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Characterizing the Central Hemodynamic Response to Orthostasis: Influence of Sex, Fitness and Body Composition

Benjamin Schreck

The University of Southern Mississippi

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by

Benjamin Schreck

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Approved by:

Daniel Credeur, Ph.D., Thesis Adviser
Assistant Professor
School of Kinesiology and Nutrition

Scott Piland, Ph.D.
Professor and Director
School of Kinesiology and Nutrition

Ellen Weinauer, Ph.D., Dean
Honors College

Abstract

Inter-individual responses to orthostasis (i.e., ability to maintain consciousness in the upright posture) exist. However, few studies provide insight into the potential mechanisms for this variation. The purpose of this thesis project was to explore individual differences (i.e., sex, fitness, and body composition) on the central hemodynamic response to a modified head-up tilt table test (HUT). Fourteen volunteers with an average age of 22±1 years and an average body mass index (BMI) of 8±1 kg/m^2 underwent assessments of pulse wave analysis, heart rate variability, and perfusion determination via near-infrared spectroscopy over the gastrocnemius muscle while supine, followed by a 5-min HUT (torso; 70°). Aerobic fitness (VO_2 peak; 3-min step test) and body composition (body fat percentage; skinfolds) were estimated. During HUT, heart rate (+5±1 bpm; $p<0.001$), reflection magnitude (+4±2%; $p=0.017$), and gastrocnemius perfusion (total hemoglobin—tHB) increased (+4±1 μM), with no change occurring in augmentation index (AIx: $p=0.31$) and mean arterial pressure ($p=0.95$). The low-high frequency component ratio increased during HUT (LF/HF: +2.8±1.5 AU), but was only significant at $p=0.08$. Females exhibited an increase in AIx to HUT (females=+7±2 vs. males=-1.9±3%; $p=0.38$). Independent of sex, there was a relationship between VO_2 peak and LF/HF change to HUT ($r=0.68$; $p=0.02$). No interactions were noted for body fat percentage and HUT. These preliminary findings indicate that individual differences (i.e., sex and fitness) influence the cardiovascular response to orthostasis.

Keywords: Orthostasis, hemodynamic response, HUT, perfusion

Dedication

To my late grandparents, Armando and Rosa Ortiz, I love and miss you.

To the members of Eagle Catholic, thank you for reminding me, through all of the stress and trials of college, to always seek to live according to His will.

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To Dr. Credeur, thank you for your patience and your dedication to my personal and academic development. Your guidance has aided me tremendously and this entire experience would not have been possible without you. Congratulations and good luck on your journey of fatherhood.

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List of Abbreviations

AIx	Augmentation Index
AU	Arbitrary Uni
BMI	Body Mass Index
bpm	Beats Per Minute
BRS	Baroreflex Sensitivity
ECG	Electrocardiogram
HbA1c	Glycated Hemoglobin
HUT	Head-up Tilt Table Test
LF/HF	Low-High Frequency Component Ratio
NIRS	Near-Infrared Spectroscopy
PWA	Pulse Wave Analysis
SRS	Spatially Resolved Spectroscopy
tHB	Total Hemoglobin
VO_2	Oxygen Consumption
YMCA	Young Men's Christian Association

Chapter 1: Introduction

Autonomic responses to physiological demands such as an orthostatic challenge (i.e., ability to maintain consciousness in the upright posture) are readily observed as markers for cardiovascular health (Sarafian & Miles-Chan 2017). A head-up tilt-table test (HUT) is a common assessment used in clinical settings to test for abnormalities in hemodynamic responses to the upright posture. An individual with adequate cardiovascular health and fitness typically displays normal hemodynamic responses to the orthostatic stressor like the tilt test, characterized by an increase in heart rate with little to no change in arterial blood pressure. The increase in heart rate is also accompanied by an increase in peripheral vascular resistance mediated by elevations in sympathetically-induced vasoconstriction (Stoner et al. 2015). These sympathetic responses in peripheral vascular resistance may be attributed to increases in gravitational force on the vasculature during an orthostatic tilt challenge (Pucci et al. 2016). However, there appear to be inter-individual fluctuations in physiological response to an upright tilt, which may place some individuals at greater risk for developing orthostatic hypotension. Some of the variation in the response to the HUT stimulus may stem from differences in cardio-vagal baroreflex sensitivity (BRS), the reflexive physiological ability to respond to the peripheral pooling of blood caused by HUT (Ramírez-Marrero et al. 2007). Gaining a greater understanding of these differences and contributing mechanisms will enhance treatment and early detection of individuals with autonomic nervous system impairment and subsequent cardiovascular disease risk.

The purpose of this thesis project was to explore individual differences (i.e., sex, fitness, and body composition) on the central hemodynamic response to a modified head-

up tilt. The use of the modified torso-only HUT presents a more accessible yet still reliable option for observing effects of orthostasis (Stoner et al. 2017). Utilizing pulse wave analysis to evaluate changes in blood pressure and central hemodynamics, electrocardiography to monitor cardio-vagal responses, and near-infrared spectroscopy to monitor leg blood volume changes, during and following HUT should allow for an understanding of variation in inter-individual responses to the orthostatic challenge. The use of different demographical populations coupled with subsequent aerobic fitness testing may yield further insight on the physiological basis for inter-individual variations in the orthostatic response, as previous research has not fully indicated if factors such as age, gender or body composition have a significant effect on hemodynamic responses to the orthostatic challenge (Tahvanainen et al. 2009).

Chapter 2: Literature Review

In recent decades, cardiovascular disease has become a leading cause of death among individuals throughout the world, especially within the United States (CDC 2015). In addition, to traditional clinical tests, i.e., blood pressure, other novel assessments have been developed to diagnose cardiovascular irregularities. Along these lines, this study will evaluate the utilization of a modified head up tilt-table (HUT) test as an assessment test for central hemodynamic abnormalities. The HUT serves as an orthostatic stressor (i.e., ability to maintain consciousness in the upright posture), which challenges the arterial baroreflex (Vanoli & Adamson 1994). Essentially, a healthy individual in a supine position has normal blood flow throughout the body. If the individual's trunk is tilted, as in the case of someone beginning to sit up, blood will temporarily pool in the lower extremities as gravitational forces will increase blood flow to the legs (Taylor et al. 2013). In most individuals, a reflex response which originates from receptors within the aortic arch and carotid sinus causes an increase in heart rate, and/or increases in peripheral vascular resistance, which in turn prevents a significant decrease in arterial blood pressure (Grubb et al. 1997). However, in some individuals, the orthostatic stressor will yield an augmented parasympathetic, i.e. vasovagal, response (Van Lieshout et al. 1997). The vagus nerve, as an efferent modulator in the parasympathetic nervous system, functions to decrease heart rate by decreasing autonomic stimulation of the sinoatrial node. Vagal stimulation is important in avoiding tachycardia and other associated symptoms, but excessive vagal stimulation in response to HUT can induce syncope in individuals with poor cardiovagal regulation (Halliwill & Minson 2005). The orthostatic stressor allows for an increased gravitational effect on the vasculature and the subsequent

pooling of blood in the legs (Sundblad et al. 2016). Vasoconstriction of peripheral vasculature through sympathetic innervation and skeletal muscle pump increase blood flow back to the heart, ensuring proper tissue oxygenation and normal function. A healthy individual's heart will typically be stimulated to momentarily increase heart rate to accommodate the brief drop in blood pressure due to pooling in the legs, thereby maintaining homeostatic levels of cardiac output (Wyller et al. 2011). Increased sympathetic outflow from the brainstem will also promote lower extremity vasoconstriction, thus ensuring normal levels of blood flow to other vital organs, such as the brain, following the orthostatic challenge (Stewart 2012). However, in individuals not possessing the normal central hemodynamic reflex response to the orthostatic stressor, symptoms such as hypoxia and syncope may occur. Thus, it is important for researchers to study the physiological mechanisms governing central hemodynamic responses to a HUT, which may allow clinicians to better prescribe treatments to prevent orthostatic intolerance in 'at-risk' individuals.

