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Does attenuated skin blood flow lower sweat rate and the critical environmental limit for heat balance during severe heat exposure?

Matthew N. Cramer[1,2], **Daniel Gagnon**[1], **Craig G. Crandall**[1], and **Ollie Jay**[3,✉]

[1]Institute for Exercise and Environmental Medicine, Texas Health Presbyterian Hospital Dallas and the University of Texas Southwestern Medical Center, Dallas, TX, USA

[2]School of Human Kinetics, Faculty of Health Sciences, University of Ottawa, ON, CANADA

[3]Thermal Ergonomics Laboratory, Faculty of Health Sciences, University of Sydney, NSW, AUSTRALIA

Abstract

Attenuated skin blood flow (SkBF) is often assumed to impair core temperature (T_c) regulation. Profound pharmacologically-induced reductions in SkBF (~85%) lead to impaired sweating but whether the smaller attenuations in SkBF (~20%) more associated with ageing and certain diseases lead to decrements in sweating and maximum heat loss potential is unknown. Seven healthy males (28±4y) completed a 30-min equilibration period at 41°C and a vapour pressure (P_a) of 2.57 kPa followed by incremental steps in P_a of 0.17 kPa every 6-min to 5.95 kPa. Differences in heat loss potential were assessed by identifying the critical vapour pressure (P_{crit}) at which an upward inflection in T_c occurred. Three separate treatments elicited changes in plasma volume to achieve three distinct levels of SkBF: control (CON), diuretic-induced iso-osmotic dehydration to lower SkBF (DEH), and continuous saline infusion to maintain SkBF (SAL). T_c, mean skin temperature (T_{sk}), heart rate, mean laser-Doppler flux (forearm, thigh; LDF_{mean}), mean local sweat rate (forearm, thigh; LSR_{mean}), and metabolic rate were measured. In DEH, a 14.2±5.7% lower plasma volume resulted in a ~20% lower LDF_{mean} (DEH: 139±23, CON: 176±22, SAL: 186±22 PU; P=0.034). However, LSR_{mean} and whole-body sweat losses were unaffected by treatment throughout (P>0.482). P_{crit} for T_c was similar between treatments (CON: 5.05±0.30, DEH: 4.93±0.16, SAL: 5.12±0.10 kPa; P=0.166). Further, no differences were observed in the $T_{sk}-T_a$ gradient, metabolic rate, or changes in T_c (P>0.197). In conclusion, a ~20% reduction in SkBF alters neither sweat rate nor the upper limit for heat loss from the skin during non-encapsulated passive heat stress.

✉**Address for correspondence:** Dr. O. Jay, Thermal Ergonomics Laboratory, Faculty of Health Sciences, University of Sydney, Lidcombe, NSW, 2141, AUSTRALIA, Tel: +61 2 93519328, Fax: +61 2 9351 9204, ollie.jay@sydney.edu.au.

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Keywords

core temperature; critical vapour pressure; cutaneous vascular conductance

INTRODUCTION

In response to rising core and/or skin temperatures, reflex and locally-mediated mechanisms initiate cutaneous vasodilatation, leading to greater skin blood flow (SkBF). Since internal heat flux to the skin surface is governed primarily by the core-to-skin temperature gradient and SkBF, it is reasonable to suggest that physiological conditions impairing cutaneous vasodilatation and/or SkBF, can diminish the rate of whole-body heat loss from the skin to the external environment (Johnson & Proppe, 1996; Charkoudian, 2010).

Fundamentally, heat exchange between the skin and the environment is driven by the physical properties of the skin-air interface; specifically, dry heat transfer is governed by the skin-air temperature gradient, while evaporative heat loss is dependent on the skin-air vapour pressure gradient and the area of skin sweat coverage. Under fixed ambient conditions, attenuated SkBF could thereby influence heat exchange with the environment through changes in mean skin temperature (T_{sk}) and/or diminished sweat production. Exposure to very high ambient temperatures favours dry heat gain, but higher T_{sk} secondary to greater SkBF would theoretically assist core temperature regulation by reducing the negative skin-air temperature gradient. With respect to a possible relationship between SkBF and sweating, local ischaemia following arterial occlusion abolishes reflex sweating in warm and hot environments (Randall *et al.*, 1948; Elizondo, 1973), and noradrenaline-induced reductions in SkBF attenuate the rate of local sweat production by as much as 50% for a given change in core temperature (ΔT_c) during passive heating in a water-perfused suit (Wingo *et al.*, 2010). It must be noted however that the ~85–100% reductions in SkBF achieved with noradrenaline infusion and local ischaemia are well above the ~20% reduction in SkBF typically reported with ageing (Minson *et al.*, 1998), disease (Carberry *et al.*, 1992; Cui *et al.*, 2005; Green *et al.*, 2006; Wick *et al.*, 2006; Sokolnicki *et al.*, 2009), or dehydration (Nadel *et al.*, 1980; Montain & Coyle, 1992*a*, 1992*b*). Therefore, whether reductions in SkBF of a more physiologically relevant magnitude diminish sweating and thereby maximum evaporative heat loss, have not to the best of our knowledge been previously examined.

Many previous studies have examined cutaneous vasodilatory and SkBF responses during exercise with submaximal thermolytic requirements (i.e., compensable conditions) or during passive heating in encapsulated conditions such as a water-perfused garment, which yields an extremely high T_{sk} under the suit while local skin temperature at the SkBF measurement site is held constant. However, in order to assess the upper limit for heat loss from the skin surface, a non-encapsulated approach that identifies the transition from compensability to uncompensability must be adopted, such as an incremental humidity protocol consisting of short-duration steps of increasing ambient vapour pressure at a constant air temperature and metabolic rate. Above a critical ambient vapour pressure (P_{crit}), an upward inflection in core temperature is observed, indicating that the thermolytic requirements—a combination of

metabolic heat production and any dry heat gain from the environment—have exceeded the maximum rate of heat loss that can be physiologically attained via evaporation. Values for P_{crit} can then be compared between different conditions in which SkBF levels are manipulated to assess whether skin surface heat loss is meaningfully altered. Historically, this approach has been used to define critical environmental limits between populations (Kamon *et al.*, 1978; Kenney & Zeman, 2002; Dougherty *et al.*, 2010), at various air velocities and ambient temperatures (Belding & Kamon, 1973; Kamon & Avellini, 1979; Ravanelli *et al.*, 2015), and with different clothing ensembles (Belding & Kamon, 1973; Kamon *et al.*, 1978; Kenney *et al.*, 1993), and may be especially useful to assess whether physiological differences in SkBF are sufficient to alter maximum heat loss potential in a non-encapsulated heat stress condition.

The current investigation sought to determine if physiologically relevant reductions in SkBF attenuate sweating rates and whole-body heat loss to the extent that the P_{crit} for core temperature is ultimately lowered. It was hypothesized that (i) diminished SkBF would result in lower sweat rates and a lower P_{crit} for core temperature inflection, and (ii) the maintenance of a higher SkBF would preserve sweat rates and the P_{crit} for core temperature inflection.

METHODS

Subjects

Seven healthy young males completed the study (age: 28 ± 4 years; body mass: 82.3 ± 17.2 kg; height: 1.76 ± 0.07 m; body surface area: 1.98 ± 0.23 m^2). Based on previously reported data (Ravanelli *et al.*, 2015), and using conventional β (0.20) and α (0.05) values, a sample size of seven subjects was estimated to be sufficient to detect a significant difference in the P_{crit} for core temperature (G*power version 3.1.9.2). Subjects were non-smokers; reported no history of cardiovascular, metabolic, respiratory, or neurological disease; were not taking any medications; and were not acclimated to the heat. The protocol was explained to each subject before obtaining written informed consent, and a complete medical history was obtained prior to testing. The experimental protocol was approved by the University of Ottawa Health Sciences and Science Research Ethics Board and the Institutional Review Boards of the University of Texas Southwestern Medical Center and Texas Health Presbyterian Hospital Dallas. All procedures conformed to the standards set forth by the Declaration of Helsinki.

