

The impact of rate of thermal acquisition on cerebral oxygenation and haemodynamics, cerebral neural function, perceptual decision-making and salivary cortisol concentration

By

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MSc Kinesiology and Health, Louisiana State University – Shreveport, 2012

A Dissertation Submitted in Partial Fulfillment of the
Requirements for the Degree of
DOCTOR OF PHILOSOPHY
In the School of Exercise Science, Physical and Health Education

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University of Victoria

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Abstract

This study examined the effects of rapid and uncompensable core temperature (T_c) acquisition on cerebral oxygenation and haemodynamics, cerebral neural function, decision-making, and rate and magnitude salivary cortisol appearance. Fourteen male subjects (mean age, 33.6 ± 12.1 years) performed an incremental treadmill exercise test to a termination criterion in a control session (CON) and an experimental session (PPE). The incremental treadmill exercise test protocol included an initial 5-minute stage at 3.5 mph and a 0% grade, the second stage was 5-minutes at 3.5 mph at 4% grade, the third stage was 50-minutes at 3.5 mph and an 8% grade, and the final stage was 1-hour at 3.5 mph and a 12% grade. The Instrumentation included a near-infrared spectroscopy (NIRS) monitor, MUSE EEG monitoring system, Equivital integrated physiological monitoring system, T_c capsules, and salivary cortisol oral swabs and ELISA kit for salivary analysis. Important physiological results were significant differences in the physiological strain index (PSI) at all common points of measurement. Important cerebral oxygenation and haemodynamics results were a plateau in left-side prefrontal cortex (PFC) HbO₂ and tHb at roughly T_c 38°C in both CON and PPE, 80% of TTT in CON, and 60% of TTT in PPE. Additionally, there was higher left-side PFC activation during PPE as indicated by a significant decrease in TSI % from start to end of exercise and double the decrease in TSI % per minute in PPE when compared to CON. There were no significant differences during the CON session. An analysis of frontal theta EEG power results showed a significant decrease when comparing pre- and post-exercise values during a Go/No-go test in PPE ($F(1,13) = 6.069$, $p \leq 0.05$). There was also a significant difference when evaluating incorrect responses between pre- and post-exercise values in PPE ($F(1,13) = 12.785$, $p \leq 0.01$); these differences were not observed during CON. There was also a difference in the rate of cortisol appearance (CON =

0.002 $\mu\text{g dL}^{-1} \text{min}^{-1}$; PPE = 0.018 $\mu\text{g dL}^{-1} \text{min}^{-1}$). In the PPE condition, mean cortisol values between start of exercise and the measurement point associated with T_c 38°C and between the start and end of exercise during PPE were significantly different ($F(1,13) = 22.71$, $p \leq 0.01$). Lastly, there was a significant difference between magnitude of cortisol values at the termination between CON and PPE. These data suggest that rapid and uncompensable T_c acquisition during PPE caused an altered cerebral oxygenation and haemodynamic response in the left-side PFC when compared to CON. The left PFC could be working harder to prevent fatigue in PPE. This could have implications for cognitive processes during and/or following exercise in the heat while wearing PPE. These data also suggest rapid and uncompensable T_c acquisition results in decreased cognitive control. This could have implications for individuals whose occupation requires PPE and critical decision making while experiencing rapid T_c heat storage. Lastly, these results show a difference between PPE and CON in regards to rate and magnitude of salivary cortisol appearance, potentially affecting individuals chronically exposed to acute heat stress. Increased acute cortisol concentration decreases anabolic response, cognitive performance, and mood states. The chronic effects of increased cortisol concentration are many: largely related to atherosclerosis development and subsequent cardiovascular disease. Additional issues include anthropometric, endocrine, metabolic, and haemodynamic disturbances. This study makes a strong argument for the rate of thermal acquisition factor. CON and PPE differences in PSI at all measurement points provides justification and support for the changes in other variables. Rapid and uncompensable T_c acquisition needs to be taken into account, as it potentially puts the lives of employees who wear PPE and those around them at risk.

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List of Abbreviations

DLPFC	Dorsolateral Prefrontal Cortex
EEG	Encephalography
HbO ₂	Oxyhemoglobin
HHb	Deoxyhemoglobin
HbDiff	Hemoglobin difference = HbO ₂ – HHb
HR	Heart Rate
μM	Micromolar, measure of concentration of hemoglobin variables
μg/dL	Micrograms Per Deciliter
NIRS	Near-infrared Spectroscopy
OFC	Orbitofrontal Cortex
PAR-Q	Physical Activity Readiness Questionnaire
PFC	Prefrontal Cortex
PPE	Personal Protective Equipment
RPE	Rating of Perceived Exertion
T _c	Core Temperature
TCS	Thermal Comfort Scale
tHb	Total hemoglobin = HbO ₂ + HHb
TS	Thermal Sensation
TSI	Tissue Saturation Index = HbO ₂ /tHb
TTT	Time to Termination
$\dot{V}_E / \dot{V}_{O_2}$	Ventilatory Equivalent for Oxygen
$\dot{V}_{O_2}$	Oxygen Consumption

$\dot{V}O_{2\max}$ Maximal Oxygen Consumption

Acknowledgements

We would like to express our appreciation for all of the volunteer subjects who participated in our study. Funding for the research was provided by the University of Victoria Centre for Occupational Research. Additionally, WorkSafe BC provided the principal investigator with a research training award. We would like to express our gratitude for financially supporting this research. The principal investigator would like to thank his family for their support during this research.

CHAPTER 1: INTRODUCTION

1.1 Overview

Rapid and uncompensable core temperature (T_c) acquisition is an important variable to consider for individuals working in hyperthermic conditions while wearing personal protective equipment (PPE). Uncompensable T_c acquisition is defined as the T_c storage that occurs while an individual is subject to uncompensable heat stress. Uncompensable heat stress is a state where the evaporative capacity of the immediate external environment is less than the evaporative dissipation necessary to maintain heat balance (Cheung, McLellan, Tenaglia, 2000). Several occupations are exposed to rapid and uncompensable T_c acquisition: firefighting, hazardous waste disposal, military, mining, etc. High ambient temperatures accompanied by the microclimate created by the PPE creates a scenario where rapid heat storage/acquisition is possible (Taylor, Lewis, Notley, & Peoples, 2012). The microclimate often contains several layers: each acting as their own individual microclimate (Cheung, McLellan, & Tenaglia, 2000). Evaporative thermoregulation becomes difficult as a result of the lack of permeability these microclimates possess.

During rapid T_c acquisition, enhanced thermoregulation or delayed T_c acquisition is necessary because increased rate of thermal acquisition could have physiological, cognitive, or stress response consequences. The human body is very capable of adapting to large fluctuations in environmental temperatures and exercise conditions; T_c fluctuates very little from rest to exercise in the heat as long as the heat can escape via sweating to the external environment. Temperature fluctuations of $\sim 3^\circ\text{C}$ can lead to very serious thermal injury or even death. Thermoregulation occurs via four major methods: evaporation, convection, conduction, and radiation. The major means of thermoregulation during heat stress is the elevation of skin blood

flow for convective/conductive heat exchange and sweating for the purpose of evaporative heat exchange. Without sweating, the human body would reach close to unsafe core temperatures within 10 minutes of moderate exercise (Kenney & Johnson, 1992).

The brain deals with heat stress in a different way than the rest of the body. The human brain produces between 15 and 20% of the body's resting metabolic heat; this is very significant as the brain only makes up roughly 2% of total body mass (Nelson & Nunneley, 1998). This large degree of cerebral heat production results in the brain having a higher mean temperature than the rest of the body that ranges between 0.39 to 2.5°C (McIlvoy, 2004). The brain accomplishes thermoregulation largely through convection between the brain tissue and the surrounding capillaries (Pennes, 1948). The brain also accomplishes thermoregulation by exchanging heat between areas of the brain. The superficial areas of the brain can exchange heat with the cortical vessels, which ultimately reaches the environment via the scalp; deep structures rely primarily on convection with blood vessels to remove heat (Karbowski, 2009).

During periods of heat stress, the brain has to work very hard to meet the metabolic and thermoregulatory demands. For example, the brain receives input from chemo-, mechano-, and barosensitive sensory endings throughout the body to ultimately divert the majority of systemic O₂ to working skeletal muscle during exercise in the heat at an enhanced perfusion pressure (Gonzalez-Alonso et al., 2004). Heat stress whether it be passive heat stress (Brothers, Zhang, Wingo, Hubing, & Crandall, 2009; Fan et al., 2008; Fujii et al, 2008), prolonged moderate exercise in the heat (Nybo & Nielsen, 2001), or maximal exercise in the heat (Gonzalez-Alonso et al., 2004) causes a decrease in cerebral perfusion; decreases in cerebral perfusion are met by increases in oxygen uptake by the brain to allow for sustained cerebral functioning (Gonzalez-Alonso et al., 2004).

Rapid and uncompensable Tc acquisition, as which occurs in various occupational scenarios, could cause considerable decrements in brain blood flow, which could ultimately effect the brain's neuronal activity. This has not been studied previously; thereby providing importance for this study. These consequences could impair the decision-making process, which would be detrimental for individuals in occupations where critical, life-threatening decisions need to be made quickly.

Heat stress has also been shown to affect the stress response through increased cortisol production. Cortisol is a product of the hypothalamic-pituitary-adrenal (HPA) axis. The ultimate goal of cortisol is to bring the stressed body back to a state of homeostasis. The problem arises when the body is in a state of chronic stress, leading to chronically elevated cortisol. Chronically elevated cortisol has been linked to accelerated atherosclerosis and subsequent cardiovascular issues (Dekker et al., 2008). Chronically elevated cortisol is prominent amongst firefighters due to several factors: anticipation of the fire call (Smith, Deblois, Kales, & Horn, 2016), altered sleep (Wolkow, Aisbett, Reynolds, Ferguson, & Main, 2015), and excessive physical work (Wolkow et al., 2015). Whether or not regular exposure to heat stress has an effect on the cumulative cortisol response has not been studied. Cardiac related issues are the leading cause of line-of-duty death among firefighters. Statistics show that 45% to 50% of all firefighter duty-related fatalities are a result of sudden cardiac death (Smith et al., 2016). In addition to this, there are 17 to 25 duty-related nonfatal cardiovascular events for every fatal event (Fahy, Leblanc, & Molis, 2015; Haynes & Molis, 2015). Exercise in the heat increases plasma cortisol levels when compared to exercise in a normothermic condition (Brenner, Zamecnik, Shek, & Shephard, 1997). Acute bouts of rapid and uncompensable Tc acquisition due to PPE and ambient heat exposure could result in an elevated cortisol response when compared to gradual and

compensable heat stress scenarios. This has not been studied previous to this study. Firefighters in larger centres who respond to regular fire calls are exposed to acute heat stress chronically.

1.2 Purpose of the Study

The purpose of this study was to examine the impact of rapid and uncompensable Tc acquisition on cerebral oxygenation and haemodynamics, neural function, decision-making, and rate and magnitude of salivary cortisol appearance. Tc was analyzed to portray heat acquisition profiles.

1.3 Research Questions

The following research questions were addressed in this study:

1. What effect does exercise while wearing PPE and the resulting rapid and uncompensable Tc acquisition have on cerebral oxygenation and haemodynamics?
2. What effect does exercise while wearing PPE and the resulting rapid and uncompensable Tc acquisition have on cerebral neural function and decision-making performance?
3. What effect does exercise while wearing PPE and the resulting rapid and uncompensable Tc acquisition have on the rate and magnitude of salivary cortisol appearance?

1.4 Hypotheses

1. H_0 : Exercise while wearing PPE and the resulting rapid and uncompensable Tc acquisition will have no effect on cerebral oxygenation and haemodynamics.
2. H_0 : Exercise while wearing PPE and the resulting rapid and uncompensable Tc acquisition will have no effect on cerebral neural function and decision-making performance.
3. H_0 : Exercise while wearing PPE and the resulting rapid and uncompensable Tc acquisition will have no effect on the rate and magnitude of salivary cortisol appearance.

1.5 Delimitations

1. Only subjects between the ages of 20 – 55 years of age were recruited to participate in the study.
2. Only healthy male subjects as indicated by the physical activity readiness questionnaire (PAR-Q) were recruited.
3. There was a 2-hour time limit for the control and experimental sessions.
4. Only subjects who had a $\text{VO}_{2\text{max}}$ of greater than $35 \text{ ml kg}^{-1} \text{ min}^{-1}$ were able to participate in the study.

1.6 Limitations

1. This study was only able to heat subjects to a T_c of 39.5°C (University of Victoria ethics requirement)

1.7 Assumptions

1. Participants followed all criteria required to participate in the study related to alcohol, drugs, nicotine, caffeine, dietary intake, and physical activity.

Assumptions associated with NIRS data

The following assumptions are stated in the Artinis Portalite Manual (Artinis Medical Systems BV, 2011, p.21):

1. Slope estimations are based on the assumption that the source-detector separation is much larger than the source size and the scattering mean free pathlength
2. The algorithm assumes homogeneous and infinite tissue
3. The light enters the tissue perpendicular and without any air-tissue transition
4. A constant scattering coefficient is assumed, and it is estimated to follow a linear relation to the wavelength

1.8 Operational definitions

1. Healthy: No chronic diseases including any vascular disorders.
2. Cerebral oxygenation and haemodynamics: changes in oxygenated hemoglobin, deoxygenated hemoglobin, total hemoglobin, and tissue saturation index measured at the prefrontal cortex using a NIRS.
3. Cerebral neural function: measured by changes in frontal and posterior delta, theta, alpha, and beta dynamics.
4. Decision-making performance: indicated by the amount of incorrect responses during the Go/No-go test pre- and post-exercise.
5. Rate of salivary cortisol appearance: measured as the $\mu\text{g.dL}^{-1}$ of salivary cortisol per minute.
6. Magnitude of salivary cortisol appearance: measured as the absolute value of cortisol in $\mu\text{g.dL}^{-1}$ at particular time or temperature point.

CHAPTER 2: REVIEW OF LITERATURE

2.1 Introduction

Individuals who work in occupations requiring the use of PPE have the potential for rapid and uncompensable Tc acquisition. Rapid and uncompensable Tc acquisition could lead to detrimental effects in relation to cerebral oxygenation and haemodynamics, neural function, decision-making, and stress response (cortisol) when compared to gradual, compensable heat stress scenarios. It is important to mediate these effects, as each of these issues could cause safety concerns.

This review of literature will present substantial evidence that directly relates to this doctoral research project. Section one of this review of literature will begin by discussing topics related to the effects of heat stress on the rate and magnitude of cortisol appearance. This section will begin by discussing the validity of salivary cortisol collection and evaluation. One must determine the most effective procedure for measuring the presence of cortisol to obtain a quantitative representation of systemic cortisol. This section will discuss in detail the means of salivary collection and analysis, as well as the correlation between salivary and blood measures for cortisol. The last paragraph in section 2.3 provides justification for the use of oral swab collection of salivary cortisol during this study. This section will also provide direct evidence for the effect of heat stress on cortisol appearance. Section two of this review will discuss the haemodynamics of passive heat stress, exercise in the heat, and uncompensable heat stress. Within this area, there will be a specific discussion of the cerebral haemodynamic response to these various heat stress modalities; it is important to discuss the haemodynamic response to various forms of heat stress as they each pose specific challenges. This research intended to understand the specific nature of rapid and uncompensable Tc acquisition during exercise in a

hyperthermic ambient environment; therefore, understanding various modes of heat stress helps to compare between rapid and uncompensable Tc acquisition and gradual, compensable Tc acquisition that occurred during this study. The third section of this review will discuss subtopics related to the effects of heat stress on neural function and decision-making. Lastly, limitations of the literature and a summary of this review are reported.

Section 1

2.2 Means of Salivary Collection and Analysis

When measuring for the presence of cortisol, one must determine whether salivary measurements are adequate when compared to bloodletting. Blood is regarded as the most accurate body fluid for the measurement of systematic processes (Williamson, Munro, Pickler, Jo Grap, Elswick, 2012); however, there are potential risks associated with blood-letting as it can cause discomfort, bruising, potential infection at the venipuncture site, and anemia if large amounts are drawn (Williamson et al., 2012). On the other hand, salivary collection is relatively non-invasive. A potential change from blood collection to salivary measurements is appealing as the risks associated with the collection of blood are eliminated. Saliva can be collected and measured using a variety of techniques including unstimulated whole saliva, unstimulated saliva from a specific gland, unstimulated saliva from a pair of glands, and stimulated salivary collection (Navanesh & Kumar, 2008).

Stimulated salivary collection is generally considered to be less accurate than unstimulated sampling, as stimulated saliva contains a varied composition due to the mechanism by which stimulated flow is obtained. For example, saliva stimulating agents, such as gum, may react with the saliva causing a change in the acid-base balance (Anderson & Orchardson, 2003). However, the stimulated oral swab method is considered to be a very effective method of

salivary cortisol collection (Poll et al., 2007; Raff, Raff, & Findling, 1998). This method will be discussed in detail in section 2.3 of this review.

Saliva is a hypotonic fluid that is made up of mostly water, electrolytes, and organic molecules. Blood components of saliva are derived from vasculature that originates from the common carotid arteries (Johnson, 2001). This interaction between the salivary glands and systemic circulation potentially makes saliva an important fluid for diagnostic means.

There are differing means by which unstimulated saliva is collected. One method is the ‘draining’ method, where pooled saliva is expectorated every 30 seconds. Another method is the passive drool method, where saliva is collected over the course of a 30 second period. This method is considered the “gold standard” when it comes to unstimulated salivary collection (Williamson et al., 2012). Lastly, unstimulated salivary collection can be performed by placing filter paper in the sublingual pocket (Ameringer, Munro, & Elswick, 2012). This method has several benefits: one benefit being that the subject can remain in an upright position during collection (Williamson et al., 2012). The other benefit of this method is that filter paper samples are easy to transport and can, for the most part, be stored at room temperature. Passive drool samples, depending on the analyte being measured, need to be frozen at -20°C for short-term storage (Monea et al., 2014) and -70 to -80°C for long-term storage [Poll et al., 2007].

Analysis of blood and salivary contents can be evaluated by two major means: ELISA and multiplex suspension array technologies. ELISA allows for analysis of a single biomarker per test, while multiplex suspension array technologies allow for analysis of multiple biomarkers simultaneously. ELISA are the time-tested and most validated method of biomarker measurement; therefore, ELISA tests are considered the gold standard clinical diagnostic tool for biomarker measurement (Thiha & Ibrahim, 2015). Multiplex suspension array technologies,

while convenient, have been found to lack precision, particularly at the batch level when testing cytokine concentrations (Browne et al., 2013). Multiplex arrays are also in the primitive stage of development, and further studies using this technology will add to its validity.

2.3 Correlation between Salivary and Blood Measurements and Analysis for Cortisol

Saliva is produced by three major salivary glands: sublingual, submandibular, and parotid. These salivary glands have continuous interaction with blood vessels from which a portion of saliva is filtered and processed. This filtration occurs via passive and active transport and causes several specific soluble biological markers (biomarkers) from blood to be present in saliva. Not all biomarkers within saliva originate in the bloodstream; some biomarkers originate in the mouth and are not adequate indicators of the systemic concentration of that particular biomarker. For example, salivary norepinephrine is not an adequate measure of changes in systemic sympathetic activity. This inadequacy is due to the fact that penetration of blood norepinephrine into saliva is slow, and salivary sympathetic nerves contribute to the overall concentration of norepinephrine in saliva (Kennedy, Dillon, Mills, & Zeigler, 2001). When determining the relationship between salivary and blood concentrations of a specific biomarker, a connection must be drawn in that a correlation must be present.

Cortisol is a glucocorticoid synthesized from cholesterol, secreted by the adrenal cortex, and released into the blood. Elevated cortisol levels have been linked to hypertension, central obesity, insulin resistance, glucose intolerance (Phillips et al., 2008), and atherosclerosis (Dekker et al., 2008). As such, cortisol is one of the most widely studied salivary biomarkers of stress.

In regards to the correlation of salivary cortisol to blood cortisol, there are many factors that need to be considered. Saliva contains free, biologically active cortisol as opposed to total cortisol which is present in blood. This is significant because 80 – 95% of total cortisol in blood

is bound to cortisol-binding globulin (CBG). It is not the bound content of cortisol which produces the physiologic function of the hormone but, rather, the free content in a biologically active form (le Roux et al., 2003; Raff, Raff, & Findling, 1998). Free salivary cortisol is not dependent on saliva flow rate as it enters saliva via the intracellular route which is caused by passive diffusion from blood. As such, salivary cortisol closely resembles the unbound, free concentration of cortisol in blood (Vining, McGinley, & Symons, 1983). Due to this passive diffusion of cortisol into saliva, there is a potential delay in the accurate representation of blood concentrations (Soto-Mendez et al., 2015). This may have implications for measuring the effects of cortisol change during rapid heat acquisition. Another factor of consideration is that the process of taking venous blood samples could increase stress and, therefore, cause an overestimation of results (Aardal-Eriksson, Karlberg, & Holm, 1998).

There are a few studies that analyzed the correlation between salivary cortisol and free blood cortisol. Poll et al. (2007) used oral swabs (a stimulated salivary collection method) as well as passive drool to collect saliva. There was a stronger correlation between the oral swab method and free serum cortisol ($r = 0.836$) than the passive drool method. These authors also used an ELISA method to determine the salivary cortisol concentration. They also determined the correlation between the oral swab method and total blood cortisol and found a strong and significant correlation ($r = 0.813$). Raff et al. (1998) also found that a correlation existed between blood free cortisol and salivary cortisol ($r = 0.86$, $P < 0.001$). These authors also used the stimulated oral swab method for salivary collection. Several additional studies have examined the correlation between salivary cortisol and total blood cortisol and have found a significant and positive correlation (Burke et al., 1985; Calixto, Martinez, Jorge, Moreira, Marinelli, 2002; Raff

& Trivedi, 2013; VanBruggen, Hackney, McMurray, & Ondrak, 2011; Wong, Yan, Donald, & Mclean, 2004).

2.4 Firefighting, Stress Response, and Hyperthermia

Chronic exposure to various stressors has been related to a higher risk of cardiovascular disease (CVD). One of the major responses to stress is dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis. Physical stress ultimately results in the increased presence of circulating cortisol (Gawel, Park, Alaghband-Zadeh, & Rose, 1979), which causes the mobilization of free fatty acids, decrease of growth and sex hormone levels, an increase in cardiac output and blood pressure, and a decrease in immune system response (Bjornthorp, 2001; Chrousos & Gold, 1992; Whitworth, Williamson, Mangos, & Kelly, 2005). The ultimate goal of cortisol is to bring the stressed body back to a state of homeostasis; however, issues arise when the body is in a state of chronic stress, which leads to chronically elevated cortisol. Chronically elevated cortisol has been linked to accelerated atherosclerosis and subsequent cardiovascular issues (Dekker et al., 2008). In addition to this, cortisol levels associated with stress have been related to anthropometric, endocrine, metabolic, and haemodynamic disturbances (Rosmond, Dallman, & Björntorp, 1998).

