J Appl Physiol 138: 634–650, 2025.
First published January 17, 2025; doi:10.1152/japplphysiol.00775.2024

american physiological society | JOURNAL OF APPLIED PHYSIOLOGY

RESEARCH ARTICLE

Effect of condensed heat acclimation on thermophysiological adaptations, hypoxic cross-tolerance, exercise performance, and deacclimation

Charlotte E. Stevens,[1,2] Joseph T. Costello,[1] Michael J. Tipton,[1] Ella F. Walker,[3] Alex A. M. Gould,[1] John S. Young,[4] Ben J. Lee,[5] Thomas B. Williams,[1] Fiona A. Myers,[6] and Jo Corbett[1]

[1]*Extreme Environments Laboratory, School of Psychology, Sport and Health Sciences, University of Portsmouth, Portsmouth, United Kingdom;* [2]*Occupational Performance Research Group, University of Chichester, Chichester, United Kingdom;* [3]*Defence Science and Technology Laboratory, Porton Down Salisbury, United Kingdom;* [4]*National Horizons Centre, Teesside University, Darlington, United Kingdom;* [5]*Occupational and Environmental Physiology Group, Centre for Sport, Exercise and Life Sciences, Faculty of Health and Life Sciences, Coventry University, Coventry, United Kingdom; and* [6]*School of the Environment and Life Sciences, University of Portsmouth, Portsmouth, United Kingdom*

Abstract

Short duration heat acclimation (HA) (≤5 daily heat exposures) elicits incomplete adaptation compared with longer interventions, possibly due to the lower accumulated thermal "dose." It is unknown if matching thermal "dose" over a shorter timescale elicits comparable adaptation to a longer intervention. Using a parallel-groups design, we compared: *1)* "condensed" HA (CHA; $n = 17$ males) consisting of 4×75 min·day^{-1} heat exposures [target rectal temperature (T_{rec}) = 38.5 °C] for two consecutive days, with *2)* "traditional" HA (THA; $n = 15$ males) consisting of 1×75 min·day^{-1} heat exposure (target T_{rec} = 38.5°C) for eight consecutive days. Physiological responses to exercise heat stress, hypoxia, and normoxic exercise performance were evaluated pre- and postintervention. Thermal (T_{rec} over final 45 min: CHA = 38.45 ± 0.17°C, THA = 38.53 ± 0.13°C, $P = 0.126$) and cardiovascular strain were not different during interventions, indicating similar thermal "dose," although CHA had lower sweating rate, higher starting T_{rec}, and greater inflammation, gastrointestinal permeability, and renal stress ($P < 0.05$). However, CHA elicited an array of thermophysiological adaptations that did not differ from THA [reduced indices of peak thermal (e.g., Δ peak T_{rec} CHA = −0.28 ± 0.26°C, THA = −0.36 ± 0.17°C, $P = 0.303$) and cardiovascular strain, inflammation, and renal stress; blood and plasma volume expansion; improved perceptual indices], although improvements in resting thermal strain (e.g., Δ resting T_{rec} CHA = −0.14 ± 0.21°C, THA = −0.35 ± 0.29°C, $P = 0.027$) and sweating rate were less with CHA. Both interventions improved aspects of hypoxic tolerance, but effects on temperate normoxic exercise indices were limited. The diminished thermal strain was well-maintained over a 22-day decay period. In conclusion, CHA could represent a viable acclimation option for time-restricted young healthy males preparing for a hot, and possibly high-altitude, environment.

NEW & NOTEWORTHY This study has shown, for the first time, that a novel condensed heat acclimation program can elicit an array of thermophysiological adaptations, many of which do not differ from traditional heat acclimation. These findings suggest that accumulated thermal "dose" is an important factor contributing to the adaptive responses to heat stress and that condensed heat acclimation may represent a viable option for time-restricted individuals (e.g., military personnel, firefighters, and athletes) preparing to enter a hot environment.

acclimatization; cross-tolerance; environmental physiology

INTRODUCTION

Occupational groups (e.g., military personnel and firefighters) and sports people are often exposed to environments where high ambient temperatures and humidity, the physical demands of the role, and clothing and uniform requirements interact to create conditions of high heat stress (1, 2). Compared with cool conditions, exercise under high heat stress augments skin (T_{sk}) and deep-body (core) temperature (T_c), increases cardiovascular strain and perceived exertion, and reduces thermal comfort (3). Together, these responses diminish aerobic exercise performance (4) and can increase the risk of exertional heat illness (5).

Heat acclimation (HA) refers to repeated frequent exposure to artificially created (i.e., laboratory) heat stress sufficient to elicit within-life phenotypic changes that improve homeostatic ability during subsequent heat exposure (6). The heat-adapted phenotype is characterized by expanded plasma volume (7), elevated cutaneous blood flow (8), augmented secretion of sweat with a reduced electrolyte content

Correspondence: J. Corbett (jo.corbett@port.ac.uk).
Submitted 9 October 2024 / Revised 23 October 2024 / Accepted 3 January 2025

(9), and decreased heart rate (10), T_{sk} and T_c (11) during exercise in the heat. These adaptations improve thermal comfort, reduce perceived exertion, attenuate heat-related reductions in work capacity, and reduce exertional heat illnesses during heat exposure (12, 13).

It is generally accepted that the adaptive process is near-complete within 7 to 10 days (14–16). HA guidance for athletes advocates heat exposures over at least seven consecutive days (13), and the current UK Joint Service Publication 375 guidance [Chapter 41, Annex E (17)] recommends exercise to raise and maintain an elevated body temperature for at least 1 h each day for 10–14 days before deployment, followed by a 7-day heat acclimatization program (50–100 min·day^{-1}) upon deployment. However, these approaches may not be possible in contexts where individuals need to be deployed to a hot environment at short notice, or for athletes before competition, and HA rates remain low among groups likely to benefit from their implementation (18).

These challenges have prompted research examining shorter ($\leq$5 days) HA durations (e.g., see Refs. 19–23), but this typically results in a partial (e.g., no change in some HA indices) or diminished (e.g., reduced magnitude) adaptation (15, 19, 20, 23–31). For example, Petersen et al. (20) reported a reduced heart rate and sweat electrolyte concentration during exercise in the heat, but trivial effects on T_c, T_{sk}, and sweat rate after four consecutive daily heat exposures, whereas Sunderland et al. (19) evidenced a modest reduction in exercise T_c and an increased amount of work performed in the heat, but no change in resting T_c, plasma volume, or sweating rate over the same number of days of HA. Similarly, Neal et al. (25) reported that the reduction in T_c, mean T_{sk} ($\bar{T}_{sk}$), and mean body temperature ($\bar{T}_b$) during exercise in the heat was greater after 10 days of HA compared with 5 days of HA, with recent data showing most individuals derive further benefit when HA is extended from 5 to 8 days (31).