Commonly, these 'at risk' individuals lack the ability to withdraw parasympathetic vagal stimulation in order to allow for the necessary increase in heart rate. As a result, these individuals exhibit orthostatic hypotension, a sharp decrease in blood pressure, in response to the orthostatic challenge (Luther et al. 2008). Blood is not able to circulate at a normal rate, resulting in a decrease in oxygenated blood being delivered to the brain. This hypoxic response and lack of oxygen, glucose, and other necessary nutrients being delivered to the brain can cause syncope. Normal function of sympathetic regulatory responses can aid in avoiding orthostatic intolerance, including vasovagal syncope and orthostatic hypotension (Stewart et al. 2012). Individuals who

suffer symptoms of orthostatic intolerance during a HUT are returned to a supine position and will typically return to consciousness and normal hemodynamic levels. This study utilized a modified head-up tilt procedure, manipulating only the torso in order to attenuate symptomatic effects observed in full supine-to-upright tilt procedures. Full and modified head-up tilt procedures can induce symptoms of vasovagal syncope in individuals who may be predisposed to autonomic dysfunction (Shinohara et al. 2014). The procedure used in this study, a modified head-up tilt of seventy degrees from the hips, can induce a similar orthostatic response to traditional head-up tilt methods; however, this modified form is non-invasive, does not require direct medical supervision, and poses far less risk to the subject. This modified head-up tilt was found to be more appropriate for use in the current research setting. The presence of an irregular response to an orthostatic challenge, however, can be indicative of an underlying pathological issue (Chi et al. 2008). As such, the HUT test utilized in this study can serve as diagnostic tool for health professionals. The impaired vasoconstrictive response associated with orthostatic intolerance can lead to abnormal hemodynamic responses in both exercise and functional settings (Raine et al. 2001). An individual predisposed to orthostatic hypotension and bradycardia in response to the orthostatic challenge may suffer from autonomic dysfunction and possible cardiovascular disease (Grubb et al. 1997). This study will follow previous research in assessing individual central hemodynamic responses to the HUT orthostatic challenge. Additionally, there is a shortage of research evaluating the potential effects of sex, fitness level, body composition and other markers on orthostatic stress responses to the HUT. The purpose of this thesis project was to

explore individual differences (i.e., sex, fitness, and body composition) on the central hemodynamic response to a modified head-up tilt table test.

Chapter 3: Methodology

Participants

This study utilized 14 volunteer subjects (age range=18-55 years) who were recruited from The University of Southern Mississippi and the surrounding area. Subjects were recruited via paper announcement, email and word-of-mouth. Subjects had to be 18-55 years old, possess minimal cardiovascular risk factors, not engage in strenuous activity for at least 12 hours pre-study, not consume alcohol for at least 12 hours pre-study and be fasted for at least 2 hours pre-study. This study was approved for proper human subjects research ethics by the Institutional Review Board at The University of Southern Mississippi. Study procedures were completed within the School of Kinesiology and Nutrition at The University of Southern Mississippi. All subjects completed an informed consent form approved by the Institutional Review Board of The University of Southern Mississippi.

Experimental Measures

Following completion of a medical health history form and physical activity questionnaire, our research team (Dr. Credeur, graduate assistant Raymond Jones, and myself) performed a cardio-metabolic health assessment on each subject to collect data for later correlational analysis. These data measurements taken at baseline included blood sampling (via finger stick) for fasting glucose and HbA1c levels and body composition (body fat percentage) determined via 3-site skinfold test with skin calipers. Following collection of baseline data, the subject rested on an examination table with an adjustable back. Device instrumentation (placement and calibration) was completed prior to baseline measurements. Mean arterial pressure, forward and backward pressure waveforms,

reflection magnitude, augmentation pressure, augmentation index, and heart rate-corrected augmentation index were measured using a telemetric blood pressure monitor utilizing pulse wave analysis (Stoner et al. 2015). Low-high frequency component ratio, heart rate, and R-R interval (interval between peaks of QRS complexes observed via ECG) ratio were measured via electrocardiogram. Gastrocnemius perfusion levels including oxyhemoglobin, deoxyhemoglobin, total hemoglobin and SRS levels were measured via near-infrared spectroscopy technology placed on the medial gastrocnemius (Stone et al. 2016). Subjects rested for 10 minutes before baseline measurements were collected. Baseline measurements were collected twice to ensure reliability between readings. These measurements were taken while the subject was in supine position. Following baseline measurements in the supine position, the subject was adjusted to a 70° tilt (angle at torso from lower body, measured via goniometry) on the adjustable experimental table. Measurements were taken again at minutes 2 and 5 of tilt and, following tilt, the subject was immediately returned to the supine position, with another series of measurements performed at minutes 2 and 5 of recovery. The first tilt session, including tilt and recovery, lasted approximately 10 minutes. After an additional 5 minutes of rest post-recovery, the tilt was repeated with the previous protocol. Following the HUT, subjects completed a standard YMCA step test on a 12-inch step box (Bohannon et al. 2015). Our research team used this test to extrapolate the individual's VO_2 peak value and associated level of aerobic fitness. The subject's heart rate was monitored closely via Polar heart rate monitor during and into the recovery period of the step test.

Pulse Wave Analysis (PWA)

Pulse wave analysis (Wilkinson et al. 1998) is determined using computer technology that utilizes peripheral blood pressure readings from blood pressure monitors to create peripheral pressure waveforms and generate a corresponding central pressure waveform. These values can be used to determine augmentation index and central blood pressure values with reliability (Stoner et al. 2017). These values may also be used to measure levels of arterial stiffness.

Near-Infrared Spectroscopy (NIRS)

Using a NIRS device placed on the gastrocnemius muscle, NIRS works by producing various wavelengths (approximately 800 to 2500 nm) of light through an object that are then reflected back to the device. The light intensity from the wavelengths measured through interaction with the object diffuse as a combination of the absorbance and scattering of light waves (ThermoFisher). The collection of bond vibrations from the object will then allow for approximation of hemoglobin levels at the gastrocnemius muscle. Increases in the SRS signal from the NIRS indicate less vasoconstriction and vascular tone and more pooling within the lower extremity following the orthostatic challenge (Stone et al. 2016).

Data Analysis

Subjects were all provided with de-identified laboratory identification labels in order to identify subject information while ensuring information confidentiality. Laboratory measurement data was collected and tracked using Microsoft Excel spreadsheets as information was compiled from separate sources. For heart rate

variability, information was taken in 1-minute segments around respective time points in Powerlab and averaged. Time and frequency domain values were collected for heart rate variability measurements. NIRS measurements were collected with the Portalite system utilizing Oxysoft software; 1-minute recordings were collected at respective time points and averaged in order to obtain perfusion values throughout the procedure.

Statistical Analysis

For the whole cohort, to examine the influence of the modified HUT on primary dependent variables (i.e., HR, blood pressure, HRV, central hemodynamics, and leg blood volume), a one-way analysis of variance was performed. To determine the potential modifying role of biological sex on study outcomes, a two-way repeated measures ANOVA was performed (sex*tilt time). Body fat %, and aerobic fitness were incorporated as covariates into the analysis. Data normalities were checked using a Shapiro-Wilk test. In the event of non-normal data distributions, an ANOVA on ranks was performed (i.e., Kruskal-Wallis one way). In the event of significant interactions, Bonferroni was selected as the post-hoc test. All statistical analyses were performed using SigmaPlot (Version 12) and SPSS (Version 22) statistical software. All data are presented as mean ± standard error, and statistical significance was set *a priori* as $p>0.05$.

Chapter 4: Results

Subjects were found to exhibit increases in heart rate (+5±1 bpm; p<0.001), reflection magnitude (+4±2%; p=0.017), and gastrocnemius perfusion (+4±1 μM; **Figure 1**) during HUT. No changes were observed in augmentation index (p=0.31) and mean arterial pressure (p=0.95). Overall subject data for these factors can be found in **Table 1**. Gender-derived subject data for these factors can be found in **Table 2** and **Table 3**.

