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Complete List of Authors:	Friesen, Brian; University of Ottawa, Human Kinetics Poirier, Martin; University of Ottawa, School of Human Kinetics, Faculty of Health Sciences Lamarche, Dallon; University of Ottawa, Human Kinetics D'Souza, Andrew; University of Ottawa, Human Kinetics Kim, Jung-Hyun; Centers for Disease Control and Prevention, National Institute for Occupational Safe Notley, Sean; University of Ottawa, Faculty of Health Sciences Kenny, Glen; University of Ottawa,
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Postexercise whole-body sweating increases during muscle metaboreceptor activation in young men

¹Brian J. Friesen, ²Martin P. Poirier, ³Dallon T. Lamarche, ⁴Andrew W. D’Souza, ⁵Jung-Hyun Kim, ⁶Sean R. Notley and ⁷Glen P. Kenny

¹Human and Environmental Physiological Research Unit, Faculty of Health Sciences, University of Ottawa, Ottawa, Ontario, Canada, K1N 6N5; bfrie051@uottawa.ca

²Human and Environmental Physiological Research Unit, Faculty of Health Sciences, University of Ottawa, Ottawa, Ontario, Canada, K1N 6N5; mpoir026@uottawa.ca

³Human and Environmental Physiological Research Unit, Faculty of Health Sciences, University of Ottawa, Ottawa, Ontario, Canada, K1N 6N5; dlama059@uottawa.ca

⁴Human and Environmental Physiological Research Unit, Faculty of Health Sciences, University of Ottawa, Ottawa, Ontario, Canada, K1N 6N5; adsou102@uottawa.ca

⁵Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, Pittsburgh, USA; inr3@cdc.gov

⁶Human and Environmental Physiological Research Unit, Faculty of Health Sciences, University of Ottawa, Ottawa, Ontario, Canada, K1N 6N5; snotley@uottawa.ca

⁷Human and Environmental Physiological Research Unit, Faculty of Health Sciences, University of Ottawa, Ottawa, Ontario, Canada, K1N 6N5; gkenny@uottawa.ca

Corresponding author:

Glen P. Kenny
University of Ottawa
125 University Ave.
Ottawa, ON, Canada, K1N 6N5
Phone: +1 613 562 5800 ext. 4282; Fax: +1 613 562 5497
E-mail: gkenny@uottawa.ca

Running head: Nonthermal modulation of heat dissipation

ABSTRACT

We assessed the effect of metaboreceptor activation on whole-body evaporative heat loss (WB-EHL) in twelve men (24 ± 4 years) in the early-to-late-stages of a 60-min exercise recovery in the heat. Metaboreceptor activation induced by 1-min isometric-handgrip (IHG) exercise followed by 5-min forearm ischemia to trap metabolites increased WB-EHL by 25-31% and 26-34% during the ischemic period relative to IHG-Only and Control (natural recovery only) respectively throughout recovery. We show that metaboreceptor activation enhances WB-EHL in recovery.

Key words: exercise, heat loss, calorimetry, nonthermal, isometric, sweat rate.

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INTRODUCTION

An increasing number of studies demonstrate that nonthermal factors associated with the activation of sensory end organs of baroreceptors, osmoreceptors and metaboreceptors play an important role in the regulation of heat loss responses during heat stress (Kenny et al. 2010; Kondo et al. 2010). For instance, studies show that independent of thermal control, nonthermal factors can simultaneously act on the thermoregulatory system to modulate heat dissipation during the postexercise recovery period (Kenny and Journeay 2010; Kenny et al. 2016; Kenny and McGinn 2017). Upon cessation of exercise, the rapid decrease in metabolic heat liberation is paralleled by a decline in local and whole-body heat loss to pre-exercise resting levels despite sustained elevations in body temperatures (i.e. core and muscle) and therefore body heat storage (Kenny et al. 2008; Kenny and Journeay 2010). This response, which has been shown to last for up to 120 minutes, has been primarily attributed to the overriding influences of nonthermal factors on postexercise thermoregulatory function (Kenny et al. 2008; Kenny and Journeay 2010).