Stress has also been shown to have an effect on the sympathomedullo-adrenal (SMA) axis (Lutgendorf, Garand & Buckwalter, 2001). This pathway involves the release cytokines such as C-reactive protein (CRP), an acute phase protein released from the liver which increases its response following interleukin-6 (IL-6) secretion. IL-6 is an important pro-inflammatory cytokine. CRP is a sensitive marker in systemic inflammation, and chronically elevated values are an independent risk factor for cardiovascular disease in both children and adults (Cook et al., 2000; Ridker, Buring, Cook & Rifai, 2003). A link has been drawn between the HPA axis and

the SMA axis. It has been suggested that high concentrations or prolonged presence of inflammatory cytokines such as IL-6 stimulate the secretion of adrenocorticotrophic hormone (ACTH) from the pituitary gland and cortisol from the adrenal cortex (Nijm & Johansson, 2009).

Hyperthermia is a relevant stressor in several occupations, including firefighting, where workers are chronically exposed to acute heat stress. Firefighters wear very thick, multi-layered, cumbersome equipment. This personal protective equipment (PPE) is beneficial because it defends against environmental hazards and injury; however, the equipment is also detrimental in its limited permeability. The limited permeability of the PPE creates a microclimate with its own temperature and relative humidity. Rapid and uncompensable T_c acquisition may occur in this microclimate. Thermoregulation is hindered due to this microclimate while working in high ambient temperatures, high relative humidity, and extreme exertion (Cheung, McLellan & Tenaglia, 2000). Salivary cortisol is increased during simulated firefighting drills (Perroni et al., 2009). Additionally, it is known that passive heat stress significantly elevates cortisol levels in rats (Wang, Liu, Luo, Zhu, & Li, 2015) and humans (Follenius et al., 1982). It is also known that exercise in the heat increases plasma and serum cortisol levels when compared to exercise in a normothermic condition (Brenner, Zamecnik, Shek, & Shephard, 1997; Hoffman et al., 1996). Rapid and uncompensable T_c acquisition has not been compared to compensable T_c acquisition when analyzing the rate of salivary cortisol appearance. This comparison is essential as individuals who wear PPE and work in hyperthermic ambient environments may be in a unique and detrimental stress response situation.

Section 2

2.5 Haemodynamics and Passive Heat Stress

When the amount of heat gain outweighs heat loss, there is a net gain in core body temperature. Core/internal temperature gains of $\sim 3^{\circ}\text{C}$ above “normothermia” can severely strain physiological systems and can potentially lead to death (Bouchama & Knochel, 2002). Studies that use passive heat as a method of elevating core body temperature typically use one of three methods: water-perfused suits, warm water immersion of the entire body or legs only, or exposure to a warm environment using a climatic chamber. During passive heat studies, the objective is to elevate T_c by elevating skin temperature (Crandall & Gonzalez-Alonso, 2010).

Each method of passive heat exposure will cause T_c to increase via conductive heat exchange from the environment to the body, but the environmental influence varies. Water-perfused suits heat individuals by pumping hot water ($45 - 50^{\circ}\text{C}$) through a tube-lined suit; this elevates skin temperature to a range of $37-40^{\circ}\text{C}$ and T_c to as high as 40°C (Crandall & Wilson, 2015). This is an uncompensable method, in that the body is unable to maintain a thermal steady state (Cheung et al., 2000). Warm water full body immersion is most likely the quickest method of passive heat stress. Skin temperature rapidly equilibrates to the water temperature, and subsequently, the heat is rapidly transferred to the core. One major disadvantage to this method is the water-induced hydrostatic pressure which causes central displacement of the blood and ultimately diuresis (Crandall & Wilson, 2015). Lower body water immersion is a slower method of passively heating the body than whole body immersion but offers some distinct advantages over whole body immersion: There is less central blood displacement, which allows for a more natural thermal response. Additionally, electronic devices can be used on non-immersed skin. With this approach, areas of the body that are not exposed to water have increases in blood flow

via reflex vasodilation. The third method for increasing T_c is exposure to warm ambient temperatures where the entire body is exposed to a hyperthermal environment and warm air is inhaled throughout the warming process. This is a relatively slower method of T_c elevation in that it is compensable and therefore requires long periods of exposure to high ambient temperatures.

Passive heat exposure to elevate T_c causes a significant shift of blood volume from the central splanchnic region to the cutaneous circulation. Skin blood flow is estimated to increase from $\sim 300 \text{ ml min}^{-1}$ to $\sim 7500 \text{ ml min}^{-1}$ (Rowell, 1974; Rowell, 1986). This large shift of blood volume to the cutaneous region causes very significant reductions in central venous pressure: the blood pressure in the venae cavae near the right atrium of the heart. Crandall et al. found that heat stress caused a reduction in central venous pressure from 5.5 ± 0.7 to $0.2 \pm 0.6 \text{ mmHg}$ ($p < 0.001$). Along with this marked decrease in central venous pressure, they also found that there were large reductions in thoracic, heart, liver, and spleen blood volume (Crandall et al., 2008).

In order to mitigate the large decline in central venous pressure due to displacement of blood volume from central regions to the cutaneous circulation, there must be marked increase in cardiac output. Cardiac output can increase to as high as 13 L min^{-1} in pronounced passive heat stress (Rowell, 1986b). Cardiac output is primarily increased via increased heart rate, as stroke volume either does not change or is slightly increased in healthy, young, heat-stressed subjects (Crandall et al., 2008). An increase of 1.0°C in internal temperature in humans will increase heart rate by $7.15 \pm 0.19 \text{ bpm}$ (Johnson, 1992). Forty percent of increased heart rate due to heat stress in baboons was a result of increased cardiac temperature, while the other 60% was due to autonomic nervous system activity (Gorman & Proppe, 1984). Based on these studies, there are 2 major mechanisms that attribute to heat induced increases in heart rate: 1) direct effects of

temperature on cardiac nodal cells (sinoatrial and atrioventricular) and conduction velocity 2) autonomic effects on cardiac nodal cells and impulse propagation through the heart (Crandall & Wilson, 2015). Heat increases the phase IV slope of the cardiac action potential in nodal cells and shortens the action potential duration of both the sinoatrial and atrioventricular nodes. The slope of phase IV in nodal cells is necessary to increase membrane potential to trigger a subsequent depolarization (Strom, 1960; White, 2006). Elevated cardiac temperature increases the speed of delivering the pacemaker signal to adjacent cardiac myocytes; this is a result of temperature on gap junction conduction (Chen & DeHaan, 1993). Heat stress decreases cardiac parasympathetic response, which causes an increase in heart rate (Yamamoto, Iwamoto, Inoue, & Harada, 2007).

The decrease in central venous pressure due to the migration of blood to the cutaneous circulation along with a decrease in plasma and interstitial fluid volume from sweating causes a decrease in the preload of the heart. The tension created by the lengthening ventricular myocytes during the end-diastolic phase of the cardiac cycle equates to ventricular preload (Crandall & Wilson, 2015). The relationship between cardiac preload, force production, and stroke volume is known as the Frank-Starling relationship (Frank, 1895; Patterson & Starling, 1914). The Frank-Starling relationship states that an increase in left ventricular end-diastolic cross sectional diameter increases the ability of the left ventricle to produce force and stroke volume. Heat stress causes a leftward shift of the Frank-Starling hyperbolic curve: for a given reduction in ventricular filling pressure there is a greater reduction in stroke volume. One study (Wilson et al., 2009) confirmed this relationship between heat stress, left ventricular filling pressure, and stroke volume. They used pulmonary capillary wedge pressure to measure left ventricular filling pressure. This technique involves wedging a pulmonary catheter with an inflated balloon in the

pulmonary arterial branch. They found that heat stress shifted the operating point to a steeper portion of the Frank-Starling curve as opposed to normothermic conditions (Wilson et al., 2009). This explains how stroke volume does not decrease during passive heat stress conditions. If heat causes a leftward shift of the Frank-Starling curve, a decrease in pulmonary wedge pressure as seen during the Wilson and Crandall (2011) study would not have an effect on stroke volume. The presence of another variable, such as orthostatic challenge, could cause further decreases in preload and subsequent decreases in stroke volume.

As previously discussed, during heat stress there is a decrease in pulmonary wedge pressure which is representative of decrease in left ventricular preload. Coupled with this decrease is a contrary response in that there is no decrease in stroke volume and in some cases a slight increase during heat stress (Wilson, Cui, Zhang, Witkowski, & Crandall, 2002). The mechanisms which allow for the maintenance of stroke volume during heat stress are alteration in cardiac afterload and an increase in inotropy. Cardiac afterload is the systemic resistance in which the heart needs to overcome to eject blood. During passive heat stress, there is a decrease in mean pulmonary artery pressure (Wilson et al., 2007). This is coupled with a decrease in left ventricular wall stress during systole and an overall decrease in systemic vascular resistance (Crandall & Gonzalez-Alonso, 2010). These alterations in cardiac afterload allow for the maintenance or increase of stroke volume as there is less resistance for the heart to overcome to eject blood. In addition to the effects of afterload on the maintenance of stroke volume during passive heat stress, there is also evidence for an increase in inotropy. An increase in inotropy causes an increase in the force of cardiac muscle contractions. Two studies have shown through radionucleotide multi-gated acquisition and echocardiography data that there is an increase in ejection fraction during passive heat stress (Crandall et al., 2008; Wilson et al., 2009). In

addition, there is isovolumetric acceleration of the septal and mitral annulus (Brothers et al., 2009). Coupled with all of these factors showing positive inotropy, Nelson et al. observed an increase in left ventricular twist rates during passive heat stress (Nelson et al., 2010). These explain the maintenance or increase in stroke volume observed during passive heat stress.

2.6 Passive Heat Stress and Cerebral Circulation

Passive heat has a direct effect on cerebral perfusion. Transcranial doppler measures show a decrease in cerebral perfusion during passive heat stress (Brothers et al., 2009; Fan et al., 2008; Fujii et al., 2008). The degree to which cerebral perfusion is decreased is temperature dependent. Heat stress that results in an internal temperature increase of 0.5 to $\sim 1.2^{\circ}\text{C}$ has little to no effect on mean cerebral perfusion (Low et al., 2009; Wilson, Cui, Zhang, Crandall, 2006; Wilson et al., 2002); however, passive heat that elevates internal temperatures 1.5°C or more results in 20 – 30% reductions in mean cerebral perfusion (Fan et al., 2008; Fujii et al., 2008; Nelson et al., 2011; Ross et al., 2012).

The mechanisms by which passive heat stress decreases cerebral perfusion is not fully apparent, but some causes have been established. One cause of the decrease in cerebral perfusion during heat stress is perfusion pressure. An increase in internal temperature $\sim 1.5^{\circ}\text{C}$ reduces arterial pressure measured from the radial artery during passive heat stress (Ganio, Brothers, Lucas, Hastings, & Crandall, 2011). To mitigate the effects of decreased perfusion pressure, an adjustment occurs to increase vascular tone (Bain et al., 2013; Nelson et al., 2011; Ross et al., 2012; Wilson et al., 2002). Another explanation for the decrease in perfusion pressure during passive heat stress is heat stress induced hyperventilation, which decreases PaCO_2 . The internal temperature threshold where hyperventilation occurs and PaCO_2 begins to decrease is between ~ 1 and 1.5°C above normal temperature levels (Wilson et al., 2002). This decrease on PaCO_2 due

to hyperventilation continues as internal temperature increases (Fan et al., 2008; Fujii et al., 2008; White, 2006). Cerebral vasculature is very sensitive to these decreases in PaCO₂. Changes in PaCO₂ during passive heating may be the main contributing factor to decreased cerebral perfusion. There is a 2 – 4% decrease in cerebral perfusion for each 1 mmHg reduction in PaCO₂ (Ringelstein, Van Eyck, & Mertens, 1992). In addition to perfusion pressure and PaCO₂ influence on cerebral perfusion, sympathetic stimulation has also been postulated as a mechanism for decreasing cerebral perfusion. Evidence suggests that cerebral vasculature may be under the influence of sympathetic stimulation (van Lieshout & Secher, 2008). If this is the case, an increase in sympathetic activity in the brain would decrease cerebral perfusion via vasoconstriction.

2.7 Heat Stress and Exercise Haemodynamics

Passive heat stress alone causes significant cardiovascular adjustments to take place; combined heat stress and physical exercise can cause far-reaching challenges to the cardiovascular system. The greatest challenges exist for individuals who are untrained, unacclimated, and hypohydrated (Crandall & Gonzalez-Alonso, 2010). Trained distance runners exhibit a decreased physiological strain compared to untrained individuals during exercise in the heat (Piwonka, Robinson, Gay, Manalis, 1965). Some classic adaptations following heat acclimation are increased and earlier sweating response, decreased heart rate, decreased core and skin temperature, and decreased perceived exertion during exercise in the heat (Nadel, Pandolf, Roberts, Stolwijk, 1974; Rowell, 1974; Wyndham, 1973). At 5% hypohydration, termination of exercise due to volitional maximum occurred at a significantly lower T_c than while euhydrated (Rowell, Marx, Bruce, Conn, & Kusumi, 1966).

Some of the key effects on the cardiovascular system during moderate exercise in the heat are significantly lower stroke volume, central blood volume, aortic pressure, cardiac output, and an increased heart rate (Rowell et al., 1966). Rowell et al. (1966) found a 16% decrease in stroke volume and in central blood volume during moderate exercise in a high ambient temperature of 43.3°C as compared to the control values at 25.6°C. Additionally, they found that cardiac output decreased during the high ambient temperature trial by 1130 – 1240 ml.min⁻¹, and heart rate reached near maximal values in 3 of the subjects during the third out of four workloads. During moderate to severe exercise of short duration at high ambient temperatures, a repartitioning of cardiac output occurs rather than an increase. The fall in central blood volume and stroke volume was due to a redistribution of blood from the core to the periphery at the high ambient temperature of 43.3°C. They determined that the failure to provide adequate increments in cardiac output in these conditions is an important contributing factor limiting man's capacity to work in the heat. In another study, Rowell, Kraning, Kennedy, and Evans (1967) found that walking in a very hot environment caused cardiac output to increase over time due to increases in heart rate. From this, it can be assumed that the effects of exercise in the heat is intensity dependent.

The repartitioning of cardiac output during exercise between active limb muscle and skin perfusion has been widely investigated. It was suggested in early studies that blood flow to active muscles would decrease at the expense of elevated skin circulation for thermoregulatory purposes (Rowell, 1974). This would suggest that combined heat stress and exercise would cause the heart to not meet the joint blood requirements for active limbs and skin; however, a more recent study has shown that blood flow to active limbs and tissues is maintained during moderate exercise in the heat (Savard, Nielsen, Laszczynska, Larsen, & Saltin, 1988). Additionally,

cutaneous vasodilation is noticeably restrained during exercise in the heat as compared to resting levels in a hot environment (Johnson, 1992). This evidence, during submaximal exercise, would suggest to the contrary of the early studies which suggested a priority of blood flow to cutaneous circulation over active muscles during exercise in the heat. The question then arises as to the response of systemic circulation during maximal exercise in the heat. Intense exercise in severe heat stress conditions reduces VO_2max by accelerating the declines in cardiac output and mean arterial pressure that lead to decrements in exercising muscle blood flow, O_2 delivery, and O_2 uptake (Gonzalez-Alonso & Calbet, 2003). During the last 2 minutes of maximal exercise in the heat, there was no decline in leg or systemic vascular conductance despite the fact that arterial norepinephrine concentration increased over time which is indicative of enhanced sympathetic vasoconstrictor activity. This shows that fatigue and decrements in performance during maximal exercise in heat stress is associated solely with a lowering of systemic and skeletal muscle O_2 delivery, not with excess blood flow to the periphery. One explanation for the offset of the vasoconstrictor activity is that maximal exercise in the heat showed an enhanced accumulation of ATP in active legs, which is a strong vasodilator (Gonzalez-Alonso & Calbet, 2003; Van Ginneken, Meijer, Verkaik, Smits, & Rongen, 2004). This would assist in maintaining limb muscle vascular conductance.

When looking specifically at stroke volume during maximal exercise in the heat and in normothermic conditions, stroke volume fell further before exhaustion in normothermic conditions than before exhaustion in hyperthermic conditions (Gonzalez-Alonso & Calbet, 2003). In both trials during this study, it was determined that the last two minutes of fatiguing exercise resulted in a decline in mean arterial pressure, internal body temperature of $>39^\circ\text{C}$, and an almost-maximal heart rate. They concluded that decline in stroke volume could be related to

simple restriction in left ventricular filling time and left ventricular end-diastolic volume that accompanies severe tachycardia. Human studies have found that stroke volume was decreased during heat induced tachycardia (Fritzche, Switzer, Hodgkinson, & Coyle, 1999). Additionally, it could be possible that a small attenuation in myocardial perfusion-to-work relationship could lead to myocardial disfunction (Crandall & Gonzalez-Alonso, 2010). It can then be inferred that decline in stroke volume during the latter part of maximal exercise prior to exhaustion in hyperthermic and normothermic conditions can be attributed to restriction in left ventricular filling time, left ventricular end-diastolic volume, tachycardia, and potential blunting of myocardial oxygen supply (Crandall & Gonzalez-Alonso, 2010; Gonzalez-Alonso & Calbet, 2003).

2.8 Cerebral Circulation during Heat Stress and Exercise

The brain receives input from chemo-, mechano-, and barosensitive sensory endings throughout the body to divert the majority of systemic O₂ to working skeletal muscle at an enhanced perfusion pressure (Gonzalez-Alonso et al., 2004). Left common carotid artery and left internal carotid artery blood flow increases by 33% and 17%, respectively, during moderate exercise. Additionally, middle cerebral artery blood velocity (MCA V) increases by 14% during moderate exercise (Hellstrom, Fischer-Colbrie, Wahlgren, & Jogestrand, 1996). As exercise continues to volitional maximum, there is a decreasing effect on middle cerebral artery mean blood velocity (MCA V (mean)). Nybo and Nielsen (2001) showed that the prolonged moderate exercise in the heat until volitional maximum caused a marked reduction in MCA V(mean) by 26 +/- 3 %.

Maximal exercise has a more intense effect on cerebral blood flow. After the first 90 seconds of maximal exercise with or without heat stress, there is a decrease in left and right

MCA V. This is accompanied by an increase in brain extraction of O₂, glucose, and lactate (Gonzalez-Alonso et al., 2004). There was a 45% increase in brain extraction of O₂ following the first 90 seconds of maximal exercise; this signifies that, although cerebral perfusion is declining following the first 90 seconds of maximal exercise, there are mechanisms in place to maintain brain function and metabolism. The physiological repercussions of reductions in brain perfusion are largely met by the brain's large oxygen reserve as one approaches exhaustion.

The critical question that arises is what causes the decreases in brain blood flow during maximal exercise. During orthostatic challenge, MCA V (mean) declined drastically when arterial and central venous pressures were decreased (Van Ginneken et al., 2004). Additionally, MCA V (mean) decreases with heat stress during submaximal exercise; this happens in parallel with the drop in arterial and venous pressures during heat (Gonzalez-Alonso et al., 2004). Therefore, the drop in MCA V (mean) and cerebral perfusion that occurs during maximal exercise can most likely be attributed to a decline in arterial and central venous pressures. Studies have examined the effect of cardiac output on cerebral perfusion because a decrease in cardiac output by cardioselective β_1 -adrenergic blockade has been associated with a reduction in MCA V (mean); however, during maximal exercise, cardiac output increased when MCA V (mean) decreased (Ide, Pott, van Lieshout, & Secher, 1998). Another scenario for decreased cerebral perfusion during maximal exercise with or without heat has been proposed: local factors reduce vasodilation and increase vasoconstriction in brain vessels during maximal exercise. This was debunked though because both the potent vasodilator ATP in the jugular vein and the uptake of catecholamines by the brain increase on exhaustion during maximal exercise (Gonzalez-Alonso et al., 2004). It seems that the most viable explanation for the decrease in cerebral

perfusion during maximal exercise is associated with a decrease in arterial and central venous pressures.

2.9 Haemodynamics of Uncompensable Heat Stress

Various athletic and occupational settings require the use of personal protective equipment (PPE) to protect an individual from environmental hazards or from injury. When PPE is used in warm or hot environments, there is the potential for uncompensable heat stress: a state where the evaporative capacity of the immediate external environment is less than the evaporative dissipation necessary to maintain heat balance (Cheung, McLellan, Tenaglia, 2000).

During periods of heat stress, a large portion of circulation is diverted to the cutaneous region in order to allow for rapid dissipation of heat. Whole-body and local heat stress cause attenuated cutaneous adrenergic vasoconstrictor responsiveness (Wilson & Crandall, 2011). This allows for increased vasodilation of the cutaneous circulation in order to allow for a greater portion of blood flow to reach the periphery. This increased cutaneous circulation allows for increased conductive/convective heat exchange to the periphery and provides increased potential for elevated fluid in the interstitial spaces for the purposes of sweating and evaporative heat exchange. A large problem occurs when evaporative heat loss is restricted due to high ambient temperature, relative humidity, or the wearing of PPE. The potential for evaporative heat loss is determined by the water vapour pressure gradient between the human body and the external environment. High relative humidity can largely disturb the ideal water vapour pressure gradient and cause a large degree of heat storage. All indices of heat strain are elevated when ambient water vapour pressure increases from 1.1 to 4.8 kPa during both light and heavy exercise (McLellan, Pope, Cain, & Cheung, 1996). PPE has been shown to increase energy cost of physical performance causing increased metabolic heat production and increase the risk of

overheating (Duggan, 1988). PPE creates a microenvironment: the initial environmental layer that the body interacts with upon heat dissipation (Cheung et al. 2000). This microenvironment has its own thermal characteristics of temperature and humidity through which metabolically generated heat must pass through before being dissipated to the ambient environment (Sullivan & Mekjavic, 1992). Elevation in metabolic heat production and a decrease in evaporative efficiency due to PPE hinders heat dissipation and T_c acquisition becomes apparent.