Table 1. Collective Hemodynamic Response (Cohort Total)

		Tilt	
	Baseline	**2 mins**	**5 mins**
MAP (mmHg)	78.6 ± 2.9	79.0 ± 2.6	78.7 ± 2.7
HR (bpm)	64.6 ± 2.7	67.1 ± 2.9*	69.9 ± 2.7*
P_f (mmHg)	30.4 ± 1.4	28.8 ± 1.5	29.2 ± 1.4
P_b (mmHg)	14.1 ± 0.7	13.7 ± 0.5	14.6 ± 0.9
RM (%)	46.3 ± 1.6	48.3 ± 1.9	50.1 ± 1.6*
AP (mmHg)	3.9 ± 1.0	3.6 ± 1.1	4.1 ± 1.1
AIx (%)	10.7 ± 2.5	10.8 ± 3.2	11.4 ± 2.7
AIx75 (%)	4.9 ± 3.2	7.8 ± 3.0	7.5 ± 2.6

**Denotes p<0.05 vs. Baseline.*

Table 2. Collective Hemodynamic Response (Men)

			Tilt	
	MEN	**Baseline**	**2 mins**	**5 mins**
MAP (mmHg)		79 ± 3.4	79.1 ± 2.3	78.6 ± 2.7
HR (bpm)		68.5 ± 2.4	73.8 ± 2.9	72.8 ± 2.5
P_f (mmHg)		31.6 ± 1.8	30.8 ± 1.7	29.6 ± 1.8
P_b (mmHg)		14.4 ± 0.8	14.1 ± 0.5	13.9 ± 0.9
RM (%)		45.7 ± 1.0	46.1 ± 1.2	47.2 ± 0.3
AP (mmHg)		3.7 ± 1.0	2.3 ± 0.9	2.2 ±0.7
AIx (%)		10.3 ±2.6	6.9 ± 2.7	6.6 ± 1.9
AIx75 (%)		6.1 ± 3.5	5.1 ± 3.1	4.3 ± 2.5

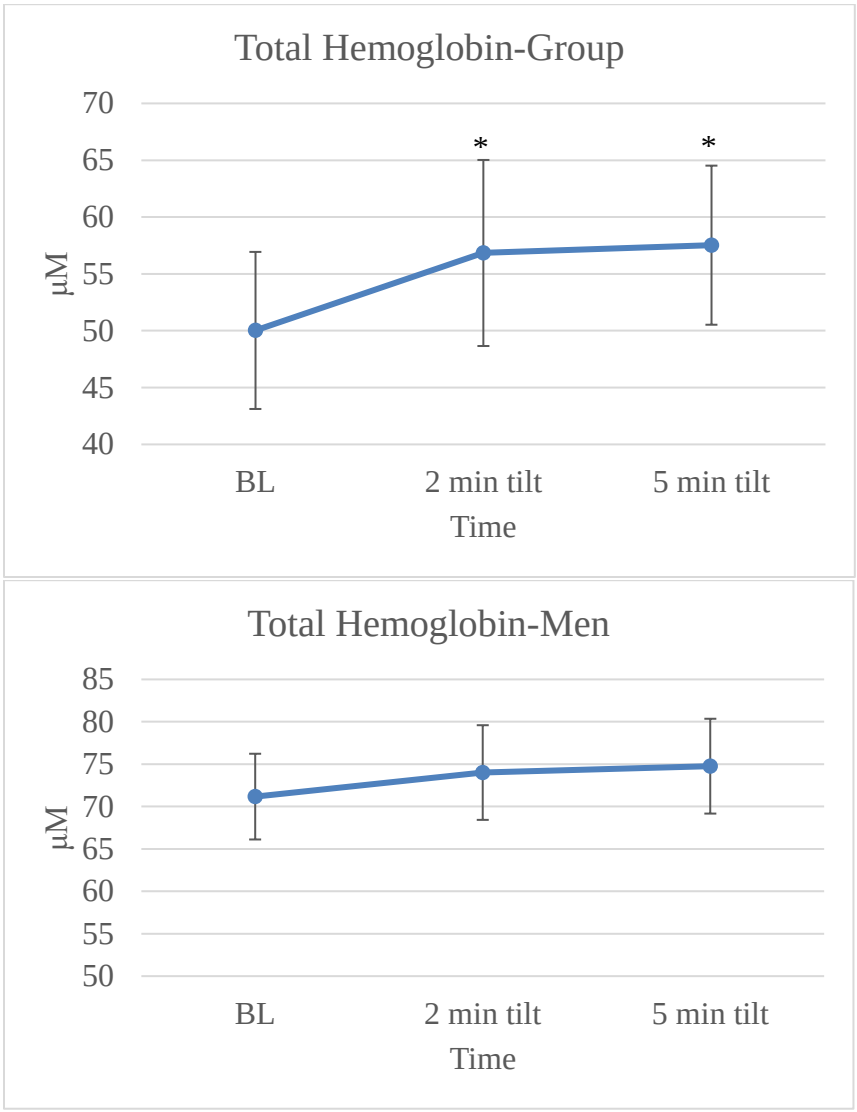
Table 3. Collective Hemodynamic Response (Women)

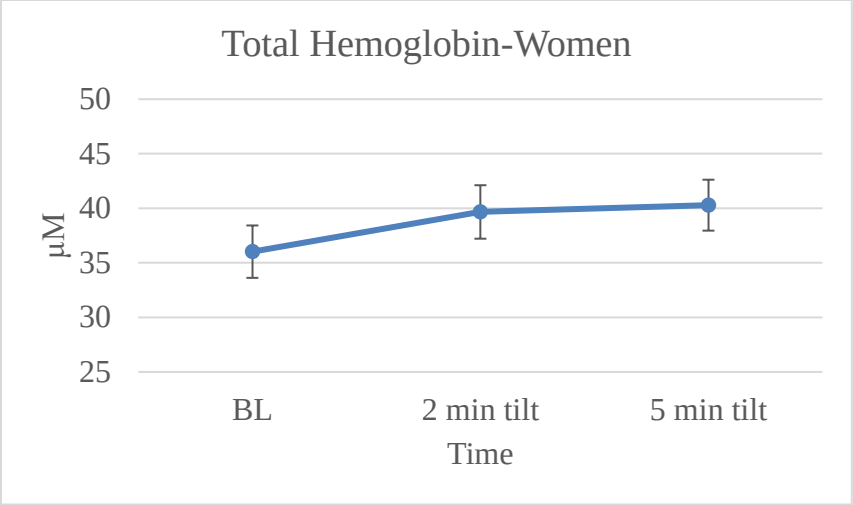
			Tilt	
	WOMEN	**Baseline**	**2 mins**	**5 mins**
MAP (mmHg)		78.2 ± 2.4	78.9 ± 3.1	78.9 ± 3.0
HR (bpm)		62.0 ± 3.0	64.4 ± 2.3	66.8 ± 2.2*
P_f (mmHg)		29.1 ± 0.7	26.8 ± 1.0	28.3 ± 0.9
P_b (mmHg)		13.8 ± 0.8	13.4 ± 0.6	15.31 ± 0.9
RM (%)		47.0 ± 2.1	50.4 ± 2.3	53.1 ± 1.9*
AP (mmHg)		4.0 ± 1.1	4.9 ± 1.0	5.9 ± 1.3*
AIx (%)		11.0 ± 2.7	14.8 ± 3.3	16.2 ± 2.7
AIx75 (%)		3.8 ± 3.0	10.4 ± 2.8*	10.8 ± 2.5*

**Denotes p<0.05 vs. Baseline.*

Figure 1. Total Hemoglobin Change (Total and Gender Comparison)

**Denotes p<0.05 vs. Baseline.*





***Data collected via NIRS, showing increases in total hemoglobin levels at the gastrocnemius at baseline (BL) and into the duration of the HUT.**

The low-high frequency component ratio increased during HUT (LF/HF: +2.8±1.5 AU; p=0.08). There was a tendency for females to exhibit an increase in AIx to HUT (females=+7±2 vs. males=-1.9±3%; p=0.05). For men and women, there was a relationship observed between VO_2 peak and LF/HF change to HUT (r=0.68; p=0.02). No interactions were noted for body fat percentage and HUT response. No interactions were noted for blood glucose and HbA1c levels and HUT response.

