ACUTE EFFECTS OF NORMOBARIC HYPOXIA
AND COLD WATER HAND IMMERSION
ON THERMOREGULATORY RESPONSE AND COGNITIVE FUNCTION

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INTRODUCTION: Cold-induced vasodilation (CIVD) is a mechanism that protects the peripheries from cold-related injury. There is a need to elucidate mechanisms that attenuate reduced cognitive and motor performance in hypoxic environments.

PURPOSE: The purpose of the present study was to investigate the effects of cold-water hand immersion (CWI) on changes in thermoregulation, measures of CIVD, executive function, mood, and memory in normobaric hypoxia before and following submaximal exercise. METHODS: 10 apparently healthy men (23±3 years) volunteered for this study. The two experimental trials (13% O₂, 21% O₂) were counterbalanced and blinded from the participants. Following a 60-min. acclimation the experimental trials consisted of two 15-min. exposures to 5°C water of the non-dominant hand. The exposures were separated by a 30-min. bout of submaximal exercise producing the equivalent of 400 watts (W) of metabolic heat. Executive function (Stroop), total mood disturbance (TMD), memory (RMCPT), mean body temperature (MBT), oxygen saturation (SaO2), and thermal sensation (TS) of the arm were collected during the final 5 min. of each stage. CIVD was measured pre- and post-exercise during each of the cold water exposures on the nailbed of the middle finger on the non-dominant hand. RESULTS: No significant interaction or main effects of time or condition were reported for any score of executive
function ($F \leq 3.12, p \geq 0.069$) or mood ($F \leq 0.773, p \geq 0.477$). A significant time by condition interaction exists for throughput score ($F = 3.19, p = 0.039$), a measure of RMCPT. The score during CWI in the 13% $O_2$ condition was significant lower compared to the 21% $O_2$ condition ($p = 0.05$), as well as when compared to acclimation of the 13% $O_2$ condition ($p = 0.02$). However, the worsening TMD trend led to positive associations between skin temperature during CWI and TMD scores at baseline ($r = 0.753, p = 0.012$), acclimation ($r = 0.653, p = 0.041$), and CWI ($r = 0.657, p = 0.039$) in the 13% $O_2$ condition. A main effect of time is observed for MBT ($F = 42.477, p < 0.001$) in that both exercise and CIVDpost values of MBT are significantly greater than values observed at baseline, acclimation, and CIVDpre ($p < 0.001$ in all instances). A significant time (baseline, acclimation, CIVDpre, exercise, and CIVDpost) by condition (13% $O_2$, 21% $O_2$) interaction was observed for SaO$_2$ ($F = 38.4, p < 0.001$). Significant differences between conditions exist at all time points with the exception of baseline ($p < 0.001$ in all instances). Onset time was significantly later in 13% $O_2$ ($p = 0.043$) compared to the 21% $O_2$ condition at time point CIVDpre. A main effect of time was observed for amplitude temperature ($F = 20.034, p < 0.001$). Both peak time and amplitude temperature were significantly different ($p \leq 0.03$) across conditions during CIVDpost. **CONCLUSION:** CWI has no effect on executive functioning in both normoxia and normobaric hypoxia. The decreased skin temperature observed during CWI correlates to reduced mood throughout all time points in a hypoxic state. It appears that during rest in normobaric hypoxia, a cold stress test has minimal effect on MBT and the CIVD response. During exercise, reduced CIVD amplitude is associated with reduced SaO$_2$. It is clear that a
submaximal bout of cycling exercise is not the proper stimulus to acutely induce a CIVD response to the magnitude at which positive physiological adaptations occur. Further research is necessary to elucidate mechanisms to improve mood in normobaric hypoxia.
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CHAPTER I

INTRODUCTION

Environmental stress influences simple and complex cognitive tasks, motor control, core temperature and thermoregulation during exercise, and physiologic hemodynamics (Bradley, 2003; Kryskow, 2013; Kamon, 1974; Makinen, 2006; Qian, 2013). The reductions observed in cognitive performance and motor control are often transient or reversed (altered) with different stimuli. Two of these stimuli include an acute bout of exercise and exposure to extreme environmental conditions.

Reduced cognitive performance can result from an alteration in thermoregulation. Thermoregulatory balance is the product of heat production and heat loss. Four modes of heat exchange include radiation, conduction, convection, and evaporation. Cheung (2010) describes these factors and their individual and collective effect on thermoregulation in great detail. Radiation (R) is the transfer of heat via electromagnetic waves, typically involving a combination of the sun’s radiation, the ground’s reflected radiation, and the surface area of exposure.

Sometimes conduction and convection are described together, and even paired into a single term when referencing the first law of thermodynamics. This first law of thermodynamics is outlined as follows: \( S = M \pm W_k \pm R \pm C \pm K - E \) (W * m\(^{-2}\)). In this equation, “C” often refers to both conduction and convection, although a difference does exist. Conduction refers to interaction and contact with predominantly solid surfaces, like ice, while convection often refers to contact with fluids or gases like water or air.
Evaporation (E), measured in Watts * m$^{-2}$, is the only method of heat exchange classified as a wet, or evaporative pathway. While dry heat exchange is dependent on temperature gradients between surfaces, wet heat loss occurs when sweat evaporates off of the body, which depends on the gradient of water pressure between the environment and surface of the skin. (Cheung, 2010). As these methods of heat exchange take place, the resulting shift in skin and core temperature may lead to decrements or improvements in both cognitive and motor function.

This change in cognition is dependent on the magnitude of change in temperature, the means of achieving the change, as well as the type of cognitive tasks performed. For example, in 2014, Watkins observed no change in simple cognitive tasks in a sample of goal-line soccer officials, who were passively exposed to 30°C ambient temperature for 90 minutes (Watkins, 2014). However, this study neglected to assess complex cognitive tasks which examined dual tasks, working memory, and executive function. Furthermore, in this study the individual’s core temperature was passively increased over the course of 90 minutes, with a simulated half-time, 15 minutes in duration without environmental exposure. Similarly, following a 90 minute exposure to normobaric hypoxia, at a simulated altitude of 6,096 meters (10% O$_2$), complex attention, executive function, and cognitive flexibility were all significantly impaired (Turner, 2015). However, this study examined the acute and passive exposure to an environmental stress whereby the stressor was a reduction in oxygen concentration in ambient air. In another study conducted in the field by Kramer (1993), deficits in short-term memory and reaction time resulted from the short-term exposure to an altitude of 4,328 meters. This study demonstrated that these
same impairments remained following 2-weeks post-exposure for all participants (Kramer, 1993). These data indicate a need to elucidate if there is a means to improve the reduction often observed in cognition during a change that may ensue in hypoxia due to this passive environmental stress.

Hypoxia elicits physiological adaptations or changes which may distract volunteers from completing the cognitive and/or motor task that they are assigned to complete during an experimental protocol. This theory is called the distraction theory (Teichner, 1958). Specifically, a recent study conducted by Muller in 2012 indicates that cold exposure as mild as 10°C may be cold enough to distract participants from the cognitive task presented during the protocols (Muller, 2012). In this study, 10 men were exposed to 10°C air on three consecutive days. Throughout the exposure, working memory, choice reaction time, and executive function declined. These results contribute to the distraction theory, in which the participants, Muller suggested were too preoccupied with adjusting to the stressor of the cold, or other the environmental exposure, to focus on the experimental tasks presented (working memory and choice reaction time tasks).

Prior to the research conducted by Muller in 2012, Mäkinen observed in 2006 that cold acclimation and/or acclimatization results in reduced vasoconstriction, increased skin temperature and reduced thermal discomfort (Mäkinen, 2006). Limiting thermal discomfort would potentially allow participants to focus less on their surroundings and more on cognitive tasks. Despite this expected outcome, 10 days of repeated exposure to
10°C did not alter cognitive function, further demonstrating the need for a type of stimulus (perhaps exercise) to improve cognition in environmental stress.

Although an acute bout of submaximal cycling exercise has been found to improve cognition in a hypoxic state relative to baseline (Seo, 2015), physical activity is a significant predictor of the prevalence of another variable often observed during exposure to altitude, Acute Mountain Sickness (AMS). AMS is characterized by fatigue, weakness, nausea and dizziness. These symptoms can lead to vomiting and gastrointestinal issues after rapid exposure to altitude. In 2013, Beidleman found physical activity to be the third most significant factor at predicting the prevalence of AMS, behind only altitude and time spent at a given altitude (Beidleman, 2013). Thus, during hypobaric hypoxia, exercise may be a detriment or predictor of AMS, while during normobaric hypoxia it actually may alter mood state and improve cognitive function. Therefore, these stressors may vary in intensity and their countermeasures may also vary as well.

A commonly studied countermeasure to AMS is acetazolamide. This drug has been proven effective at reducing symptoms of AMS. When the medication is taken before arriving to altitude, as well as a short time after arrival, it is shown to have positive effects in symptom reduction (Forwand et al., 1968; Gray et al., 1971; Evans et al., 1976). This is further displayed by Grissom et al. (1992) after monitoring 12 climbers who ascended to a research station on Mt. McKinley (4200m) in Alaska. Of the 12 climbers who were all diagnosed with AMS upon arrival to the research station, 6 were treated with acetazolamide and 6 were not. Five of the 6 who were treated with the medication
became symptom-free, while the entire group who received placebo still displayed symptoms of AMS (Grissom et al., 1992). Another drug, dexamethasone, is used to treat cerebral edema, but has also been shown to reduce symptoms of AMS. Specifically, in a population of 6 adult males, during 48 hours of hypobaric exposure, administration of dexamethasone reduced symptoms of AMS by 63% while the group receiving the placebo had a minimal reduction of 23% (Levine et al., 1989). The administration of these drugs has been shown to improve the symptoms of AMS, which can also lead to increased focus and possibly stimulate improved cognition.

Cold water immersion (CWI) is believed to attenuate reduced cognitive performance. The phenomenon was first outlined by Lewis in 1930, and has since been emerging in research pertaining to the field of environmental physiology as a mechanism to improve performance in extreme environmental conditions. Cold water immersion causes an immediate reduction in peripheral blood flow, which is reversed following 5 to 10 minutes of exposure in 5°C water. This shift in blood flow, as indicated by fluctuations in temperature, is thought to be a protective mechanism for exposure to extreme cold, and is termed cold-induced vasodilation (CIVD) (Lewis, 1930).

Previous research within the environmental physiology laboratory at Kent State University has investigated the effects of different exercise intensities on cognitive and motor performance. The protective mechanism of cold induced vasodilation will be investigated in the present study. The expected shift in blood flow could potentially lead to an attenuated reduction in cognitive performance; a reduction that has been previously monitored in response to different modalities and intensities of exercise.
Statement of the Problem

There is a need to elucidate countermeasures that may improve cognitive and vascular responses in normobaric hypoxia for the various populations of military personnel, recreational exercisers, and athletes that are regularly exposed to these ambient environments. This study will evaluate the physiological variables in responses to acute cold exposure and submaximal exercise in normobaric hypoxia. In a state of hypoxia, the body’s physiological responses change to maintain homeostasis. The reduction in core body temperature can lead to decrements in cognition. With the vasodilation induced via cold water exposure, increased blood flow to the extremities may or may not attenuate this reduced cognitive function. Having an understanding of the specific mechanism involved with cold induced vasodilation in hypoxia (i.e., countercurrent heat exchange mechanism) will assist exercisers and military personnel in maintaining safety and attenuating the risk of cold injury when exposed, and working in similar environments.

Purpose of the Study

The first purpose of the study is to elucidate the varying effects of acute normobaric hypoxia (13% O₂), mean body temperature, and cold-induced vasodilation on acute mountain sickness (AMS), oxygen saturation, as well as thermal sensation. The second purpose of this study is to examine differences in cognitive performance tasks (ANAM4) between 2 different percentages of normobaric hypoxia (13% O₂ and 17% O₂) and normoxia (21% O₂). In addition, changes in cognitive function will be correlated to changes in heart rate, stroke volume, blood pressure, and cold-induced vasodilation.
Hypothesis

Based on previous studies, the following hypotheses were formed:

1: Mean body temperature will be significantly lower in 13% O₂ compared to 21% O₂.

2: There will be greater magnitude of CIVD response in 13% O₂ compared to 21% O₂, both pre- and post-exercise.

3: The magnitude of CIVD response in 13% O₂ condition will be significantly, positively correlated to AMS (lower score), SaO₂, and thermal sensation, but not mean body temperature.

4: The magnitude of CIVD response in 21% O₂ condition will be significantly, positively correlated to thermal sensation and mean body temperature, but not correlated to AMS or SaO₂.

5: Measures of executive function, memory and mood will be significantly impaired following acclimation in 13% O₂, relative to baseline.

6. The minimum temperature during CWI in 13% and 17% O₂ conditions will be significantly, positively correlated to TMD and cognitive performance, relative to baseline in respective conditions.

7: The 13% O₂ condition will elicit significantly lower performance measures of cognitive function, memory, and mood at all time points, compared to the 21% O₂ condition.
A state of hypoxia (low oxygen) may lead to a decrease in metabolic heat production and an increase in heat loss which results in a lower core body temperature in humans (DiPasquale, Kolkhorst, & Buono, 2015) as well as animals (Bonora & Gautier, 1989; Dupre, Romero, & Wood, 1988; Tattersall, Blank, & Wood, 2002). The decreased heat production, increased heat loss, and the resulting reduction in core body temperature can have various adverse effects on human physiologic homeostasis.

**Cognition in Hypoxia**

One of the main effects on the human physiologic response from exposure to hypoxia is impaired cognitive and motor function. When core temperature increases in humans via heat exposure or some other external stimulus such as exercise, there is a concomitant decrease in cognitive function observed (Simmons, 2008). The risk associated with assessing cognition in extreme environmental conditions is considerable.

In the cold, the cold pressor test (CPT) has been widely used in medical research with low-risk. This test activates the sympathetic nervous system and hypothalamic–pituitary–adrenal axis (Lovallo, 1975; McRae et al., 2006; Velasco, Gómez, Blanco, & Rodriguez, 1997). The CPT has been used to examine the effects of stress on memory function (Buchanan, Tranel, & Adolphs, 2006; Cahill, Gorski, & Le, 2003; Smeets, Otgaar, Candel, & Wolf, 2008).

Cognitive function plays an important role in optimizing performance and safety during work and recreational activities, even daily life. Impairment of cognitive function
and mood state have been reported at high altitude (>3500 m) and hypoxic conditions (Bahrke & Shukitt-Hale, 1993; Crow & Kelman, 1971). A number of previous studies indicated that stress is a potent modulator of cognitive function, with regard to learning and memory processes (de Kloet, Oitzl, & Joëls, 1999; Lupien & Lepage, 2001; McEwen & Sapolsky, 1995; Sandi, 2004; Warren, Castro, Rudy, & Maier, 1991). Previous studies have reported a positive effect on cognitive function when the concentration of a stress hormone, cortisol, is not very high (Andreano & Cahill, 2006; Jelici, Geraerts, Merckelbach, & Guerrieri, 2004; Steidl, Mohi-Uddin, & Anderson, 2006).

