EFFECT OF WORK-TO-REST CYCLES ON CARDIOVASCULAR DRIFT AND MAXIMAL OXYGEN UPTAKE DURING HEAT STRESS

by

ANNE M. MULHOLLAND

JONATHAN E. WINGO, COMMITTEE CHAIR
MARK T. RICHARDSON
STEFANIE A. WIND

A THESIS

Submitted in partial fulfillment of the requirements
for the degree of Master of Arts
in the Department of Kinesiology
in the Graduate School of
The University of Alabama

TUSCALOOSA, ALABAMA

2020

ABSTRACT

Cardiovascular (CV) strain, indexed as CV drift—a progressive increase in heart rate (HR) and decrease in stroke volume (SV) during prolonged exercise—is exacerbated by environmental heat stress and is accompanied by a decrease in maximal work capacity ($\dot{V}O_{2max}$). To attenuate CV strain, work:rest ratios have been recommended by the National Institute for Occupational Safety and Health (NIOSH). Whether these guidelines sufficiently mitigate CV drift and preserve $\dot{V}O_{2max}$ is unknown. PURPOSE: To test the hypothesis that during moderate work (201-300 kcal/h) in hot conditions [indoor wet-bulb globe temperature ($WBGT_{in}$)=29 °C] utilizing the recommended 45:15 work:rest ratio, CV drift will 'accumulate' over time, and the magnitude of accumulated CV drift will be proportional to decrements in $\dot{V}O_{2max}$ after 120 min. METHODS: Eight subjects [5 women; (mean±SD) age=25±5 y; body mass=74.8±11.6 kg; $\dot{V}O_{2max}$=42.9±5.6 mL/kg/min] completed 3 sessions on different days. The first visit involved measurement of $\dot{V}O_{2max}$ ($WBGT_{in}$=18.1±1.2 °C). The following 2 experimental trials were counterbalanced ($WBGT_{in}$=29.0±0.6 °C). Moderate work was achieved by 2.5 min of arm curls (4.5 kg at 20/min) and 20 min of walking ($\dot{V}O_2$=1.0–1.1 L/min) on a treadmill, repeated once for a total of 45 min of work, and then followed by 15 min of seated rest. HR and SV were measured at 15 and 45 min of each work bout to evaluate CV drift. The 120-min trial consisted of 2 full work-rest cycles followed by measurement of $\dot{V}O_{2max}$; the 15-min trial replicated the first 15 min of the 120-min visit followed by measurement of $\dot{V}O_{2max}$ and was necessary to measure $\dot{V}O_{2max}$ before CV drift occurred. RESULTS: CV drift accumulated between 15 and 105 min: HR increased 16.7% (18±9 bpm, P=0.004) and SV decreased 16.9% (-12.3±5.9 mL, P=0.003), but

$\dot{V}O_{2max}$ was not affected after 2 full work-rest cycles (*P*=0.14). Core body temperature increased by 0.5±0.2 °C (*P*=0.006) over 2 h. CONCLUSION: Although CV drift occurred after two 45:15 work:rest cycles, $\dot{V}O_{2max}$ was unaffected. Work capacity is preserved during 2 hours of work in the heat with rest cycles patterned like those in this study, but CV and thermal strain persist unabated.

DEDICATION

For Ryan Curtis and Courteney Benjamin,

who just laughed when I told them I hated my internship. Thank you for being supportive mentors and letting me figure that out all on my own.

And for Mr. Bradford,

who encouraged all his students to be the best they could be. Thank you for believing in me.

LIST OF ABBREVIATIONS AND SYMBOLS

ACGIH	American Conference of Governmental Industrial Hygienists
ANOVA	Analysis of variance
$(a\text{-}\bar{v})O_2$	Arteriovenous oxygen content difference
bpm	Beats per minute
CDC	Centers for Disease Control and Prevention
cm	Centimeter
CNTRL	Control trial (first laboratory visit)
CO_2	Carbon dioxide
CV	Cardiovascular
dL	Deciliter
°	Degree
g	Gram
gi	Gastrointestinal
GXT	Graded exercise test
h	Hour
HR	Heart rate
J	Joule
kcal/h	Kilocalories per hour
kg	Kilogram
kph	Kilometers per hour

L	Liter
$\dot{M}$	Metabolic rate
m	Meter
mg	Milligram
min	Minute
mL	Milliliter
mmol	Millimole
mOsm	Milliosmole
$\dot{M}$-$\dot{W}$	Metabolic heat production
NIOSH	National Institute for Occupational Safety and Health
$\dot{Q}$	Cardiac output
RER	Respiratory exchange ratio
RH	Relative humidity
RPE	Rating of perceived exertion
RTS	Rating of thermal sensation
s	Second
SD	Standard deviation
STPD	Standard conditions for temperature and pressure
SV	Stroke volume
$\overline{T}_b$	Mean body temperature
T_{gi}	Gastrointestinal temperature
T_{gi}-$\overline{T}_{sk}$	Core-to-skin temperature gradient
$\overline{T}_{sk}$	Mean skin temperature

TWA	Time weighted average
USG	Urine specific gravity
$\dot{V}O_2$	Rate of oxygen uptake
$\dot{V}O_{2max}$	Maximal rate of oxygen uptake
W	Watt
$\dot{W}$	External work rate
WBGT	Wet-bulb globe temperature
$WBGT_{in}$	Wet-bulb globe temperature, indoor calculation
y	Year
120MIN	120-min experimental trial
15MIN	15-min experimental trial

ACKNOWLEDGEMENTS

This project would not have been possible without the help and support of so many people, but first and foremost I want to thank my advisor, Dr. Wingo—I am so grateful for the opportunity you've allowed me, and your support and guidance throughout this process means so much. I came to UA not really knowing what I wanted out of my grad school experience. I knew I liked research, and for some reason, the heat chamber but I never could have known what a fantastic experience this would be. While sometimes it was challenging (the good kind of challenging, where you learn something in the end), I am a better researcher because of it. And when all else failed, somehow you were always in your office when I sprinted down there because something wasn't working. We've accomplished some pretty cool things already, I think, and I am looking forward to continuing my education with you.

I also want to thank Hillary Yoder for her assistance with this project: it was whatever I needed, which was a little bit (a lot) of everything. Hillary, you have been a wonderful and supportive mentor, peer, and friend, and I am so lucky to have had your help and your friendship every step of the way. I am looking forward to continuing to work alongside you these next few years at UA, and hopefully many more after that.

This project would not have been possible without the help of every single graduate and undergraduate student who volunteered their time. This was a big undertaking, and I could not have done it on my own. From piloting to data collection to data analysis to even just asking questions about the process, you have contributed to a better final product and I thank you for that. I especially want to thank Brooke Titshaw and Aley Fox, their stellar commitment to this project and to Dr. Wingo's lab group did not go unnoticed. While we wish that they could stay forever I am so excited to see what they accomplish next!

Thank you so much to all of my participants—it is literally your blood and sweat (but hopefully not tears) that make up this data set. I am grateful to each and every one of you for volunteering your time, and to everyone who gave up coffee for data collection: I'm sorry and I appreciate you so much.

Dr. Richardson and Dr. Wind, thank you for serving on my thesis committee. I sincerely appreciate the time and effort you have put in, and your input on this project has been invaluable. I am looking forward to additional opportunities to hopefully work with you again in the future!

Thank you to Dr. Casa, Gabrielle Giersch, and Courteney Benjamin for their help with the IRB process.

CONTENTS

LIST OF TABLES

LIST OF FIGURES

INTRODUCTION

Self-paced work performed in hot conditions results in diminished productivity because of the negative effects of prolonged exposure to environmental heat stress on psychological, behavioral, and physiological function (Maresh et al. 2014). This decrease in productivity is partly attributable to behavioral thermoregulation, a self-preservation process involving slowing of pace in response to the perception of heat stress (Schlader et al. 2011). Other reasons for decreased productivity during heat stress include hyperthermia, dehydration, fatigue, and cardiovascular strain (Cheuvront et al. 2010; Wingo et al. 2005; Flouris 2010). Regardless of the mechanism, understanding heat stress limitations to worker productivity is important because productivity has economic impacts and because the preservation of worker productivity under heat stress presents ongoing occupational health and safety issues.

The physiological strain workers experience under heat stress can be characterized by examining cardiovascular strain, represented as cardiovascular (CV) drift. CV drift is a well-established phenomenon that occurs during continuous, submaximal, steady-state exercise in which there is a progressive increase in heart rate and decrease in stroke volume over time. Cardiac output is maintained, but the drift in heart rate and stroke volume is related to a decrease in maximal work capacity, indexed as maximal oxygen uptake ($\dot{V}O_{2max}$) (Wingo et al. 2005). Additionally, heat stress and hyperthermia have been shown to amplify CV drift and accompanying decrements in maximal work capacity in as little as 45 minutes during exercise (Wingo et al. 2005; Lafrenz et al. 2008).

As CV drift occurs and $\dot{V}O_{2max}$ decreases during steady-state exercise, the relative intensity of physical activity for a given absolute workload represents a greater percentage of $\dot{V}O_{2max}$, and therefore results in greater physiological and perceptual strain. “Criteria for a Recommended Standard – Occupational Exposure to Heat and Hot Environments” is the document published by the National Institute for Occupational Safety and Health (NIOSH), in conjunction with the Centers for Disease Control and Prevention (CDC), which outlines acceptable work standards for hot conditions (Jacklitsch et al. 2016). According to their recommendations, an acceptable intensity of continuous work is 30% to 40% of maximal work capacity ($\dot{V}O_{2max}$), without the presence of environmental heat stress (Jacklitsch et al. 2016). While achieving maximal work capacity may not be required in an occupational setting, progressive reductions in $\dot{V}O_{2max}$ as a result of CV drift could result in submaximal work intensities that exceed this recommended range, which may also negatively impact worker productivity and safety.

If pace is not reduced, such as in an effort to preserve productivity, there is an elevated risk of developing dangerously high body temperature and heat injury. For example, between 2008 and 2010 in North Carolina, heat illness was the most common work-related reason for an emergency room visit for people age 19–45 years (Rhea et al. 2012).