Chapter 5: Discussion

The purpose of this study was to explore the inter-individual differences, namely gender, aerobic fitness and body composition, on the central hemodynamic response to a modified head-up tilt. We found that heart rate, reflection magnitude, and gastrocnemius perfusion all displayed increases during HUT. No changes were observed in augmentation index and mean arterial pressure in response to HUT. Also, during HUT the low-high frequency component ratio increased. An increase in augmentation index

was observed in female subjects only. Across the group, a relationship was observed between VO_2 peak and changes in the low-high frequency component ratio in response to tilt. There were no interactions observed between body fat percentage and the orthostatic response.

Cardio-Vagal Response

Increases in the low-high frequency component ratio may be indicative of parasympathetic withdrawal and sympathetic innervation in response to the orthostatic challenge. Observed increases in heart rate in response to HUT may be indicative of the shift toward sympathetic stimulation of the autonomic nervous system as a method of addressing the gravitational impact imposed on the body by the orthostatic challenge. A study conducted by Kamiya and colleagues asserted that the body maintains arterial pressure and circulation via compensatory mechanisms for addressing gravitational stress; among these compensatory mechanisms is sympathetic activation to deter gravitational effects that could induce orthostatic hypotension and vasovagal syncope (Kamiya et al. 2009). The observed increase in heart rate as mean arterial pressure decreased or stabilized in participants can further support the presence of sympathetic activation in the cardio-vagal response to the orthostatic challenge. Additionally, a relationship was observed between VO_2 peak levels and variation in low-high frequency component ratio. This may suggest that individuals with higher VO_2 levels and subsequent aerobic health may be more readily adaptable to the orthostatic challenge through an increased sympathetic activation. Males showed a slight decrease in heart rate at 5 minutes of tilt whereas females showed a steady increase in heart rate upon and

throughout tilt. Body fat percentage did not present any significant effect on the cardio-vagal response to the orthostatic challenge.

Central Hemodynamics

Augmentation index and mean arterial pressure remained relatively stable throughout HUT. Although a previous study assessing the reliability of oscillometric pulse wave analysis to measure responses to tilt indicated increases in central diastolic and systolic blood pressure, a significant change in these factors was not observed in the present study (Stoner et al. 2015). However, an increase in reflection magnitude was observed in response to HUT. Increases in reflection magnitude may be indicative of increased arterial stiffness associated with peripheral vasoconstriction often observed in the orthostatic response (Sarafian & Miles-Chan 2017). While an increase in reflection magnitude was observed across the group, females showed a greater increase throughout HUT compared to males. No changes were observed in HUT in response to participant blood glucose or HbA1c levels. Body composition did not present any significant effect on the central hemodynamic response to the orthostatic challenge. The observed increase in reflection magnitude in response to the orthostatic challenge may be recognized as an additional compensatory mechanism.

Leg Blood Volume Changes

Although the modified HUT utilized in this study did not test participants' orthostatic tolerance levels by bringing individuals to a standing, upright position, the modified protocol did produce similar results as total hemoglobin increased throughout the progression of HUT. This observation suggests that the modified 70º degree torso-only tilt may be able to induce a response to the orthostatic challenge similar to what has

been observed in traditional HUT methods (Chi et al. 2008). The modified HUT protocol utilized in the present study may prove useful for further research on the orthostatic response without the need for direct medical supervision or intravenous injections and with lower risk presented to participants. Throughout HUT, increases in total hemoglobin levels (measured at the medial gastrocnemius via NIRS) were observed across the group. Overall, men typically had greater absolute total hemoglobin levels, but females also experienced an increase in total hemoglobin. Increases in gastrocnemius perfusion levels confirm that pooling of blood in the lower extremities occurs in response to HUT as gravitational force creates a fluid shift. Aerobic fitness and body fat percentage levels did not produce observed significant effects for leg blood volume variables.

Limitations

The findings in this study indicate that individual differences influence the central hemodynamic response to orthostasis. Hormonal differences between men and women may also impact the inter-individual response to an orthostatic challenge. Future studies should evaluate the influence of other factors and modifiers to orthostatic challenge response. This study does not address the hemodynamic response to the orthostatic challenge in aged, diseased, and otherwise non-normative individuals. Subjects included within this study were generally healthy and of minimal cardiovascular risk. Individuals with various conditions may exhibit varied responses to the orthostatic challenge. Additionally, the test used for aerobic fitness approximation was sub-maximal and direct measure of oxygen consumption was not performed. Sample size within this study may have been limited. A larger sample size may provide greater statistical power for examination of variables within the cardiovascular response to tilt.

Chapter 6: Conclusion

The present study found that individual differences can influence the central hemodynamic response to orthostasis. Subjects exhibited increases in heart rate, reflection magnitude, gastrocnemius perfusion and low-high frequency component ratio in response to the modified HUT. Females exhibited an increase in augmentation index, a potential indicator of vascular stiffness. We observed an association between aerobic fitness and low-high frequency component ratio that may indicate aerobic fitness as a factor affecting the cardiovascular response to tilt. Future studies should further examine the influence of these and other factors on the cardiovascular response to the orthostatic challenge among a variety of populations.

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Appendix A

University of Southern Mississippi, Laboratory of Applied Physiology Medical Health History Form	
All of the information provided in this form is voluntary.	
Date:	Biographical information:
Last Name:	First: MI:
Occupation:	Email:
Home Phone: ( )	Work: ( ) Cell: ( )
Address:	
DOB: / /	Age: Gender M / F Height: Weight:
Highest Education Achieved:	
Race:	What race do you consider yourself to be? Select one or more of the following:
	Hispanic or Latino - A person of Mexican, Puerto Rican, South or Central American, or oth Spanish culture or origin, regardless of race. The term "Spanish origin," can be used in addition "Hispanic or Latino."
	American Indian or Alaska Native - A person having origins in any of the original peopl of North, South, of Central America, and who maintain a tribal affiliation or community attachmer
	Asian- A person having origins in any of the originals peoples of the Far East, Southeast Asia, the Indian subcontinent, including, for example, Cambodia, China, India, Japan, Korea, Malaysia Pakistan, the Philippine Islands, Thailand, and Vietnam. (Note: Individuals from the Philippine Islands have been recorded as Pacific Islanders in the previous data collection strategies.)
	Black or African American - A person having either origins in any of the black racial grou of Africa. "Haitian" can be used in addition to "Black" or "African American."
	Native Hawaiian or Pacific Islander - A person having origins in any of the original peoples of Hawaii, Guam, Samoa, or other Pacific Islands.
	White - A person having origins in any of the original peoples of Europe, the Middle East, or North Africa.
Primary Care Physician:	
Name:	Office Phone:
Address:	
Emergency Contact:	
Name:	Relationship: Phone #
Medications: Include over the counter drugs/ oral contraceptive/ dietary supplements	
Name/ Dosage/ How often taken:	

Allergies:

Smoking History:	
Do you smoke	Cigarettes? Pipe/ Cigar? Other? If you quit, what year did you quit?
# of packs smoked per day _____	For how many years _____

Medical Health History Form **Page 2**

Alcohol Consumption History:
Do you currently drink alcohol? If you drank alcohol previously, when did you stop?
If you ever did drink alcohol, what is (was) the volume consumed? _____# ounces / day for _____ # of years

Medical History:		
NO	YES	*Please explain any "YES" answers*
		high blood pressure
		chest pain/ history of heart attack
		extra heart beats or racing
		abnormal electrocardiogram (ECG)
		other heart trouble (e.g. murmur, valve problems)
		high cholesterol
		diabetes
		seizures
		stroke
		fainting spells
		anxiety (diagnosed)
		depression (diagnosed)
		recurrent fatigue
		insomnia
		thyroid problems
		difficulty breathing
		emphysema/ asthma/ chronic bronchitis
		tuberculosis
		chronic infection
		stomach/ GI problems
		hepatitis
		bleeding disorder
		kidney/ urinary problems
		joint injuries/ joint pain
		arthritis (rheumatoid or osteoarthritis)
		migraine headaches
		vision problems (exclude corrected near/ far sightedness)
		surgical procedures
		For premenopausal females, Pregnant?
		For premenopausal females, Early follicular phase, i.e., start of menstrual cycle?