**Cognition in Cold**

Recreational, occupational and military activity may involve exposure to extreme environments. A reduction in work capacity as well as cognitive function may be observed in different environments, often dictated by severity of exposure paired with imposed demands on the body. Current fitness level can also yield different levels of cognitive maintenance and work capacity. For example, in a study comparing elite alpine skiers to age-matched controls, cognitive function and proprioceptive acuity was maintained in both normal and cold temperature (8°C) environments. No difference was observed between conditions. The control group displayed similar cognitive function in the normal thermal environment, but significantly reduced cognition and proprioceptive acuity in the cold environment (Racinais et al., 2016), reinforcing the importance of fitness level on both mental and proprioceptive acuity in extreme environmental conditions.
Exposure to cold temperatures between -20-10°C leads to decrements in memory (both simple and complex tasks). Shurtleff (1994) attempted to alleviate memory impairments which are commonly observed in the cold. By administering a supplemental dose of tyrosine (a catecholamine), brain catecholamine levels were maintained in both 8- and 16-sec delayed matching, accuracy delayed responses. By maintaining normal catecholamine levels in the brain, a significant improvement was noticed in simple working memory tasks. Despite this improvement following tyrosine supplementation, Shurtleff observed an initial reduction in matching accuracy from exposure to 4°C air with no supplementation. This is consistent with findings from Patil in 1995. Patil employed a 45-second test consisting of 20 words to assess working memory in volunteers. Following the display of 20 consecutive words within 45 seconds, volunteers were given 90 seconds to write down as many words as possible from memory. The results of this short-term memory assessment revealed that 2-3°C cold water immersion reduced the capacity for maintaining short-term memory (Patil, 1995). This finding from Patil is in contrast to a more recent study conducted by O’Brien (2007), who found no cognitive alterations following cold water immersion in temperatures between 10-15°C. Ten enlisted male soldiers volunteered for up to 8 immersions in two temperatures (10 or 15°C), two depths (waist or chest) and two walking intensities (.44 or .88 m/sec) for 1 hour. All cognitive tests (matching, reaction time, logical reasoning, serial addition/subtraction, and repeated acquisition) were performed immediately following the bout of exercise, and results demonstrated no statistical significance between trials for any of the cognitive assessments (O’Brien, 2007). In 2006, Makinen observed an increase
in response time during cold exposure (10°C), but significantly reduced accuracy and efficiency (Makinen, 2006). It is hypothesized that the distraction theory, as first described by Teichner in 1958, is largely responsible for observed reductions in cognitive function. Specifically, this theory explains the cold stimulus as an interruption for those who would otherwise be able to fully focus on cognitive and motor tasks at hand. The research related to cognitive and motor impairments resulting from cold exposure is equivocal, but, this area remains unclear and warrants investigation. Thermoregulation in the heat and hypoxia, has been on the forefront as our US Army has been deployed to Afghanistan and Iraq (which may be at high altitude), and other locations across the world. There is a need to better understand how the soldier should be prepared to ascend safely and quickly for duty.

Cognition in Heat

Similarly, heat exposure has been found to alter cognition and operative task performance. In a similar relationship to the effects of acute cold exposure, acute heat exposure can alter cognition and negatively affect task performance. In 1983, Ramsey et al. observed 17,000 safety tasks among factory workers across a 14-month period. The relationship between temperature and unsafe behavior formed a U-shaped curve. Essentially, when temperatures were outside of the safety range of 17-23°C, the rate of unsafe behavior significantly increased (Ramsey et al., 1983).

In terms of short operative tasks, cognitive performance and motor skills are not significantly changed (Berg, 2015), but further examination is necessary regarding tasks of longer duration. When evaluating short-term memory during acute environmental
exposures, the effects of heat and cold exposures are often quite different. For example, Gaoua et al. (2011) observed significant reductions in short-term memory due to heat exposure compared to cold exposure. Regular administration of cold packs to heated areas reduced the effect of hyperthermia on short-term memory only. From this study specifically, it was concluded that heat exposure led to a significant reduction in cognitive processes, and these reductions were minimized with the administration of acute localized cold exposure.

In studies without any cold exposure, the heat has been found to reduce accuracy (Simmons et al., 2008). Impaired executive function has been observed in temperatures of 50°C, with humidity ranging from 30-40% relative humidity (Sun et al., 2012; Liu et al., 2013). Regardless of the precise temperature, heat exposure ranging from 40-50°C has been found to impair both simple and complex cognitive tasks (Lenzuni et al., 2014; Racinais et al., 2008). However these findings are equivocal to Gaoua et al. in 2011, who suggested that although complex cognitive tasks were significantly reduced following a 45-minute exposure to 50°C, 50% relative humidity environment, simple cognitive tasks such as tracking, reaction time, and numerical vigilance were unchanged (Gaoua et al., 2011). Thus, further evaluating this line of inquiry is necessary in order to evaluate specific stressors in the environment that may facilitate less of a cognitive reduction. Thereby potentially facilitating or aiding in task completion and perhaps, during exposure to normobaric hypoxia one can provide an overall safer less “stressful” environment for recreational, occupational and/or military personnel.
Thermoregulation

A recent published study by DiPasquale et al. (2015) reported that core body temperature decreased by an average of 0.13°C, 0.25°C, and 0.3°C during hypoxia (14% O2, 12% O2, and 10% O2, respectively) compared to normoxia during the resting state in humans. This reduction in core body temperature has also elicited gender differences in cognition. Specifically, males have demonstrated increased cognitive perturbation compared to their female counterparts when acutely exposed to whole-body cold water immersion (Solianik, 2014).

Exposure to heat sometimes leads to alterations in thermoregulatory response (skin temperature, core temperature and oxygen saturation). In a hyperoxic environment, when observing elite cycling athletes in 2 different environments, 21°C or 33°C, Zinner et al. utilized both a normoxic condition (21% O₂) as well as a hyperoxic condition (40% O₂) to observe differences in thermoregulatory response. Following 30 minutes of submaximal cycling in each of these conditions, no difference between core temperature, skin temperature, or muscle activity was observed. In this study, the hyperoxic environment did not alter thermoregulation (Zinner et al., 2016).

A large factor influencing the body’s ability to acclimate to extreme environments is age. Specifically, older men typically exhibit more variable thermoregulatory responses than younger men (Inoue et al., 1992). When exposed to two different cold-air environments (17°C and 12°C), a group of older men (61-70 years old) exhibited significantly larger variations in rectal temperature, skin temperature and metabolic heat production compared to a group of younger men (20-25 years old) matched for body fat.
and body surface area. As we know as discussed by Glickman-Weiss et al. (1991) there are a number of factors that influence thermoregulation; age, gender, race, ethnicity, training status, body composition, and some even suggest surface-area-mass ratio. Thus, the present investigation will control for all of the above variables and only measure Caucasian males of average fitness.

**Cold Water Exposure**

A popular mode of altering cognitive function, performance, safety, and recovery following strenuous exercise involves whole-body water immersion. This method, along with many others, has limited research either supporting or opposing the efficacy. For example, whole-body water immersion has been reported to have no effect in aiding muscle recovery following exercise in adults (Costello, 2015), but has been found to improve recovery time in thermoneutral environments following high intensity bouts of exercise (Kruger, 2015). Thus, the impact of cold exposure on muscle recovery, and potentially cognitive function may be further impacted by the type and intensity of exercise, along with factors relating to previous training status and physical conditioning.

Previous studies indicate that hand immersion for 1 minute into cold water (0-2°C) facilitated eye-blink conditioning and spatial navigation performance in healthy men (Duncko, Cornwell, Cui, Merikangas, & Grillon, 2007). However, another study evaluated that hand immersion for 1 minute into cold water (0-2°C) improved reaction time and impaired accuracy in working memory (Duncko, Johnson, Merikangas, & Grillon, 2009).
The phenomenon of hand or limb immersion is intended to induce reactive hyperemia. This increased blood flow in the extremity can lead to improved cognitive performance. In 1991, Ducharme et al. observed that cold-induced vasodilation (CIVD) may not be a phenomenon related solely to the vasculature of the immersed limb. By implanting a small sensor into the axis of the forearm, researchers concluded that following a 3-hour cold water immersion in 15°C water, the observed cycling muscle tissue fluctuations in temperature indicate that CIVD may occur in the muscle as well as the vasculature of the exposed limb (Ducharme et al., 1991). The fluctuations in muscle blood flow could potentially lead to correlations between blood flow and motor performance.

Muller et al. (2012) evaluated working memory, choice-reaction time and executive functioning during and following exposure to 10°C air. In this research protocol significant impairments were observed during this exposure, as well as up to 60 minutes following the exposure, during the rewarming period. The study concluded that participants may not only be at risk of injury during cold exposure, but this risk of injury exists for up to 60 minutes following removal of the stimulus (Muller, 2012), suggesting that another stimulus may be required to aid in a safe recovery.

In a study conducted by Aquiar et al. in 2016, 4 weeks of cold water immersion following high intensity interval training did not improve exercise performance (Aquiar et al., 2016). Exercise performance was measured with a 15 kilometer cycling time trial pre- and post-intervention. No differences between the cold water immersion group and control group was found.
When cold water immersion is used prior to exercise, it appears that physiological improvements and performance enhancements are observed during and after exercise. Nine trained male runners completed 5-kilometer running trials on a treadmill. Each runner underwent 3 separate trials; pre-exercise cold water immersion, intermittent facial spray during exercise, and control. Only the pre-cooling group observed lowered rectal temperature both pre- and throughout exercise. Both of the cooling strategies improved performance compared to control (Stevens et al., 2016). It is clear that cooling in some capacity is beneficial for athletic performance. Whether or not this benefit translates to enhanced occupational and military activity is not fully clear, thus rendering further investigation in this area.

**Cold-Induced Vasodilation**

Exposure to high altitude greater than 2800 meters is also associated with local cold injury (Harirchi et al., 2005; Hashmi et al., 1998). At high altitude, there can also be environmental factors (cold, wind and sometimes heat) and behavioral factors (low physical activity and energy intake) that can also influence the risk for cold injury (Keramidas, Kölegård, Mekjavic, & Eiken, 2014). A number of studies reported that hypoxia attenuated a cold-induced vasodilation (CIVD) response (Daanen & Van Ruiten, 2000; Mathew, Purkayastha, Selvamurthy, & Malhotra, 1977; Purkayastha et al., 1999; Takeoka et al., 1993). Even though this cold-induced vasodilation has been reported, not all studies have found similar findings. The primary reason for equivocal findings is due to the methodological differences between studies, the stressors and the populations
examined, as well as the technological advances that have driven the research methodology.

Lewis, in 1930, reported that CIVD can occur in temperatures below 15°C. For this reason, temperatures ranging from 0-15°C have primarily been used. Water temperature, immersion site and depth, and other standardization factors have not been held consistent in recent years, leading to discrepancies in the literature. Typically, whole-hand immersion into cold water is used to measure CIVD (Bernie et al., 2012).

Keramidas et al. (2014) discovered that the acute exposure to normobaric hypoxia did not alter the effects of cold-induced vasodilation in the upper extremities of males. This suggests that further research is needed to classify conditions which facilitate limb warming, as well as limb blood flow during acute exposure to cold in normobaric hypoxia. The vasodilation resulting from an acute exposure, predominantly observed in the extremities, is somewhat of a protective mechanism. The vasodilation found in the limbs acts to widen the blood vessels, decreasing vascular resistance, and increasing the delivery of oxygen to the localized limb. The increase of oxygen delivery is due to the increased blood flow, which occurs in in an effort to attenuate physiological injury such as hypothermia.

Although no standardized measurement for CIVD exists, the recent literature has assessed the following parameters; minimum finger temperature, maximum finger temperature, the difference between minimum and maximum finger temperature, the time from immersion to the minimum finger temperature (also termed the onset of CIVD), and lastly the time between minimum and maximum finger temperature (also termed peak
time). Although previous studies have utilized fingers on the dominant hand, in the present study, the middle and ring fingers of each participant’s non-dominant hand will be used for assessment, allowing each participant to use their dominant hand to conduct the cognitive testing.

**Effects of Exercise**

An acute bout of exercise between low to moderate intensities has been proposed to prevent or restore the cognitive dysfunction in hypoxia (Ando et al., 2013; Seo et al., 2015). However, performing exercise is not always available during occupational and military activities. Thus, finding countermeasures to improve or restore cognitive dysfunction would likely promote performance and safety in hypoxia. For example, the implementation of different methods post-exercise can facilitate physiological recovery, making it possible to continue exercise and/or service in occupational or military environments. Although both cold and heat have been demonstrated to facilitate muscle repair and recovery after exercise or strenuous activity, cold exposure research suggests that cold may be more beneficial to heat exposure in terms of pain reduction and muscle recovery (Petrofsky, 2015).

**Exercise and Cold**

Thermoregulatory responses to exercise are often observed in a variety of environmental conditions. Specifically, mechanisms for maintaining thermoregulatory responses during exercise in the cold need to be discussed, both in terms of practicality as well as maintaining safety. Castellani et al. (2001) examined the effect of pre-exhaustive exercise on thermoregulatory response during exercise in the cold. Specifically, a 4-hour
exhaustive exercise protocol was performed continuously for 7 days, while a group of controls did not perform this exercise. Following the exhaustive exercise bout, participants walked in the cold for 45 minutes. Rectal temperature was found to be lower, and the change in rectal temperature was greater in the experimental group. Following this 7-day study, the warmer skin temperature observed in the experimental group indicates that pre-exertional fatigue places subjects at higher risk for reduced thermoregulatory control and hypothermia (Castellani et al., 2001).

Toner and McArdle (1988) reported that the increased O₂ consumption in the cold was directly related to increased shivering, suggesting the peripheral vasoconstriction may not be sufficient in maintaining core temperature. This implies that the cold leads to a significantly reduced capacity to maintain submaximal exercise intensities, largely in part due to the body’s inability to maintain core temperature and O₂ consumption. Galloway and Maughan (1997) were the first to conduct an experiment to volitional fatigue at a set submaximal exercise intensity (70% VO₂max) in 4 different ambient air temperatures; 4, 11, 21 and 31°C. The time to exhaustion was greatest at 11°C, and shortest at 31°C. Research later conducted by Parkin et al. in 1999 demonstrated that time to exhaustion was greatest at 3°C. Among three different temperatures, 3, 20 and 40°C, the high temperature condition (40°C) elicited the greatest core temperature, and no difference was observed between the normal temperature (20°C) and cold temperature (3°C) condition. This increase in core temperature alters the endocrine and substrate utilization, and can alter exercise performance as well. Thus, it
appears that the maximal performance of sustained moderate activity according to these protocols may be in the range of 3-11°C.