To prevent hyperthermia and reduce the risk of heat injury or illness, an alternative strategy to slowing of pace is incorporation of work-to-rest ratios. Rest intervals allow for the mitigation of heat-related physiological strain while maintaining work intensity and thereby productivity. Use of work-to-rest ratios is not a novel idea, but their use with regards to blunting CV drift and accompanying decrements in maximal work capacity has not been investigated. Most prior studies investigating CV drift and effects on $\dot{V}O_{2max}$ utilized continuous work protocols (Wingo and Cureton 2006b; Lafrenz et al. 2008; Ganio et al. 2006; Wingo et al. 2005), and one that incorporated rest included only one work bout of varying submaximal intensities followed by a single prolonged rest period prior to the maximal exercise test (Åstrand et al. 1964). Therefore, the results of previous CV drift studies are not generalizable for characterizing CV responses over the course of a work shift, or for predicting any potential decrement in $\dot{V}O_{2max}$ when using the recommended work-to-rest ratios.

CV drift and a concomitant decrease in $\dot{V}O_{2max}$ have been observed during physical activity in the heat over a 45-min period, so it is plausible that drift occurs during a work period (that is part of a longer overall work shift) of the same duration. Depending on work intensity and rest conditions (e.g., ambient conditions, availability of fluid, cooling modalities), a 45:15-minute work-to-rest ratio—the minimum work-to-rest ratio recommended by NIOSH (Jacklitsch et al. 2016) —may not be enough for full recovery, especially if body temperature does not return to pre-exercise levels. If full recovery is not attained, then some amount of 'accumulated' CV drift would be expected over multiple work/rest cycles, meaning that despite return of heart rate and stroke volume to near resting levels during rest breaks, over a 2-hour work bout heart rate will still drift upward and stroke volume will still drift downward (relative to initial values measured during the first 10–15 min) over time, which could result in reduced maximal work capacity ($\dot{V}O_{2max}$).

Without an understanding of the extent to which work capacity is reduced, optimizing work-to-rest ratios and other countermeasures designed to mitigate physiological strain during work in heat stress is an improbable task. The purpose of the proposed study is to test the hypothesis that during moderate-intensity work utilizing a recommended 75%:25% work:rest ratio, CV drift will ‘accumulate’ over time. Furthermore, it is hypothesized that the magnitude of ‘accumulated’ CV drift will be proportional to decrements in maximal work capacity ($\dot{V}O_{2max}$).

METHODS

Research Design

A repeated measures research design was utilized in which all participants were tested under all conditions. Participants completed 3 sessions on different days, each separated by at least 2 days. Every effort was made to complete visits not more than 1 week apart, but due to participant availability and the menstrual cycle, this was not possible for every subject. The first visit involved measurement of $\dot{V}O_{2max}$ and familiarization with the CO_2-rebreathing technique used to estimate cardiac output (Jones 1975). The remaining 2 experimental trials occurred in counterbalanced order, and the counterbalanced treatment orders were randomly assigned to the participants. For one experimental trial, participants performed simulated work at a moderate intensity for 15 min, immediately followed by measurement of $\dot{V}O_{2max}$. For the other experimental trial, participants performed simulated work at a moderate intensity for 120 min divided into two 45-min:15-min work:rest cycles. The purpose of the separate 15- and 120-min trials was so that $\dot{V}O_{2max}$ could be assessed before and after CV drift occurred, respectively, since $\dot{V}O_{2max}$ could not be assessed twice within the same 120-min trial. Other than duration, all other aspects of the 15- and 120-min trials were identical.

All sessions occurred in a climate-controlled environmental chamber at approximately the same time of day for each participant to control for circadian variation in core temperature, and each female participant completed all experimental visits within a single phase of the menstrual cycle to control for fluctuations in baseline core body temperature. Environmental conditions were verified using indoor wet-bulb globe temperature ($WBGT_{in}$), an index of "feelslike” temperature, which takes into account air temperature, percent relative humidity (RH), and radiant and convective heat exchange (Budd 2008). The first visit occurred in temperate conditions (22 °C, 40% RH, to achieve approximately 17 °C $WBGT_{in}$), whereas the remaining visits occurred in hot conditions (34 °C, 55% RH, to achieve 29 °C $WBGT_{in}$). The hot conditions were based on data from the National Weather Service for the southeastern United States and were chosen to mimic the WBGT workers in this region might experience on a near daily basis for the summer months (NWS 2018). Air flow (measured as wind speed) generated by the environmental chamber accounted for both the NIOSH assumption of ‘perceptible air flow’ and the likelihood of air movement during outdoor work. The 45:15 work-to-rest ratio was from the NIOSH Recommended Alert Limits and the adjusted temperature for the test environment (Jacklitsch et al. 2016). The assigned workload was based on a prescription of “moderate” work, as defined by the American Conference of Governmental Industrial Hygienists (ACGIH) and NIOSH as between approximately 201–300 kcal/h (Jacklitsch et al. 2016; ACGIH 2017).

Participants

A power analysis revealed 8 participants were needed to observe a meaningful effect of CV drift on $\dot{V}O_{2max}$, based on means, SDs, and an effect size from a prior study (Wingo et al. 2005) using G*Power 3.1.9.4 (Faul et al. 2007). In order to account for the individual characteristic assumptions of the NIOSH heat stress guidelines given in Table 6-2 (Jacklitsch et al. 2016), participant inclusion criteria were healthy men and women who were “physically fit, well-rested, fully hydrated, [and] under age 40.” Since NIOSH does not provide a specific definition of fitness, and in order to assess ‘physical fitness’ in an appropriate manner, this criterion was considered met if participants self-reported that they participated in regular, moderate-to-vigorous physical activity and met the public health recommendations of ≥150 min of moderate-intensity physical activity per week or the equivalent (U.S. Department of Health and Human Services 2018). Additional exclusion criteria included a history of metabolic, renal, and cardiovascular diseases, gastrointestinal issues, or contraindications to exercise in the heat. Participants were instructed to arrive for all trials hydrated, rested, and having refrained from eating 2 hours prior, as well as to avoid use of alcohol and tobacco and consumption of caffeine 24 hours prior to testing.

Procedures

Initial Visit

After providing written informed consent, participants completed a medical history form, physical activity history form, and a 24-hour history questionnaire (detailing food and drink consumption, physical activity, and sleep during the preceding 24 hours). Women were asked to self-report the first and last day of previous menses. Blood pressure and resting heart rate measurements were then taken while participants remained in the seated position. Next, hydration status was assessed via urine specific gravity (USG) and had to be $\leq$1.020 for participants to be considered adequately hydrated (Sawka et al. 2007). Percent body fat was calculated using the sum of skinfolds at 3 sites (Jackson and Pollock 1985). Height was measured using a stadiometer (model no. 213 1821009, Seca, Chino, CA). Body mass was measured using a digital scale while the participant was wearing shorts, socks, sports bra (females) and tank top. Participants were then provided with trousers (50% polyester, 50% cotton) and a long sleeve shirt (65% polyester, 35% cotton) and instrumented with a heart rate monitor around their chest (model H10, Polar USA, Bethpage, NY). Finally, participants were familiarized with the questions and scales for rating of perceived exertion (RPE) and rating of thermal sensation (RTS) (Borg 1982; Young et al. 1986).

After a 5-min warm-up at a moderate intensity and a brief rest period, a graded exercise test (GXT) was administered on a treadmill to measure $\dot{V}O_{2max}$. Participants ran at an initial stage of 2.5% grade and approximately 9.0 kph (starting speed varied slightly from one participant to another based on the self-selected intensity and heart rate responses during warm-up) and the test progressively increased in grade by 2.5% every 2 min until volitional exhaustion. RPE and heart rate were recorded 15 s before the end of each stage, and at maximum. A 2-mL blood sample was drawn from a superficial forearm vein or a sample was obtained via fingerstick approximately 3 minutes after the end of the test to assess blood lactate. After completing the GXT, participants cooled down and rested for 20 min. Then, participants completed a $\dot{V}O_{2max}$ plateau verification protocol during which they ran to exhaustion; if the final stage of the GXT lasted less than 1 min, verification occurred at the same workload, but if it was ≥ 1 min, it occurred at the workload for the next stage (+2.5% grade). Next, participants cooled down and rested for another 20 min before walking an additional 10–15 min at the exercise intensity to be used during the experimental trials [4.0 kph and 1.0–6.0% grade, to elicit a $\dot{V}O_2$ of 1.0–1.1 L/min in order to achieve the desired energy expenditure (201-300 kcal/h)]. During this time, participants practiced the CO_2-rebreathing technique that was used to non-invasively determine cardiac output during exercise, in order to familiarize them with the procedure and to determine starting gas concentrations and volumes used during the experimental trials. Cardiac output and heart rate measurements during exercise were then used to calculate stroke volume. All procedures during the initial visit occurred in a temperate environment [~17 °C $WBGT_{in}$, confirmed using a Kestrel 4400 Heat Stress Meter (Kestrel Meters, Boothwyn, PA)].

Experimental Trials

Upon arrival, participants re-consented to study procedures and completed a 24-hour history questionnaire. A wireless temperature-sensing pill (eCelsius Performance, BodyCap Medical, France), used for the measurement of core temperature (T_{gi}), was provided for ingestion 5 hours prior to arrival—6 hours prior to the start of exercise—to ensure passage into the gastrointestinal tract and to avoid confounding by water consumption (Byrne and Lim 2007). Gastrointestinal temperature has a mean bias of −0.02 °C compared to rectal temperature during exercise in the heat (Ganio et al. 2009). Blood pressure, resting heart rate, USG, and nude body mass were assessed before exercise began. Participants were again provided with trousers and a long sleeve shirt for all experimental trials. Skin temperature was assessed at the calf, thigh, chest, and deltoid using wireless data loggers (iButton model no. DS1921H, Embedded Data Systems, Lawrenceburg, KY), and the weighted average of the 4 sites was used to calculate mean skin temperature ($\overline{T}_{sk}$) using the following equation (Ramanathan 1964):

$$\overline{T}_{sk} = 0.3(T_1 + T_2) + 0.2(T_3 + T_4)$$

where T_1, T_2, T_3, and T_4 correspond to skin temperature of the chest, lateral deltoid, quadriceps, and gastrocnemius, respectively. T_{gi} and $\overline{T}_{sk}$ were then used to calculate mean body temperature ($\overline{T}_b$) using a weighted average (Stolwijk and Hardy 1965):

$$\overline{T}_b = 0.8(T_{gi}) + 0.2(\overline{T}_{sk})$$

A 2-mL blood sample was then obtained via venipuncture for the baseline assessment of blood lactate concentration, plasma osmolality, hematocrit, and hemoglobin concentration. Hematocrit and hemoglobin concentration were used to calculate changes in plasma volume (Dill and Costill 1974). Participants entered an environmental chamber maintained at a $WBGT_{in}$ of 29 °C and sat quietly in a chair for 20 min to allow for equilibration to the hot environment.