At present, it is unclear whether short HA interventions are less effective than longer HA interventions by virtue of the reduced number of days, or the lower thermal "dose" (e.g., total minutes of heat exposure) accumulated over the shorter timescale. Indeed, it has recently been suggested that the thermal dose (i.e., total accumulated time with elevated T_c, and $\bar{T}_{sk}$) is more important than HA structure (i.e., frequency or number of days) (32). This raises the possibility that accumulating a larger thermal dose over a shorter duration could elicit similar adaptations to those occurring when the same thermal dose is delivered over a longer time scale. However, excessive stress may cause maladaptation (33) and accumulating a large thermal dose within a brief time period could increase gastrointestinal permeability and inflammation (34, 35), augment renal stress and injury (36), and impair subsequent thermoregulation (37, 38).

An emerging body of evidence suggests that thermally mediated adaptations that enhance convective oxygen delivery and utilization (e.g., plasma volume expansion, improved myocardial mechanics, and increased metabolic efficiency), as well as common intracellular pathways [e.g., hypoxia inducible factor-1α; heat shock proteins (HSPs)], might also attenuate physiological strain in a hypoxic environment (39–41) and confer ergogenic benefit under temperate conditions (42–45). However, these adaptations may be partly underpinned by the exercise component common in most HA interventions [i.e., a 'training' effect rather than a 'heat' effect (43, 46)]. Therefore, investigating potential cross-adaptation to hypoxia and effects on temperate exercise performance is important within a comprehensive evaluation of any novel HA intervention, and such an intervention should minimize the potential confounding influence of exercise training.

Finally, understanding the rate of deacclimation following HA is important for optimizing the timing of such interventions (e.g., before deployment or competition). Early studies suggested that thermophysiological adaptations decay quickly, with ~1 day of HA lost for every 2 days of deacclimation (47, 48), and that the adaptations that are induced most rapidly (e.g., plasma volume and cardiovascular stability) decay most rapidly (16, 47, 49). More recent research using meta-analysis and stepwise multiple regression indicates that when at least 5 days of HA are undertaken, heart rate and T_c decay at a rate of ~2.5% per day, but an increased daily heat exposure duration reduces the rate of decay in T_c, whereas the decay in sweating rate is affected by the number of HA days, with a longer HA intervention leading to a slower decay (50). Together this suggests that the rate of decay differs for different thermophysiological variables and that the length of daily exposure and intervention may influence this process, but data from shorter duration HA interventions are limited.

In summary, traditional HA approaches consisting of daily heat exposures for $\geq$7 days are often impractical. Although some adaptation can be elicited within $\leq$5 days, the adaptation profile is typically incomplete. However, the lower total thermal dose accumulated over the shorter HA timescale has not previously been considered, and it is unknown whether increasing the daily thermal dose will elicit similar adaptations to those occurring when the same thermal dose is delivered over a longer a timescale. Accordingly, we investigated: *1)* whether thermophysiological adaptations elicited by a "condensed" HA intervention consisting of four heat exposures per day over two consecutive days (CHA) differed from those induced by a "traditional" once-daily heat exposure HA intervention delivering a similar total thermal dose over eight consecutive days (THA); *2)* the extent to which either HA intervention conferred cross-acclimation to a hypoxic environment or enhanced endurance performance parameters in a temperate environment; and *3)* the decay of any adaptations induced by CHA or THA following a deacclimation period. It was hypothesized that CHA and THA would not differ in the magnitude and profile of: *1)* thermophysiological adaptations evident during exercise heat stress; *2)* cross-acclimation to a hypoxic environment and alterations to endurance performance parameters; and *3)* the decay in thermophysiological adaptations following a deacclimation period.

METHODS

Experimental Design

A parallel-groups research design was used with participants allocated to either: *1)* CHA, consisting of 4×75 min·day^{-1} heat exposure for two consecutive days; or *2)* THA, consisting of 1×75 min·day^{-1} heat exposure for eight consecutive days. Group allocation was determined by order of study enrolment but adjusted where necessary due to logistical and scheduling constraints. Each HA intervention was preceded and followed

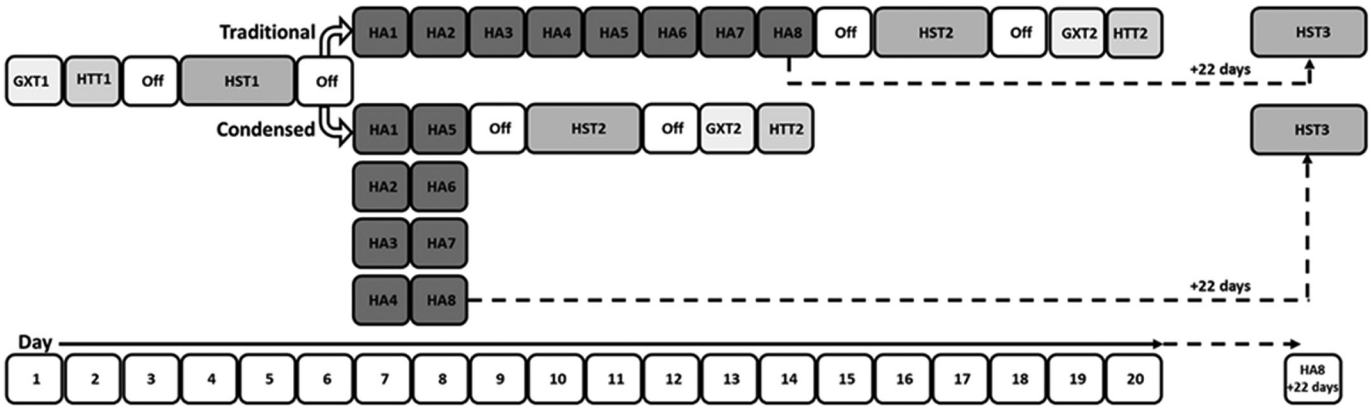

Figure 1. Protocol schematic for a parallel groups study comparing a "traditional" once-daily heat exposure heat acclimation intervention over 8 days and a novel "condensed" four-daily heat exposures over 2 days heat acclimation intervention. GXT, graded exercise test; HA = 75-min isothermal strain heat acclimation session; HST, heat stress test (undertaken on either of the specified days); HTT, hypoxic tolerance test; Off = no laboratory visit.

by: *1)* a heat stress test (HST) for assessing thermophysiological responses to exercise heat stress; *2)* a hypoxic tolerance test (HTT) for assessing cross-adaptation to a hypoxic environment; and *3)* a graded exercise test (GXT) for assessing endurance performance parameters [$\dot{V}O_{2max}$, gross mechanical efficiency, lactate threshold indices, and peak power output (PPO)] in a temperate normoxic environment. A subset of participants undertook a further HST 22 ± 1 days after the final HA session to provide an index of deacclimation. The experimental design and timeline are summarized in Fig. 1.