**Exercise and Heat**

There are many factors to that alter temperature homeostasis during exercise in the heat, some of which can be altered or controlled by acclimation. When exercising for 9-12 consecutive days in 40°C, acclimation is observed by improving endurance, lowering rate of increased heart rate, as well as increased sweating (Nielsen et al., 1993) and perhaps altering blood volume long term. Eight participants were asked to exercise at 60% of maximum VO₂ to volitional fatigue. Over the 9-12 consecutive days, time to fatigue increased from 48-80 minutes, and exhaustion was most closely correlated to a rise in core temperature to 39.7°C.

The question of hydration status is certainly relevant as it pertains to exercise and thermoregulatory response in the heat. Often times, sweating rate will exceed the intake of water, leading to hypohydration, which can increase heat storage due to the reduced sweating rate and skin blood flow. Very few studies have looked at the effect of hydration status on thermoregulation and performance in the heat. A study by Blyth and Burt in 1961 examined differences in time to exhaustion of 18 male participants exercising in an ambient temperature of 120°F, in three states of hydration; normal water balance, dehydration, and superhydration. Researchers observed no difference in time to exhaustion between superhydration and normal water balance conditions. Only the dehydrated condition led participants to significantly reduced performance and time to exhaustion (Blyth & Burth, 1961).
Similarly, other research has suggested that a rate limiting factor of endurance performance in the heat is directly related to high body temperature (Cheung and McLellan, 1998; Nielsen et al., 1993). On the contrary, Gonzalez-Alonso et al. have observed time to exhaustion in hot environments to be inversely related to initial temperature and directly related to the rate of heat storage, as elucidated by a water-perfused jacket (Gonzalez-Alonso et al., 1999).

**Exercise and Hypoxia**

Acute Mountain Sickness (AMS) is a condition characterized by dizziness, lightheadedness and fatigue, often experienced as the result of rapid ascension to altitude or exposure to hypoxic (reduced oxygen) environments. By using the Lake Louise Score (LLS) for diagnosis of AMS, researchers can diagnose AMS on the following: presence of a headache plus the presence of at least one other symptom (Gastrointestinal, Fatigue and/or weakness, Dizziness/lightheadedness, or Difficulty sleeping). Each of these symptoms ranges in potential value from 0-3. A combined score of 3-5 is diagnosed as mild AMS, while a combined score of 6 or greater is diagnosed as severe AMS (Roach et al., 1993). Repeated exposures to altitude or normobaric hypoxia will induce acclimatization and possibly reduce the symptoms of AMS. For example, Fulco et al. observed acclimatization in a hypobaric hypoxic condition in the form of increased oxygen saturation (SaO₂) during sleep. This increased SaO₂ is expected to have influenced the lessening symptoms of AMS, although it had no influence on exercise performance (Fulco et al., 2011).
A study conducted by the U.S. Army Research Institute of Environmental Medicine in Natick (USARIEM), MA observed differences in work capacity and rating of perceived exertion (RPE) in maximal and submaximal exercise performed at sea level and after rapid ascension to altitude (4300m). Participants’ VO\textsubscript{2} max was, on average, 27% less in high altitude compared to sea level. This reduction has since been used in normobaric hypoxic studies as a correction factor for calculating submaximal values to be used in normobaric hypoxia after testing maximal oxygen consumption in a normoxic environment (Seo et al., 2015). Average power output was found to be 189 watts at sea level, and 140 watts at high altitude (4300m). Perceived exertion was largely influenced by central factors such as ventilation rate and cardiac output as opposed to localized muscular fatigue from the Monark ergometer (Young et al., 1982).

Another study conducted by the USARIEM examined the effect of altitude on simple and complex motor tasks. The simple motor task used in the study involved disassembly and assembly of an M-16 rifle, and complex task involved rifle marksmanship. The primary finding of this study was that simple psychomotor performance was not affected by exposure to altitudes ranging from 2500-4300m, while complex psychomotor performance was degraded at 4300m and was significantly correlated to feelings of sleepiness. The decrement in complex task performance was in the form of reduced speed in order to maintain accuracy. Symptoms of AMS increased only from sea level to 2500m, and was not associated with the decreased performance observed at 4300m (Kryskow et al., 2013).
Exercise and Water

Exercising in cold water, as opposed to cold air, presents a plethora of physiologic changes to maintain homeostasis. First and foremost, water is 25 times more conductive than air, which leads the body to lose heat at a rate of 3-5 times faster than in ambient air of the same temperature (Smith and Hames, 1962). Water directly in contact with the skin acts as an insulator layer, if it is not circulated. But when the water or subject’s body begin to move through the water, the insulator mechanism is reduced, as water is drawn away via convection (Toner and McArdle, 1988). Thus when one stirs the water it reduces the body’s ability to be insulated, leading to an increase in heat loss, as opposed to maintaining a static position in the water as is the case with a water circulator.

Often times, the proper stimulus is not applied during or after exercise to facilitate the subjects in the re-cooling process, or to stimulate cognitive function and/or maintain motor control. Hand cooling is a technique that has been used following exercise to aid in maintaining homeostasis, and ultimately cognitive function and core temperature homeostasis. Adams et al. (2016) observed a greater cooling rate following exercise in the heat when immersing a hand into cool water. The exercise consisted of 2, 60-minute bouts of submaximal cycling exercise. In the population of volunteers acclimated to the heat, no difference in hand cooling was observed. The population of volunteers who were not acclimated to the heat demonstrated significantly faster re-cooling following exercise when immersing a limb into cold water (Adams et al., 2016).

With the large body of literature pertaining to both hot and cold exposure, it is certainly a relevant question to ask; how are cognitive function and vasculature
parameters affected following exposure? In this case, the present study will examine acute cold exposure in a normobaric hypoxic environment. The magnitude of the cold induced vasodilation (CIVD) response will be observed, and correlated to cardiovascular and cognitive variables between conditions.
CHAPTER III

METHODOLOGY

Participants

Ten healthy college-age males (18-30 years old) will be recruited for participation in this study. All participants will be recreationally active and free of any cardiovascular, pulmonary, and metabolic disease. Participants will also be free of previously experienced frostbite, loss of consciousness at high altitude, Raynaud’s disease, and sickle cell anemia. No subjects will be included if they were currently using any medication that would affect circulation and other cardiovascular variables. A medical history questionnaire will be administered during the initial session, followed by a graded maximal exercise protocol, which will allow researchers to identify possible limitations for inclusion in the study. Orientation with the subsequent three experimental conditions will consist of familiarization with all cognitive assessments as well as the protocol followed in the hypoxic chamber. The current study was reviewed and approved by the Institutional Review Board at Kent State University in Kent, Ohio.

Procedures

On the day of the initial session, participants will report to the laboratory for consent and medical history paperwork, anthropometric assessments, familiarization, and a graded maximal exercise test. The pre-experimental visit to the laboratory will begin with consent and a medical history questionnaire. Following participant consent, researchers will review medical history to ensure the participant is free of all exclusion criteria as previously defined. Resting heart rate (RHR), Oxygen Saturation (SaO2) and
blood pressure (BP) will be recorded. Height, weight, and body fat (via 7-site skinfold analysis) will be recorded before the participant can begin familiarization. Following all anthropometric data, participants will be familiarized with the hypoxic chamber and protocol to be carried out over the course of the next three sessions. Before the VO\textsubscript{2} max test, participants will be familiarized with the cognitive assessments in order to control for a learning effect on the day of testing. Subjects then perform a graded maximal exercise test on a cycle ergometer through stages of increasing resistance. The protocol will begin at 20 watts, and increase by 25 watts every minute until volitional fatigue (Amann, 2004). VO\textsubscript{2} will be measured with a TrueOne 2400 metabolic cart (ParvoMedics, Sandy, Utah) and heart rate will be assessed with a Polar heart rate monitor (Polar RS800 CX, Polar Electro Oy, Kempele, Finland). Participants will be required to maintain a cadence between 60-80 revolutions per minute through increasing intensity, and the test will end when participants can no longer maintain this cadence. The VO\textsubscript{2} max test will allow researchers to calculate a relative intensity for each participant to produce 400 watts of metabolic heat.

The equation is as follows; $M \text{ (W/m2)} = \text{VO}_2 \times \frac{[(\text{RER}-0.7)/0.3*\text{ec}) + (1-\text{RER}/0.3*\text{ef})]/60$, where ec is the caloric equivalent of a liter of oxygen when carbohydrates are oxidized (21.1kj) and ef is the caloric equivalent of a liter of oxygen when fat is oxidized (19.6 kj) (Cena & Clark, 1981).
Following the maximal exercise test, participants will be encouraged to rest before performing a second familiarization trial with the cognitive assessments.

On days of experimental testing, participants will arrive to the laboratory, instructed to abstain from a meal for 3 hours, as well as strenuous exercise and alcohol for the previous 24 hours. The 3 hour fast is to stabilize substrate utilization and reduce the risk of subjects becoming nauseous during exercise in the hypoxic chamber. Each of the experimental conditions will be separated by a minimum of 48 hours to ensure full recovery of the participants. The three experimental conditions, 21%, 17% and 13% Oxygen, will be randomized, counterbalanced, and blinded to the participant. Time points of assessment include measurement of the following variables: VO₂, SaO₂, heart rate (HR), stroke volume (SV), BP, RPE, thermal sensation (TS), mean weighed skin temperature (T_{sk}), core temperature (T_{c}), total mood disturbance (TMD), cognition, and acute mountain sickness (AMS). Following an initial baseline measurement outside of the chamber, participants will be moved into the chamber for a 60 minute acclimation period. During this 60 minutes, all variables with the exception of TMD and cognition will be reported at 15 minutes, 30 minutes, and 45 minutes. The 60 minute assessment time point includes all measurements. After the 60 minute acclimation to the hypoxic chamber, participants will then immerse their non-dominant hand into 5°C water for 15 minutes. All variables will be assessed again in the final 5 minutes of this cold water exposure. Cognitive assessments will be performed with the participant’s dominant hand. A 30 minute exercise protocol at a predetermined submaximal intensity will be performed by the participant in order to produce 400 watts of metabolic heat. This intensity is
approximately 50-60% VO\textsubscript{2} max. All measurements will be taken again during the final 5 minutes of exercise. Following the exercise, subjects will be taken back to the cold water bath, and their hand will be immersed for another 15 minutes. All measurements will be collected during the final 5 minutes of cold water exposure.

**Measurement and Instrumentation**

Subjects will be equipped with ICG in order to assess heat rate, stroke volume, and brachial artery blood pressure via BioZ-Dx impedance cardiography system. The BioZ-Dx measures the change in impedance using a high-frequency (60-kHz minimum, low-amplitude (4.0-mA rms maximum) alternating electrical current (Cardio dynamics, San Diego, CA). Rectal temperature will be measured by a thermistor inserted 13 cm past the anal sphincter (ITP010-11, Nikkiso - Therm Co., Ltd., Japan). Skin and hand temperature will be measured using thermocouples (ITP082-25, Nikkiso - Therm Co., Ltd., Japan). To determine metabolic rate, oxygen consumption and carbon dioxide production, we will be using indirect open circuit spirometry (True Max 2400, Parvo Medics, Sandy, UT). This system includes a mouthpiece with two one-way valves and an expiratory gas air hose.

A perception scale of thermal sensation, thermal comfort, Rating of Perceived Exertion, and Acute Mountain Sickness (AMS) will be assessed at predetermined time points. AMS is a condition characterized by dizziness, lightheadedness and fatigue, often experienced as the result of rapid ascension to altitude or exposure to hypoxic (reduced oxygen) environments. By using the Lake Louise Score (LLS) for diagnosis of AMS, researchers can diagnose AMS on the following: presence of a headache plus the
presence of at least one other symptom (Gastrointestinal, Fatigue and/or weakness, Dizziness/lightheadedness, or Difficulty sleeping). Each of these symptoms ranges in potential value from 0-3. A combined score of 3-5 is diagnosed as mild AMS, while a combined score of 6 or greater is diagnosed as severe AMS (Roach et al., 1993).

Cognitive function tests will be assessed with Automated Neuropsychological Assessment Metrics-4th Edition (ANAM4), a computerized cognitive test battery first developed by the Department of Defense with subtests designed to assess a variety of cognitive domains. Specific subtests utilized for this study include the Running Memory Continuous Performance Task (RMCPT), Stroop Color Word Test (SCWT), and Mood State.

RMCPT assesses attention, concentration, and working memory. Single characters are presented on the display in rapid sequence. The user presses designated buttons to indicate if the displayed character matches or does not match the preceding character.

SCWT assesses processing speed, selective attention, interference, and executive functioning. The SCWT consists of three 45-second tests. The first test involves pressing a corresponding key for each word (1 for red, 2 for green, 3 for blue). The next test requires pressing the corresponding key based on color. A series of colors including red, green or blue are presented on the screen. In the final test, a series of words (red, green, blue) are presented in a color that does not match the name of the color displayed by the word. The participants are required to press the response key assigned to color.
Mood state test is designed to assess seven categories of mood; anger, anxiety, depression, fatigue, happiness, restlessness, and vigor. Specifically, through the use of a laptop, 42 words expressing various emotions were presented to the subject and they are simply instructed to choose a number between 0 and 6; 0 representing “Not at all” and 6 representing “Very Much” for each emotion presented. These emotions are associated with the seven categories of mood state. The calculation for total mood disturbance (TMD) involves subtracting all of the positive scores from the negative scores. Thus, a higher score indicates a greater negative mood, while a lower score indicates a greater positive mood.

**Statistical Analysis**

Data will be presented as mean and standard deviation for each condition. Analysis of variance will be used to assess differences in dependent variables (VO2, HR, Tre, Tsk, Cog, TMD, CIVD, all ICG variables, SaO2, TS, TC, RPE, and AMS) between the three conditions (13%, 17%, and 21% Oxygen). Correlation analysis will be used to assess the relationship between two variables, and the change in these correlations between conditions will be reported. All analyses will be performed using the SPSS statistical software package (SPSS v.23.0, IBM, Somers, NY).
CHAPTER IV

THE EFFECTS OF NORMOBARIC HYPOXIA ON COLD-INDUCED VASODILATION, MEAN BODY TEMPERATURE, AND OXYGEN SATURATION BEFORE AND AFTER A BOUT OF SUBMAXIMAL EXERCISE

Abstract

Cold-induced vasodilation (CIVD) is a mechanism that protects the peripheries from cold-related injury. PURPOSE: The purpose of the current study was to investigate the effects of normobaric hypoxia on the thermoregulatory and CIVD response before and following submaximal exercise. METHODS: 10 apparently healthy men (23±3 years) volunteered for two experimental trials and differing O$_2$ saturations. These two trials (13% O$_2$, 21% O$_2$) were counterbalanced and blinded from the participant. Following a 60-min. acclimation the experimental trials consisted of two 15-min. exposures to 5°C water of the non-dominant hand. The exposures were separated by a 30-min. bout of submaximal exercise producing the equivalent of 400 watts (W) of metabolic heat. Mean body temperature (MBT), oxygen saturation (SaO2), and thermal sensation (TS) of the arm were collected during the final 5 min. of each stage. CIVD was measured pre- and post-exercise during each of the cold water exposures on the nailbed of the middle finger on the non-dominant hand. RESULTS: No significant difference across time or condition exists for MBT. ANOVA revealed a significant time (baseline, acclimation, CIVDpre, exercise, and CIVDpost) by condition (13% O$_2$, 21% O$_2$) interaction for SaO$_2$ ($F = 38.4, p < 0.001$). Significant differences ($p < 0.001$) between conditions existed at all time-points with the exception of baseline ($p = 1.0$). No significant difference across time or condition was found for overall TS. A main effect of
time was observed for amplitude temperature \((F = 20.034, p < 0.001)\), which was significantly greater \((p < 0.001)\) at CIVDpost compared to CIVDpre (CIVDpost: 1.13°C; CIVDpre: 0.28°C). In the 13% O\(_2\) condition, the reduction in SaO\(_2\) during exercise (81.5%) was positively associated \((r = 0.656, p = 0.039)\) with amplitude temperature at CIVDpost (0.69°C), which was significantly greater \((p < 0.05)\) compared to CIVDpre (0.14°C). CONCLUSION: It appears that during rest in normobaric hypoxia, a cold stress test has minimal effect on MBT and the CIVD response. During exercise, reduced CIVD amplitude is associated with reduced SaO\(_2\). It is clear that a submaximal bout of cycling exercise is not the proper stimulus to acutely induce a CIVD response to the magnitude at which positive physiological adaptations occur.

