Efficacy of Head and Torso Rewarming
by Using a Human Model for Severe Hypothermia

by

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A Thesis submitted to the Faculty of Graduate Studies of

The University of Manitoba

in partial fulfillment of the requirements of the degree of

MASTER OF SCIENCE

Faculty of Kinesiology and Recreation Management

University of Manitoba

Winnipeg, Manitoba

ABSTRACT

This study determined the core rewarming effectiveness of the same amount of heat applied to the head or torso using a human model of severe hypothermia. Six male subjects were cooled three times in 8˚C water for 60 minutes or to a core temperature of 35˚C. Shivering was inhibited by intravenous meperidine (1.5 mg/kg), administered during the last ten minutes of immersion, and during warming, to a maximum cumulative dose of 3.3 mg/kg. After exiting from the cold water and were rewarmed for 120 minutes by one of the following methods: Spontaneous warming, and a charcoal heater applied to the Head, or Torso. No significant differences were found in the afterdrop amount or core rewarming rates among the conditions. In non-shivering cold subjects, head warming is a viable alternative if torso warming is contraindicated.

ACKNOWLEDGEMENTS

Dedicated to my late mother

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AD	Afterdrop
ANOVA	Analysis of variance
AVA	Arterio-venous anastomoses
BMI	Body mass index
BF	Body fat
BSA	Body surface area
HFT	Heat flux measured by transducer in (W/m^2)
HF_{Total}	Total heat flux
HF_{UTorso}	Upper torso heat flux
HF_{Head}	Head heat flux
HL	Heat Loss
HR	Heart rate
ITS	Integrated thermal signal
MHP	Metabolic heat production
MSQHS	Medical screening questionnaire for hypothermia study
NHG	Net heat gain
N.S.	Not significant
PAR-Q & YOU	Physical activity readiness-questionnaire & you
RER	Respiratory exchange rate
RHL	Respiratory heat loss
SFSF	Sum of four skinfolds
SD	standard deviation
T_a	Ambient temperature
T_{co}	Core temperature
T_{es}.	Esophageal temperature
T_{sk}	Skin temperature
$T_{skTotal}$	Total skin temperature

$T_{skUTorso}$	Upper torso skin temperature
T_{skHead}	Head skin temperature
$\dot{V}O_2$	Oxygen consumption

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INTRODUCTION

Canada experiences extreme winters when temperatures drop to as low as -20˚C in most parts of the country. On average, in Canada the number of deaths attributable to cold between 2007-2011 was 94 per year. [1] Prolonged immersion in cold water results in accidental hypothermia (i.e., a fall in core temperature (T_{co}) to <35˚C). [2] Factors affecting the rate of core cooling are: water or air temperature; insulation; body mass; anthropometrics; amount of body surface area exposed to the water; sea state; body position and movement. [3]

Exposure to cold stress causes short-term or long-term imbalance between heat gain and heat loss to the environment. This results in net heat loss causing the T_{co} to decline. [2,4] Cold stress can be classified into four levels. Briefly, if a person is cold stressed but not hypothermic (T_{co}>35˚C), the thermoregulatory mechanisms (i.e. shivering) are engaged and some physical performance decrement is present. In mild hypothermia (T_{co} 35 - 32˚C), the person is conscious, physiologically stable, has significant physical decrement and shivers intensely. In moderate hypothermia (T_{co} 32 - 28˚C), there is impaired consciousness, significant physical performance decrement and the shivering intensity wanes, until it completely stops. In severe hypothermia (T_{co}<28˚C) the person is unconscious, and at risk for cardiac arrest or ventricular fibrillation (VF). [2,5,6]

The basic principles of treating a hypothermic patient are to provide supportive measures and appropriate rewarming techniques. During rescue from cold water, the hypothermic patient should be handled gently and horizontally. [2] Gentle handling is paramount in reducing the risk of ventricular fibrillation. [2] Horizontal positioning of the hypothermic patient is important to reduce the effects of decreased hydrostatic pressure during rescue. [2] Sudden decrease in hydrostatic pressure may lead to hypotension, especially orthostatic hypotension. [3,7] During rescue, it is

important not to allow the hypothermic patient to put in any physical effort, like climbing the ladder of the rescue boat. [2] Any physical work will increase the blood flow to the cold tissues in the exercising limbs, which, when it returns to the core, contributes towards the afterdrop (i.e. continued core cooling after removal from the cold exposure). [2,8–12]

The next priority for the treatment of the hypothermic subject is to reduce further heat loss by drying and insulating the patient from the environment. [2,13] After the hypothermic patient has been protected from further heat loss, the next step is to promote a safe and steady rate of rewarming. Rewarming techniques can be broadly classified under invasive (e.g., extracorporeal membrane oxygenation, cardiopulmonary bypass, body cavity lavage) [14,15] and non-invasive. The problem with the invasive rewarming techniques are that they normally can only be used in a hospital setting. In the field, as the sources of heat are limited, non-invasive rewarming techniques are required. [5] Various non-invasive rewarming techniques have been studied in the past, like using a charcoal heater,[16,17] body-to-body contact, [18] heating pads, [19,20] chemical heat packs, [20] and the arteriovenous anastomoses (AVA) warming (immersion of distal limbs in warm water). [21]

Generally, it is advised that if any form of external heating modalities are available and if they are practical, they should be applied to the areas of high surface-heat transfer. [6,22] These areas in particular are the axillae, anterior chest, and upper back. [22] In mildly hypothermic intensely shivering patients, vigorous shivering can increase the heat production by 5-6 times the resting metabolic rate. [23–25] In mild hypothermia, in which the individual is physiologically stable, vigorous shivering provides an efficient core rewarming rate of 3 – 4 °C/hr. [6,16,17,20,26] Related studies have shown that in mildly hypothermic shivering subjects the application of an external heating modality increases the skin temperature and thereby inhibits the shivering heat production

by the amount roughly equal to the heat provided, thus making the rewarming rates similar to shivering rewarming alone. [17–19,27,28]

In some cases, the application of heat on the anterior chest is contraindicated because of the presence of the open wounds or if the emergency personnel are performing cardio-pulmonary resuscitation (CPR) on the patient. It is therefore important to find alternate areas for rewarming the patient when application of heat is contraindicated on the chest. The head is one such option. The effectiveness of transferring heat via the head in a non-shivering cold subject is not known.

Pretorius and colleagues [29] evaluated the effects of cooling the head on heat transfer and thermoregulatory responses. They found that, isolated head cooling in 17˚C water significantly increased shivering heat production by 33% when the body was not cooled, but head cooling did not increase shivering heat production when the body was also cooled. A possible mechanism for this result is that isolated head cooling provided enough relative decrease in the total mean skin temperature to elicit a shivering response. However, when head cooling was added to body cooling, there was not enough decrease in the total mean skin temperature to significantly increase shivering heat production.

A subsequent study from our laboratory evaluated the effects of warming the head. [16] The same amount of exogenous heat was donated with a charcoal heater (a combustion chamber which blows heated air through a set of flexible tubes) to the head or torso of mildly hypothermic shivering participants. The authors hypothesized that, compared to torso warming, head warming would result in a smaller increase in total mean skin temperature, less inhibition of shivering heat production, and a greater net heat gain and rate of rewarming. However, they found that head and torso warming elicited a similar increase in total mean skin temperature, head warming did not inhibit shivering heat production, and rewarming rates were similar for both conditions. The

limitation of this study was that in these mildly hypothermic shivering subjects the shivering heat production potentially masked the differences in head and torso warming conditions.

We therefore used a human model for severe hypothermia to evaluate the rewarming effectiveness, when the same amount of heat is provided to the head or torso. The purpose of the study was to evaluate the rewarming effectiveness of the same amount of heat donated, using a charcoal heater to the head or torso by using a human model for severe hypothermia where shivering is pharmacologically inhibited in mildly hypothermic subjects. [8,20,30,31] Specifically, we intended to evaluate the core temperature afterdrop and subsequent core rewarming rates during recovery using three conditions: 1) Spontaneous warming with no exogenous heat donation; 2) Torso warming with a charcoal heater; and 3) Head warming with a charcoal heater. Subjects were immersed in cold water (8ºC) until they were mildly hypothermic. During the ten minutes before exit, meperidine (Demerol) was infused to inhibit shivering. Under these conditions the subjects were only mildly hypothermic but their shivering was abolished.

We hypothesized that torso warming would be the most effective in decreasing the afterdrop, provide greater net heat gain and higher core rewarming rate, followed by head warming which would be greater than spontaneous warming. Even though the same amount of heat was applied to the head and torso, greater heat donation was expected in torso warming because: 1) the torso has a higher surface area compared to the head; 2) there is greater insulation in torso warming because the entire heat source is contained within the sleeping bag, whereas during head warming some heat is lost through the face opening of the sleeping bag, and 3) the head is smaller than the torso, therefore some of the flexible tubes will overlap during head warming and heat donation will be less efficient.

LITERATURE REVIEW

ACCIDENTAL HYPOTHERMIA

Accidental hypothermia occurs when the body's core temperature unintentionally drops below 35˚C. [19,26,32] Accidental hypothermia can be caused due to sudden cold exposure to the human body. This exposure can be either to a cold ambient air environment or cold water immersion. Accidental hypothermia can occur in any age group. It mainly occurs in people involved in outdoor work or people who frequently perform outdoor recreation activities like skiing.

CLASSIFICATION OF ACCIDENTAL HYPOTHERMIA

There are several classification systems for describing accidental hypothermia. [26,32,33] Commonly, accidental hypothermia is classified using core temperature: mild hypothermia 35-32˚C; moderate hypothermia 32–28 ˚C and severe hypothermia <28˚C. [26] Recently, Zafren et. al., [2] have added the category "Cold Stressed, but Not Hypothermic" relating to core temperatures ranging from 37 ˚C to 35 ˚C.

FACTORS CONTRIBUTING TO ACCIDENTAL HYPOTHERMIA

The main causes of accidental hypothermia are exposure to cold; it can be cold water immersion and exposure to cold environmental air. [26] The factors that contribute to hypothermia are water or air temperature and sea state; thermal protection; body morphology; body exposure, position and movement; age; and alcohol and drug ingestion.

Water or air temperature and sea state

Cold water immersion can cool the core body temperature much more rapidly than exposure to cold air because the thermal conductivity of cold water is about 25 times greater than that of air at the same temperature. [34]

Thermal protection

Clothing can either aid or attenuate the occurrence of hypothermia in an individual. In extreme cold weather, clothing provides insulation and reduces heat loss. [22] Especially wet and inadequate clothing increases the risk of hypothermia. Previous studies conducted [35] on the relationship between various types of protective clothing with heat loss and cooling rates show that, in calm water "dry suits" and insulated garments give better insulation than "wet suits" and insulated garments. Waves decrease the insulation provided by "dry" suits and thereby increased the heat loss. [36]

Giesbrecht et al., [22] gives three principles for choosing cold weather clothing: firstly; a complete ensemble of clothing must be selected keeping in mind the weather and workload conditions one is expected to encounter. Secondly; one should have a complete understanding of how clothing works and how to use it properly, and lastly; moisture accumulation must be minimal in clothing.

Body morphology (mass, size and composition)

The rate of heat loss is generally proportional to surface area, whereas the amount of heat that can be lost is proportional to mass. [3] As compared to obese individuals, thin individuals have a higher risk of succumbing to hypothermia due to decreased mass and fat insulation. Body fat works as an insulation which minimizes heat loss. [37] Its been demonstrated that obese individuals

showed hardly any reduction in core body temperature when immersed in 15˚C water, whereas in thin individuals the temperature dropped by 2.5˚C within the first 30 minutes. [37,38]

Body exposure, position and movement

Greater skin surface exposed to cold air or water, results in higher heat loss through the skin. It is very important to reduce the skin surface area which is exposed, either by adding layers of clothing over the skin or by getting as much of the body out of the water as possible. Once immersed in cold water, one is advised to assume the H.E.L.P (Heat Escape Lessening Position) position. [22,39] In this position the arms are pressed against the chest and legs are pressed together. This position helps in reducing the body surface area of high heat transfer exposed to cold water and thereby reduces the heat loss. [22] When three or more people are immersed in cold water, huddling (with each person pressing their legs together while forming a tight circle) is preferred. [39] This position helps in keeping the survivors together to facilitate rescue, increasing thermal insulation and providing moral support. The huddle position is most efficient when there are three to five people. If there are more than six people immersed, then it is advised to divide the immersees into smaller groups of three to five.

Age

Elderly subjects and very young subjects are at higher risk for hypothermia. [40] Weinberg (1993) suggests that because infants have a larger body surface relative to total mass compared to adults, this results in greater relative heat loss. The heat production capability in infants and older adults is reduced compared to healthy young adults. For example, elderly subjects have low metabolic rate than young adults, therefore its difficult for the elderly subjects to maintain their core body temperature if the ambient temperature drops below 18˚C. [40]

Alcohol and drug ingestion

Alcohol and some drugs impair shivering heat production [40,41] and cause cutaneous vasodilation which, in turn increases cutaneous heat loss. [41] Alcohol and drugs impair judgement and decrease the ability to gain protection from the cold. [37] Alcohol decreases shivering thermogenesis in cold water by 10% to 20%, thus reducing the metabolic heat production. [42,43] Alcohol also results in decreased perception to cold. [42] Thus, alcoholics and drug addicts are more susceptible to acquiring hypothermia, whereas social drinking can result in carelessness which may potentiate in hypothermia. [3]

MAINTENANCE OF CORE BODY TEMPERATURE

Humans can normally maintain their core body temperature at a relatively constant core temperature (~37˚C) despite being exposed to a wide range of ambient temperatures. [44] This constant core temperature at ~37˚C is maintained through a dynamic balance between heat gain and heat loss. [4]

MECHANISMS OF HEAT TRANSFER

Heat can be lost from the body through four main mechanisms: conduction, convection, radiation and evaporation. [4,22,45] Heat loss due to conduction occurs when the human body is in direct contact with a solid or liquid which is cooler than the skin. The amount of heat loss due to conduction is primarily dependent on the temperature gradient between the human skin and the surface that it is directly in contact with. Other factors that play an important role in conduction are thermal conductivities and area of contact between the two surfaces. At the same temperature, water has about 25 times greater heat conductivity than air at the same temperature, thus heat

conductivity of the surface or fluid in contact with the body plays a very important role in heat exchange. [22] This is very important when a person accidentally falls in cold water.

Convection refers to the heat transfer between the surrounding fluid (water or air) surface which has a lower temperature than that of the body, when it contacts the skin, is warmed by the warm skin, and travels away from the skin carrying heat along. [22] The fluid which gets warmed expands, becomes less dense and rises replacing the cooler fluid. In case of fluid, the convective heat loss occurs when the warm skin is exposed to cool stirred water. The cool stirred water contacts the warm skin, it is warmed and due to stirring the warm water is replaced by cold water. A temperature gradient is created between the surrounding fluid and the body which results in heat loss. If the body's temperature is higher than the surrounding fluid, heat will be lost by the body. In still air or water, the air or water warmed by the body remains adjacent to the skin forming a layer of insulation to reduce further conductive heat loss. However, in the event of air movement (as in wind blowing), the warm air is blown away by cooler air which gains more heat from the body. In a cold windy environment or in a cold flowing river, convective heat loss is a major mechanism by which the body loses heat. Due to greater density of water, higher specific heat and thermal conductivity, convection is much greater in water compared to air. [22,26] A layer of insulation by means of protective clothing helps in reducing the effect of convective heat loss. [22,26]

Radiation refers to the heat exchange between the body and the environment by the means of electromagnetic waves. [4,22] At room temperature (20-22˚C), radiation is the largest source of heat loss, [22] at a thermoneutral environment (~28 ˚C) approximately forty-five percent of heat loss occurs in the form of radiation. Radiant heat loss depends on the number of radiating objects around the body, surface temperature of the radiating objects and of the body and lastly on the

body's clothing insulation. [22,26] The proximity of the cold radiant object to the warm body also impacts the heat loss; the closer the cold object is to the body, the more the radiant heat loss. [22]

Evaporation is the only means of heat loss when the environmental temperature exceeds that of body temperature. Heat energy is needed to convert a water molecule from liquid into a gas, so heat is removed from the surface where evaporation takes place. When water on the skin, which is mainly produced by the eccrine glands within the skin as sweat, evaporates from the skin, the process transfers heat to the environment. Approximately 2400 kJ of heat energy are transferred from the skin to the environment with full evaporation of every 1 liter of sweat from the skin. For evaporative heat loss to work, it is important that the sweat is evaporated from the skin before it drops off the body or is towel dried. Evaporative heat loss is primarily dependent on the skin surface area where evaporation is taking place, air velocity, skin wettedness and the humidity levels in the environment. [4,22]

In addition to the above-mentioned mechanisms of heat loss which primarily occurs from the skin, heat exchange can also occur between the respiratory tract and the environment during respiration. This respiratory heat loss increases when minute ventilation ($\dot{V}_E$) increases in cold air.[26,45] During inspiration, cold dry air is warmed by direct conductive warming and evaporation as liquid water in the airway lining evaporates to humidify the air. Most of the heat is lost during expiration.

HEAT PRODUCTION AND DONATION

The body gains heat by internal and external means: internally through metabolic heat production (general heat production, hormone output, exercise and shivering) and externally by

heat donation to the body, either by external heating methods (e.g., charcoal heater) or from the warm environment itself.

When exposed to cold, the body's first reaction is to increase metabolic heat production which it does by raising the resting metabolic rate and by increasing muscular activity which can be voluntary and involuntary. While a subject is resting, the energy expended by the subject is called resting metabolic rate. [46] This energy is the sum of all the metabolic processes which occur in active cells to maintain normal functions at rest. Heat production can also be increased by voluntary and involuntary muscle activity. Exercise is a form of voluntary activity and shivering is a form of involuntary muscular activity which generates metabolic heat.

During prolonged cold exposure, the body shivers vigorously as core temperature decreases (until ~32°C). [1,24] Vigorous shivering increases oxygen consumption ($\dot{V}O_2$). This higher $\dot{V}O_2$ is the same as a human body achieves by voluntarily exercising. [46] Shivering heat production can be an effective defence against hypothermia as it increases the metabolic heat production up to 5-6 times the resting metabolic rate. [17]

The human body also increases the internal heat production by releasing epinephrine and norepinephrine during cold exposure. These hormones raise the resting metabolic rate to increase heat production internally. [46]

External heat can be applied to a hypothermic victim by using heating pads such as chemical heating pads, hot-water bottles and a charcoal heater. These rewarming methods have been studied extensively in mildly-hypothermic, vigorously shivering individuals. [16,17] These methods increase skin temperature (T_{skin}), reduce the thermal stimulus for shivering, and thereby suppress shivering heat production. Generally, the rate of rewarming has been shown to be similar

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for the external rewarming and shivering only methods. [16–18] This could be due to the fact that the amount of heat donated by these external sources is just enough to compensate for the shivering heat production that is inhibited. However, they provide other advantages such as increased thermal comfort, preservation of energy stores and reduced cardiovascular stress. These sources would be beneficial (i.e., increase core rewarming) when there is no shivering heat production or shivering is inhibited (i.e., during severe hypothermia).