Appendix B

Godin Leisure-Time Exercise Questionnaire

INSTRUCTIONS

In this excerpt from the Godin Leisure-Time Exercise Questionnaire, the individual is asked to complete a self-explanatory, brief four-item query of usual leisure-time exercise habits.

CALCULATIONS

For the first question, weekly frequencies of strenuous, moderate, and light activities are multiplied by nine, five, and three, respectively. Total weekly leisure activity is calculated in arbitrary units by summing the products of the separate components, as shown in the following formula:

Weekly leisure activity score = (9 · Strenuous) + (5 · Moderate) + (3 · Light)

The second question is used to calculate the frequency of weekly leisure-time activities pursued "long enough to work up a sweat" (see questionnaire).

EXAMPLE

Strenuous = 3 times/wk

Moderate = 6 times/wk

Light = 14 times/wk

Total leisure activity score = (9 · 3) + (5 · 6) + (3 · 14) = 27 + 30 + 42 = 99

Godin, G., Shephard, R. J.. (1997) Godin Leisure-Time Exercise Questionnaire. Medicine and Science in Sports and Exercise. 29 June Supplement: S36-S38.

Godin Leisure-Time Exercise Questionnaire

1. During a typical **7-Day period** (a week), how many times on the average do you do the following kinds of exercise for **more than 15 minutes** during your free time (write on each line the appropriate number).

	Times Per Week
a) STRENUOUS EXERCISE **(HEART BEATS RAPIDLY)** (e.g., running, jogging, hockey, football, soccer, squash, basketball, cross country skiing, judo, roller skating, vigorous swimming, vigorous long distance bicycling)	_____
b) MODERATE EXERCISE **(NOT EXHAUSTING)** (e.g., fast walking, baseball, tennis, easy bicycling, volleyball, badminton, easy swimming, alpine skiing, popular and folk dancing)	_____
c) MILD EXERCISE **(MINIMAL EFFORT)** (e.g., yoga, archery, fishing from river bank, bowling, horseshoes, golf, snow-mobiling, easy walking)	_____

2. During a typical **7-Day period** (a week), in your leisure time, how often do you engage in any regular activity **long enough to work up a sweat** (heart beats rapidly)?

OFTEN	SOMETIMES	NEVER/RARELY
1.	2.	3.

Appendix C

THE UNIVERSITY OF SOUTHERN MISSISSIPPI

INSTITUTIONAL REVIEW BOARD
118 College Drive #5147 | Hattiesburg, MS 39406-0001
Phone: 601.266.5997 | Fax: 601.266.4377 | www.usm.edu/research/institutional.review.board

NOTICE OF COMMITTEE ACTION

The project has been reviewed by The University of Southern Mississippi Institutional Review Board in accordance with Federal Drug Administration regulations (21 CFR 26, 111), Department of Health and Human Services (45 CFR Part 46), and university guidelines to ensure adherence to the following criteria:

- The risks to subjects are minimized.
- The risks to subjects are reasonable in relation to the anticipated benefits.
- The selection of subjects is equitable.
- Informed consent is adequate and appropriately documented.
- Where appropriate, the research plan makes adequate provisions for monitoring the data collected to ensure the safety of the subjects.
- Where appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of all data.
- Appropriate additional safeguards have been included to protect vulnerable subjects.
- Any unanticipated, serious, or continuing problems encountered regarding risks to subjects must be reported immediately, but not later than 10 days following the event. This should be reported to the IRB Office via the "Adverse Effect Report Form".
- If approved, the maximum period of approval is limited to twelve months.
  Projects that exceed this period must submit an application for renewal or continuation.

PROTOCOL NUMBER: 18020601
PROJECT TITLE: Validity and Reliability of Ambulatory Pulse Wave Analysis for Determination of Central Hemodynamic Changes during an Orthostatic Challenge
PROJECT TYPE: New Project
RESEARCHER(S): Daniel Credeur, Ph.D.
COLLEGE/DIVISION: College of Health
DEPARTMENT: Kinesiology
FUNDING AGENCY/SPONSOR: N/A
IRB COMMITTEE ACTION: Expedited Review Approval
PERIOD OF APPROVAL: 02/27/2018 to 02/26/2019
Lawrence A. Hosman, Ph.D.
Institutional Review Board

ORI | Office of Research Integrity

INSTITUTIONAL REVIEW BOARD

HUMAN SUBJECTS RESEARCH APPLICATION

HUMAN SUBJECTS RESEARCH APPLICATION PROCEDURES

Use this form to apply for IRB review. IRB approval is required before human subjects research can begin. Always use the most recent version of the form, which can be found at http://www.usm.edu/research/irb-forms

- In order for your application to be complete, you will need to attach to this form both CITI certificates for all USM-affiliated investigators ("Common Course" and "Human Subjects Research Course"), completed consent forms, and additional supporting documents, such as research instruments and external permission letters. All of these documents must be attached **as icons** (see instructions at the bottom of this form) in order for this application to be accepted.
- Review the information included on the sample consent forms and the FAQ section of the IRB website: http://www.usm.edu/research/institutional-review-board.
- Student investigators must send the completed form with all attachments to Research Advisors (Honor's Thesis Advisor, Master's Thesis Director, or Dissertation Director) for review. Faculty researchers should send the form directly to Department Chairs.
- Student Research Advisors must review the form, attach their own CITI certificates, and provide authorization where indicated before sending the application to Departmental Chairs.
- Department Chairs must review the completed form, provide authorization where indicated, and submit completed versions of this form to irb@usm.edu from their USM email address.

Last Edited April 3, 2017

SECTION 1: INVESTIGATOR INFORMATION

1. Project Title: Validity and Reliability of Ambulatory Pulse Wave Analysis for Determination of Central Hemodynamic Changes during an Orthostatic Challenge

2.Principal Investigator: Daniel P. Credeur

3. Campus ID: w944855

4. USM Email: Daniel.Credeur@USM.edu

5. Department: Kinesiology

6. Purpose (check one):

☐Undergraduate Project
☒Honor's Thesis Project
☒Graduate Project
☒Faculty or Staff Project
☐Master's Thesis
☐Doctoral Dissertation

Student Research Advisor (if applicable)	Funding Agency/Sponsor (if applicable)
7. Name:	9. Organization:
8. USM Email:	10. Grant #:

11. Describe your expertise and qualifications related to this research:

Dr. Daniel Credeur, PhD (Research Advisor; PI) has a research interest in studying the physiological mechanisms governing blood flow and blood pressure regulation at rest, and during varying modes of therapy in human health and disease. To do this, his laboratory utilizes sphygmanometry, electrocardiography, Doppler-ultrasonography, applanation tonometry, and near-infrared spectroscopy (NIRS) to non-invasively assess blood pressure, heart rate, blood flow and peripheral vascular function and structure. Dr. Credeur is proficient in all of these techniques, and has conducted numerous studies using them in a variety of human subject populations. Dr. Credeur will provide project oversight. Importantly, Dr. Credeur is certified in CPR and AED through the Amercian Red Cross (Certificate attached).

12. List other USM affiliated investigators; completion of CITI Common and Human Subjects Research Courses must be attached. (Students need not list committee members or chairs.)	Name	Faculty or Staff	Graduate Student	Under-graduate	Project Role
	Stephanie McCoy	☒	☐	☐	Co-Investigator
	Raymond Jones	☐	☒	☐	Graduate Assistant
	Benjamin Schreck	☐	☐	☒	Honors Thesis Advisee
	Sabina Miller	☐	☒	☐	Graduate Assistant

13. List all Non-USM affiliated investigators**;** attach evidence of their research ethics training.	Name	University or Institution	Project Role

14. If other individuals will be involved in data collection, describe their role and their training.

Benjamin Schreck (Honors Undergraudate Advisee): Benjamin is an undergrduate student in the exercise science program in the school of Kinesiology at USM. Over this past Fall semester he has worked closely with Dr. Credeur (thesis advisor) to gain experience in the research lab, and to learn more about the cardiovascular system. Dr. Credeur, will be supervising him for multiple aspects of the proposed study including study design, participant recruitment, administration of the informed consent and questionnaires, collection of study data, and data analysis. In addition, data collected from this study will be used towards his Honor's thesis project, to prepare an abstract for the southeast regional American College of Sports Medicine (SEACSM) meeting, and for a peer-reviewed publication.