**Introduction**

Mean body temperature (MBT) and thermoregulation are both known to change from environmental stress (Bradley, 2003; Kryskow, 2013; Kamon, 1974; Makinen, 2006; Qian, 2013). The four modes of heat exchange; radiation, conduction, convection, and evaporation; have both individual and collective effects on human thermoregulation (Cheung, 2010). As these methods of heat exchange interact, there is a resulting shift in skin, core, and mean body temperature. Furthermore, a state of normobaric hypoxia leads to decreased metabolic heat production, as well as an increase in heat loss (Dipasquale, 2015). This results in reduced core and mean body temperature, which can lead to various adverse physiological side effects.

The mechanism of Cold-Induced Vasodilation (CIVD) is hypothesized to serve as a protective mechanism to these potentially adverse side effects of reduced core and
mean body temperature. This mechanism is induced via cold-water exposure of the hand (Bernie, 2012), and the shift in temperature measured with skin thermistors indicates any oscillations in blood flow to the extremity. CIVD acts to widen the blood vessels, decreasing vascular resistance, and increasing the delivery of oxygen to the exposed limb. CIVD can occur in temperatures as warm as 15°C, but is predominantly observed in temperatures ranging from 0-15°C (Lewis, 1930).

While some studies have reported that hypoxia attenuates the CIVD response (Keramidas, 2014; Daanen, 2000; Mathew, 1977; Purkayastha, 1999; Takeoka, 1993), the standardization of CIVD measurement is still lacking, which leads to the need to explore a standardized method, as well as conditions within research that will facilitate limb warming and increase limb blood flow. The need to elucidate countermeasures that may improve vascular responses in normobaric hypoxia is relevant to a variety of populations; EMT’s, recreational exercisers, athletes, and military personnel who may be regularly exposed to these ambient environments. For that reason, the purpose of the present study is twofold; first, we will investigate the effects of normobaric hypoxia on the thermoregulatory and CIVD responses before and after a bout of submaximal exercise; second, we intend to assess the association between CIVD amplitude and thermal sensation (TS), SaO₂, and MBT. We hypothesize that MBT will be significantly lower in normobaric hypoxia compared to normoxia. We also hypothesize a significant positive correlation between CIVD amplitude and thermal sensation (TS), oxygen saturation (SaO₂), and MBT.
Methods

Participants

10 apparently healthy Caucasian men (23 ± 3 years) volunteered for this study. All participants were recreationally active and free of any cardiovascular, pulmonary, or metabolic disease. No participants had reported previously experiencing frostbite. Similarly, no participant had Raynaud’s disease, sickle-cell anemia, or any other condition or medication that affected circulation or other cardiovascular variables. All participants reported they had never experienced loss of consciousness at altitude. A medical history questionnaire assessed these responses, and the study was reviewed and approved by the Institutional Review Board at Kent State University in Kent, Ohio.

Pre-Experimental Trial

All participants reported to the Environmental Physiology Laboratory at Kent State University for the pre-experimental session. This initial session began with consent and a medical history questionnaire. Following consent, researchers reviewed the medical history questionnaire in detail to ensure the participant was free of all exclusion criteria and fully aware of the outlined protocol for the subsequent experimental sessions. Resting heart rate (RHR), oxygen saturation (SaO₂), and blood pressure (BP) were recorded after the participant was rested in a seated position for at least 10 minutes. Following this resting period, the participant’s body fat was assessed via the 7-site skinfold method. Two measurements were recorded at each of the following sites; subscapular, chest, midaxillary (side), suprailium, abdomen, triceps, and thigh. If the two measurements deviated greater than 2mm, a third measurement was taken. The average
for each skin fold site was recorded. Height and weight were recorded, and BMI was calculated as weight divided by the squared height (kg/m²).

Following baseline anthropometrics, the participant was familiarized with the normobaric hypoxic chamber, as well as the protocol to be carried out over the course of the subsequent sessions. After familiarization with the chamber, participants performed a maximal VO₂ test on a cycle ergometer. The protocol for this test is outlined by Amann in 2004. Participants begin the test at an intensity of 20 Watts (W). Each stage of the test is 1 minute long, and involves increasing the intensity by 25 watts to volitional fatigue. Participants are required to maintain a cadence between 60-80 rpm throughout the maximal protocol. Oxygen consumption (VO₂) was measured with a TrueOne 2400 metabolic cart (Parvo Medics, Sandy, Utah), while heart rate was constantly recorded with a Polar heart rate monitor (Polar RS800 CS, Polar Electro Oy, Kempele, Finland). When the pedaling cadence was no longer maintained, or the subject stopped cycling, the test was ended, and maximal VO₂ was recorded along with maximum heart rate and final power output in Watts. This allowed researchers to calculate a relative intensity for each participant in order to produce 400W of metabolic heat. This intensity was kept constant between the two experimental trials (13% O₂ and 21% O₂). The equation for calculating relative intensity is as follows: 

\[ M \text{ (W/m²)} = \text{VO}_2 \times \left( \frac{(\text{RER}-0.7/0.3*\text{ec}) + (1-\text{RER}/0.3*\text{ef})}{60} \right) \],

where \( \text{ec} \) is the caloric equivalent of a liter of oxygen when carbohydrates are oxidized (21.1kJ) and \( \text{ef} \) is the caloric equivalent of a liter of oxygen when fat is oxidized (19.6 kJ) (Cena & Clark, 1981).
Experimental Trials

On days of experimental testing, participants arrived to the laboratory having abstained from a meal for 3 hours, as well as strenuous exercise and alcohol for the previous 24 hours. The 3-hour fast was in place to control for substrate utilization during the session and reduce the risk of nausea. Each of the experimental sessions was separated by a minimum of 48 hours to ensure full recovery. The two conditions, 13% O$_2$ and 21% O$_2$, were randomized and blinded to the participants. Upon arrive to the laboratory, participants were outfitted with skin thermistors to measure skin temperature, core temperature, and mean body temperature (MBT). MBT was calculated using a method established by Burton in 1934; $MBT = 0.64(T_{core}) + 0.36(T_{skin})$, where $T_{core} =$ core temperature and $T_{skin} =$ average skin temperature, calculated from the 5 site temperatures; calf, thigh, triceps, chest, forearm, and rectal temperature (Burton, 1934).

To measure CIVD, a skin thermistor was placed laterally on the non-dominant middle finger nailbed. This thermistor was placed on the non-dominant middle finger so the participants would have free range of motion with their dominant hand, the hand they were using to complete the cognitive testing. Time points of assessment include measurements of the following variables: VO$_2$, SaO$_2$, HR, BP, Thermal Sensation (TS), mean skin temperature ($T_{skin}$), and core temperature ($T_{core}$).

Following an initial baseline measurement outside of the chamber, participants moved into the chamber for a 60-min. acclimation period. During the final 5 minutes of the acclimation, all variables were assessed a second time. Following acclimation, participants immersed the non-dominant hand into 5°C water for 15 min. All variables
were assessed a third time during the final 5 min. of this stage. All CIVD variables were recorded during this cold-water immersion. After the 15 min. of cold-water immersion, participants cycled on a cycle ergometer for 30 min. in order to produce 400 W of metabolic heat. Throughout the 30 min. of cycling, participants were required to maintain a cadence between 60-80 rpm. The cycling intensity was between 50-60% VO\(_2\) max. Measurements were taken again during the final 5 min. of cycling. Following the submaximal bout of exercise, participants immersed their non-dominant hand back into 5°C water for another 15 min. The final data collection time point occurred in the final 5 min. of this cold-water immersion. CIVD variables were recorded during this second cold-water immersion as well.

**Measurement and Instrumentation**

Arrival to the laboratory on days of experimental trials began with the application of all skin thermistors (ITP082-25, Nikkiso – Therm Co., Ltd., Japan). Body sites for thermistor application include middle finger, calf, thigh, triceps, chest, and forearm. The middle finger, forearm, and triceps were all placed on the non-dominant side of the body, while calf, thigh and chest were placed on the dominant side of the body. The placement of thermistors was based on each participant’s dominant side of the body, which was used for cognitive testing. A rectal thermistor was inserted 13 cm past the anal sphincter to measure core temperature (ITP010-11, Nikkiso – Therm Co., Ltd., Japan). To assess metabolic rate, \(O_2\) consumption and \(CO_2\) production, we used indirect open circuit spirometry (True Max 2400, Parvo Medics, Sandy, UT). The system included a mouthpiece, two Hans Rudolph one-way valves, and an expiratory gas air hose.
Heart rate (HR) was constantly recorded with a Polar heart rate monitor (Polar RS800 CS, Polar Electro Oy, Kempele, Finland). HR and BP were also monitored through the use of a BioZ-Dx, which measures changes in impedance using a high-frequency (60-kHz minimum, low-amplitude, 4.0-mA rms maximum) alternating electrical current, as well as automated BP analysis (Cardio dynamics, San Diego, CA). SaO$_2$ was assessed through the use of a manual pulse oximeter placed onto the ring finger, which detect oxygenated hemoglobin through the absorption of specific wavelengths emitted by the oximeter.

CIVD was analyzed via recorded skin temperature on the non-dominant middle finger nailbed. Five separate parameters of CIVD were recorded. Minimum finger temperature ($T_{fmin}$) was recorded as the lowest temperature reached during the 15 min. immersion. Maximum finger temperature ($T_{fmax}$) was recorded as the highest temperature reached after $T_{fmin}$ during the 15 min. immersion. The temperature difference between $T_{fmin}$ and $T_{fmax}$ was reported as $T_{amp}$. Onset time of CIVD ($\Delta t_{onset}$) was defined as the time from immersion to $T_{fmin}$. Peak time ($\Delta t_{peak}$) was defined as the time from $T_{fmin}$ to $T_{fmax}$ (Kim, 2013). Each of these variables were recorded during the pre-exercise cold-water immersion and the post-exercise cold-water immersion.

TS was reported via a thermal perception scale introduced by Glickman-Weiss et al. (1994). Participants reported scores of 0 if they did not feel cold at all, and higher scores if they did feel some level of cold. Scores ranged from 0 (nothing at all) to 10 (unbearably cold) (Glickman-Weiss et al., 1994).
Statistical Analysis

A two-way repeated measures analysis of variance (ANOVA) was used to assess differences in MBT, SaO$_2$, TS, and all CIVD variables (onset and peak time, minimum temperature, and amplitude) across the two experimental conditions (13% O$_2$, 21% O$_2$) and the following time points: baseline, acclimation (60 minutes of passive environmental exposure), CIVDpre, exercise, and CIVDpost. Post-hoc analysis on any significant main or interaction effects were performed via paired-samples t-tests. Pearson’s correlation analyses were performed to assess the relationships between CIVD amplitude (T$_{amp}$) both pre- and post-exercise and SaO$_2$ pre-, during, and post-exercise. Further correlation analyses were performed to assess the relationship between CIVD amplitude (T$_{amp}$) and MBT recorded at baseline and both pre- and post-exercise.

Results

Anthropometrics

The participants’ age, BMI, percentage of body fat, resting heart rate, and VO$_2$ max are included in Table 2.

Mean Body Temperature (MBT)

Results of the analysis of variance reveal no significant main effect or interaction ($F \leq 2.261, p \geq 0.082$) (Table 3).

Oxygen Saturation (SaO$_2$)

There was a significant time by condition interaction ($F = 38.4, p < 0.001$) for SaO$_2$ (Table 4, Figure 1). Post-hoc analysis revealed significant differences across conditions at all time points ($p < 0.001$ in all instances), with the exception of baseline ($p$
A main effect of time \((F = 35.48, p < 0.001)\) and condition \((F = 115.61, p < 0.001)\) was observed. The main effect of time is further explained by the significant differences relative to baseline in the 13% \(O_2\) condition observed at all time points \((p < 0.001)\). \(SaO_2\) was significantly lower in the 13% \(O_2\) condition compared to acclimation \((p = 0.014)\), CIVDpre \((p = 0.01)\), and CIVDpost \((p = 0.06)\). The main effect of condition is further explained by the significant differences observed at all time points across conditions \((p < 0.001)\), with the exception of baseline \((p = 1.0)\).

**Thermal Sensation (TS)**

Results of the analysis of variance reveal no significant main effect or interaction \((F \leq 0.184, p \geq 0.678)\) (Table 5).

**Cold-Induced Vasodilation (CIVD)**

No significant interaction \((F = 0.237, p = 0.633)\) or main effect of time \((F = 0.642, p = 0.433)\) was observed for onset time (Table 6).

A main effect of time was observed for amplitude temperature \((F = 20.034, p < 0.001)\) (Figure 2). Post-hoc analysis revealed significantly greater amplitude temperature between CIVDpost compared to CIVDpre \((p < 0.001)\) (Table 7).

Minimum temperature elicited a main effect of time \((F = 34.662, p < 0.001)\) (Figure 3), in that minimum temperature was significantly greater \((p < 0.001)\) across conditions at CIVDpost compared to CIVDpre (Table 7).

In the 13% \(O_2\) condition, the \(SaO_2\) value during exercise was positively associated \((r = 0.656, p = 0.039)\) with the amplitude temperature of CIVDpost following exercise (Figure 4).
In the 21% O\textsubscript{2} condition, MBT recorded after acclimation was found to be negatively associated ($r = -0.697$, $p = 0.025$) with the onset time of CIVDpost following exercise (Figure 5).

The 21% O\textsubscript{2} condition elicited further positive associations between baseline MBT and the amplitude temperature of CIVDpre ($r = 0.761$, $p = 0.011$) (Figure 6), as well baseline MBT and the amplitude temperature of CIVDpost ($r = 0.66$, $p = 0.038$) (Figure 7).