Instrumentation and Measurements

To assess SkBF, cutaneous red blood cell flux was measured using laser-Doppler velocimetry (Moor Instruments Ltd., Devon, UK) on the dorsal forearm and the mid-point of the anterior thigh. Skin blood flow data are reported as the mean of both sites as absolute laser-Doppler flux in arbitrary perfusion units (LDF_{mean}), as a percentage of maximum laser-Doppler flux ($\%LDF_{max}$), as cutaneous vascular conductance (CVC_{mean}), which was calculated as the quotient of LDF_{mean} and mean arterial pressure (MAP), and as the percentage of the maximum cutaneous vascular conductance ($\%CVC_{max}$). Additionally, forearm blood flow (FBF) was measured via venous occlusion plethysmography (Whitney,

1953) with an indium-gallium strain gauge (Hokanson, Bellevue, WA, USA) every 12 min during the first 72 min of the protocol, and then every 6 min thereafter. Forearm vascular conductance (FVC) was subsequently calculated as the quotient FBF and MAP. Maximum laser-Doppler flux was assessed by heating each measurement site for ~45 min by setting the local heater to 44°C. Arterial blood pressures were measured with an electrosphygmomanometer (Tango, SunTech Medical Instruments, Inc., Raleigh, NC, USA), with MAP values calculated as (pulse pressure/3) + diastolic blood pressure. Heart rate was taken from an electrocardiogram (Solar 8000M, GE Medical Systems, Madison, WI, USA). Venous blood samples (4 ml) were collected from a forearm vein in lithium-heparin tubes (BD Vacutainer, Franklin Lakes, NJ, USA) and analysed in triplicate for haemoglobin concentration (Hemoximeter, OSM3, Radiometer, Copenhagen, Denmark), haematocrit, and plasma osmolality (Micro-Osmometer, Model 3MO plus, Advanced Instruments Inc., Norwood, MA, USA). Changes in blood, cell, and plasma volumes were estimated with the equations of Dill and Costill (1974).

Oesophageal temperature was measured with a general-purpose thermocouple probe (Mon-a-therm, Mallinckrodt Medical, St. Louis, MO, USA) inserted to a maximum depth of 40 cm, which is a level estimated to be adjacent to the left ventricle and aorta (Mekjavic & Rempel, 1990). Skin temperatures were measured on the chest, shoulder, abdomen, lower back, thigh, and calf using thermocouples secured to the skin with soft cloth medical tape (Medipore, 3M), and T_{sk} was calculated as a weighted average of these six sites (Taylor *et al.*, 1989). Oesophageal and skin temperatures were measured with thermocouple readers (Sable Systems International, Las Vegas, NV, USA). Gastrointestinal temperature was also measured in six subjects using a telemetric pill (HQ Inc., Palmetto, FL, USA) ingested ~4 h prior to baseline data collection.

Local sweat rates were measured using two 4.1-cm^2 ventilated capsules placed adjacent to each laser-Doppler probe. Nitrogen gas was supplied to each capsule at a flow rate of 300 ml min^{-1}, and the effluent air was analysed for vapour concentration using capacitance hygrometry (Vaisala, Vantaa, Finland). Local sweat rate for each site was calculated as the product of the vapour concentration and flow rate relative to the skin surface area covered by a sweat capsule ($mg \cdot cm^{-2} \cdot min^{-1}$). Local sweat rate ($LSR_{mean}$) values are reported as the average of the two sites.

Expired gases were analysed with a metabolic cart (TrueOne 2400, Parvo Medics, Sandy, UT, USA). The rate of oxygen uptake (VO_2) and the respiratory exchange ratio (RER) were used to determine metabolic rate (M) via indirect calorimetry:

$$M = VO_2 \frac{\left(\left(\frac{RER-0.7}{0.3}\right) e_c\right) + \left(\left(\frac{1.0-RER}{0.3}\right) e_f\right)}{(60)} (1000)[W]$$

Where: e_c and e_f are the energetic equivalents for carbohydrate (21.13 kJ L O_2^{-1}) and fat (19.62 kJ L O_2^{-1}), respectively. Dry heat exchange was calculated as the sum of convection (C) and radiation (R) using the following equations, which assumed negligible clothing insulation:

$$C = h_c(T_{sk} - T_a)[W\,m^{-2}\,K^{-1}]$$

$$R = h_r(T_{sk} - T_r)[W\,m^{-2}\,K^{-1}]$$

The value of the convective heat transfer coefficient (h_c) was taken as 3.1 W m^{-2} K^{-1} since air velocity inside the thermal chamber was measured to be <0.2 m s^{-1} (Mitchell, 1974). Ambient temperature (T_a) and mean radiant temperature (T_r) were assumed to be equal. Ambient temperatures were measured in degrees Celsius, but converted to Kelvin degrees to calculate dry heat transfer coefficients. The radiant heat transfer coefficient (h_r) was calculated as:

$$h_r = 4\varepsilon\sigma \cdot (A_r\,A_D{}^{-1}) \cdot [(T_{sk} + T_r)/2 + 273.15]^3[W\,m^{-2}\,K^{-1}]$$

Here, ε is the emissivity of the skin, assumed to be 0.95 (no dimensions); σ is the Stefan-Boltzmann constant ($5.67 \cdot 10^{-8}$ W m^{-2} K^{-4}); $A_r\,A_D{}^{-1}$ is the effective radiant surface area (non-dimensional), which was taken as 0.7 (Guibert & Taylor, 1952; Kerslake, 1972).

Experimental Protocol

In a randomized, counterbalanced order separated by at least 3 days, subjects performed three experimental trials: a control condition (CON) in which no treatment was administered, a diuretic-induced iso-osmotic dehydration trial (DEH) with the goal of lowering SkBF relative to CON, and a continuous saline infusion trial (SAL) with the goal of elevating SkBF relative to CON. Prior to experimentation, subjects were instructed to avoid cold, allergy, and anti-inflammatory medicines for 36 h, alcohol consumption and exercise for 24 h, and caffeine intake for 12 h. They were also asked to consume plenty of water the night before and the morning of each visit to ensure adequate hydration, and to eat breakfast before leaving for the laboratory.

Subjects arrived at the lab between 0800 and 0900. Nude body mass, standing height, and urine specific gravity (USG) were first recorded, with euhydration accepted at a USG ≤ 1.025 (Kenefick & Cheuvront, 2012). A forearm venous catheter was then inserted, and after 30 min of supine rest, an initial blood sample was drawn. In DEH, 40–80 mg of furosemide was then administered orally, after which the subjects rested for ~3.5 h to allow the drug to take effect (Ikegawa *et al.*, 2011). Furosemide was selected to induce hypovolemia without any change in plasma osmolality, which can independently affect sweating responses (Fortney *et al.*, 1984). In CON and SAL, subjects rested for an equivalent duration to ensure that heating commenced at a similar time of day during each visit. Drinking water was provided *ad libitum* during the initial rest period in CON and SAL only, but a small volume of fluid was ingested in DEH to facilitate insertion of the oesophageal temperature probe during instrumentation. Urine output was also recorded during this period. Nude body mass was measured again at the end of the rest period.

Following instrumentation, subjects entered the chamber. The experimental protocol began with a 30-min baseline equilibration period at 41°C, 33% RH (2.57 kPa) during which steady-state sweat rates and core temperature were attained. After, an incremental humidity protocol began with P_a increased by 0.17 kPa every 6 min from 2.57 to 5.95 kPa (maximum: 20 stages or 120 min). Throughout baseline and the incremental humidity protocol T_a was controlled at 41.0 ± 0.1°C. This T_a was selected to elicit skin temperatures similar to those achieved in encapsulated protocols (e.g. water-perfused suit studies), and induce high sweating rates that would facilitate examination of a link between SkBF and LSR. The pattern of change in P_a over time was nearly identical between trials, resulting in steps of 0.17 ± 0.01 kPa per 6-min stage. Termination criteria were (i) completion of the 20th stage, (ii) reaching a 1.0°C ΔT_c from baseline, (iii) hypotension (systolic blood pressure < 80 mmHg), or (iv) voluntary withdrawal due to excessive discomfort. Trials were conducted in an upright seated position (n=4) on a steel-framed mesh chair (height: 83 cm) or in a supine position (n=3) on a hospital bed. Experimentation was conducted initially in the upright seated posture, but because of episodes of hypotension in some DEH trials, testing was completed in a supine posture by the remaining three subjects to minimize the possibility of syncope. Each subject conducted his trials in the same posture. During SAL, 0.9% saline was infused continuously at a rate of 0.05 ml $kg^{-1}min^{-1}$ throughout the incremental humidity trial (total: 479 ± 105 ml). Core and skin temperatures, local sweat rates, skin blood flow, and heart rate were measured throughout. Blood pressure was measured at the end of each stage; expired gases were sampled at baseline and every four stages. Upon completion of the incremental humidity protocol, a final blood sample was drawn and the thermal chamber was cooled. Local heating of the laser-Doppler measurement sites was performed for ~45 min to induce maximum LDF values. A final nude body mass measurement was then performed.