2.10 Cerebral Haemodynamics during Uncompensable Heat Stress

There has been no research for the effects of rapid and uncompensable heat stress on cerebral haemodynamics; although, there is data to show a decrease in cerebral blood flow during both passive heat stress (Brothers et al., 2009; Fan et al., 2008; Fujii et al., 2008; Nelson et al., 2011; Ross et al., 2012), prolonged moderate exercise in the heat (Nybo & Nielsen, 2001), and during maximal exercise in the heat (Gonzalez-Alonso et al., 2004). Studies using extreme heat stress scenarios have found that cerebral haemodynamics are largely affected. Kao et al. (1994) induced heat stroke in rats and found that there was very significant drop in local cerebral blood flow (~ 40% decrease). This could lead to ischemic injury of brain tissue. Additionally, they found an increase in hypothalamic dopamine release. Brain dopamine decreases brain neuronal damage resulting from ischemic injury. The large decrease in brain blood flow that occurs in extreme cases of hyperthermia may cause neuronal damage, which could have implications for the decision-making process. Rapid and uncompensable T_c acquisition could have increased detrimental effects on cerebral oxygenation and haemodynamics when compared to compensable scenarios.

2.11 Near-infrared Spectroscopy

Near-infrared spectroscopy (NIRS) started with a publication by Frans Jobsis in 1977 (Jobsis, 1977). The purpose of NIRS is to measure cerebral and muscle oxidative metabolism in a non-invasive fashion. The basis of NIRS is the differential absorption properties of various chromophores in the near-infrared range of 700-1000 nm (Neary, McKenzie, & Bhambhani, 2002). The two chromophores of interest in cerebral and muscle metabolism measurements are oxygenated haemoglobin (HbO₂) and deoxygenated haemoglobin (HHb). HbO₂ absorbs near-infrared wavelength's around 850 nm and HHb absorbs near-infrared wavelengths around 760 nm. From the differential absorbency patterns of HbO₂ and HHb it is possible to infer the oxidative status and blood volume changes in muscle and brain tissue during exercise and during standardized motor and cognitive tasks (Neary et al., 2008).

Section 3

2.12 The Basis of Decision-Making

Any decision, whether it be simple or complex, is an attempt to maximize rewarding outcomes or utility (Mill, 1879). The study of decision-making attempts to understand one's ability to process multiple alternatives and ultimately choose an optimal decision or course of action (Sanfey, 2007).

Decision making theories have traditionally fallen into two major categories: economic theories and reinforcement learning theories. Economic theories of decision-making assign values to alternatives such that one choice has more value than others; this choice is made solely in an attempt to maximize utility. This is a very agnostic approach to decision making (Lee, Seo, & Jung, 2012). The reinforcement learning theory is a computational approach which emphasizes learning by direct interaction with the environment. There is no reliance on

exemplary supervision or models of the environment in which they inhabit. RL theory proposes that each action has a value based on the predicted reward or punishment. The learner is never told which actions are to be taken, but they must navigate various actions and determine that which yields the greatest reward (Sutton & Barto, 1998; Rescorla & Wagner, 1972). One of the defining characteristics of this theory of learning and decision-making is the idea of prediction error: the discrepancy between the actual and predicted value of the reward or punishment (Krigolson, Hassall, & Handy, 2014). This discrepancy diminishes over the course of the learning process, and the predicted value of the reward or punishment begins to resemble the actual reward or punishment as learning progresses. For example, someone with no prior knowledge is presented with two choices (A and B). Their previous knowledge would cause them to give equal value to the choices. If they choose A and are rewarded, they assign a new increased value to the choice A. If they are presented with this choice multiple times and choose A every time and are rewarded every time, they will continually add value to choice A. Ultimately, the predicted value of A will represent the actual value of A. Not only does the value of the choices increase or decrease, but the actual choice state value itself changes. Assume that the choice between A and B is represented as choice state X. As the value of choice A increases, the value of choice state X also increases. Early in the learning process, the prediction errors occur at the time of the actual reward being given. After learning, the prediction error occurs once presented with choice state X as choice state X now has increased value. When monkeys are initially given a reward there is a phasic increase in the firing rate of dopaminergic neurons in the substantia nigra pars compacta. If the monkeys' reward is consistently paired with a predictive stimulus, the phasic increase in dopamine firing rate diminishes over time, and it is

ultimately associated with the presentation of the predictive stimulus (Schultz, Dayan, & Montague, 1997).

Economic models of decision-making do not hold much value based on the fact that humans use two cognitive systems to think and make decisions. System 1 works easily and automatically making judgements based on patterns that are familiar. An example of system 1 would be one's reaction to a disturbing image. Alternatively, System 2 takes more effort; this system requires intense focus and tends to operate methodically (Kahneman, 2011). System 2, for example, would be used when solving a difficult math problem or learning a complicated movement in sport. There is interaction, exchange, and collaboration between the two systems. Humans mostly live in a System 1 world; we typically rely on fast processing as it is very efficient. When one needs to focus and think intensely about something, they will switch to System 2. One great example of these two systems working together is when trying to solve a skill-testing question like $(2 \times 4) + (3 \times 10)$. System 1 would compute the obvious answers: 2×4 and 3×10 . Most adults can easily compute those answers to be 8 and 30. When solving the equation as a whole, one will typically move into System 2 processing. The system that one uses also depends on the amount of effort necessary. For example, if someone is driving on a known route and listening to music, they will mostly operate in System 1. If they change to an unknown route, they will move into System 2 in order to navigate appropriately. If they feel like they may be lost, it is not uncommon to turn the music off as all of their processing will require intense effort. The nervous system requires more glucose than most other parts of the body. Effortful mental activity, as which would occur if one is lost while driving, will require exponentially more glucose than non-effortful mental activity (Gailliot & Baumeister, 2007).

Not only do humans think and make decisions using two systems, but it has been proposed that humans operate with two “selves:” the “experiencing self” and the “remembering self.” The “experiencing self” lives one’s life in the moment, while the “remembering self” recalls past experiences, learns lessons from them, and makes decisions about the future based on those past experiences. These “selves” are constructed by the two mental systems discussed earlier. Mental System 1 is intertwined with the “experiencing self,” while mental System 2 constructed the “remembering self” (Kahneman, 2011). The whole duality of the two mental systems and selves refutes the possibility of the economic theory of decision-making. People do not always act rationally and choose the option that optimizes utility in all cases. The economic theory of decision-making diminishes the fact that humans are not robots and rely on several factors when thinking and making decisions. Emotions and cognition both guide thinking and decision-making (Camerer, Loewenstein, & Prelec, 2005).

Experimental economics, and more specifically game theory, additionally supports the idea that humans do not always think and make decisions by acting rationally. Most experimental studies of decision-making have examined choices with clearly defined probabilities and outcomes; this discounts the fact that we live in a social environment and that most of our decisions are made within the context of social interaction (Sanfey, 2007). Game theory is an assortment of models that seek to understand scenarios where individuals interact with each other (von Neumann & Morgenstern, 1947). Most game theoretical analyses assume that players are rational and self-interested. It is assumed that players will make decisions based on the Nash equilibrium which states that players will make decisions in which no player can increase his or her own payoff unilaterally (Nash, 1950). One great example of this is in the Prisoner’s Dilemma game (PDG) (Sally, 1995). The PDG states that two players reside in

opposite cells in prison and receive the same offer from a public prosecutor. If each of the prisoners confesses to the crime and betrays their fellow inmate, they will both get 10 years in prison. If one confesses and betrays while the other stays quiet, the snitch will go free, and the other will go to prison for life. If both prisoners remain quiet, they will both receive one year in jail. In the case of the PDG, the Nash equilibrium assumes that both prisoners will confess and betray resulting in the 10-year sentence for each. The best scenario would occur if both prisoners remained silent or exhibited mutual cooperation as opposed to mutual defection. The Nash equilibrium assumes that both players will attempt to get the best possible scenario for themselves at the expense of the other; although, it has been generally observed in many game theoretical scenarios that decision makers are generally less selfish and strategic than the Nash equilibrium suggests. Game players seem to value social factors such as reciprocity and equity (Sanfey, 2007).

A meta-analysis of 35 years of published experiments testing decision making in prisoners' dilemmas has shown that a model of pure self-interest is incongruent with the results of experimental decision-making (Sally, 1995). Another example of this inconsistency with the Nash equilibrium prediction is in the Ultimatum game (UG) (Guth, Schmittberger, & Schwarze, 1982). In the UG, two players must divide a sum of money with the proposer indicating the division of money. If the responder accepts the offer, the money is divided as proposed. If the responder rejects the offer, both parties receive nothing. The Nash equilibrium predicts that the responder and the proposer are motivated by self-interest; therefore, the responder will accept any offer, and the proposer will offer the smallest non-zero amount. Actual results from the UG indicate that the modal offer is a 50-50 split. Additionally, offers of 20% or less are rejected about 50% of the time (Guth et al., 1982). These examples provide further evidence for the

disproval of economic theories of thinking and decision-making and support reinforcement learning and decision-making theories.

2.13 The Neuroanatomy of Decision-Making

The cognitive process is extremely important; approximately 40% of deaths are associated with decision-making deficits at the most basic level of self-regulation (Schroeder, 2007). Although a formal decision making network has not been established, there are models that have been proposed. Wallis suggests that decisions are made using interactions within the prefrontal cortex, which is a higher order cortical area, as well as interactions between the prefrontal cortex and subcortical regions. The major structures of the prefrontal cortex involved in the decision making process are the orbitofrontal cortex (OFC), anterior cingulate cortex (ACC), and dorsolateral prefrontal cortex (DLPFC). The OFC has very rich “limbic system” connections, and it has been suggested that it plays a key role in processing reward as it integrates many sources of information regarding the reward outcome to calculate a value signal (Wallis, 2007). The medial portion of the OFC monitors and decodes rewards, whereas the lateral portion evaluates punishment (O’Doherty, Kringelbach, Rolls, Hornak, & Andrews, 2001). The DLPFC is necessary when making decisions that require evaluation of multiple sources of information. The DLPFC is also involved in maintaining and manipulating information in the working memory (Krawczyk, 2002). Lastly, the ACC along with the ventral cingulate cortex is involved in sorting among conflicting options and signalling outcome relevant information (Krawczyk, 2002). In regards to a particular decision, the OFC assigns a value to a specific reward; the DLPFC then uses this information to construct a plan for the reward; the ACC then evaluates the likelihood of success for the plan generated by the DLPFC (Wallis,

2007). The prefrontal cortex is associated with long term outcomes such as value assessment, emotion, self-control, preferences, and cognition (Johnstone, Wallestedt, & Silva, 2013).

While the prefrontal cortex is associated with long term outcomes, subcortical structures are associated with outcomes that are more immediate. All prefrontal areas that are involved in the decision-making process send projections to the caudate nucleus/putamen through the subcallosal fasciculus of Muratoff or the external capsule (Schmahmann & Pandya, 2006; Schmahmann, Smith, Eichler, & Filley, 2008). These structures, as well as various other important decision making structures, are associated with an area of the brain known as the basal ganglia (BG): a group of subcortical nuclei that are responsible for motor control, motor learning, executive functions and behaviors, and emotions (Lanciego, Luquin, & Obeso, 2012). The BG system is specialized to slowly integrate positive and negative outcomes over many trials, which results in the instilling of motor habits. The system uses a Go/No-Go signaling procedure for learning; it implements a go signal when the responses generally lead to positive outcomes and a no-go signal when the outcome will be negative (Frank & Claus, 2006). The go and no-go signals are associated with two pathways, or projections, through the BG: direct and indirect pathways. The direct and indirect pathways involve a dopamine projection, which differentially modulates the go and no-go cells, from the substantia nigra to the dorsal striatum. The go cells express the D₁ receptor, and the no-go cells express the D₂ receptor. These have different effects on the thalamus and the premotor cortex. The go cells facilitate the execution of a response considered in the cortex, while the no-go cells suppress competing responses.

The interaction between the BG and the prefrontal cortex can be explained by the top-down biasing that occurs via the prefrontal cortex on the BG. For example, the medial and lateral areas of the OFC store the positive and negative outcomes of decisions, respectively. The OFC

actively maintains the information from the BG in terms of positive and negative outcomes in working memory. These OFC areas then have a top-down biasing effect on the response selection process of the BG (Frank & Claus, 2006). The BG incorporates slow learning to make decisions based on the frequencies of positive versus negative reinforcement. When decisions become more complicated, representations in the OFC are necessary to provide top-down biasing on decision outputs. The BG system is a more primitive system, while the prefrontal cortex is part of the neocortex and is associated with higher level functions.

2.14 Functional Neuroanatomy of Perceptual Decision Making

Perceptual decision-making is an area of cognition in which sensory information provides the basis for the choice of one or many actions. Perceptual decision-making is relevant to occupations working in extreme circumstances where rapid decision-making is necessary due to various sensory stimuli; the field of firefighting is especially relevant to this concept. In 2007, there was a large fire in Edmonton, Alberta, Canada; the fire spread very rapidly due to building codes that allowed the use of lightweight construction. Eighty firefighters and 20 apparatus responded to the blaze in the first 20 minutes. The fire consumed 149 condominium suites and 78 duplexes. This situation would require perceptual decision-making.

The functional anatomy of perceptual decision-making involves various brain structures. One model, which was described during a study by Kayser, Buchsbaum, Erickson, & D'Esposito (2010), suggests a simple model in which motion information from the primary visual cortex is extracted by the middle temporal complex and transformed in the intraparietal sulcus; there is top down control of these signals from areas such as the middle frontal gyrus. The possible responses/decisions are then reduced by various structures, such as anterior insula and anterior cingulate cortex, that are related to task set, uncertainty, and/or conflict (Botvinick, 2007;

Dosenbach et al., 2006; Grinband, Hirsch, & Ferrera, 2006). Ultimately, this information is brought to motor structures, such as the premotor cortex, for action production. Another model was proposed by Heekeren et al. (2008) which computes a decision variable by accumulating and comparing sensory evidence. The sensory evidence moves from visual cortex areas, such as the fusiform face area and the parahippocampal place area, to areas that compute a decision variable, such as the DLPFC of the prefrontal cortex. In this particular model, the system that represents decision variables extends to the motor and premotor structures; this is a simple progression from perception to action. There is also a subsystem that operates alongside this progression in a heterarchical manner that detects perceptual uncertainty or difficulty. This system includes structures such as the anterior insula and the inferior frontal gyrus and signals when more attentional resources are needed to process a task effectively. In addition to this subsystem, Heekeren et al. also suggests that there is a subsystem that monitors performance. This performance subsystem uses the posterior medial prefrontal cortex to detect when errors occur and when alterations are needed to increase performance (Heekeren, Marrett, & Ungerleider, 2008).

2.15 Prefrontal Cortex and Cognitive Control

The prefrontal cortex (PFC) plays an important role in cognitive control. Endogenously generated motor responses and exogenously generated responses cause a pattern phase reset and an increased power signal in midfrontal sensors during EEG measurement. This signal is mostly represented in the frontal theta band (Cavanagh & Frank, 2014) which demonstrates the PFC relationship to adaptive control. Additional studies using electroencephalography (EEG) demonstrate the possibility to measure the engagement of cognitive control processes within the prefrontal cortex (Cohen & Van Gaal, 2012; Van Driel, Ridderinkhof & Cohen, 2012; Wessel &

Aron, 2013). In particular, power in the theta frequency band appears to be related to the engagement of cognitive control. Generic and reactive medial PFC processes are represented by theta band activities (Cavanagh, Zambrano-Vazquez & Allen, 2012). Theta synchronization has been proposed to act in organizing decision points. More specifically, it has been proposed to play an important role in the selection of a choice during goal-directed behavior (Womelsdorf, Vinck, Leung, & Everling, 2010). Frontal midline theta has been suggested to play an important role in implementing control during an array of scenarios (Cavanagh & Frank, 2014). Theta dynamics are enhanced following events that require increased cognitive control (Cavanagh et al., 2012).

2.16 Decision-Making Neuroanatomy and the Effects of Heat Stress

Hyperthermic conditions affect several areas of the brain. A single hyperthermic event may cause short term neurological and cognitive dysfunction, which may become prolonged (Walter & Carraretto, 2016). Cognition can be attributed to mental abilities and processes: memory, knowledge, attention, reasoning/decision making, problem solving, and comprehension (Walter & Carraretto, 2016). Hyperthermia has a negative effect on attention (Sun et al., 2012), memory (Racinais et al., 2008), processing of information (Sun et al., 2011), and decision-making (Cheema & Patrick, 2012).

Functional neuroimaging has shown that many cortical and subcortical structures associated with the cognitive processes described above are adversely affected by heat stress. For the sake of this section, the focus will be on the structures that are associated with decision-making.

Cerebellar dysfunction is the most predominant condition mentioned and discussed in relation to heat stress and brain function. Most research on cerebellar dysfunction is associated

with extreme hyperthermia resulting in heat stroke. The cerebellum plays a major role in the decision making process, specifically the neo-cerebellum which monitors the consequences of actions (Blakemore et al., 2001). The cerebellum is particularly intolerant to the effects of heat stress; the most common neuropathological issue due to heat stress is the loss of purkinje cells associated with heat shock protein 70 expression (Bazille et al., 2005). Heat shock response is an indicator of central nervous system cells undergoing stress (Nowak, Osborne, Suga, 1993). Heat shock proteins play a role in the folding, assembly, and transport of proteins, as well as, preventing the aggregation of mis-assembly of nascent or denatured peptides (Polla et al., 1993). Heat shock protein-72 (HSP-72) rapidly responds to a variety of stresses which include hypoxia, ischemia, acidosis, energy depletion, cytokines such as tumor necrosis factor- α (TNF- α), ultraviolet radiation, and thermal stress (Kregel, 2002).

Several pathways/connections are acutely affected in hyperthermia. Sun et al. (2013) identified several changes in connectivity correlations. They showed a total of 65 disturbed functional connectivities during the hyperthermia trial (50°C for one hour) compared to the control trial (25°C for one hour). Of these 65 disturbed functional connectivities, 50 of them were decreased, and 15 were increased. The decreased correlations mainly involved the medial orbitofrontal cortex, temporal lobe, and occipital lobe, while the increased correlations mainly involved the areas of the “limbic system.” In addition to the findings by Sun et al. (2013), studies show that hyperthermia causes increased activity in the DLPFC (Jiang et al., 2013), which plays a major role in the decision making process. In terms of persisting effects after hyperthermia, damage has been reported in the cerebral cortex and the basal ganglia (Biary, Madkour, & Sharif, 1995).

2.17 Heat Stress and Neural Function

There has been very limited research done to analyze the effects of heat stress of any mode on neural function. Studies evaluating the effects of environmental heat stress have demonstrated that the brain is very vulnerable to heat stress and that there is a graded effect based on the magnitude and severity of the heat stress. Total electroencephalogram (EEG) spectrum changes during passive heat stress are in proportion to the rise of T_c up to $\sim 41.8^\circ\text{C}$. There is an inverse relationship between total EEG activity and passive and uncompensable T_c acquisition (Dubois et al., 1980). Additionally, neural function is affected by exercise accompanied by heat stress. Neilsen, Hyldig, Bidstrup, Gonzalez-Alonso, and Christoffersen (2001) used a water-perfused jacket to elevate T_c during exercise at 60% of $\dot{V}O_{2\text{ max}}$ and found that the α/β index was significantly elevated, reflecting suppressed arousal, during exercise in a hot (42°C) environment. No studies have evaluated the effects of heat stress on neural function during a decision-making task.

2.18 Heat Stress and Decision-Making Performance

There is very limited research available that has specifically investigated the effects of heat stress on decision-making performance. It is accepted and well supported that hyperthermia has a detrimental effect on cognition (Cheema & Patrick, 2012; Racinais et al., 2008; Stubblefield, Cleary, Garvey, & Eberman, 2006; Sun et al., 2012). A meta-analysis of performance response under thermal stressors demonstrated that thermal stress causes individuals to reallocate attentional resources to appraise and cope with the thermal threat. This reduces one's ability to process task-relevant information (Hancock, Ross, & Szalma, 2007). Hyperthermia has a negative effect on response speed and processing speed (Stubblefield et al., 2006); this may limit one's ability to make rapid decisions. In occupations such as firefighting,

these may be life and death decisions. Studies related specifically to the effects of heat stress on decision-making report a negative effect. Warm temperatures deplete resources, increase system 1 processing, and have a negative impact on performance during complex choice tasks (Cheema & Patrick, 2012). No studies can be found examining the effects of uncompensable heat stress on decision-making.

2.19 Summary

There is a lack of information regarding the effects of rapid thermal acquisition resulting from uncompensable heat stress on cerebral oxygenation and haemodynamics (pre-frontal cortex). The research to date has analyzed the effects of compensable heat stress on cerebral blood flow and oxygenation. This is important to evaluate, as this differentiates between PPE-related occupational heat stress and compensable heat stress. There is limited research available analyzing the effects of compensable heat stress on neural function and decision-making performance but none that analyzes the effects of rapid and uncompensable T_c acquisition. Lastly, there is a lack of information regarding the effects of rapid and uncompensable thermal acquisition on cortisol secretion. It is well known that heat stress increases cortisol production (Follenius et al., 1982; Brenner et al., 1997), but the differentiating effect of rapid and uncompensable heat stress on cortisol production is unknown. This missing information is necessary to fully understand the effects of PPE in hyperthermic conditions.

It is important to distinguish between rapid and uncompensable T_c acquisition and more gradual, compensable T_c acquisition. Research to date has, for the most part, assumed that T_c acquisition is T_c acquisition and that the body behaves similarly at set core temperatures regardless of the rate at which the thermal acquisition occurs. The following research provides valuable information related to the effects of rapid and uncompensable T_c acquisition on the

human body. The results of this research will have far-reaching impacts on occupations that work in extreme hyperthermic conditions where rapid thermal acquisition is a reality.

CHAPTER 3: METHODS

3.1 Participants

Fourteen healthy male adults participated in this study. Mean $\pm$ 95% CI were reported for age, height, body mass, and $\text{VO}_{2\text{max}}$. Participants were between the ages of 20 and 53 years of age (33.6 ± 12.1 years). The subjects had a mean height of 180.8 ± 7.6 cm, a mean pre-exercise body mass of 84.3 ± 9.2 kg, and a mean $\text{VO}_{2\text{max}}$ of 52.3 ± 5.9 ml $\text{kg}^{-1} \text{min}^{-1}$. The participants were considered to be healthy and had no barriers to physical activity based on the Physical Activity Readiness Questionnaire (PAR-Q). Additionally, it was determined that the participants did not have esophageal constriction which could contribute to inability to swallow a Tc capsule (VitalSense, Health Canada License # 70240). The Human Research Ethics board at the University of Victoria approved this research study, and each participant provided written informed consent.

3.2 Preparation and Questionnaire

Following recruitment and confirmation of the inclusion criteria, participants were scheduled their testing sessions; this began with scheduling the initial VO_2 max testing session followed by the other two experimental testing sessions. All testing took place at the University of Victoria. Upon arrival to the initial VO_2 max session, the experimental procedures were explained to each participant verbally by the principal investigator. Following the explanation, the subjects filled out and signed the Par-Q form (Appendix 1), signed the written consent form (Appendix 2), and filled out the Ingestion of a Core Temperature Capsule safety screening form (Appendix 3).