Refer to Figure 1 for an illustration of the 120-min protocol (120MIN). After the 20-min acclimation period, resting $\dot{V}O_2$ was measured while standing on the treadmill, and then participants began the simulated work protocol. The simulated work bout featured 2.5 min of arm curls followed by 20 min of walking, repeated once for a total of 45 min of exercise. Arm curls were completed while standing, using a total weight of 4.5 kg (2.25 kg in each hand); participants performed 20 curls per minute in time with a metronome. After the 45 min of exercise, participants rested while sitting in a chair in the environmental chamber for 15 min. Next, they repeated the exercise bout and rest period for a total duration of 2 hours. Around min 15 and just before min 45 of each exercise bout, $\dot{V}O_2$, rating of perceived exertion, rating of thermal sensation, and cardiac output were measured. Core temperature, heart rate, and skin temperature were recorded continuously. At the end of the submaximal exercise bout and final rest period (120-min mark), participants immediately began a GXT with progressively increasing workloads in stages identical to the initial visit, running until volitional exhaustion to determine $\dot{V}O_{2max}$. Three to 5 min after the GXT, a final 2-mL blood sample was obtained via venipuncture for the assessment of changes in blood lactate concentration, plasma osmolality, hematocrit, hemoglobin concentration, and plasma volume from baseline. Participants were allowed to drink cool water (~20 °C) ad libitum during exercise and rest, provided they were not presently engaged in a task related to the collection of data or the work protocol. Water temperature was measured before exercise, and during rest breaks at 60 and 120 min. Cardiovascular drift was assessed between 15 and 45, 75, and 105 min of intermittent exercise using heart rate and stroke volume data.

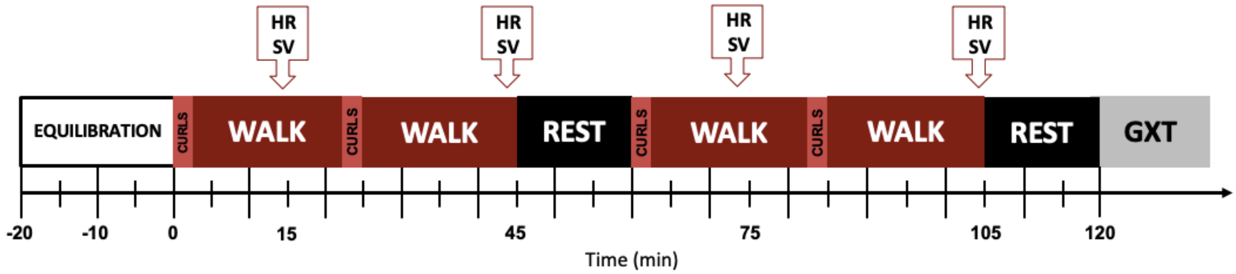

Figure 1. Procedures during the 120-min visit (120MIN). All "baseline" values were obtained during the equilibration period and before the start of exercise, except for hematological measures, which were taken before the participant entered the environmental chamber. HR, heart rate; SV, stroke volume; GXT, graded exercise test.

On a different day, participants completed a 15-min trial (15MIN) with the environmental conditions and work protocol identical to the first 15 min of the 120-min trial (2.5 min of arm curls followed by 12.5 minutes of walking at the grade identical to the 120-min trial, to elicit a $\dot{V}O_2$ of 1.0–1.1 L/min), immediately after which they completed a GXT to measure $\dot{V}O_{2max}$. Again, a 2-mL blood sample was drawn from a superficial forearm vein or a sample was obtained via fingerstick approximately 3 minutes after the end of the test to assess blood lactate. Experimental trials (15MIN and 120MIN) were performed at least 48 hours apart. The purpose of the 15-min trial was to determine $\dot{V}O_{2max}$ after the first 15 min of work so that $\dot{V}O_{2max}$ could be assessed before CV drift occurred. As such, heart rate, T_{gi}, and $\dot{V}O_2$ were recorded during 15MIN; $\overline{T}_{sk}$ and cardiac output were assessed during 120MIN only.

After exercise, participants were asked to towel off before the measurement of nude body mass. Changes in body mass were used to calculate whole body sweat losses, adjusted for fluid consumed, blood drawn, and estimated respiratory water loss and respiratory mass loss (Montain and Coyle 1992). Total water consumption was determined by the difference in pre- and post-weight of the participant's water bottle.

Metabolic heat production during submaximal exercise was calculated as the difference between metabolic rate and external work rate. Metabolic heat production ($\dot{M}$-$\dot{W}$) was calculated separately for arm curls, walking, and rest using the equation for metabolic rate ($\dot{M}$) and the corresponding equations for external work rate ($\dot{W}$), and then a time-weighted average was calculated to reflect mean $\dot{M}$-$\dot{W}$ over the two-hour protocol; NIOSH represents all $\dot{M}$-$\dot{W}$ thresholds as time-weighted averages. $\dot{V}O_2$ (L/min; STPD) was used to estimate $\dot{M}$ with the following equation (Kenny and Jay 2013):

$$\dot{M} = \frac{\left(\dot{V}O_2\left[\frac{RER - 0.7}{0.3}e_c + \frac{1 - RER}{0.3}e_f\right]\right)}{60}$$

where $\dot{M}$ is expressed in Watts, e_c is 21,130 J (the caloric equivalent per liter of oxygen for the oxidation of carbohydrates), e_f is 19,630 J (the caloric equivalent per liter of oxygen for the oxidation of fat), and RER is the respiratory exchange ratio. Metabolic rate for arm curls was calculated using a single measured value for $\dot{V}O_2$ and RER; metabolic rate for walking was calculated using $\dot{V}O_2$ and RER at 15, 45, 75, and 105 min and averaged. At rest, $\dot{V}O_2$ was assumed to be 3.5 mL/kg/min and RER was assumed to be 0.85 for all participants to account for individual variations in resting RER (Goedecke et al. 2000).

$\dot{W}$ was determined for treadmill walking using the following equation (Cramer and Jay 2016):

$$\dot{W} = m_b(g)(v)\sin\alpha$$

where $\dot{W}$ is expressed in Watts, m_b is body mass in kg, g is gravitational acceleration (9.81 m/s^2), v is velocity in m/s, and α is the angle of treadmill incline. External work during arm curls and during rest was assumed to be 0. Estimated metabolic heat production was determined by multiplying kcal/h by 1.16, as recommended by NIOSH (pg. 4, Jacklitsch et al. 2016).

Data Analysis

All statistical analyses were performed using SPSS for Windows v.25 (IBM Corporation, Somers, NY). Mean data were generated on the indicated outcome measures. Paired samples t-tests were used to test the significance of mean differences in $\dot{V}O_{2max}$ between 15 and 120 min, and hematological variables pre- and post-exercise. For other continuous variables, such as cardiovascular, temperature, and metabolic measures, a one-way repeated measures analysis of variance (ANOVA) was conducted to compare values across time. If sphericity was violated, the Greenhouse-Geisser correction was used, and normality was inspected by visual observation of Q-Q plots; outcomes of assumptions are reported in Appendix A. For ordinal variables (rating of perceived exertion and rating of thermal sensation) a nonparametric Friedman one-way repeated measures ANOVA was used. In the event of a significant omnibus test, pairwise comparisons with a Bonferroni α correction were performed and partial η^2 was reported to quantify the magnitude of variance explained by the protocol. All significance tests used an α level of 0.05.

RESULTS

Eight participants volunteered to complete all study procedures. Participant characteristics are listed in Table 1. Menstrual cycle phase and birth control use for female participants are reported in Appendix B. Table 2 indicates that the environmental conditions for all visits were achieved as intended.

Table 1. Descriptive characteristics for all participants (mean ± SD).

N							
Female	**Male**	**Age (y)**	**Weight (kg)**	**Height (m)**	**% Body Fat**	**$\dot{V}O_{2max}$ (L/min)**	**$\dot{V}O_{2max}$ (mL/kg/min)**
5	3	25 ± 5	74.8 ± 11.6	1.73 ± 0.10	24.0 ± 9.0	3.27 ± 0.91	42.9 ± 5.6

$\dot{V}O_{2max}$, maximal oxygen uptake

Table 2. Environmental conditions for all visits (mean ± SD).

	Ambient temperature (°C)	**Relative humidity (%)**	**$WBGT_{in}$ (°C)**	**Wind speed (m/s)**
CNTRL	23.1 ± 0.8	44.3 ± 10.4	18.1 ± 1.2	0.4 ± 0.6
15MIN	34.5 ± 0.6	54.3 ± 3.4	29.0 ± 0.7	1.4 ± 0.1
120MIN	34.3 ± 0.4	55.9 ± 2.5	29.0 ± 0.4	1.4 ± 0.1

$WBGT_{in}$, wet-bulb globe temperature (indoor calculation); CNTRL, initial laboratory visit; 15MIN, 15-min experimental trial; 120MIN, 120-min experimental trial

Responses During Submaximal Exercise and Rest Intervals

Hydration

Participants were adequately hydrated at the beginning of all laboratory visits, verified by USG ≤ 1.020 [(mean ± SD) CNTRL = 1.008 ± 0.003; 15MIN = 1.007 ± 0.007; 120MIN = 1.009 ± 0.005]. Plasma osmolality at baseline was 291 ± 5 mOsm/kg. Over 2 h, participants consumed 0.44 ± 0.30 L of water (21.4 ± 4.4 °C) ad libitum. Water consumption did not fully replace sweat losses of 1.2 ± 0.1 L [$t(7) = -5.79$; P=0.001], which likely explains the body mass loss of 0.9 ± 0.4% and elevated plasma osmolality post-exercise relative to baseline [305±10 mOsm/kg; $t(7) = 4.62$; P=0.002]. In addition, ad libitum fluid consumption did not meet the NIOSH recommendation of 0.95 L/h [$t(7) = -13.58$; P<0.001; Table 8-1, Jacklitsch et al. 2016]. Plasma volume decreased 7.5 ± 3.1% from baseline to end of exercise [$t(7) = 6.85$; P<0.001].