**Discussion**

The sample of participants in the present study was extremely homogenous. Although average BMI was in the range of overweight, it is likely due to the high amount of lean mass. The American College of Sports Medicine’s (ACSM) Guidelines for Exercise Testing and Prescription explains that a BMI over 25 kg/m\textsuperscript{2} puts an individual at increased risk of Type 2 diabetes mellitus, dyslipidemia, hypertension, and certain cancers (Lewis, 2009). However, the average body fat percentage for participants in this study was 10.67%. This puts the average body fat % in the present study into the category of excellent for males ranging in age from 20-29 years old (ACSM, 2014). The average VO\textsubscript{2} max of 44.11 places this group of participants into the average-above average category for males within this age range (YMCA, 2000). Overall, the participants included in this pool of subjects were at least average fitness level and body composition. In addition, the sample of individuals to control for thermoregulation were recruited and reported to be all Caucasian (Farnell, 2008; Glickman-Weiss, 1991).
The consistent MBT over time was somewhat unexpected. Previous research has shown that body temperature is reduced upon entering a state of hypoxia (Dipasquale, 2015). Researchers expected notable differences between conditions. This did not occur in the present study. There was no difference across conditions in MBT values recorded at any time points. The increased thermoregulatory response that appeared during exercise remained elevated during CIVDpost. This is consistent with the previous research of Gagge et al. in 1967, who found that increasing body temperature from heat exposure or some other stimulus may alter thermoregulatory response within 10-30 minutes, while reducing body temperature over the course of 2 hours still might not effect thermoregulatory control (Gagge, 1967). The submaximal exercise protocol in the present study appears to be a significant stimulus to induce alterations in thermoregulatory control.

The significant difference in SaO$_2$ observed between conditions at all time points with the exception of baseline was not expected. SaO$_2$ has previously been found to increase during both intermittent and chronic hypoxic exercise (Beidleman, 1997; Bender, 1989; Schoene, 1984; Vogul, 1974; Katayama, 2001). However, in the 13% O$_2$ condition, SaO$_2$ dropped during exercise.

Significantly greater amplitude was observed across conditions at CIVDpre and CIVDpost. No other temperature differences were observed between conditions for CIVD variables. Previous research shows that no difference between acclimated and non-acclimated persons exists in terms of minimum or maximum finger temperature, although each is reduced at altitude (Daanen, 2004). The CIVD response was trending towards a
later onset in the 13% O₂ condition. Peak time in the 13% O₂ condition was trending towards an earlier occurrence compared to the 21% O₂ condition. Each of these trends were observed at time point CIVDpost. Previous research had indicated this trend in both onset time and peak time of CIVD in hypoxia (O’Brien, 2015).

It appears that the beginning MBT recorded at baseline in 21% O₂ significantly affects both timing of the onset of CIVD as well as amplitude. Specifically, baseline MBT was found to be significantly correlated to amplitude temperature of CIVDpre and CIVDpost, well as the onset time of CIVDpost. This is in agreement with previous findings, which indicate the CIVD response is initiated and more noticeable by increasing body temperature (Flouris, 2008). However, in the present study, no difference between groups was observed for MBT, rejecting one of the initial hypotheses, which predicted a significant difference would exist across conditions.

Furthermore, the SaO₂ value during exercise in the 13% O₂ condition was positively associated with amplitude following exercise. This aligns with the researcher’s hypothesis that a positive association would exist between SaO₂ and CIVD amplitude, further suggesting that the magnitude of change in amplitude temperature during normobaric hypoxic exposure can induce a positive response in SaO₂, and potentially other physiological responses.

The present study does present experimental limitations. First, the subject population was limited to recreational active males. No females were included in the pool of participants, making the results less generalizable to large groups of firefighters, military, or first responders. In addition, the present study also focused solely on
recreational active, average-above average, male participants. The results are therefore not generalizable to sedentary or extremely active populations. The sample size appears to be small, and researchers believe more significant interactions would have been noted with a larger homogenous sample. Furthermore, a field study would be more directly applicable to a military or first responder scenario, as opposed to a normobaric hypoxic chamber. Despite the limitations, the researchers believe maintaining a consistent work level in both conditions strengthened the study.

**Conclusion**

These data demonstrate the importance of inducing a CIVD response in hypoxic environments. Despite similar effects of other vasoconstrictive substances such as caffeine during the initial minutes of CWI (Daniels, 1998; Poehlman, 1985), the subsequent paradoxical vasodilation that occurs from CWI may lead to increased blood flow and improved executive function. In addition, this increased blood flow serves as a protective mechanism against cold injury. Inducing the CIVD response may serve to elicit greater improvements in cognitive function when compared to other vasoconstrictive stimuli.

The current exercise stimulus led to significantly greater amplitude temperature following exercise during the cold-water immersion. This is a positive physiological parameter which was found to be significantly associated with baseline MBT. We intend to extend our research with hopes of finding a proper stimulus to induce the CIVD response in a hypoxic environment prior to exercise. This response could lead to improved physiological parameter such as SaO₂, and this improvement could extend
throughout exercise. With the significant correlation of CIVD time and temperature variables to the baseline MBT in 21% O₂ and acclimation MBT in 13% O₂, the researchers conclude that a high emphasis should be placed on ensuring homeostatic MBT prior to ascension to altitude, in order to remain in the safest condition during exercise or while performing various military duties. Further research is necessary to elucidate mechanisms that induce a positive thermoregulatory response in normobaric hypoxia both pre- and post-exercise.
CHAPTER V
THE EFFECTS OF COLD-WATER HAND IMMERSION ON EXECUTIVE FUNCTION, MOOD, AND MEMORY IN NORMOBARIC HYPOXIA

Abstract

PURPOSE: The purpose of the present study was to investigate the effects of cold-water hand immersion (CWI) on changes in executive function, mood, and memory in normobaric hypoxia. METHODS: 10 apparently healthy men (23±3 years) volunteered for this study. The two experimental trials (13% O_2, 21% O_2) were counterbalanced and blinded from the participant. Following a 60-min. acclimation the experimental trials consisted of a 15-min. exposure to 5°C water of the non-dominant hand. Executive function (Stroop), total mood disturbance (TMD), and memory (RMCPT) were recorded during the final 8 min. of each baseline, acclimation, and cold-water hand immersion.

RESULTS: Condition (13% O_2, 21% O_2) by time (baseline, acclimation, CWI) ANOVA’s revealed no significant interaction or main effects of time or condition for any score of executive function ($F \leq 3.12, p \geq 0.069$) or mood ($F \leq 0.773, p \geq 0.477$). A significant time by condition interaction exists for throughput score ($F = 3.19, p = 0.039$), a measure of RMCPT. The score during CWI in the 13% O_2 condition was significantly lower compared to the 21% O_2 condition ($p = 0.05$), as well as when compared to acclimation of the 13% O_2 condition ($p = 0.02$). The worsening TMD trend led to positive associations between skin temperature during CWI and TMD scores at baseline ($r = 0.753, p = 0.012$), acclimation ($r = 0.653, p = 0.041$), and CWI ($r = 0.657, p = 0.039$) in the 13% O_2 condition. In the 21% O_2 condition, TMD at acclimation was significantly associated with skin temperature during CWI ($r = 0.716, p = 0.02$). CONCLUSION:
Despite no effect on executive function in both normoxia and normobaric hypoxia, it appears CWI impairs measures of memory. The decreased skin temperature observed during CWI correlates to reduced mood throughout all time points in a hypoxic state. Further research is necessary to elucidate mechanisms to improve mood in normobaric hypoxia.

**Introduction**

Cognitive function and mood are often altered during exposure to normobaric hypoxia (Simmons, 2008). Reductions in cognitive performance often occur due to a change in core temperature and thermoregulatory response (Watkins, 2014; Turner, 2015), and this change is largely dependent on the magnitude of change in temperature. Reductions in memory and executive function occur as the result of both normobaric hypoxic exposure, as well as cold-water immersion (CWI). In 1958, Teichner outlined the distraction theory, which states the ambient environment may be stressful enough to distract participants from tasks at hand, whether simple or complex (Teichner, 1958). Muller et al. observed significant reductions in cognitive function. These reductions were attributed to the distraction theory, in that the participants were too preoccupied with the increasing physiological stress due to the changing environment to focus on tasks of working memory and choice reaction (Muller, 2012).

A field study conducted by Kramer on Mount Denali in Alaska observed cognitive impairments following exposure to 4,328 meters of altitude. The participants performed multiple cognitive and motor tasks before, during, and after the ascent to altitude. Not only did the climbers display a worse performance than a matched control
group, but these same impairments remained relevant following 2-weeks post-exposure for all participants (Kramer, 1993). The fact that these impairments remained significantly relevant two weeks following the climb leads researchers to believe exposure to a hypoxic climate may lead to long-term deficits in memory and cognitive function.

Recent literature has suggested that acclimatization to cold temperatures may result in reduced vasoconstriction and reduced thermal discomfort (Mäkinen, 2006). The concept of limiting thermal discomfort allows participants to focus less on their surrounding environmental stress, and more on cognitive and motor tasks. Another stimulus that has been found to reduce thermal discomfort is exercise. In short, finding a stimulus to reduce the effects of the distraction theory, as originally defined by Teichner in 1958, can attenuate the cognitive reduction observed in a hypoxic state.

While a number of studies have indicated high altitude (>3500m) impairs cognitive function and mood state (Bahrke, 1993; Crow, 1971), there has been emerging evidence that suggests different forms of stressors may modulate cognitive function, specifically with regard to learning and memory (de Kloet, 1999; Lupien, 2001; McEwen, 1995; Sandi, 2004; Warren, 1991). In 2015, Seo et al. observed that submaximal cycle ergometry (40% and 60% VO₂ max) served to significantly reduce the attenuation in cognition and memory observed in normobaric hypoxia. Specifically, at each exercise intensity, throughput score of the Running Memory Continuous Performance Task (RMCPT) and total mood disturbance (TMD) were significantly improved relative to baseline scores (Seo, 2015).
Another stimulus that has been found to reduce the attenuation of cognitive function and mood in hypoxia is CWI. CWI has been found to facilitate eye-blink conditioning and spatial navigation performance in healthy men after only 1 minute of hand exposure (Duncko, 2007). However, impaired reaction time has been observed during CWI in temperatures between 0-2°C (Duncko, 2009). CWI has also been shown to lower core temperature (Stevens, 2016; DiPasquale, 2015), which can potentially lead to improved athletic and cognitive performance in different ambient environments. For that reason, the purpose of the present study is twofold; first, we plan to investigate the effects of normobaric hypoxia and CWI on executive function, mood, and memory; second, we intend to assess the association between mean skin temperature and measures of cognitive function, mood and memory. We hypothesize that executive function, memory, and mood will be significantly reduced at baseline in 13% O₂ compared to 21% O₂. We also hypothesized that a reduced skin temperature during CWI would be significantly associated with reduced scores for executive function, mood, and memory.

Methods

Participants

10 apparently healthy Caucasian men (23 ± 3 years) volunteered for this study. All participants were recreationally active and free of any cardiovascular, pulmonary, or metabolic disease. No participants had reported previously experiencing frostbite. Similarly, no participant had Raynaud’s disease, sickle-cell anemia, or any other condition or medication that affected circulation or other cardiovascular variables. All participants reported they had never experienced loss of consciousness at altitude.
medical history questionnaire assessed these responses, and the study was reviewed and approved by the Institutional Review Board at Kent State University in Kent, Ohio.

Pre-Experimental Trial

All participants reported to the Environmental Physiology Laboratory at Kent State for the pre-experimental session. This initial session began with consent and a medical history questionnaire. Following consent, researchers reviewed the medical history questionnaire in detail to ensure the participant was free of all exclusion criteria and fully aware of the outlined protocol for the subsequent experimental sessions. Resting heart rate (RHR), oxygen saturation (SaO$_2$), and blood pressure (BP) were recorded after the participant was rested in a seated position for at least 10 minutes. Following this resting period, the participant’s body fat was assessed via the 7-site skinfold method. Two measurements were recorded at each of the following sites; subscapular, chest, midaxillary (side), suprailium, abdomen, triceps, and thigh. If the two measurements deviated greater than 2mm, a third measurement was taken. The average for each skin fold site was recorded. Height and weight were recorded, and BMI was calculated as weight divided by the squared height (kg/m$^2$).

Following baseline anthropometrics, the participant was familiarized with the normobaric hypoxic chamber, as well as the protocol to be carried out over the course of the subsequent sessions. After familiarization with the chamber, all participants were familiarized with the cognitive and mood assessments in order to control for a learning effect on the day of testing. The cognitive tests included a Running Memory Continuous
Performance Task (RMCPT), Stroop test, and finally an analysis of total mood disturbance (TMD).

**Experimental Trials**

On days of experimental testing, participants arrived to the laboratory having abstained from a meal for 3 hours, as well as strenuous exercise and alcohol for the previous 24 hours. The 3-hour fast was in place to control for substrate utilization during the session and reduce the risk of nausea. Each of the experimental sessions was separated by a minimum of 48 hours to ensure full recovery. The two conditions, 13% O₂ and 21% O₂, were randomized and blinded to the participants. Upon arrive to the laboratory, participants were outfitted with skin thermistors to measure skin temperature at various sites, as well as core temperature. Skin temperature was recorded on the non-dominant middle finger during the CWI.

Following an initial baseline measurement outside of the chamber, participants moved into the chamber for a 60-min. acclimation period. During the final 5 minutes of the acclimation, all variables were assessed a second time. Following acclimation, participants immersed the non-dominant hand into 5°C water for 15 min. All variables were assessed a third time during the final 5 min. of this stage.

**Measurement and Instrumentation**

Arrival to the laboratory on days of experimental trials began with the application of the skin thermistor to the non-dominant middle finger (ITP082-25, Nikkiso – Therm Co., Ltd., Japan). To assess metabolic rate, O₂ consumption and CO₂ production, we used indirect open circuit spirometry (True Max 2400, Parvo Medics, Sandy, UT). The system
included a mouthpiece, two Hans Rudolph one-way valves, and an expiratory gas air hose.

Heart rate (HR) was constantly recorded with a Polar heart rate monitor (Polar RS800 CS, Polar Electro Oy, Kempele, Finland). HR and BP were also monitored through the use of a BioZ-Dx, which measures changes in impedance using a high-frequency (60-kHz minimum, low-amplitude, 4.0-mA rms maximum) alternating electrical current, as well as automated BP analysis (Cardio dynamics, San Diego, CA).

Cognitive function tests will be assessed with Automated Neuropsychological Assessment Metrics-4th Edition (ANAM4), a computerized cognitive test battery first developed by the Department of Defense with subtests designed to assess a variety of cognitive domains. Specific subtests utilized for this study include the Running Memory Continuous Performance Task (RMCPT), Stroop Color Word Test (SCWT), and Mood State.

RMCPT assesses attention, concentration, and working memory. Single characters are presented on the display in rapid sequence. The user presses designated buttons to indicate if the displayed character matches or does not match the preceding character.