A previous study that used a human model for severe hypothermia [20] evaluated the effectiveness of four field-appropriate torso-warming modalities. In this study, shivering was pharmacologically inhibited in mildly hypothermic subjects. Hot-water bottles and chemical heating pads provided high initial heat delivery to a large surface area as they cover the upper back area and the anterior chest area. Thus hot-water bottles and chemical heating pads reduced the amount and duration of the core temperature (T_{co}) afterdrop, whereas a charcoal heater that delivered heat to a relatively smaller surface area was effective in reducing only the duration of T_{co} afterdrop. The charcoal heater and hot-water bottles provided high continuous heat delivery, and thus produced a steady core rewarming rate, whereas the chemical heating pad had a smaller core rewarming rate as it provided initial high heat delivery that gradually declined over time. All of these sources have been recommended for pre-hospital treatment of severely hypothermic victims. [20]

Goheen et al., [8] evaluated the efficacy of forced air and inhalation rewarming using a human model for severe hypothermia. A new forced air warming system was used which consisted of a mobile wooden warming box which supported a webbed stretcher. The rostral portion of the box contained two 1,200-W electric heaters and six circulating fans below the webbed stretcher. Two more 1,200-W heaters and three fans were contained on the top of the wire frame just above

the subject's chest. Forced air warming provided a significantly higher rewarming rate (2.40˚C/h) compared to control (0.41˚C/h) and inhalation warming (0.23˚C/h). The authors noted that forced air warming provided a high heat gain whereas in the other two conditions, there was an overall heat loss during rewarming phase. Forced air warming also significantly reduced the afterdrop compared to inhalation rewarming and control.

Hultzer et al., [31] used a human model for severe hypothermia to compare the effectiveness of five active warming techniques. The authors cooled subjects in 8˚C water to a core temperature of 35˚C and then rewarmed for 120 minutes using: 1) forced-air warming with a 600-W heater and commercial soft warming blanket; 2) a 600-W heater and rigid cover; 3) an 850-W heater and rigid cover; or 4) a charcoal heater on the chest; 5) direct body-to-body contact with a normothermic partner. They found that compared to control (spontaneous warming) all the other warming systems were found effective in rewarming the core temperature and reducing the core temperature afterdrop. They concluded that the modalities used in the study were practical and can be used in the field for the treatment of the severely hypothermic subject.

HUMAN THERMOREGULATION

Integrated thermal signal

Normal human core temperature is 37 ± 0.5˚C. The human body tries to maintain this temperature for normal functioning of various metabolic activities. Any shift in the core temperature whether higher or lower initiates physiological mechanisms to help bring the temperature back to normal. Humans can maintain this almost constant core temperature even in dynamic temperatures. [22] These mechanisms are controlled two ways: voluntary and involuntary. Involuntary responses are those which increase or decrease the heat loss and heat gain whenever

required. These involuntary responses are regulated by the temperature control center in the brain called the hypothalamus. [22,45,47] Voluntary responses are behavioral responses which provide greater protection from the external environment than can be provided by the involuntary responses alone. Examples of these types of responses include wearing heavier clothing or adding layers while in extreme cold regions or removing layers or turning on the air conditioner in warmer environments. [47]

Involuntary responses are regulated by the hypothalamus which receives information through the thermal afferents from the peripheral body and the body core and are integrated into an overall thermal signal within the hypothalamus. [45] These signals are referred to as the integrated thermal signal (ITS). [22] The functioning of the hypothalamus in thermoregulation can be explained by a simple analogy of a household thermostat. In a household thermostat once the temperature goes above or below the "set-point", it initiates either heating or cooling based on the set temperature. In humans, the temperature set-point (36.5˚ – 37.5˚C) where there is no thermoregulatory response, is known as inter-threshold range. [22] The hypothalamus compares the ITS with the target set-point and initiates voluntary and involuntary responses as required.

Cooling responses are initiated if the ITS is above the set point. These cooling responses include peripheral vasodilation, sweating and cooling by behavioral changes. In warm conditions, the peripheral blood vessels dilate, which increases the blood flow to the periphery. When large quantities of warmed blood from the core of the body are carried to the skin heat loss may occur via radiation, convection, and conduction. [22] Sweating increases heat loss through evaporation. [22,26,45] Behavioural changes include removing extra layers of clothing, turning on the air conditioner, and avoiding the heat.

Warming responses are activated when the ITS is below the set-point. Warming responses include peripheral vasoconstriction, shivering and behavioural changes. The human body's first line of involuntary defence against cold exposure is peripheral vasoconstriction and shivering. Peripheral vasoconstriction reduces blood flow to, and from the skin surface thereby reducing heat loss. [34,48] Shivering is involuntary muscular contractions that produce metabolic heat. The lower the ITS below the set-point, the higher the intensity of shivering that occurs before it reaches the plateau of maximum response. [45] Behavioral responses include adding extra layers of clothing, and being near a heater or fireplace.

MUSCULAR FUNCTION IN COLD

Voluntary muscle contraction

Studies in the past have reported that temperature has an effect on skeletal muscle performance, whereby cold exposure to the body will significantly reduce the temperature in the muscles which will reduce the function of the various neuromuscular and biochemical properties, and affect the overall working of the muscle. [49,50] A study by Giesbrecht and Bristow [51] reported the decrease in maximal voluntary force production and manual dexterity due to a decrease in core body temperature. They evaluated three manual arm tasks (flexion and extension of fingers, handgrip strength and manual dexterity) before and after cold water immersion. They reported significant decreases in all three manual arm task scores after the core temperature decreased 0.5°C. They concluded that peripheral cooling on sensorimotor function, with a potential additional effect of central cooling on cerebral function, may have resulted in decrement of performance. The increased accumulation of metabolites in the muscles might be the causing factor for suboptimal performance of the muscle.

To understand the independent contributors of local cooling and/or core cooling in decreasing the manual performance Giesbrecht et. al., [51] developed a protocol to independently cool the arm (local) and the rest of the body (core). They cooled six subjects in a body tank under three conditions: 1) cold body-cold arm (CB-CA); 2) warm body-cold arm (WB-CA); and 3) cold body-warm arm (CB-WA). They had a separate arm tank where they cooled or warmed the dominant arm. Six tests requiring fine or gross motor movements were performed by the subjects before and after the immersion (at 15, 45 and 70 minutes). They reported that cooling the body and/or the arm elicited decrements in finger, hand and arm performance. No significant differences were found in the CB-WA condition for the physical test. For the other two conditions (CB-CA and WB-CA), there were significant decrements (43-85%) in all the tests. Increased local effects of cooling which may be physical (increased viscosity of synovial fluid in the joints) or neuromuscular (decreased excitability of nerve membranes and nerve conduction velocity) could have been the reasons for the results reported in the study. These could be the possible reasons why performing the fine motor movements is difficult and sometimes impossible for people facing situations where their life is at risk, during cold water immersion. Cheung et. al., [52] reported a significant decline in manual dexterity after short term hand and forearm immersion in cold water. They immersed the participants' hands and forearms up to the level of the epicondyle of the humerus for approximately 5 minutes in 10°C water and found that, the participants took a significantly longer time to complete simple performance tasks compared to the control group.

Cahill et. al., [53] used a novel approach to study the effect of cold exposure on voluntary activation during a fatiguing contraction. Cahill and colleagues used electrical and single-pulse transcranial magnetic stimulation (TMS) to define the role(s) of central neural control in contraction and fatigue of cold muscle. Magnetic and electrical stimuli were imposed during

various intensities of muscle contraction to provide the following measures (and interpretation): torque (voluntary muscle activation); amplitude of TMS motor evoked potential (MEP) [excitability of the cortical cells and spinal cord]; length of subsequent EMG silent period (inhibition in the cortical area); time to peak force and force relaxation rate (contractile properties of muscle); and ratio of, the increment in force evoked during a contraction, to the amplitude of evoked response, in the potentiated relaxed muscle (proportion of total drive ascribed to voluntary activation). The study reported that whole body hypothermia reduced maximal muscle torque and attenuated the rate of fatigue during sustained fatiguing contractions, an effect occurring centrally, at and/or above the level of the spinal cord. Thus, peripheral mechanisms are primarily involved which results in decreased MVCs in hypothermia and central mechanisms are responsible for the fatigue development.

Involuntary muscle contraction: -Shivering (Control, Capacity and Endurance)

Figure 1. Model for shivering intensity changes with respect to core temperature. [Xu et al., [54]] Note: Permission obtained from the copyright holder, Dr. Gordon G. Giesbrecht.
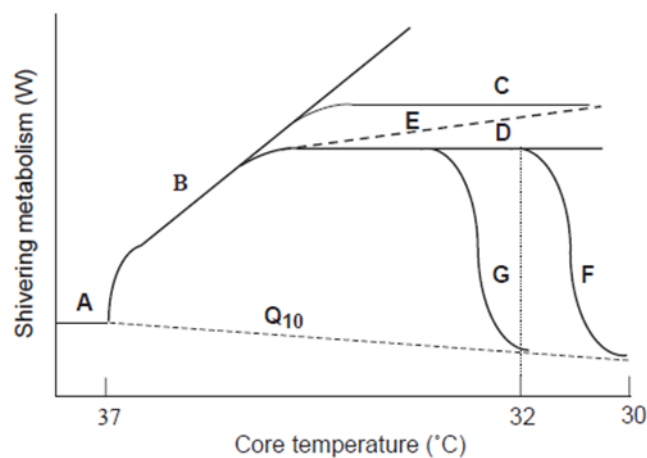
Shivering is an important defence mechanism against cold exposure. A mildly hypothermic vigorously shivering patient rewarms at a rate of 3-4°C/h. [17] When exposed to cold, the skin

temperature decreases and the shivering response is initiated. Previous studies have shown that there is an inverse relationship between the core body temperature and shivering metabolism. [23,55] In a paper by Xu et al., the authors refined a long term cold exposure model for shivering (see Fig. 1). This study reported that shivering increases (line B) when the core body temperature drops from 37°C to 32°C (line B), to a theoretical maximum (line C). When core temperature remains constant and the skin temperature is below 20°C, a lower shivering plateau is observed (line D). Line E is observed when shivering intensity is expected to increase when the body core temperature decreases or skin temperature nears 20°C. Thermoregulatory inhibition decreases the shivering intensity when the core body temperature further drops below 32°C (line F). However, when the core body temperature is above 32°C the decline in shivering is attributed to reduced substrate availability (line G). As previously described, shivering heat production may mask differences between active warming methods in shivering subjects. Since, shivering heat production cannot be eliminated in the body through fatigue (Line G) or thermoregulatory inhibition (Line F), a process of pharmacological inhibition of shivering heat production is used to eliminate shivering experimentally.

HYPOTHERMIA TREATMENT

Pre-hospital treatment of hypothermia includes removal of the patient from the cold exposure, removing all the wet clothing (if any), providing proper insulation and rewarming using the external heating modalities. As explained before, the body can gain heat endogenously and exogenously. Studies have shown that shivering alone can rewarm the mildly hypothermic patient with the rate of 3˚- 4˚C/hr. [18,21,26,28] Shivering should be fueled by providing warm glucose filled fluids, for example a warm chocolate milk. If the patient is not shivering as in severe hypothermia, [2,26] heat donation using external heating modalities becomes important to rewarm the patient.

REWARMING METHODS

An external heat source should be applied at the areas of high surface-heat transfer, particularly the axilla, anterior chest and upper back. Various kinds of exogenous rewarming methods have been studied in the past; arterio-venous anastomosis (AVA) rewarming, [21] forced-air warming, [28] and charcoal heaters. [16,20]

AVA Rewarming

Arteriovenous anastomoses (AVA) are physical pre-capillary connections between the arteries and veins and are most abundant in the fingers and toes. [22] When subjected to a cold environment, the AVAs constrict in order to reduce cutaneous heat loss by reducing the peripheral blood flow. Warming the distal extremities opens the AVAs which increase the blood flow in the distal extremities and thus increases the heat exchange between the distal extremities and environment. [22] Vanggaard and colleagues conducted a study of AVA rewarming. They cooled six subjects in 8°C water to a T_{co} of 34.3 ± 0.8 (± SD) °C (mild hypothermia). These subjects were then rewarmed by shivering heat production alone, or by immersing the distal extremities (hands, forearms, feet and lower legs) in either 42 °C or 45 °C water. They found that the post cooling T_{co} afterdrop was reduced by both 42 °C and 45 °C water immersion (0.4 ± 0.2 °C) compared with shivering alone (0.6 ± 0.4 °C; $p < 0.05$). Core rate of rewarming with 45 °C water immersion was significantly greater at 9.9 ± 3.2 °C/h than both rewarming with 42 °C water immersion (6.1 ± 1.2 °C/h) and shivering alone (3.4 ± 1.5 °C/h). In response to distal extremity immersion in warm water (45 °C and 42 °C), AVAs opened up resulting in an increased heat delivery to the heart via blood flow from the superficial veins in the distal extremities. The limitation of AVA rewarming is that the method is not practically viable in the field treatment of hypothermia.

Forced-Air Warming

Forced-air warming (FAW) injects warm air (outlet temperature ~43˚C) through a connecting hose into a disposable plastic or paper quilt-like cover. The warm air flows through the holes on the patient side of the cover and provides convective warming to the skin. These systems provide convective heat transfer of 60-70 W [28] over the body. Giesbrecht et. al., [28] evaluated the efficacy of this system for the treatment of mild immersion hypothermia. They found no significant differences in core rewarming rates during forced air warming (3.26˚C/hr) from shivering (3.02˚C/hr). The possible mechanism for the similar core rewarming rate is that the FAW increased the skin temperature and inhibited shivering heat production roughly equal to the heat provided. Thus, making the core rewarming rates similar.

Charcoal Heater

The charcoal heater is the most effective portable rewarming device. [17] A charcoal heater consists of a charcoal briquette in a canister and a fan which circulates the heat through flexible tubing. Once the briquette is ignited and burns for about ten minutes it provides 250 W of heat for eight to twelve hours and requires only a D-cell battery to power the fan.

The charcoal heater has been studied previously in mildly hypothermic shivering subjects. [16,17] Giesbrecht et. al., [17] studied the effectiveness of three field treatments for induced mild hypothermia. The authors cooled the subjects in 8˚C cold water to a T_{co} of 33˚C and subsequently rewarmed the subjects by either spontaneous warming, external heat (charcoal heater) or treadmill exercise. They found that the rate of core rewarming for exercise was 4.9˚C/h which was significantly higher than both shivering (3.5˚C/h) and the charcoal heater (3.7˚C/h). The authors concluded that although the rate of core rewarming was higher during exercise compared to

shivering and external heat, there was a greater afterdrop length and amount and there was no difference in total recovery times among the three treatments.

Sran et. al., [16] evaluated the effectiveness of head and torso warming. The same amount of heat was donated with a charcoal heater to the head or torso of mildly hypothermic shivering participants. They cooled six subjects (1 female) in 8ºC water to a core temperature of 35ºC. The subjects were rewarmed by spontaneous warming, charcoal heater applied to the head; or charcoal heater applied to the torso. They noted that there were no significant differences in core rewarming rates among the three conditions. As demonstrated in the previous studies [18,28] application of external heating devices increased the skin temperature and inhibited shivering heat production by the amount roughly equal to the heat provided, thus making the core rewarming rates similar to shivering rewarming alone. The researchers concluded that head warming was as effective as torso warming for rewarming mildly hypothermic shivering victims.

It was shown that, cooling of the head in 17˚C water has similar core cooling rates compared to body cooling, and head cooling only does not stimulate shivering heat production. Whereas, when the rewarming effectiveness was studied between head and torso, both the conditions had similar rewarming rate and head warming did inhibit shivering. The limitation of the study was that, the shivering heat production masked the differences between the head and torso warming conditions. The purpose of this study was to evaluate the rewarming effectiveness of the same amount of heat donated using a charcoal heater to the head or torso by using a human model of severe hypothermia. We hypothesized that torso warming would be the most effective in decreasing the afterdrop, provide greater net heat gain and higher core rewarming rate, followed by head warming which would be greater than spontaneous warming.

METHODS

SUBJECTS

The protocol was approved by Health Canada and the Biomedical Research Ethics Board at the University of Manitoba (Appendix A).

The study was open to both males and females, however only males volunteered. Six healthy and physically active men (aged 28.7 ± 3.2 years) were tested in this study. Participants were asked to complete a Physical Activity Readiness Questionnaire (PAR-Q and Medical Screening Questionnaire for Hypothermia Study (MSQHS) (Appendices B and C). Prior to participation a signed informed consent form was obtained from each participant (Appendix D).

INCLUSION AND EXCLUSION CRITERIA

Inclusion Criteria

Healthy adults aged 18-45 years, who answered "No" to all the questions on the PAR-Q and MSQHS forms.

Exclusion Criteria

Subjects were excluded from the study if they gave a positive answer to any PAR-Q questions or any of the questions on the MSQHS form. They were also excluded if they had, or have, any cardiorespiratory disease, renal dysfunction, Raynaud's syndrome, and if they were taking recreational drugs or had any other condition(s) that can be aggravated by cold exposure. Subjects who had contraindications for meperidine administration or had any of the conditions listed below, were also excluded from the study:

    i)   hypersensitivity to meperidine or any ingredients in the formulation

ii)   known or suspected mechanical GI obstruction or any diseases/conditions that affect bowel transit

iii)   suspected surgical abdomen (i.e. acute appendicitis or pancreatitis)

iv)   severe CNS depression, head injury, increased cerebrospinal or intracranial pressure

v)   convulsive disorder, delirium tremens

vi)   hypothyroidism

vii)   prostatic hypertrophy or urethral stricture

viii)   sickle cell anemia

ix)   Addison's disease

x)   Pheochromocytoma

xi)   Known sensitivity or intolerance to the drug metoclopramide

xii)   Use of medications that might interact negatively with meperidine. Examples include Monoamine oxidase (MAO) inhibitors at the time of screening or within 14 days of screening; CNS depressants; phenytoin; cimetidine; ritonavir; aclyclovir; skeletal muscle relaxants.

xiii)   pregnant women, breastfeeding women, and women planning on becoming pregnant

POWER ANALYSIS

To determine the sample size for this study, a power analysis was performed using the following equation: [56]

$$n = (PI \times \sigma/\mu d)^2$$

Where:

n = number of subjects,

PI = power index, determined from the desired power of the study.

μd = true mean difference between individual values for two treatment methods

σ = true standard deviation of the differences

In order to have 80% power to detect a difference between any two treatment methods:

PI was determined based on the assumptions of 5% chance of committing a Type I error (e.g. failure to detect a real difference) ($\alpha = 0.05$) and 20% chance of committing a Type II error (e.g. detecting a difference when none exists) ($\beta = 0.20$). A previous rewarming study done in our lab demonstrated a significant difference of 0.6˚C/h (mean) in T_{co} rewarming rate (120 min) between two protocols (Hot-water bags and Spontaneous warming) with a standard deviation of 0.55. [20]

Thus,

PI = 1.64 (0.05 α, one-tailed) + 0.84 (0.20 β, one-tailed) = 2.48 n = $(2.48 \times 0.55/0.6)^2$

n = 5.22

Thus, this study required a minimum of six subjects to achieve the power of 80%.

ANTHROPOMETRIC DATA

Age (yrs), weight (kg), height in meters (m) and measurements of skin fold thickness at four sites- biceps (on the anterior midline of the upper arm over the belly of the biceps muscle), triceps (measure halfway between the acromion and olecranon processes), subscapularis (located 1 to 2 cm below the inferior angle of the scapula), and suprailiac (located 1 cm above the anterior superior iliac crest) were determined. An average of three repetitions at each site were used for calculation of body surface area and % body fat. [57]

Using the following equation based on height and weight, body surface area (BSA, in m^2) was calculated: [58]

$$BSA \ (m^2) = weight^{0.425} \ (kg) \times height^{0.725} \ (cm) \times 0.007184$$

Using the equation by Durnin and Womersley [59] body density (Db) was calculated using the sum of four skinfolds and constants specific for gender and age group (Appendix E).