Work Intensity

$\dot{V}O_2$ was maintained at an average of 1.08 ± 0.05 L/min (35.8 ± 9.1% CNTRL $\dot{V}O_{2max}$) during treadmill walking [F(3, 21) = 9.17; P<0.001; partial $\eta^2 = 0.57$], but despite statistical significance, the mean differences across all time points were not greater than 0.05 L/min. $\dot{V}O_2$ was 0.54 ± 0.08 L/min (17.5 ± 3.2% CNTRL $\dot{V}O_{2max}$) during arm curls. Three participants' relative workload remained below 30% CNTRL $\dot{V}O_{2max}$, 3 participants' relative workload was between 30%–40% of CNTRL $\dot{V}O_{2max}$, and, even though mean $\dot{V}O_2$ remained within the prescribed range (1.0–1.1 L/min for treadmill walking) throughout the entirety of the protocol, 2 participants still exceeded the upper end of the NIOSH recommended relative intensity range (40% $\dot{V}O_{2max}$). Table 3a provides $\dot{V}O_2$ and % CNTRL $\dot{V}O_{2max}$ values at specific time points throughout the protocol. Although there was no meaningful change in relative workload (i.e., %$\dot{V}O_{2max}$) observed over time, RPE also drifted [$\chi^2(3) = 13.70$; P=0.003]. Participants reported a

2-unit increase in RPE at the end of the second work bout compared to the first 15 min of exercise. (*P*=0.02; Table 3a).

All participants' work intensity was categorized as moderate based on NIOSH guidelines when work intensity was expressed as kcal/h (248 ± 12) and estimated $\dot{M}$-$\dot{W}$ (279 ± 15 W), but not when $\dot{M}$-$\dot{W}$ was calculated from metabolic measures (231± 30 W). Figure 2 illustrates estimated and calculated $\dot{M}$-$\dot{W}$ for each participant, and how the values compare to the NIOSH range for moderate-intensity work.

Cardiovascular Drift

Over 2 hours of intermittent, moderate intensity exercise, heart rate [$F(1.31, 9.16) = 28.92$; $P<0.001$; partial $\eta^2 = 0.81$] and stroke volume [$F(3, 21) = 24.73$; $P<0.001$; partial $\eta^2 = 0.78$] were different across time. CV drift occurred as demonstrated by a 16.7% increase in heart rate (*P*=0.004) and 16.9% decrease in stroke volume (*P*=0.003) between 15 and 105 min. Furthermore, CV drift accumulated over consecutive work bouts (Figures 3 and 4): heart rate increased from 15 to 45 min (*P*=0.001), was not different between 45 and 75 min (*P*=1.00), and increased again from 75 to 105 min (*P*=0.04). During arm curls, heart rate was measured during the last minute of each set (at 2, 24, 62, and 84 min). Heart rate during arm curls also exhibited accumulated drift [$F(3, 21) = 31.65$; $P<0.001$; partial $\eta^2 = 0.82$], increasing from set 1 to set 2 (*P*=0.003), not different between sets 2 and 3 (*P*=0.30), and increasing again from set 3 to set 4 (*P*=0.03), for an overall mean increase of 28.8% from set 1 to set 4 (*P*=0.002). Cardiac output was not able to be measured during arm curls, so stroke volume data are not available for these time points.

Baseline resting heart rate was 68 ± 10 bpm, and heart rate remained elevated during the first (83 ± 11 bpm; *P*=0.004) and second (92 ± 14 bpm; *P*<0.001) rest breaks (Figure 3) [*F*(1.88, 13.14) = 35.96; P<0.001; partial η^2 = 0.84]. Heart rate at the end of the first rest break was also lower than heart rate at the end of the second rest break, immediately prior to measurement of $\dot{V}O_{2max}$ (P=0.03).

Stroke volume during treadmill walking followed a similar pattern as heart rate in terms of overall decrease (Table 3a), with a decrease between 15 and 45 min (P=0.002) and no difference between 45 and 75 min (P=0.09). The mean decrease of 4.2 mL between 75 and 105 min was not significant (P=0.37).

Thermal Responses

As a result of technical difficulties, T_{gi} data were not available for 1 participant at 45, 75, and 105 min and therefore were excluded from statistical analyses. T_{gi} changed over the duration of the 2 hour protocol [F(6, 36) = 18.21; P<0.001; partial η^2 = 0.75]. At 120 min, T_{gi} was elevated 0.5 ± 0.2 °C from baseline (P=0.006; Figure 5). Neither 15-min rest break was sufficient to significantly decrease T_{gi} from the end of the preceding work bout (both P=1.00). $\overline{T}_{sk}$ also changed throughout the duration of the protocol [F(2.49, 17.46) = 6.37; P=0.006; partial η^2 = 0.48]. $\overline{T}_{sk}$ was elevated at 45 min compared to the end of the first (P=0.02) and second (P=0.047) rest breaks but not compared to baseline (P=0.29; Figure 6). $\overline{T}_{sk}$ was also elevated at 105 min compared to the end of the rest break that immediately followed (P=0.002). Over 120 min, the core-to-skin temperature gradient (T_{gi}-$\overline{T}_{sk}$) gradually increased (Table 3a and 3b) due to a slowly rising T_{gi} and the return of $\overline{T}_{sk}$ to baseline during each rest break [F(1.99, 11.97) = 5.27; P=0.023; partial η^2 = 0.47]. $\overline{T}_b$ exhibited a similar slow rise over time (Table 3a and 3b) [F(6, 36) = 16.02; P<0.001; partial η^2 = 0.73].

Rating of thermal sensation (RTS) was different over time [χ^2(6) = 31.99; P<0.001]. Based on RTS, participants felt "cooler" at baseline than during work at 45, 75, or 105 min

(*P*=0.009, *P*=0.001, and *P*<0.001, respectively; Figure 7). RTS was not different between baseline and the first or second rest breaks (both *P*=0.78). Figures 6 and 7 demonstrate that RTS and $\overline{T}_{sk}$ followed similar patterns throughout work and rest bouts.

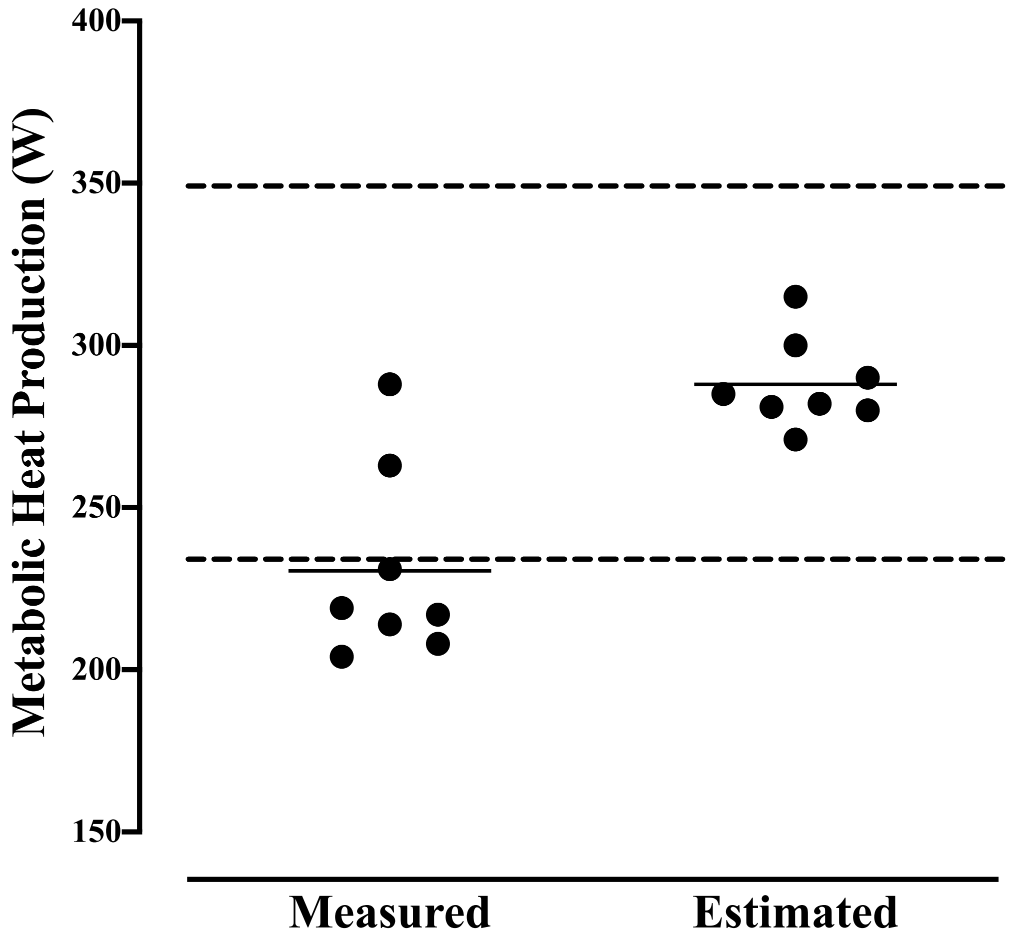

Figure 2. Time weighted average of measured vs. estimated metabolic heat production for each participant. The horizontal solid lines represent group means, and dashed lines indicate the upper and lower thresholds for moderate intensity work (234–349 W) as defined by NIOSH.

Table 3a. Responses to submaximal exercise during treadmill walking (mean ± SD).