Participants

Thirty-two healthy males participated, with group characteristics (CHA, $n = 17$; THA, $n = 15$) summarized in Table 1. Our primary outcome measure was the pre to postintervention change (i.e., Δ) in peak T_{rec} recorded during the HST. An a priori sample-size estimate (G*power 3.1.9.7) using the previously reported reduction in peak T_{rec} during exercise heat stress with a once daily HA for 2 days [~0.20°C (15, 51)] compared with once daily HA for ≥7 days [~0.55°C (15, 25)], and previously reported standard deviation [SD (52)] indicated that a minimum of 7 participants/group would enable detection of a between-groups difference in this parameter with sufficient power ($\beta \geq 0.80$) at a (two-tailed) α-level of 0.05. Over-recruitment beyond this minimum sample size was to account for potential participant dropout and to support secondary outcome measures. Groups did not differ for key parameters known to affect thermoregulation, with the exception of a small difference in estimated percent body fat (calculated from sum of 4 skinfolds) (53). However, the difference was well within recommend limits for between-groups designs (54), and this parameter has minimal influence on thermoregulation compared with metabolic heat production per unit of body mass, and a smaller influence on thermoregulation during exercise than the other anthropometric factors (e.g., mass specific area) (55), which were similar between groups.

Potential participants completed a health history questionnaire with medical opinion sought for any questionable response. Individuals were excluded if they had engaged in any formal HA regime or used saunas or prolonged hot baths, in the 2 mo before participation. For most individuals, data collection commenced outside of the UK summer months, with the exception of one participant in each group, where data collection commenced in June due to delays arising from COVID-19 lockdown restrictions, but any acclimatization effects would likely be minimal (56). Serum sodium was assessed within 48 h before commencing either HA program; individuals with a serum sodium concentration below 135 mmol·L^{-1} were deemed to be at an elevated risk of hyponatremia and were excluded from participation. The study was approved by the Ministry of Defense Research Ethics Committee (1017/MoDREC/19) and conducted in accordance with the Declaration of Helsinki (2013). Participants provided their written informed consent before participation, and database registration was completed before data analysis (identifier NCT05600452).

Experimental Procedures

Participants were instructed to abstain from alcohol throughout the experimental period and from caffeine for 8 h before laboratory visits, to consume a similar (high carbohydrate) diet before each test and to ensure that they arrived for each session well-hydrated, having consume at least 0.5 L of water before arriving for any experimentation in the heat. Euhydration was verified by mid-stream urine

Table 1. *Group characteristics (mean ± SD) for individuals undertaking either a condensed (n = 17) or traditional (n = 15) heat acclimation intervention*

	Condensed HA	Traditional HA	*P* Value
Age, yr	25 ± 6	23 ± 5	0.282
Height, m	1.76 ± 0.07	1.79 ± 0.07	0.360
Mass, kg	73.7 ± 6.9	71.4 ± 8.3	0.406
Body mass index, kg·m^{-2}	23.9 ± 3.0	22.4 ± 1.9	0.122
Estimated body fat, %	16 ± 4	12 ± 2	**<0.001**
Body surface area, m^2	1.90 ± 0.09	1.89 ± 0.13	0.884
Mass specific surface area, cm^2·kg^{-1}	258 ± 16	266 ± 14	0.189
$\dot{V}O_{2max}$, mL·min^{-1}·kg^{-1}	48.3 ± 6.0	46.7 ± 7.4	0.486
Peak power output, W	318 ± 24	303 ± 56	0.362

$\dot{V}O_{2max}$, maximal rate of oxygen uptake. HA, heat acclimation. *P* value = significance value from statistical analysis. Bold typeface denotes statistically significant between-groups difference at stated *P* value.

osmolality upon arrival at the laboratory for any exercise session in the heat (Osmo 1, Advanced Instruments Inc., Norwood); the same equipment was also used for the assessment of plasma osmolality. On the rare occasion that participants reported with a urine osmolality >800 mOsm·kg^{-1}, they were provided with additional water (minimum of 300 mL) to consume at least 30 min before commencing any subsequent test. Participants also avoided strenuous exercise in the 24 h before HSTs, HTTs, and GXTs but were instructed to try and maintain their normal exercise around the HA sessions within the THA program.

Heat acclimation.

The HA sessions were identical for both groups, with the exception of frequency of administration. Each session lasted 75-min and was undertaken in a hot-dry environment (T_{air} 45°C; 20% r.h.) utilizing a pseudo-passive controlled hyperthermia approach to elicit and maintain a target T_{rec} of 38.50 ± 0.25°C. To facilitate an initial increase in T_{rec} toward the target T_{rec}, each session commenced with 10-min of light stepping exercise (25 cm step × 18 steps·min^{-1}) in vapor-impermeable clothing [PVC-lined hooded long-sleeved top and trousers (AQF Sports, Worsley, UK), neoprene gloves and socks (Olaian, Decathlon, Villeneuve-d'Ascq, France)], with shorts, t-shirt, and underwear worn underneath, followed by 5 min of seated rest and a further 5 min of stepping. This process was typically sufficient to elicit a rising T_{rec}, but where this was not the case an additional 5-min block of rest and light-stepping was undertaken. Once a rising T_{rec} had been achieved, participants sat on a chair in the vapor impermeable clothing assembly until reaching a T_{rec} of ~38.20°C, at which point clothing was removed [in the following order: hood, gloves and socks, suit top, and trousers (if required)] to attenuate the rise in T_{rec}. Thereafter, clothing was manipulated as required (added or removed) to alter evaporative heat loss to the hot-dry environment and maintain the target T_{rec} for the remainder of the session. Where required, participants were permitted to use a fan on the face and upper torso (airspeed ~2–3 m·s^{-1}) to provide perceptual relief. Our pseudo-passive approach was informed by pilot work and was designed to standardize the thermal stimulus above the adaptation threshold (25, 57), while minimizing the exercise component and facilitating completion. During each HA session, participants were provided with an electrolyte drink (Go Hydro, Science in Sport, UK) that had been placed in the environmental chamber at least 2 h before each session and were instructed "drink to thirst."

For the THA program, the once-daily HA sessions were scheduled to take place, as far as possible, at ~0800 h (i.e., separated by ~24 h), with fluids and food consumed "to thirst and hunger" around their daily HA sessions; this was repeated on eight consecutive days. For the CHA program, the first HA session of each day commenced at ~0800 h, and the subsequent sessions were separated by 60 min resting in shorts and t-shirt in a cool room outside of the environmental chamber (e.g., second daily HA session started at ~1015 h; third daily HA session started at ~1230 h; and fourth daily HA session stated at ~1445 h). After the first and third HA session of the day, participants consumed a snack consisting of a Powerbar [Energize C2, PowerBar, CA (201 kcal)] and pretzels [KP snacks, Slough, UK (118 kcal)]; a standard meal was consumed after the second HA session [chicken and bacon pasta bowl; Co-op, Manchester, UK (415 kcal); McCoy's salt and vinegar crisps, KP snacks, Slough, UK (251 kcal)] and were able to consume additional fluids "to thirst" between the sessions. Once the participants left the laboratory after their fourth session of the day, they were free to consume additional fluids and food "to thirst and hunger." This process was repeated on two consecutive days.

Heat stress test.