Data Analysis

Continually measured variables were sampled at 25 Hz (MP150, Biopac Systems, Inc., Santa Barbara, CA). For each 6-min stage, data were averaged over the final 2 min. In accordance with recent work, these values were subsequently used to define P_{crit} for core temperature and heart rate using segmental regression analysis (Ravanelli *et al.*, 2015).This latter statistical approach is based on the biphasic core temperature response during an incremental humidity protocol: the first phase is a baseline phase during which the slope of the relationship between core temperature and P_a is approximately zero, and an “inflected” phase during which core temperature rises abruptly and linearly from its baseline level as the heat loss requirement has exceeded heat loss potential due to increasing P_a. The segmental regression analysis identifies the P_a value at the intersection between these two slopes, which is then accepted as P_{crit} (see Figure 1). The core temperature P_{crit} was determined from oesophageal temperature in six subjects, and gastrointestinal temperature in one subject.

Statistical Analysis

Data are presented as means ± standard deviations. A one-way repeated measured analysis of variance (ANOVA), using the independent factor of treatment (3 levels: CON, DEH, SAL), was employed to compare USG, fluid intake and urine output during rest, whole-body

sweat loss, P_{crit} values, and metabolic rate. A two-way repeated measures ANOVA, with the independent factors of treatment (3 levels: CON, DEH, SAL) and time, was also employed to compare changes in blood and plasma volumes and plasma osmolality (4 levels: initial, baseline, at 60 min, and at the end of the protocol); LDF_{mean}, $\%LDF_{max}$, CVC_{mean}, $\%CVC_{max}$, LSR_{mean}, T_{sk}, ΔT_c, $T_{sk}-T_a$, and dry heat exchange (15 levels: baseline and every 6-min stage to ~5.0 kPa or 84 min of the protocol); as well as FBF and FVC (8 levels: baseline and every 2 stages to ~4.8 kPa or 78 min of the protocol). A Greenhouse-Geisser correction was applied if the assumption of sphericity had been violated. In the event of a significant time-by-treatment interaction, post-hoc analysis was performed using Tukey's range test for multiple comparisons. All remaining statistical analyses were performed with Prism 6 for Windows (GraphPad, Software, La Jolla, CA, USA). Alpha was set at the 0.05 level.

RESULTS

Initial Rest Period

Initial USG values upon arrival were not different between trials (CON: 1.014 ± 0.007, DEH: 1.012 ± 0.007, SAL: 1.013 ± 0.006; P = 0.633). *Ad libitum* fluid intake in CON (613 ± 239 ml) and SAL (614 ± 184 ml) was greater than in DEH (253 ± 109 ml) (P = 0.002). Diuretic ingestion resulted in greater urine output in DEH (1997 ± 633 ml) compared to CON (566 ± 361 ml) and SAL (878 ± 507 ml) (P < 0.001). Consequently, blood volume declined to a greater extent during this time in DEH compared to CON and SAL due to a contraction of plasma volume, but not cell volume (P < 0.001, Table 1). Fluid intake, urine output, changes in blood, cell, and plasma volumes, and body mass changes were not different between CON and SAL during the initial rest period (P > 0.168).

Incremental Humidity Protocol

The greater reduction in blood and plasma volumes during DEH persisted throughout the incremental humidity protocol (P < 0.001), but no differences in plasma osmolality were observed between treatments (P = 0.546) (Table 1). This greater hypovolemia in DEH mitigated the increase in laser-Doppler SkBF during the protocol (Figure 2). Significant main effects of treatment were found for LDF_{mean} (P = 0.034), $\%LDF_{max}$ (P = 0.003), and $\%CVC_{max}$ (P = 0.016), while CVC_{mean} tended to show an effect of treatment (P = 0.056). Treatment-related effects resulted in an ~20% difference in each laser-Doppler index of SkBF between DEH and CON, as well as DEH and SAL (Figure 2), while no differences were observed between CON and SAL treatments. A similar pattern of change in all indices of SkBF were observed between forearm and thigh sites. No effect of treatment was evident for FBF and FVC (P ≥ 0.769).

Despite the attenuation of SkBF, no treatment effect was observed for LSR_{mean} (P = 0.279, Figure 3), while changes in body mass, indicating whole-body sweat loss, were not different between conditions (P = 0.482; Table 1). Similarly, no effects of treatment on T_{sk} (Figure 3), the $T_{sk} - T_a$ thermal gradient, and the calculated rate of dry heat exchange (Figure 4) were found between trials (P > 0.193). Moreover, metabolic rate was not different between treatments, averaging 119 ± 13, 115 ± 15, and 109 ± 18 W in CON, DEH, and SAL,

respectively (P = 0.121). Consequently, P_{crit} for core temperature was not different across treatments (P = 0.166, Figure 5). A similar rate of increase in ΔT_c was also observed post-inflection between trials (CON: 0.020 ± 0.003°C min^{-1}, DEH: 0.019 ± 0.004°C min^{-1}, SAL: 0.018 ± 0.002°C min^{-1}; P = 0.353).

Baseline MAP was not different between treatments (CON: 87 ± 7, DEH: 84 ± 7, SAL: 84 ± 10 mmHg; P = 0.740), and no differences in ΔMAP were observed during the protocol (Figure 6; P = 0.189). Volume depletion caused a significantly higher HR throughout DEH compared to CON and SAL (P = 0.009, Figure 6), amounting to a consistent difference of 8 ± 2 beats/min in CON *versus* DEH, and 11 ± 2 beats min^{-1} in SAL *versus* DEH.

DISCUSSION

In the present study, the influence of physiologically-relevant differences in SkBF on sweating and skin surface heat loss potential were assessed by employing an incremental humidity protocol that enabled us to identify the critical ambient vapour pressure (P_{crit}) above which T_c could no longer be compensated. That is, above P_{crit}, rates of metabolic heat production and dry heat gained from a 41°C environment could no longer be balanced by the total rate of evaporative heat loss from the skin. Using an iso-osmotic volume-depletion model, a ~20% reduction in SkBF had no effect on sweating (Figure 4) and ultimately the P_{crit} for core temperature (Figure 6) compared to control and volume-infusion treatments, suggesting that sudomotor output and the upper limit of heat dissipation from the skin is not sufficiently compromised by an attenuated SkBF within the parameters presently employed.

Changes in body mass (−2.4%) and plasma volume (−14.0%) following oral furosemide administration, but prior to heat exposure, were consistent with those reported previously (Romero *et al.*, 2011; Ikegawa *et al.*, 2011). It is particularly noteworthy that the subsequent reduction in SkBF (Figure 3) was similar to that observed with exercise- (Montain & Coyle, 1992*a*) and diuretic-induced (Ikegawa *et al.*, 2011) hypohydration compared to euhydration. Despite the lower SkBF in DEH (Figure 3), LSR (Figure 4), whole-body sweat rate, and P_{crit} (Figure 6) were similar relative to CON and SAL, suggesting that maximum heat dissipation was not affected by lower SkBF. At a constant metabolic rate and ambient temperature, a difference in heat loss potential (i.e., P_{crit}) secondary to altered SkBF would theoretically arise from changes in the physical properties of the skin surface—T_{sk}, maximum skin wettedness, and/or evaporative efficiency—that alter heat exchange with the environment. Specifically, if attenuated SkBF caused a lower T_{sk}, a wider skin-air temperature gradient would follow and the rate of dry heat gain (convection and radiation) would rise. Similarly, if SkBF compromised sweat production and/or efficiency, the rate of evaporative heat loss would be reduced. In the present study, since ambient temperature was constant (41°C) and T_{sk} was not different between treatments, no differences in the skin-air temperature gradient and the rate of dry heat exchange were observed (Figure 5). Furthermore, it stands to reason that evaporative heat loss was similar between conditions given the absence of any differences in local and whole-body sweating responses, T_{sk}, and the P_{crit} for core temperature (Figures 4–6). Although a functional relationship between SkBF and sweating has been reported previously (Wingo *et al.*, 2010), the supra-physiological reduction in local SkBF induced pharmacologically (noradrenaline infusion) in the study of Wingo *et al.*

cannot be compared to the whole-body observations reported in the present study. Importantly, we show that physiologically-relevant reductions in SkBF, such as those that occur with ageing (Kenney *et al.*, 1997; Minson *et al.*, 1998), and disease (Kenney & Kamon, 1984; Green *et al.*, 2006), are unlikely to affect whole-body heat loss potential.