Body fat percentage (%BF) was calculated using the following equation: [59]

$$\%BF = (4.95/Db - 4.50) \times 100$$

Body mass index (BMI) was calculated using the following equation:

$$BMI = weight \ (kg) / \ height^2 \ (m)$$

INSTRUMENTATION

Subjects wore a swim suit and were instrumented at an ambient temperature of ~22°C as follows:

<u>Skin temperature (T_{skin} in ˚C) and cutaneous heat flux (HF in W)</u>

Twelve heat flux disks (2 cm in diameter; Concept Engineering, Old Saybrook, CT) were taped to the skin according to the standard lab procedures to measure skin temperature and heat transfer from the skin at the following sites: forehead, left cheek, top of the head, dorsum of the head, right axilla, anterior chest, anterior abdomen, upper back, left anterior upper-arm, right anterior fore-arm, right anterior thigh and left posterior thigh. Flux is defined as positive when heat flows from skin towards the environment (i.e., heat loss).

The data was acquired, averaged and stored on a computer at 30-seconds intervals.

<u>Core temperature (˚C)</u>

Core temperature was estimated by esophageal temperature (T_{es}). This was measured with a disposable thermocouple (Mallinckrodt Medical Inc., St Louis, MO) inserted into the esophagus to the level of the heart. This site provides the best non-invasive measure for intra-cardiac temperature [60,61] and is a standard procedure in our laboratory. The thermocouple is inserted through a nostril, and pushed through the pharynx to the esophagus to the level of the heart.

<u>Electrocardiogram (ECG)</u>

Electrocardiogram (ECG) leads were affixed to the skin (right and left shoulders and the left axilla) to monitor ECG and heart rate (HR) continuously with a Hewlett-Packard monitor/defibrillator (model 43100A) throughout the experiment. Heart rate was averaged and recorded at 30-s intervals in digital format.

<u>Oxygen consumption ($\dot{V}O_2$ in l/min)</u>

Oxygen consumption ($\dot{V}O_2$) was measured continuously with an open circuit metabolic cart (Vmax 229 by Sensormedics, Yorba Linda, Ca) from expired minute volume and inspired and mixed-expired gas concentrations sampled from a mixing box. Oxygen consumption was recorded at 30-s intervals.

<u>Intravenous line</u>

An intravenous (IV) line was inserted by the physician before the start of each trial to administer meperidine (Demerol) to inhibit shivering. The arm where the IV line is inserted was kept out of water so that the broken skin site was never exposed to the water.

REWARMING METHODS

<u>Spontaneous warming</u>

No exogenous heat source was used in the spontaneous warming trials.

<u>Head warming</u>

A charcoal heater (HEATPAC Personal heater, Emergco Tech. Solutions, Vancouver) was applied to the head. It consisted of a combustion chamber, charcoal fuel briquette, and a branched, flexible, but non-compressible, heating duct. It is small and light ($23 \times 12 \times 6$ cm, 1,100 g). This heater produces 250 W of heat (1,800 kJ over 120 minutes). Once the charcoal fuel is ignited, the fuel is placed in the chamber and the heated air is blown through the branched ducts by a fan within the charcoal heater. The heater was set to "high" mode and was ignited at least 15 minutes before being applied to the participant. The heater can produce maximum heat for ~8 hours. The combustion chamber was placed on the right side of the face/head (the chamber is insulated to

prevent skin burning) and the ducts were wrapped around anteriorly over the forehead, nose, chin, not covering the eyes or the mouth, then going over the dorsum of the head, top of the head and again over the left side of the face/head and under the chin (Figure 2). The participants were breathing ambient air (~22˚C).

Torso warming

The charcoal heater was applied to the torso. The combustion chamber was placed on the anterior chest with the flexible ducts travelling posteriorly over the shoulders and then anteriorly under the arms to cross over the lower anterior chest (Figure 3). The participants were breathing ambient air at room temperature (~22˚C).

Figure 2. Head warming- Charcoal heater on the head

Figure 3. Torso warming- Charcoal heater on the torso

PROTOCOL

Each participant served as his own control for comparative evaluation of each of the warming modalities and were cooled on three different occasions, separated by at least five days. The minimum of five days allowed for an adequate washout of meperidine from the body. The subjects were cooled at the same time of the day to control for circadian effects. The order of trials followed a modified random balanced design, with spontaneous warming being the first modality tested for each subject. External heat donation increases the skin temperature and reduces the thermal stimulus for shivering. Thus, the shivering stimulus is expected to be maximum in the spontaneous warming condition. Therefore, a higher dose of meperidine was required to inhibit shivering in the spontaneous warming condition compared with the active warming (head and torso warming) conditions. To control for pharmacological effects, the same (maximum) drug doses were given to each subject for all conditions. The results from spontaneous warming served both as comparative control and for determination of the meperidine dose for the subsequent trials.

Instrumentation (explained above) took about 45 minutes. The participants then sat quietly and baseline measurements were recorded for 10 minutes at an ambient temperature of ~22˚C. The subjects were then immersed to the level of the sternal notch in a 21˚C stirred water bath. The water temperature was lowered to 8˚C over a period of 5-10 minutes by addition of about 60 kg of ice. Participants then remained in the water until one of the following criteria was met: core temperature reached 35˚C, a researcher advised exit for any reason, a time period of 60 minutes was elapsed, or the participant wished to exit.

During the last 10 minutes of immersion 1.5 mg/kg of IV meperidine (diluted in 10 ml of saline) was infused slowly in five 2-mL aliquots (i.e., 0.3 mg/kg meperidine per injection) over

successive 2-minute intervals. The participants then exited the water, were dried off and laid in a vapor barrier within a hooded sleeping bag for 120 minutes of rewarming.

In the spontaneous warming condition, a maximum of 1.8 mg/kg of additional IV meperidine was infused, as required to inhibit subsequent shivering. It was infused in amounts of 0.3 mg/kg (diluted in 2-mL aliquots injected slowly at a minimum of 2-minute intervals) to a maximum cumulative dose of 3.3 mg/kg.

Treatment continued either for a period of 120 minutes or until the core temperature returned to normal values (~36.5-37˚C). If the participants' core temperature did not return to the normal values, they were then placed in a warm water bath (40-42˚C) until they were comfortable and core temperature returned to a normothermic level.

DATA ANALYSIS

The following variables were calculated for all three conditions:

Rate of core cooling

Rate of core cooling (˚C/h) was calculated by linear regression for T_{es} data during the final 10 minutes of immersion.

Afterdrop (AD)

Afterdrop was calculated as the difference between T_{es} on exit from cold water and its nadir.

Rate of core rewarming

Rate of core rewarming (˚C/h) was calculated by linear regression for T_{es} data from a point of steady increase in T_{es}.

Heat flux for each site (W)

Heat flux (HF) was measured from 12 sites (listed below) using thermal flux transducers (Concept Engineering, Old Saybrook, CT). It is defined as positive when heat flows from skin to the environment (i.e., heat loss) and values for each transducer (HFT)(W/m^2) were used to calculate the heat flux for each site (in W) using the following equation:

$$HF_{site} (W) = HFT_{site} (W/m^2) \times \text{Body Surface Area } (m^2) \times \text{Regional percent of the site} \times 0.01$$

The following regional percentages were assigned based on Layton et. al., [62]: forehead (centre of the forehead) (2%); left cheek (belly of the masseter muscle) (1%); top of the head (vertex-skull) (3%); dorsum of the head (vertex-skull) (3%); the top head and dorsum head probes are ~2cm apart from each other on the vertex; right axilla (~5cm below the axilla) (6%); anterior chest (~2cm medial to the left nipple) (6%); anterior abdomen (~2cm above the umbilicus) (18%); upper back (~5cm medial to the left scapula) (6%); left anterior upper arm (belly of the biceps muscle) (7%); right anterior forearm (~5cm below and lateral to the elbow line) (12%); right anterior thigh (the mid-point of the anterior surface of the thigh) (18%); and left posterior thigh (the mid-point of the posterior surface of the thigh) (18%).

HF was then calculated for the following areas:

Head heat flux (HF_{Head}) (W) = $HF_{Forehead}$ + $HF_{Left\ Cheek}$ + $HF_{Top\ of\ the\ Head}$ + $HF_{Dorsum\ of\ the\ Head}$

Upper torso heat flux ($HF_{UpperTorso}$) (W) = $HF_{Anterior\ Chest}$ + $HF_{Right\ Axilla}$ + $HF_{Upper\ Back}$

Total cutaneous heat flux (HF_{Total}) (W) = HF_{Head} + $HF_{Upper\ Torso}$ + $HF_{Left\ Anterior\ Upper\ Arm}$ + $HF_{Right\ Anterior\ Forearm}$ + $HF_{Left\ Posterior\ Thigh}$ + $HF_{Right\ Anterior\ Thigh}$

Metabolic Heat Production (M)

Metabolic heat production was determined from the oxygen consumption ($\dot{V}O_2$) by using the following equation [21]:

M (W) = $\dot{V}O_2$ (l O_2/min) × 69.7 (W/Kcal/min) × [4.686 (Kcal/l O_2) + (0.83 – 0.707) × 1.232 (Kcal/l O_2)]

Respiratory Heat Loss (RHL)

Respiratory heat loss was calculated using the following equation [63]:

RHL (W) = 0.09 × M (W)

Net heat gain (W)

Net heat gain (W) was calculated by subtracting the respiratory heat loss and total cutaneous heat flux from the metabolic heat production. Positive values of total heat flux (HF_{Total}) indicate heat loss.

Net heat gain (W) = M (W) – RHL (W) – HF_{Total} (W)

Data from the three conditions were compared using repeated measures analysis of variance (ANOVA) for all the variables. Post hoc analysis for significant differences between treatments were accomplished using Tukey's test. Results are reported as means ± SD; $p < 0.05$ was used to identify statistically significant differences.

RESULTS

Six male subjects were studied. Table. 1 shows the descriptive data for all the subjects. The subjects were (mean ± SD) 28.7 ± 3.2 years old, 180.5 ± 6.1 cm tall, weighed 83.5 ± 18.4 kg, had 2 ± 0.2 m^2 body surface area, 16.2 ± 6.5% body fat and 25.5 ± 5 BMI.

Table 1. Descriptive data for six subjects.

Subject	Gender	Age (yr)	Height (cm)	Weight (Kg)	BSA (m^2)	SFSF (mm)	%Body Fat	BMI
1	M	29.0	175.0	62.0	1.8	18.0	11.9	20.2
2	M	32.0	188.0	80.0	2.1	35.1	17.8	22.6
3	M	29.0	184.0	87.0	2.1	52.4	19.4	25.7
4	M	32.0	172.0	65.0	1.8	16.3	14.8	22.0
5	M	24.0	180.0	109.0	2.3	74.3	23.8	33.6
6	M	26.0	184.0	98.0	2.2	53.7	19.7	28.9
Mean		28.7	180.5	83.5	2.0	41.6	16.2	25.5
SD		3.2	6.1	18.4	0.2	22.7	6.5	5.0

CORE TEMPERATURE

Baseline T_{es} was 37.4 ± 0.2 ˚C and the core cooling rate was -2.4 ± 1.7 ˚C/h (Figure 4). Three subjects were immersed for the entire 60 min period (Table 2) whereas, one subject reached the target T_{es} before 60 min, and was therefore removed early. The other two subjects opted to end the cooling before the 60 min period was completed. There were no significant differences in exit T_{es} between conditions.

Postcooling afterdrop compared with Spontaneous condition (1.5 ˚C) tended to be less than the Head (1.3˚C) and Torso (1.2 ˚C) conditions but there were no significant differences between the three conditions (Table 3, Figure 4).

Table 2. Length of the immersion period and core temperature on removal from the cold water (Exit T_{es}) for each subject in the Spontaneous, Head and Torso conditions.

Subject	Immersion Time (min)			Exit T_{es} (°C)		
	Spontaneous warming	Head warming	Torso warming	Spontaneous warming	Head warming	Torso warming
1	51.0	43.0	44.0	35.1	35.0	34.9
2	35.0	35.0	35.0	35.4	36.1	35.7
3	60.0	60.0	60.0	37.1	36.3	36.3
4	32.5	32.5	32.5	36.4	36.9	37.2
5	60.0	60.0	60.0	35.8	35.5	35.8
6	60.0	60.0	60.0	35.4	35.3	35.5
Mean	49.8	48.4	48.6	35.9	35.9	35.9
SD	12.9	13.2	13.1	0.8	0.7	0.8

Table 3. Core temperature responses during baseline, and cooling periods for Spontaneous, Head and Torso conditions (means ± standard deviation).

Condition	Baseline T_{es}, ˚C	Cooling Rate (-10 to 0 min), ˚C/h	Afterdrop Amount, ˚C	Time to T_{es} Nadir, min	Change in T_{es} (0-120 min), ˚C
Spontaneous warming	37.4 ± 0.3	-2.3 ± 1.5	-1.5 ± 0.4	41.3 ± 21.1	-0.5 ± 0.7
Head warming	37.4 ± 0.2	-2.4 ± 1.5	-1.3 ± 0.4	42.3 ± 23.4	-0.3 ± 0.7
Torso warming	37.3 ± 0.2	-2.5 ± 2.2	-1.2 ± 0.3	37.0 ±17.7	-0.1 ± 0.6

T_{es} decreased during immersion after the meperidine administration, and continued to decrease until exit from the cold water (Figure 4). No significant differences were found between the three conditions during the baseline and cold water immersion periods. Cooling rates for the Spontaneous condition was 2.3 ± 1.5 ˚C/h, Head was 2.4 ± 1.5 ˚C/h and Torso was 2.5 ± 2.2 ˚C/h. Core rewarming rates during 60-120 min warming periods were not significant between conditions; Spontaneous (0.7 ± 0.2˚C/h), Head (0.8 ± 0.3˚C/h) and Torso (0.8 ± 0.3˚C/h) (see Table

4, Figure 4). However, T_{es} was significantly lower in Spontaneous than Torso condition at 90 min

($p < 0.05$) and at 120 min ($p < 0.01$) (Figure 4).

Table 4. Core temperature responses during warming periods for Spontaneous, Head and Torso conditions (means ± standard deviation).

Condition	Rewarming Rate (60-120 min), ˚C/h
Spontaneous warming	0.7 ± 0.2
Head warming	0.8 ± 0.3
Torso warming	0.8 ± 0.3

Figure 4. Mean change in esophageal temperature (˚C) during baseline, up to 60 minutes of immersion in 8˚C water, and during 120 minutes of warming in the Spontaneous, Head and Torso conditions. Time 0 minutes and temperature 0˚C indicate exit from cold water (bars, SD). Only 3 subjects were immersed for the entire 60-minute period in all conditions. With the other three subjects ranging from 32.5 to 51 minutes of immersion. To show what the whole group did at the beginning and the end of immersion, data for the immersions less than 60 minutes are presented for the first 20 minutes, with the remainder adjusted so that the exit time is lined up for everyone at time 0. As a result, n=6 for data from -60 to -40 minutes and from -12.5 to 0 minutes. In the period between -40 and -12.5 minutes, n=4-5. For clarity, SD bars are only included for top and bottom lines. * Significantly lower in Spontaneous than the Torso condition (90 min, p < 0.05) † Significantly lower in Spontaneous than the Torso condition (120 min, p < 0.01).
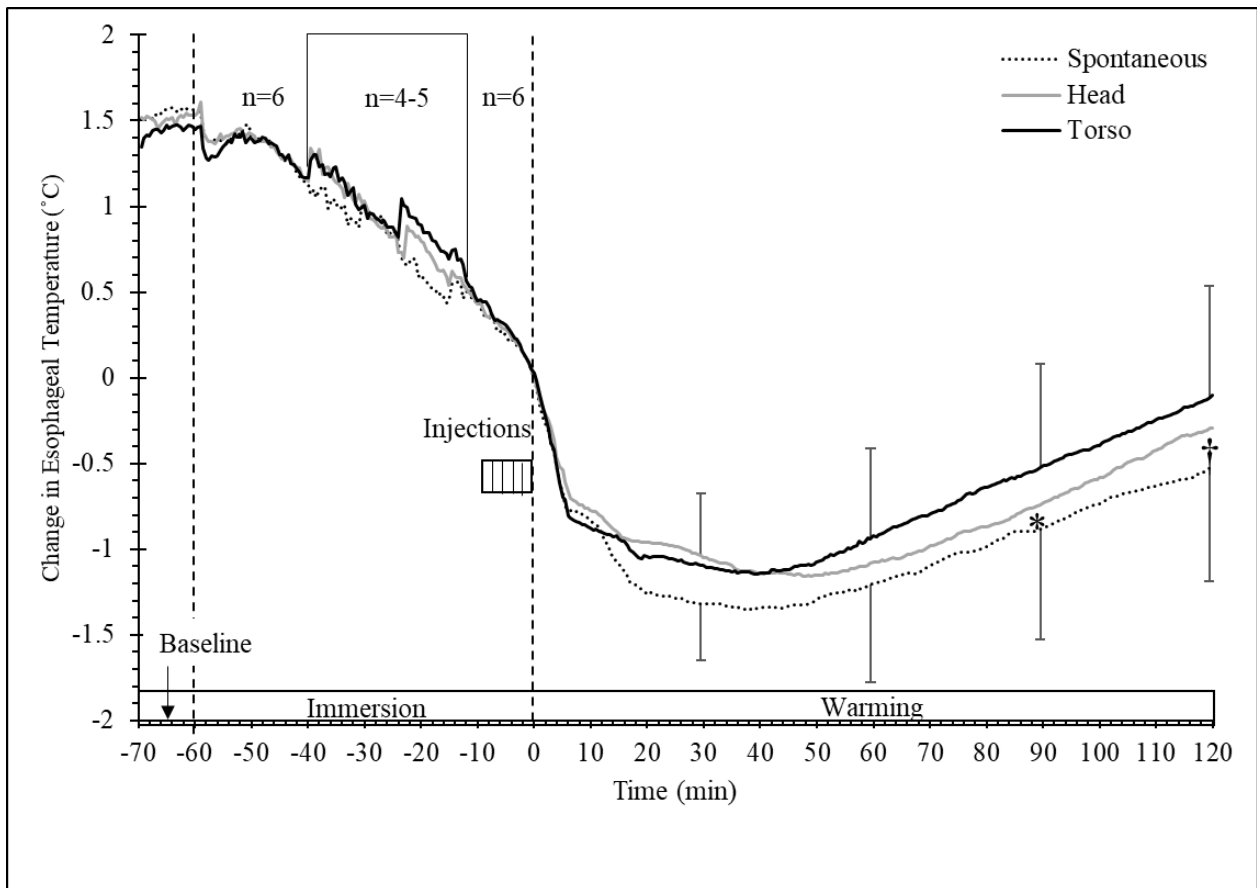
AVERAGE SKIN TEMPERATURE

There were no significant differences between the three conditions for $T_{skTotal}$ during the baseline and cooling periods (Figure 5). $T_{skTotal}$ decreased rapidly from baseline values of 32.3 ± 0.01°C to 15.5 ± 3.3°C during cooling. $T_{skTotal}$ was significantly higher at 90 min and 120 min of warming in the Torso condition (32.7 ± 1°C and 33.7 ± 0.9°C respectively) than the Spontaneous condition (31.8 ± 1.1°C ($p < 0.05$) and 32.8 ± 0.8°C ($p < 0.01$) respectively), but neither of these conditions were significantly different from the Head condition (32.5 ± 0.8°C and 33.4 ± 0.6°C). There were no significant differences in $T_{skTotal}$ between the three conditions at 30 min and 60 min of warming.