Prior to any testing, the subjects were informed of the pre-testing protocol needed to standardize the results. This pre-testing protocol had the subjects refrain from caffeine, alcohol,

and nicotine 12 hours prior to testing. In addition to this, the subjects followed a pre-testing dietary protocol. The subjects drank at least 3.7 liters of water in the 24-hour period prior to testing and also drank at least 500 ml of water 2 hours prior to the testing protocol (Convertino et al., 1996). They were also instructed to eat their last meal a minimum of 2 hours prior to the test. In addition to this, the two experimental testing sessions were scheduled for the same time of day to maintain consistency and to limit the potential diurnal effects. Lastly, all subjects voided their bladders 30 minutes prior to testing.

3.3 Study Design

Upon arrival to the laboratory, the subject's anthropometric values were measured. Height was measured using a stadiometer (Tanita, USA). Body mass was measured pre- and post-exercise on a weigh scale (Health-o-meter, Continental Scale Corporation, USA). Following the measurement of the descriptive data variables, the subjects were fitted with the Equivital Integrated physiological monitoring system for heart rate (HR) measurement. They were also given a Jonah Tc capsule (VitalSense, Health Canada License # 70240) to ingest for real-time Tc observation and analysis. The Jonah Tc capsule was ingested 40-45 min prior to exercise testing; this time period allowed for the Tc capsule to read roughly 37°C. The starting Tc was $37.0 \pm 0.2^{\circ}\text{C}$ in the control session (CON) and $36.9 \pm 0.2^{\circ}\text{C}$ in the experimental session (PPE). To increase thermal acquisition, the laboratory was kept at an ambient temperature of 25 – 26°C in both CON and PPE.

The design of the experiment was crossover and true experimental in nature with the fourteen subjects acting their own control. Each participant was required to come to the laboratory three times. The first session was an initial maximal oxygen consumption ($\text{VO}_2 \text{ max}$) test; this was used as a determinant of fitness status. Any subject with a relative $\text{VO}_2 \text{ max}$ of less

than $35 \text{ ml kg}^{-1} \text{ min}^{-1}$ was excluded from participation. The second and third sessions were CON and PPE and were assigned in random order. CON and PPE were separated by a minimum of 24 hours. During both CON and PPE EEG data was collected pre-exercise and post-exercise during a Go/No-Go test. The analysis of the EEG data was done in the neuroeconomics laboratory at the University of Victoria. The protocol of CON and PPE included two 10-minute rest periods lying in the supine position before and after a treadmill graded-exercise protocol. The participants wore shorts, t-shirt, socks, and running shoes in the CON (Figure 3.1) and firefighter PPE in the PPE (Figure 3.1). Participants wore shorts and a t-shirt during the rest periods in both CON and PPE. During the CON, participants wore a backpack with mass equal to the mass of firefighter PPE. The backpack (CON)/firefighter PPE (PPE) was added following the initial 10-minute rest period and removed prior to the final 10-minute rest period. Participant descriptive data were obtained before the initial 10-minute rest period and after the final 10-minute recovery period. Assessment of both left and right PFC oxygenation status was measured using near infrared spectroscopy (NIRS) probes (Artinis Medical Systems). NIRS was used to monitor PFC tissue oxygenation and haemodynamic changes. The NIRS probes were worn during all aspects of the testing. In addition to this, metabolic variables were monitored using a metabolic cart (Parvomedics, USA) during the treadmill graded-exercise protocol. All participants completed a standard Go/No-Go task following the initial 10-minute rest period and prior to the final rest period while EEG data were recorded via a MUSE headband. The MUSE EEG headband has been validated as an efficient measure of EEG (Krigolson, Williams, Norton, Hassall, & Colino, 2017). This was done so that the subjects would complete the Go/No-Go test right before and immediately following the graded-exercise protocol. The Go/No-Go test protocol allowed for the best representation of immediate pre- and post-exercise values. The treadmill graded-exercise

protocol included an initial 5-minute stage at 3.5 mph and a 0% grade, the second stage was 5-minutes at 3.5 mph at 4% grade, the third stage was 50-minutes at 3.5 mph and an 8% grade, and the final stage was 1-hour at 3.5 mph and a 12% grade. Treadmill graded-exercise protocol was terminated at the onset of any of the following three termination criteria: (1) core-temperature reached 39.5°C (2) the subject reached a volitional maximum (3) the subject reached the 2-hour time limit. Volitional maximum in this study was defined as the inability of the subject to maintain exercise intensity and thereby voluntarily stepping off of the treadmill.

3.4 Measured Experimental Parameters

Table 3.1.

Experimental parameters, instrumentation, and points of data collection

Parameters Measured	Instrument for Collection and/or Analysis	Points when Collection took Place
Salivary Cortisol Analysis	Salivary Cortisol ELISA Kit; SalivaBio Oral Swab (Salimetrics, LLC)	At each 0.5°C Increase in Tc
Height (cm)	Stadiometer (Tanita, USA)	Pre-Exercise
Body Mass (kg)	Health-o-meter, Continental Scale Corporation (USA)	Pre-, and Post-Exercise
Tc (°C)	Equivital Integrated Physiological Monitoring System and Jonah Tc capsules (VitalSense, Health Canada License # 70240)	Continuous
HR (bpm)	Equivital Integrated Physiological Monitoring System	Continuous
TS	9-point thermal sensation scale	At each 0.5°C Increase in Tc
TCS	5-point thermal comfort scale	At each 0.5°C Increase in Tc
RPE	8 - point rating of perceived exertion scale	At each 0.5°C Increase in Tc
Ventilatory Variables (VO ₂ , VCO ₂ , VE, RER)	Metabolic cart via a regulator (Parvomedics, USA)	Continuous
Pre-frontal Cortex Brain Oxygenation (TSI%, HbO ₂ , tHb, HHb, HbDiff)	Near-Infrared Spectroscopy (NIRS) monitor (Portalite, Artinis Medical Systems BV, The Netherlands; Oxysoft version 2.1.6)	At each 0.5°C Increase in Tc
Electroencephalography (EEG)	MUSE (Interaxon Inc., Canada)	Pre-, and Post-Exercise
Perceptual Decision-Making Performance	Go/No-Go Test (Peer Analytics)	Pre-, and Post-Exercise

Anthropometric measures

Height was measured upon arrival to the laboratory using a stadiometer (Tanita, USA). Body mass was measured pre- and post-exercise on a weigh scale (Health-o-meter, Continental Scale Corporation, USA).

Core Temperature

T_c was monitored every 30 seconds using the Equivital Integrated Physiological Monitoring System. T_c was directly measured from the ingested Jonah T_c capsules (VitalSense, Health Canada License # 70240). Measurement from this system was used to verify all T_c measurement points including the termination criterion of T_c 39.5°C.

Heart Rate

HR (bpm) was continuously measured with an Equivital Integrated Physiological Monitoring System. HR data was used for safety purposes and to understand the state of the cardiovascular system. HR was also used to monitor pre-testing status, exercise intensity, exertion, and post-exercise recovery status.

Ventilatory variables

Participants were connected to the metabolic cart via a regulator which sampled expired air from the participant as they inhaled normoxic air from the environment. Ventilatory measurements were averaged at 30 second intervals throughout all exercise sessions. VO₂ (ml/kg/min), VCO₂ (ml/kg/min), VE (L/min), and RER (respiratory exchange ratio) were calculated by computer software (Parvomedics, USA).

Cerebral Oxygenation and Haemodynamics

Throughout the experimental procedures, a continuous wave Near-Infrared Spectroscopy (NIRS) monitor (Portalite, Artinis Medical Systems BV, The Netherlands; Oxysoft version

2.1.6) was used to measure changes in chromophore concentrations of oxy-haemoglobin (HbO_2) and deoxy-haemoglobin (HHb), in $\mu\text{M cm}^{-1}$. Total haemoglobin (tHb) was also reported in $\mu\text{M cm}^{-1}$ and represents the total HbO_2 and HHb at any given point. Additionally, haemoglobin difference (HbDiff) was reported and represents the difference between HbO_2 and HHb. Total Saturation Index (TSI %) was expressed as a ratio between HbO_2 and THb. The data was collected at 10Hz with a brain measurement differential pathlength factor (DPF) determined by a scattering medium formula based on age and wavelengths set at 761nm and 848nm. The DPF accounts for the increase in optical pathlength due to scattering in the tissue. Two NIRS sensors were used to account for differences in oxygenation between the left and right sides of the pre-frontal cortex. The sensors were placed at a height of 15% of the nasion-inion distance from nasion and at 7% of the head circumference to the left and right from midline, to avoid measuring the midline sinus. These locations are used to measure left and right Brodmann's area (BA) 10 and the dorsolateral and anterior PFC (Maidan et al., 2018). The NIRS sensors were also wrapped in thin plastic to prevent sweat from altering the measurement. Lastly, the NIRS sensors were covered with dark fabric to keep out ambient light. A NIRS event related design and time to termination (TTT) % design was used to analyze PFC oxidative metabolism. NIRS events (Table 3.2) were marked at the start and end of each rest period, the start of the treadmill graded-exercise protocol, at each 0.5°C increase in T_c , and at the termination of exercise. TTT % was recorded at each 10% increase. Data around each event marker was averaged and recorded for further analysis and the determine trends.

Table 3.2.

Experimental protocol events with event label, body position details, and NIRS Marker

Event Label	Details	NIRS Marker
Start Initial Rest Period	Supine, quiet	A
End Initial Rest Period	Supine, quiet	B
Start Exercise	Upright, Moving	C
Tc 37.5°C	Upright, Moving	D
Tc 38°C	Upright, Moving	E
Tc 38.5°C	Upright, Moving	F
Tc 39°C	Upright, Moving	G
End Test	Upright, Stationary	H
Start Final Rest Period	Supine, quiet	I
End Final Rest Period	Supine, quiet	J

Note. Not all subjects reached each temperature point in both CON and PPE.

Saliva Sampling and Analysis

Saliva samples were collected at the start of exercise, at each 0.5°C increase in T_c, and at the end of exercise. Saliva was collected using the SalivaBio Oral Swab (SOS) method (Salimetrics, Inc., State College, PA) and were stored at -20°C. Samples were thawed and processed in duplicate using a highly sensitive enzyme immunoassay with a range of sensitivity from < 0.003 to 3.0 µg/dL and average intra- and inter-assay coefficients of variation of 4.6% and 6%, respectively (Salimetrics, Inc., State College, PA). Averaged duplicate scores were used for statistical analyses.

Go/No-Go Task

A Go/No-Go test (PEER Analytics) was used to measure the subjects perceptual decision-making ability pre- and post-exercise in both the CON and PPE (Perri, Berchicci, Lucci, Spinelli, & Di Russo, 2016). The Go/No-Go task was done in a quiet room with limited visual and auditory stimuli. The Go/No-Go test consisted of 4 blocks of 50 trials in which either a green or blue circle would appear on a black screen. In line with previous studies, participants were instructed to respond to the green circles by touching the screen which appeared more frequently and to not respond when a blue circle appeared. The green circles (Go) appeared 70% of the time, while the blue dots (No-Go) appeared 30% of the time. The presentation order of the circles was completely random and the meaning of the circles (Go, No-Go) was randomly counterbalanced between sessions.

EEG data was collected with a MUSE EEG headband during performance of the Go/No-Go task with pre-set collection parameters (256 Hz sampling rate, no onboard data processing: InteraXon, Ontario, Canada). The MUSE EEG headband has five electrodes (AF7, AF8, Fpz, TP9, TP10) with electrode Fpz being utilized as the reference. Data from the MUSE EEG system

was streamed to an iPad (Apple Inc., California, U.S.A.) via Bluetooth to the PEER application. Signal quality was determined by ongoing calibration within the Go/No-Go software (PEER Analytics) using a criteria based on the average variance per second in the EEG data. Variance at each channel needed to be less than $150 \mu\text{V}^2/\text{s}$ in order to maintain signal quality (Krigolson et al., 2017). This was maintained by onboard calibration.

EEG Data Processing

Post experiment, the EEG data was imported into Brain Vision Analyzer 2 software (Version 2.1.1, Brainproducts, GmbH, Munich, Germany) using methods that were previously used by the Neuroeconomics Laboratory at the University of Victoria (see <http://www.neuroeconlab.com/data-analysis.html>). First, the EEG data were filtered with a zero-phase shift Butterworth filter with a passband of 0.1 Hz to 15 Hz in addition to a 60 Hz notch filter. Subsequent to this, the frontal EEG channels (AF7, AF8) were re-referenced to an average of the posterior channels (TP9, TP10) given the proximity of the physical reference at Fpz. Given a preliminary analysis of the data in which hemispheric differences were not observed, the two frontal electrodes were pooled (AF7, AF8), and the two posterior electrodes (TP9, TP10) into new channels AF and TP. Next, the EEG data was epoched using a window from -200 ms to 600 ms after the onset of the visual stimulus. Epochs with an absolute difference of more than $75 \mu\text{V}$ were discarded with no participants being removed as a result of the artifact rejection procedure. Following the artifact rejection procedure, a Fast Fourier Transformation (FFT) was used to extract EEG power using maximum resolution, non-complex output, on the full spectrum with a Hanning Window with a 10% taper and a resolution of 0.48 Hz. Epochs were zero-padded for a length of 2048 ms generating 1024 points. Power was determined for the individual epochs and averaged across epochs for each frequency (1 –30 Hz) for each participant. Finally, mean

power was computed for each frequency band (delta: 1–3 Hz, theta: 4–7 Hz, alpha: 8–12 Hz, beta: 13–30 Hz).

3.5 Statistical Analysis

All statistical analyses were conducted in R Studio (Version 1.1.456 – © 2009-2018 RStudio, Inc.). The alpha level for significance was set at $p \leq 0.05$. All results in this study were calculated as mean values $\pm$ 95% confidence intervals.

All mean NIRS values (TSI%, HbO₂, HbDiff and tHb) were compared using a 2 x 3 repeated measures ANOVA design - two conditions (PPE, CON) by three times (start, Tc 38°C, end). Additionally, 95% confidence levels were reported when necessary. Mauchly's test was used to test for the assumption of sphericity.

All NIRS parameter data were averaged and separated into 60 s sections representative of each NIRS event or TTT %. The 600 data points (60 s of data) were then averaged to give a mean value, representative the NIRS data around a specific NIRS event. Examples of the NIRS events are displayed in Table 3.2 under the “Event Label” column. Magnitude of change in the NIRS parameters was determined as the difference between a given start and end value. The differences were all compared to the initial start value. For example, the NIRS data at Tc 38°C were referenced to the NIRS data at rest prior to exercise. The mean start value was set at 0 and the subsequent values were compared to that start point to show the change over time to 100% TTT or at increasing Tc points.

Post-exercise mean values related to EEG frequency bands, and Go/No-Go error occurrence were compared to baseline (pre-exercise) values in both CON and PPE using a 2x2 repeated measures ANOVA design - two conditions (PPE, CON) by two times (pre, post). Additionally, post-exercise comparisons between CON and PPE were evaluated using a 2x2

repeated measures ANOVA design - two conditions (PPE, CON) by two times (pre, post). 95% confidence levels were reported whenever inferential statistics were used. The alpha level for significance was set at $p \leq 0.05$. Mauchly's test was used to test for the assumption of sphericity.

Mean values of cortisol values were compared using a 2 x 3 repeated measure ANOVA - two conditions (PPE, CON) by three times (start, TC 38°C, end). 95% confidence levels were reported for all significant mean cortisol CON and PPE comparisons. The alpha level for significance was set at $p \leq 0.05$. Mauchly's test was used to test for the assumption of sphericity.

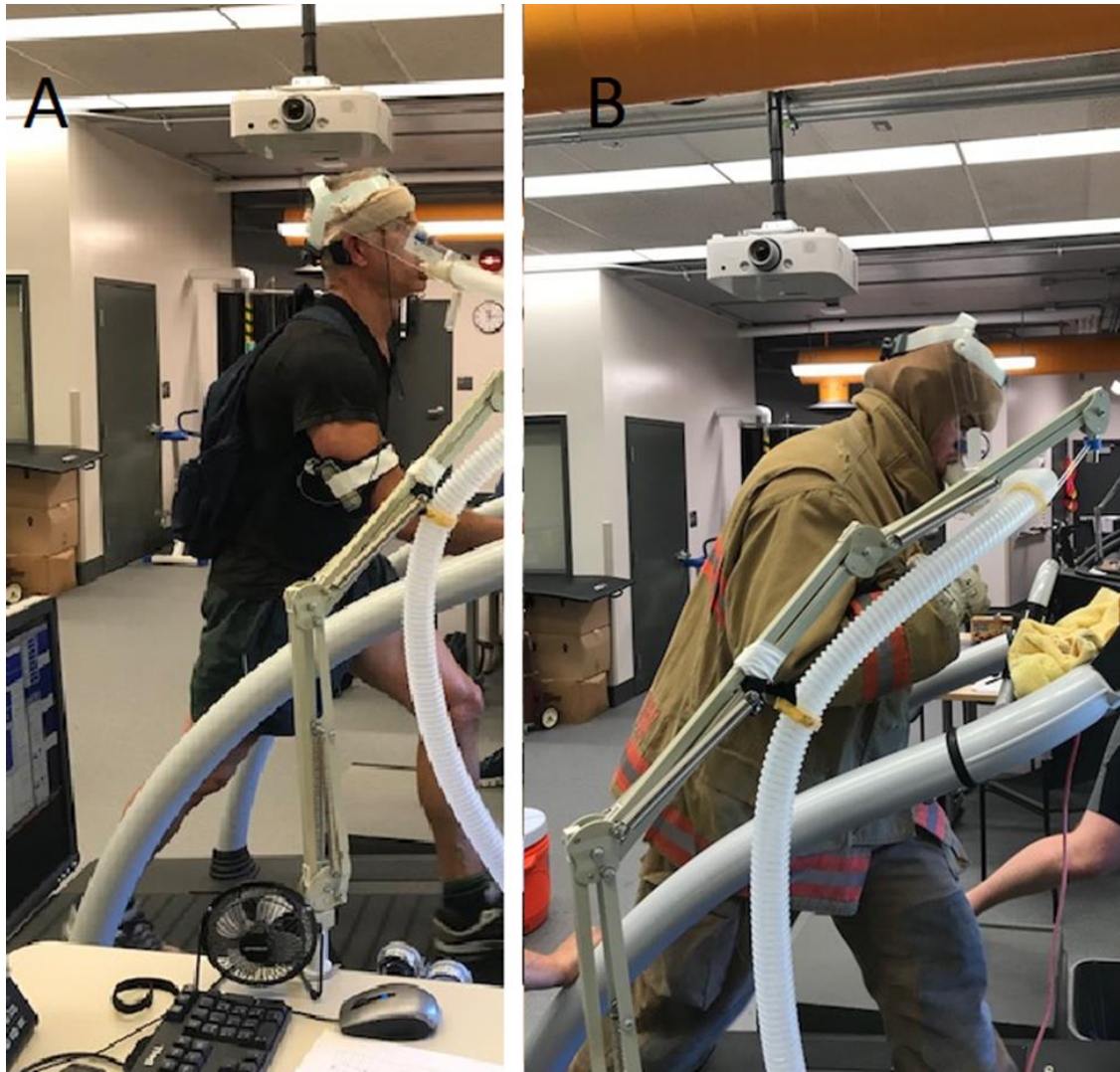


Figure 3.1. The difference between the attire in CON and PPE. (A) The subject is wearing shorts, t-shirt, and the backpack representing the mass of the firefighter PPE. (B) The subject is wearing the full firefighter PPE. The NIRS probes are under a black headband, which is secured by a tensor bandage.

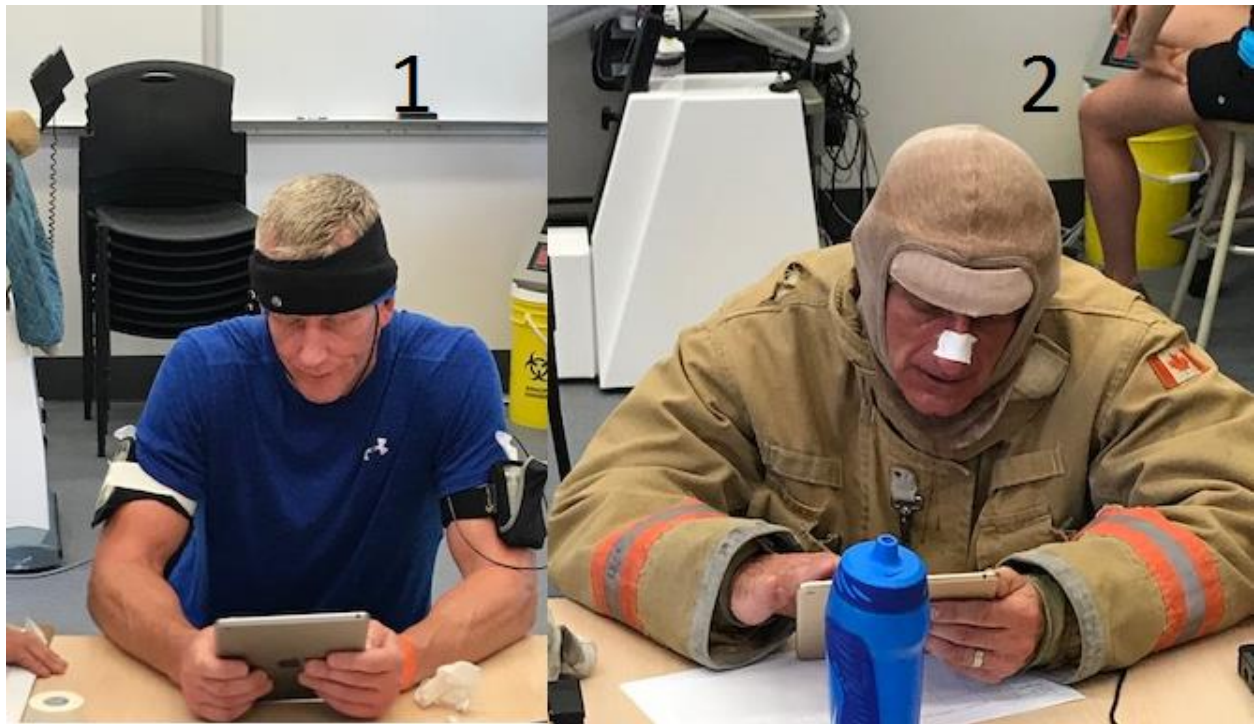


Figure 3.2. The difference between the attire in CON and PPE during the Go/No-Go test. (1) The subject is wearing shorts and a t-shirt; (2) The subject is wearing the full firefighter PPE. The MUSE headband and NIRS probes are under a black headband, which is secured by a tensor bandage.