SCWT assesses processing speed, selective attention, interference, and executive functioning. The SCWT consists of three 45-second tests. The first test involves pressing a corresponding key for each word (1 for red, 2 for green, 3 for blue). The next test requires pressing the corresponding key based on color. A series of colors including red, green or blue are presented on the screen. In the final test, a series of words (red, green,
blue) are presented in a color that does not match the name of the color displayed by the word. The participants are required to press the response key assigned to color.

Mood state test is designed to assess seven categories of mood: anger, anxiety, depression, fatigue, happiness, restlessness, and vigor. Specifically, through the use of a laptop, 42 words expressing various emotions were presented to the subject and they are simply instructed to choose a number between 0 and 6; 0 representing “Not at all” and 6 representing “Very Much” for each emotion presented. These emotions are associated with the seven categories of mood state. The calculation for total mood disturbance (TMD) involves subtracting all of the positive scores from the negative scores. Thus, a higher score indicates a greater negative mood, while a lower score indicates a greater positive mood.

**Statistical Analysis**

A two-way repeated measures analysis of variance (ANOVA) was used to assess differences in measures of executive function, mood and memory across the two experimental conditions (13% O₂, 21% O₂) and the following time points: baseline, acclimation (60 minutes of passive environmental exposure), and CWI. Post-hoc analyses on any significant main or interaction effects were performed via paired-samples t-tests. Pearson’s correlation analyses were performed to assess the relationships between finger temperature during CWI and TMD scores collected at all time points.
Results

Anthropometrics

The participants’ age, BMI, percentage of body fat, resting heart rate, and VO₂ max are included in Table 2.

Stroop Test

No significant interaction or main effect of time or condition was observed for Color score \( (F \leq 3.12, p \geq 0.069) \) (Table 8). No significant interaction or main effect of time or condition was observed for Word score \( (F \leq 2.878, p \geq 0.124) \) (Table 9). No significant interaction or main effect of time or condition was observed for Word-Color score \( (F \leq 1.425, p \geq 0.263) \) (Table 10). No significant interaction or main effect of time or condition was observed for Interference score \( (F \leq 2.14, p \geq 0.147) \) (Table 11).

Running Memory Continuous Performance Task (RMCPT)

A significant condition by time interaction \( (F = 3.19, p = 0.039) \) exists for throughput score of RMCPT (Figure 8). Post-hoc analysis revealed a significant difference across conditions \( (p = 0.05) \) during CWI, in that the 21% O₂ condition elicited a greater throughput score than the 13% O₂ condition. No other significant differences across conditions were found at any other time points \( (p \geq 0.105) \). In the 21% O₂ condition, a significantly greater score at acclimation compared to baseline was observed \( (p = 0.041) \), while no other differences across time were observed \( (p \geq 0.318) \). In the 13% O₂ condition, a significantly lower score at CWI compared to acclimation was observed \( (p = 0.02) \), while no other differences across time were observed \( (p \geq 0.158) \) (Table 12). No significant interaction or main effect of time or condition was observed for percentage
of correct responses ($F \leq 3.162, p \geq 0.08$) (Table 13). No significant interaction or main effect of time or condition was observed for mean response time ($F \leq 3.092, p \geq 0.07$) (Table 14).

**Total Mood Disturbance (TMD)**

No significant interaction or main effect of time or condition was observed for TMD ($F \leq 0.773, p \geq 0.477$) (Table 15).

**Cold-Water Immersion (CWI)**

Temperature at all time points is reported in Table 16.

The 13% $O_2$ condition elicited significant positive associations between skin temperature during CWI and TMD scores at baseline ($r = 0.753, p = 0.012$) (Figure 9), acclimation ($r = 0.653, p = 0.041$) (Figure 10), and CWI ($r = 0.657, p = 0.039$) (Figure 11).

The 21% $O_2$ condition led to further positive associations. In this condition, TMD score at acclimation was found to be significantly associated to skin temperature during CWI ($r = 0.716, p = 0.02$) (Figure 12).

**Discussion**

The sample of participants in the present study was extremely homogenous. Although average BMI was in the range of overweight, it is likely due to the high amount of lean mass. The American College of Sports Medicine’s (ACSM) Guidelines for Exercise Testing and Prescription explains that a BMI over 25 kg/m$^2$ puts an individual at increased risk of Type 2 diabetes mellitus, dyslipidemia, hypertension, and certain cancers (Lewis, 2009). However, the average body fat percentage for participants in this
study was 10.67%. This puts the average body fat % in the present study into the category of excellent for males ranging in age from 20-29 years old (ACSM, 2014). The average VO_{2} max of 44.11 places this group of participants into the average-above average category for males within this age range (YMCA, 2000). Overall, the participants included in this pool of subjects were at least average fitness level and body composition.

No interaction or main effect of time or condition was observed for any measure of the Stroop test, which tests executive function. This conflicts with previous research, which demonstrates improved cognitive performance in cold environments (Mäkinen, 2006). The cold environment used in the present study may, in fact, have been too cold for participants to improve executive function. Another possibility of this unlikely finding could relate to the length of exposure, which may have been too long, ultimately passing the opportune window of time for improved executive functioning.

Researchers hypothesized differences in memory to be observed at baseline. The present differences conflict with this hypothesis. A significant condition by time interaction for throughput score was further explained by observed differences between conditions during CWI. In fact, throughput score was significantly less during the normobaric hypoxic condition during CWI, but not at any other time points. The score at CWI in the 13% O_{2} condition was significantly lower compared to acclimation, indicating the CWI led to further attenuation of memory. No other variables associated with memory led to main effects or significant interactions. This finding is not in agreement with previous research by Seo et al. in 2015, who found significant
improvements relative to baseline in short term memory during exercise in normobaric hypoxia (Seo, 2015).

The temperature during CWI was found to be significantly correlated to TMD at baseline, acclimation, and during CWI. Although not significant, the increasingly worse scores for TMD were correlated to average finger temperature during CWI. This aligns with the second hypothesis of the researchers, displaying that reduced skin temperature is associated with a reduced mood. This is further supported by previous research conducted by Lieberman et al., showing cold exposure expectedly decreases overall mood (Lieberman, 2009).

The present study does have some experimental limitations that need to be addressed. First, the subject population was limited to recreational active males. No females were included in the pool of participants, making the results less generalizable to large groups of firefighters, military, or first responders. The present study also focused solely on recreational active, average-above average, Caucasian male participants. The results are therefore not generalizable to sedentary or extremely active populations. Further research using various ethnic and racial groups is necessary to truly quantify thermoregulatory differences that may exist.

**Conclusion**

To our knowledge, this is one of the first studies to quantify change in mood from CWI during normobaric hypoxia. The practical importance of this study extends to emergency personnel, firefighters, and members of the military who serve in extreme environments. Further research is necessary to elucidate mechanisms that may prevent
the attenuation of memory and mood in a hypoxic environment. The importance of improving mood can extend to improved simple and complex psychomotor tasks (Kryskow, 2013) in various military, first responder, and firefighter populations. Specifically, the reduced finger temperature during CWI was significantly correlated to a reduction in mood at all time points. A reduced memory or mood can lead to worsened physical performance, ultimately placing military personnel in danger. Furthermore, despite the positive effect of normobaric hypoxia on executive function during CWI, more research is rendered to find mechanisms to improve memory and mood in normobaric hypoxia.
CHAPTER VI

SUMMARY

These data demonstrate the importance of inducing a CIVD response in hypoxic environments. With elevated fluctuations in CIVD amplitude comes improved SaO\textsubscript{2}. This improved oxygen saturation may lead to improved mood and physical performance. Despite increased amplitude being significantly associated with improved SaO\textsubscript{2}, the reduction in skin temperature led to worsened mood, and this relationship was also a significant association.

Improved CIVD time and temperature variables was significantly associated with baseline MBT in normoxia, and acclimation MBT in normobaric hypoxia. For that reason, the researchers conclude that a high emphasis should be placed on ensuring homeostatic MBT prior to ascension to altitude, in order to remain in the safest condition during exercise or while performing various military duties.

The practical importance of this study extends to emergency personnel, firefighters, and members of the military who serve in extreme environments. Improved executive function, memory, and mood at altitude may lead to increased safety and likelihood to carry out military and first-responder tasks.

In conclusion, more research is necessary to find mechanisms to improve memory, executive functioning, and mood in normobaric hypoxia. Similar mechanisms do exist to induce a vasoconstrictive response. However, the CIVD response, which leads to a paradoxical vasodilation, seems to serve as a protective mechanism against the cold
via increased blood flow. Researchers suggest that inducing a positive thermoregulatory response in hypoxia may lead to such improvements.

Finally, finding the proper stimulus to elicit this improved thermoregulatory response is crucial, leading to the need to expand the current body of literature related to thermoregulation, CIVD, and both cognitive and motor performance tasks in normobaric hypoxia.

*Figure 1* Interaction between condition and time displayed for SaO$_2$. A significant time by condition interaction displayed for SaO$_2$ ($F = 38.4, p < 0.001$), computed using alpha = 0.05.
Figure 2 Main effect of time displayed for amplitude temperature. A main effect of time for amplitude ($F = 20.034, p < 0.001$), computed using alpha = 0.05.

Figure 3 Main effect of time displayed for minimum temperature. A main effect of time for minimum temperature ($F = 34.662, p < 0.001$), computed using alpha = 0.05.
Figure 4 SaO₂ and Amp. Correlation in 13% O₂ condition between SaO₂ during exercise and amplitude temperature at CIVDpost ($r = 0.656$, $p = 0.039$), computed using alpha = 0.05.
**Figure 5** MBT and Onset Time. Correlation in 21% O$_2$ condition between MBT following acclimation and onset time at CIVDpost ($r = -0.697$, $p = 0.025$), computed using alpha = 0.05.

![MBT and CIVDpre Amp](image)

**Figure 6** MBT and CIVDpre Amp. Correlation in 21% O$_2$ condition between baseline MBT and amplitude at CIVDpre ($r = 0.761$, $p = 0.011$), computed using alpha = 0.05.
Figure 7 MBT and CIVDpost Amp. Correlation in 21% O₂ condition between baseline MBT and amplitude at CIVDpost (r = 0.66, p = 0.038), computed using alpha = 0.05.

Figure 8 Throughput score: RMCPT. Significant time by condition interaction (F = 3.19, p = 0.039) displayed for Throughput score, computed using alpha = 0.05.
Figure 9 CWI Skin Temperature and baseline TMD. Correlation in 13% O\textsubscript{2} condition between CWI skin temp and baseline TMD ($r = 0.753$, $p = 0.012$), computed using alpha = 0.05.

Figure 10 CWI Skin Temperature and acclimation TMD. Correlation in 13% O\textsubscript{2} condition between CWI skin temp and acclimation TMD ($r = 0.653$, $p = 0.041$), computed using alpha = 0.05.
Figure 11 CWI Skin Temperature and CWI TMD. Correlation in 13% O₂ condition between CWI skin temp and CWI TMD ($r = 0.657$, $p = 0.039$), computed using alpha = 0.05.

Figure 12 CWI Skin Temperature and acclimation TMD. Correlation in 21% O₂ condition between CWI skin temp and CWI TMD ($r = 0.716$, $p = 0.02$), computed using alpha = 0.05.
Table 1 *Pre-Experimental and Experimental Trial Design*

<table>
<thead>
<tr>
<th>Pre-Experimental Trial</th>
<th>Consent, Prescreening, Familiarize, VO2max</th>
</tr>
</thead>
<tbody>
<tr>
<td>Session 1 (13% O2) (3600m) (12000 ft)</td>
<td>Baseline 60min Acclimation CIVD 15min 30min Exercise CIVD 15min</td>
</tr>
<tr>
<td>Session 2 (17% O2) (1500m) (5000 ft)</td>
<td>↑ ↑ ↑ ↑ ↑ ↑ ↑</td>
</tr>
<tr>
<td>Session 3 (21% O2) (0m) (0 ft)</td>
<td></td>
</tr>
</tbody>
</table>

VO2, HR, Tre, Tsk, Cog, TMD, and all ICG variables measured continuously throughout each session. ↑ Denotes collection of SaO2, TS, TC, RPE, and AMS, along with recording of all continuously measured variables.

Table 2 *Baseline participant anthropometrics*

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>23.4 ± 2.88</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.86 ± 2.7</td>
</tr>
<tr>
<td>Body Fat (%)</td>
<td>10.67 ± 5.98</td>
</tr>
<tr>
<td>RHR (bpm)</td>
<td>62.8 ± 8.39</td>
</tr>
<tr>
<td>VO2 Max (ml/kg/min)</td>
<td>44.11 ± 7.11</td>
</tr>
</tbody>
</table>

Data are mean ± SD

Table 3 *MBT*

<table>
<thead>
<tr>
<th>Condition</th>
<th>Baseline</th>
<th>Acclimation</th>
<th>CIVDpre</th>
<th>Exercise</th>
<th>CIVDpost</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>35.18 ± .33</td>
<td>35.07 ± .36</td>
<td>35.12 ± .37</td>
<td>35.84 ± .40</td>
<td>35.78 ± .22</td>
</tr>
<tr>
<td>2</td>
<td>35.40 ± .35</td>
<td>35.25 ± .41</td>
<td>35.21 ± .37</td>
<td>35.8 ± .52</td>
<td>35.78 ± .34</td>
</tr>
<tr>
<td>Total</td>
<td>35.29 ± .34</td>
<td>35.16 ± .39</td>
<td>35.17 ± .37</td>
<td>35.82 ± .46</td>
<td>35.78 ± .28</td>
</tr>
</tbody>
</table>

Data are mean ± SD. Values are percentages. Condition 1 = 21% O2. Condition 2 = 13% O2. Values are reported in °C.
Table 4 $SaO_2$

<table>
<thead>
<tr>
<th>Condition</th>
<th>Baseline</th>
<th>Acclimation</th>
<th>CIVDpre</th>
<th>Exercise</th>
<th>CIVDpost</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>97.7 ± .68</td>
<td>97.8 ± .63*</td>
<td>98.2 ± .63*</td>
<td>97.3 ± 1.16*</td>
<td>97.8 ± .63*</td>
</tr>
<tr>
<td>2</td>
<td>97.7 ± 1.16</td>
<td>86.0 ± 4.69</td>
<td>85.8 ± 4.42</td>
<td>81.5 ± 4.5</td>
<td>85.9 ± 4.75</td>
</tr>
<tr>
<td>Total</td>
<td>97.7 ± .92</td>
<td>91.9 ± 2.66</td>
<td>92 ± 2.53</td>
<td>89.4 ± 2.83</td>
<td>91.85 ± 2.69</td>
</tr>
</tbody>
</table>

Data are mean ± SD. Values are percentages. Condition 1 = 21% $O_2$. Condition 2 = 13% $O_2$.