Figure 5. Total skin temperature (°C) during baseline, up to 60 min of immersion in 8°C water, and during 120 min of warming in the Spontaneous, Head, and Torso conditions Time 0 minutes and temperature 0˚C indicate exit from cold water (bars, SD). Only 3 subjects were immersed for the entire 60-minute period in all conditions. With the other three subjects ranging from 32.5 to 51 minutes of immersion. To show what the whole group did at the beginning and the end of immersion, data for the immersions less than 60 minutes are presented for the first 20 minutes, with the remainder adjusted so that the exit time is lined up for everyone at time 0. As a result, n=6 for data from -60 to -40 minutes and from -12.5 to 0 minutes. In the period between -40 and -12.5 minutes, n=4-5. For clarity, SD bars are only included for top and bottom lines. * Spontaneous is significantly lower than the Torso ($p<0.05$) at 90 min of warming. † Spontaneous is significantly lower than the Torso ($p<0.01$) at 120 min of warming.
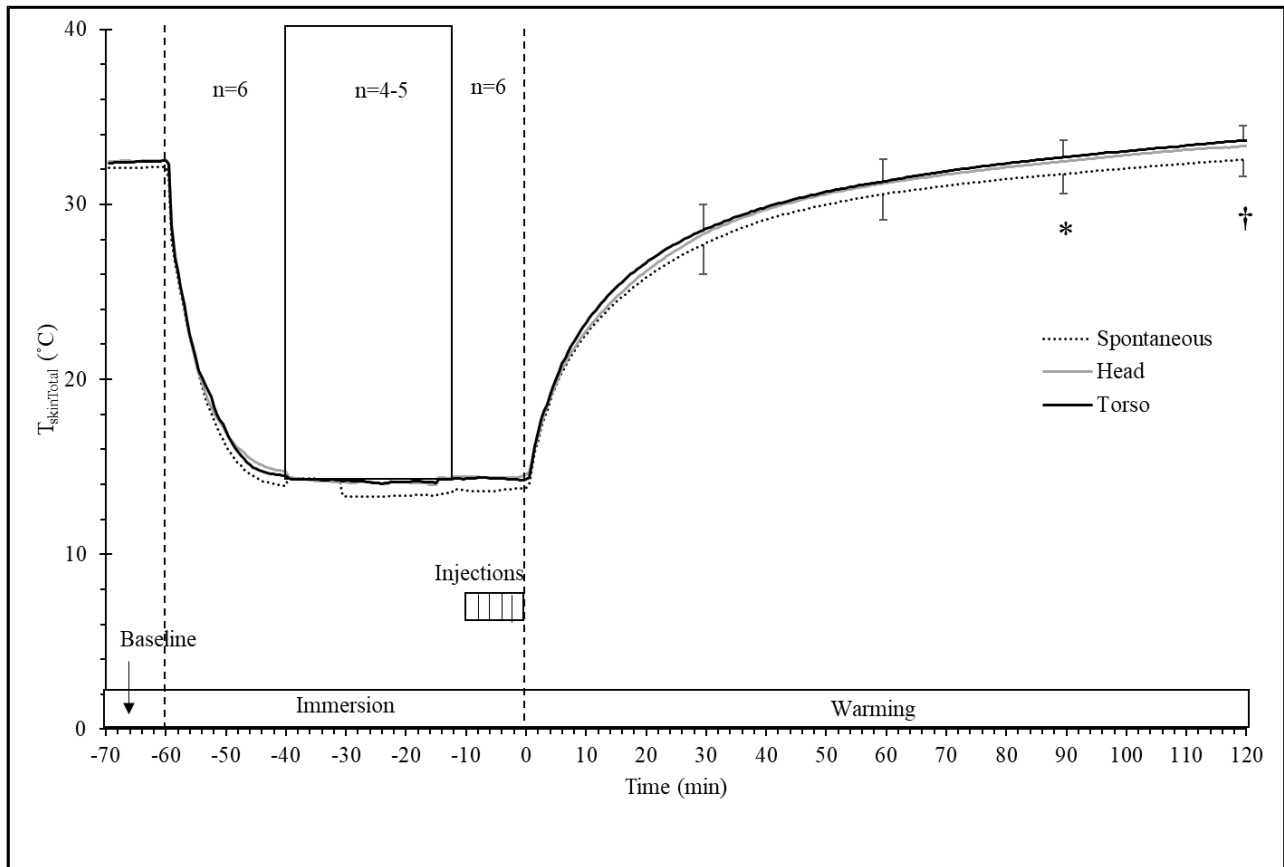
There were no significant differences between the three conditions for T_{skHead} during the baseline (32.1 ± 0.0°C) or cooling (31.3 ± 0.5°C) periods (Figure 6). T_{skHead} increased to 37.9 ± 1.9°C warming in the Head condition, whereas it returned to near baseline values in the Spontaneous (33.0 ± 0.5°C) and Torso (33.0 ± 0.6°C) conditions. T_{skHead} then continued to increase gradually in all the conditions with the average T_{skHead} at 30 min, 60 min, 90 min and 120 min of warming being significantly higher in the Head condition (38.3 ± 0.5°C, 38.6 ± 1.2°C, 38.7 ± 1.2°C and 39 ± 1.4°C respectively) than both the Spontaneous (33.1 ± 1.1°C, 33 ± 1°C, 33.2 ± 1°C and 33.5 ± 1.1°C respectively) ($p < 0.001$) and Torso [32.9 ± 1.4°C, 33 ± 1.3°C, 33.4 ± 1.3°C ($p < 0.001$) and 33.8 ± 1.4°C ($p < 0.01$)] conditions. There were no significant differences for T_{skHead} between the Spontaneous and Torso conditions.

Figure 6. Head skin temperature (°C) during baseline, up to 60 min of immersion in 8°C water, and during 120 min of warming in the Spontaneous, Head, and Torso conditions. Time 0 minutes and temperature 0˚C indicate exit from cold water (bars, SD). Only 3 subjects were immersed for the entire 60-minute period in all conditions. With the other three subjects ranging from 32.5 to 51 minutes of immersion. To show what the whole group did at the beginning and the end of immersion, data for the immersions less than 60 minutes are presented for the first 20 minutes, with the remainder adjusted so that the exit time is lined up for everyone at time 0. As a result, n=6 for data from -60 to -40 minutes and from -12.5 to 0 minutes. In the period between -40 and -12.5 minutes, n=4-5. For clarity, SD bars are only included for top and bottom lines. * Significantly higher in the Head than the Spontaneous and Torso conditions (p<0.001).
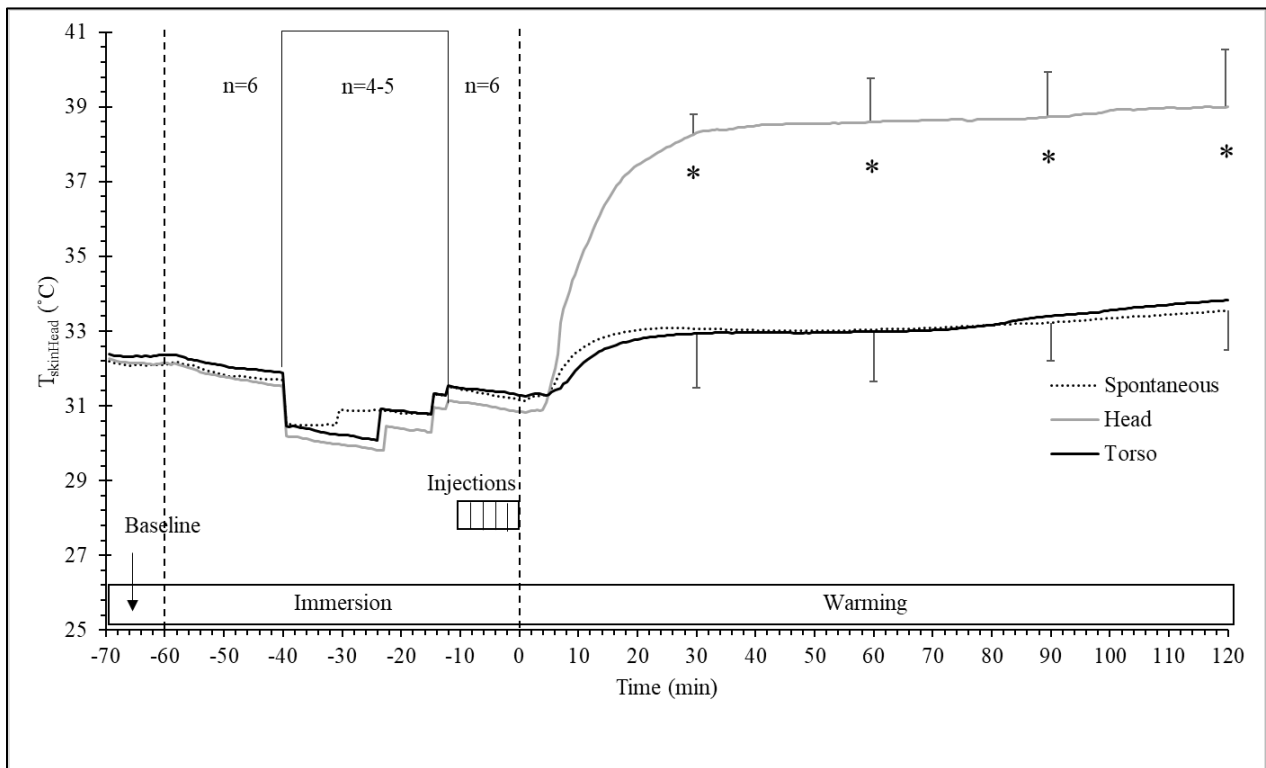
There were no significant differences between the three conditions for $T_{skUTorso}$ during the baseline and cooling periods (Figure 7). $T_{skUTorso}$ decreased from baseline of $32.9 \pm 0.1°C$ to $11.5 \pm 4.3°C$ during cooling. Following cooling, $T_{skUTorso}$ rapidly increased to $33.5 \pm 5.2°C$ during warming in the Torso condition whereas, it was still below the baseline values for the Spontaneous ($31.1 \pm 4.6°C$) and Head ($30.9 \pm 4.7°C$) conditions. $T_{skUTorso}$ then continued to increase in all the conditions, with average $T_{skUTorso}$ at 30 min, 60 min, 90 min and 120 min of warming being significantly higher in the Torso condition ($32.8 \pm 1.8°C$, $35.4 \pm 1.3°C$, $36.7 \pm 0.5°C$ and $37.1 \pm 0.5°C$ respectively) than both the Spontaneous ($30.1 \pm 2.9°C$ ($p < 0.01$), $32.9 \pm 1.6°C$, $34 \pm 1°C$ and $34.6 \pm 0.7°C$ ($p < 0.001$)] and Head [$29.8 \pm 2.4°C$ ($p < 0.01$), $32.4 \pm 1.1°C$, $34.7 \pm 0.5°C$ and $34.8 \pm 0.4°C$ ($p<0.001$)] conditions. There were no significant differences between the Spontaneous and Head conditions for the warming periods.

Figure 7. Upper torso skin temperature (°C) during baseline, up to 60 min of immersion in 8°C water, and during 120 min of warming in the Spontaneous, Head, and Torso conditions. Time 0 minutes and temperature 0˚C indicate exit from cold water (bars, SD). Only 3 subjects were immersed for the entire 60-minute period in all conditions. With the other three subjects ranging from 32.5 to 51 minutes of immersion. To show what the whole group did at the beginning and the end of immersion, data for the immersions less than 60 minutes are presented for the first 20 minutes, with the remainder adjusted so that the exit time is lined up for everyone at time 0. As a result, n=6 for data from -60 to -40 minutes and from -12.5 to 0 minutes. In the period between -40 and -12.5 minutes, n=4-5. For clarity, SD bars are only included for top and bottom lines. † Significantly higher in the Torso condition than the Spontaneous and the Head conditions (p<0.01). * Significantly higher in the Torso condition than the Spontaneous and the Head conditions (p<0.001).
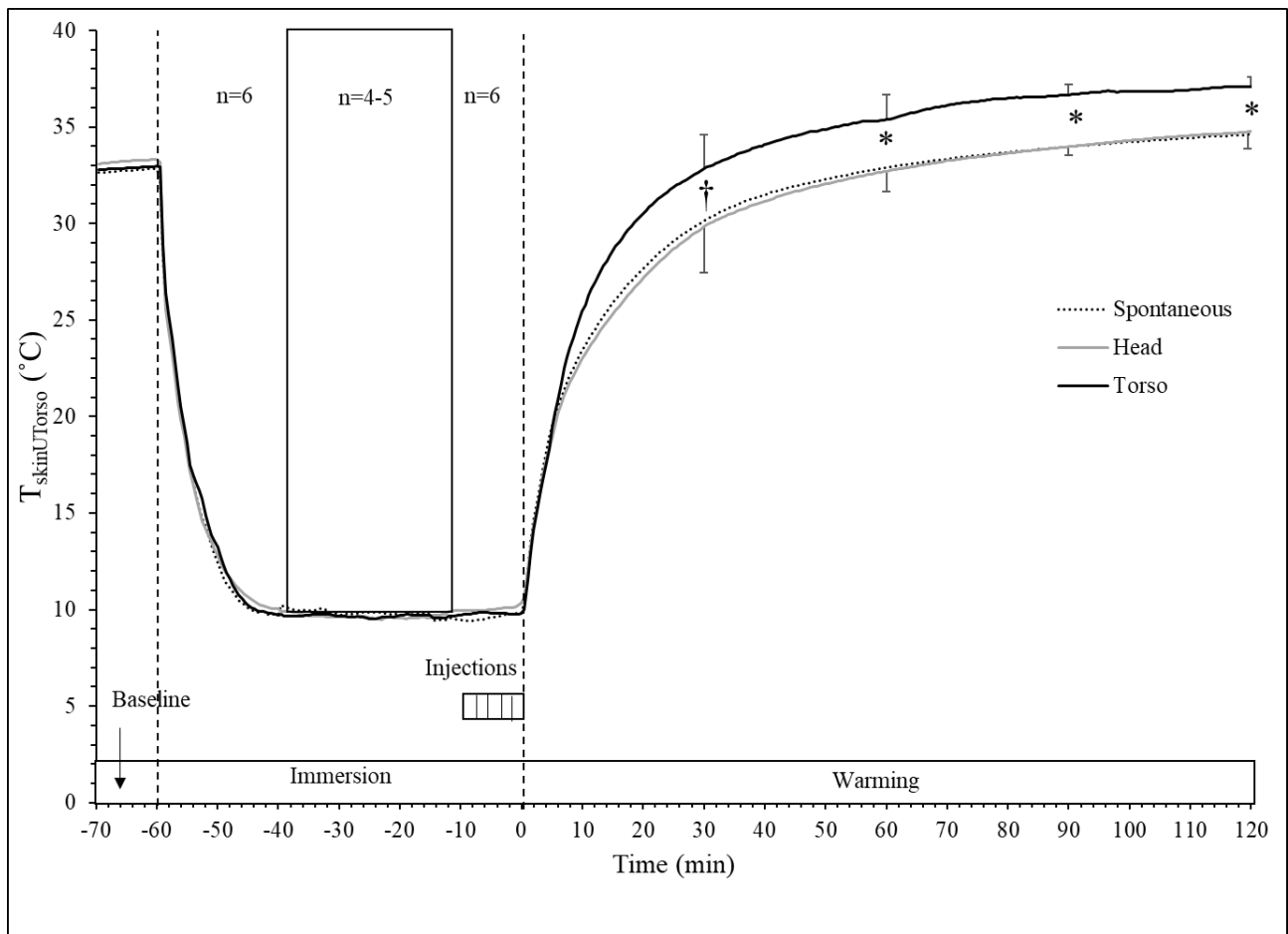
HEART RATE

No significant differences were found between the different conditions (Figure 8). Heart rate significantly increased during cooling from baseline values of 77 ± 10 beats/min to 84 ± 12 beats/min ($p < 0.05$), just before the meperidine administration. During the warming periods heart rate significantly declined to 64 ± 7 beats/min ($p < 0.05$).

Figure 8. Heart rate (b/min) during baseline, up to 60 min of immersion in 8°C water, and during 120 min of warming in the Spontaneous, Head, and Torso conditions. Time 0 minutes and temperature 0˚C indicate exit from cold water (bars, SD). Only 3 subjects were immersed for the entire 60-minute period in all conditions. With the other three subjects ranging from 32.5 to 51 minutes of immersion. To show what the whole group did at the beginning and the end of immersion, data for the immersions less than 60 minutes are presented for the first 20 minutes, with the remainder adjusted so that the exit time is lined up for everyone at time 0. As a result, n=6 for data from -60 to -40 minutes and from -12.5 to 0 minutes. In the period between -40 and -12.5 minutes, n=4-5. For clarity, SD bars are only included for top and bottom lines.

METABOLIC HEAT PRODUCTION

No significant differences were found for metabolic heat production among the three conditions during baseline, cooling and warming periods (Figures 9 and 10). Metabolic heat production significantly increased from 98.2 ± 12.7 W during baseline to 268.9 ± 111 W ($p < 0.001$) during cooling until the meperidine infusion. Meperidine suppressed shivering, and heat production returned to 93.6 ± 32.1 W during the warming period.

Figure 9. Metabolic heat production (W) plotted continuously (at 30-sec intervals) during baseline, up to 60 min of immersion in 8°C water, and during 120 min of warming in the Spontaneous, Head, and Torso conditions. Time 0 minutes and temperature 0˚C indicate exit from cold water (bars, SD). Only 3 subjects were immersed for the entire 60-minute period in all conditions. With the other three subjects ranging from 32.5 to 51 minutes of immersion. To show what the whole group did at the beginning and the end of immersion, data for the immersions less than 60 minutes are presented for the first 20 minutes, with the remainder adjusted so that the exit time is lined up for everyone at time 0. As a result, n=6 for data from -60 to -40 minutes and from -12.5 to 0 minutes. In the period between -40 and -12.5 minutes, n=4-5. For clarity, SD bars are only included for top and bottom lines.