Although this is the first study to investigate a direct link between altered SkBF and the potential for skin surface heat loss, previous data suggest that high levels of SkBF may not be advantageous for core temperature regulation. For example, a 15% reduction in FVC did not alter local sweat rates, T_{sk}, or ΔT_c in hypoxic *versus* normoxic conditions (Miyagawa *et al.*, 2011), or following a 2.6% reduction in body mass with diuretic-induced hypohydration (Ikegawa *et al.*, 2011) during exercise. Additionally, chronic heart failure patients with a 20% lower CVC demonstrated similar ΔT_c and T_{sk} (sweat rate was not measured) compared to healthy controls during non-encapsulated passive heat stress (38°C, 50% RH) (Green *et al.*, 2006). Similarly, a 40% reduction in FBF in older *versus* younger individuals resulted in similar ΔT_c, T_{sk}, or sweat rates during exercise in the heat despite similarities in the rate of metabolic heat production, body size, and aerobic fitness between groups (Kenney, 1988). Although this has not been a consistent finding in aged *versus* younger groups (Kenney *et al.*, 1997), it is important to note that elderly individuals also demonstrate attenuated sudomotor responses and rates of evaporative heat loss, which perhaps contribute to greater ΔT_c independently of any parallel reductions in SkBF (Anderson & Kenney, 1987; Larose *et al.*, 2013). Collectively, current and previous data suggest that core temperature is regulated similarly despite a ≥15% lower SkBF, provided that sweating and evaporative heat loss are not physiologically limited. It follows that populations demonstrating concurrent vasodilatory and sudomotor impairments, such as the elderly (Minson *et al.*, 1998), type-2 diabetics (Wick *et al.*, 2006; Sokolnicki *et al.*, 2009), skin graft recipients (Davis *et al.*, 2007, 2009), and spinal cord injury victims (Freund *et al.*, 1984), may be at greater risk of thermal injury during severe heat stress due to problems associated with sudomotor function and/or evaporation, and perhaps not due to impairments of skin blood flow *per se*.

In many previous studies, physiological regulation of cutaneous vasodilatation and SkBF has been examined during passive heating to a fixed elevation in core temperature using a water-perfused suit [e.g., (Freund *et al.*, 1984; Minson *et al.*, 1998; Wick *et al.*, 2006; Davis *et al.*, 2007, 2010)], which controls skin temperature under the suit at a set level (~38°C) and simultaneously impedes evaporative heat loss over most of the skin surface. Given the mostly encapsulated nature of water-perfusion suit studies, the influence of SkBF on sweating and whole-body heat loss cannot be established with this experimental approach. Similarly, studies conducted during exercise (Montain & Coyle, 1992*a*, 1992*b*) or non-encapsulated passive heat stress (Green *et al.*, 2006) with submaximal heat loss requirements would not necessarily observe any effect on core temperature as any reductions in skin surface heat loss due to lower SkBF are likely to be physiologically compensated by increased sweat production and evaporation. In contrast, the incremental humidity protocol used presently permits the evaluation of whole-body heat loss potential in non-encapsulated conditions of high environmental heat stress. The basis for this approach lies in examining how various factors/interventions affect the heat loss side of the conceptual heat balance equation. Since the rate of heat storage is equal to the difference between rates of heat production and loss, P_{crit} represents the threshold ambient vapour pressure above which

thermal balance (i.e., a rate of heat storage equal to zero) cannot be maintained. Therefore, a shift in P_{crit} at a fixed metabolic heat production and ambient temperature, attributed to the factor/intervention in question, directly indicates a change in maximum whole-body skin surface heat loss. The current experiment represents a novel use of this classic protocol (Belding & Kamon, 1973).

Although the current iteration of the incremental humidity protocol used similar stepwise increases in P_a (~0.17 kPa per stage) and stage durations (6 min) as in previous studies (Belding & Kamon, 1973; Kenney *et al.*, 1993; Ravanelli *et al.*, 2015), it could be argued that the present approach may lack the sensitivity required to detect differences in P_{crit} secondary to a reduction in SkBF. One way to demonstrate the sensitivity of the current protocol is through the effect of stepwise increases in P_a on the skin wettedness required for heat balance (Gagge, 1937). Theoretically, skin wettedness reflects the fraction of the skin surface that must be covered with sweat to achieve a certain rate of evaporative heat loss, while maximum skin wettedness refers to the value of skin wettedness at the threshold for compensability (i.e., P_{crit}). Presently, stepwise increases in P_a of 0.17 kPa corresponded to average elevations in skin wettedness of 0.05 ± 0.02 (range: 0.02–0.10). Given that interventions (e.g. heat acclimation) alter maximum skin wettedness by ~0.15, a possible shift in the maximum skin wettedness by < 0.05 (and thus P_{crit}) by an attenuated SkBF response would have been trivial. Furthermore, a lack of any effect of lowered SkBF on P_{crit} is supported by a similar rate of change in core temperature above P_{crit}. If a true shift in P_{crit} to a lower ambient vapour pressure due to lowered SkBF was not detected using the present analysis, a higher rate of change in core temperature would have been expected above P_{crit} in the DEH trial; however, this was not the case.

Continuous or rapid saline infusion has been an effective approach to elevate SkBF above non-infusion levels, resulting in a higher FBF during exercise (Nose *et al.*, 1990). The lack of any effect of saline infusion (0.05 ml kg^{-1} min^{-1}) on indices of SkBF, LSR_{mean}, T_{sk}, and ultimately ΔT_c (Figures 2 and 5) in the present study is perhaps explained by the relatively modest infusion rate compared to previous studies. While a higher infusion rate could have shifted P_{crit} to a higher value by affecting SkBF and sweating, this possibility requires further investigation.

Estimates of SkBF are typically expressed in a variety of ways, including absolute LDF or FBF, CVC or FVC values that are normalized to arterial blood pressure, or as a percentage of maximum LDF or CVC. While indices of SkBF expressed relative to blood pressure or a percentage of maximum flux indicate aspects of vasomotor control, it must be recognized that heat exchange between cutaneous blood and skin tissue will be dependent on the absolute level of blood flow through cutaneous vessels, as well as the blood-skin thermal gradient, not absolute CVC or CVC normalized to maximum values. Absolute SkBF was represented herein by the LDF_{mean} value, which was consistently lower in DEH, while $\%LDF_{max}$, CVC_{mean}, and $\%CVC_{max}$ were also included given the conventional use of these parameters (Figure 2). Regardless of how it was expressed, interpretation of the SkBF data was similar. Absolute SkBF was also estimated using venous occlusion plethysmography to determine FBF in the present study; however, unlike previous investigations using a volume-depletion experimental model (Nadel *et al.*, 1980; Fortney *et al.*, 1983), no treatment effect

was detected. Previously, Johnson et al. (1984) demonstrated good agreement between LDF and FBF values measured during passive heating. However, in that study, the experimental conditions were very different to those of the present investigation; specifically, LDF and FBF measurements would have been performed on an arm exposed to the ambient air, with skin much cooler than skin under the heating garment (Johnson *et al.*, 1984). As such, LDF and FBF values would have represented reflex drive for vasodilatation only. While the severity of the heat stress imposed in the present study would have likely induced reflex- and locally-mediated cutaneous vasodilation, there is no conspicuous reason for the present discrepancy between laser-Doppler and plethysmographic measurements, unless alterations in cutaneous blood flow were balanced by changes in blood flow through underlying tissues. Nevertheless, the consistent attenuation of LDF_{mean} observed among all subjects during DEH in the present study (Figure 2) suggests that blood flow in cutaneous vascular beds was consistently altered as expected.