	15 min	45 min	75 min	105 min
$\dot{V}O_2$ (L/min)	1.05 ± 0.05	1.08 ± 0.04*	1.07 ± 0.05	1.10 ± 0.06*‡
% CNTRL $\dot{V}O_{2max}$	34.9 ± 9.2	36.1 ± 9.3*	35.7 ± 8.8	36.5 ± 9.2*‡
SV (mL)	73.1 ± 14.2	66.9 ± 15.1*	64.9 ± 15.5*	60.7 ± 13.3*
$\dot{Q}$ (L/min)**	7.8 ± 0.6	7.9 ± 0.6	7.6 ± 0.6	7.5 ± 0.6
T_{gi}-$\overline{T}_{sk}$ (°C)**	1.3 ± 0.4	1.5 ± 0.7	1.7 ± 0.8	1.7 ± 0.9
$\overline{T}_b$ (°C)	36.9 ± 0.4	37.2 ± 0.4	37.2 ± 0.4	37.4 ± 0.4*‡
RPE	10 ± 2	12 ± 2	11 ± 2	12 ± 3*

$\dot{V}O_2$, oxygen uptake; SV, stroke volume; $\dot{Q}$, cardiac output; T_{gi}-$\overline{T}_{sk}$, gastrointestinal-to-skin temperature gradient; $\overline{T}_b$, mean body temperature; RPE, rating of perceived exertion. For T_{gi}-$\overline{T}_{sk}$ and $\overline{T}_b$, N = 7 because technical difficulties were encountered for 1 participant and data are missing at 45, 75, and 105 min. For all other variables, N = 8. * $P<0.05$ compared to 15 min; ‡ $P<0.05$ compared to 75 min. ** $P<0.05$ for the omnibus test.

Table 3b. Responses during rest intervals (mean ± SD).

	Baseline	60 min	120 min
T_{gi}-$\overline{T}_{sk}$ (°C)**	1.6 ± 0.4	2.1 ± 1.1	2.2 ± 1.1
$\overline{T}_b$ (°C)	36.7 ± 0.3	37.0 ± 0.4	37.1 ± 0.3*

T_{gi}-$\overline{T}_{sk}$, gastrointestinal-to-skin temperature gradient; $\overline{T}_b$, mean body temperature. N = 7 because technical difficulties were encountered for 1 participant and data are missing at 45, 75, and 105 min. * $P<0.05$ compared to baseline; ** $P<0.05$ for the omnibus test.

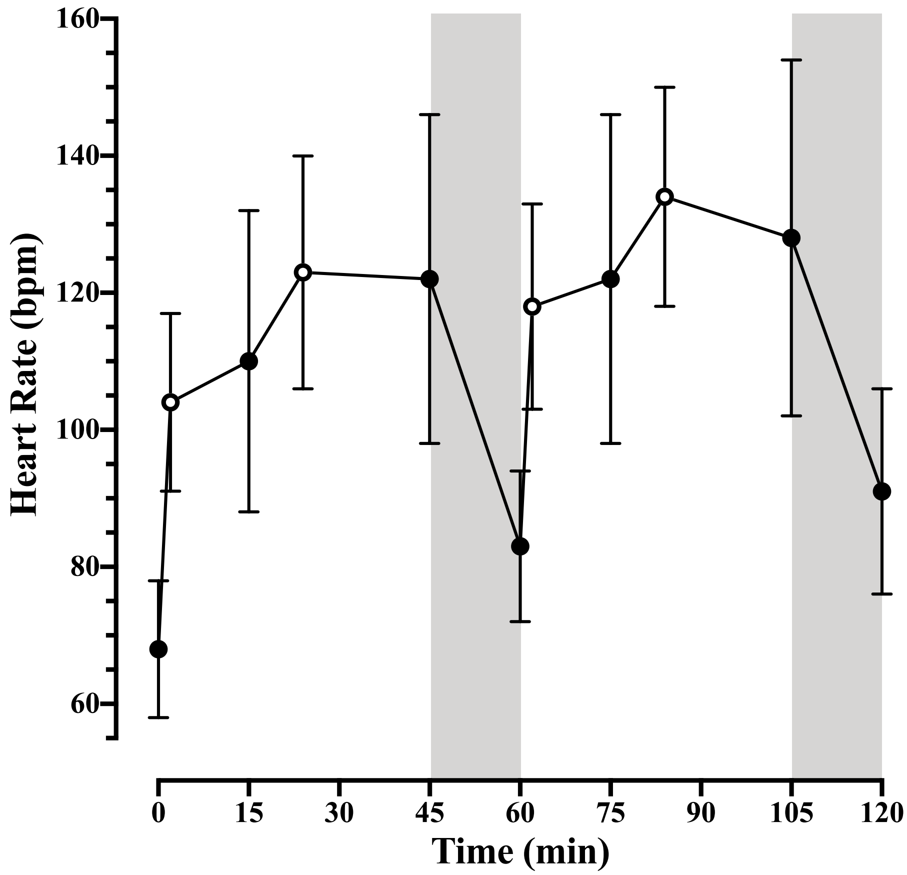

Figure 3. Mean ± SD heart rate over two 45:15 work:rest cycles. Open circles indicate mean heart rate at the end of each set of arm curls and solid circles indicate mean heart rate during treadmill walking and rest; shaded areas indicate rest breaks.

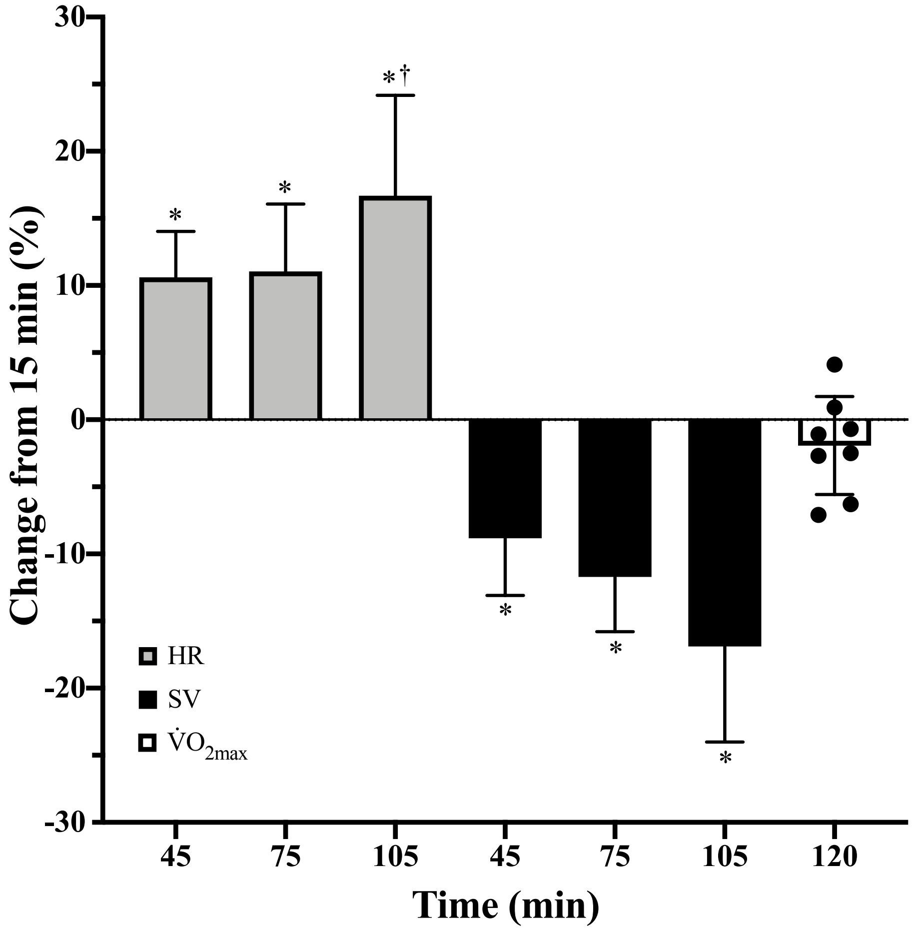

Figure 4. Mean ± SD percent change from 15 min for heart rate (HR), stroke volume (SV), and maximal oxygen uptake ($\dot{V}O_{2max}$). For $\dot{V}O_{2max}$, the bar represents mean data and the dots represent individual responses. * P<0.05 compared to 15 min; † P<0.05 compared to 75 min.

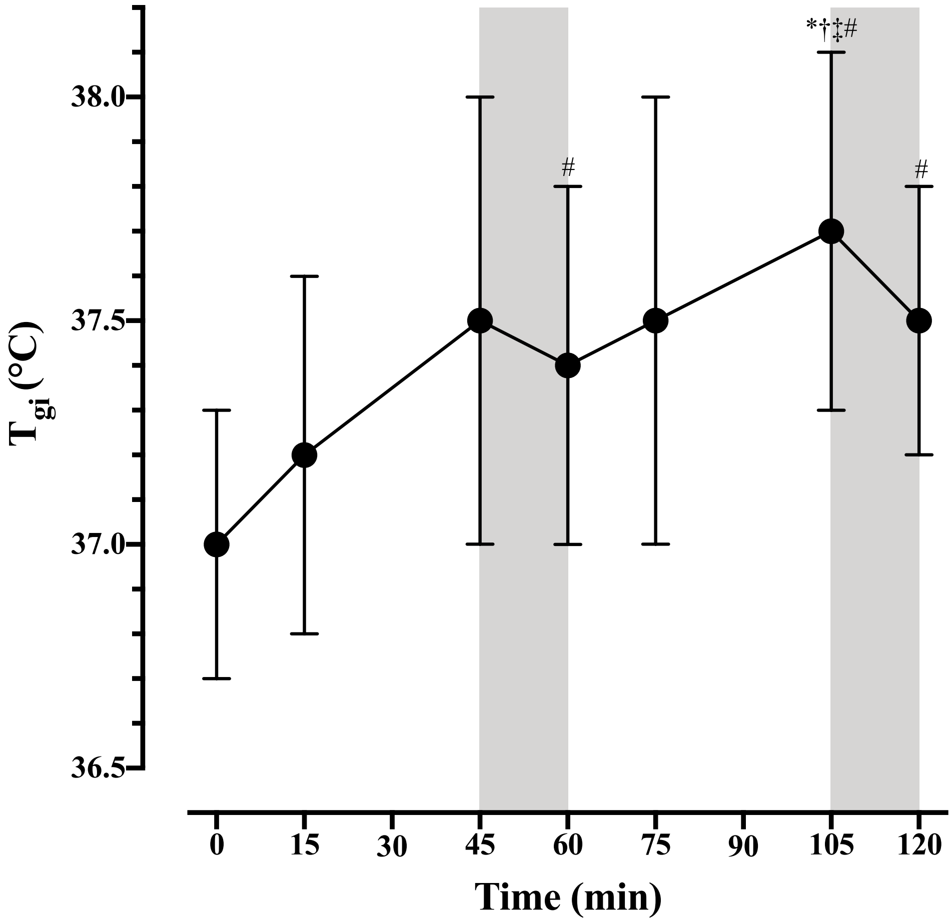

Figure 5. Mean ± SD gastrointestinal temperature (T_{gi}) over two 45:15 work:rest cycles. Shaded areas represent rest breaks. N = 7 because technical difficulties were encountered for 1 participant and data are missing at 45, 75, and 105 min. * P<0.05 compared to 15 min; † P<0.05 compared to 45 min; ‡ P<0.05 compared to 75 min; # P<0.05 compared to baseline (0 min).