Figure 10. Metabolic heat production (W) during baseline, up to 60 min of immersion in 8°C water, and during 120 min of warming in the Spontaneous, Head, and Torso conditions. Time 0 minutes and temperature 0˚C indicate exit from cold water (bars, SD). Only 3 subjects were immersed for the entire 60-minute period in all conditions. With the other three subjects ranging from 32.5 to 51 minutes of immersion. To show what the whole group did at the beginning and the end of immersion, data for the immersions less than 60 minutes are presented for the first 20 minutes, with the remainder adjusted so that the exit time is lined up for everyone at time 0. As a result, n=6 for data from -60 to -40 minutes and from -12.5 to 0 minutes. In the period between -40 and -12.5 minutes, n=4-5. Each data point represents average of 30 min except for the -65 min which represents the average of 10 min baseline. For clarity, SD bars are only included for top and bottom lines. * Significantly greater than all other points for all three conditions.
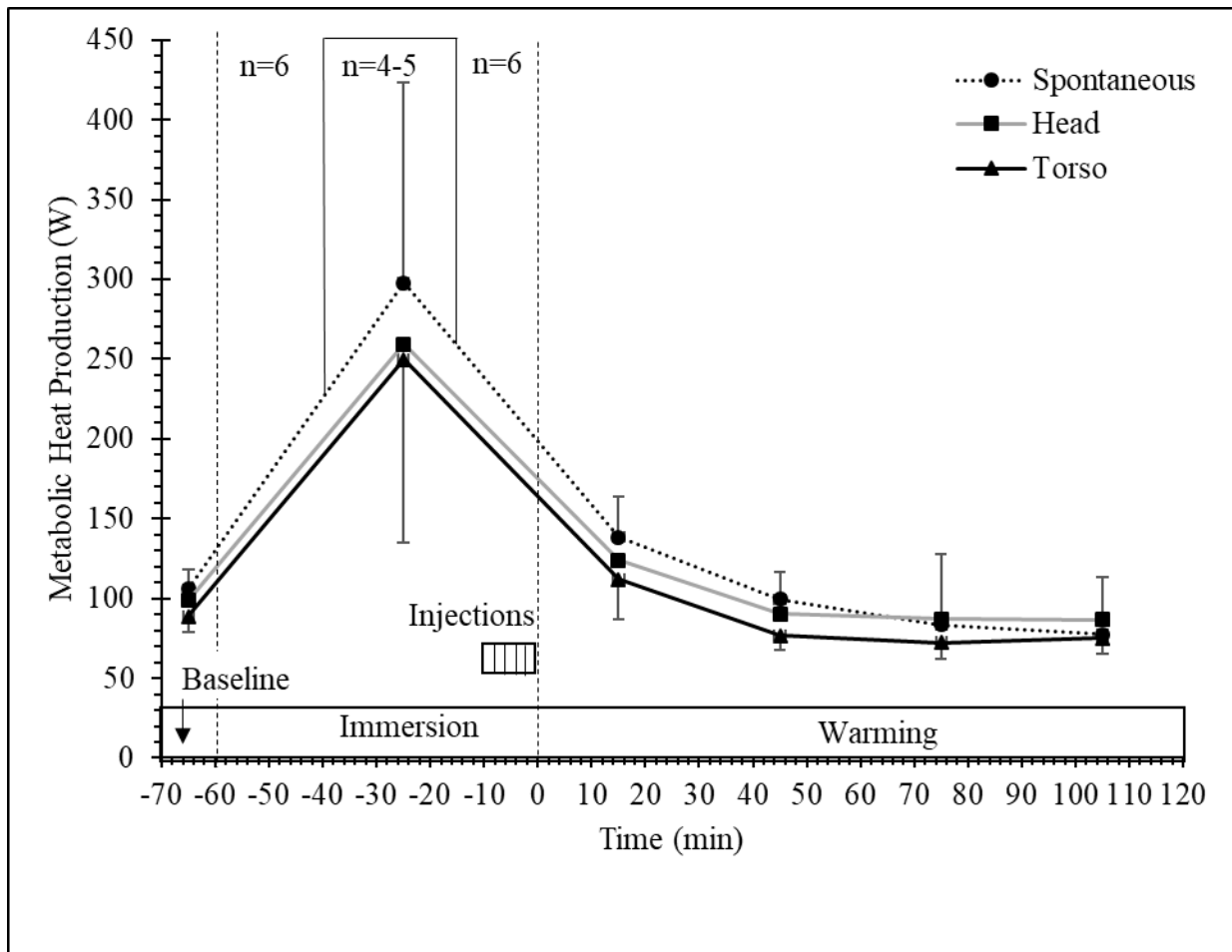
HEAT FLUX

No significant differences were found for HF_{Total} between the three conditions during baseline and cooling periods (Figure 11). Total heat loss increased from the baseline values of 104.2 ± 18.3 W to a peak value of 558.1 ± 35.4 W during cold-water immersion.

At 30, 60, 90 and 120 min of warming (Table 5), there was significantly less heat gain in the Spontaneous condition (18.2 ± 9.7 W, 14.1 ± 9 W, 13.1 ± 9 W and 13.9 ± 8.4 W respectively) than both the Head [-6.1 ± 12.5 W, -8.2 ± 5.2 W, -7.7 ± 4.6 W ($p < 0.001$) and -5.7 ± 4.1 W ($p < 0.01$)] or Torso (-11.8 ± 12.3 W, -15.6 ± 7.1 W, -15.1 ± 6.1 W and -11.4 ± 7) ($p < 0.001$) conditions. However, there were no significant differences between the Head and Torso conditions.

Figure 11. Total heat flux (W) during 120 min of warming in the Spontaneous, Head, and Torso conditions. Negative values indicate heat gain and positive values indicate heat loss. For clarity, SD bars are only included for top and bottom lines. * Spontaneous significantly different from the Head (p<0.05) and the Torso (p<0.001) conditions.

Table 5. Results of total heat flux at 30 min, 60 min, 90 min and 120 min of warming

Variable	Spontaneous warming	Head warming	Torso warming
HF$_{Total}$ 30 min, W	18.2 ± 9.7^b	-6.1 ± 12.5	-11.8 ± 12.3
HF$_{Total}$ 60 min, W	14.1 ± 9^b	-8.2 ± 5.2	-15.6 ± 7.1
HF$_{Total}$ 90 min, W	13.1 ± 9^b	-7.7 ± 4.6	-15.1 ± 6.1
HF$_{Total}$ 120 min, W	13.9 ± 8.4^a	-5.7 ± 4.1	-11.4 ± 7

[a] Significantly different from head (p < 0.01) and torso warming (p < 0.001)
[b] Significantly different from the other two conditions (p < 0.001)

There were no significant differences between the three conditions for heat loss from the head during the baseline (11.2 ± 0.1 W) or cooling (10.8 ± 0.4 W) periods (Figure 12 and Table 6). During warming at 30 min, 60 min, 90 min and 120 min, the head had significantly higher heat gain in the Head condition (-16.0 ± 4.6 W, -16.1 ± 4.7 W, -15.8 ± 4.9 W and -15.5 ± 4.3 W respectively) than in the Spontaneous (3.0 ± 0.5 W, 2.9 ± 0.3 W, 2.9 ± 0.4 and 3.1 ± 0.4 W) ($p < 0.001$) and Torso conditions (2.4 ± 0.8 W, 2.2 ± 0.9 W, 2.3 ± 0.9 W and 2.5 ± 1.0 W) ($p<0.001$).

There were no significant differences between the Spontaneous and Torso conditions.

Figure 12. Head heat flux (W) during 120 min of warming in the Spontaneous, Head, and Torso conditions. Negative values indicate heat gain and positive values indicate heat loss. For clarity, SD bars are only included for top and bottom lines. * Significantly greater heat gain in the Head condition (p<0.001).
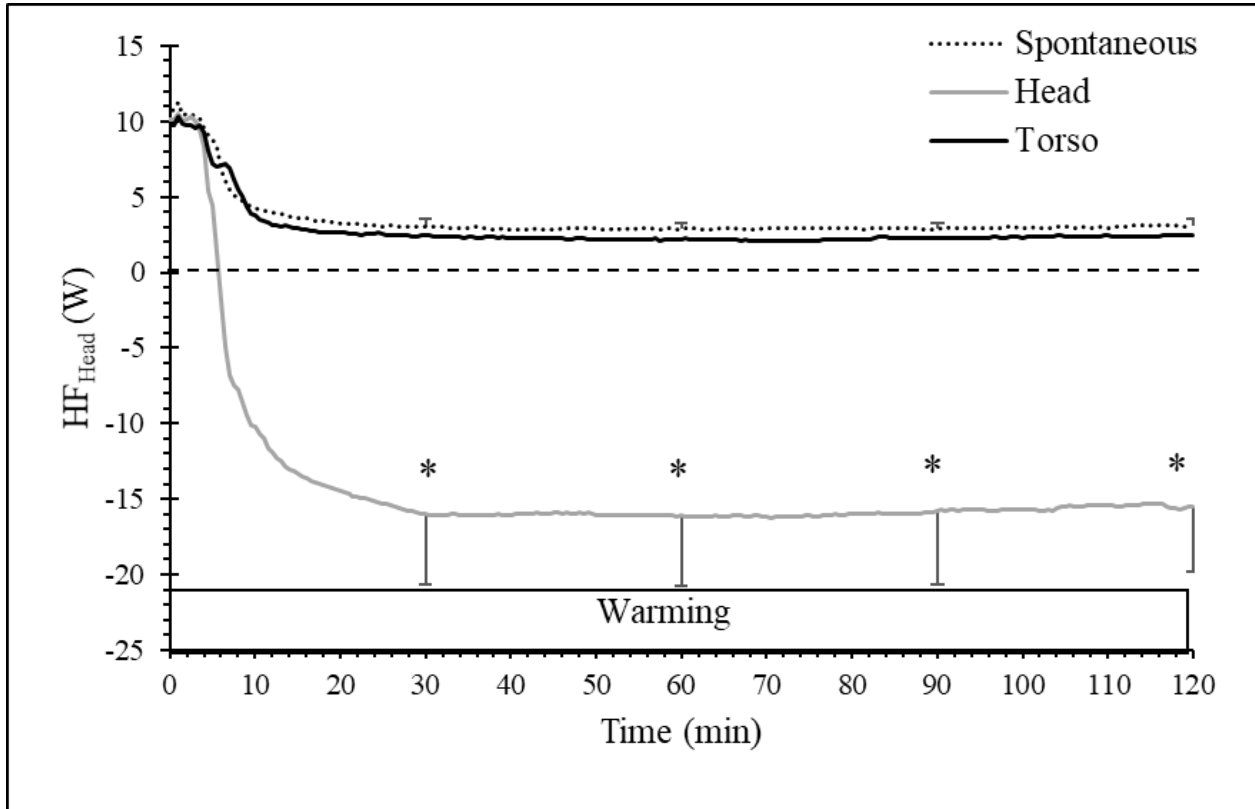
Table 6. Results of head heat flux at 30 min, 60 min, 90 min and 120 min of warming

Variable	Spontaneous warming	Head warming	Torso warming
HF$_{Head}$ 30 min, W	3 ± 0.5	-16 ± 4.6 [b]	2.4 ± 0.8
HF$_{Head}$ 60 min, W	2.9 ± 0.3	-16.1 ± 4.7 [b]	2.2 ± 0.9
HF$_{Head}$ 90 min, W	2.9 ± 0.4	-15.8 ± 4.9 [b]	2.3 ± 0.9
HF$_{Head}$ 120 min, W	3.1 ± 0.4	-15.5 ± 4.3 [b]	2.5 ± 1

[b] Significantly different from the other two conditions (p < 0.001)

There were no significant differences between the three conditions for HF_{UTorso} during the baseline and cooling periods (Figure 13 and Table 7). Heat loss from the upper torso increased rapidly from a baseline value of 20.2 ± 0.7 W to a peak value of 146.1 ± 34.9 W during cold-water immersion. At 30 min, 60 min, 90 min and 120 min of warming, there was significantly greater heat gain from the upper torso in the Torso condition (-18.0 ± 8.5 W, -19.7 ± 6.1 W, -19.6 ± 3.8 and -19 ± 4.3 W respectively) than the Spontaneous (3.5 ± 2.1 W, 1.5 ± 1.8 W, 0.9 ± 1.2 W and 0.6 ± 1 W) ($p < 0.001$) and Head (3.4 ± 3.4 W, 2.5 ± 2.1 W, 1.5 ± 1.6 W and 0.7 ± 1.2 W) ($p<0.001$) conditions.

There were no significant differences between the Spontaneous and Head conditions.

Figure 13. Upper Torso heat flux (W) during 120 min of warming in the Spontaneous, Head, and Torso conditions. Negative values indicate heat gain and positive values indicate heat loss. For clarity, SD bars are only included for top and bottom lines. * Significantly greater heat gain in the Torso condition (p<0.001).
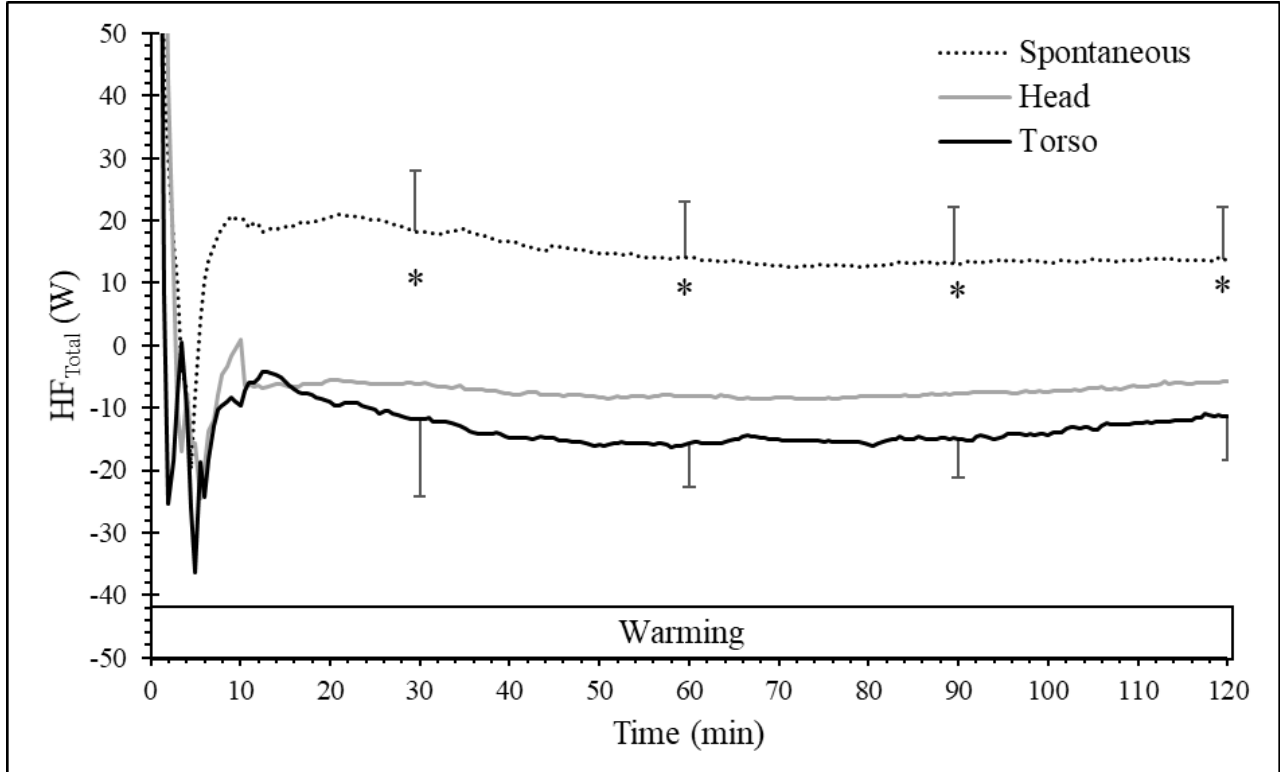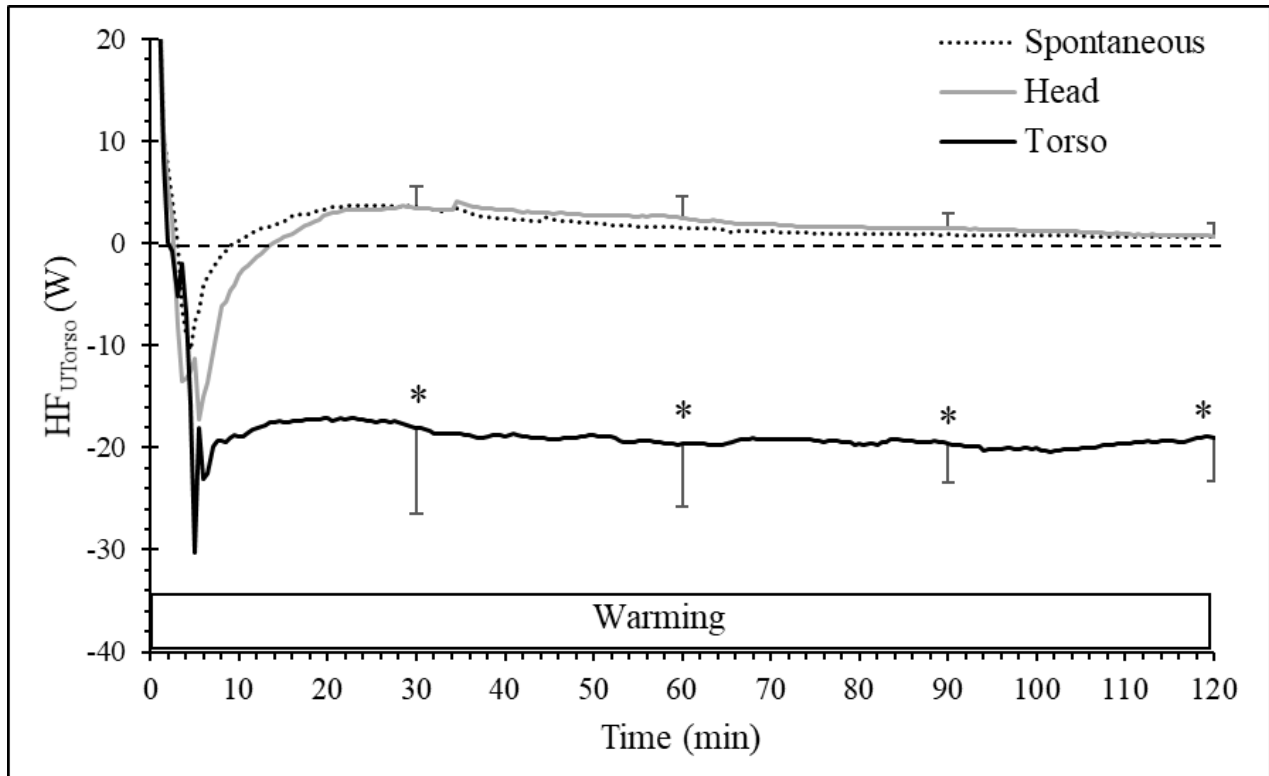

Table 7. Results of upper torso heat flux at 30 min, 60 min, 90 min and 120 min of warming

Variable	Spontaneous warming	Head warming	Torso warming
HF_{UTorso} 30 min, W	3.5 ± 2.1	3.4 ± 3.4	-18 ± 8.5 [b]
HF_{UTorso} 60 min, W	1.5 ± 1.8	2.5 ± 2.1	-19.7 ± 6.1 [b]
HF_{UTorso} 90 min, W	0.9 ± 1.2	1.5 ± 1.6	-19.6 ± 3.8 [b]
HF_{UTorso} 120 min, W	0.6 ± 1	0.7 ± 1.2	-19 ± 4.3 [b]

[b] Significantly different from the other two conditions (p < 0.001)

NET HEAT GAIN

There were no significant differences between the three conditions during the baseline and cooling periods (Figure 14). During baseline, there was a net heat loss (-15.1 ± 7.6 W) which increased rapidly to a peak value of -368.7 ± 195.4 W during cold-water immersion. Results for the net heat gain were analyzed at four different data points during warming: at 15, 45, 75 and 105 minutes. Each data point represents the average data for 30 mins. 15 represents the data for 0 min to 30 mins, 45 represents the data from 30 to 60 mins, 75 represents the data from 60 to 90 mins and 105 represents the data from 90 to 120 mins. At 105, net heat gain was significantly higher in Head (85.8 ± 25.3) and Torso condition (81.5 ± 6.3) than the Spontaneous (56.9 ± 12.0) ($p < 0.05$). However, for the remaining three data points 15, 45 and 75 there were no significant differences between the Spontaneous (96.3 ± 35.3 W, 74.6 ± 15 W and 63 ± 11.4 W respectively), Head (103.9 ± 58.3, 89.7 ± 41.3 W and 87.5 ± 39.1 W), and Torso (98.9 ± 32.4 W, 84.6 ± 12 W and 81.1 ± 8.6 W) conditions.