CHAPTER 4: GENERAL RESULTS AND DISCUSSION RELATED TO ALL MEASURED VARIABLES

4.1 Descriptive, Exercise Capacity, and Physiological Data Results

Fourteen subjects reached one or more of the three termination of exercise criteria, and all had a $\text{VO}_{2\text{max}}$ greater than $35 \text{ ml kg}^{-1} \text{ min}^{-1}$ ($52.3 \pm 5.9 \text{ ml kg}^{-1} \text{ min}^{-1}$). One subject did not reach one of the three termination criteria and was excluded from the study.

Body mass index (BMI) for the subjects was $25.8 \pm 1.9 \text{ kg/m}^2$. A correlation analysis was done between BMI and post-exercise T_c in both CON and PPE. There were no significant correlations between BMI and post-exercise T_c in either CON or PPE, indicating BMI had no impact on the ability to tolerate T_c acquisition. A correlation analysis was also completed between BMI and TTT in both CON and PPE. No significant correlations were found indicating that BMI also had no influence on TTT in either CON or PPE.

There was a significant difference ($p \leq 0.01$) when comparing TTT (CON = 77.3 ± 12.6 min; PPE = 50.3 ± 6.9 min), pre-exercise HR (CON = 76.8 ± 4.8 bpm; PPE = 86.5 ± 5.1 bpm), T_c 37.5°C HR (CON = 124.3 ± 7.8 bpm; PPE = 143.3 ± 9.2 bpm), T_c 38°C HR (CON = 140.7 ± 9.2 bpm; PPE = 162.7 ± 8.5 bpm), and post-exercise HR (CON = 161.1 ± 11.9 bpm; PPE = 179.6 ± 6.8 bpm). Additionally, there were significant differences between CON and PPE end-exercise T_c (CON = $38.57 \pm 0.3^\circ\text{C}$; PPE = $39.01 \pm 0.3^\circ\text{C}$), thermal comfort scale (TCS) (CON = 3.57 ± 0.6 ; PPE = 4.63 ± 0.3), and thermal sensation (TS) (CON = 7.57 ± 0.5 ; PPE = 8.67 ± 0.3). Physiological strain index (PSI) (Moran, Shitzer, & Pandolf, 1998) was measured and there were significant differences between conditions at T_c 37.5°C , T_c 38°C , and end of exercise. Lastly, the rate of T_c acquisition was significantly different with acquisition averaging 0.04°C/min increase in T_c during PPE and 0.02°C/min increase in T_c during CON.

4.2 Rate of Thermal Acquisition Results

The time at which the subjects reached various measurement points (start, Tc 37.5°C, Tc 38°C, end) can be used as an indicator of the rate of thermal acquisition. Overall, the subjects reached each point earlier in the PPE session. There were significant differences ($p \leq 0.05$) at Tc 37.5°C (CON = 20.3 ± 4.0 min; PPE = 16.7 ± 3.0 min), at Tc 38°C (CON = 47.7 ± 10.4 min; PPE = 27.7 ± 3.0 min), and at end (CON = 77.3 ± 2.9 min; PPE = 50.3 ± 5.7 min). Tc 37.5°C and Tc 38°C were points where all subjects reached in both CON and PPE. Not all subjects reached the remaining measurement points of Tc 38.5°C (CON = 12; PPE = 13), Tc 39°C (CON = 7; PPE = 11), and Tc 39.5°C (CON = 1; PPE = 6). That being said, all subjects reach the end NIRS event point. The end point is associated with the meeting of one of the termination criteria.

Table 4.1

Summary of termination of exercise temperature, thermal comfort, thermal sensation, and rating of perceived exertion for CON and PPE

Variable	Condition	Mean $\pm$ 95% CI	Effect Size (Cohen's d)
Start Tc (°C)	CON	37.0 $\pm$ 0.2	0.04
	PPE	36.9 $\pm$ 0.2	
End Tc (°C)	CON	38.6 $\pm$ 0.3	0.68
	PPE	39.1 $\pm$ 0.3 *	
TCS	CON	3.57 $\pm$ 0.6	1.29
	PPE	4.63 $\pm$ 0.3 *	
TS	CON	7.57 $\pm$ 0.5	1.3
	PPE	8.67 $\pm$ 0.3 *	
RPE	CON	7.2 $\pm$ 1.3	0.12
	PPE	7.6 $\pm$ 1.2	

Note. Start Tc (°C), core temperature pre-exercise; End Tc (°C), core temperature post-exercise; TCS, thermal comfort scale; TS, thermal sensation; RPE, rating of perceived exertion. Significant differences (* $p \leq 0.05$) between CON and PPE during exercise.

Table 4.2

Summary of physiological data (mean $\pm$ 95% CI) for the CON and PPE sessions.

Variable	CON	PPE
TTT (min)	77.3 $\pm$ 12.6	50.3 $\pm$ 6.9 **
Pre HR (bpm)	76.8 $\pm$ 4.8	86.5 $\pm$ 5.1 **
Tc 37.5°C HR (bpm)	124.3 $\pm$ 7.8	143.3 $\pm$ 9.2 **
Tc 38°C HR (bpm)	140.7 $\pm$ 9.2	162.7 $\pm$ 8.5 **
Post HR (bpm)	161.1 $\pm$ 11.9	179.6 $\pm$ 6.8 **
Pre-Body Mass (kg)	84.3 $\pm$ 9.2	84.5 $\pm$ 9.4
Post-Body Mass (kg)	82.8 $\pm$ 9.2	83.1 $\pm$ 9.4
$\dot{V}_E/\dot{V}O_2$ (Start)	24.2 $\pm$ 3.4	23.2 $\pm$ 2.4
$\dot{V}_E/\dot{V}O_2$ (End)	29.2 $\pm$ 3.9	31.2 $\pm$ 3.5 *

Note. TTT, time to termination; HR, heart rate. Significant differences (** $p \leq 0.01$, * $p \leq 0.05$) between the CON and PPE sessions.

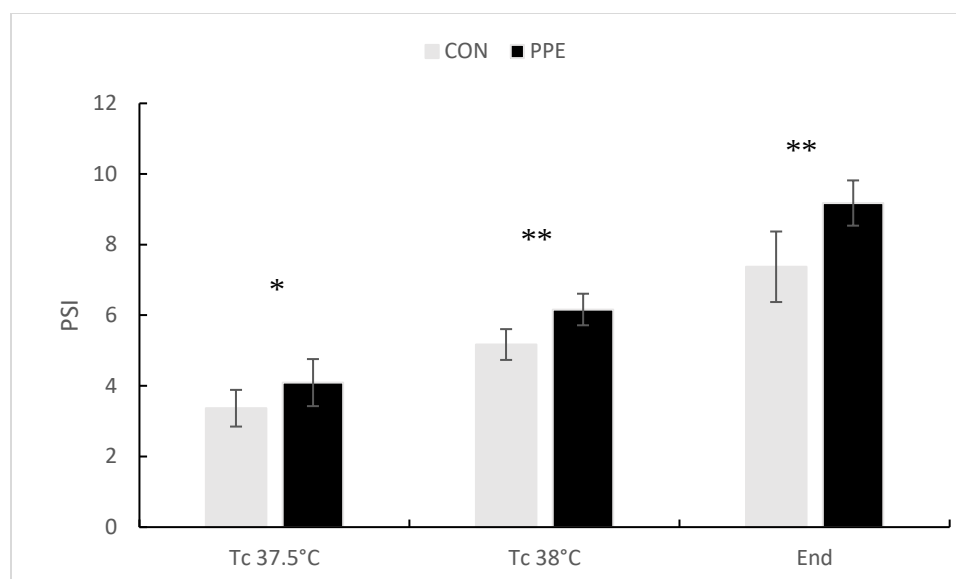


Figure 4.1. Physiological strain index (PSI) at Tc 37.5°C, Tc 38°C, and end of exercise.

Significant differences (* $p \leq 0.05$, ** $p \leq 0.01$) between CON and PPE during exercise. Error bars = 95% confidence intervals.

4.3 Descriptive, Exercise Capacity, and Physiological Data Discussion

There was a difference in this study when analyzing end of exercise Tc. This difference cannot be sufficiently argued as the means of explaining the results throughout this study. There was a difference in HR and PSI at all common measurement points. PSI (Moran et al., 1998) is a 10-point scale which measure physiological heat strain based on a comparison between HR and Tc. Traditionally the PSI has been measured by using rectal temperature, which is a Tc measurement. This study used the results from the Tc capsule system to calculate PSI. The PSI was different (Figure 4.1) at all common points of measurement (Tc 37.5°C, Tc 38°C, and End) when comparing CON and PPE. This indicating that at each measurement point there was not only a difference in TS and TCS, but there was also a physiological strain difference. The physiological strain difference means that at each common measurement point there was

increased demand for oxygen and nutrients in all working areas of the body during PPE when compared to CON. Additionally, there was increased blood delivery to the periphery for thermoregulatory purposes in PPE when compared to CON. This is important as it provides support for the rate of thermal acquisition argument. If rate of thermal acquisition was not a factor, the PSI should be the same or have non-significant differences at common T_c points. This needs to be kept in mind when analyzing the results, discussion, and conclusions throughout this study.

CHAPTER 5: RESULTS AND DISCUSSION FOR CEREBRAL OXYGENATION AND HAEMODYNAMICS VARIABLES

Research Question: What effect does exercise while wearing PPE and the resulting rapid and uncompensable Tc acquisition have on cerebral oxygenation and haemodynamics?

5.1 Prefrontal Cortex Oxygenation and Haemodynamics Results

Figures 5.1 – 5.7 demonstrate the group means for all of the NIRS variables that were measured for during CON and PPE. There was a gradual increase from rest (set at 0) to 80% TTT ($6.7 \pm 4.2 \mu\text{M cm}^{-1}$) in CON (Figure 5.10) and from rest to 60% TTT ($6.2 \pm 5.9 \mu\text{M cm}^{-1}$) in PPE (Figure 5.8) when evaluating left-side PFC HbO₂. There was also a gradual increase from rest (set at 0) to 80% TTT ($9.1 \pm 6.9 \mu\text{M cm}^{-1}$) in CON (Figure 5.11) and from rest (set at 0) to 60% TTT ($8.8 \pm 8.8 \mu\text{M cm}^{-1}$) in PPE (Figure 5.9) when evaluating left-side PFC tHb. These increases in both CON and PPE were followed by a plateau and then a decrease until 100% of TTT. HHb values increased from rest to 100% of TTT in both CON and PPE. HbDiff values increased to 60% of TTT in PPE and 80% of TTT in CON and then plateaued and decreased to 100% of TTT. Right-side values for HbO₂, tHb, HHb, and HbDiff during CON and PPE were also measured and closely resembled left-side values. Therefore, only left-side values are reported to avoid replication. V_E/VO₂ deflection points were compared to HbO₂ and tHb peaks during CON and PPE. There were deflection points in the V_E/VO₂ measurements at 60% of TTT in PPE (Figures 5.8 & 5.9) and at 80% of TTT in CON (Figures 5.10 & 5.11). HbO₂ (Figure 5.4), tHb (Figure 5.5), HHb (Figure 5.6), and HbDiff (Figure 5.7) were also evaluated in relation to specific NIRS points. There was a gradual increase from start (set at 0) to Tc 38°C when evaluating HbO₂, tHb, and HbDiff. There was a plateau in HbO₂ following Tc 38°C in both the

CON and PPE sessions. Additionally, there was a plateau in tHb starting at Tc 38°C in PPE. HHb values increased from start until end of exercise.

When evaluating TSI %, there was a statistically significant difference ($F(1,13) = 3.906$, $p \leq 0.05$; Effect size = 0.78) in regards to magnitude of change during PPE when evaluating left-side PFC values. It should also be noted that there was also a significant difference ($p \leq 0.05$) in regard to magnitude of change between start of exercise and Tc 38°C in left-side TSI % values in PPE. There were no TSI % magnitude of change differences when evaluating the right-side PFC during PPE. There was additionally no significant magnitude of change differences on either the right-side or left-side during the CON session. The TSI % in the left PFC decreased at a rate of roughly 0.06%/min during PPE and roughly 0.03%/min during CON. This showing that there was roughly double the oxygenation decrease per minute during PPE in the left PFC when compared to the left PFC in CON.

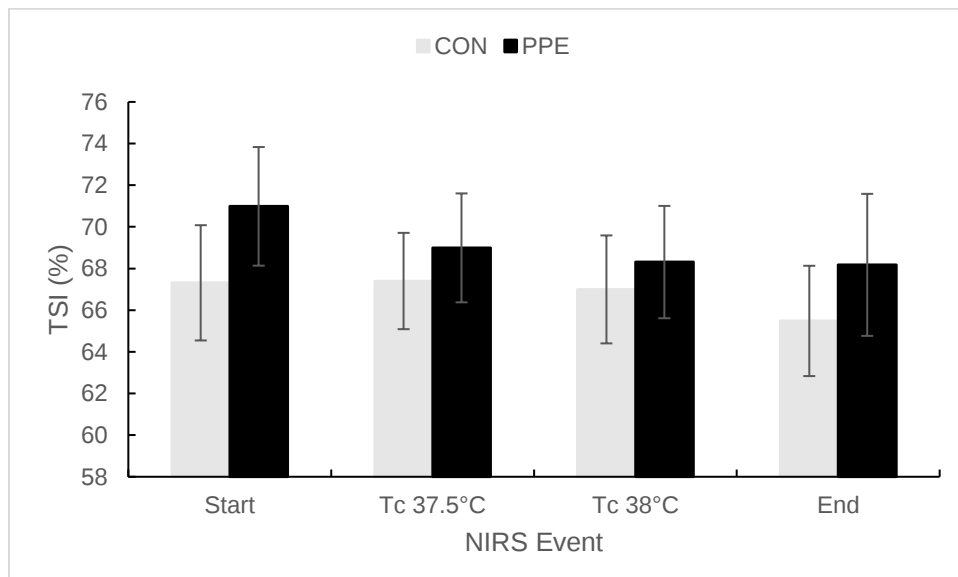


Figure 5.1. Mean left PFC TSI % comparison between CON and PPE when evaluating NIRS event points. Error bars = 95% confidence intervals.

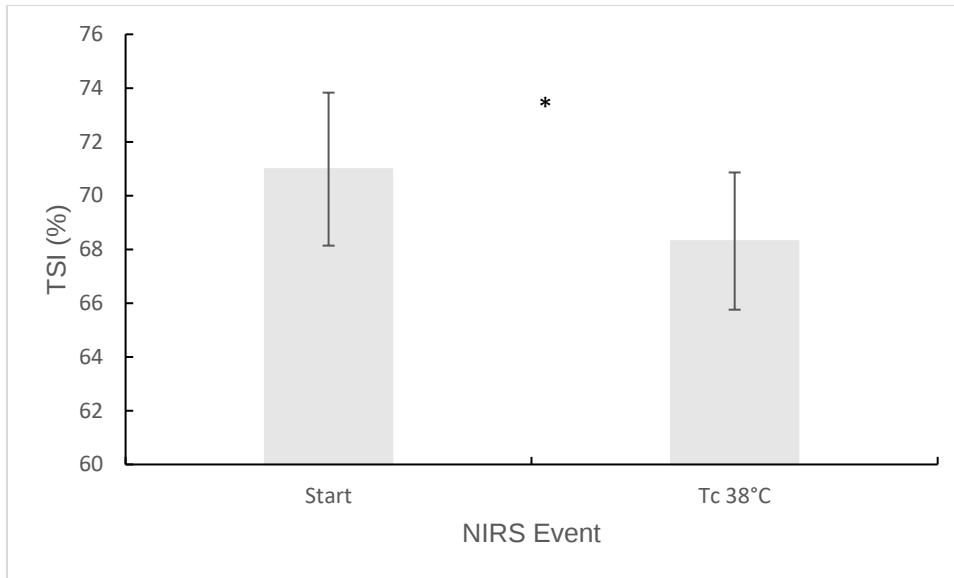


Figure 5.2. Mean left PFC TSI % comparison between start of exercise and Tc 38°C during PPE. Significant difference (* $p \leq 0.05$). Error bars = 95% confidence intervals.

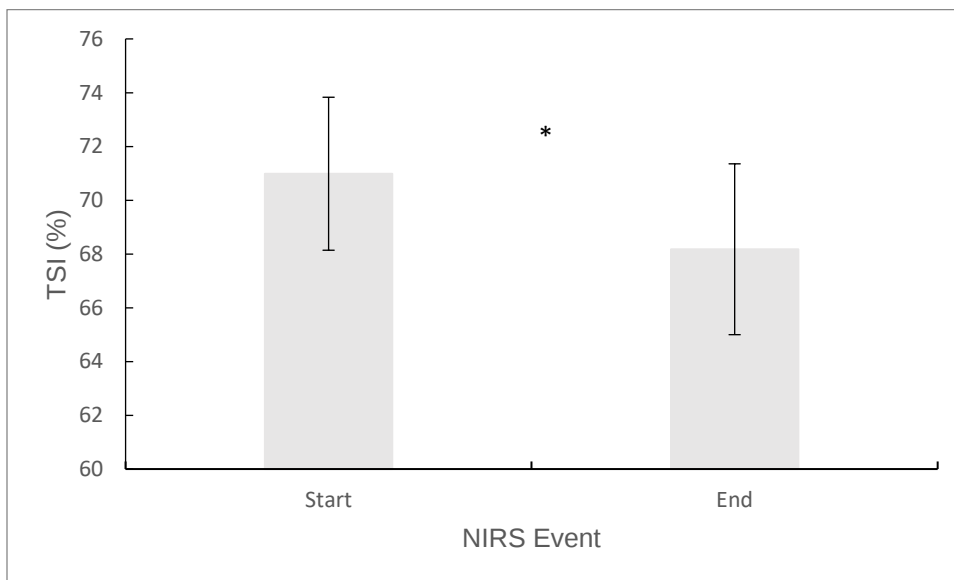


Figure 5.3. Mean left PFC TSI % comparison between start of exercise and end of exercise during PPE. Significant difference (* $p \leq 0.05$). Error bars = 95% confidence intervals.

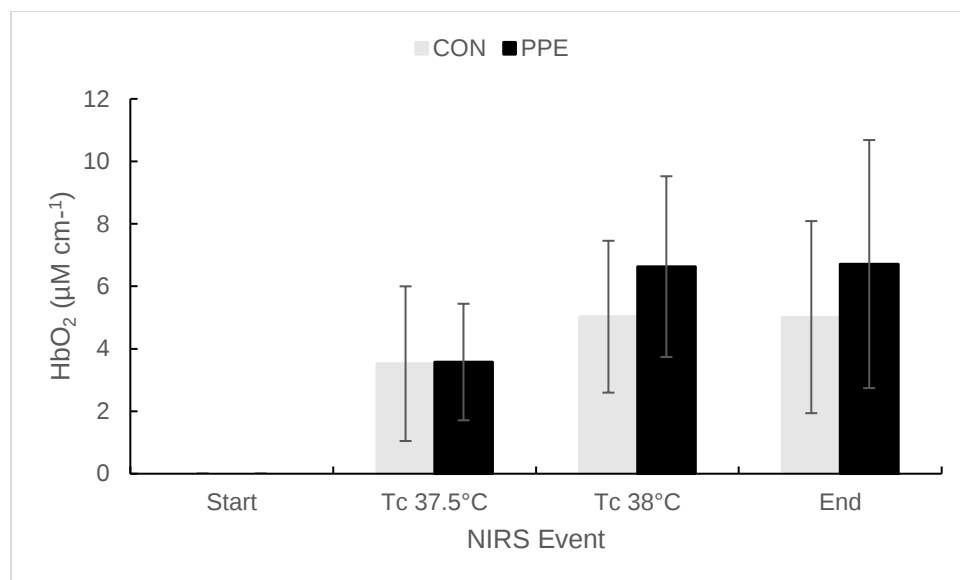


Figure 5.4. Mean left PFC changes in HbO₂ from baseline (Start) between CON and PPE when evaluating NIRS event points. Error bars = 95% confidence intervals.

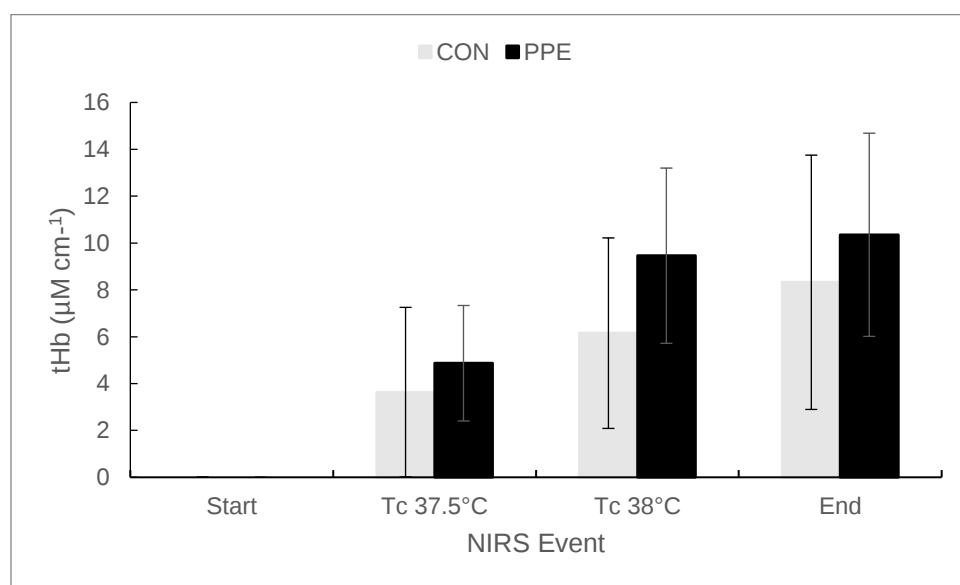


Figure 5.5. Mean left PFC changes in tHb from baseline (Start) between CON and PPE when evaluating NIRS event points. Error bars = 95% confidence intervals.