Limitations and Future Research

Due to instances of hypotension following volume depletion, body posture was adjusted from an upright seated position to a supine posture (note: seven total subjects were tested, with four seated in the upright and three supine). Although postural differences with heat stress influence baroreflex control of SkBF (Lind *et al.*, 1968), it should be noted that (i) all analyses were performed within-subject with the position of a given subject consistent between all three trials; (ii) perturbations that unload baroreceptors do not appear to alter thermoregulatory sweat rate (Wilson *et al.*, 2005; Kenny *et al.*, 2010; Lynn *et al.*, 2012); and (iii) comparisons within posture still revealed no effect of treatment on P_{crit} for core temperature, metabolic rate, whole-body sweat rate, LSR_{mean}, and T_{sk}; (iv) the slightly higher P_{crit} for core temperature in the upright seated position (CON: 5.2 ±0.1, DEH: 5.0 ± 0.2, SAL: 5.2 ± 0.1 kPa; n=4) compared to the supine posture (CON: 4.9 ±0.4, DEH: 4.9 ± 0.1, SAL: 5.1 ± 0.1 kPa; n=3) can be explained by the greater effective skin area from which heat loss could occur while seated.

The applicability of the present findings is limited to healthy young male subjects at one high ambient temperature (~41°C), under resting conditions, and with minimal clothing. Future studies should examine the implications of lower SkBF on physiological compensability to environmental heat stress in special populations with well-known impairments of cutaneous vasodilatation, between sexes, at different ambient temperatures, with various clothing ensembles, and even during exercise at different metabolic rates.

Conclusion

The present study examined whether physiologically relevant reductions in SkBF alter sweating and subsequently lower the potential for skin surface heat loss during non-encapsulated passive whole-body heat stress. Despite a ~20% lower SkBF achieved using a volume-depletion model, sweating and heat loss potential were not altered compared to control and continuous saline infusion treatments.

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ABBREVIATIONS

C	rate of convective heat exchange
CON	control trial
CVC	cutaneous vascular conductance
DEH	dehydration trial
FBF	forearm blood flow
FVC	forearm vascular conductance
LDF	laser Doppler flux
LSR	local sweat rate
M	metabolic rate
MAP	mean arterial pressure
$\mathbf{P_{crit}}$	critical ambient vapour pressure
R	rate of radiant heat exchange
SAL	saline infusion trial
SkBF	skin blood flow
$\mathbf{T_c}$	core temperature
$\mathbf{T_{sk}}$	mean skin temperature
$\mathbf{VO_2}$	rate of oxygen uptake

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New Findings

What is the central question of this study?

- Does attenuated skin blood flow (SkBF) diminish sweating and reduce the critical environmental limit for heat balance, which indicates maximum heat loss potential, during severe heat stress?

What is the main finding and its importance?

- Iso-osmotic hypovolaemia attenuated SkBF by ~20%, but did not result in different sweating rates, mean skin temperatures, or critical environmental limits for heat balance compared to control and volume-infusion treatments, suggesting that lower levels of skin blood flow commonly observed in aged and diseased populations may not diminish maximum whole-body heat dissipation.

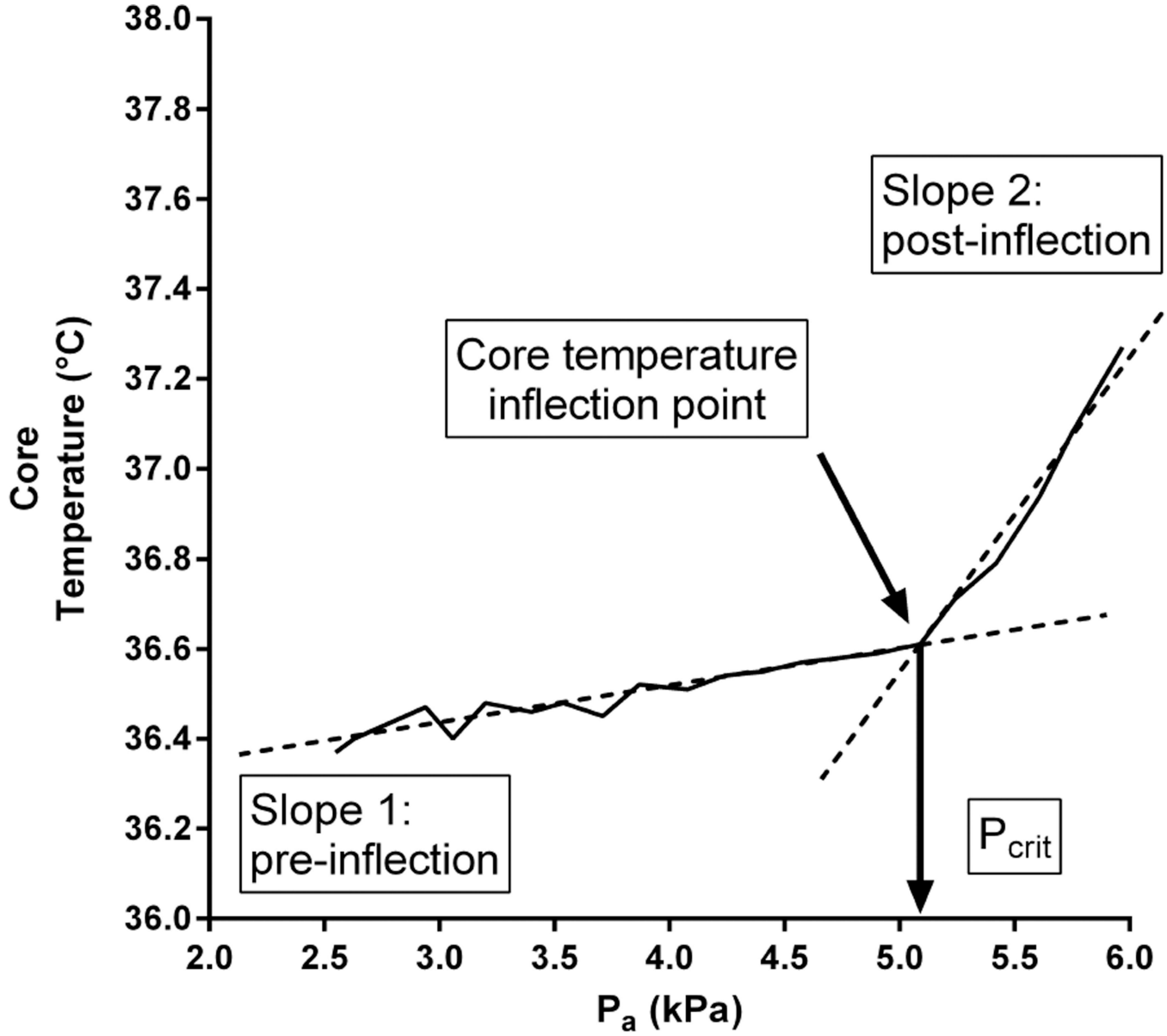

Figure 1.

Representative core temperature data from the incremental humidity protocol, demonstrating the determination of acritical ambient vapour pressure (P_{crit}). After 30-min baseline at 41°C with 2.57 kPa (30%RH), ambient vapour pressure was elevated by 0.17 kPa (~2% RH) every 6 min while air temperature remained fixed. Core temperature stayed relatively stable despite the rising ambient vapour pressure. At P_{crit}, core temperature inflects and rises rapidly. The value of P_{crit} is identified as the intersection of the two slopes (Slope 1, pre-inflection; Slope 2, post-inflection), determined via segmental regression analysis.