Until recently, the nonthermal mediated postexercise disturbance in thermal homeostasis was largely ascribed to a baroreflex-mediated response associated with postexercise hypotension (Kenny and Journeay 2010). However, recent findings reveal that other nonthermal factors associated with metaboreceptor activation may be involved (Kenny and McGinn 2017, McGinn et al. 2014; Paull et al. 2015). The accumulation of metabolites within the active skeletal muscle has been shown to stimulate group III and IV afferent neurons which in turn evoke a reflex increase in muscle sympathetic nerve activity, known as the muscle metaboreflex (Rowell and O'Leary 1990). The activation of metaboreceptors have been shown to modulate heat loss

responses during both passive heat stress and exercise (Crandall et al. 1998; Shibasaki et al. 2001; Boushel 2010) with recent studies extending their influence to the postexercise period (McGinn et al. 2014; Paull et al. 2015). These latter studies demonstrate that the influence of baroreceptors may be limited to the control of local skin blood flow whereas metaboreceptors, and not baroreceptors, may largely influence the regulation of local sweating (McGinn et al. 2014; Paull et al. 2015); an important avenue of heat dissipation during heat stress. Specifically, metaboreceptor activation, induced by a brief isometric handgrip (**IHG**) exercise followed by forearm ischemia to trap metabolites, was shown to delay the rapid reduction in local sweating occurring in the early stages of recovery (≤ 20 min)(McGinn et al. 2014; Paull et al. 2015) while increasing local sweating during the mid-to-late stages of recovery (30- to 60-min of recovery)(Paull et al. 2015) relative a natural recovery (no IHG or ischemia). Despite regional variations in absolute local sweat rate, a consistent response was observed across different body regions (i.e., chest, forearm and upper back)(Paull et al. 2015) during the activation of metaboreceptors. Taken together, these findings indicate that the metaboreceptor-mediated modulation of local sweating may have an important effect on whole-body sweating. In this context, it is possible that changes in metaboreceptor activity in the postexercise period may play an important role in the observed disruption of thermal homeostasis.

Thus, in the present study, we examined the effect of metaboreceptor activation on whole-body sweating by assessing whole-body evaporative heat loss (WB-EHL) during the early- (15 min), mid- (30 min) and late- (45 min) stages of recovery following a 45-min moderate intensity exercise bout in the heat (35°C, 20% relative humidity). To evaluate this response, we used direct calorimetry to precisely measure WB-EHL (Kenny et al. 2017). We evaluated the hypothesis that following dynamic exercise, WB-EHL would increase in response

to the activation of metaboreceptors induced by a period of post-IHG ischemia throughout the early-to-late stages of the 60-min recovery period relative to both IHG exercise only and a natural recovery.

METHODS

Ethical approval

The experimental protocol was approved by the University of Ottawa Health Sciences and Science Research Ethics Board and agrees with the *Declaration of Helsinki*. Written and informed consent was obtained from all participants prior to their participation in the study.

Participants

Twelve healthy habitually active young males (age: 24±4 years; height: 1.7±0.7 m; body mass: 76.0±8.1 kg; body surface area: 1.90±0.11 m²; peak oxygen consumption ($\dot{V}O_{2peak}$): 49.4±7.7 mL O_2 /kg/min; body fat percentage: 16.9±5.4%) participated in this study.

Experimental Design

Participants completed one preliminary and three experimental sessions each separated by at least 48 hours. For all sessions, participants refrained from exercise, alcohol or caffeine 24 hours prior to experimentation. During the preliminary session, the participant's physical characteristics (height, weight, and body composition) was assessed. Additionally, aerobic fitness (defined by $\dot{V}O_{2peak}$) was determined through an incremental cycling exercise protocol. Participants performed two 5-sec maximal voluntary contractions (**MVC**) to establish the