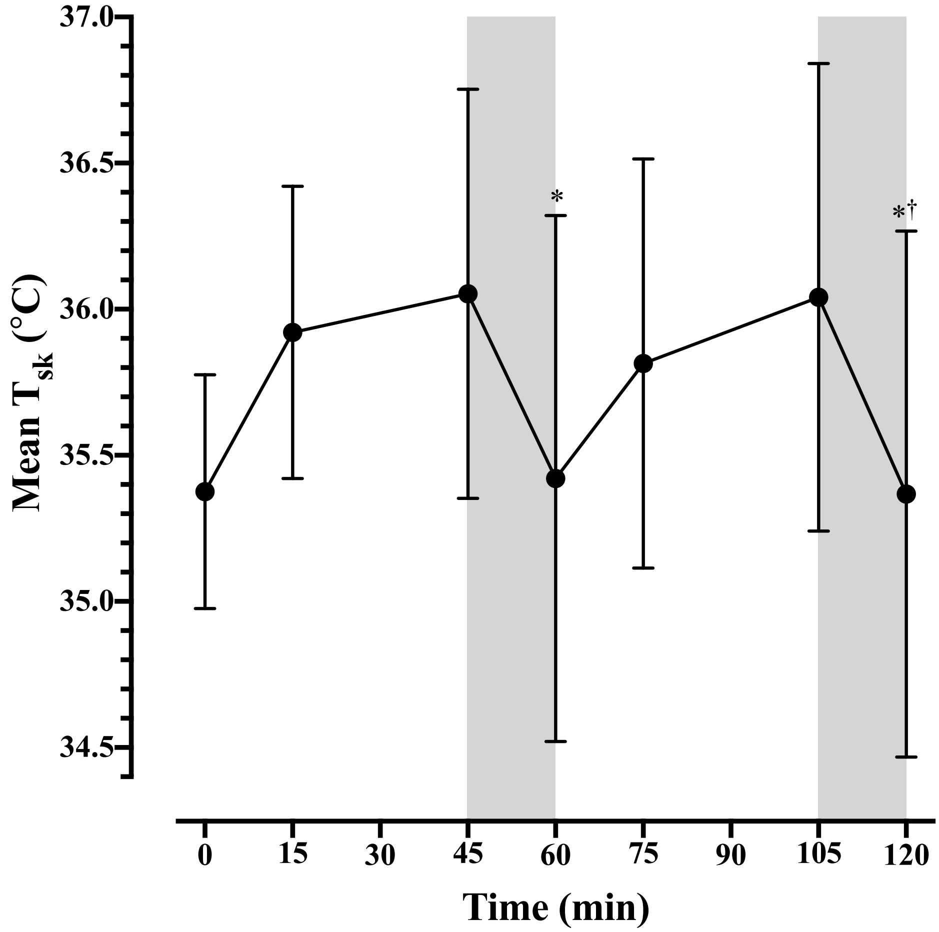

Figure 6. Average ± SD mean skin temperature (T_{sk}) over two 45:15 work:rest cycles. Shaded areas represent rest breaks. * P<0.05 compared to 45 min. † P<0.05 compared to 105 min.

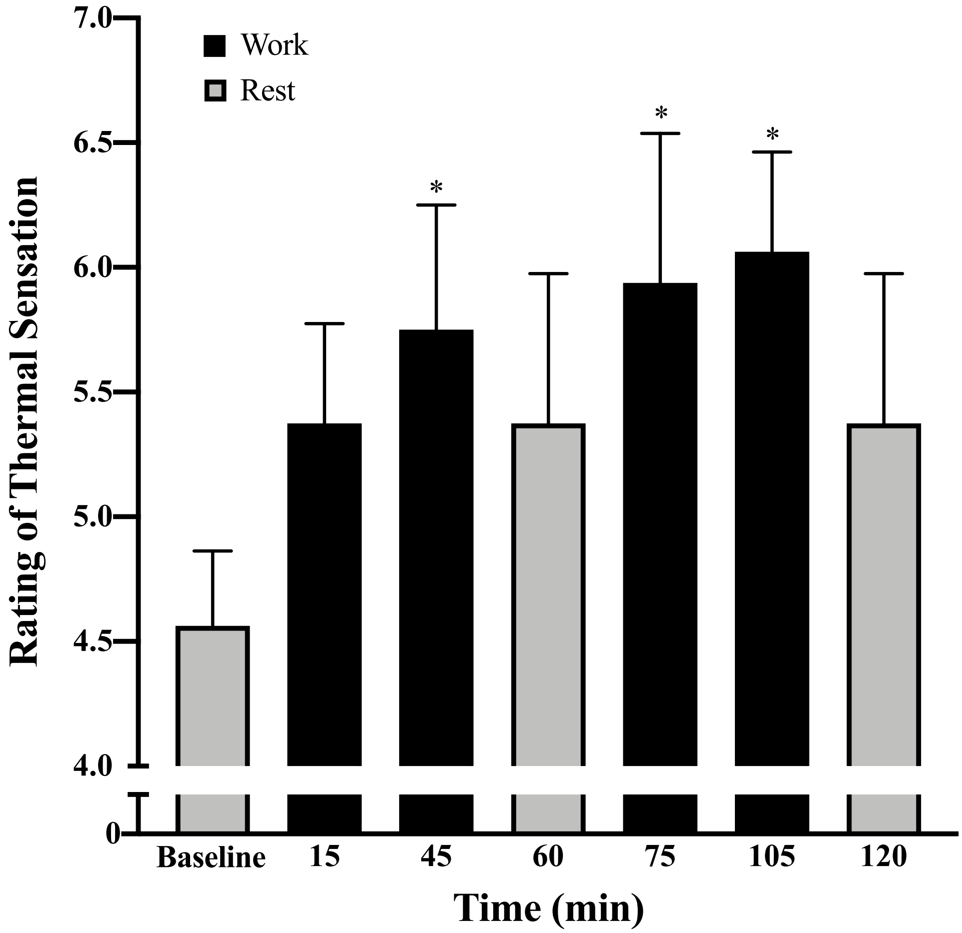

Figure 7. Mean ± SD rating of thermal sensation before and throughout the 120-min protocol.
* P<0.05 compared to baseline.

Responses to Maximal Exercise

Despite an increase in heart rate and a decrease in stroke volume over time, $\dot{V}O_{2max}$ was not different between 15 min and 120 min [$t(7) = -1.53$; P=0.17; Figure 4 and Table 4]. Along with absolute and relative $\dot{V}O_2$, RPE, RTS, and blood lactate responses showed no differences among maximal exercise bouts (all P>0.05). RER was greater during CNTRL compared to 120MIN (P=0.02). Average maximal heart rate achieved during 120MIN was 1% lower than that during CNTRL (P=0.01; Table 4), but all participants achieved a maximal heart rate within 5 beats of their CNTRL maximal heart rate. With the exception of one participant, the final workload (treadmill grade and speed) during each GXT for each participant was identical.

T_{gi} is based on N = 7 because of missing data for 1 participant as a result of technical difficulties. While T_{gi} increased over time during 120MIN, the rest break just prior to the GXT was sufficient to render T_{gi} at the end of the GXT comparable (P=0.25) to T_{gi} at the end of the GXT in 15MIN. The longer running duration during the 15MIN GXT, reported in Table 4, might have also contributed to a comparable T_{gi} in 120MIN despite the shorter submaximal exercise period before measurement of $\dot{V}O_{2max}$ during 15MIN.

Table 4. Responses to maximal exercise (mean ± SD). All ANOVA omnibus results presented here have (2, 14) degrees of freedom.

	CNTRL	15MIN	120MIN	ANOVA results		
				F	***P*-value**	**Partial η^2**
$\dot{V}O_2$ (L/min)	3.20 ± 0.90	3.22 ± 0.95	3.16 ± 0.92	1.35	0.29	0.16
$\dot{V}O_2$ (mL/kg/min)	42.0 ± 5.7	42.3 ± 6.3	41.5 ± 6.1	1.12	0.36	0.14
RER	1.16 ± 0.06	1.12 ± 0.07	1.10 ± 0.08*	5.70	0.02	0.45
HR (bpm)	191 ± 5	188 ± 6	189 ± 5*	4.39	0.03	0.39
T_{gi} (°C)	–	37.6 ± 0.3	37.8 ± 0.3	–	0.25	–
RPE	19 ± 1	19 ± 1	19 ± 1	–	0.94	–
RTS	–	7.0 ± 0.5	7.1 ± 0.4	–	0.32	–
Blood lactate (mmol/L)	6.3 ± 1.4	5.9 ± 2.0	6.0 ± 3.1	1.77	0.22	0.26
Treadmill grade (%)	11.1 ± 1.5	11.1 ± 2.8	10.8 ± 2.7	0.23	0.80	0.03
Speed (km/h)	8.2 ± 0.8	8.3 ± 0.8	8.3 ± 0.8	1.00	0.39	0.13
GXT duration (min:sec)	8:00 ± 1:06	6:40 ± 1:06	5:21 ± 1:28*†	17.87	<0.001	0.72

$\dot{V}O_2$, oxygen uptake; RER, respiratory exchange ratio; HR, heart rate; T_{gi}, gastrointestinal temperature; RPE, rating of perceived exertion; RTS, rating of thermal sensation; GXT, graded exercise test. Data for T_{gi} are based on N = 7; data for all other variables are based on N = 8. T_{gi} and RTS were not collected during the CNTRL visit and the associated *P*-values represent the results of a paired samples t-test; RPE and RTS were analyzed using nonparametric statistics. Three values included in the means for blood lactate were measured from a handheld device using a fingerstick blood sample (1 each for CNTRL, 15MIN, 120MIN; 3 different participants) due to venipuncture or equipment difficulties. * *P*<0.05 compared to CNTRL, † *P*<0.05 compared to 15 min.