The HSTs were performed on a cycle ergometer (Corival, Lode BV, The Netherlands) in a hot environment (T_{air} = 40.2 ± 0.2°C; r.h.=50 ± 1%) using an established test (25, 58) that provides sufficient thermal stimulus to evidence thermophysiological adaptation, while limiting the time that T_{rec} is elevated above 38.50°C (which could act as an additional adaptation stimulus). HSTs were conducted at the same time of day (~0800 h). Following a 5-min seated rest period, participants cycled at 35% of the power output for the final completed stage of the initial GXT (105 ± 15 W; described subsequently), for a total of 60 min. They were provided with 500 mL of electrolyte drink at 0 and 30 min of the exercise period, which they were instructed to consume over the subsequent 30 min. The same clothing was worn for each session (shorts, underwear, socks, and trainers), and convective cooling (2.7 m·s^{-1}; Meterman, Wavetek, New York) was provided by a fan directed on the face and upper torso.

Graded exercise test.

GXTs took place in a temperate environment (T_{air} 21°C; 50% r.h.) using cycle ergometry. Participants cycled at a power output of 75 W for 3 min, at which point a fingertip capillary blood sample was obtained and assayed for blood lactate concentration (Biosen lactate analyzer, EFK Diagnostics, Leipzig, Germany), and power output was increased by 25 W. This process was repeated until a blood lactate concentration [Lac] ≥4 mmol·L^{-1}, at which point work rate was increased 25 W·min^{-1} until volitional exhaustion. The first lactate threshold (LT) was defined as the power output eliciting a [Lac] of 2 mmol·L^{-1} with the second lactate threshold defined as the power output eliciting a [Lac] of 4 mmol·L^{-1}. Gross mechanical efficiency (GME) was calculated at 125 W (highest work rate below the initial increase in [Lac] achieved by most participants; for 2 participants 100 W was used) from the ratio of external work to energy expenditure, with the latter calculated according to Cramer and Jay (59). $\dot{V}O_{2max}$ was defined as the highest 15 s average $\dot{V}O_2$ during the GXT.

Hypoxic tolerance test.

The HTTs were undertaken in normobaric hypoxia (F_{IO_2} = 0.1504 ± 0.0017; Sporting Edge, Basingstoke, UK) and in temperate conditions (T_{air} 21°C; 50% r.h.) using a protocol adapted from Lunt et al. (60). During the HTT participants breathed through a facemask and falconia tubing. After 10 min seated rest on the cycle ergometer breathing normoxic air, the air supply was switched to the hypoxic air for a further 10-min rest period. Thereafter, participants commenced cycle ergometer exercise at an external work rate of 100 W for 10 min while breathing the hypoxic air. Data for each rest or exercise stage were calculated as the average over the last 5 min of the stage.

General Procedures

During GXTs and HTTs minute ventilation, oxygen uptake and carbon dioxide production, as well as heart rate (HRM-Dual, Garmin; Kansas) and peripheral capillary oxygen saturation (Sa_{O_2}) at the ear lobe (during HTTs only; Nonin Medial Inc, Plymouth), were recorded on a metabolic cart (Quark B2, COSMED, Rome, Italy) calibrated before use with gases of known concentration (15% O_2, 5% CO_2 for GXTs; 10% O_2, 5% CO_2 for HTTs) and a calibrated 3 L syringe. During HSTs, $\bar{T}_{sk}$ was determined according to Ramanathan (61), T_{rec} was measured according to Miller et al. (62), and $\bar{T}_b$ was calculated from the weighted mean of T_{rec} (0.9) and $\bar{T}_{sk}$ (0.1) (63). If a participant terminated the pre- or postintervention HST before the 60-min period, the iso-time data were used for prepost intervention comparison. This occurred for four participants in THA during the preintervention HST (test duration = 48 ± 7 min); the iso-time data were also used for the subset of these participants (two) who also completed a third HST to assess deacclimation. In addition, one participant (in CHA) terminated the deacclimation HST before the 60-min period (test duration = 55 min) having previously completed the pre- and postintervention HSTs; the iso-time data for this individual were used for the postintervention versus deacclimation HST comparison only. Heart rate was measured by a chest strap and short-range telemetry (Polar Electro, Kempele, Finland), local sweat rate was measured using a ventilated capsule on the right scapula (Q-Sweat, WR Medical Electronics, Maplewood), and peripheral blood flow was assessed using a laser Doppler probe positioned on the right thumb pad (Moor Instruments, Axminster, UK); a biological zero was obtained before each trial by occlusion of blood flow at the base of the thumb. During the HST, expired gases (Douglas bag method), RPE (64), thermal sensation, and thermal comfort (20 cm visual analogue scale) were measured at 20-min intervals, and a sample of sweat was collected for determining sodium concentration using a custom patch constructed from Tegaderm dressing (3 M, St. Paul) and Fisherbrand clear plastic wrap (Fisher Scientific; Loughborough, UK) and positioned on the right scapula (adjacent to the Q-sweat device), with the area cleaned with deionized water before application. Nude body mass (dry) was measured before and after each laboratory session (Model I10, Ohaus Corporation, Parsippany) to determine whole body sweat rate (WBSR), adjusted for fluid ingested, and metabolic heat production (MHP) was calculated according to Cramer and Jay (59).

Venous blood samples were obtained by venipuncture from a prominent forearm vein, following 10 min of seated rest before and after HSTs, before HA 1, and after HA 4 and 8; in instances where participants did not compete all HA sessions, the blood sample was obtained after their final HA session. Blood was collected into K2E EDTA vacutainers (Becton Dickinson & Co., Plymouth, UK) and SST vacutainers (Becton Dickinson & Co., Plymouth, UK) for serum, with the latter left to clot for 30 min. Hemoglobin concentration (201+ HemoCue, Ängelholm, Sweden) and hematocrit (Hawksley, Lancing, UK) were assessed in triplicate from the whole blood sample and used to calculate changes in blood volume (BV) and plasma volume (PV) using the method of Dill and Costill (65). All biological samples were centrifuged at 4,350 *g* for 10 min at 4°C, and the supernatant aliquoted into Eppendorf tubes with 20 μL of plasma assayed to determine osmolality. Thereafter, biological samples were frozen to −80°C until subsequent analysis.