Figure 14. Net heat gain (W) during 120 min of warming in the Spontaneous, Head, and Torso conditions. Positive values indicate heat gain. For clarity, SD bars are only included for top and bottom lines. * Significantly lower net heat gain in the Spontaneous condition than the Head and Torso condition (p < 0.05) at 105 (average of 90 min to 120 min).
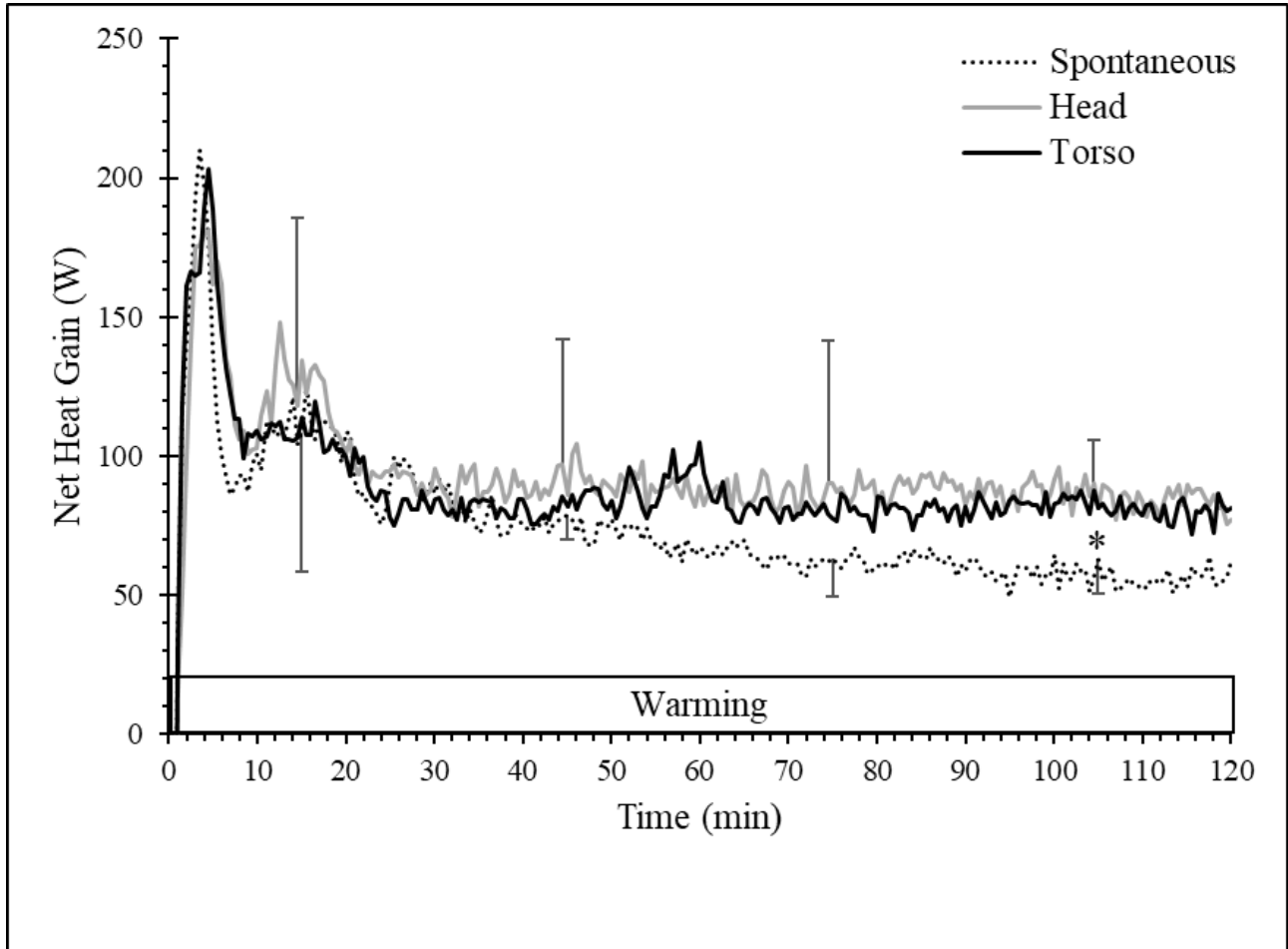
DISCUSSION

This study is the first study to compare the effectiveness of the same amount of heat donation through the head or torso for rewarming mildly hypothermic individuals in whom the shivering was pharmacologically inhibited. In this study the subjects were immersed in 8°C on three different occasions for a period of 60 min or until they met the exit criteria. All the subjects were then rewarmed by one of three methods: spontaneous warming; head warming; or torso warming.

We hypothesized that compared to head warming, torso warming would result in greater net heat gain, a smaller afterdrop, and a greater rate of core rewarming. Our results did not support these hypotheses, as we did not find any significant differences between the torso and head warming conditions for net heat gain, afterdrop amount or rate of core rewarming. The positive aspect of these results is that the head provides a viable alternative for heat donation when torso warming is contraindicated.

Torso warming resulted in significantly higher total heat flux at 30 min, 60 min, 90 min and 120 min during warming compared to spontaneous warming condition. Torso warming had significantly higher net heat gain at 105 min and significantly higher total skin temperature at 90 min and 120 min during warming than the spontaneous warming condition. There were no differences found between torso and head warming in any of these variables.

Head warming also had significantly higher total heat flux at 30 min, 60 min, 90 min and 120 min during warming than the spontaneous warming condition. Net heat gain was also significantly higher in head condition than the spontaneous warming at 105 min during warming.

RELATION TO PREVIOUS LITERATURE

We expected that torso warming would result in a lower afterdrop amount and a higher rate of core rewarming compared to spontaneous warming. Our study showed that the afterdrop amount and core body rewarming rates were similar for all the three conditions. In our study the afterdrop amount values for the spontaneous warming condition (1.5˚C) and torso warming condition (1.2˚C) were within the range previously reported for non-shivering subjects (1.4 – 2.2˚C and 1.0 – 1.8˚C respectively). [8,20,30] A previous study by Goheen et. al., [8] reported that using forced-air warming reduced the afterdrop amount by 30-40%. The lower afterdrop values reported by Goheen may be due to the high source of heat used in their study (forced-air warming which provided up to 270 W) vs. 13 W in the present study provided by the charcoal heater on the torso.

During the spontaneous warming condition, our non-shivering subjects rewarmed at a higher rate (0.7˚C/h) than reported in previous studies (between 0.1 and 0.4˚C/h). [8,20,31] The higher rewarming rate in our study may be due to higher metabolic heat production during the first 30 min post immersion. Baseline values of metabolic heat production in the spontaneous warming condition were 106 W, post immersion during the first 30 min, the metabolic heat production increased 31% (138 W) although, this difference was not significant. In a study by Giesbrecht et al., [30] reported core rewarming rate of 1.2˚C/h (meperidine condition) with a metabolic heat production increased up to 42% post immersion. Therefore, our lack of difference between the core rewarming rates between the torso warming and control conditions is due to higher core rewarming in control compared to torso and head warming conditions.

The core rewarming rate in the head warming condition was as effective in rewarming the core as torso warming when a similar source of heat donation was used in both the conditions. This result was similar to the results reported in a previous study where the authors investigated

the thermal effects of head cooling on non-shivering subjects. [64] In this study the authors found that isolated head cooling had similar effects on core cooling rates as similar to body only cooling.

POSSIBLE MECHANISMS FOR THE RESULTS

Unlike the previous studies [20,31] where torso warming resulted in a significantly higher core rewarming rate, in this study torso warming resulted in similar rewarming rates compared to the spontaneous warming, although, the core rewarming rate in the torso condition (0.8˚C/h) is well within the range as shown in the previous studies. In the torso warming condition, we found that core temperature and total skin temperature was significantly higher at 90 and 120 min compared to spontaneous warming condition. The amount of heat donated through the torso warming (~13 W) was significantly higher than the spontaneous warming condition where there was a net heat loss. The net heat gain during the last 30 min of warming was significantly higher compared to the spontaneous warming condition. These results show that torso warming is advantageous compared to spontaneous warming in providing steady rate of core rewarming in severely hypothermic patients.

For the first 90 min of warming, the net heat gain was similar for all three conditions. In the last 30 min, net heat gain was significantly lower in the spontaneous warming condition compared to head warming and torso warming. There were no differences found between the head warming and torso warming conditions. Head warming provided a core rewarming rate of (0.8˚C/h), total skin temperature was similar to the spontaneous warming condition. Head warming provided a heat gain (~7 W) which is significantly higher compared to spontaneous warming condition where there was a total heat loss.

It is noteworthy that when the same amount of heat is donated on the head and torso, head warming had similar core rewarming rates compared to the torso warming when the confounding

effects of shivering had been diminished. This phenomenon could be potentially explained by the size of the effective perfused mass. When exposed to cold, there is a generalized vasoconstriction which further decreases the thermal core by reducing the peripheral blood flow. Therefore, any heat donation to the head and torso would have similar effect on that smaller perfused tissue.

Further work is needed to quantify the tissue temperature and blood flow to confirm the mechanisms of these results.

PRACTICAL IMPLICATIONS

It has been recommended in the previous literature to actively warm the severely hypothermic patients in whom shivering is absent. In the absence of active warming, core temperature can continue to drop, especially in severely hypothermic subjects in whom the shivering heat production is abolished. It is important to provide external heat to the severely hypothermic patient to provide a safe and steady core rewarming rate and to attenuate the afterdrop. Due to the proximity to the heart, the torso is the most efficient area to provide external heat.

Torso warming is beneficial for providing safe and steady rate of rewarming in hypothermic subjects in whom shivering is either diminished or impaired. Providing active warming to the torso can be potentially beneficial as warming a larger surface area perfuses more tissues with warm blood, thus providing more warm blood into the circulation. Also, in this study we found that the application of the charcoal heater was much easier for the torso than the head. Applying the charcoal heater on the torso and then wrapping the body with a vapor barrier and a sleeping bag would help reduce heat loss to the environment compared to head warming.

In this study, we found that the core rewarming rates for torso warming and head warming were similar. Although, torso warming is more preferred and a more comfortable method of providing active warming to the hypothermic subject than head warming, head warming provides

a viable alternative to donate external heat to hypothermic subjects in whom torso warming may be contraindicated. Torso warming may be contraindicated when there is an open wound on the anterior chest or emergency personnel are performing cardiopulmonary resuscitation on the patient. In some cases, the hypothermic subject is insulated and wrapped in a sleeping bag, thus getting an access to the torso may be difficult. Providing heat to the head can prove to be beneficial especially in an extreme cold environment.

LIMITATIONS

Our study did not follow a strictly balanced design as the spontaneous warming condition was conducted first according to previous work. [9,32] This modified balanced design is unlikely to have any affect on the important comparisons between torso and head warming.

CONCLUSION

In conclusion, external heat delivery to the head and torso provided similar core rewarming rates. The data indicates that external heat donation to the head may be beneficial in severely hypothermic subjects in whom the active warming to torso is contraindicated. A charcoal heater, which is light, portable, and easy-to-use can be an effective modality to provide a safe and steady rate of core rewarming in severely hypothermic patients. The charcoal heater does not need any external power supply and can be used safely by lay persons, and Search and Rescue personnel during rescue operations to provide prehospital warming to cold patients.

REFERENCES

1.   Gower S, Bassil K, Kim M, et al. Health Impacts of Cold Weather. *Toronto Public Heal*.
      2014. http://www.mississauga.ca/file/COM/Health Impacts of Cold Weather.pdf.

2.   Zafren K, Giesbrecht GG, Danzl DF, et al. Wilderness Medical Society Practice
      Guidelines for the Out-of-Hospital Evaluation and Treatment of Accidental Hypothermia:
      2014 Update. *Wilderness Environ Med*. 2014;25:S66-S85.
      doi:10.1016/j.wem.2014.10.010.

3.   Giesbrecht GG, Steinman AM. Immersion into Cold Water. In: *Auerbach P, Ed.
      Wilderness Medicine. Management of Wilderness and Environmental Emergencies*.
      Mosby, St. Louis; 2017:162-197.

4.   Cramer MN, Jay O. Biophysical aspects of human thermoregulation during heat stress.
      Auton Neurosci Basic Clin. 2016;196:3-13. doi:10.1016/j.autneu.2016.03.001.

5.   Giesbrecht GG. Emergency treatment of hypothermia. *Emerg Med*. 2001;13(1):9-16.
      doi:10.1046/j.1442-2026.2001.00172.x.

6.   Giesbrecht GG. Prehospital treatment of hypothermia. *Wilderness Environ Med*.
      2001;12:24-31. doi:10.1580/1080-6032(2001)012[0024:PTOH]2.0.CO;2.

7.   Golden FS, Hervey GR, Tipton MJ. Circum-rescue collapse: collapse, sometimes fatal,
      associated with rescue of immersion victims. *J R Nav Med Serv*. 1991;77(3):139-149.
      http://www.ncbi.nlm.nih.gov/pubmed/1815081.

8.   Goheen MSL, Ducharme MB, Kenny GP, et al. Efficacy of forced-air and inhalation
      rewarming by using a human model for severe hypothermia. *J Appl Physiol*.

1997;83(5):1635-1640. http://jap.physiology.org/content/83/5/1635.

9.   Giesbrecht GG, Bristow GK. The convective afterdrop component during hypothermic exercise decreases with delayed exercise onset. *Aviat Sp Environ Med*. 1998;69(1):17-22.

10. Osborne L, El-Din ASK, Smith JE. Survival after prolonged cardiac arrest and accidental hypothermia. *Br Med J (Clin Res Ed)*. 1984;289(6449):881.

11. Lee CH, Van Gelder C, Burns K, Cone DC. Advanced cardiac life support and defibrillation in severe hypothermic cardiac arrest. *Prehospital Emerg Care*. 2009;13(1):85-89.

12. Giesbrecht GG, Bristow GK. A second postcooling afterdrop: more evidence for a convective mechanism. *J Appl Physiol*. 1992;73(4):1253-1258. http://search.ebscohost.com/login.aspx?direct=true&db=cmedm&AN=1447067&site=eho st-live.

13. Thomassen Ø, Færevik H, Østerås Ø, et al. Comparison of three different prehospital wrapping methods for preventing hypothermia-a crossover study in humans. *Scand J Trauma Resusc Emerg Med*. 2011;19(1):41.

14. D. D. *Accidental Hypothermia. In: Auerbach's Wilderness Medicine*. Elsevier Health Sciences; 2012.

15. Morrison G. Management of acute hypothermia. *Medicine (Baltimore)*. 2017.

16. Sran BJK, McDonald GK, Steinman AM, Gardiner PF, Giesbrecht GG. Comparison of Heat Donation Through the Head or Torso on Mild Hypothermia Rewarming. *Wilderness Environ Med*. 2014;25(1):4-13. doi:10.1016/j.wem.2013.10.005.

17.   Giesbrecht GG, Bristow GK, Uin a, Ready a E, Jones R a. Effectiveness of three field treatments for induced mild (33.0 degrees C) hypothermia. *J Appl Physiol*. 1987;63(6):2375-2379. http://www.ncbi.nlm.nih.gov/pubmed/3436871.

18.   Giesbrecht GG, Sessler DI, Mekjavic IB, et al. Treatment of mild immersion hypothermia by direct body-to-body contact Treatment of mild immersion hypothermia by direct body-to-body contact. *J Appl Physiol*. 1994;76(6):2373-2379. https://www.researchgate.net/profile/Igor_Mekjavic/publication/15270097_Treatment_of_mild_immersion_hypothermia_by_direct_body-to-body_contact/links/54736e3c0cf2d67fc0373703.pdf.

19.   Collis ML, Steinman AM, Chaney RD. Accidental hypothermia: an experimental study of practical rewarming methods. *Aviat Sp Environ Med*. 1977;48(7):625-632.

20.   Lundgren JP, Henriksson O, Pretorius T, et al. Field Torso-Warming Modalities: A Comparative Study Using a Human Model. *Prehospital Emerg Care*. 2009;13(3):371-378. doi:10.1080/10903120902935348.

21.   Vanggaard L, Eyolfson D, Xu X, Weseen G, Giesbrecht GG. Immersion of distal arms and legs in warm water (AVA rewarming) effectively rewarms mildly hypothermic humans. *Aviat Sp Environ Med*. 1999;70(11):1081-1088.

22.   Giesbrecht GG, Wilkerson JA. *Hypothermia, Frostbite and Other Cold Injuries: Prevention, Survival, Rescue, and Treatment*. The Mountaineers Books; 2006.

23.   Eyolfson DA, Tikuisis P, Xu X, Weseen G, Giesbrecht GG. Measurement and prediction of peak shivering intensity in humans. *Eur J Appl Physiol*. 2001;84(1-2):100-106. doi:10.1007/s004210000329.

24. Iampietro PF, Vaughan JA, Goldman RF, Kreider MB, Masucci F, Bass DE. Heat production from shivering. http://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.964.6348&rep=rep1&type=pdf. Accessed March 5, 2017.

25. Bristow GK, Giesbrecht GG. Contribution of exercise and shivering to recovery from induced hypothermia (31.2 degrees C) in one subject. *Aviat Space Environ Med*. 1988;59(6):549-552.

26. Giesbrecht GG. Cold stress, near drowning and accidental hypothermia: A review. *Aviat Sp Environ Med*. 2000;71(7):733-752.

27. Sterba JA. Efficacy and safety of prehospital rewarming techniques to treat accidental hypothermia. *Ann Emerg Med*. 1991;20(8):896-901. doi:10.1016/S0196-0644(05)81434-9.

28. Giesbrecht GG, Schroeder M, Bristow GK. Treatment of mild immersion hypothermia by forced-air warming. *Aviat Sp Environ Med*. 1994;65(9 I):803-808.

29. Pretorius T, Cahill F, Kocay S, Giesbrecht GG. Shivering heat production and core cooling during head-in and head-out immersion in 17??C water. *Aviat Sp Environ Med*. 2008;79(5):495-499. doi:10.3357/ASEM.2165.2008.

30. Giesbrecht GG, Goheen MS, Johnston CE, Kenny GP, Bristow GK, Hayward JS. Inhibition of shivering increases core temperature afterdrop and attenuates rewarming in hypothermic humans. *J Appl Physiol*. 1997;83(5):1630-1634. http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=9375331%5Cnhttp://www.ncbi.nlm.nih.gov/pubmed/9375331.

31. Hultzer M V., Xu X, Marrao C, Bristow G, Chochinov A, Giesbrecht GG. Pre-hospital torso-warming modalities for severe hypothermia: A comparative study using a human model. *Can J Emerg Med*. 2005;7(6):378-386.

32. Mallet ML. Pathophysiology of accidental hypothermia. *QJM - Mon J Assoc Physicians*. 2002;95(12):775-785. doi:10.1093/qjmed/95.12.775.