relative intensity (determined using the higher of the two values) for the isometric handgrip (IHG) exercise. The detailed procedures are reported elsewhere (McGinn et al. 2014; Paull et al. 2015). For each experimental session, following instrumentation, participants rested inside the direct air calorimeter regulated at 35°C (20% relative humidity) for a 20-min resting period (**Pre-exercise resting**) followed by a 45-min bout of cycling at a fixed rate of metabolic heat liberation of 400 W (to maintain a constant thermal drive for sweating between conditions) and a 60-minute recovery. During recovery, they performed either: 1) a 1-min IHG exercise at 60% of their predetermined MVC (**IHG-Only**), 2) a 1-min IHG at 60% of MVC followed by a 5-min forearm ischemia (**IHG+OCC**) or 3) a natural recovery with no IHG or OCC (**Control**). Forearm occlusion was achieved by inflating a blood pressure cuff to supra-systolic levels which was then deflated rapidly for a 5-min recovery period. The protocols were repeated in the early (15 min), mid (30 min) and late (45 min) stages of the 60-min recovery data collection period. During the period of muscle ischemia, it is thought that the accumulation of metabolites within the muscle triggers chemosensitive afferents (group III and IV afferents) and reflexively raises arterial blood pressure which is used to confirm the activation of metaboreceptors (Rowell and O'Leary 1990).

Instrumentation

The modified Snellen direct air calorimeter was used to perform continuous measurements of whole-body evaporative (WB-EHL) and dry heat loss (**WB-DHL**), and metabolic heat liberation was calculated by indirect calorimetry (Kenny et al. 2017). Esophageal temperature was measured using a thermocouple probe (Mallinckrodt Medical Inc., St-Louis, MO, USA) estimated to be in the region bounded by the left ventricle and aorta. Skin temperature was measured using 0.3-mm diameter T-type (copper/constantan) thermocouples

integrated into heat flow sensors (Concept Engineering, Old Saybrook, CT, USA) affixed to the chest, biceps, thigh, and calf temperatures (Concept Engineering, Old Saybrook, CT, USA). Mean skin temperature was calculated using the following weightings: chest, 30%; bicep, 30%; thigh, 20; and calf, 20% (Ramanathan 1964). Calorimetry and temperature data were recorded continuously on a personal computer with LabVIEW software (version 7.0; National Instruments, Austin, TX, USA). Mean arterial blood pressure (MAP) (Finapres Medical Systems, Amsterdam, The Netherlands) was measured continuously. Isometric handgrip exercise was performed using a Smedley Hand Dynamometer (Model 19117, Stoelting Co, Wood Dale, IL, USA).

Data analysis

Pre-exercise resting and end-exercise values were averaged over the last 5-min. For the postexercise recovery, values for each of the three recovery periods were assessed based on the four time stages for the metaboreceptor activation protocol as follows: 1) 1-min period preceding the IHG (**Pre-IHG**), 2) last 15 sec of the IHG exercise (**IHG**), 3) the final 15 sec of the postexercise forearm occlusion (**OCC**), and 4) final 15 sec of the post-OCC recovery period (**REC**). Body heat storage was calculated as the temporal summation of metabolic heat liberation and heat loss within the 5-min occlusion phase during each recovery stage.

Statistical analysis

A one-way analysis of variance (ANOVA) with the non-repeated factor of condition (Control, IHG-Only, IHG+OCC) was conducted for all dependent variables for pre-exercise resting, end-exercise as well as for the change in body heat storage across conditions. When a main effect of condition was measured, post-hoc analysis was conducted using paired sample t-

tests corrected for multiple comparisons using the Bonferroni procedure. During recovery, a two-way repeated measures ANOVA was performed to compare the dependent variables at each stage (Pre-IHG, IHG, OCC, REC) as well as between the three experimental conditions (3 levels: Control, IHG-Only, IHG+OCC) for each recovery period. When a significant main effect or interaction was observed, post hoc comparisons were carried out using paired-sample t-tests corrected for multiple comparisons using the Bonferroni procedure. Results are presented at means $\pm$ SD. All statistical analyses performed using IBM SPSS Statistics v24.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

Pre-exercise resting and End-exercise

Pre-exercise resting and end-exercise responses for body temperatures (esophageal: $36.9 \pm 0.3^{\circ}\text{C}$, $37.3 \pm 0.4^{\circ}\text{C}$; mean skin: $34.4 \pm 0.5^{\circ}\text{C}$, $35.0 \pm 0.5^{\circ}\text{C}$), MAP (92 ± 5 mmHg, 94 ± 7 mmHg), metabolic heat liberation (108 ± 18 W, 390 ± 31 W), and heat loss (WB-EHL: 86 ± 38 W, 373 ± 51 W; WB-DHL: -10 ± 18 W, -25 ± 19 W) respectively were similar between conditions (all $P > 0.05$).