Raymond Jones (Graduate Assistant), a doctoral student in KIN, will also assist with data collection and analysis. In addition, data collected from this study will be used to prepare an abstract to be submitted at the regional and annual American College of Sports Medicine (ACSM) meetings, and for a peer-reviewed publication. Importantly, Raymond will be trained and supervised directly by the PI (Credeur) and Co-Invesitgator (McCoy) for all aspects of the study, including data collection.

Sabina Miller (Graduate Assistant), a Masters student in KIN, will also assist with data collection, and analysis. Sabina will also be trained and supervised directly by the PI (Credeur) for all aspects of the study, including data collection.

SECTION 2: RESEARCH PROCEDURES

15. Briefly describe the project and its goal(s) in two to three paragraphs.

The goal of this project is to explore potential mechanisms associated with autonomic dysfunction by performing an orthostatic stress test, known as the modified head-up tilt-table test (HUT). The typical physiological response to a HUT test is characterized by a baroreflex-mediated increase in heart rate and peripheral vasoconstriction which normally occurs as a means to restrain decreases in arterial blood pressure when transitioning the torso upright (60 degree tilt) after a period of supine rest. Interestingly, there seems to be variations in this response between individuals, which may be related to factors such as age, biological sex, cardio-metabolic health risk, and aerobic fitness. To better understand the reasons for discrepant responses to a HUT, we aim to recruit and study a range of individuals stratified as low-moderate cardiovascular health risk (via ACSM risk factor stratification), and perform several non-invasive cardiovascular assessments, including; aortic mean arterial blood pressure, heart rate variability, augmentation index, and peripheral (medial soleus) skeletal muscle perfusion via near-infrared spectroscopy during a HUT. A secondary aim will be to test the validity of a novel oscillometric ambulatory blood pressure monitor (Oscar-2, from AtCor medical) for collection of central hemodynamic variables during the HUT. To do this, data from the Oscar-2 collected during HUT will be compared against the industry standard (SphygmoCor XCEL, from AtCor medical). Within testing reliability will also be examined and compared between the two devices. Collectively, these data will allow for a heightened understanding of potential mechanisms underlying the varied physiological responses to an orthostatic challenge, such as the HUT test. Importantly, the results from this study may be aid in development and or modification of current treatment strategies for patients with cardiovascular and autonomic disorders.

16. Are any of the participants under 18 years of age?

☐Yes ☒No

Note: Parental consent is required for participants under the age of 18.

17. Describe participant population, number of participants to be included, and criteria for selection.

This study will require 20 volunteer subjects. Inclusion for participation: men and women between the ages of 18-55 years; free of any diagnosed cardiovascular, metabolic, or neurological disease; and not-pregnant. Eligible women will have a normal menstrual cycle (i.e., menstruate once per month), and will be studied during the early follicular phase of their cycle (days 1-7), or during the placebo phase of oral contraceptive use.

18. How will participants be recruited?

☒Class announcement ☒Oral Announcement ☒Email announcement
☒Posted campus advertisement ☐Television, Radio or Newspaper ad ☐Advertising Agency
☐Other (explain):

19. For adult participants, how will you verify that individuals are over 18?

☒Questionnaire or interview
☐No adults will be participating in this research
☐Other (explain):

20. Indicate consent procedures (check all that apply):

☒Standard Informed Consent
☐Oral Presentation & Signed Consent
☐Parental Consent
☐Minor Assent
☐Translation Verification
☐Request for Waiver of Consent

21. Detail procedures for obtaining participants' consent or justify request for waiver.

Participants will sign a University of Southern Mississippi approved Informed Consent document. Prior to this, study personnel will read through and explain all experimental protocols and procedures which will be performed. In addition, potential risks and benefits associated with study participation will also be highlighted.

22. How many interactions will be required with each participant?

☒1
☐2 - 3
☐4 – 9
☐10 or more

23. Maximum length of each interaction:

☐Less than 10 minutes
☐Less than an hour
☒Less than three hours
☐Three hours or more.
☐No direct interaction with participants

24. Where will interactions take place? (check all that apply):

☒USM campus
☐Off campus
☐Online

25. Indicate means of data collection (check all that apply).

☐Personal Interview ☒Questionnaire
☐Audio or video recording ☐Behavioral Observation
☐Focus Group Inquiry ☒Other (explain below):

Numerical data gained from instrumentation.

26. Do any of the following apply to your study?

Use of human biological samples	☒Yes	☐No
Use of physical exercise	☒Yes	☐No
Medical examinations or procedures	☐Yes	☐No
Use of drugs or biological products	☐Yes	☐No

27. Give a step by step explanation of data collection procedures.

Experimental Protocols:

Following completion of an informed consent form, medical health history, and physical activity questionnaire, we will perform a varitey of cardiovascular health assessments on each subject. Data to be collected at baseline will include blood sampling (finger stick) for fasting glucose and lipids, and body composition (via 3-site skinfold test with skin calipers). Following collection of baseline data, the subject will be positioned on an examination table with an adjustable back. The subject will rest for 10 minutes and initial measurements of central blood pressure, heart rate variability, pulse wave analysis, and skeletal muscle perfusion levels via near-infrared spectroscopy will be collected. The industry standard blood pressure monitor will be utilized on one arm (randomized) at the brachial artery and the Oscar2 will be used simultaneously in the corresponding location of the contralateral limb.

Baseline measurements will be collected twice to ensure reliability between readings. The aforementioned measurements will be taken while the subject is at a 60° tilt (angle at torso from lower body, measured via

goniometry) on the adjustable experimental table. Measurements will be taken again at minutes 2 and 5 of tilt and immediately returned to the supine position, with another series of measurements performed at minutes 2 and 5 of recovery. After an additional 5 minutes of rest, the tilt will be repeated. Following the HUT, subjects will complete a standard YMCA 3-min step test on a 12-inch step box. Researchers will use this test to approximate the individual's VO2 max value and associated level of aerobic fitness. The subject's heart rate will be monitored closely during and into the recovery period of the step test.

Experimental Procedures:

Subjective Questionnaires- A detailed medical health history questionnaire, and a separate physical activity questionnaires, the Godin Leisure-Time Exercise Questionnaire, will be administer prior to data collection. These data will be used to characterize the amount of structured and habitual physical activity levels performed by the subjects.

Cardio-metabolic Health Measures- Using minimally invasive procedures, glucose, lipid panel, and HbA1c will be determined using commercially available devices (i.e., Cardio-check, and HbA1c-Now+). To do this, a small capillary of blood (<1 mL) will be obtained from a finger prick on the left ring or middle finger(s) using a sterilized lancet. Importantly, this amount of blood will not exceed Federal Regulations as described below:

(a) for healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or

(b) from other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.

Additional measures will include heart rate monitored via Lead-II surface electrocardiography (ECG).

Blood Pressure- Both systemic (i.e., brachial) and central BP will be determined using the SphygmoCor XCEL (industry standard) and Oscar2 (portable BP onitor) devices. To do this, a traditional BP cuff will be positioned around the upper arm to determine systolic, diastolic and mean BP. For central BP, a sub-systolic pressure (80-100 mmHg) will be applied to the cuff and a brachial pulse wave will be examined using a transducer embedded in this cuff (oscillometric). This waveform will undergo a proprietary transfer function to estimate aortic BP (systolic, diastolic and mean) from the brachial BP waveform.

Muscle Perfusion- A continuous wave near-infrared spectroscopy (NIRS) device (Portalite, Artinis Medical Systems BV, Zetten, Netherlands) will be placed over the right or left calf muscle. To measure perfusion, total hemoglobin will be monitored continuously during baseline, titlt and into recovery.