33. Danzl D, Pozos R. Accidental hypothermia. *N Engl J Med*. 1994;367(20):1930-1938. doi:10.1056/NEJMra1114208.

34. Nadel ER. Energy exchanges in water. *Undersea Biomed Res*. 1984;11(2):149-158. http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=6485144.

35. Nunneley SA, Wissler EH, Allan JR. Immersion cooling: effect of clothing and skinfold thickness. *Aviat Space Environ Med*. 1985;56(12):1177-1182.

36. Ducharme MB, Brooks CJ. The effect of wave motion on dry suit insulation and the responses to cold water immersion. *Aviat Space Environ Med*. 1998;69(10):957-964.

37. Turk EE. Hypothermia. *Forensic Sci Med Pathol*. 2010;6(2):106-115.

38. Keatinge WR. The effects of subcutaneous fat and of previous exposure to cold on the body temperature, peripheral blood flow and metabolic rate of men in cold water. *J Physiol*. 1960;153(1):166.

39. Hayward JS, Eckerson JD, Collis ML. Effect of behavioral variables on cooling rate of man in cold water. *J Appl Physiol*. 1975;38(6):1073-1077.

40. Weinberg AD. Hypothermia. *Ann Emerg Med*. 1993;22(2 Pt 2):370-377.

41. Johnston CE, Bristow GK, Elias DA, Giesbrecht GG. Alcohol lowers the vasoconstriction threshold in humans without affecting core cooling rate during mild cold exposure. *Eur J Appl Physiol Occup Physiol*. 1996;74(3):293-295.

42. Fox GR, Hayward JS, Hobson GN. Effect of alcohol on thermal balance of man in cold water. *Can J Physiol Pharmacol*. 1979;57(8):860-865.

43. Martin S, Cooper KE. Alcohol and respiratory and body temperature changes during tepid water immersion. *J Appl Physiol*. 1978;44(5):683-689.

44. Brown DJA, Brugger H, Boyd J, Paal P. Accidental hypothermia. *N Engl J Med*. 2012;367(20):1930. doi:10.1056/NEJMra1114208.

45. Cheung SSS. *Advanced Environmental Exercise Physiology*.; 2010. http://books.google.co.uk/books/about/Advanced_Environmental_Exercise_Physiolo.html ?id=kMVuQYzG420C&pgis=1%5Cnhttp://books.google.com/books?hl=en&lr=&id=nuY NX8zRgXcC&oi=fnd&pg=PR1&dq=Advanced+environmental+exercise+physiology&ot s=FEXpmdDKqW&sig=98bVmd_QVQ.

46. McArdle WD, Katch KI KV. *Exercise Physiology: Nutrition, Energy, and Human Performance*.; 2009. doi:10.1161/01.STR.25.4.793.

47. Boulant JA. Hypothalamic mechanisms in thermoregulation. *Fed Proc*. 1981;40(14):2843-2850. http://www.ncbi.nlm.nih.gov/pubmed/6273235. Accessed March 7, 2017.

48. Mekjavic IB, Sundberg CJ, Linnarsson D. Core temperature" null zone." *J Appl Physiol*. 1991;71(4):1289-1295.

49.   Bigland-Ritchie BR, Thomas CK, Rice CL, Howarth J V, Woods JJ. Muscle temperature, contractile speed, and motoneuron firing rates during human voluntary contractions. *J Appl Physiol*. 1992;73(7):2457-2461.

50.   Davies C, Young K. Effect of temperature on the contractile properties and muscle power of triceps surae in humans. *J Appl Physiol*. 1983;55(1 Pt 1):191-195.

51.   Giesbrecht GG, Bristow GK. Decrement in manual arm performance during whole body cooling. *Aviat Sp Environ Med*. 1992;63(12):1077-1081.

52.   Cheung SS, Montie DL, White MD, Behm D. Changes in manual dexterity following short-term hand and forearm immersion in 10 C water. *Aviat Space Environ Med*. 2003;74(9):990-993.

53.   Cahill F, Kalmar JM, Pretorius T, Gardiner PF, Giesbrecht GG. Whole-body hypothermia has central and peripheral influences on elbow flexor performance. *Exp Physiol*. 2011;96(5):528-538. doi:10.1113/expphysiol.2010.054973.

54.   Xu X, Tikuisis P, Gonzalez R, Giesbrecht G. Thermoregulatory model for prediction of long-term cold exposure. *Comput Biol Med*. 2005;35(4):287-298. doi:10.1016/j.compbiomed.2004.01.004.

55.   Tikuisis P, Giesbrecht GG. Prediction of shivering heat production from core and mean skin temperatures. *Eur J Appl Physiol Occup Physiol*. 1999;79(3):221-229.

56.   Hassard TH. *Understanding Biostatistics*. Mosby year book; 1991.

57.   Norton K, Whittingham N, Carter L, Kerr D, Gore C, Marfell-Jones M. Measurement techniques in anthropometry. *Anthropometrica*. 1996;1:25-75.

58.   Du Bois D, Du Bois EF. A formula to estimate the approximate surface area if height and

       weight be known. 1916. *Nutrition*. 5(5):303-11-3.

       http://www.ncbi.nlm.nih.gov/pubmed/2520314.

59.   Durnin JVGA, Womersley J. Body fat assessed from total body density and its estimation

       from skinfold thickness : measurements on 481 men and women aged from 16 to 72 years.

       Br J Nutr. 1973;32(1):77-97. doi:10.1079/BJN19740060.

60.   Cooper KE, Ferres HM, Kenyon JR, Wendt F. A comparison of oesophageal, rectal and

       para-aortic temperatures during hypothermia in man. In: *JOURNAL OF PHYSIOLOGY-

       LONDON*. Vol 130. CAMBRIDGE UNIV PRESS 40 WEST 20TH STREET, NEW

       YORK, NY 10011-4211; 1955:P10-P10.

61.   Hayward JS, Eckerson JD, Kemna D. Thermal and cardiovascular changes during three

       methods of resuscitation from mild hypothermia. *Resuscitation*. 1984;11(1-2):21-33.

62.   Layton RP, Mints WH, Annis JF, Rack MJ, Webb P. Calorimetry with heat flux

       transducers: comparison with a suit calorimeter. *J Appl Physiol*. 1983;54(5):1361-1367.

63.   Fanger PO. Thermal comfort - Analysis and applications in environmental engineering.

       McGraw-Hill B Co. 1970:244 p.

       http://www.cabdirect.org/abstracts/19722700268.html%5Cnpapers2://publication/uuid/5C

       E163C3-F9AC-4937-A143-1238F1D806C5.

64.   Pretorius T, Bristow GK, Steinman AM, Giesbrecht GG. Thermal effects of whole head

       submersion in cold water on nonshivering humans. *J Appl Physiol*. 2006;101(2):669-675.

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UNIVERSITY OF MANITOBA

Research Ethics - Bannatyne
Office of the Vice-President (Research and International)

BIOMEDICAL RESEARCH ETHICS BOARD (BREB)
CERTIFICATE OF FINAL APPROVAL FOR AMENDMENTS AND ADDENDUMS

PRINCIPAL INVESTIGATOR: Dr. Gordon Giesbrecht	INSTITUTION/DEPARTMENT: U of M/Kinesiology and Recreation Management	ETHICS #: HS18816 (B2015:101)
BREB MEETING DATE (If applicable):	**APPROVAL DATE:** May 19, 2017	
STUDENT PRINCIPAL INVESTIGATOR SUPERVISOR (If applicable):		

PROTOCOL NUMBER: NSERC Discovery Grant (2010-16)	PROJECT OR PROTOCOL TITLE: NSERC Discovery Grant (2010-16) Efficacy of Head and Torso Rewarming by Using a Human Model for Severe Hypothermia (Linked to B2012:024)
SPONSORING AGENCIES AND/OR COORDINATING GROUPS: NSERC	

REMINDER: THE CURRENT BREB APPROVAL FOR THIS STUDY EXPIRES: **February 22, 2018**

REVIEW CATEGORY OF AMENDMENT:	Full Board Review ☐	Delegated Review ☒
Submission Date of Investigator Documents: April 24 and May 19, 2017	**BREB receipt date of Documents:** April 24 and May 19, 2017	

THE FOLLOWING AMENDMENT(S) and DOCUMENTS ARE APPROVED FOR USE:

Document Name	Version(if applicable)	Date

Protocol:
Revised Protocol   April 21, 2017
Consent and Assent Form(s):
Research Participant Information and Consent Form   April 21, 2017

Other:
Medical Screening Questionnaire for Hypothermia Study   April 21, 2017

CERTIFICATION
The University of Manitoba (UM) Biomedical Research Board (BREB) has reviewed the amendment to the research study/project named on this *Certificate of Approval* as per the category of review listed above and was found to be acceptable on ethical grounds for research involving human participants. The amendment and documents listed above were granted final approval by the Chair or Acting Chair, UM BREB.

BREB ATTESTATION
The University of Manitoba (UM) Biomedical Research Board (BREB) is organized and operates according to Health Canada/ICH Good Clinical Practices, Tri-Council Policy Statement 2, and the applicable laws and regulation of Manitoba. In respect to clinical trials, the BREB complies with the membership requirements for Research Ethics Boards defined in

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Division 5 of the Food and Drug Regulations of Canada and carries out its functions in a manner consistent with Good Clinical Practices.

QUALITY ASSURANCE
The University of Manitoba Research Quality Management Office may request to review research documentation from this research study/project to demonstrate compliance with this approved protocol and the University of Manitoba Policy on the Ethics of Research Involving Humans.

CONDITIONS OF APPROVAL:
1. This amendment is acceptable on scientific and ethical grounds for the ethics of human use only. *For logistics of performing the study, approval must be sought from the relevant institution(s).*
2. This research study/project is to be conducted by the local principal investigator listed on this certificate of approval.
3. The principal investigator has the responsibility for any other administrative or regulatory approvals that may pertain to the research study/project, and for ensuring that the authorized research is carried out according to governing law.
4. **This approval is valid until the expiry date noted on this certificate of approval.** A Bannatyne Campus Annual **Study Status Report** must be submitted to the REB within 15-30 days of this expiry date.
5. Any changes of the protocol (including recruitment procedures, etc.), informed consent form(s) or documents must be reported to the BREB for consideration in advance of implementation of such changes on the **Bannatyne Campus Research Amendment Form.**
6. Adverse events and unanticipated problems must be reported to the REB as per Bannatyne Campus Research Boards Standard Operating procedures.
7. The UM BREB must be notified regarding discontinuation or study/project closure on the **Bannatyne Campus Final Study Status Report**.

Sincerely,

Lindsay Nicolle, MD, FRCPC
Chair, Biomedical Research Ethics Board
Bannatyne Campus

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Please quote the above Human Ethics Number on all correspondence.
Inquiries should be directed to the REB Secretary **Telephone:** (204) 789-3255/ **Fax:** (204) 789-3414

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Physical Activity Readiness
Questionnaire - PAR-Q
(revised 2002)

PAR-Q & YOU

(A Questionnaire for People Aged 15 to 69)

Regular physical activity is fun and healthy, and increasingly more people are starting to become more active every day. Being more active is very safe for most people. However, some people should check with their doctor before they start becoming much more physically active.

If you are planning to become much more physically active than you are now, start by answering the seven questions in the box below. If you are between the ages of 15 and 69, the PAR-Q will tell you if you should check with your doctor before you start. If you are over 69 years of age, and you are not used to being very active, check with your doctor.

Common sense is your best guide when you answer these questions. Please read the questions carefully and answer each one honestly: check YES or NO.

YES	NO		
☐	☐	1.	Has your doctor ever said that you have a heart condition <u>and</u> that you should only do physical activity recommended by a doctor?
☐	☐	2.	Do you feel pain in your chest when you do physical activity?
☐	☐	3.	In the past month, have you had chest pain when you were not doing physical activity?
☐	☐	4.	Do you lose your balance because of dizziness or do you ever lose consciousness?
☐	☐	5.	Do you have a bone or joint problem (for example, back, knee or hip) that could be made worse by a change in your physical activity?
☐	☐	6.	Is your doctor currently prescribing drugs (for example, water pills) for your blood pressure or heart condition?
☐	☐	7.	Do you know of <u>any other reason</u> why you should not do physical activity?

If

you

answered

YES to one or more questions

Talk with your doctor by phone or in person BEFORE you start becoming much more physically active or BEFORE you have a fitness appraisal. Tell your doctor about the PAR-Q and which questions you answered YES.

- You may be able to do any activity you want — as long as you start slowly and build up gradually. Or, you may need to restrict your activities to those which are safe for you. Talk with your doctor about the kinds of activities you wish to participate in and follow his/her advice.
- Find out which community programs are safe and helpful for you.

NO to all questions

If you answered NO honestly to <u>all</u> PAR-Q questions, you can be reasonably sure that you can:

- start becoming much more physically active — begin slowly and build up gradually. This is the safest and easiest way to go.
- take part in a fitness appraisal — this is an excellent way to determine your basic fitness so that you can plan the best way for you to live actively. It is also highly recommended that you have your blood pressure evaluated. If your reading is over 144/94, talk with your doctor before you start becoming much more physically active.

DELAY BECOMING MUCH MORE ACTIVE:
- if you are not feeling well because of a temporary illness such as a cold or a fever — wait until you feel better; or
- if you are or may be pregnant — talk to your doctor before you start becoming more active.

PLEASE NOTE: If your health changes so that you then answer YES to any of the above questions, tell your fitness or health professional. Ask whether you should change your physical activity plan.

<u>Informed Use of the PAR-Q:</u> The Canadian Society for Exercise Physiology, Health Canada, and their agents assume no liability for persons who undertake physical activity, and if in doubt after completing this questionnaire, consult your doctor prior to physical activity.

No changes permitted. You are encouraged to photocopy the PAR-Q but only if you use the entire form.

NOTE: If the PAR-Q is being given to a person before he or she participates in a physical activity program or a fitness appraisal, this section may be used for legal or administrative purposes.

"I have read, understood and completed this questionnaire. Any questions I had were answered to my full satisfaction."

NAME _____

SIGNATURE _____   DATE_____

SIGNATURE OF PARENT _____   WITNESS _____
or GUARDIAN (for participants under the age of majority)

Note: This physical activity clearance is valid for a maximum of 12 months from the date it is completed and becomes invalid if your condition changes so that you would answer YES to any of the seven questions.

© Canadian Society for Exercise Physiology www.csep.ca/forms

Revised: April 21, 2017

Name: _____   Signature: _____   Date:_____

Medical Screening Questionnaire for Hypothermia Study	
Please <u>circle</u> answer for each question below:	
1. Do you have any history of cardiac diseases (e.g., heart murmur or palpitations, chest pain on exertion)?	Yes / No
2. Do you have any history of respiratory disease (e.g., asthma, chronic bronchitis)?	Yes / No
3. Do you have diabetes or thyroid disease?	Yes / No
4. Do you have any negative reactions caused by cold exposure (e.g., Raynaud's phenomenon, hives, rashes, trouble breathing)?	Yes / No
5. Do you have a history of seizures?	Yes / No
6. Do you have epilepsy or delirium tremens?	Yes / No
7. Do you have any other neurological diseases such as multiple sclerosis?	Yes / No
8. Do you have any history of kidney disease?	Yes / No
9. Do you have any history of liver disease?	Yes / No
10. Are you presently taking any prescribed and/or non-prescribed medications that cause sedation or drowsiness (such as sleep aids, antihistamines, or anything containing codeine)?	Yes / No
11. Do you now, or have you ever, used illicit (non-prescription) opioids (narcotics) such as oxycodone, fentanyl, morphine, meperidine (Demerol) or heroin?	Yes / No

12. Do you have sensitivity or intolerance to the drug metoclopramide (Maxeran), meperidine (Demerol) or naloxone (Narcan)?	Yes / No If yes, which drug(s)? _____
13. Do you have any diseases/conditions (such as mechanical GI obstruction) that affect bowel transit?	Yes / No
14. Did you undergo any surgical procedure of abdomen (i.e. acute appendicitis or pancreatitis)	Yes / No
15. Do you have severe CNS depression, head injury, increased cerebrospinal or intracranial pressure?	Yes / No
16. Do you have prostatic hypertrophy (enlarged prostrate) or urethral stricture?	Yes / No
17. Do you have sickle cell anemia, Addison's disease or pheochromocitoma?	Yes / No
18. Do you have acute alcoholism (alcohol poisoning)?	Yes / No
19. Are you using medications that might interact negatively with meperidine. Examples include MAO inhibitors at the time of screening or within 14 days of screening; CNS depressants; phenytoin; cimetidine; ritonavir; aclyclovir; skeletal muscle relaxants?	Yes / No
20. Are you pregnant, planning to become pregnant, or breast feeding?	Yes / No
21. Is your skin hypersensitive to heat: do you burn easily or do you get hives or any other type of skin reactions to heating?	Yes / No

Reviewed by: _____   **Signature:** _____
             (Qualified Investigator)

UNIVERSITY OF MANITOBA | **Faculty of Kinesiology and Recreation Management**

APPENDIX D

REVISION APRIL 21, 2017

PART II: INFORMED CONSENT FOR CLINICAL TRIALS

RESEARCH PARTICIPANT INFORMATION AND CONSENT FORM

Title of Study: <u>Efficacy of head and torso rewarming by using a human model for severe hypothermia</u>

Protocol number: **HS18816 (B2015: 101)** NSERC Discovery Grant (2010-17)
Principal Investigator: Gordon Giesbrecht
211 Max Bell Centre, University of Manitoba,
Winnipeg, MB - R3T 2N2
Phone: 474-8646
Co-Investigator: None
Sponsor: NSERC
350 Albert Street,
Ottawa, ON – K1A 1H5

You are being asked to participate in a Clinical Trial (a human research study). Please take your time to review this consent form and discuss any questions you may have with the study staff. You may take your time to make your decision about participating in this

clinical trial and you may discuss it with your regular doctor, friends and family before you make your decision. This consent form may contain words that you do not understand. Please ask Dr. Giesbrecht or his study staff to explain any words or information that you do not clearly understand.

The Principal Investigator (Dr. Gordon Giesbrecht) is receiving financial support (from the Natural Sciences and Engineering Research Council) to conduct this study.

Public registration of the study

ClinicalTrials.gov is a website that provides information about federally and privately supported clinical trials. A description of this clinical trial will be available on http.//ClinicalTrials.gov. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

Purpose of Study

This Clinical Trial is being conducted to study the effectiveness of simple rewarming techniques for the treatment of mild hypothermic humans who are given meperidine (Demerol) to inhibit shivering; resulting in thermal responses similar to severely hypothermic, non-shivering patients. This procedure has been used safely and successfully in this lab for the past 20 years. You are being asked to take part in this study because you have fulfilled the criteria of being a healthy adult between the ages of 18-45 years with no adverse responses to cold exposure nor any cardiorespiratory disease. A total of eight participants will participate in this study.

The purpose of this study is to compare the effectiveness of core rewarming techniques of the same amount of heat donation through the head or torso in core rewarming using a human model for severe hypothermia.

Study procedures

The order of experiments will follow a randomized balanced design. The order of the three rewarming methods will be randomly assigned to each participant so that all participants have a different order of treatments. This design allows the researchers to ensure that all participants do not undergo the experiments in an exactly same order.

Neither you nor the study staff will be blinded to the treatment groups.