Enzyme-linked immunoassay analyses were performed in duplicate using commercially available kits to examine biomarkers of stress and inflammation [plasma interleukin 6 (IL-6; R&D systems human IL-6 assay; CV = 4.5%); plasma cortisol (R&D systems human cortisol assay; CV = 4.5%); serum heat shock protein 70 (HSP 70; R&D systems human HSP70 duoset; CV = 4.8%)], gastrointestinal stress [serum intestinal fatty acid binding protein (IFABP; R&D systems human IFABP duoset; CV = 2.2%); plasma lipopolysaccharide binding protein (LBP; R&D systems human LBP duoset; CV = 3.7%); plasma soluble cluster of differentiation 14 (sCD14; R&D systems human sCD14 duoset; CV = 2.0%)], and renal stress [plasma and urine neutrophil gelatinase-associated lipocalin (NGAL; R&D systems human lipocalin2/NGAL duoset; plasma CV = 3.2%; urine CV = 2.4%); urine tissue inhibitor of metalloproteinase-2 (TIMP-2; R&D systems human TIMP-2 duoset; CV = 5.4%); urine insulin-like growth factor binding protein-7 (IGFBP-7; R&D systems human IGFBP-7 duoset; CV = 2.5%); kidney injury molecule-1 (KIM-1; R&D systems human KIM-1 duoset; CV = 3.5%)]. Serum creatine was also assessed as a further index of renal stress (Randox Daytona +; Randox Laboratories, County Antrim, Northern Ireland) with acute kidney injury (AKI) defined according to the Acute Kidney Injury Network (AKIN) criteria, with *stage 1* AKI defined as an increase in serum creatinine of >26.5 $\mu mol \cdot L^{-1}$ from baseline, and *stage 2* AKI defined as an increase in serum creatinine of two- to threefold of the baseline measurement (66).

For blood biomarkers assessed during HSTs, all values were corrected to account for PV changes relative to the sample obtained before HST 1, thereby accounting for both the within-HST (e.g., due to dehydration) and between-HST (e.g., due to hypervolemia) effects of PV changes on blood biomarker concentration relative to a common baseline; the resultant PV corrected values were used to determine the within HST change (Δ) of the blood biomarkers. For blood biomarkers assessed during the HA sessions, values were corrected to account for PV changes relative to the sample obtained before HA 1 and used to determine the Δ from the HA1 baseline value following HA *sessions 4* and *8*, thereby accounting for changes in PV over the intervening HA sessions relative to a common baseline. Urine biomarkers were normalized to urine osmolality (67), and sweat sodium concentration was measured in duplicate (Sweat-check, EliTech, UT; CV = 0.33%) and adjusted to ion chromatography equivalent values according to Goulet et al. (68).

Data Analyses

Statistical analyses were undertaken using SPSS (v. 27, IBM, New York, NY) with statistical significance set a priori as $P < 0.05$. Parametric data are presented as means ± SD, with nonparametric data (assessed by Shapiro–Wilks' test and skewness and kurtosis) presented as median (interquartile range; IQR). Simple between-groups analysis of parametric data (e.g., participant characteristics; thermophysiological responses to the HA interventions) was done

by using independent samples t test, with equality of variances assessed by Levene's test. For analysis of our primary outcome measure (peak T_{rec} during the HST), as well as other (normally distributed) indices of thermophysiological adaptation, hypoxic cross-tolerance and temperate exercise performance, the within (pre HA vs. post HA) HST, between (CHA vs. THA), and interaction (time × group) effects were assessed using 2 × 2 mixed model ANOVA; the P value for the interaction term in this type of ANOVA is identical to that calculated by independent samples t test of the pre- to postintervention Δ analysis on which the study was powered. For the subset of participants who undertook a third HST for assessing deacclimation effects, the same analysis approach was undertaken to compare the post HA versus decay HST data (i.e., HST2 vs. HST3). Post hoc analysis of significant interaction effects was done by using paired samples t test for within-group comparisons and independent samples t test for between-group comparison. For nonparametric data, the effect of time was assessed by Wilcoxon's signed-ranks test, with the effect of group (analyzed at each time point), and the between-groups difference in the pre- versus post-HA Δ value (analogous to the interaction effect for this study design) assessed by Mann–Whitney U tests using the "exact" P value.

RESULTS

Thermophysiological Responses during CHA and THA Interventions

The thermophysiological responses over the course of the CHA and THA interventions (i.e., during the HA sessions) are summarized in Table 2. Average T_{rec} ($t_{27} = 0.774$, $P = 0.446$), time to T_{rec} target ($t_{30} = -1.116$, $P = 0.273$) and T_{rec} over the final 45 min of the HA session ($t_{30} = -1.574$, $P = 0.126$) did not differ between the interventions, with the latter in accordance with the target T_{rec} of 38.50 ± 0.25°C. Average heart rate within HA sessions was also similar between groups ($t_{25} = -0.297$, $P = 0.769$). Together, this indicates that that the isothermal strain technique was effectively applied and that thermal and cardiovascular strain were similar across the HA groups. However, starting T_{rec} was higher during CHA than THA ($t_{29} = 2.746$, $P = 0.010$) and WBSR was lower across the CHA intervention than THA ($t_{30} = -4.062$, $P < 0.001$), and a small between-groups difference was evident for the average RPE ($t_{23.9} = 2.338$, $P = 0.028$). In addition, the lower bound of the target T_{rec} was not reached for four of the 136 scheduled HA sessions within CHA (i.e., early removal of clothing and request for fanning due to perceptual discomfort; peak $T_{rec} = 37.96 \pm 0.34$°C) but the participant remained in the hot environment for the entire period; three of these sessions were from the same participant and sessions where the target T_{rec} was not achieved were not included in the analysis of time to T_{rec} target. Session completion rates did not differ between groups ($U = 150$, $P = 0.411$), but in the CHA group one participant withdrew before HA *session 7* (dizziness and nausea) and two participants withdrew before HA *session 8* (discomfort, $n = 1$; volitional withdrawal, $n = 1$).

A significant time effect was evident for Δ serum IFABP, which was higher after HA8 than HA4 ($Z = 1.994$, $P = 0.046$), although the median values after HA8 remained similar to the pre-HA baseline. A significant interaction effect was evident for Δ plasma cortisol ($U = 144$, $P = 0.033$), but at each time point in both conditions the median value remained below baseline levels. Significant group effects were evident for the Δ serum creatinine ($F_{1,25} = 6.359$, $P = 0.018$), Δ plasma IL-6 (at HA4: $U = 41$, $P = 0.041$), and Δ plasma LBP (at HA8; $U = 28$, $P = 0.003$), each of which were higher during the CHA intervention compared with THA. The *stage 1* AKI threshold was reached by two participants in CHA at HA4 and three participants at HA8. No participants in THA group met the criteria for *stage 1* AKI at either time point and no participants in either group met the *stage 2* AKI threshold at either timepoint. It should also be noted that three participants at HA4 and three participants at HA8 exceeded the detection limit for urine IGFBP-7 in CHA and were not included in the analysis. However, using imputation of the upper-limit values for these individuals and undertaking a nonparametric group analysis, which utilizes rank rather than absolute values, group effects remained nonsignificant at each time point. In contrast, the change in urine KIM-1 was lower in the CHA intervention compared with THA at HA4 ($U = 119$, $P = 0.005$) and HA8 ($U = 111$, $P = 0.022$). Changes in biomarkers of inflammation, gastrointestinal barrier integrity, and renal stress over the course of each HA intervention are summarized in Supplemental Table S1.