28. Are your participants anonymous? ☐Yes ☒No	**Note: 'Anonymous' means that even investigators cannot associate the data with individual participants and vice versa, not merely that identities will not be revealed. Electronic surveys must be conducted via websites that do not link responses to email addresses or other identifiers. Personal interviews are not anonymous.**
29. Does your research involve sensitive information? ☐Yes ☒No	**Note: Sensitive information may include (but is not limited to) information about sexual activity, drug usage, criminal behavior, financial or medical data, and religious views.**
30. Does your research involve hidden video or audio recordings or deception? ☐Yes ☒No	**Note: Deception includes any information or procedure that misleads a participant intentionally.**

SECTION 3: RISKS AND BENEFITS

31. Indicate all potentially vulnerable participants involved in the study. ☐Children ☐Mentally ill patients ☐Nursing home patients ☐Pregnant females ☐Prisoners ☐HIV positive individuals ☐Other ☒Not applicable	32. Detail the methods that will be employed to protect vulnerable participants.

33. If your research involves prisoners, explain how it is directly relevant to prisoners or the prison system (check all that apply):

☐the causes and/or effects of incarceration
☐the process of incarceration
☐prisons as institutional structures
☐the conditions of prisons or prisoners
☐procedures for improving the well-being of prisoners
☐other (explain):

Note: All research involving prisoners requires compliance with federal regulations pertaining to biomedical and behavioral research involving prisoners as listed in FR 53655 Subpart C. Research must be directly relevant to prisons or prisoners (e.g. the effects of incarceration, criminal behavior, prison infrastructures, etc.). Completion of the CITI Research with Prisoners Module is also required.

34. How will you maintain confidentiality?

☐Anonymous data
☒Electronic data will be password protected
☒Physical data will be locked in a file drawer
☐Public/non-confidential data
☐Other (explain):

35. Describe final disposition of data.

All participant information and data will be handled according to university policies and will be kept by the principal investigator (Dr. Daniel Credeur) in a locked filing cabinet in KIN 224, to which only the principal investigator and Co-Investigators will have access. Individual subject codes will be used for each participant during data collection and analysis. The investigators are aware of the confidentiality requirements and the proper conduct of such a study. All participant data will be de-identified when transferred electronically to an external hard-drive for data back-up, as well to spreadsheets for analysis, which will performed on a password protected computer. Only aggregate, de-identified, group data will be presented at conferences or published in peer reviewed journals. Following completion of the study, all hard copies of participant data will remain on file in a locked filing cabinet, and electronic data will remain encrypted on a designated external laboratory hard-drive.

36. Risks, inconveniences, or discomforts participants are likely to experience (check all that apply):

☒Physical
☐Psychological
☐Financial
☐Occupational
☐Legal
☐Social
☐Other
☐None

37. Detail potential risks, inconveniences and discomforts participants are likely to experience, if any.

The orthostatic challenge (tilt) may cause temporary dizziness for some individuals. In the event a subject experiences any symptoms, they will be immediately returned to the supine position. Imporatntly, their heart rate and blood pressure will be monitored continuously throughout all procedures by a trained research member who is CPR certified.

ECG: Some people may have a skin irritation from the patches that connect the wires on the chest to the computer. Skin and hair are pulled slightly when the patches are removed after the test. Research personnel will attach and remove the patches as carefully as possible.

Blood pressure cuff inflation: The blood pressure cuff will squeeze the arm tightly; however, any discomfort will be alleviated as soon as the pressure in the cuff is released.

Moderate Intensity Exercise: Engaging in moderate intensity physical activity will cause your heart rate and blood pressure to increase. This is a normal physiological response. In addition, your breathing rate will also increase. You may also experience some slight discomfort in your leg muscles due to fatigue. However, these sensations will subside upon stopping the exercise bout. The exercise protocols used in this study do not pose a great threat to your health.

38. Describe the methods that will be employed to mitigate any potential risks, inconveniences or discomforts.

Each individual will be monitiored closely for any signs or symptoms suggestive of any emergency situation. As stated previously, the subjects will be screed prior to participating in any facet of the study to exclude individuals with any known pathology. Furthermore, the PI is CPR/AED certified, and will be present during all screening and experimental study visits, and will be able to respond quickly to any emergency situation. A functioning Automated External Defibrillator (AED) device is located on the first and second floor of the KIN building, with the closest on the first floor being ~100 feet from the research laboratory. All participants will be instructed to wear comfortable clothing, empty their bladder prior to research activities and blood pressure and heart rate will be monitored throughout the study. In the unlikely event that a medical emergency were to occur, research activity would cease, CPR/AED will be administered if necessary, and medical emergency services (911) would be called immediately if needed.

39. Describe any potential benefits participants may gain as a result of participation.

While there is no direct benefit to the subject for participating, the knowledge gained from this research will benefit the scientific community and will potentially lead to the development of future recommendations used for the detection and the prevention and/or treatment of cardiovascular disease.

40. List all incentives participants will receive for their participation.

No incentives other than knowledge regarding their body composition and cardiovascular health parameters will be given to the subjects.

Note: If class credit will be given for participation, describe what other options exist for nonparticipants to receive the same credit.

41. If individuals are unwilling or unable to complete their participation, how will their incentives be distributed?

☒Not Applicable (no incentives will be offered)
☐They will still receive all incentives.
☐They will be informed that they will receive no incentives.
☐They will receive partial incentives (explain):

SECTION 4: CHECKLIST AND AUTHORIZATION

42. The following documents must be attached to this form:

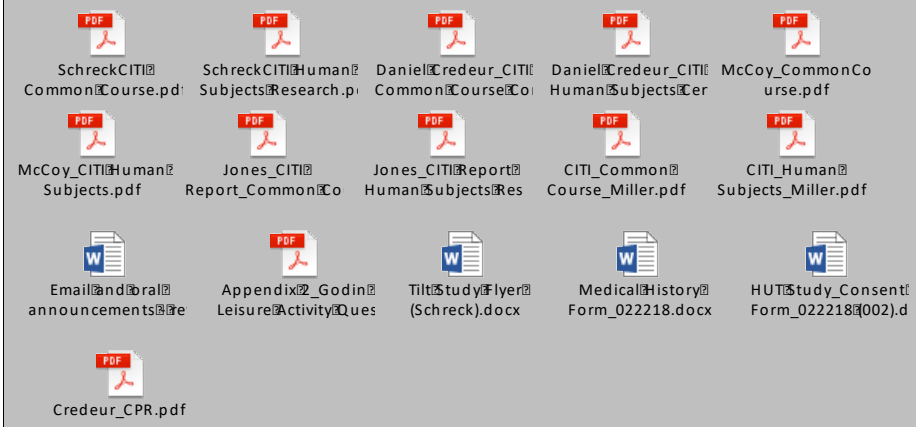
☒CITI Common Course Certificate (mandatory for all USM investigators and student advisors)
☒CITI Human Subjects Course Certificate (mandatory for all USM investigators and student advisors)
☐Both CITI certificates or alternative documentation of research ethics training for all non-USM investigators
☐Research proposal approval from Dissertation or Master's Thesis Committee (if applicable)
☒Study recruitment documents (if applicable)
☐Research Instrument (if applicable)
☐Permission letter from external organization participating in the project (if applicable) on official letterhead
☐Assent form for minors (if applicable)
☒Consent forms (long or short) and any related documents
☐Letter to parents (if applicable)

Instructions for Attaching Documents:

1) Place the cursor where you want the attachment to appear.
2) Select the “Insert” tab at the top of MS Word.
3) Select “Object,” located on the far right of the tool bar (PC) or the bottom of the list (MAC)
4) Select the “Create from File” tab and **check the box that states “Display as Icon.”** Note: Do not check the box that says "link to file."
5) Browse to the location of your document, and double click on it.
6) Repeat these steps for each document to be attached.

Note for Mac Users: Word for Mac is unable to attach .pdf files, so Mac users will have to first save the Citi certificates or any other .pdf files as .doc or .rtf files before attaching them. There are several ways to accomplish this. You may use Adobe to open the file and then select “File” and “Save as” and change the file type to an .rtf or .doc format. Alternatively, you may also download or create your own .pdf to .doc application or simply save the application and then open the file on a PC to attach as instructed above.