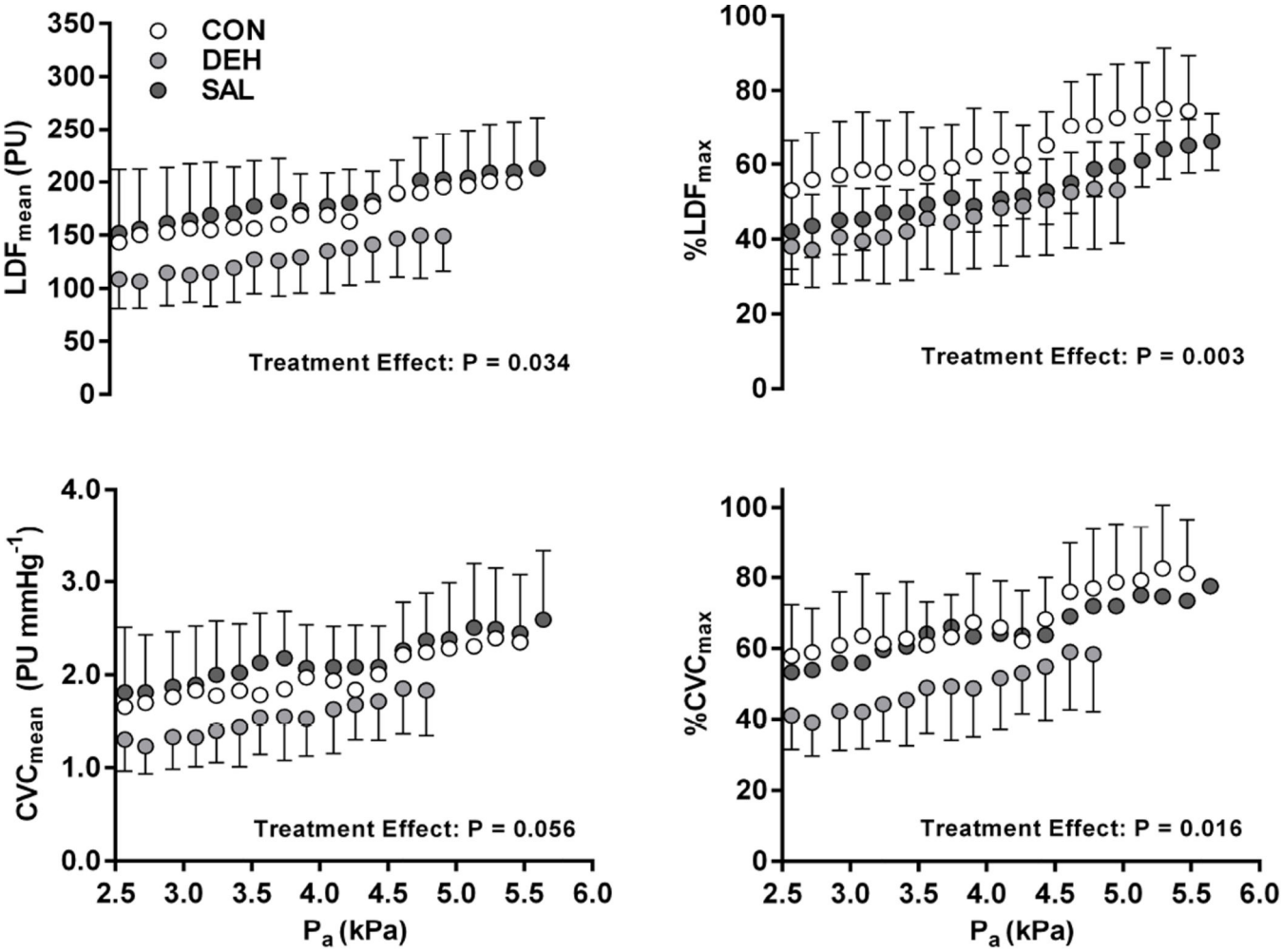

Figure 2.

Laser-Doppler derived skin blood flow responses in a control condition without treatment (CON), following diuretic following diuretic-induced dehydration (DEH), and with continuous saline infusion (SAL). Four indices of skin blood flow are presented: mean absolute laser-Doppler flux (LDF_{mean}), mean laser-Doppler flux expressed as a percentage of maximum values ($\%LDF_{max}$), mean cutaneous vascular conductance (CVC_{mean}), and mean cutaneous vascular conductance expressed as a percentage of maximum values ($\%CVC_{max}$). Analyses were performed for seven subjects up to ~5 kPa (84 min), after which early termination criteria were met at different times. A significant main effect of treatment was observed for LDF_{mean}, $\%LDF_{max}$, and $\%CVC_{max}$ ($P < 0.05$). A trend towards an effect of treatment on CVC_{mean} was also observed.

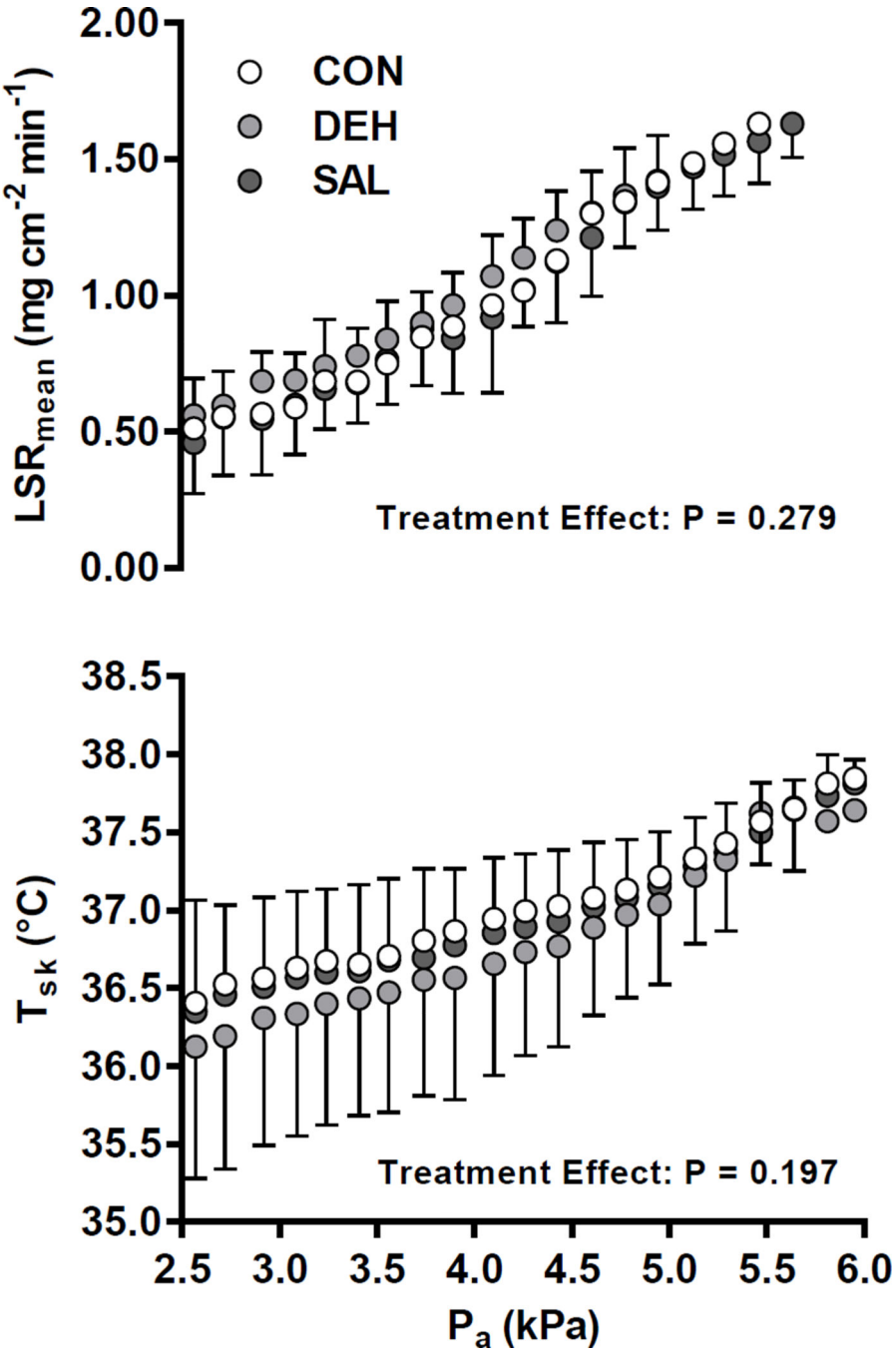

Figure 3.