Thermophysiological Adaptations to CHA and THA

The thermophysiological, perceptual, and metabolic responses during the HSTs undertaken before and after each

Table 2. *Thermophysiological responses (grand mean ± SD) and session completion rates [median (IQR)] for participants undertaking either a condensed (n = 17) or traditional (n = 15) heat acclimation intervention*

	Condensed HA	Traditional HA	*P* Value
T_{rec} over final 45 min, °C	38.45 ± 0.17	38.53 ± 0.13	0.126
Time to target T_{rec} range, min[a]	33 ± 7	35 ± 6	0.273
Average T_{rec} (°C; $n = 29$)	38.11 ± 0.19	38.06 ± 0.15	0.446
Starting T_{rec} (°C; $n = 31$)	37.23 ± 0.26	36.99 ± 0.23	**0.010**
Whole body sweat rate, L·h^{-1}	0.93 ± 0.23	1.33 ± 0.32	**<0.001**
Average heart rate, beats·min^{-1}; $n = 27$	121 ± 9	122 ± 12	0.769
Average RPE (6–20 scale)	9 ± 2	8 ± 1	**0.028**
Number of HA sessions completed (count)	8 (0)	8 (0)	0.411

HA, heat acclimation; RPE, rating of perceived exertion; T_{rec}, rectal temperature; [a]Data omitted for four sessions within condensed HA where target T_{rec} range was not achieved. P value = significance value from statistical analysis. Bold typeface denotes statistically significant between-groups difference at stated P value.

Table 3. *Thermophysiological responses to a heat stress test, undertaken pre and post a condensed (n = 17) or traditional (n = 15) heat acclimation (HA) intervention*

	Condensed HA			Traditional HA			*P* Value		
	Pre	Post	Delta	Pre	Post	Delta	Time	Group	Interaction
Thermal									
Resting T_{rec}, °C	36.92 ± 0.33	36.78 ± 0.33*	−0.14 ± 0.21	37.07 ± 0.36	36.72 ± 0.29***	−0.35 ± 0.29	<**0.001**	0.661	**0.027**
Exercise T_{rec}, °C	37.65 ± 0.33	37.47 ± 0.32	−0.18 ± 0.19	37.78 ± 0.23	37.44 ± 0.24	−0.34 ± 0.26	<**0.001**	0.643	0.055
Peak T_{rec}, °C	38.50 ± 0.41	38.21 ± 0.43	−0.28 ± 0.26	38.58 ± 0.30	38.22 ± 0.34	−0.36 ± 0.17	<**0.001**	0.749	0.303
Resting $\bar{T}_{sk}$, °C	35.81 ± 0.53	35.95 ± 0.52	0.14 ± 0.54	36.23 ± 0.46	36.03 ± 0.38	−0.20 ± 0.46	0.746	0.092	0.063
Exercise $\bar{T}_{sk}$, °C	37.67 ± 0.42	37.34 ± 0.44	−0.33 ± 0.32	37.70 ± 0.41	37.21 ± 0.34	−0.49 ± 0.32	<**0.001**	0.703	0.167
Peak $\bar{T}_{sk}$, °C	38.30 ± 0.54	37.84 ± 0.43	−0.46 ± 0.41	38.22 ± 0.45	37.75 ± 0.37	−0.47 ± 0.53	<**0.001**	0.538	0.965
Resting $\bar{T}_{b}$, °C	36.81 ± 0.32	36.69 ± 0.32*	−0.11 ± 0.20	36.98 ± 0.35	36.65 ± 0.28***	−0.33 ± 0.29	<**0.001**	0.520	**0.017**
Exercise $\bar{T}_{b}$, °C	37.65 ± 0.33	37.47 ± 0.30**	−0.18 ± 0.19	37.77 ± 0.22	37.41 ± 0.21***	−0.35 ± 0.24	<**0.001**	0.713	**0.032**
Peak $\bar{T}_{b}$, °C	38.46 ± 0.42	38.15 ± 0.42	−0.31 ± 0.26	38.51 ± 0.28	38.12 ± 0.31	−0.39 ± 0.16	<**0.001**	0.926	0.340
Thermoregulatory									
Whole-body sweat rate, $L \cdot h^{-1}$	1.06 ± 0.18	1.27 ± 0.20***#	0.21 ± 0.10	1.15 ± 0.32	1.49 ± 0.33***#	0.34 ± 0.11	<**0.001**	0.094	**0.002**
Exercising upper-back sweat rate, $mL \cdot m^{-2} \cdot h^{-1}$	8.9 (2.4)	9.9 (2.6)	1.0 (4.2)	9.4 (4.2)	10.5 (3.4)	1.6 (3.5)	**0.005**	Pre = 0.278 Post = 0.246	1.000[a]
Sweat sodium, $mmol \cdot L^{-1}$; $n = 27$	88 ± 27	65 ± 19	−23 ± 21	70 ± 30	62 ± 33	−8 ± 17	<**0.001**	0.295	0.061
Exercising skin blood flow (a.u.; $n = 30$)	251 ± 54	263 ± 48	11 ± 53	263 ± 60	285 ± 54	23 ± 84	0.197	0.264	0.658
Exercise heart rate, $beats \cdot min^{-1}$	146 ± 15	141 ± 14	−5 ± 7	149 ± 14	140 ± 10	−9 ± 11	<**0.001**	0.805	0.227
Peak heart rate $beats \cdot min^{-1}$	166 ± 16	158 ± 15	−8 ± 8	167 ± 14	160 ± 9	−7 ± 13	<**0.001**	0.692	0.746
Δ resting plasma volume, %; $n = 31$			7.5 ± 7.9			5.1 ± 7.2		0.374	
Δ resting blood volume, %; $n = 31$			4.7 ± 4.6			2.7 ± 3.9		0.219	
Perceptual									
Exercise RPE (6–20 scale)	12 ± 2	11 ± 2	−1 ± 2	12 ± 2	11 ± 2	−1 ± 1	0.057	0.920	0.751
Exercise thermal sensation (20 cm VAS)	16.1 ± 1.0	15.3 ± 1.6	−0.8 ± 1.8	16.6 ± 1.1	15.5 ± 1.4	−1.1 ± 1.2	**0.002**	0.430	0.549
Exercise thermal comfort (20 cm VAS)	9.2 ± 3.7	11.9 ± 3.7	2.7 ± 3.1	8.1 ± 2.6	9.7 ± 2.8	1.6 ± 2.7	<**0.001**	0.121	0.265
Hydration									
Baseline urine osmolality, $mOsm \cdot kg^{-1}$	597 ± 331	552 ± 290	−45 ± 262	488 ± 306	484 ± 289	−3 ± 154	0.536	0.386	0.594
Baseline plasma osmolality, $mOsm \cdot kg^{-1}$	291 ± 3	290 ± 3	−1 ± 4	293 ± 3	292 ± 3	−1 ± 3	0.185	0.083	0.788
Metabolic									
Exercise metabolic heat production, $W \cdot kg^{-1}$	6.4 ± 0.8	6.7 ± 0.8	0.3 ± 0.8	6.9 ± 0.8	6.7 ± 1.0	−0.1 ± 0.4	0.505	0.350	0.077
Exercise $\dot{V}O_2$, $L \cdot min^{-1}$	1.68 ± 0.18	1.73 ± 0.13	0.05 ± 0.15	1.72 ± 0.22	1.68 ± 0.22	−0.33 ± 0.07	0.739	0.931	0.072
Exercise RER (ratio)	0.91 (0.09)	0.92 (0.11)	0.04 (0.10)	0.91 (0.09)	0.92 (0.08)	0.00 (0.04)	0.083	Pre = 0.411 Post = 0.970	0.069[a]