Postexercise recovery

Metabolic heat liberation did not differ between conditions during Pre-IHG, OCC or REC phases in all recovery stages (all $P > 0.05$), averaging 113 ± 17 , 110 ± 19 and 108 ± 15 W (early), 106 ± 13 , 108 ± 18 and 104 ± 12 W (mid) and 110 ± 16 , 114 ± 17 and 107 ± 14 W (late) across conditions, respectively. Metabolic heat liberation was also similar between conditions during IHG exercise during the early-stage ($P = 0.11$; mean across conditions: 123 ± 18 W), yet was

elevated in the mid- and late-stages relative to Control (107 ± 15 and 101 ± 11 W, respectively) in the IHG+OCC condition (124 ± 21 and 124 ± 18 W, respectively; $P=0.02$ and $P=0.01$) and in the IHG-only condition in the mid- (122 ± 12 W; $P=0.04$), but not the late-stage (114 ± 18 W; $P=0.26$). WB-DHL did not differ between conditions or phases in each recovery stage (all $P>0.05$), averaging -5 ± 17 , -2 ± 19 and 1 ± 18 W across phases during the early-, mid- and late-stages, respectively. For all recovery stages, WB-EHL increased during the IHG exercise for the IHG-only and IHG+OCC conditions relative to Control (all $P<0.05$), and remained elevated during the OCC phase for the IHG+OCC condition relative to the Control and IHG-only conditions (all $P<0.05$; Figure 1). Heat stored during OCC was reduced during the early-, mid- and late-stages in the IHG+OCC condition (-20 ± 10 , -15 ± 2 and -10 ± 2 kJ, respectively) relative to Control (-9 ± 3 , -2 ± 3 and 2 ± 10 kJ, respectively; all $P=0.03$) as well as between IHG-only (-6 ± 6 kJ) and Control during the mid-stage ($P=0.04$).

In all recovery stages, MAP did not differ between conditions during Pre-IHG and REC phases (all $P>0.05$), but increased during IHG exercise for IHG-only and IHG+OCC conditions relative to the Control condition (all $P<0.05$) and remained elevated during OCC in the IHG+OCC condition relative to the IHG-only and Control conditions (all $P<0.05$; Figure 1). Esophageal and mean skin temperatures remained elevated above baseline but similar between conditions during the early- (esophageal: $37.1 \pm 0.3^\circ\text{C}$, mean skin: $34.7 \pm 0.5^\circ\text{C}$), mid- (esophageal: $37.1 \pm 0.3^\circ\text{C}$, mean skin: $34.6 \pm 0.5^\circ\text{C}$) and late-stages (esophageal: $37.1 \pm 0.3^\circ\text{C}$, mean skin: $34.6 \pm 0.4^\circ\text{C}$; all $P>0.05$).

DISCUSSION

We show for the first time that the activation of muscle metaboreceptors augments whole-body evaporative heat loss (and therefore whole-body sweating) and that the level of influence (as defined by the relative increase in WB-EHL of ~45 W) remains constant throughout the early-to-late stages of recovery despite a progressive decay in body temperatures. Specifically, we showed that metaboreceptor activation induced by 1-min isometric-handgrip (IHG) exercise followed by 5-min forearm ischemia to trap metabolites increased WB-EHL by 25-31% and 26-34% during the ischemic period relative to IHG-Only and Control (no-IHG or ischemia, natural recovery) respectively throughout recovery. Moreover, despite the relatively short duration of the period of stimulation (i.e., 5-min ischemia), the metaboreceptor-mediated increase in evaporative heat loss was associated with a concomitant reduction in body heat storage. Taken together, our findings demonstrate that the metaboreceptor modulation of whole-body sweating is an important factor mediating the postexercise disturbance in thermal homeostasis.