*p < 0.001, significantly different compared to condition 2 (13% $O_2$)

Table 5 $TS$

<table>
<thead>
<tr>
<th>Condition</th>
<th>Baseline</th>
<th>Acclimation</th>
<th>CIVDpre</th>
<th>Exercise</th>
<th>CIVDpost</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.0 ± .00</td>
<td>0.0 ± .00</td>
<td>0.3 ± .35</td>
<td>0.0 ± .00</td>
<td>0.3 ± .42</td>
</tr>
<tr>
<td>2</td>
<td>0.0 ± .00</td>
<td>0.0 ± .00</td>
<td>0.35 ± .34</td>
<td>0.0 ± .00</td>
<td>0.3 ± .35</td>
</tr>
<tr>
<td>Total</td>
<td>0.0 ± .00</td>
<td>0.0 ± .00</td>
<td>0.33 ± .35</td>
<td>0.0 ± .00</td>
<td>0.3 ± .39</td>
</tr>
</tbody>
</table>

Data are mean ± SD. Values are percentages. Condition 1 = 21% $O_2$. Condition 2 = 13% $O_2$.

Table 6 CIVDpre and CIVDpost time values

<table>
<thead>
<tr>
<th>Condition</th>
<th>Onset</th>
<th>Peak</th>
</tr>
</thead>
<tbody>
<tr>
<td>CIVDpre</td>
<td>1</td>
<td>541.3 ± 187.1</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>686 ± 220.84</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>613.65 ± 212.6</td>
</tr>
<tr>
<td>CIVDpost</td>
<td>1</td>
<td>520.8 ± 211.61</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>602.2 ± 221.27</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>561.5 ± 214.82</td>
</tr>
</tbody>
</table>

Data are mean ± SD. Condition 1 = 21% $O_2$. Condition 2 = 13% $O_2$. Values are reported in seconds.
Table 7 CIVDpre and CIVDpost temperature values

<table>
<thead>
<tr>
<th>Condition</th>
<th>Amplitude</th>
<th>Min</th>
</tr>
</thead>
<tbody>
<tr>
<td>CIVDpre</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>0.43 ± .63</td>
<td>10.03 ± .45</td>
</tr>
<tr>
<td>2</td>
<td>0.14 ± .22</td>
<td>9.99 ± .24</td>
</tr>
<tr>
<td>Total</td>
<td>0.28 ± .48</td>
<td>10.01 ± .35</td>
</tr>
<tr>
<td>CIVDpost</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>1.56 ± 1.43</td>
<td>10.37 ± .54</td>
</tr>
<tr>
<td>2</td>
<td>0.69 ± .69</td>
<td>10.33 ± .50</td>
</tr>
<tr>
<td>Total</td>
<td>1.13 ± 1.18*</td>
<td>10.35 ± .51*</td>
</tr>
</tbody>
</table>

Data are mean ± SD. Condition 1 = 21% O₂. Condition 2 = 13% O₂. Values are reported in °C.

* p < 0.001, significantly different compared to “CIVDpre”

Table 8 Color score: Stroop test

<table>
<thead>
<tr>
<th>Condition</th>
<th>Baseline</th>
<th>Acclimation</th>
<th>CWI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>67.7 ± 11</td>
<td>67.5 ± 11.13</td>
<td>67.1 ± 12.3</td>
</tr>
<tr>
<td>2</td>
<td>66 ± 12.62</td>
<td>69.6 ± 12.92</td>
<td>64.4 ± 13.41</td>
</tr>
<tr>
<td>Total</td>
<td>66.85 ± 11.81</td>
<td>68.55 ± 12.03</td>
<td>65.75 ± 12.86</td>
</tr>
</tbody>
</table>

Data are mean ± SD. Condition 1 = 21% O₂. Condition 2 = 13% O₂. Values are represented in milliseconds (ms).

Table 9 Word score: Stroop test

<table>
<thead>
<tr>
<th>Condition</th>
<th>Baseline</th>
<th>Acclimation</th>
<th>CWI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>64.7 ± 10.71</td>
<td>67.8 ± 11.1</td>
<td>68.4 ± 11.98</td>
</tr>
<tr>
<td>2</td>
<td>68.6 ± 12.37</td>
<td>70.3 ± 11.76</td>
<td>67.6 ± 14.74</td>
</tr>
<tr>
<td>Total</td>
<td>66.65 ± 11.54</td>
<td>69.05 ± 11.43</td>
<td>68 ± 13.36</td>
</tr>
</tbody>
</table>

Data are mean ± SD. Condition 1 = 21% O₂. Condition 2 = 13% O₂.

Table 10 Word-Color score: Stroop test

<table>
<thead>
<tr>
<th>Condition</th>
<th>Baseline</th>
<th>Acclimation</th>
<th>CWI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>59.2 ± 13.91</td>
<td>59.7 ± 14.66</td>
<td>60.8 ± 15.49</td>
</tr>
<tr>
<td>2</td>
<td>58.2 ± 16.46</td>
<td>59.4 ± 16.8</td>
<td>61.5 ± 18.26</td>
</tr>
<tr>
<td>Total</td>
<td>58.7 ± 15.19</td>
<td>59.55 ± 15.73</td>
<td>61.15 ± 16.88</td>
</tr>
</tbody>
</table>

Data are mean ± SD. Condition 1 = 21% O₂. Condition 2 = 13% O₂.
Table 11 *Interference score: Stroop test*

<table>
<thead>
<tr>
<th>Condition</th>
<th>Baseline</th>
<th>Acclimation</th>
<th>CWI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>26.2 ± 9.25</td>
<td>26.0 ± 9.58</td>
<td>27.0 ± 9.71</td>
</tr>
<tr>
<td>2</td>
<td>24.5 ± 11.24</td>
<td>24.7 ± 10.97</td>
<td>28.5 ± 12.2</td>
</tr>
<tr>
<td>Total</td>
<td>25.35 ± 10.25</td>
<td>25.35 ± 10.28</td>
<td>27.75 ± 10.96</td>
</tr>
</tbody>
</table>

Data are mean ± SD. Condition 1 = 21% O₂. Condition 2 = 13% O₂.

Table 12 *Throughput score: RMCPT*

<table>
<thead>
<tr>
<th>Condition</th>
<th>Baseline</th>
<th>Acclimation</th>
<th>CWI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>119.9 ± 24.56</td>
<td>127.5 ± 24.54†</td>
<td>122.9 ± 21.07</td>
</tr>
<tr>
<td>2</td>
<td>120.9 ± 20.61</td>
<td>122.0 ± 25.13</td>
<td>115.1 ± 25.7*#</td>
</tr>
<tr>
<td>Total</td>
<td>120.4 ± 22.59</td>
<td>124.75 ± 24.84</td>
<td>119.0 ± 23.34</td>
</tr>
</tbody>
</table>

Data are mean ± SD. Condition 1 = 21% O₂. Condition 2 = 13% O₂.

* p = 0.05, significantly different compared to condition 1 (21% O₂).

# p = 0.02, significantly different compared to condition 2 (13% O₂) acclimation.

† p = 0.041, significantly different compared to condition 1 (21% O₂) baseline.

Table 13 *Percent correct: RMCPT*

<table>
<thead>
<tr>
<th>Condition</th>
<th>Baseline</th>
<th>Acclimation</th>
<th>CWI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>98.3 ± 2.16</td>
<td>98.6 ± 1.26</td>
<td>97.9 ± 1.73</td>
</tr>
<tr>
<td>2</td>
<td>97.5 ± 2.64</td>
<td>96.6 ± 3.5</td>
<td>96 ± 4.14</td>
</tr>
<tr>
<td>Total</td>
<td>97.7 ± 2.4</td>
<td>97.6 ± 2.38</td>
<td>96.95 ± 2.94</td>
</tr>
</tbody>
</table>

Data are mean ± SD. Condition 1 = 21% O₂. Condition 2 = 13% O₂.

Table 14 *Mean Response Time: RMCPT*

<table>
<thead>
<tr>
<th>Condition</th>
<th>Baseline</th>
<th>Acclimation</th>
<th>CWI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>512 ± 125.6</td>
<td>483.5 ± 120.82</td>
<td>495.3 ± 123.63</td>
</tr>
<tr>
<td>2</td>
<td>494.9 ± 119.08</td>
<td>502.3 ± 145.38</td>
<td>528 ± 180.87</td>
</tr>
<tr>
<td>Total</td>
<td>503.45 ± 122.34</td>
<td>492.9 ± 133.1</td>
<td>511.65 ± 152.25</td>
</tr>
</tbody>
</table>

Data are mean ± SD. Condition 1 = 21% O₂. Condition 2 = 13% O₂.

Table 15 *TMD score*

<table>
<thead>
<tr>
<th>Condition</th>
<th>Baseline</th>
<th>Acclimation</th>
<th>CWI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>-70.5 ± 63.09</td>
<td>-67.4 ± 86.71</td>
<td>-71.8 ± 61.29</td>
</tr>
<tr>
<td>2</td>
<td>-73.2 ± 54.33</td>
<td>-64.5 ± 56.21</td>
<td>-61.6 ± 62.68</td>
</tr>
<tr>
<td>Total</td>
<td>-71.85 ± 58.71</td>
<td>-65.95 ± 71.46</td>
<td>-66.7 ± 61.99</td>
</tr>
</tbody>
</table>

Data are mean ± SD. Condition 1 = 21% O₂. Condition 2 = 13% O₂.
Table 16 *Temp during Cold-Water Immersion (CWI)*

<table>
<thead>
<tr>
<th>Condition</th>
<th>Baseline</th>
<th>Acclimation</th>
<th>CWI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>32.32 ± 3.66</td>
<td>31.66 ± 2.79</td>
<td>10.18 ± .59</td>
</tr>
<tr>
<td>2</td>
<td>32.92 ± 3.07</td>
<td>31.4 ± 3.26</td>
<td>10.12 ± .33</td>
</tr>
<tr>
<td>Total</td>
<td>32.62 ± 3.37</td>
<td>31.53 ± 3.03</td>
<td>10.15 ± .46</td>
</tr>
</tbody>
</table>

Data are mean ± SD. Condition 1 = 21% O$_2$. Condition 2 = 13% O$_2$. Values are displayed in °C.
APPENDICES
APPENDIX A

Informed Consent
Appendix A

Informed Consent

Informed Consent to Participate in a Research Study

Study Title: *Acute effects of normobaric hypoxia and cold water hand immersion on thermoregulatory response and cognitive function*

**Principal Investigator:** Hayden Gerhart, M.S., Ellen Glickman, PhD,

This document provides you with information on the research project, what you will need to do, and the associated risks and benefits of the research. Your participation is voluntary and it is important that you read this form carefully. We encourage you to ask questions so that you can make an informed decision about whether you want to participate. You will receive a copy of this document to take with you.

**Purpose**

It is the purpose of the proposed study to determine the effect of acute normobaric hypoxia on thermoregulation and vasomotor responses of the hand during rest and recovery from exercise-induced mild hyperthermia. The second purpose of this study is to examine and quantify the effects of cold water hand immersion on cognitive function in normobaric hypoxia.

**Procedures**

If you decide to volunteer as a research subject for this project, you will be asked to come to the lab on 4 different days. In total, we estimate that the time commitment to participate in this research as a volunteer will be approximately 8 hours and 15 minutes:

- Session 1 – approximately 60 minutes
- Session 2 – approximately 145 minutes
- Session 3 – approximately 145 minutes
- Session 4 – approximately 145 minutes

You may not qualify to be a participant in this research if you have certain health conditions or have previous experiences of heart-related symptoms (such as shortness of breath with low-level activity, pain, pressure, tightness, heaviness in the chest, neck, jaw, back and/or arms). It is very important that you tell us about these or any other unusual symptoms that you experience during the research procedures.

You are responsible for disclosing your medical history on the health history form prior to your participation in the research. You are also expected to report all medications (including non-prescription) taken recently to the research staff prior to participating in each research session.
If you decide to participate in this research, we will ask you to complete the following procedures:

**VO2 max test** – This test involves you pedaling on an exercise cycle at progressively harder workloads while wearing a mask and a mouthpiece with a breathing valve to collect expired gases. This will only be conducted in the first session.

**Submaximal cycling test** - three lighter intensity cycling exercise sessions, 30 minutes in duration, with 15 minutes of hand exposure into 5°C water before and after the exercise bout (visits 2, 3, and 4) in a chamber under:

1. A reduced oxygen (hypoxic) condition. In this first condition, oxygen within the chamber will be adjusted to 13%, rather than the normal level of 20%. This simulates a reduced oxygen level comparable to being at Pike’s Peak in Colorado (14,110 feet above sea level).
2. A reduced oxygen (hypoxic) condition. In this second condition, oxygen within the chamber will be adjusted to 17%, rather than the normal level of 20%. This simulates a reduced oxygen level comparable to being in Boulder, Colorado (5,000 feet above sea level).
3. A normal oxygen (normoxic) condition. In this condition, the oxygen level of the chamber will not be modified. Normal oxygen levels are about 20%.

During these tests, we will monitor:

- Blood pressure – using a stethoscope and a sphygmomanometer
- Heart rate – using an elastic and rubber chest strap, and a watch
- Blood oxygen levels – using a pulse-oximeter (clips onto the end of the finger)
- Oxygen consumption – using a metabolic measuring system which measures expired gasses (pictured above).
- Rectal temperature – inserting a thermistor 13 cm into rectum.
- Skin temperature – using thermocouples
- Water temperature
- Impedance cardiography
- Thermal sensation
- Thermal comfort
- Rating of perceived exertion
- Acute mountain sickness
Cognitive Function and Mood Assessment tests
For these tests we will ask that you use a computer to complete the Automated Neuropsychological Assessment Metric 4th edition (ANAM4) test. The results of this tests provide us with information about your attention and concentration level, reaction time, memory, processing speed and decision-making.

Benefits
Participants will learn about their aerobic fitness levels and tolerance to altitude. This information may be applicable to future exercise or travel plans.

Risks and Discomforts
- Exercise-induced fatigue (becoming tired resulting from the exercise)
- Lightheadedness
- Shortness of breath
- Muscular soreness
- Discomfort with insertion of rectal thermistor
- Cardiovascular event (extremely rare cases)
- Increased breathing rate
- Increased heart rate
- Headache
- Acute Mountain Sickness (dizziness, headache)
- Discomfort associated with immersion of hand into 5°C water

Every effort will be made to minimize these risks by evaluation of preliminary information relating to your health and fitness and by careful observations during testing. Emergency equipment and trained personnel are available to deal with unusual situations that may arise. Researchers conducting this study are not medical doctors and are not qualified to diagnose a participant’s illness or state of disease.

We may stop the test at any time because of signs of fatigue or changes in your heart rate, blood pressure, or symptoms you may experience and you may decide to stop your participation at any time.

Privacy and Confidentiality
Your personal information will be kept confidential. Any identifying information will be kept in a secure location that only the researchers will have access to. Research participants will not be identified in any publication or presentation of research results; only aggregate data will be used.

Your research information may, in certain circumstances, be disclosed to the Institutional Review Board (IRB), which oversees research at Kent State University, or to certain federal agencies. Confidentiality may not be maintained if you indicate that you may do harm to yourself or others.
Compensation
Four $10 payments will be made. A $10 payment will be given after each of the four sessions, totaling $40 in the form of a gift card to Target.