Data are mean ± SD or median (IQR) for nonparametric data. a.u., arbitrary units; RER, respiratory exchange ratio; RPE, rating of perceived exertion; T_{rec}, rectal temperature; $\bar{T}_{sk}$, mean skin temperature; $\bar{T}_{b}$, mean body temperature; VAS, visual analogue scale; $\dot{V}O_2$, rate of oxygen uptake. [a]Where data did not meet the assumption of normality, the interaction term was assessed by between group analysis of the delta value by Mann–Whitney *U* test. *P* value = significance value from statistical analysis. Where a significant interaction effect was identified: *Pre vs. post within-group difference, $P < 0.050$; **pre vs. post within-group difference, $P < 0.010$; ***pre vs. post within-group difference, $P < 0.001$; #between-groups difference for that time point, $P < 0.050$. Bold typeface denotes statistically significant time, group, or interaction effect at stated *P* value.

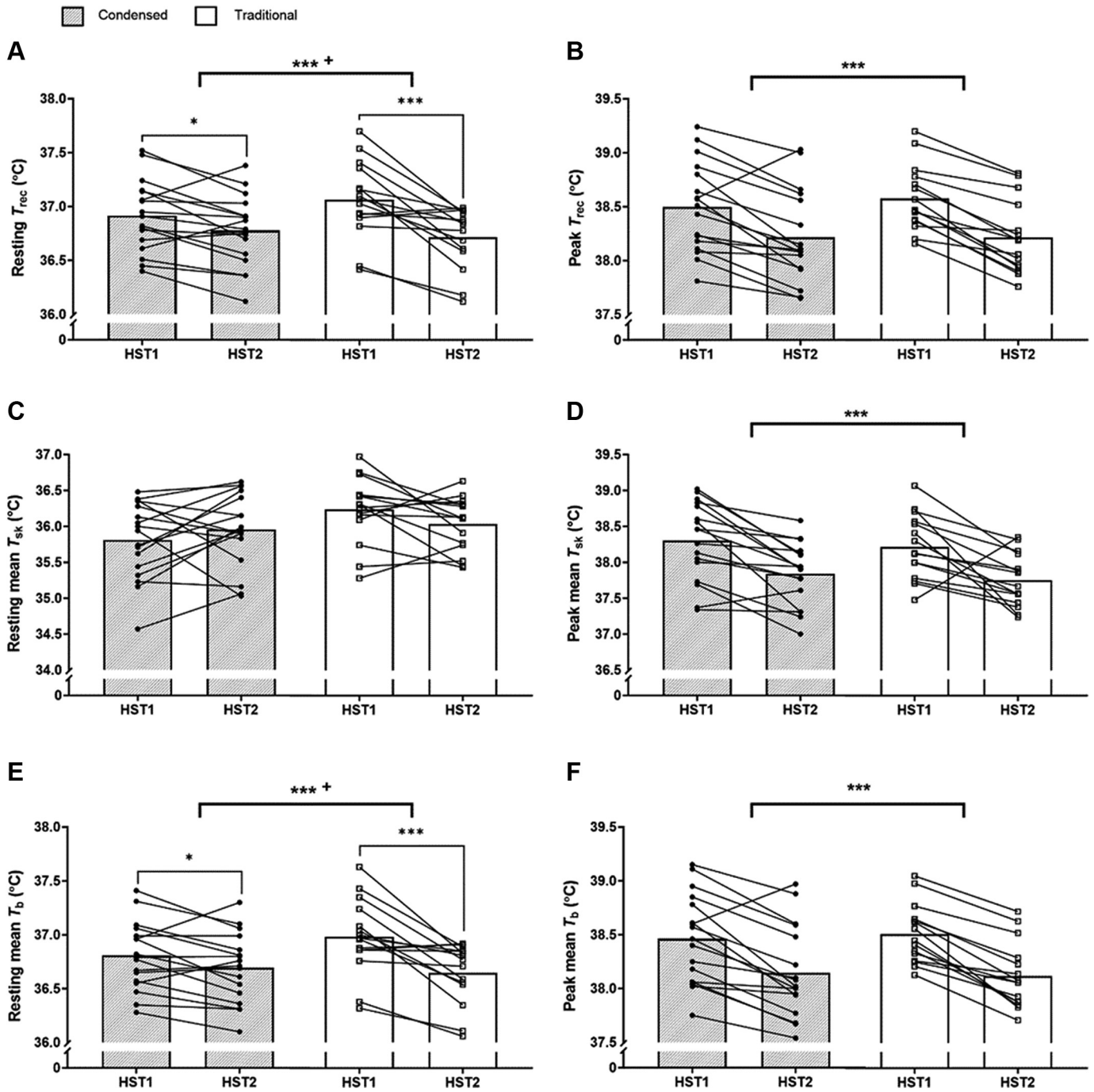

Figure 2. Mean and individual data for resting and peak rectal (T_{rec}; *A* and *B*), mean skin ($\bar{T}_{sk}$; *C* and *D*), and mean body ($\bar{T}_b$; *E* and *F*) temperature for participants undertaking either a condensed or traditional heat acclimation (HA) intervention. HST1, heat stress test 1, undertaken prior to the HA intervention; HST2, heat stress test 2, undertaken after the HA intervention. *Effect of time $P < 0.050$; ***effect of time $P < 0.001$; + interaction effect $P < 0.050$.

HA intervention are summarized in Table 3. Both HA interventions induced a range of beneficial thermophysiological adaptations to heat, indicated by a significant main effect of time for each of the thermal, thermoregulatory, or perceptual indices of adaptation, apart from resting $\bar{T}_{sk}$, exercising skin blood flow and RPE. Moreover, there was no significant main effect of HA group for any of the measured variables, although significant interaction (time × condition) effects were evident for resting T_{rec} ($F_{1,30} = 5.385$, $P = 0.027$), resting $\bar{T}_b$ ($F_{1,30} = 6.419$, $P = 0.017$), average exercising $\bar{T}_b$ ($F_{1,30} = 5.038$, $P = 0.032$), and WBSR ($F_{1,30} = 11.478$, $P = 0.002$) indicating a between-groups difference in the pre- to postintervention Δ for that variable. Post hoc analysis of the significant interaction effects showed that there were no between-groups differences in resting T_{rec}, resting $\bar{T}_b$, and exercising $\bar{T}_b$ before or after the intervention, and significant within-participant reductions in each of these variables following both HA interventions. Similarly, WBSR did not differ between groups before the HA interventions ($t_{30} = -1.037$, $P = 0.308$) and increased over time in both the THA ($t_{16} = -8.632$,

$P < 0.001$) and CHA groups ($t_{14} = -11.644$, $P < 0.001$). However, after the HA intervention, WBSR was higher in the THA group than the CHA group ($t_{30} = -2.313$, $P = 0.028$). The improvements in peak thermophysiological (e.g., peak T_{rec}, peak $\bar{T}_{sk}$, and peak $\bar{T}_b$), cardiovascular responses (e.g., average exercising and peak heart rate), perceptual indices (e.g., thermal comfort and sensation), and hematological indices were not different between groups (see Fig. 2 and Fig. 3).