Previous studies have demonstrated that the activation of metaboreceptors play an important role in the regulation of local forearm sweating (McGinn et al. 2014; Paull et al. 2015) as well as back and upper chest sweating (Paull et al. 2015) during the postexercise period. This response was shown to be independent of any changes in baroreceptor loading status that occurs during the occlusion period (McGinn et al. 2014). While previous studies showed that the activation of metaboreceptors preserved but did not augment local sweating in the early stages of recovery (i.e., ≤ 20 -min) (McGinn et al. 2014; Paull et al. 2015), we observed a consistent increase in whole-body sweating throughout the early-to-late stages of recovery. This disparity may in part be due differences in the level of hyperthermia achieved during the exercise. In

previous studies, the level of hyperthermia prior to the start of the metaboreceptor activation protocol was greater (as defined by a greater rise in core temperature of $\sim 0.3\text{--}0.6^{\circ}\text{C}$; equivalent to $\geq 37.4^{\circ}\text{C}$) relative to that recorded in the present study ($\sim 37.0^{\circ}\text{C}$). In keeping with this observation, previous work showed that thermal control predominates over nonthermal factors at core temperatures above $\sim 37.4^{\circ}\text{C}$ (Gagnon et al. 2008). Differences in the duration of the period of ischemia may also contribute to this response. While prior studies employed a 2 min period of ischemia, we used an extended period of ischemia (5 min) to ensure that a metaboreceptor-mediated response, if any, would be captured in our calorimetric measurement of whole-body sweating. It remains to be determined if the increase in whole-body sweating would have been observed with a shorter period of ischemia.

In summary, we show that metaboreceptor activation enhances whole-body WB-EHL and therefore whole-body sweating, throughout the early-to-late stages of the postexercise recovery period in the heat. This was associated with a 56, 88 and 115% greater amount of heat stored during the natural recovery (i.e. Control) relative to recovery with the activation of metaboreceptors (i.e. IHG+OCC) performed in the early-, mid- and late-stages respectively. Our findings demonstrate that independent of thermal control (i.e. changes in skin and/or core temperatures), changes in nonthermal metaboreceptor activity during the postexercise period play an important role in the observed disruption in whole-body thermal homeostasis. In the context of exercise or work performed in the heat, our findings demonstrate that nonthermal factors can influence the rate of heat dissipation and therefore the restoration of thermoregulation after exercise in the heat.

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DISCLOSURES

No conflict of interest, financial or otherwise, are declared by the author(s). The results of the study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation.

AUTHOR CONTRIBUTIONS

G.P.K. and B.J.F. conceptualized and designed the research; B.J.F., M.P.P., D.T.L. and A.W.D. performed experiments; B.J.F. and M.P.P. analyzed the data; all authors interpreted the results of experiments; G.P.K. drafted the manuscript; all authors edited and revised the manuscript and approved final version of manuscript.

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303

304 **FIGURE CAPTION**

305 **Figure 1.** Whole-body evaporative heat loss (W) (Panel A) and mean arterial pressure (mmHg)
306 (Panel B) during Pre-isometric hand grip exercise (Pre-IHG, 1 min prior to IHG), last 15 sec of
307 isometric handgrip exercise (IHG), last 15 sec of forearm occlusion (OCC) and last 15 sec of
308 recovery from forearm occlusion (REC, 5 min after the end of OCC) during Control, IHG-Only
309 and IHG+OCC conditions. Measurements were performed in the early- (15 min), mid- (30 min)
310 and late- (45 min) stages of postexercise recovery. *Significantly different between IHG+OCC
311 and Control. †Significantly different between IHG-Only and Control. ‡Significantly different
312 between IHG+OCC and IHG-Only. Significance level accepted at $P \leq 0.05$. Values are presented
313 as mean $\pm$ SD.

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A

● Control □ IHG+OCC ▲ IHG Only

B