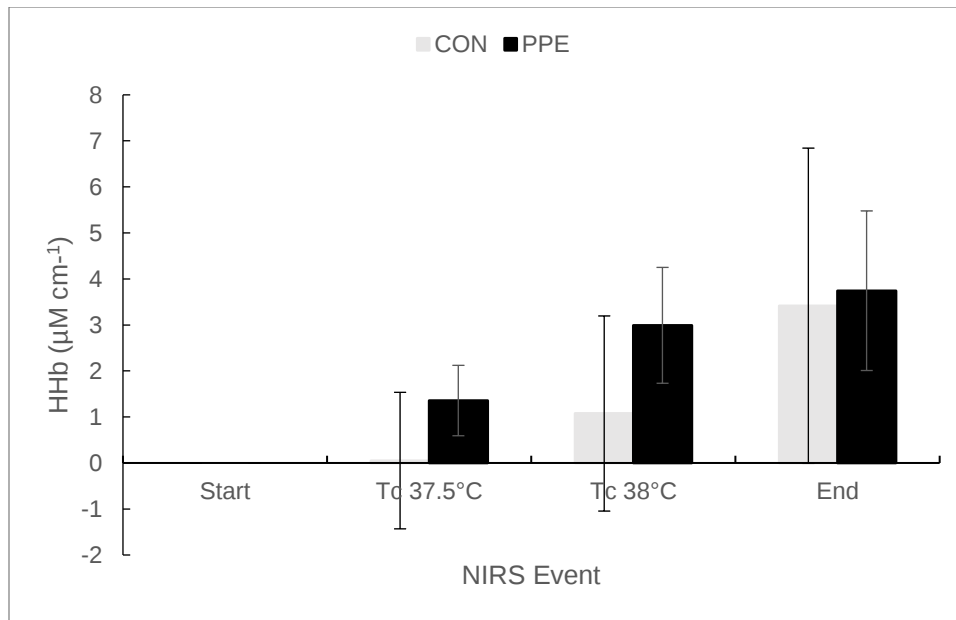


Figure 5.6. Mean left PFC changes in HHb between CON and PPE when evaluating NIRS event points. Error bars = 95% confidence intervals.

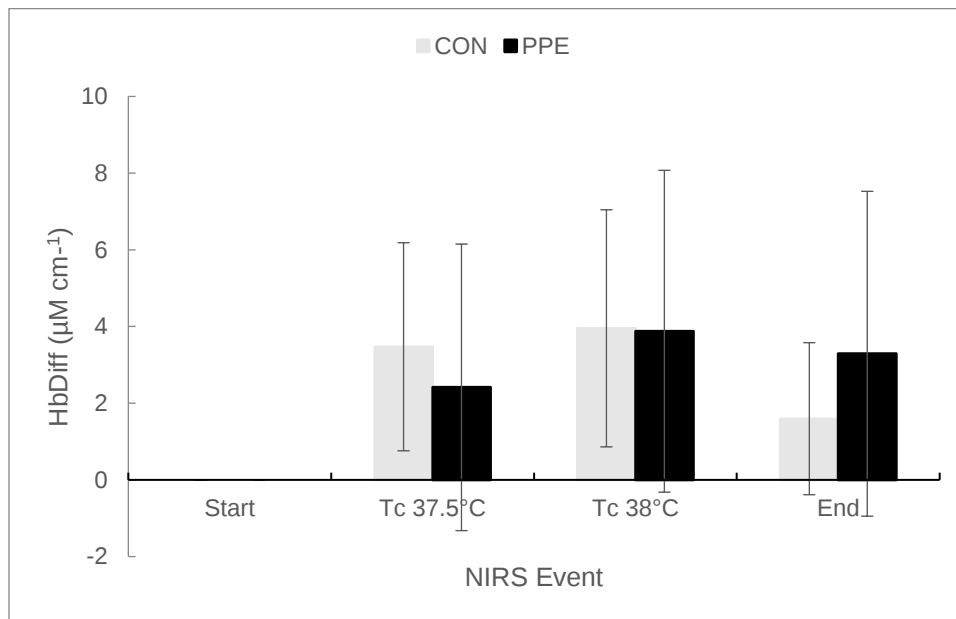


Figure 5.7. Mean left PFC HbDiff changes between CON and PPE when evaluating NIRS event points. Error bars = 95% confidence intervals.

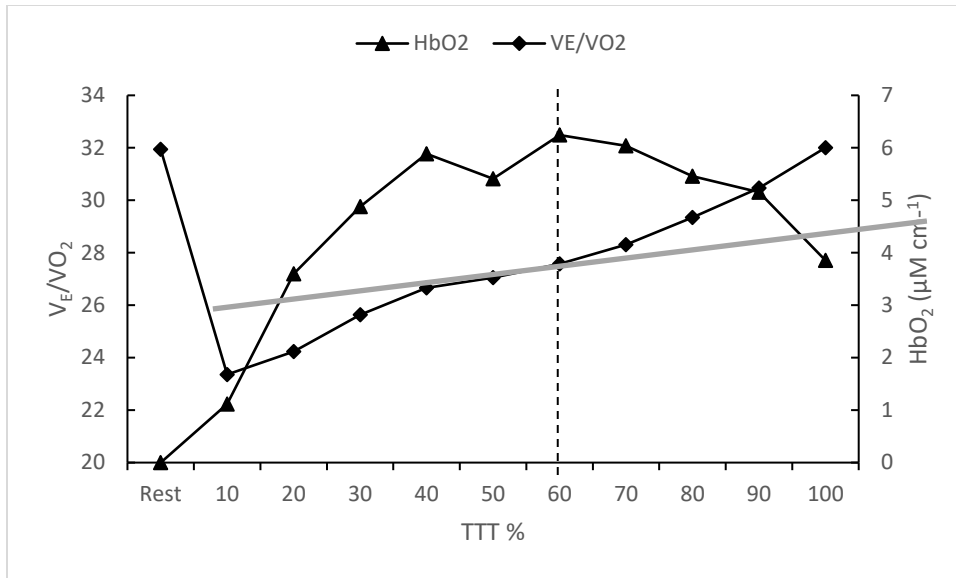


Figure 5.8. Evaluation of V_E/VO_2 and HbO_2 during PPE. Vertical broken line represents the break point for V_E/VO_2 and the point in which HbO_2 begins to decrease. This point is referred to as the respiratory compensation threshold (RCT). The grey line is used to emphasize the deflection point.

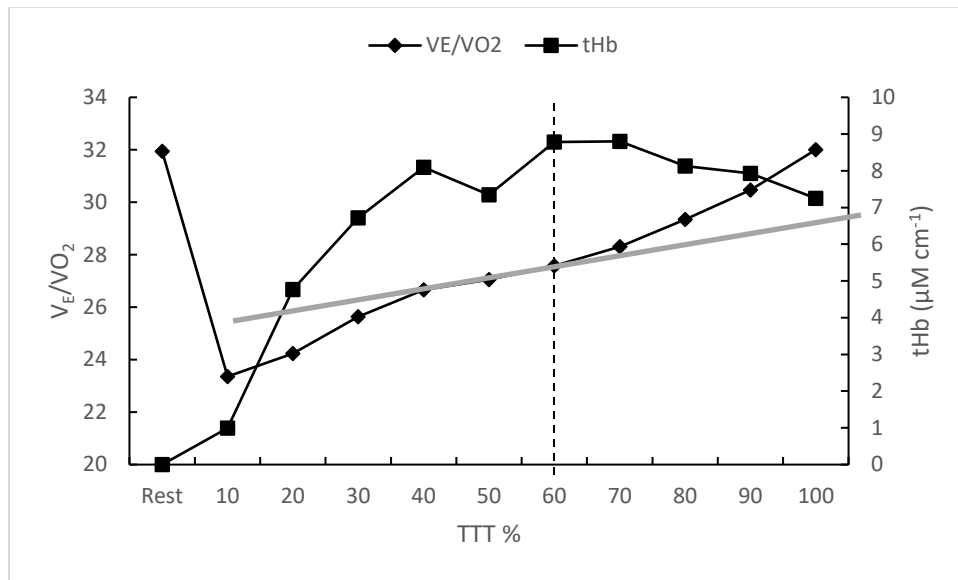


Figure 5.9. Evaluation of V_E/VO_2 and tHb during PPE. Vertical broken line represents the break point for V_E/VO_2 and the point in which tHb begins to decrease. This point is referred to as the respiratory compensation threshold (RCT). The grey line is used to emphasize the deflection point.

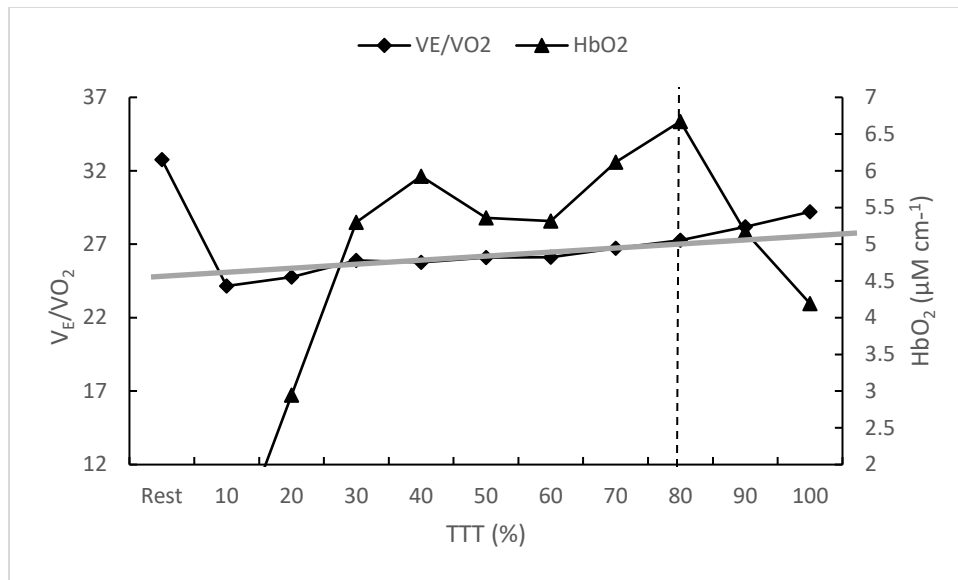


Figure 5.10. Evaluation of V_E/VO_2 and HbO_2 during CON. Vertical broken line represents the break point for V_E/VO_2 and the point in which HbO_2 begins to decrease. This point is referred to as the respiratory compensation threshold (RCT). The grey line is used to emphasize the deflection point.

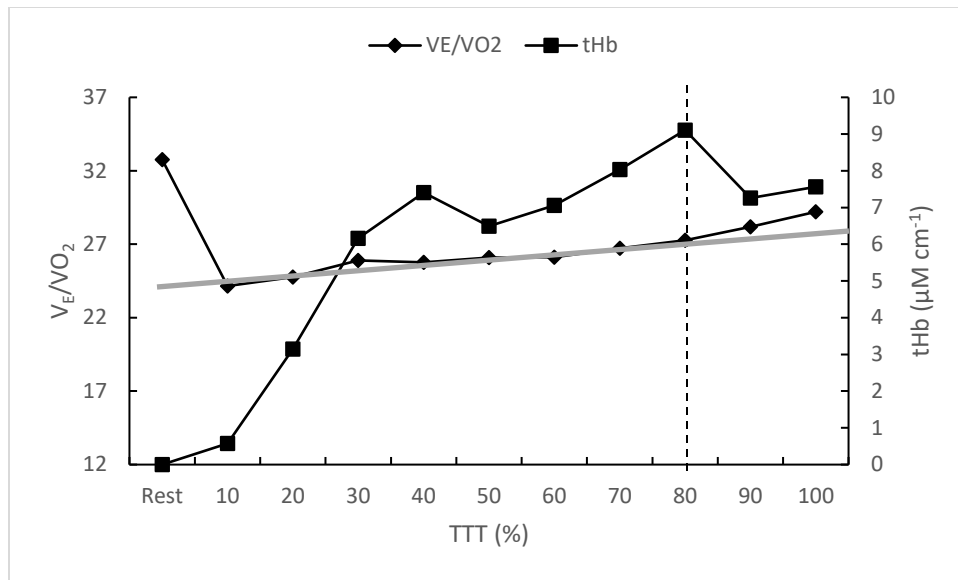


Figure 5.11. Evaluation of V_E/V_{O_2} and tHb during CON. Vertical broken line represents the break point for V_E/V_{O_2} and the point in which tHb begins to decrease. This point is referred to as the respiratory compensation threshold (RCT). The grey line is used to emphasize the deflection point.

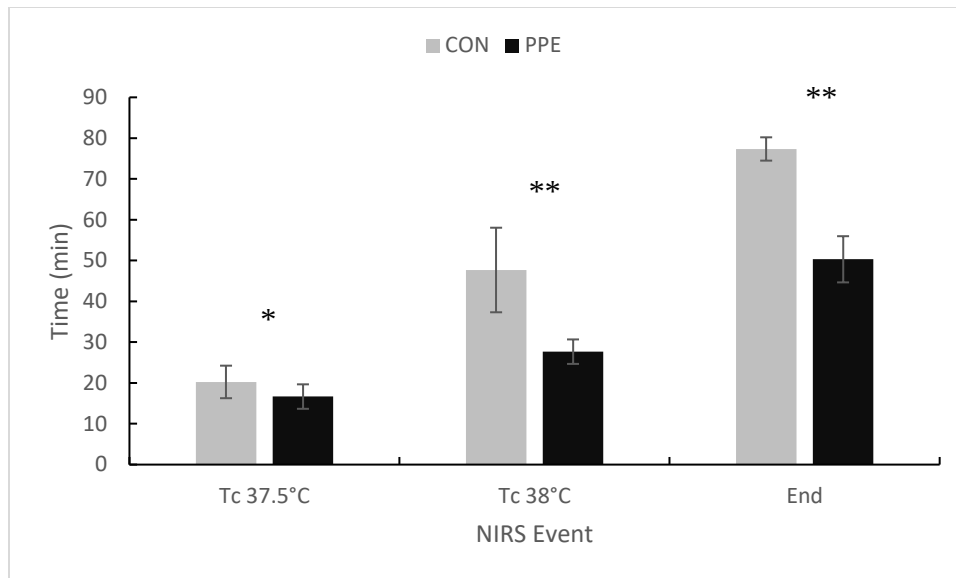


Figure 5.12. Comparison of exercise time difference between CON and PPE at Tc 37.5°C, Tc 38°C and termination of exercise (End). Significant differences (* $p \leq 0.05$, ** $p \leq 0.01$) between CON and PPE during exercise. Error bars = 95% confidence intervals.

5.2 Prefrontal Cortex Oxygenation and Haemodynamics Discussion

This study using NIRS is the first study to demonstrate a potential Tc point associated with a peak, plateau, and subsequent decrease in cerebral oxygenation and haemodynamics. Additionally, it is the first study to demonstrate an increased left-side PFC activation when exercising to a termination point in PPE. This was indicated by a significant decrease in TSI % from start to end of exercise and also double the decrease in TSI % per minute during PPE when compared to CON. This supports the hypothesis that rapid Tc acquisition has an increased influence on cerebral oxygenation and haemodynamics when compared to CON.

During a long duration incremental exercise to a termination criterion, there was activation of the PFC in both CON and PPE as indicated by increases in HbO₂, HHb and tHb. These increases are representative on increased neuronal activation (Ferrari, Mottola, & Quaresima, 2004). It is accepted that oxygen uptake is increased in the brain during exercise (Ferrari et al., 2004; Bhambhani, Malik, & Mookergjee, 2007). The NIRS measurements indicated increased activation in the left-side PFC during PPE:

A) there was a significant decrease in TSI %, reflecting increased O₂ extraction, from start to Tc 38°C and from start to termination of exercise. It should be mentioned that the mean TSI % drop of 2.78% in the left-side PFC during PPE is not considered to be a clinically significant drop. A TSI % drop of -13% is the necessary threshold for significant cerebral ischemia (Al-Rawi, & Kirkpatrick, 2006). That being said, the drop observed in this study does indicate that there was increased neuronal activation in the left-side PFC during PPE when compared to right-side and CON values.

B) There was double the oxygen extraction per minute during PPE. This demonstrates an effect of rate of thermal acquisition on the rate of oxygen uptake by the left PFC. Previous

research shows that decreases in TSI% are also a result of increased neuronal activation (Ferrari et al., 2004). Previous research has found that increases in the left-side PFC activation are associated with the approach-related emotion, whereas increased right pre-frontal activation is associated with the withdrawal emotion (Davidson, 2002; Fox, 1991; Schmidt & Trainor, 2001). This most likely indicates that the participants in this study were approaching PPE with a higher approach-related emotional state. This is further supported by the significant difference in HR prior to the exercise portion. Mean HR was significantly higher prior to exercise in PPE when compared to CON. This is potentially indicative of an anticipatory effect of wearing the PPE.

Higher left-side PFC activation, as reflected by the changes in oxygenation parameters while undergoing rapid Tc acquisition, could have implications for cognitive processes. Increased PFC activation is associated with compensatory efforts to maintain a desired level of performance (Liu, 2014). Additionally, there is a relationship between the left PFC and motor areas (Wu, Liu, Huang, & Han, 2017). Although speculative, the left PFC could be working harder to prevent fatigue in PPE. This could have implications for cognitive processes following exercise in the heat while wearing PPE. Hyperthermia causes increased activity in the dorsolateral PFC (Jiang et al., 2013), which plays a major role in the decision-making process. Further research is warranted to confirm these results.

There was a peak in HbO₂ followed by a plateau at Tc 38°C in both CON and PPE. During PPE, there was also a peak in tHb followed by a plateau at Tc 38°C. It should be noted that at the peak and subsequent decrease in HbO₂ and tHb occurred earlier in PPE. The peak, plateau, and subsequent decrease in cerebral oxygenation is associated with declining end-tidal CO₂ (PETCO₂) and arterial CO₂ content (PaCO₂) that happens beyond the respiratory compensation threshold (RCT) (Bhambhani et al., 2007). When exercise continues past the RCT,

decreased PaCO_2 results in decreased cerebral blood flow (Bhambhani et al., 2007; Nybo & Rasmussen, 2007). This was evident in this study by a decline in tHb (a representation of blood flow) (Nioka et al., 2006)) following 60% of TTT in PPE and following 80% of TTT in CON. This was additionally supported in this study when evaluating V_E/VO_2 during CON and PPE. A deflection point in V_E/VO_2 occurred at roughly 80% of TTT in CON and roughly 60% of TTT in PPE; these deflection points are representative of RCT (Simon, Young, Gutin, Blood, & Case, 1983) and further support the statement that there was a decrease in cerebral oxygenation blood flow at an earlier percentage in PPE. This is extremely important as it shows an effect of rate of thermal acquisition. The fact that HbO_2 and tHb started to decrease earlier in PPE means that at the point of termination of exercise there was a further decrease in cerebral oxygenation and blood flow in PPE when compared to CON. This can in part be explained by the PSI differences at each measurement point. Less overall oxygen and blood flow were available in PPE as compared to CON. This is due to the redistribution of oxygen and blood flow to meet the increased exercise and thermoregulatory demands in PPE. In most cases the termination point was associated with volitional maximum. This indicates that in an occupational setting where rapid and uncompensable T_c acquisition occurs and an individual reaches an exercise termination point, there is decreased oxygenation and brain blood flow compared to a normothermic scenario. This could result in neuronal consequences if the situation becomes severe. These neuronal consequences could result in disruption of cognitive processes. Disruption of cognitive processes will put the life of the employee at risk and in life-saving occupations, the lives of others at risk.

CHAPTER 6: RESULTS AND DISCUSSION FOR CEREBRAL NEURAL FUNCTION AND DECISION-MAKING PERFORMANCE VARIABLES

Research Question: What effect does exercise while wearing PPE and the resulting rapid and uncompensable Tc acquisition have on cerebral neural function and decision-making performance?

6.1 Incorrect Responses Results

Evaluation of the frequency of incorrect responses during the pre-and post-exercise Go/No-Go tests revealed that there was a significant difference between mean pre- and post-exercise values ($F(1,13) = 12.785$, $p \leq 0.01$; Effect size = 1.17) in PPE (Figure 6.1). Decision-making performance was compromised post-exercise in PPE when compared to pre-exercise. There was no significant difference between mean pre-and post-exercise values in CON.

6.2 EEG Frontal Theta Power Results

All EEG frequency band data was measured and analyzed from the frontal and posterior electrode sites during the Go/No-Go test pre- and post-exercise in CON and PPE. There was a significant difference between mean post-exercise frontal theta power when compared to the mean pre-exercise baseline ($F(1,13) = 6.069$, $p \leq 0.05$) in PPE (Figure 6.2). Frontal theta power decreased post-exercise when compared to the pre-exercise values in PPE. No difference was observed in other frequency bands at the frontal electrode sites (delta, alpha, and beta) (Figure 6.2) or at the posterior electrode sites (delta, theta, alpha, and beta) (Figure 6.3) (all p 's > 0.05).

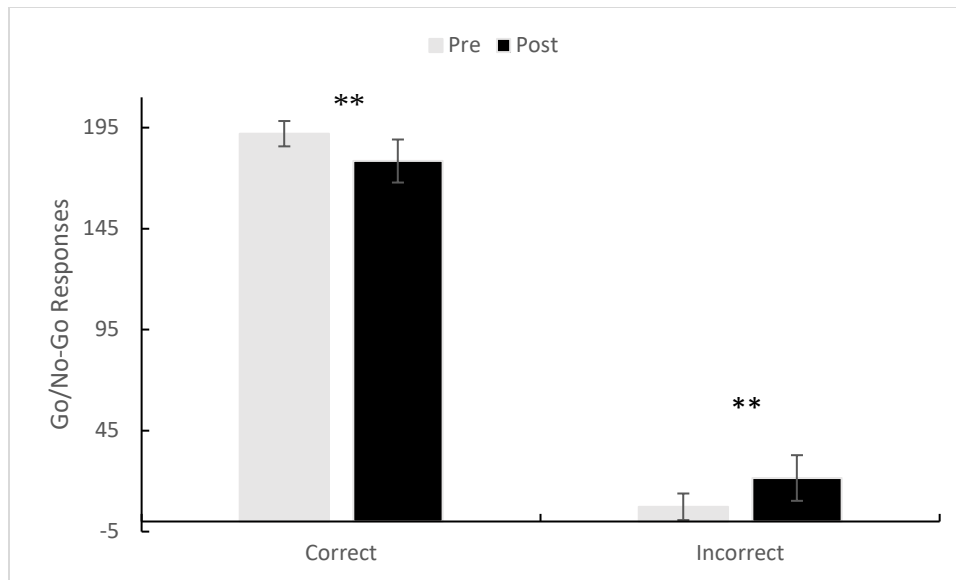


Figure 6.1. Mean correct and incorrect responses during Go/No-Go test pre- and post-exercise in PPE. Significant differences (** $p \leq 0.01$). Error bars = 95% confidence intervals.