DISCUSSION

The purpose of this study was to determine the extent to which CV drift ‘accumulated’ over consecutive work:rest cycles and the subsequent impact this had on maximal work capacity, indexed as $\dot{V}O_{2max}$. The primary finding was that the hypothesis that CV drift would accumulate over multiple work bouts was confirmed, but $\dot{V}O_{2max}$ was unaffected. The nonsignificant 2% decrease in $\dot{V}O_{2max}$ after 2 work:rest cycles in 120MIN compared to 15MIN corresponded to comparable GXT durations and final workloads in the majority of participants. The observed mean decrease in $\dot{V}O_{2max}$, as well as the magnitude of all individual responses, was within the day-to-day variability that has been reported for repeated $\dot{V}O_{2max}$ testing (Katch et al. 1982).

The magnitude of CV drift in the current study was comparable to other studies involving prolonged exercise in the heat. For example, Gliner et al. (1975) observed responses over 4 hours of 50:10 work:rest at 35% $\dot{V}O_{2max}$ in the heat (35 °C dry bulb temperature, 30% RH), and they found similar magnitudes of drift in heart rate and stroke volume—+23% and approximately -23%, respectively. However, they did not assess $\dot{V}O_{2max}$ at the conclusion of the protocol, so it is impossible to determine whether maximal work capacity was affected over time. Other studies that measured CV drift and $\dot{V}O_{2max}$ concurrently observed a magnitude of CV drift comparable to this study and a decrement in $\dot{V}O_{2max}$ of 9%–19% (Ganio et al. 2006; Lafrenz et al. 2008; Wingo et al. 2005; Wingo and Cureton 2006a, b), but despite the similar magnitudes of CV drift, $\dot{V}O_{2max}$ was unaffected in the current study.

Contrary to other studies that have demonstrated that the elevated heart rate associated with CV drift reflects an increased relative metabolic intensity as a result of accompanying decreases in $\dot{V}O_{2max}$ (Wingo et al. 2005; Wingo and Cureton 2006a; Ganio et al. 2006), the increase in heart rate in the present study appeared to be dissociated from relative metabolic intensity since $\dot{V}O_{2max}$ was preserved after 2 work:rest cycles. Despite the preservation of relative metabolic intensity over the 120-min period, RPE increased over consecutive work bouts. This is consistent with the observed upward drift in heart rate that is associated with CV drift, but the precise explanation for this result is elusive since we did not observe a change in relative metabolic intensity (i.e., %$\dot{V}O_{2max}$). The ~0.5 °C increase in T_{gi} between 15 and 105 min may have contributed, as RPE has been shown to be amplified by elevated body temperature (Nybo and Nielsen 2001; Nielsen and Nybo 2003).

Although the relative magnitudes of drift (i.e., % change) in heart rate and stroke volume in the present study were comparable to the studies cited above, the absolute values for heart rate and stroke volume were lower in this study. The absolute and relative work intensities utilized in this study were lower compared to others, which resulted in a lower absolute metabolic demand and elicited heart rates of 110–130 bpm during exercise, compared to 150–170 bpm in other studies (Ganio et al. 2006; Lafrenz et al. 2008; Wingo et al. 2005; Wingo and Cureton 2006a, b). This difference in working heart rate resulted in a greater cardiac reserve (difference between exercise values and maximum values) in the present study, which may have been even further improved during the rest period implemented prior to measurement of $\dot{V}O_{2max}$, and which the other studies lacked. It may be that there is a minimum threshold work intensity and accompanying CV drift involving higher absolute heart rates and stroke volumes, and therefore greater reductions in cardiac reserve—rather than a given magnitude of CV drift per se—that is most strongly associated with reductions in $\dot{V}O_{2max}$ during prolonged work in the heat.

Given that previous studies observed a decrease in $\dot{V}O_{2max}$ preceded by a similar magnitude of CV drift, why was $\dot{V}O_{2max}$ unaffected in the current study after 120 min? The data collected do not permit a definitive answer to this question, but preservation of stroke volume during maximal exertion is the likely explanation. Compared to other studies (Lafrenz et al. 2008; Wingo et al. 2005; Wingo and Cureton 2006a, b), this study featured a lower exercise intensity, longer duration, and inclusion of rest breaks. As a result, rates of $\dot{M}$-$\dot{W}$ were 2–3 times higher in the other studies than the 231 W observed here. Greater rates of $\dot{M}$-$\dot{W}$ caused greater increases in core temperature (even over shorter exercise durations) that likely exacerbated CV strain—i.e., reduced stroke volume—during submaximal exercise and persisted during the maximal exercise that immediately followed. In contrast, despite a similar magnitude of CV drift in the current study, thermal strain was mild. This may have resulted in preservation of stroke volume—and thereby maximal cardiac output—during maximal exercise. This notion is supported by findings from Saltin and Stenberg (1964) who observed a comparable magnitude of CV drift—increase in heart rate and decrease in stroke volume of approximately 15% each—during prolonged, intermittent, submaximal exercise (70% $\dot{V}O_{2max}$, 195 min), but only a small reduction (-5%; -0.1 L/min) in $\dot{V}O_{2max}$ after a 90-min rest period. Despite this magnitude of decrease in stroke volume and cardiac output during the submaximal exercise period, these variables were restored during maximal exercise, essentially preserving $\dot{V}O_{2max}$. The authors attributed the ability to achieve maximal stroke volume and thereby maximal cardiac output to a reduced skin blood flow requirement. It may be that a rest period shorter than 90 min, like the 15 min utilized in the current study, is sufficient in reducing skin blood flow requirements under conditions of relatively low exercise intensity and thermal strain. While we did not measure skin blood flow, the return of $\overline{T}_{sk}$ to baseline values before the GXT to measure $\dot{V}O_{2max}$ suggests skin blood flow decreased as well (Vuksanović et al. 2008). Since maximal heart rate was achieved and since $(a\text{-}\bar{v})O_2$ would not be expected to be different under these conditions (González-Alonso and Calbet 2003), restoration of maximal stroke volume would have permitted achievement of maximal cardiac output and thereby $\dot{V}O_{2max}$.

A limitation of this study is that we were not able to measure skin blood flow due to constraints regarding the instrumentation and the movement artifact associated with exercise, and so we can only speculate regarding the redistribution of blood flow to the skin. While skin temperature can be an adequate substitution for measurement of skin blood flow, participants in this study wore a long sleeve shirt and pants which creates a microenvironment that could have artificially elevated skin temperatures and overestimated the assumption of elevated skin blood flow.

Although NIOSH assumptions (age, physical fitness, health status, hydration, sleep, work intensity, environmental conditions, etc.) were largely accounted for in subject recruitment and study design, participants were probably not representative of the average worker and so the extent to which these findings are applicable in the work place is limited by the sample population. By design, they did not have any co-morbidities, they were under 40 years old (18–35 y), and they arrived at all laboratory visits prepared for peak performance: well-rested, hydrated, and having not consumed alcohol or caffeine in the previous 24 hours. This ‘ideal’ scenario is likely an infrequent reality, and as such generalization of these results to what workers experience over a more prolonged workday warrants caution. Because of time constraints related to study execution, data were collected between October and January and as such the NIOSH assumption that workers are heat acclimatized was left unmet. However, the lack of heat acclimated participants probably had a limited, if any, impact on the findings. Two trials conducted in the heat would not likely have induced any degree of acclimation, and counterbalanced treatment orders should have eliminated any systematic acclimation effect on results if there had been one. Heat acclimation alters physiological set points: for a given submaximal exercise intensity, heart rate, core body temperature, skin temperature, and perceived exertion are lower, while sweat rate is higher, due to changes in the homeostatic mechanisms through which they function (Aoyagi et al. 1997). So, while absolute values might have been different if participants had been heat acclimated, the nature of the responses between 15 and 120 min should not have been affected.

Future research should expand upon the relationship between CV drift and $\dot{V}O_{2max}$ at varying work intensities, environmental conditions, clothing requirements, work:rest ratios, and over longer durations. The next steps should include direct assessment of changes in skin blood flow (instead of using $\overline{T}_{sk}$ as a proxy) to better understand the extent to which blood flow demand impacts cardiac reserve and $\dot{V}O_{2max}$. Also, the exploration of CV drift in a sample population that is more representative of the actual working population is recommended, since it is unknown whether co-morbid conditions impact the relationship between CV drift and $\dot{V}O_{2max}$.

This study examined the relationship between work intensity, CV drift, and $\dot{V}O_{2max}$ over 120 min of intermittent exercise in the heat. The primary finding was that although elevations in both CV and thermal strain persisted over consecutive 45-min work bouts coupled with 15-min rest periods, $\dot{V}O_{2max}$ was unaffected. Fifteen-min rest periods were not sufficient to fully return heart rate or T_{gi} to initial resting values but were sufficient to preserve (or restore) maximal work capacity.