Attach all relevant documents in this section:



43. Instructions for Authorization:

1) Type your name and date in the appropriate box.
2) Students should email the form to their advisors, who should type their name below and then send to Department Chairs for review. Department Chairs should type their name below and send the completed form to irb@usm.edu.

By typing my name below, I acknowledge that I have read, understood, and approve of the information herein.

Daniel Credeur		**Scott Piland**
Principal Investigator	**Student Research Advisor (if applicable)**	**Department Chair**
1/31/2018		**1/31/2018**
Date	**Date**	**Date**

Appendix D

ORI | Office of Research Integrity

INSTITUTIONAL REVIEW BOARD

STANDARD (SIGNED) INFORMED CONSENT

STANDARD (SIGNED) INFORMED CONSENT PROCEDURES
This completed document must be signed by each consenting research participant. · The Project Information and Research Description sections of this form should be completed by the Principal Investigator before submitting this form for IRB approval. · Signed copies of the consent form should be provided to all participants. Last Edited July 20th, 2017

Today's date:		
PROJECT INFORMATION		
Project Title: Validity and Reliability of Ambulatory Pulse Wave Analysis for Determination of Central Hemodynamic Changes During an Orthostatic Challenge		
Principal Investigator: Daniel P. Credeur	Phone:	Email: daniel.credeur@usm.edu
College: Health	Department: Kinesiology	

RESEARCH DESCRIPTION

1. **Purpose**:

I am being asked to participate in this to help understand the changes to my heart and blood vessels that occur when I go from a lying to upright position

2. **Description of Study:**

Following completion of an informed consent form and medical health history questionnaire, researchers will perform a variety of cardiovascular health assessments. These measurements will be performed at baseline, including blood sampling (finger stick) for fasting glucose and lipids, and body composition (via 3-site skinfold test with skin calipers). Following baseline, I will be positioned on an examination table with an adjustable back. After 10 minutes of quiet rest, initial measurements for blood pressure, heart rate, and blood flow will be performed.

Baseline measurements will be collected twice to ensure reliability between readings. All measurements will be taken again after I am repositioned upright (60° tilt). Measurements will be taken again at minutes 2 and 5 of the tilt, and then I will be immediately returned to the supine position, with another series of measurements performed at minutes 2 and 5 of recovery. After an additional 5 minutes of rest, the tilt will be repeated. Following the tily, I will complete a standard YMCA 3-min step test on a 12-inch step box. This test to will be used to estimate my aerobic fitness level. My heart rate will be monitored closely during, and into the recovery period of the step test. The estimated time for this experiment is ~2.5 hours.

Experimental Procedures:

Body Composition - My percentage of body fat and lean body mass will be determined by a non-invasive process called bioelectrical impedance amplitude (BIA). During this test, I will stand barefoot on a specialized scale for ~2 minutes while a very low level, electrical current is passed through your body. The magnitude of electrical current is used to estimate percentage of body fat and also lean body mass (e.g., muscle). This is an FDA approved, widely used, and very safe, commercial assessment of body composition.

3-min step test - After resting quietly for 5 mins in a chair, my resting heart rate will be determined manually by the investigator placing 2 fingers over my wrist and feeling for a heartbeat. The step test requires that I step up and down, alternating legs on a standardized box for 3 minutes at a cadence of 24 steps per minute. After 3 minutes of stepping are completed I will stop and another heart rate will be measured immediately. A third heart rate will be measured 15, 30 and 60 sec into recovery from test.

Blood Pressure (BP) - A blood pressure cuff will be wrapped around both upper arms to periodically measure blood pressure.

Heart Rate (HR) - Electrodes (patches) will be placed on the surface of my chest for heart rate measurements.

Muscle Blood Flow- Blood flow will be measured non-invasively through a light-emitting sensor.

Blood sample- Using minimally invasive procedures my glucose and lipid levels will be determined. To do this, a small drop of blood (<1 mL) will be obtained from a finger prick on my left ring or middle finger(s) using a sterilized lancet. Importantly, this amount of blood will not exceed Federal Regulations as described below:

(a) for healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or

(b) from other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.

3. **Benefits:**

I may gain a better understanding of my cardiovascular health as indicated by heart rate and blood pressure measurements, and performance on the YMCA 3-min step test. Data collected may be later applied to future research to address maladaptive cardiovascular responses to the orthostatic challenge.

4. **Risks:**

The orthostatic challenge (tilt) may cause temporary dizziness for some individuals. If I experience any symptoms, I will be immediately returned to the supine position. My heart rate and blood pressure will be monitored continuously throughout all procedures by a trained research member who is CPR certified.

ECG: Some people may have a skin irritation from the patches that connect the wires on the chest to the computer. Skin and hair are pulled slightly when the patches are removed after the test. Research personnel will attach and remove the patches as carefully as possible.

Blood pressure cuff inflation: The blood pressure cuff will squeeze my arm tightly; however, any discomfort will be alleviated as soon as the pressure in the cuff is released.

Moderate Intensity Exercise: Engaging in moderate intensity physical activity will cause my heart rate and blood pressure to increase. This is a normal physiological response. In addition, my breathing rate will also increase. I may also experience some slight discomfort in my leg muscles due to fatigue. However, these sensations will subside upon stopping the exercise bout. The exercise protocols used in this study do not pose a great threat to my health.

For the reasons stated above the investigators will observe me closely while giving the treatments described and, if I have any worrisome symptoms or symptoms that the investigator has described, I will notify the investigator immediately.

5. **Confidentiality:**

Information produced by this study will be stored in the investigator's file and identified by a code number only. The code key connecting your name to specific information about you will be kept in a separate,

secure location. Information contained in your records may not be given to anyone unaffiliated with the study in a form that could identify you without your written consent, except as required by law. It is possible that your medical and/or research record, including sensitive information and/or identifying information, may be inspected and/or copied by the study sponsor and/or federal or state government agencies in the course of carrying out their duties. If your record is inspected or copied by the study sponsor (and/or its agents), or by any of these agencies, the University of Southern Mississippi will use reasonable efforts to protect your privacy and the confidentiality of your medical information. The results of this study may be published in a medical book or journal or used for teaching purposes. However, your name or other identifying information will not be used in any publication or teaching materials without your specific permission.

6. **Alternative Procedures:**

An alternative is to not participate in this research study.

7. **Participant's Assurance:**

This project has been reviewed by the Institutional Review Board, which ensures that research projects involving human subjects follow federal regulations.

Any questions or concerns about rights as a research participant should be directed to the Chair of the IRB at 601-266-5997. Participation in this project is completely voluntary, and participants may withdraw from this study at any time without penalty, prejudice, or loss of benefits.

Any questions about the research should be directed to the Principal Investigator using the contact information provided in Project Information Section above.

CONSENT TO PARTICIPATE IN RESEARCH

Participant's Name: _____

Consent is hereby given to participate in this research project. All procedures and/or investigations to be followed and their purpose, including any experimental procedures, were explained to me. Information was given about all benefits, risks, inconveniences, or discomforts that might be expected.

The opportunity to ask questions regarding the research and procedures was given. Participation in the project is completely voluntary, and participants may withdraw at any time without penalty, prejudice, or loss of benefits. All personal information is strictly confidential, and no names will be disclosed. Any new information that develops during the project will be provided if that information may affect the willingness to continue participation in the project.

Questions concerning the research, at any time during or after the project, should be directed to the Principal Investigator with the contact information provided above. This project and this consent form have been reviewed by the Institutional Review Board, which ensures that research projects involving human subjects follow federal regulations. Any questions or concerns about rights as a research participant should be directed to the Chair of the Institutional Review Board, The University of Southern Mississippi, 118 College Drive #5116, Hattiesburg, MS 39406-0001, 601-266-5997.

Include the following information only if applicable. Otherwise delete this entire paragraph before submitting for IRB approval: The University of Southern Mississippi has no mechanism to provide compensation for participants who may incur injuries as a result of participation in research projects. However, efforts will be made to make available the facilities and professional skills at the University. Participants may incur charges as a result of treatment related to research injuries. Information regarding treatment or the absence of treatment has been given above.

_____ **Research Participant**	**Person Explaining the Study**
_____ **Date**	**Date**