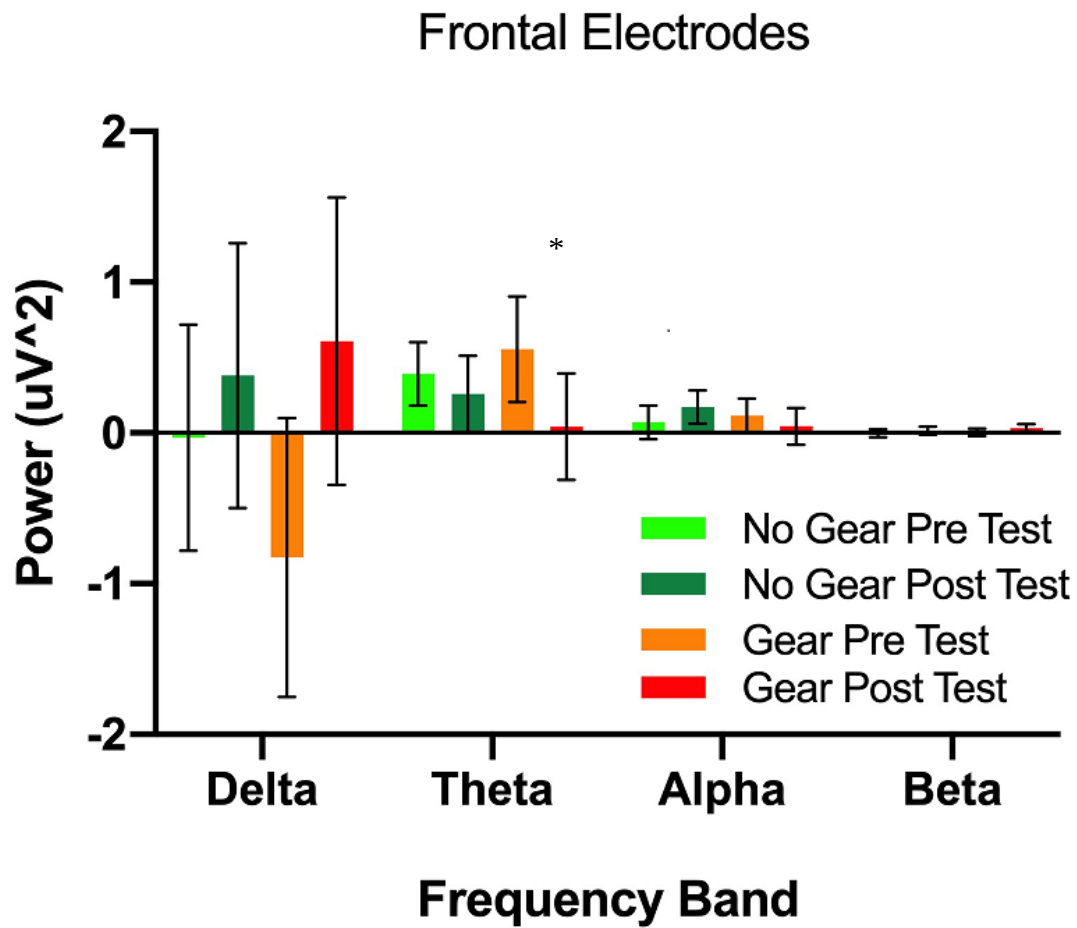


Figure 6.2. Mean delta, theta, alpha, and beta frequency band data from the frontal electrode sites during Go/No-Go test pre- and post-exercise in CON and PPE. Gear = PPE; No Gear = CON. Significant differences (* $p \leq 0.05$). Error bars = 95% confidence intervals.

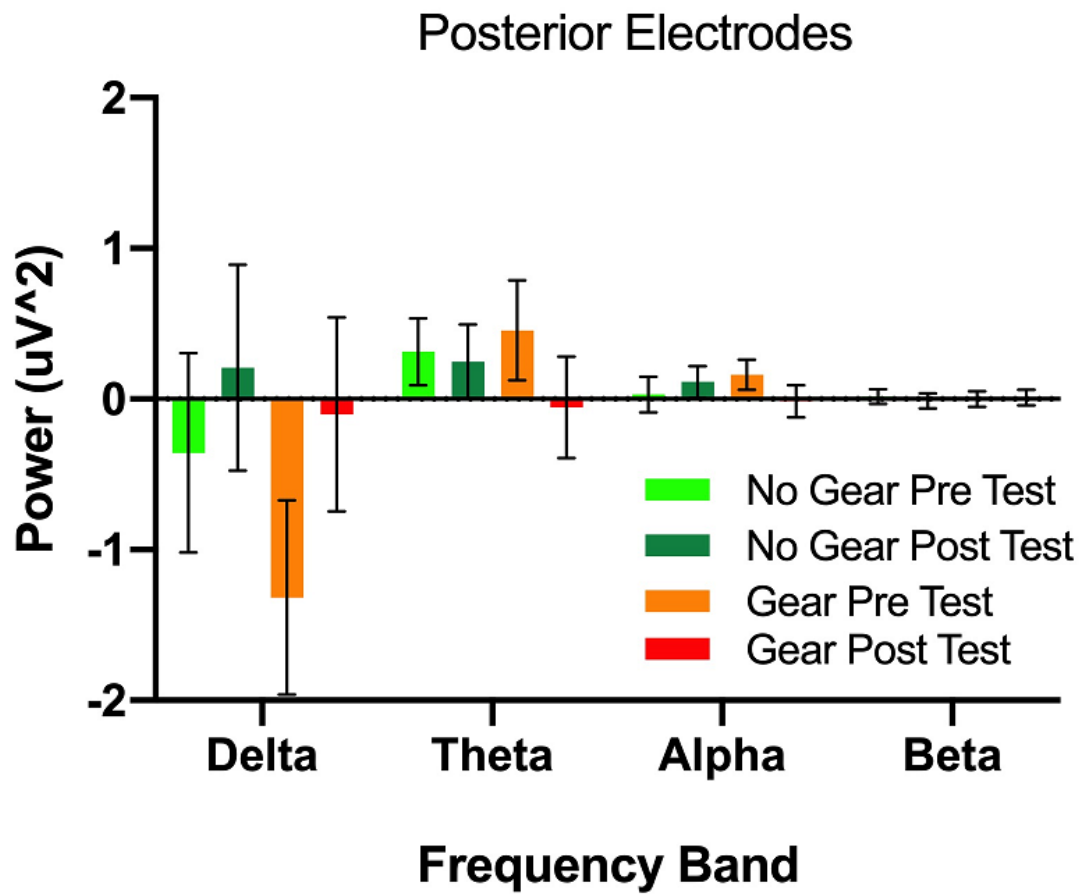


Figure 6.3. Mean delta, theta, alpha, and beta frequency band data from the posterior electrode sites during Go/No-Go test pre- and post-exercise in CON and PPE. Gear = PPE; No Gear = CON. Error bars = 95% confidence intervals.

6.3 Incorrect Responses and EEG Frontal Theta Power Discussion

The present study sought to determine the effects of rapid and uncompensable Tc acquisition on cerebral neural function and perceptual decision-making ability. Using MUSE to monitor EEG activity during a pre-and post-exercise Go/No-Go test, specific frequency band power data was acquired. This is the first study to monitor the effects of rapid Tc acquisition during exercise on frontal theta power and perceptual decision-making ability.

This study revealed significantly more incorrect responses post-exercise in PPE when compared to pre-exercise scores (Figure 6.1). This supports previous research that have found that hyperthermia has an effect on cognition (Sun et al., 2012; Racinais et al., 2008; Sun et al., 2011; Cheema & Patrick, 2012). It also shows a novel finding in that rate of thermal acquisition has an effect on decision-making performance. The subjects in this study had double the Tc acquisition per minute during exercise in PPE when compared to CON. Although speculative, this could support the statement made in the NIRS discussion that mentioned an effect of decreased cerebral oxygenation and blood flow in this study on cognitive performance. Decreased decision-making performance during rapid an uncompensable Tc acquisition will have far reaching impacts on individuals, such as firefighters, who need to make decisions in high ambient temperatures while wearing PPE. Decreased decision-making performance in these scenarios put lives many individuals at risk. One decision-making error can have far reaching impacts in these scenarios.

Using oddball stimuli during a Go/No-Go decision-making test, the study found a significant reduction in frontal theta power when comparing pre- and post-exercise mean values in PPE. There was no difference in pre- and post-exercise mean values in CON. Previous research has shown that frontal theta power is associated with cognitive control. Increased theta

power is associated with increased cognitive control (Cavanagh et al., 2012). Based on this, it can be inferred from the results of this study that the decreased frontal theta power is associated with decreased cognitive control. This decreased cognitive control could cause a decrement in decision-making ability in occupational settings that lend themselves to rapid Tc acquisition.

The decreased cognitive control, as indicated by decreased frontal theta power (Figure 4.2) when comparing pre- and post-exercise values in PPE, would have implications for the top-down cognitive processing using the PFC. The PFC is associated with top-down processing during attention-based decision-making (Frank & Claus, 2006). The PFC has also been associated with top-down processing in perceptual decision-making: an area of cognition in which sensory information provides the basis for the choice of one or many actions. One model of perceptual decision-making proposed by Heekeren, Marrett and Ungerleider (2008) relates to the computation of a decision variable by accumulating and comparing sensory evidence. In this model, the sensory evidence moves from visual cortex areas, such as the fusiform face area and the parahippocampal place area, to areas that compute a decision variable, such as the DLPFC. In this particular model, the system that represents decision variables extends to the motor and premotor structures. This is a simple progression from perception to action.

6.4 Cerebral Neural Function and Decision-Making Performance Summary and

Conclusion

This study demonstrated that exercise in a hyperthermic environment while wearing PPE causes a decrement in perceptual decision-making ability as proven by significantly reduced frontal theta power. This demonstrates a decrease in cognitive control following incremental exercise in PPE when compared to CON; this decreased cognitive control resulted in a decrease in perceptual decision-making performance in PPE. It should be mentioned that there was a

significant difference in Tc post-exercise between CON and PPE, which may have played a role in the decreased frontal theta power in PPE. Additionally, there was a significant difference between CON and PPE when evaluating end of exercise values for TCS and TS. There was increased TCS and TS during PPE. This could be a contributing factor to the significant differences in perceptual decision-making performance between the two conditions. Thermal comfort plays a role in complex decision-making ability (Cheema & Patrick, 2012). No studies could be found to analyze the effects of thermal comfort or sensation on perceptual decision-making performance. The differences in TCS and TS post-exercise does not explain the differences in frontal theta power that was observed between the two conditions. A more likely explanation for the differences in frontal theta power is related to rate of thermal acquisition. The PSI values reported earlier help to support this argument. The subjects had a higher physiological strain at each common measurement point in PPE when compared to CON. Further research is necessary to confirm whether it was the absolute post-exercise Tc value that resulted in decreased cognitive control in PPE or if the result was related to the rate of thermal acquisition difference. It should be mentioned that it is possible to measure stimulus evaluation speed during Go/No-Go tests (Guo et al., 2018) by measuring the latency of the P300 during event related potential (ERP) analysis. This study did not use ERP analysis due to the ERP data being turbulent. The ERP data was turbulent prior to the P300 wave when evaluating the grand averaged waveform.

CHAPTER 7: RESULTS AND DISCUSSION FOR CORTISOL VARIABLES

Research Question: What effect does exercise while wearing PPE and the resulting rapid and uncompensable Tc acquisition have on the rate and magnitude of salivary cortisol appearance?

7.1 Rate of Salivary Cortisol Appearance Results

In order to calculate the average rate of appearance of salivary cortisol in each exercise condition, the overall magnitude of cortisol was taken at the beginning of exercise and subtracted from the end of exercise value. That number was then divided by the mean TTT. There was a $0.018 \mu\text{g dL}^{-1} \text{min}^{-1}$ appearance in PPE and a $0.002 \mu\text{g dL}^{-1} \text{min}^{-1}$ in CON. This indicates that salivary cortisol appeared at a rate 9 times faster in PPE when compared to CON. Additionally, there was a significant difference in mean cortisol values between start of exercise and the measurement point associated with Tc 38°C ($p \leq 0.01$) (Figure 7.1) and start and end of exercise ($F(1,13) = 22.71$, $p \leq 0.01$; Effect size = 1.47) (Figure 7.2) during PPE. There were no significant differences when comparing any time or temperature values to start of exercise throughout CON.

7.2 End Salivary Cortisol Concentration Results

When analyzing the rate of salivary cortisol appearance, there was a significant difference ($t(13) = -3.4365$, $p \leq 0.01$; Effect size = 0.92) between termination point values when comparing CON and PPE (Figure 7.5). It should additionally be noted that there was a significant difference ($p \leq 0.05$) between Tc at the termination point when comparing CON and PPE.

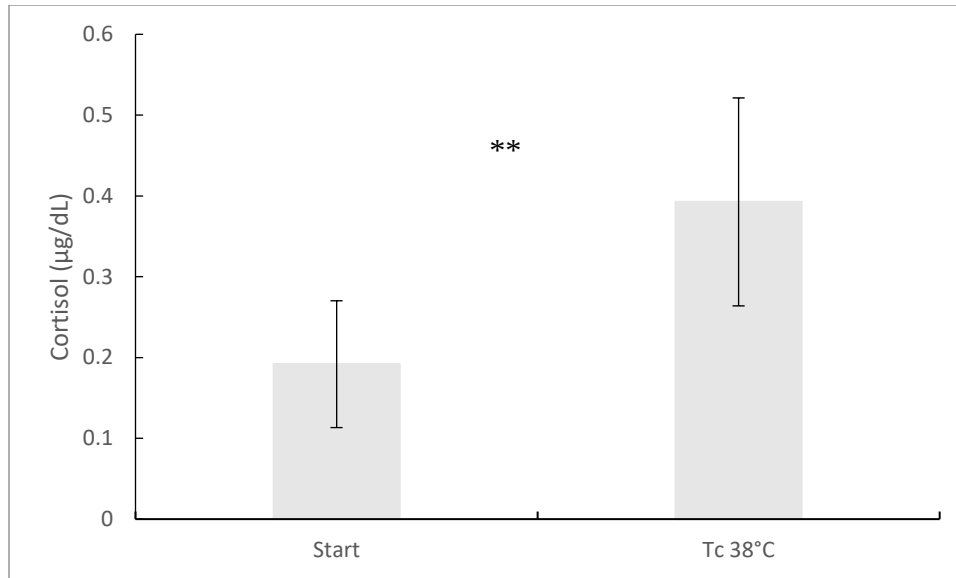


Figure 7.1. Comparison of cortisol concentration from start of exercise to the measurement point associated with Tc 38°C in PPE. Significant difference (** $p \leq 0.01$). Error bars = 95% confidence intervals.

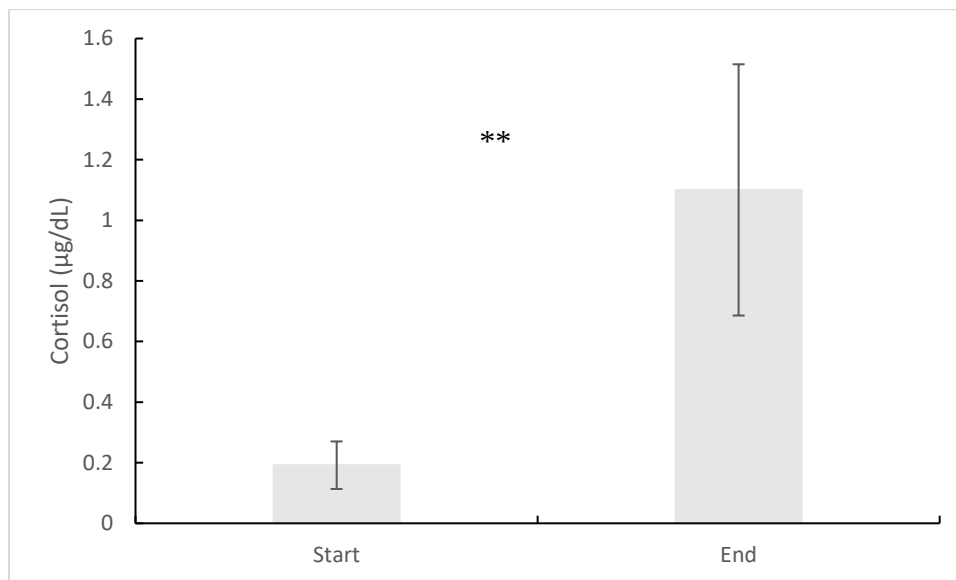


Figure 7.2. Comparison of cortisol concentration from start to end of exercise in PPE. Significant difference (** $p \leq 0.01$). Error bars = 95% confidence intervals.

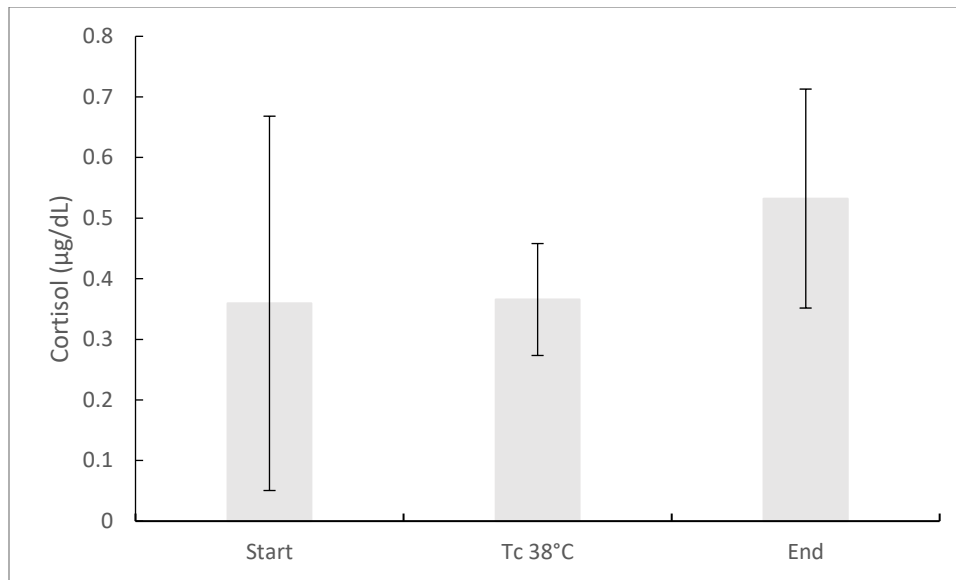


Figure 7.3. Comparison of cortisol concentration at start, Tc 38°C, and end in CON. Error bars = 95% confidence intervals.

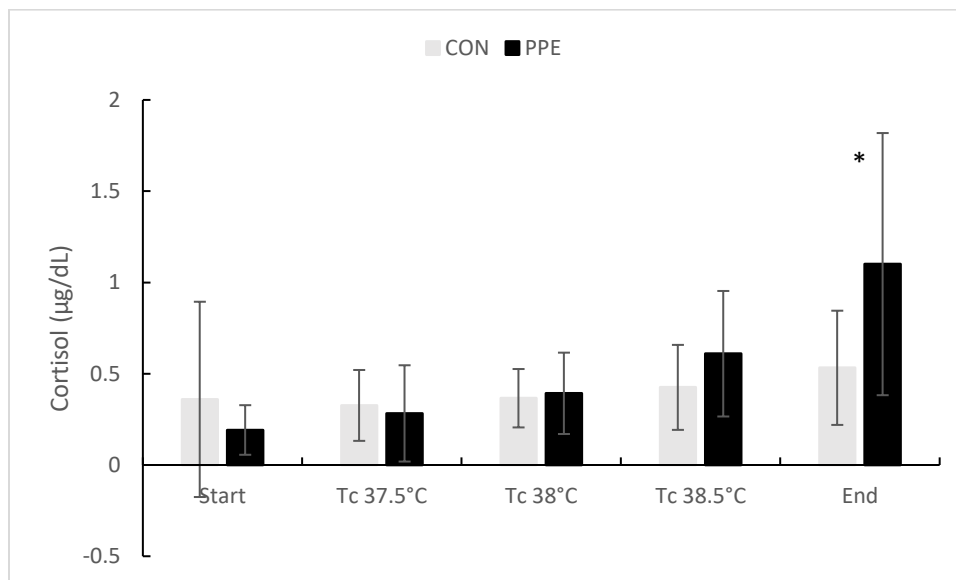


Figure 7.4. Comparison of CON and PPE mean ($\pm$ 95% CI) cortisol values at various time and temperature points. Significant difference (* $p \leq 0.01$). Error bars = 95% confidence intervals.

Note: No statistical analysis was done at Tc 38.5°C. Not all subjects reached this Tc point in both CON and PPE

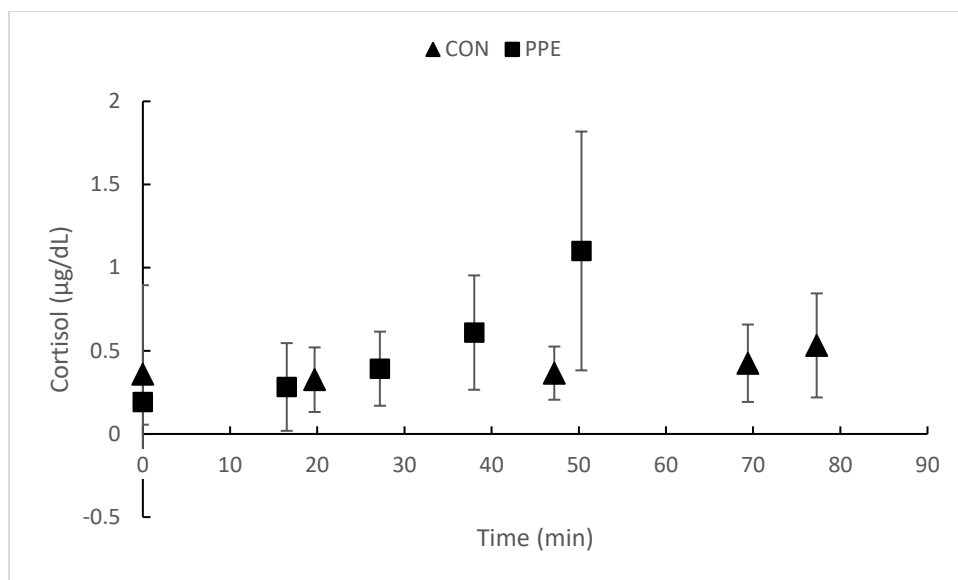


Figure 7.5. Comparison of time and cortisol concentration during CON and PPE. Error bars = 95% confidence intervals.

7.3 Rate and Magnitude of Salivary Cortisol Appearance Discussion

Previous research has demonstrated an effect of hyperthermia on cortisol appearance during exercise (Brenner et al., 1997; Hoffman et al., 1996; Mitchell et al., 2002). Based on this, it was hypothesized that rapid and uncompensable Tc acquisition during incremental exercise to a termination point would have an impact on the rate and magnitude of the appearance of salivary cortisol during PPE. This would differ from the response during CON.