Local sweating and skin temperature responses throughout the incremental humidity protocol in a control condition without treatment (CON), following diuretic-induced dehydration (DEH), and with continuous saline infusion (SAL). LSR_{mean}, mean local sweat rate (2 sites: forearm, thigh); T_{sk}, mean skin temperature; P_a, ambient vapour pressure. Analysis was performed up to ~5 kPa (84 min) in seven subjects. Beyond this point, early termination criteria were met at different times. No treatment effect was observed for LSR_{mean} and T_{sk}.

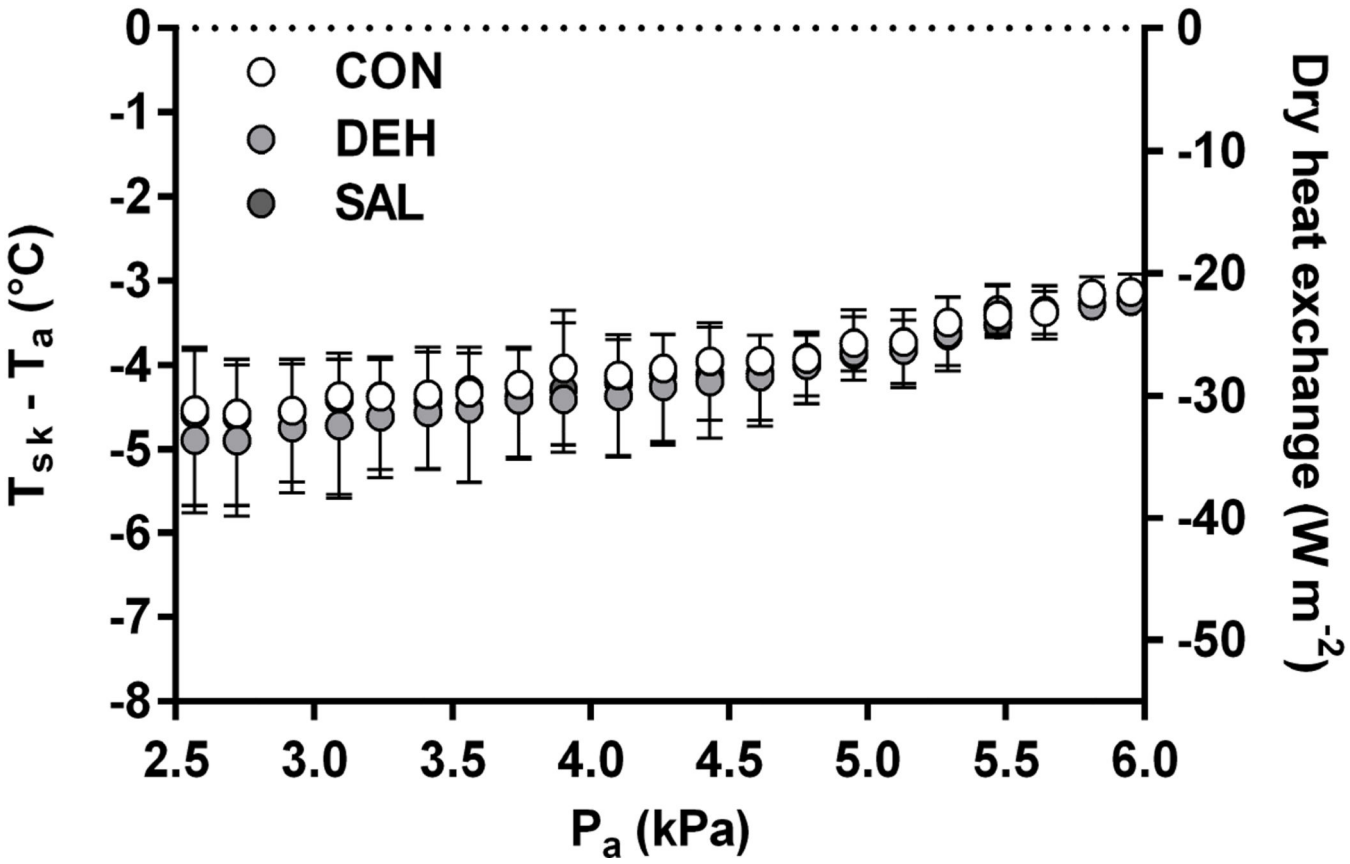

Figure 4.

The skin-air temperature gradient and the corresponding rate of dry heat exchange throughout the incremental humidity protocol in a control condition without treatment (CON), following diuretic-induced dehydration (DEH), and with continuous saline infusion (SAL). T_{sk}, mean skin temperature; T_a, ambient temperature; P_a, ambient vapour pressure. Data are for seven subjects. Note that negative values for dry heat exchange indicate dry heat gain. No effect of treatment was observed for $T_{sk} - T_a$ and dry heat exchange ($P > 0.193$).

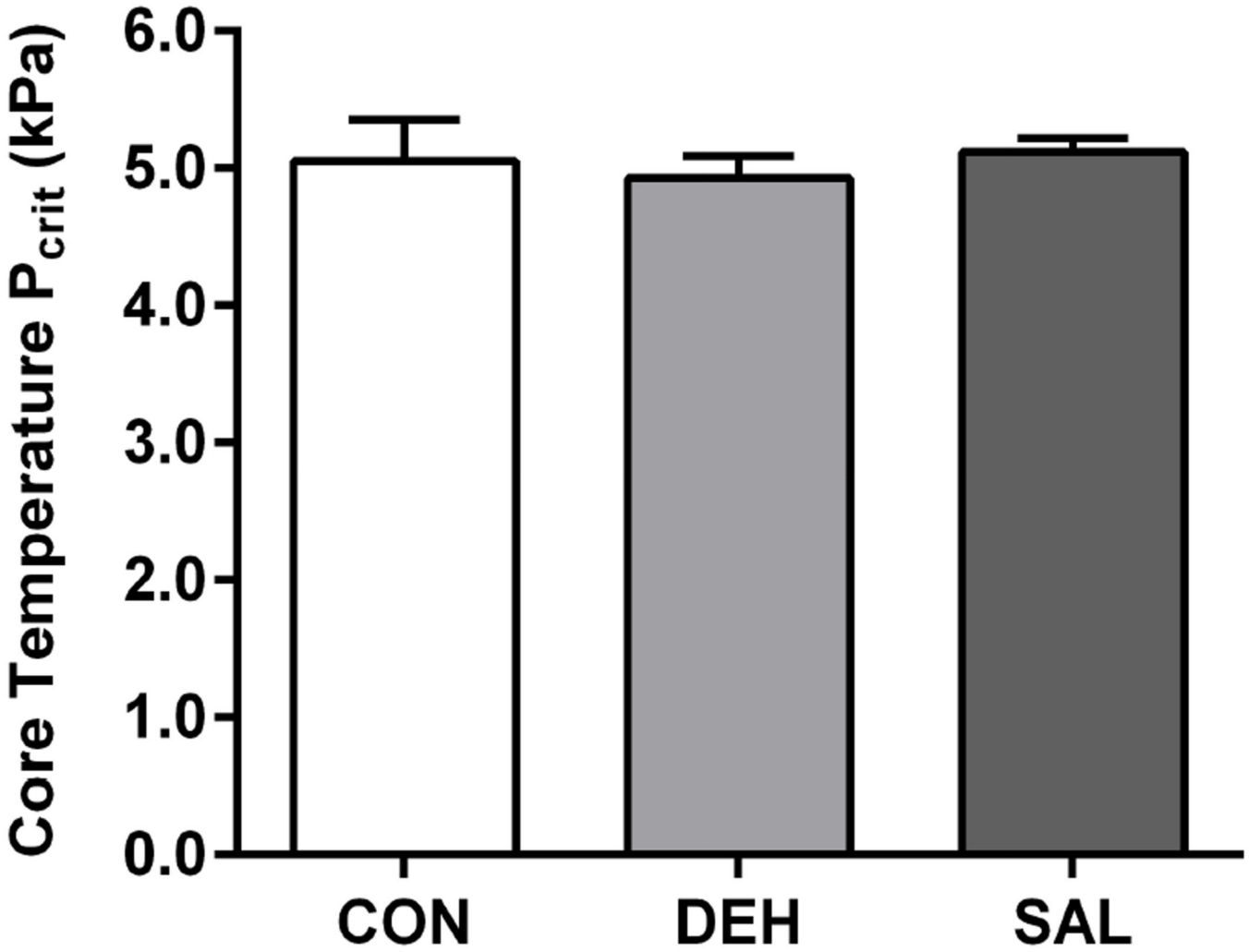

Figure 5.