For research related injuries, 911 will be called. You or your medical insurance will be billed for this service.

Voluntary Participation
Taking part in this research study is entirely up to you. You may choose not to participate or you may discontinue your participation at any time without penalty or loss of benefits to which you are otherwise entitled. You will be informed of any new, relevant information that may affect your health, welfare, or willingness to continue your study participation.

Contact Information
If you have any questions or concerns about this research, you may contact Ellen Glickman at 330-672-2930 or Hayden Gerhart at 717-371-5197. This project has been approved by the Kent State University Institutional Review Board. If you have any questions about your rights as a research participant or complaints about the research, you may call the IRB at 330.672.2704.

Consent Statement and Signature
I have read this consent form and have had the opportunity to have my questions answered to my satisfaction. I voluntarily agree to participate in this study. I understand that a copy of this consent will be provided to me for future reference.

________________________  _____________________
Participant Signature                              Date
APPENDIX B

Health History Questionnaire
Appendix B

Health History Questionnaire

KENT STATE UNIVERSITY

APPLIED PHYSIOLOGY RESEARCH LAB
MODIFIED FOR HYPOXIA RESEARCH

HEALTH HISTORY

Thank you for volunteering to be a participant for a study to be conducted in the Applied Physiology Research Laboratory. You may be asked to perform a test that requires you to exercise at or near your maximum capability. Consequently, it is important that we have an accurate assessment of your past and present health status to assure that you have no medical conditions that would make the tests dangerous for you. Please complete the health history as accurately as you can. This medical history is confidential and will only be seen by researchers to determine your qualifications for this study.

Name__________________________________________ Date___/___/____

Date of Birth___/___/____ Present Age____ yrs

Ethnic Group:  ____White

____ African American

____ Hispanic

____ Asian

____ Pacific Islands

____ American Indian

____ Other_____________
HOSPITALIZATIONS AND SURGERIES

If you have ever been hospitalized for an illness or operation, please complete the chart below. Do not include normal pregnancies, childhood tonsillectomy, or broken bones.

YEAR______________

OPERATIONS OR ILLNESS

________________________________________________

YEAR______________

OPERATIONS OR ILLNESS

________________________________________________

YEAR______________

OPERATIONS OR ILLNESS

________________________________________________

Are you under long-term treatment for a protracted disease, even if presently not taking medication? [ ] Yes [ ] No

If Yes, explain: ____________________________________________________________

________________________________________________

________________________________________________

MEDICATIONS

Please list all medications that you have taken within the past 8 weeks: (Include prescriptions, vitamins, over-the-counter drugs, nasal sprays, aspirins, birth control pills, etc.)

Check this box [ ] if you have not taken any medication.

MEDICATION______________

REASON FOR TAKING THIS

________________________________________________

MEDICATION______________

REASON FOR TAKING THIS
MEDICATION __________
REASON FOR TAKING THIS

ALLERGIES
Please list all allergies you have (include pollen, drugs, alcohol, food, animals, etc.)
Check this box [ ] if you have no allergies.
1.______________________________________________________________________
2.______________________________________________________________________
3.______________________________________________________________________
4.______________________________________________________________________

When was the last time you were “sick”? (e.g. common cold, flu, fever, etc.)
________________________________________________________________________

PROBLEMS AND SYMPTOMS
Place an X in the box next to any of the following problems or symptoms that you have had:

General
[ ] Mononucleosis
    If yes, when______________________________

[ ] Excessive fatigue
[ ] Recent weight loss while not on a diet
[ ] Recent weight gain
[ ] Thyroid disease
[ ] Fever, chills, night sweats
[ ] Diabetes
[ ] Arthritis
Sickle Cell Anemia
Heat exhaustion or heat stroke
Recent sunburn

PROBLEMS AND SYMPTOMS, continued

Heart and Lungs

Abnormal chest x-ray
Pain in chest (persistent and/or exercise related)
Heart attack
Coronary artery disease
High blood pressure
Rheumatic fever
Peripheral vascular disease
Blood clots, inflammation of veins (phelebitis)
Asthma, emphysema, bronchitis
Shortness of breath
  At rest
  On mild exertion
Discomfort in chest on exertion
Palpitation of the heart; skipped or extra beats
Heart murmur, click
Other heart trouble
Lightheadedness or fainting
Pain in legs when walking
Swelling of the ankles
Need to sleep in an elevated position with several pillows
G-U SYSTEM

[  ] Get up at night to urinate frequently
[  ] Frequent thirst
[  ] History of kidney stones, kidney disease

G.I. TRACT

[  ] Eating disorder (e.g. anorexia, bulimia)
[  ] Yellow jaundice
  If yes, when ________________________________
[  ] Hepatitis
  If yes, when ________________________________
[  ] Poor appetite
[  ] Frequent indigestion or heartburn
[  ] Tarry (black) stool
[  ] Frequent nausea or vomiting
[  ] Intolerance of fatty foods
[  ] Changes in bowel habits
[  ] Persistent constipation
[  ] Frequent diarrhea
[  ] Rectal bleeding
[  ] Unusually foul smelling or floating stools
[  ] Pancreatitis

Nervous System

[  ] Alcohol problem
[  ] Alcohol use
If yes, how many drinks ingested per week? __________________

[ ] Frequent or severe headaches
[ ] Stroke
[ ] Attacks of staggering, loss of balance, dizziness
[ ] Persistent or recurrent numbness or tingling of hands or feet
[ ] Episode of difficulty in talking
[ ] Prolonged periods of feeling depressed or “blue”
[ ] Difficulty in concentrating
[ ] Suicidal thoughts
[ ] Have had psychiatric help

Explain any items checked (when, severity, treatment)
____________________________________________________________________________
____________________________________________________________________________
____________________________________________________________________________
____________________________________________________________________________
____________________________________________________________________________

Have you ever passed out during or after exertion? YES NO
Do you have a family history of coronary artery disease YES NO
If yes, Who? (Grandparents, parents, siblings, uncles, and aunts)
____________________________________________________________________________
____________________________________________________________________________
____________________________________________________________________________

Are there any other reasons not mentioned above that you feel you should not participate in this research study? YES NO

Do you currently smoke cigarettes? YES NO
Do you currently use any smokeless tobacco products?    YES    NO

EXCLUSION CHECKLIST

This form is intended to identify any signs, symptoms, or conditions that would exclude any person from participating in a study involving hypoxia. Please mark if any of the following statements apply.

Have you ever experienced severe headache when at high altitude?
Yes [ ]    No [ ]

Have you ever experienced syncope (loss of consciousness) or dizziness during exercise at sea-level?
Yes [ ]    No [ ]

Have you been diagnosed with Anemia or Sickle-cell Anemia?
Yes [ ]    No [ ]

Have you been told that you have sickle-cell trait?
Yes [ ]    No [ ]

Have you ever coughed blood after exercising?
Yes [ ]    No [ ]

Have you been diagnosed with orthostatic hypotension, or experience extreme dizziness upon standing?
Yes [ ]    No [ ]

Have you ever been diagnosed with Raynaud’s Disease?
Yes [ ]    No [ ]
Have you ever experience Angina? (a pain or discomfort in the chest, neck, or jaw during exertion that is not attributed to muscle or joint pain)
Yes [ ]   No [ ]

Have you ever experience shortness of breath at rest or with mild exertion (Dyspnea)?
Yes [ ]   No [ ]

Do you have a history of frostbite?
Yes [ ]   No [ ]

Do you or have you ever had ankle edema? (fluid retention in the ankles causing swelling)
Yes [ ]   No [ ]

Do you every experience tachycardia or palpitations at rest? (do you ever feel that your heart is beating very rapidly and forcefully without exercise, caffeine, or another stimulus?)
Yes [ ]   No [ ]

Do you have intermittent claudication? (a pain in the leg due to exercise caused by a lack of blood flow, usually caused by a clot)
Yes [ ]   No [ ]

Have you ever been told that you have a heart murmur?
Yes [ ]   No [ ]

Are you pregnant?
Yes [ ]   No [ ]

Do you smoke, or have you quit smoking within the last 6 months?
Yes [ ]   No [ ]
APPENDIX C

Fasting Checklist
Appendix C

Fasting Checklist

When was the last meal that you ate, and what did it contain?

Have you use any recreational drugs or alcohol in the last 24 hours?

Have you performed any vigorous physical activity in the last 23 hours?
APPENDIX D

Acute Mountain Sickness (AMS) Assessment
Appendix D

Acute Mountain Sickness (AMS) Assessment

Lake Louise Score (LLS) for the diagnosis of Acute Mountain Sickness (AMS)

A diagnosis of AMS is based on:
1. A rise in altitude within the last 4 days
2. Presence of a headache
3. Presence of at least one other symptom
4. A total score of 3 or more from the questions below

Self-report Questionnaire
Add together the individual scores for each symptom to get the total score.

<table>
<thead>
<tr>
<th>Headache</th>
<th>No headache</th>
<th>0</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mild headache</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Moderate headache</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Severe headache, incapacitating</td>
<td>3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Gastrointestinal symptoms</th>
<th>None</th>
<th>0</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Poor appetite or nausea</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Moderate nausea &amp; or vomiting</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Severe nausea &amp; or vomiting</td>
<td>3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Fatigue &amp;/or weakness</th>
<th>Not tired or weak</th>
<th>0</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mild fatigue/ weakness</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Moderate fatigue/ weakness</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Severe fatigue/ weakness</td>
<td>3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Dizziness/lightheadedness</th>
<th>Not dizzy</th>
<th>0</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mild dizziness</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Moderate dizziness</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Severe dizziness, incapacitating</td>
<td>3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Difficulty sleeping</th>
<th>Slept as well as usual</th>
<th>0</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Did not sleep as well as usual</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Woke many times, poor sleep</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Could not sleep at all</td>
<td>3</td>
</tr>
</tbody>
</table>

Total score of:
- 3 to 5 = mild AMS
- 6 or more = severe AMS

Note:
- Do not ascend with symptoms of AMS
- Descend if symptoms are not improving or getting worse
- Descend if symptoms of HACE or HAPE develop
APPENDIX E

Thermal Sensation/Comfort Scales
### Appendix E

**Thermal Sensation/Comfort Scales**

<table>
<thead>
<tr>
<th>Sensation</th>
<th>Comfort</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>Very Hot</td>
<td>4</td>
</tr>
<tr>
<td>3</td>
<td>Hot</td>
<td>3</td>
</tr>
<tr>
<td>2</td>
<td>Warm</td>
<td>2</td>
</tr>
<tr>
<td>1</td>
<td>Slightly Warm</td>
<td>1</td>
</tr>
<tr>
<td>0</td>
<td>Neutral</td>
<td>0</td>
</tr>
<tr>
<td>-1</td>
<td>Slightly Cool</td>
<td>-1</td>
</tr>
<tr>
<td>-2</td>
<td>Cool</td>
<td>-2</td>
</tr>
<tr>
<td>-3</td>
<td>Cold</td>
<td>-3</td>
</tr>
<tr>
<td>-4</td>
<td>Very Cold</td>
<td>-4</td>
</tr>
<tr>
<td></td>
<td>Very Comfortable</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Just Comfortable</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Just Uncomfortable</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Very Uncomfortable</td>
<td></td>
</tr>
</tbody>
</table>
APPENDIX F

RPE Scale
### Appendix F

### RPE Scale

<table>
<thead>
<tr>
<th>Rating</th>
<th>Description</th>
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<tbody>
<tr>
<td>6</td>
<td>NO EXERTION AT ALL</td>
</tr>
<tr>
<td>7</td>
<td>EXTREMELY LIGHT</td>
</tr>
<tr>
<td>8</td>
<td>VERY LIGHT</td>
</tr>
<tr>
<td>9</td>
<td>LIGHT</td>
</tr>
<tr>
<td>10</td>
<td>SOMEWHAT HARD</td>
</tr>
<tr>
<td>11</td>
<td>HARD (HEAVY)</td>
</tr>
<tr>
<td>12</td>
<td>VERY HARD</td>
</tr>
<tr>
<td>13</td>
<td>EXTREMELY HARD</td>
</tr>
<tr>
<td>14</td>
<td>MAXIMAL EXERTION</td>
</tr>
</tbody>
</table>
APPENDIX G
Rectal Thermistor SOP
Appendix G
Rectal Thermistor SOP

S.O.P. FOR RECTAL TEMPERATURE THERMISTOR

1. A taped rectal thermistor will be given to you that is taped at the 13 cm mark, with thermistor cover already in place.

2. The tip of the thermistor was cleaned for you with an alcohol pad before placing the cover over top, to ensure the thermistor is 100% clean.

3. Apply your personal lubricant (KY Jelly) to the tip of the thermistor (now covered) and all the way down the probe to make it easier to insert (optional).

4. Gently self-insert the flexible thermistor 13 cm (marked with tape) into the rectum.

5. Once the thermistor is inserted, the rest of the wiring that is connected to the thermistor must extend out of the clothing worn. It should be extended in an upward manner so it does not “slip down.”

6. Dispose of the thermistor covering into a waste container (bio-hazard red container in the bathroom) and clean the thermistor with soap and water. After drying, use alcohol pad to clean thermistor once again.
# Appendix H

## Data Sheet

Anthropometric characteristics

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<th># Subject:</th>
<th>Date:</th>
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<table>
<thead>
<tr>
<th>Age:</th>
<th>Gender: (M/F)</th>
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<table>
<thead>
<tr>
<th>Height: (ft/in or cm)</th>
<th>Weight: (lbs/kg)</th>
<th>BMI:</th>
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<tr>
<td></td>
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<table>
<thead>
<tr>
<th>RHR:</th>
<th>Blood pressure:</th>
<th>MAP: mmHg (=1/3 *(SBP-DBP) + DBP)</th>
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<tbody>
<tr>
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</table>

### Skin fold (mm)

<table>
<thead>
<tr>
<th>Subscapular</th>
<th>Chest</th>
<th>Side</th>
<th>Suprailium</th>
<th>Abdomen</th>
<th>Triceps</th>
<th>Thigh</th>
</tr>
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\[ %BF = \frac{\text{Sum}}{} \]

\[ \text{Sum} = \]

98
<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>60min Rest</th>
<th>1st Recovery post immersion (min. 80)</th>
<th>Post Exercise (min. 120)</th>
<th>2nd Recovery Post immersion (min.145)</th>
<th>Final Recovery (min. 180)</th>
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<tr>
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<td>ANAM</td>
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<tr>
<td>Mood State</td>
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<tr>
<td>Anger</td>
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<tr>
<td>Depression</td>
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<tr>
<td>Fatigue</td>
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</tr>
<tr>
<td>Happiness</td>
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</tr>
<tr>
<td></td>
<td>Restless</td>
<td>Vigor</td>
<td>SCWT</td>
<td>Interference A</td>
<td>Word A</td>
<td>Color A</td>
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<tr>
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