There was a significant difference in the rate of salivary cortisol appearance when comparing CON and PPE as indicated by the rate per minute difference. Salivary cortisol appeared at a rate that was nine times faster in PPE than in CON. There was an exponential relationship between Tc and cortisol appearance in PPE that did not appear in CON. There were statistically significant increases in PPE, but not in CON. This increased cortisol appearance in PPE can be attributed to increased exercise intensity based on physiological measures due

rapid Tc acquisition. To support a higher exercise intensity during PPE, $\dot{V}_E / \dot{V}O_2$ was higher at the end of exercise in PPE when compared to end of exercise values in CON. The subject's ventilation increased more during PPE as a result of reaching the respiratory compensation threshold (RCT) earlier; the RCT is associated with increased ventilation necessary to lower PaCO₂ (Bhambhani et al., 2007; Nybo & Rasmussen, 2007). The increased exercise intensity in PPE is further supported by a significantly higher HR at the end of exercise in PPE when compared to CON. The increased HR in PPE at the end of exercise can be explained by relatively more blood flow redistribution to the cutaneous circulation due to the higher thermal load as well as higher oxygen demand in the working muscles during PPE. This is a result of increased exercise intensity due to the microclimate created by the PPE. Previous research has shown a correlation between exercise intensity and cortisol levels (Hill et al., 2008). Exercise at set higher intensities consistently induces greater cortisol release (Kirschbaum & Hellhammer, 1994). Additionally, incremental exercise to exhaustion results in an increase in cortisol appearance (Vega et al., 2006). This study used a long duration incremental treadmill protocol to a termination point in both conditions. The termination point was in most cases associated with volitional maximum. The variable between trials was the rate of thermal acquisition. The subjects reached each Tc point earlier in PPE (Figure 5.12).

A relationship has also been drawn between exercise duration and cortisol accumulation. Exercise at moderate intensities up to 2 hours has resulted in significant increases in plasma cortisol levels (Tremblay, Copeland & Van Helder, 2005). This same study showed no effect of exercise duration up to 80 min on cortisol appearance. Two of the subjects in this study reached the 2-hour time-cap termination point in CON; none of the subjects reached this termination point in PPE. Increased cortisol presence due to exercise intensity and/or duration can be

attributed to increased glandular secretion and not due to decreases in the metabolic clearance rate (Hill et al., 2008). This increased glandular secretion is due to increased activation of the HPA axis, which results in increased cortisol secretion (Gawel, Park, Alaghband-Zadeh, & Rose, 1979). It can be inferred from this that the subjects in this study had a higher overall glandular secretion of cortisol in PPE when compared to CON. There was also an overall difference in the magnitude of cortisol concentration at the termination point when comparing CON and PPE. This was due to the exponential increase in cortisol concentration in PPE.

It is difficult to determine if the cortisol concentration results from this study, in either the CON or PPE trials, are considered to be higher than normal. Cortisol appearance has a large diurnal effect. The subjects in this study were tested at different times of the day. Each subject completed their individual sessions at the same time of the day, but the subjects were scheduled throughout the day. Cortisol appearance is elevated early in the day and then declines as the day progresses (Nijm & Jonasson, 2009).

Studies using heat stress and exercise show cortisol accumulation at lower exercise intensities. Brenner et al. (1997) had subjects perform two 30-minute exercise bouts in both a normothermic condition and a hyperthermic condition at ~50% of VO_{2max} . They found that the individuals in the hyperthermic condition had elevated cortisol response, while there was no effect in the normothermic trial. Additionally, Mitchell et al. (2002) showed that exercise bouts at ~55% of VO_{2Peak} combined with heat stress elicited an increase in cortisol appearance when compared to a normothermic condition. Both conditions in this study were performed in a hyperthermic environment (ambient temperature was 25-26°C).

The results of this study align with a combination of previous studies completed. A study using an incremental protocol (Vega et al., 2006), a study using simulated firefighting drills

(Perroni et al., 2006), and multiple studies using heat stress and a moderate exercise protocol (Brenner et al., 1997; Mitchell et al., 2006) all showed an increased cortisol response. This study used a long duration incremental protocol while wearing PPE in a hyperthermic environment and also demonstrated an increased cortisol response during PPE over that which was seen in CON. The increase in cortisol accumulation in PPE can be attributed in part to the aforementioned means of increased cortisol appearance, but the exponential increase (Figure 7.7) needs to be attributed to the increased rate of thermal acquisition in PPE. The major difference between the conditions in this study was the rate of thermal acquisition. This exponential increase in salivary cortisol concentration due to rate of thermal acquisition in PPE is a novel finding.

The impact of rapid and uncompensable T_{c} acquisition on cortisol response has an impact for occupational workers who use PPE. Previous research has found that increased cortisol as a result of exhaustive exercise causes a decrease in testosterone levels (Anderson, Lane & Hackney, 2016; Brownlee, Moore & Hackney, 2005). Anderson et al. (2016) additionally found that cortisol levels return to baseline 48 hours following exhaustive exercise, but testosterone required roughly 72 hours for full recovery. High levels of cortisol during prolonged exhaustive exercise could result in an increased catabolic over anabolic effect. Additionally, heat stress resulting in short term increased cortisol response led to decreased performance during central executive tasks and perceptions of mood state (McMorris et al., 2006). Long term elevated cortisol has been associated with a plethora of conditions; chronically elevated cortisol has been linked to accelerated atherosclerosis and subsequent cardiovascular issues (Dekker et al., 2008) as well as anthropometric, endocrine, metabolic, and haemodynamic disturbances (Rosmond, Dallman, & Björntorp, 1998).

7.4 Rate and Magnitude of Salivary Cortisol Summary and Conclusion

The results of this study have demonstrated that exercise to a termination point while wearing PPE results in an exponential rate of cortisol appearance and an overall higher cortisol concentration. This exponential rate of cortisol appearance can be attributed to the increased rate of thermal acquisition during PPE. Acute bouts of increased cortisol concentrations result in decreased testosterone, cognitive performance, and decreased mood states. Long term effects of chronically elevated cortisol results in many conditions and ailments. Firefighters in larger centers which respond to regular fire calls are chronically exposed to acute heat stress. The leading cause of line-of-duty death among firefighters is cardiac related. Statistics show that 45% to 50% of all firefighter duty-related fatalities are a result of sudden cardiac death (Smith et al., 2016). In addition to this, there are 17 to 25 duty-related nonfatal cardiovascular events for every fatal event (Fahy, Leblanc, & Molis, 2015; Haynes & Molis, 2015).

It is suggested that future research analyze the rate of cortisol disappearance during recovery following exercise that creates rapid Tc acquisition. This study simply evaluated the effect of rate of thermal acquisition on salivary cortisol appearance during exercise. This is a preliminary step in the total understanding of the effects of rapid and uncompensable Tc acquisition on the stress response. The next step is to study the rate of cortisol disappearance differences related to these two conditions. This will help to develop a full understanding of the cumulative chronic effects of repeated bouts of rapid thermal acquisition.

CHAPTER 8: OVERALL SUMMARY AND CONCLUSIONS

8.1 Summary and Conclusions

This study has clearly demonstrated an effect of rate of thermal acquisition on cerebral oxygenation, cerebral haemodynamics, cerebral neural function, decision-making performance, and the rate and magnitude of salivary cortisol appearance. The argument for an effect of rate of thermal acquisition is supported by the differences in PSI at all measurement points in this study. The subjects were working harder at all measurements points throughout the exercise protocol in PPE when compared to CON. This is most likely due to increased demand for oxygen by all working areas of the body and increased need for thermoregulation earlier during PPE. During PPE the subjects were acquiring heat up much more rapidly. This resulted in the subjects losing blood volume at a more rapid rate due to earlier increases in the sweating response. Decreased blood volume results in significantly lower stroke volume, central blood volume, aortic pressure, cardiac output, and an increased heart rate. This elevated rate of blood volume loss during PPE resulted in earlier decreases of blood volume to the periphery for thermoregulatory purposes, to the working muscles for locomotion, and to the PFC to maintain optimal cerebral functioning. As PPE progressed, the majority of the limited blood volume would have been redirected to the working muscles for locomotion (Johnson, 1992) and to brain to maintain a desired level of performance (Liu, 2014). This ultimately would have led to an increased rate of thermal acquisition because the subjects were not directing blood flow to the cutaneous circulation later on during PPE and the PPE itself was restricting evaporation of the sweat to the external environment. The blood flow to the brain and to the working muscles decreased earlier in PPE as indicated by earlier decreases in tHb and earlier volitional maximum in most subjects. This was a result of HR not adequately accounting for the loss in cardiac output imposed by the earlier

decrease in stroke volume during PPE. This was additionally a result of decreasing end tidal PaCO_2 beyond the RCT (Ringelstein et al., 1992).

This study showed that there is a difference in unilateral prefrontal cortex activation when exercising in the heat while wearing PPE. There was overall higher activation in the left-side PFC. There was additionally a decrease in cerebral oxygenation and blood flow earlier in PPE when compared to CON. These NIRS results provide a possible explanation for the decreased frontal theta power and decision-making performance found in the Go/No-Go analysis during PPE. This study also showed that cortisol appeared nine times faster during PPE as compared to CON. This increased appearance resulted in a higher magnitude of the presence of salivary cortisol at the termination of exercise in PPE when compared to CON.

The implications of this study are applicable to occupations or athletic endeavors that require the use of PPE and are exposed to high ambient temperatures. Rapid and uncompensable Tc acquisition in these occupational and athletic situations will result in decreased decision-making ability and increased stress response when compared to compensable, normothermic conditions. The decreased decision-making performance will put the life of the employee, and in life-saving occupations, the lives of others at risk. For example, one decision-making error as a firefighter could result in the collapse of a building or loss of life. Acute bouts of increased cortisol response results in decreased testosterone, cognitive performance, and decreased mood states. Chronic effects have been linked cardiovascular disease and sudden cardiac death. Further research is warranted to understand the cumulative effects of acute bouts of exponential cortisol appearance.

The results of this study should cause alarm. It is important to for future research endeavors to find a solution to problem of rapid and uncompensable Tc acquisition. PPE

manufacturers need to come up with a solution to delay Tc acquisition in occupations that require PPE and work in high ambient temperatures. An additional proposed solution would be to require individuals in occupations that require PPE to only use PPE when necessary (ie. firefighters could wear normal clothing when responding to a non-fire related scenarios). These results should also cause concern with safety at work organizations. If a solution can be found to rapid and uncompensable Tc acquisition, there may be significantly less occupational work claims due to decision-making errors and stress related issues.

8.2 Limitations

The present study was limited by the wide age range among the subjects. Middle aged and older males show reduced evaporative cooling capacity and have the potential to store more heat during exercise in hot-dry and hot-humid conditions when compared to younger males (Larose, Boulay, Wright-Beatty, Sigal, Hardcastle, & Kenny, 2014). Additionally, age-related differences exist in regards to exercise induced heat loads when comparing older, middle-aged, and younger males (Stapleton & Kenny, 2014).

The present study was also limited to examining the effects of rapid and uncompensable Tc acquisition in healthy, male subjects. It is important to note that in order to get a full representation of the occupational groups that wear PPE females need to be included. The exact percentages of women in these occupations could not be acquired, but according to Perrot (2016) the number of women working in masculinized work places is increasing. Females were excluded from this study to limit type 1 and type 2 statistical errors.

Lastly, the present study was limited by the lack of adequate body composition measurement. This study used BMI as an indicator of body composition. It would have been more appropriate to use a validated measure to determine fat mass to fat-free mass ratios. Body

fatness has been shown as a known modifier of voluntary exercise tolerance in uncompensable heat stress scenarios (Selkirk & McLellan, 2001).

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Appendix 1: PAR-Q Questionnaire

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

PAR-Q & YOU

(A Questionnaire for People Aged 15 to 69)

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

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

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

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

If
you
answered

YES to one or more questions

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

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

NO to all questions

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

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

DELAY BECOMING MUCH MORE ACTIVE:

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

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

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

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

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

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

NAME _____

SIGNATURE _____

DATE _____

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

WITNESS _____

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



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Appendix 2: Written Participant Consent Form



**University
of Victoria**

Participant Consent Form

The impact of rate of thermal acquisition on brain blood oxygenation, decision making and salivary cortisol concentration

You are being invited to participate in a study entitled “The impact of rate of thermal acquisition on brain blood oxygenation, decision making and salivary cortisol concentration” that is being conducted by Cory Coehoorn, Dr. Lynneth Stuart-Hill, and Dr. Olav Krigolson. Cory Coehoorn is a PhD student in the School of Exercise Science, Physical and Health Education at the University of Victoria. Dr. Stuart-Hill and Dr. Krigolson are faculty members of the School of Exercise Science, Physical and Health Education at the University of Victoria. If you have any questions or concerns about the study, you may contact Dr. Stuart-Hill at 250-721-7884 or via email at lstuhill@uvic.ca.

As a graduate student, I am required to conduct research as part of the requirements for the degree of PhD in Kinesiology. It is being conducted under the supervision of Dr. Lynneth Stuart Hill and Dr. Olav Krigolson. You may contact Dr. Stuart-Hill at 250-721-7884 and Dr. Krigolson at 250-721-7843 .

The purpose of the proposed study is to examine the impact of rapid heat acquisition (RHA) on brain blood oxygenation (prefrontal cortex), brain wave activity, and decision making. Additionally, the impact of RHA on the rate and magnitude of appearance of salivary cortisol

and blood glucose will be determined. This research will contribute to two areas, both of which are involved in examining the impact of RHA on the human body. First, RHA is a significant physiological stress that causes major cardiovascular blood flow adjustments throughout the body. These adjustments can potentially limit blood flow to vital organs such as the brain, which will impair decision-making processes. Second, RHA also causes other non-positive body responses such as the release of stress hormones. The proposed research will also determine the rate and magnitude of the appearance, as well as the duration of cortisol in saliva as a result of RHA.

You are being asked to participate in this study because you are a healthy, active volunteer firefighter between the ages of 20 and 55. If you agree to participate in this study, you will perform 3 exercise trials. The first will consist of a maximal aerobic test on a treadmill to determine maximal oxygen consumption (VO₂ max). The last two trials will be randomly assigned in a crossover design to prevent an order effect. One trial will consist of the participant exercising in standard exercise gear (runners, socks, shorts, t-shirt) while the other trial will consist of the same exercise condition performed while wearing personal protective equipment (pants, jacket, balaclava, helmet and gloves).

During the testing sessions, several physiological variables will be monitored or measured including: height, body mass, urine specific gravity, blood pressure, core body temperature, skin temperature, tympanic temperature, salivary cortisol, blood glucose, ventilatory variables, heart rate, brain wave activity, and brain blood flow. Throughout testing, core temperature will be continuously monitored using a telemetry system and ingestible, biocompatible, telemetric capsules. Heart rate will be monitored continuously by a heart rate monitor. Ventilatory variables will be collected from the air you expire (blow out). To measure

brain blood flow two sensors will be placed on your forehead and attached with tape and a headband. To measure decision-making you will be asked to perform a go, no go test. The specific details of each measurement are below:

Urine analysis

Subjects will be asked small urine sample in a spill proof collection cup. A USG refractometer will be used to immediately assess USG. Excess urine and urine sample will be immediately disposed of.

Blood glucose

Blood glucose will be determined pre-test and a number of times during the test protocols. A finger prick blood sample will be obtained, immediately analyzed using a handheld glucometer. The sample will be immediately disposed.

Saliva sampling and analysis

Saliva will be sampled before exercise and 10 minutes post exercise. Samples will immediately refrigerated and then frozen at -20°C for later analysis using Salimetrics ELISA assay kits for cortisol.

Measurement of core temperature

Core temperature (T_c) will be monitored every 30 seconds using the equivital integrated physiological monitoring system. T_c will be directly measured from the ingested jonah core temperature capsules (VitalSense, Health Canada License # 70240). Participants will discontinue work bouts and a cooling protocol will be started if/when core temperature reaches 39.5°C.

Determination of heart rate

Heart rate will be continuously sampled with an equivalent integrated physiological monitoring system

Determination of ventilatory variables

Participants will be connected to the metabolic cart via a regulator that allows sampling of expired air from the participant while they inhale normoxic air from the environment.

Ventilatory measurements will be taken as 30 second averages during the work bout. VO_2 (volume of oxygen), VCO_2 (volume of carbon dioxide produced), VE (ventilation), and RER (respiratory exchange ratio) will be calculated by computer software (Parvomedics, USA).

Determination of pre-frontal cortex brain oxygenation

Throughout the experimental procedure a continuous wave near-infrared spectroscopy (NIRS) monitor (Portalite, Artinis Medical systems bv, the netherlands; oxysoft version 2.1.6) will measure changes in concentrations of: oxyhemoglobin (HbO_2), deoxyhemoglobin (HHb), total hemoglobin (tHb), and hemoglobin difference (HbDiff) in μm . The data will be collected at 10hz with a differential pathlength factor (DPF) associated with age and wavelengths set at 761nm and 848nm.

Brain wave activity

Throughout the experimental procedure a muse (Interaxon inc., Canada) will be used to measure changes in brain wave activity. The muse is placed on the forehead (similar to a headband) and uses eeg sensors to measure brain activity in the prefrontal cortex.

Go/No-Go test

Go/no-go testing is often used as a component of a behavioral neurological examination to assess inhibitory control. The subject first learns a procedure of matching a stimulus with a response.

For example, when the tester shows one finger the subject responds with an appropriate action, and when two fingers are shown they respond with an alternative action. The subject learns this protocol and then the rules change, at this point the actual Go/No-Go test begins. Go/No-Go tests are used to measure a participant's capacity for sustained attention and response control

Participation in this study may cause some inconvenience to you. This will include having to come to the lab on three separate occasions for one and a half to two hours each time.

The inclusion criteria for this study are as follows:

- Age 20-55 years; successful response to the physical activity readiness questionnaire (PAR-Q); all other characteristics are unspecified

The exclusion criteria for this study are as follows:

- Age 0-19 and 55 + years of age; unsuccessful response to the physical activity readiness questionnaire (PAR-Q); esophageal restrictions.

There are also potential risks associated with participation in this study. Participants will be exposed to risks of dehydration, elevated core temperature, physical fatigue, and discomfort due to the nature and conditions of the physical work performed during this study. Individuals who have any esophageal restrictions **BE EXCLUDED FROM THE STUDY AS IT IS NOT SAFE FOR THEM TO SWALLOW THE CORE TEMPERATURE CAPSULES.** In light of these risks, your testing sessions will be terminated if you experience any of the following:

- i) core temperature ≥ 39.5 degrees Celsius
- ii) muscle cramps
- iii) vertigo or syncope (dizziness)
- iv) nausea or vomiting
- v) 'chills' of the head or neck
- vi) Signs of confusion or changes in mental status
- vii) Inability to continue exercise (volitional fatigue, you decide to stop)

EMERGENCY ACTION PLAN

IN THE EVENT OF AN EMERGENCY THE APPROPRIATE AUTHORITIES MUST BE IMMEDIATELY CONTACTED;

911 – EMERGENCY SERVICES (INCLUDING AMBULANCE, FIRE/RESCUE, POLICE)

7599 (LOCAL) 721-7599 (OFF-CAMPUS) – CAMPUS SECURITY

TESTING LOCATION;

MCKINNON BUILDING, ROOM 171

SCHOOL OF PHYSICAL EDUCATION,

UNIVERSITY OF VICTORIA,

3800 FINNERTY ROAD

LOCATION DESCRIPTION – OUTSIDE OF RING ROAD, JUST NORTH OF THE BOOKSTORE/BUS LOOP, BETWEEN FINNERTY ROAD & GABRIOLA ROAD.

TELEPHONE NUMBER FOR MCK 171 – 721-8391

ONE OF THE TESTING STAFF WILL IMMEDIATELY COMMENCE FIRST AID AND CARDIOPULMONARY RESUSCITATION (CPR) AS REQUIRED, WHILE ANOTHER STAFF MEMBER WILL CONTACT EMERGENCY SERVICES PERSONNEL AT THE TELEPHONE NUMBERS LISTED ABOVE. IT IS IMPERATIVE THAT CAMPUS SECURITY BE NOTIFIED SO THAT THEY MAY COORDINATE WITH THE EMERGENCY SERVICES PERSONNEL TO EXPEDITE THE PROCESS OF ARRIVING AT THE EMERGENCY LOCATION.

Individuals who volunteer to participate in the study will be given information on their personal physiological responses while working under thermal challenge thus increasing their own safety while on the job. The results of this research will contribute to understanding the effects of rapid heat acquisition on brain blood flow, decision making, and the stress response.

Participation in this research must be completely voluntary. If you do decide to participate, you may withdraw at any time without any consequences or any explanation. If you do withdraw from the study your data will not be used in analysis.

In order to protect your anonymity, no data will be recorded with your name on it. However, due to the nature of this research you will not be anonymous to the researchers involved. Your confidentiality and the confidentiality of the data will be protected by assigning an ID number to you, which will be used to code all your data. The data will be stored on a password-protected

computer. Both the master list of participants and ID numbers and the password-protected computer will be locked in Office 132 in the McKinnon building. THE DATA WILL BE SECURELY STORED ELECTRONICALLY FOR 5 YEARS AFTER WHICH IT WILL BE ERASED.

It is anticipated that the results of this study will be shared with others through presentation at the local fire departments, publication in a scholarly journal, and as part of Cory Coehoorn's thesis presentation. You may also receive a copy of all your data if you wish.

In addition to being able to contact the researchers at the above phone numbers, you may verify the ethical approval of this study, or raise any concerns you might have, by contacting the RESEARCH ETHICS OFFICE at the University of Victoria (250-472-4545) or via email at ETHICS@uvic.ca.

Your signature below indicates that you understand the above conditions of participation in this study and that you have had the opportunity to have your questions answered by the researchers.

Name of Participant

Signature

Date

A copy of this consent will be left with you, and a copy will be taken by the researcher.

Visually Recorded Images. Participant to provide initials, *only if you consent to photos and purpose:*

- Photos may be taken of me for dissemination of results * _____ (Initials).

*Even if no names are used, you may be recognizable if visual images are shown in the results.

ALL UNIVERSITY OF VICTORIA DISSERTATIONS ARE POSTED ON THE LIBRARY
WEBSITE FOR PUBLIC ACCESS (“UVICSPACE”)

Appendix 3: Safety Screen – Ingestion of a Core Temperature capsule

Safety Screen – Ingestion of a Core Temperature capsule

As part of this research project you will be asked to ingest (swallow) a core temperature capsule.

The size of the core temperature capsule is like a large vitamin pill. In order to ensure it safe and easy for you to ingest the capsule please answer the following two questions.

1. Have you ever experienced difficulty with swallowing any sort of pill?

YES NO

2. Have been told by a medical doctor that you have an esophageal restriction (a narrowing of the throat)?

YES NO

Appendix 4: Pictures of Participant Data Collection