Critical ambient vapour pressures (P_{crit}) for core temperature in a control condition without treatment (CON), following diuretic-induced dehydration (DEH), and with continuous saline infusion (SAL) for seven subjects. No effect of treatment on P_{crit} for core temperature was observed (P = 0.166).

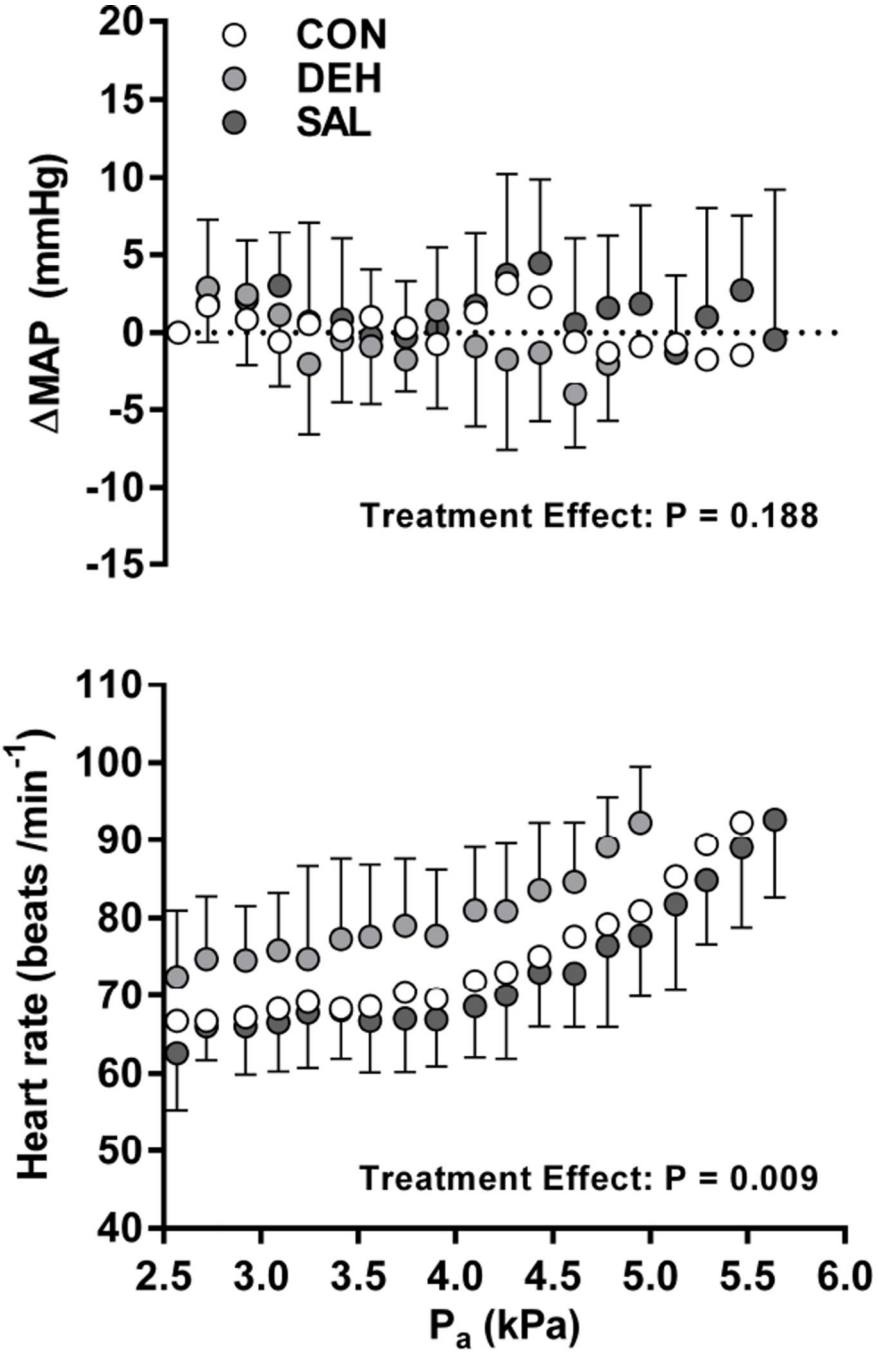

Figure 6.

Mean arterial pressure (MAP) and heart rate responses during the incremental humidity protocol in a control condition without treatment (CON), following diuretic following diuretic-induced dehydration (DEH), and with continuous saline infusion (SAL). ΔMAP, change in mean arterial pressure from baseline; P_a, ambient vapour pressure. Analyses were performed for seven subjects up to ~5 kPa (84 min), after which early termination criteria

were met at different times. A significant main effect of treatment was observed for heart rate, but not ΔMAP.

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Table 1

Changes in blood volumes, plasma osmolality, and body mass throughout experimentation.

		Rest	Baseline	60 min	End
CON	Δ Blood volume (%)	–	−1.7 ± 1.3 *a*	−2.3 ± 1.8 *ab*	−6.1 ± 2.9 *ab*
	Δ Cell volume (%)	–	0.5 ± 2.2	−0.2 ± 2.0	−0.7 ± 3.4
	Δ Plasma volume (%)	–	−3.4 ± 2.0 *a*	−4.1 ± 3.0 *ab*	−10.4 ± 3.4 *ab*
	Plasma osmolality (mOsm kg^{-1})	296 ± 5	293 ± 5	295 ± 3	297 ± 4
	Δ Body mass (kg)	–	−0.3 ± 0.5 *a*	–	−1.1 ± 0.3
	Δ Body mass (%)	–	−0.4 ± 0.6 *a*	–	−1.4 ± 0.4
DEH	Δ Blood volume (%)	–	−8.1 ± 2.5 *ac*	−9.0 ± 3.5 *ac*	−11.8 ± 2.8 *ac*
	Δ Cell volume (%)	–	−0.5 ± 2.1	−1.3 ± 1.5	−1.8 ± 2.1
	Δ Plasma volume (%)	–	−14.2 ± 5.7 *ac*	−15.3 ± 6.8 *ac*	−19.7 ± 5.1 *ac*
	Plasma osmolality (mOsm kg^{-1})	293 ± 5	293 ± 4	296 ± 7	298 ±5
	Δ Body mass (kg)	–	−2.0 ± 0.6 *ac*	–	−0.9 ± 0.4
	Δ Body mass (%)	–	−2.4 ± 0.7 *ac*	–	−1.1 ± 0.6
SAL	Δ Blood volume (%)	–	−0.7 ± 2.6 *c*	1.2 ± 3.4 *bc*	−1.6 ± 3.1 *bc*
	Δ Cell volume (%)	–	0.6 ± 1.9	0.8 ± 2.2	−0.3 ± 1.7
	Δ Plasma volume (%)	–	−1.6 ± 5.0 *c*	1.5 ± 6.8 *bc*	−2.7 ± 5.3 *bc*
	Plasma osmolality (mOsm kg^{-1})	294 ± 4	290 ± 2	294 ± 5	296 ± 5
	Δ Body mass (kg)	–	−0.4 ± 0.4 *c*	–	−1.1 ± 0.3
	Δ Body mass (%)	–	−0.5 ± 0.5 *c*	–	−1.3 ± 0.4

Data are mean ± SD for seven subjects. CON, control condition without treatment; DEH, diuretic-induced dehydration; SAL, continuous saline infusion. Note: changes in blood, cell, and plasma volumes are expressed as percentage changes from rest; changes in body mass are expressed as absolute and percentage changes from rest to baseline (i.e. from arrival until the start of the incremental humidity protocol, “Baseline”) and from baseline to the end of the incremental humidity protocol (“End”).

a, b, and c indicate differences between CON and DEH, CON and SAL, and DEH and SAL, respectively ($P < 0.05$).