REFERENCES

ACGIH Heat Stress and Strain: TLV Physical Agents Documentation. In: American Conference of Governmental Industrial Hygienists, 2017. pp 1–37

Aoyagi Y, McLellan TM, Shephard RJ (1997) Interactions of physical training and heat acclimation. Sports Medicine 23:173–210

Åstrand PO, Cuddy TE, Saltin B, Stenberg J (1964) Cardiac output during submaximal and maximal work. Journal of Applied Physiology 19 (2):268–274

Borg GA (1982) Psychophysical bases of perceived exertion. Medicine and Science in Sports and Exercise 14 (5):377–381

Budd GM (2008) Wet-bulb globe temperature (WBGT)—its history and its limitations. Journal of Science and Medicine in Sport 11 (1):20–32

Byrne C, Lim CL (2007) The ingestible telemetric body core temperature sensor: a review of validity and exercise applications. British Journal of Sports Medicine 41 (3):126

Cheuvront SN, Kenefick RW, Montain SJ, Sawka MN (2010) Mechanisms of aerobic performance impairment with heat stress and dehydration. Journal of Applied Physiology 109 (6):1989–1995

Cramer MN, Jay O (2016) Biophysical aspects of human thermoregulation during heat stress. Autonomic Neuroscience 196:3–13

Dill DB, Costill DL (1974) Calculation of percentage changes in volumes of red blood cells and plasma in dehydration. Journal of Applied Physiology 37:247–248

Faul F, Erdfelder E, Lang AG, Buchner A (2007) G*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. Behavior Research Methods 39 (2):175–191

Flouris AD (2010) Functional architecture of behavioural thermoregulation. European Journal of Applied Physiology 111:1–8

Ganio MS, Brown CM, Casa DJ, Becker SM, Yeargin SW, McDermott BP, Boots LM, Boyd PW, Armstrong LE, Maresh CM (2009) Validity and reliability of devices that assess body temperature during indoor exercise in the heat. Journal of Athletic Training 44 (2):124–135

Ganio MS, Wingo JE, Carroll CE, Thomas MK, Cureton KJ (2006) Fluid ingestion attenuates the decline in VO2peak associated with cardiovascular drift. Medicine and Science in Sports and Exercise 38 (5):901–909

Gliner JA, Raven PB, Horvath SM, Drinkwater BL, Sutton JC (1975) Man's physiologic response to long-term work during thermal and pollutant stress. Journal of Applied Physiology 39 (4):628–632

Goedecke JH, St Clair Gibson A, Grobler L, Collins M, Noakes TD, Lambert EV (2000) Determinants of the variability in respiratory exchange ratio at rest and during exercise in trained athletes. American Journal of Physiology-Endocrinology and Metabolism 279 (6):E1325–E1334

González-Alonso J, Calbet JA (2003) Reductions in systemic and skeletal muscle blood flow and oxygen delivery limit maximal aerobic capacity in humans. Circulation 107 (6):824–830

Jacklitsch B, Williams J, Musolin K, Coca A, Kim JH, Turner N (2016) NIOSH criteria for a recommended standard: Occupational exposure to heat and hot environments. Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health

Jackson AS, Pollock ML (1985) Practical assessment of body composition. Physician Sportsmed 13 (5):76–90

Jones NL (1975) Mixed venous pCO2 and the measurement of cardiac output. In: Clinical Exercise Testing. W.B. Saunders Company, Philadelphia, pp 57–62

Katch VL, Sady SS, Freedson P (1982) Biological variability in maximum aerobic power. Medicine and Science in Sports and Exercise 14 (1):21–25

Kenny GP, Jay O (2013) Thermometry, calorimetry, and mean body temperature during heat stress. Comprehensive Physiology 3 (4):1689–1719

Lafrenz AJ, Wingo JE, Ganio MS, Cureton KJ (2008) Effect of ambient temperature on cardiovascular drift and maximal oxygen uptake. Medicine and Science in Sports and Exercise 40 (6):1065–1071

Maresh CM, Sökmen B, Armstrong LE, Dias JC, Pryor JL, Creighton BC, Muñoz CX, Apicella JM, Casa DJ, Lee EC, Anderson JM, Kraemer WJ (2014) Repetitive box lifting performance is impaired in a hot environment: Implications for altered work-rest cycles. Journal of Occupational and Environmental Hygiene 11 (7):460–468

Montain SJ, Coyle EF (1992) Influence of graded dehydration on hyperthermia and cardiovascular drift during exercise. Journal of Applied Physiology 73 (4):1340–1350

Nielsen B, Nybo L (2003) Cerebral changes during exercise in the heat. Sports Medicine 33 (1):1–11

NWS (2018) Observed Weather Reports, Tuscaloosa County. National Weather Service. https://w2.weather.gov/climate/index.php?wfo=bmx.

Nybo L, Nielsen B (2001) Hyperthermia and central fatigue during prolonged exercise in humans. Journal of Applied Physiology 91 (3):1055–1060

Ramanathan NL (1964) A new weighting system for mean surface temperature of the human body. Journal of Applied Physiology 19 (3):531–533

Saltin B, Stenberg J (1964) Circulatory response to prolonged severe exercise. Journal of Applied Physiology 19 (5):833–838

Sawka MN, Burke LM, Eichner ER, Maughan RJ, Montain SJ, Stachenfeld NS (2007) American College of Sports Medicine position stand. Exercise and fluid replacement. Medicine and Science in Sports and Exercise 39 (2):377–390

Schlader ZJ, Simmons SE, Stannard SR, Mündel T (2011) The independent roles of temperature and thermal perception in the control of human thermoregulatory behavior. Physiology and Behavior 103 (2):217–224

Stolwijk JAJ, Hardy JD (1965) Partitional calorimetric studies of responses of man to thermal transients. Journal of Applied Physiology 21 (3):967–977

U.S. Department of Health and Human Services (2018) Physical Activity Guidelines for Americans. 2nd edn. U.S. Department of Health and Human Services, Washington, DC: US

Vuksanović V, Sheppard LW, Stefanovska A (2008) Nonlinear relationship between level of blood flow and skin temperature for different dynamics of temperature change. Biophysical Journal 94 (10):L78–L80

Wingo JE, Cureton KJ (2006a) Body cooling attenuates the decrease in maximal oxygen uptake associated with cardiovascular drift during heat stress. European Journal of Applied Physiology 98 (1):97–104

Wingo JE, Cureton KJ (2006b) Maximal oxygen uptake after attenuation of cardiovascular drift during heat stress. Aviation Space and Environmental Medicine 77:687–694

Wingo JE, Lafrenz AJ, Ganio MS, Edwards GL, Cureton KJ (2005) Cardiovascular drift is related to reduced maximal oxygen uptake during heat stress. Medicine and Science in Sports and Exercise 37 (2):248–255

Young AJ, Sawka MN, Epstein Y, DeCristofano B, Pandolf KB (1986) Cooling different body surfaces during upper-and-lower body exercise. United States Army Research Institute of Environmental Medicine, Natick, MA

APPENDIX

Appendix A. Outcome for all statistical assumptions checked before data analysis. Normality was assessed by visual inspection of histograms and Q-Q plots generated in SPSS and considered met if data points at the majority of the time points produced an approximately normal histogram and/or no strong pattern of deviation from the trendline of the Q-Q plot. When sphericity was violated, the Greenhouse-Geisser correction was applied.

Variable	Normality	Sphericity				
			Mauchly's *W*	χ^2	*df*	*P*-value
% CNTRL $\dot{V}O_{2max}$	Met	Met	0.166	10.267	5	0.07
Blood lactate	Met	Met	0.423	3.438	2	0.18
Body mass loss	Met	NA	–	–	–	–
GXT duration	Met	Met	0.971	0.179	2	0.91
HR (arm curls)	Met	Met	0.328	6.384	5	0.28
HR (rest)	Met	Met	0.934	0.409	2	0.82
HR (walking)	Met	Violated	0.066	15.538	5	0.009
HR_{max}	Met	Met	0.385	5.733	2	0.06
Plasma osmolality	Met	NA	–	–	–	–
Plasma volume	Met	NA	–	–	–	–
$\dot{Q}$	Met	Met	0.571	3.205	5	0.67
RER_{max}	Met	Met	0.903	0.609	2	0.74
RPE	Violated*	NA	–	–	–	–
RPE_{max}	Violated*	NA	–	–	–	–
RTS	Violated*	NA	–	–	–	–
RTS_{max}	Violated*	NA	–	–	–	–
SV	Met	Met	0.148	10.926	5	0.06
$\overline{T}_b$	Met	Met	0.000	34.055	20	0.07
T_{gi}	Met	Met	0.000	33.847	20	0.07
$T_{gi\text{-}max}$	Met	NA	–	–	–	–
T_{gi}-$\overline{T}_{sk}$	Met	Violated	0.000	45.307	20	0.004
Treadmill $grade_{max}$	Met	Met	0.499	4.165	2	0.13
Treadmill $speed_{max}$	Met	NA	–	–	–	–
$\overline{T}_{sk}$	Met	Violated	0.000	39.248	20	0.02
$\dot{V}O_2$ (walking)	Met	Met	0.321	6.502	5	0.27
$\dot{V}O_{2max}$ (L/min)	Violated	Met	0.538	3.725	2	0.16
$\dot{V}O_{2max}$ (mL/kg/min)	Violated	Met	0.579	3.275	2	0.19
$\Delta\dot{V}O_{2max}$	Met	NA	–	–	–	–
Water consumption	Met	NA	–	–	–	–

df, degrees of freedom; CNTRL, initial laboratory visit; GXT, graded exercise test; HR, heart rate; $\dot{Q}$, cardiac output; RER, respiratory exchange ratio; RPE, rating of perceived exertion; RTS, rating of thermal sensation; SV, stroke volume; $\overline{T}_b$, mean body temperature; T_{gi}, gastrointestinal temperature; T_{gi}-$\overline{T}_{sk}$, core-to-skin temperature gradient; $\overline{T}_{sk}$, mean skin temperature; $\dot{V}O_2$, rate of oxygen uptake. 'Max' denotes maximal exertion exercise data from Table 4. *indicates nonparametric statistical test. NA indicates assumption did not apply. Treadmill $speed_{max}$ was identical for all participants between 15MIN and 120MIN so the assumption of sphericity does not apply as there are not 3 unique group comparisons.

Appendix B. Self-reported menstrual cycle phase and birth control usage for female participants.

Female participant	Birth control	Type	Phase tested
Subject 1	Yes	Oral, triphasic	Luteal
Subject 2	Yes	Oral, monophasic	Follicular
Subject 3	Yes	Oral, triphasic	Luteal
Subject 4	No	–	Follicular
Subject 5	No	–	Luteal

THE UNIVERSITY OF ALABAMA® | Office of the Vice President for Research & Economic Development
Office for Research Compliance

July 22, 2019

Annie Mulholland
Department of Kinesiology
College of Education
The University of Alabama
Box 870312

Re: IRB Protocol # 19-004-ME
"Effect of Work-to-Rest Cycles on Cardiovascular Drift and Maximal Oxygen Uptake during Heat Stress"

Ms. Mulholland:

The University of Alabama Medical Institutional Review Board has granted approval for your proposed research. Your application has been given full board approval according to 45 CFR part 46.

The approval for your application will lapse on June 5, 2020. If your research will continue beyond this date, please submit a continuing review to the IRB as required by University policy before the lapse. Please note, any modifications made in research design, methodology, or procedures must be submitted to and approved by the IRB before implementation. Please submit a final report form when the study is complete.

Please use reproductions of the IRB approved stamped consent form to obtain consent from your participants.

Good luck with your research.

Sincerely,

[redacted]

358 Rose Administration Building | Box 870127 | Tuscaloosa, AL 35487-0127
205-348-8461 | Fax 205-348-7189 | Toll Free 1-877-820-3066