If you take part in this study, you will have the following tests and procedures:

You will be asked to participate in three experimental trials on three separate occasions, separated by at least five days. On each of the three trials, you will be submersed in 21˚C water up to the level of the sternal notch. The water temperature will then be lowered to 8˚C over a period of 5-10 min by addition of ~60 kg of ice. You will remain in the water until either:
1) You wish to exit;
2) The investigator or physician advises stopping for safety or other reasons;
3) Your core body temperature decreases to 35˚C; or

4) 60 minutes of immersion elapses, whichever comes first.

Ten minutes before exiting the cold water, 1.5 mg/kg of intravenous meperidine (diluted in 10 ml of saline) will be injected slowly in five 2-mL aliquots (i.e., 0.3 mg/kg meperidine per injection) in successive 2-minute intervals to inhibit shivering. After that you will then exit the water, be dried off and lie in a hooded sleeping bag, where one of the three warming procedures will be administered:

A. Spontaneous rewarming (Control) - In this control condition, up to 1.8 mg/kg of IV meperidine will be infused through the arm or hand vein, only when necessary to inhibit subsequent shivering. It will be infused in amounts of 0.3 mg/kg (diluted in 2-mL aliquots and injected slowly at minimum of 2-minute intervals) to a maximum cumulative dose of 3.3 mg/kg. If your breathing rate decreases to 8 breaths/min or any other side effect (such as nausea) occurs, no further doses will be infused to reverse the slowed breathing. If you experience nausea, a drug metoclopramide HCl (Maxeran) will be infused to alleviate these symptoms.
After towel drying you will lie on a mattress under an insulated cover without any extra heating modality. Spontaneous rewarming will be the first condition to be tested for every subject; the results will be used to determine the dosage schedule for meperidine in the other two active warming conditions.

B. Head Warming (Head) - Charcoal Heater on the Head - A charcoal heater will be placed on right side of your face/head (the heater is insulated to prevent skin burning) with ducts wrapping around the dorsum of the head, anteriorly over the forehead, nose, chin and the neck, not covering the eyes or the mouth. You will be breathing ambient air (~22˚C).

C. Torso Warming (Torso) - Charcoal Heater on the Torso - The charcoal heater will be placed on your anterior chest (the heater is insulated to prevent skin burning). The flexible ducts will be applied to the areas of high heat transfer i.e. over the shoulders, neck, and then anteriorly under the axillae to cross over the lower anterior chest. You will be breathing ambient air at room temperature (~22˚C).

Treatment will continue either for a period of 120 minutes or until your core temperature returns to normal values (~36.5-37˚C). Following that, you will be placed in a warm water bath (40-42˚C), until you are comfortable and core temperature returns to normal values (~36.5-37˚C).

If you take part in this study, you will have the following procedures:
- You will be visiting the laboratory 3 times in a period of up to 6 months. You will be required to visit at same time of the day, during weekdays.
- You will be asked to complete a PAR-Q-Activity questionnaire and Medical Screening Questionnaire for Hypothermia Study (MSQHS) prior to participating. An example of questions asked in PAR-Q is: Has your doctor ever said that you have a heart condition and that you should only do physical activity recommended by a doctor? You will also be asked a series of verbal questions to determine if you have any cardiorespiratory disease or any conditions that are stimulated by cold exposure.

- Either males or females between the ages of 18-45 years can participate in this study. There is no other screening procedure other than the PAR-Q and MSQHS.
- The study will include women of child bearing potential willing to use highly effective birth control during the trial. All women of child bearing potential will undergo a pregnancy test at screening.
- You will be instructed to abstain from alcohol, medications or vigorous physical activity for a 24 hour period prior to the study.
- You will be instructed to have a small breakfast and no other food 2-3 hours prior to the immersion.
- Anthropometric data will be collected and recorded. This includes age, weight, height, and measurements of skin fold thickness at four sites- biceps, triceps, subscapularis, and suprailiac. This will be used to calculate your body surface area and % body fat.
- Each testing session will involve whole body cooling. You will be submersed in 21°C water up to the level of the sternal notch. The water temperature will then be lowered to 8°C over a period of 5-10 min by addition of~60 kg of ice. Intravenous drug (meperidine) injection will be infused in the last 10 min of cooling to inhibit shivering. Your heart rate and electrocardiogram will be monitored continuously throughout this period. We will also visually inspect skin areas that are directly heated for any signs of excess reddening or other signs of burning. You will be asked several times throughout the study if you would like to stop. The trial will be stopped when:
  o You wish to exit (you can communicate by either asking to be removed or giving a thumbs-up hand signal);
  o The investigator advises stopping for safety or other reasons (including excess skin reddening or other signs of burning);
  o Your core body temperature decreases to 35°C;
  o Or 60 minutes of immersion elapses, whichever comes first.
- You will be instrumented as follows:
  o 12 heat flux disks (2 cm in diameter) will be taped to the skin on the legs, arms, torso and head to measure skin temperature and heat transfer from the skin.
  o Three ECG leads will be affixed to the skin.
  o Core temperature will be measured with a sterile disposable esophageal thermocouple. A thin, flexible tube will be inserted through the nose, to midway down the esophagus at the level of the heart. The esophageal probe will be inserted by Dr Giesbrecht. You will have your own thermocouple which will not be used by anyone else.
  o Metabolic rate will be continuously monitored; you will be asked to wear a face mask which will collect the expired breath, during the cooling period. The mask will be replaced with a mouth-piece during the rewarming period and a nose-clip will be placed on the nose. You will be able to speak and communicate with the investigators throughout the trials.

- o   Intravenous line on your right hand or right arm to introduce drug (meperidine).
- After removal from the water you will be dried off and lie in a hooded sleeping bag with the head inside the hood where you will be warmed by one of the three rewarming methods: A. Spontaneous rewarming; B. Head warming; and C. Torso warming. Treatment will continue either for a period of 120 minutes or until your core temperature returns to normal values ($\sim$36.5-37˚C). Following that, you will be actively rewarmed by entering a warm water bath of 40-42˚C.
- After the physician has cleared you to leave, you may go home. NOTE: because you will have had meperidine, you must not operate a motor vehicle or any other machinery for the rest of the study day. You should arrange for someone to drive you home.
- You will be asked to participate in three experimental trials. Each trial will last about 4 hours (1 hour for setup, 1 hour for cooling, and 2 hours for rewarming and removal of instrumentation). Your trials will be at least five days apart and the three tests will be completed within five-six months (June-November). Thus, your total commitment will be about 4 hours per visit and three total visits within a period of 6 months. Same procedures will be carried out for each visit except the rewarming treatment method.

Participation in the study will be for a period of up to 6 months, until you have visited the laboratory 3 times.

The researcher may decide to take you off this study if you are not able to cope with the cold stress, any of the procedures causes unexpected negative reactions or adverse events, or there are any problems with data acquisition or protocol adherence are detected which nullifies the value of collected data.

You can stop participating at any time. However, if you decide to stop participating in the study, we encourage you to talk to the study staff first.

If you are interested, we will provide an electronic copy of a summary report of the study once it is completed.

Risks and Discomforts
While on the study, you are at risk for certain side effects.

1) Hypothermia – The study in which you have been asked to participate involves lowering of body core (esophageal) temperature by a maximum of 2.0ºC (to a minimum of 35.0ºC). Submersion in cold (8°C) water may result in an unpleasant, cold sensation and may cause a transient increase in breathing; this will soon subside. As well, you may experience vigorous shivering, which is a natural response. However, intravenous injection of meperidine will be given by physician 10 min before exit from water. The criterion for stopping cooling is a maximal decrease in core temperature to the upper threshold of clinical/mild hypothermia – 35.0ºC. Therefore, cooling will be terminated before you become clinically hypothermic. The investigators have previously conducted

many cooling studies of this type and no complications were experienced as a result of the change in core temperature.

2) <u>Core temperature measurement</u> – You will have your own sterilized disposable esophageal thermocouple probe. The insertion of the esophageal probe may invoke some gag reflexes but for our technique has been well tolerated for 26 years. There is a slight risk of minor nose bleed. If it occurs, direct pressure will be applied to the nostrils until bleeding stops. Rarely, it is also possible that the probe could enter the wind pipe (trachea). This will not cause any damage but would be uncomfortable. This can be identified by difficulty in talking. If this occurs the probe will be removed.

3) <u>Skin numbness</u> – On rare occasions, extended exposure of toes and fingers to 8˚C water can cause short-term skin numbness on these areas. Although this rare problem will resolve itself (normally within a few days), this problem will be prevented by insulating the feet (with neoprene boots) and having the subject keep their hands out of the water (by holding on to a bar placed above the water).

4) <u>Skin burning</u> – On rare occasions, extended exposure of skin to a heating device my cause skin redness and if unchecked could develop into 1st (red skin) or 2nd (blister formation) degree burn. Because this trial involves warming for 120 minutes we will visually monitor your heated skin areas every 30 minutes for excess reddening. If this is noted, the warming trial will be terminated to prevent burning.

5) <u>Meperidine</u> – Meperidine is a central depressant often used for pain relief in hospital emergency departments or in post-surgical recovery rooms for pain relief or shivering suppression. Many people taking this medication do not experience any side effect. On rare occasions, nausea, vomiting, constipation, dry mouth, flushing, sweating, lightheadedness, dizziness, drowsiness, postural hypotension, trouble of breathing and pain/redness at the injection site may occur. If any side effect is noticed, the infusion of meperidine will be terminated. The investigators have previously conducted many cooling studies of this type and no complications were experienced. Using a standard method of administered and the dosage within the limits used in hospitals, side effects of meperidine can be minimized. To further minimize the side effects meperidine will be given slowly in small doses of 0.3 mg/kg (diluted in 2-mL aliquots) at a time. If nausea occurs, infusion will stop and the nausea will be treated (If necessary) with metoclopramide HCl (see below). If respiratory rate decreases to 8 breaths/min., no further meperidine will be given. If the respiratory rate decreases to 6 breaths/min., the effects of meperidine will be reversed by naloxone hydrochloride (Narcan) (see below). To minimize the occurrence of potential postural hypotension, the drug meperidine will be injected slowly in a diluted form and you will be advised to get up slowly when lying down. All drug administration will be performed by a qualified physician and the lab is equipped with all necessary drugs and respiratory support. The physician will be in attendance until the trail is over and you are   cleared   to   go   home. Meperidine can have significant negative effects on a fetus, therefore women of child bearing potential must be willing to:

1) take a pregnancy test (provided by the research team);
2) if sexually active, use highly effective birth control during the trial
   (*acceptable forms of contraception may include oral contraceptives ("the pill"), Norplant, intrauterine device (IUD), barrier (diaphragm or condom) plus spermicidal agent*); and
3) report to study staff if pregnancy occurs during the trial.

ADVERSE REACTIONS

The major hazards of meperidine as with other narcotic analgesics, are respiratory depression and, to a lesser degree, circulatory depression; respiratory arrest, shock, and cardiac arrest have occurred. The most frequently observed adverse reactions include lightheadedness, dizziness, sedation, nausea, vomiting, and sweating. These effects seem to be more prominent in ambulatory patients and in those who are not experiencing severe pain. In such individuals, lower doses are advisable. Some adverse reactions in ambulatory patients may be alleviated if the patient lies down.

Other adverse reactions include:

CNS: mood changes (such as euphoria, dysphoria), weakness, headache, agitation, tremor, muscle twitches, severe convulsions, uncoordinated muscle movements, transient hallucinations and disorientation, delirium or confusion, visual disturbances. Inadvertent injection about a nerve trunk may result in sensory-motor paralysis which is usually, though not always, transitory.

Gastrointestinal: dry mouth, constipation, biliary tract spasm.

Cardiovascular: flushing of the face, tachycardia, bradycardia, palpitation, hypotension (see WARNINGS), syncope and phlebitis following IV injection.

Genitourinary: urinary retention.

Allergic: pruritus, urticaria, other skin rashes, wheal and flare over the vein with intravenous injection, hypersensitivity reactions including anaphylaxis.

Other: pain at injection site; local tissue irritation and induration following subcutaneous injection, particularly when repeated; antidiuretic effect.

5) Metoclopramide HCl- Nausea and vomiting may occur due to meperidine infusion. Nausea will be treated with metoclopramide HCl. Occasionally; some patients experience some side effects of this drug. They are drowsiness, excessive tiredness, weakness, headache, dizziness and diarrhea.

6) Naloxone HCl– Common side effects of naloxone hydrochloride are flushing, dizziness, tiredness, weakness, nervousness, restlessness, irritability, body aches, diarrhea, stomach pain, nausea, fever, chills, goose bumps, sneezing, or runny nose.

7) <u>Intravenous (IV) line</u> – An IV line will be required to administer meperidine. On rare occasions you might face some discomfort while the IV line is inserted. There are few potential risks involved like infection at the injection site. This will be minimized by using a sterile IV needle. You might experience some pain, inflammation. Other risks of IV include deep vein thrombosis and air embolism. The study physician will be inserting the IV line to minimize all the risks associated with IV line.

Benefits
By participating in this study, you will be providing information to the study investigators that will show the effects of head vs. torso warming for the treatment of mild hypothermia using a human model for severe hypothermia. There may or may not be direct medical benefit to you from participating in this study. We hope the information learned from this study will benefit accidental victims of severe hypothermia in the future.

Costs
You will be responsible for your own parking while in the study. There will be no other expenses for you as a result of participation in this study.

Payment for participation
You will be given $100 per completed study visit to a maximum of $300 upon termination of your participation in this research study.

Once you start any immersion you will be paid an amount of $100 for that trial, whether you complete the trial or not.

Payment will be in the form of a cheque mailed after the last experiment with a delay of 3 to 6 weeks.

Alternatives
Not Applicable

Confidentiality
Information gathered in this research study may be published or presented in public forums, however your name and other identifying information will not be used or revealed. All study related documents will bear your initials, date of the experiment, and the name of the experiment. Despite efforts to keep your personal information confidential, absolute confidentiality cannot be guaranteed.

Health Canada and University of Manitoba Biomedical Research Ethics Board may review research-related records for quality assurance purposes.

Your health information will not be collected. Personal identifying information will be contained only on the Par-Q Forms, And Consent Forms, You will be assigned a code identifier which will be used on Basic Physical/Anthropometric Forms, Laboratory log book trial entries, and computer data files. The code sheet will be stored along with the

Par-Q Forms, and Consent Forms in a secure file cabinet. No identifying information will be kept on any computer. Only group data or coded individual data will be presented or exposed. Participants will not be identifier inn any written reports or publications. No identifying information that is collected on records will leave the study site.

All records which can be identified as yours will be kept in a locked secure area and only those persons identified will have access to these records. If any of your medical/research records need to be copied to any of the above, your name and all identifying information will be removed. No information revealing any personal information such as your name, address or telephone number will leave the University of Manitoba.
Only Dr. Giesbrecht and his graduate students will have access to the identity of subjects and their data. They will access the anthropometric data such as height, weight measurements of skinfold thickness etc. for the purpose of calculating the body surface area and % body fat. Dr. Gordon Giesbrecht will maintain the link to identifying information of all the participants in this study.

Voluntary Participation/Withdrawal From the Study
Your decision to take part in this study is voluntary. You may refuse to participate or you may withdraw from the study at any time. Your decision not to participate or to withdraw from the study will not affect your other care at this site. If anyone from the investigation team feels that it is in your best interest to withdraw you from the study, they will remove you without your consent. Please note that you will not receive further meperidine injections for shivering if you are required to exit cold water immersion prior to completing the last 10 minutes of the session.

We will tell you about any new information that may affect your health, welfare, or willingness to stay in this study.

Adverse Events or Medical Care for Injury Related to the Study
The study physician will be present in the laboratory for your entire visit to monitor for any side effects and to ensure it is safe for you to go home.

In case of any adverse event due to this study or if you are distressed in any way after leaving the laboratory, you will inform Dr Giesbrecht (business – 474-8646; residence – 269-5685; cell – 995-6599) for assistance. You may also notify the study physician (you will be given his contact information) or go to an emergency ward if necessary. All adverse events and unanticipated problems will be reported to the Bannatyne Campus Research Ethics Board as described on the following website:
http://umanitoba.ca/faculties/medicine/ethics/Adverse%20Event%20Reporting%20and%20Safety%20Information.html. Once you start any immersion you will be paid an amount of $100 for that trial, irrespective of whether you complete the trial or not.
You are not waiving any of your legal rights by signing this consent form nor releasing the investigator(s) or the sponsor(s) from their legal and professional responsibilities.

Questions

You are free to ask any questions that you may have about your treatment and your rights as a research participant. If any questions come up during or after the study or if you have a research-related injury, contact the study investigator and the study staff: Dr. Gordon Giesbrecht at 474-8646.

For questions about your rights as a research participant, you may contact The University of Manitoba Biomedical Research Ethics Board at (204) 789-3389

Do not sign this consent form unless you have had a chance to ask questions and have received satisfactory answers to all of your questions.

Statement of Consent

I have read this consent form. I have had the opportunity to discuss this research study with Dr. Gordon Giesbrecht and or his/her study staff. I have had my questions answered by them in language I understand. The risks and benefits have been explained to me. I believe that I have not been unduly influenced by any study team member to participate in the research study by any statement or implied statements. Any relationship (such as employee, student or family member) I may have with the study team has not affected my decision to participate. I understand that I will be given a copy of this consent form after signing it. I understand that my participation in this clinical trial is voluntary and that I may choose to withdraw at any time. I freely agree to participate in this research study. I understand that information regarding my personal identity will be kept confidential, but that confidentiality is not guaranteed.

By signing this consent form, I have not waived any of the legal rights that I have as a participant in a research study.

I would like to receive a summary report of this study once it is completed.
Yes ☐   No ☐
If yes, please provide your e-mail address:_____

I am willing to be contacted regarding participation in future studies of this type.
Yes ☐   No ☐
If yes, please provide your e-mail address and phone no.

E-mail address: _____

Phone no: _____

Participant signature_____ Date _____

                                                      (day/month/year)

Participant printed name: _____

I, the undersigned, have fully explained the relevant details of this research study to the participant named above and believe that the participant has understood and has knowingly given their consent

Printed Name: Dr. Gordon Giesbrecht   Date _____

Signature: _____

Role in the study: Primary Investigator

Relationship to study team members:_____[eg. teacher/professor or family member.]

APPENDIX E

Equations for calculating body density given by Durnin and Womersley.

Equations for different age groups in Males:

Age (yrs)	Density, Db (kg/l) = c-m x log sum of four skinfolds
17-19	Db (kg/l) = 1.1620 – 0.0630 x log sum of four skinfolds
20-29	Db (kg/l) = 1.1631 – 0.0632 x log sum of four skinfolds
30-39	Db (kg/l) = 1.1422 – 0.0544 x log sum of four skinfolds
40-49	Db (kg/l) = 1.1620 – 0.0700 x log sum of four skinfolds
50+	Db (kg/l) = 1.1715 – 0.0779 x log sum of four skinfolds
17-72	Db (kg/l) = 1.1765 – 0.0744 x log sum of four skinfolds

Equations for different age groups in Females:

Age (yrs)	Db (kg/l) = c-m x log sum of four skinfolds
16-19	Db (kg/l) = 1.1620 – 0.0630 x log sum of four skinfolds
20-29	Db (kg/l) = 1.1620 – 0.0630 x log sum of four skinfolds
30-39	Db (kg/l) = 1.1620 – 0.0630 x log sum of four skinfolds
40-49	Db (kg/l) = 1.1620 – 0.0630 x log sum of four skinfolds
50+	Db (kg/l) = 1.1620 – 0.0630 x log sum of four skinfolds
16-68	Db (kg/l) = 1.1620 – 0.0630 x log sum of four skinfolds