The within HST changes in biomarkers of inflammation, gastrointestinal barrier integrity, and renal stress during the HSTs undertaken before and after each HA intervention are summarized in Supplemental Table S2. Significant time effects were evident for the within HST Δ serum HSP70 concentration ($Z = -2.281$, $P = 0.023$) and Δ serum creatinine ($Z = -2.022$, $P = 0.043$), which were both lower post-HA. However, no group or interaction effects were evident. The *stage 1* AKI threshold was reached by one person in the CHA group, before and after the intervention, but not in any individuals within the THA group at either time point; no individuals met the *stage 2* AKI criteria.

Temperate Exercise Performance

Individual data showing the pre- versus post-HA changes for indices of endurance performance are presented in Fig. 4, with group data summarized in Supplemental Table S3. There were no significant main effects of time, condition, or interaction effect for any of the indices of endurance performance, with the exception of a significant time effect for peak heart rate ($F_{1,30} = 12.918$, $P = 0.001$), which was lower in the post HA GXT and an interaction effect for power at the 4 mmol·L^{-1} lactate threshold ($F_{1,30} = 11.689$, $P = 0.002$). Post hoc analysis identified that the power at 4 mmol·L^{-1} [Lac] was increased after THA ($t_{14} = -2.752$, $P = 0.016$) but was unchanged following CHA ($t_{16} = 1.912$, $P = 0.074$).

Hypoxic Tolerance

Two participants were unable to complete both HTTs in the traditional HA intervention (technical issues, $n = 1$; vasovagal response to venipuncture, $n = 1$) and are not included in the analysis for this portion of the study. Physiological responses during the HTT before and after each HA intervention are summarized in Table 4. No significant effect of time, condition, or interaction was detected for any of the physiological responses at rest with the exception of a time effect on O_2 pulse ($Z = 2.359$, $P = 0.018$). Similarly, a significant time effect was observed for exercising O_2 pulse ($F_{1,28} = 4.861$, $P = 0.036$), as well as exercising heart rate ($F_{1,28} = 9.643$, $P = 0.004$) and exercising Sp_{O_2} ($F_{1,28} = 7.225$, $P = 0.012$), but no other significant main or interaction effects were evident for exercising responses to hypoxia.

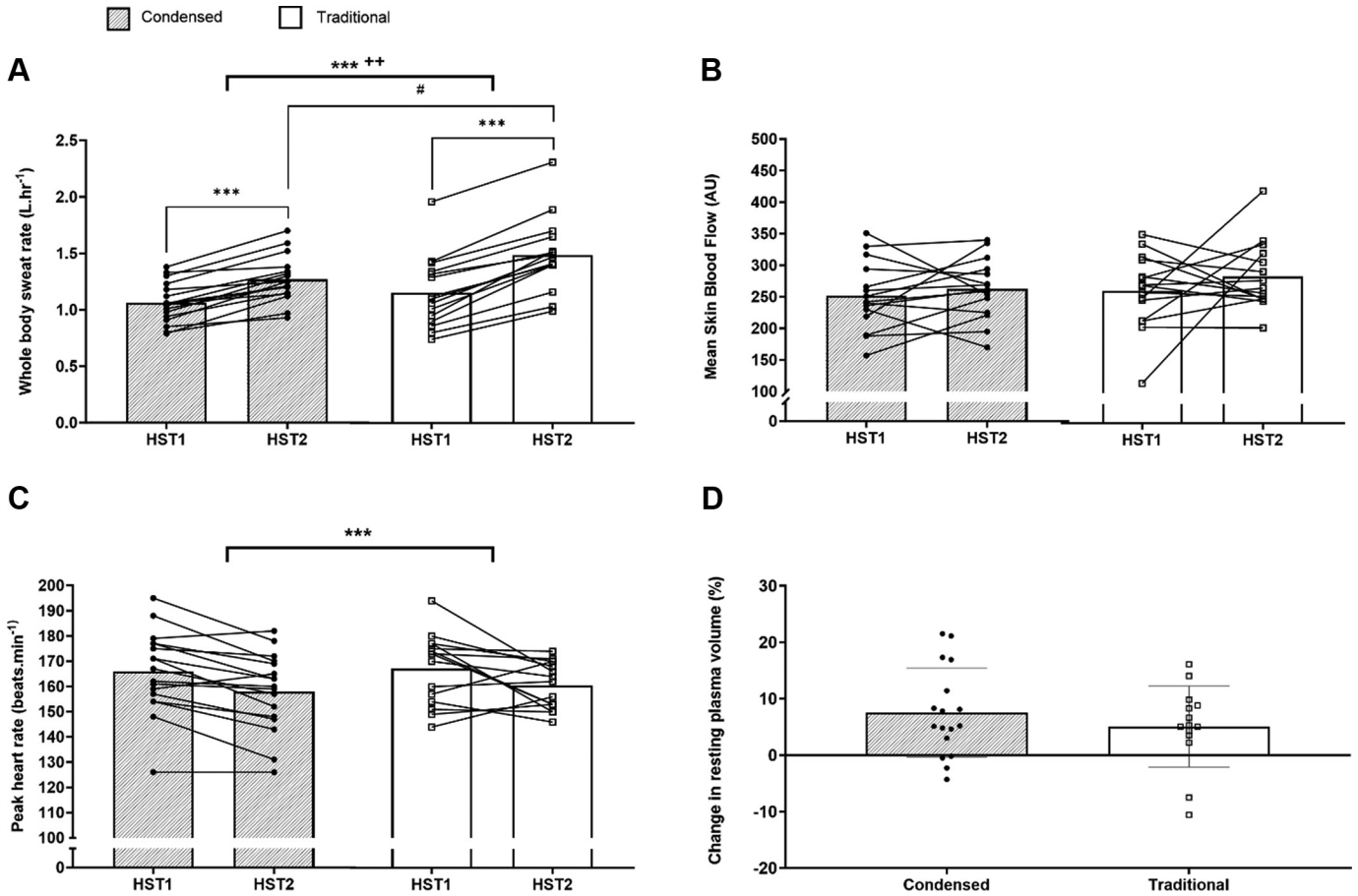

Figure 3. Mean and individual data for whole body sweat rate (*A*), mean skin blood flow (*B*), peak heart rate (*C*), and plasma volume change (*D*) for participants undertaking a condensed or traditional heat acclimation (HA) intervention. HST1, heat stress test 1, undertaken prior to the HA intervention; HST2, heat stress test 2, undertaken after the HA intervention. ***Effect of time $P < 0.001$; #effect of group $P < 0.050$; ++ interaction effect $P < 0.010$.

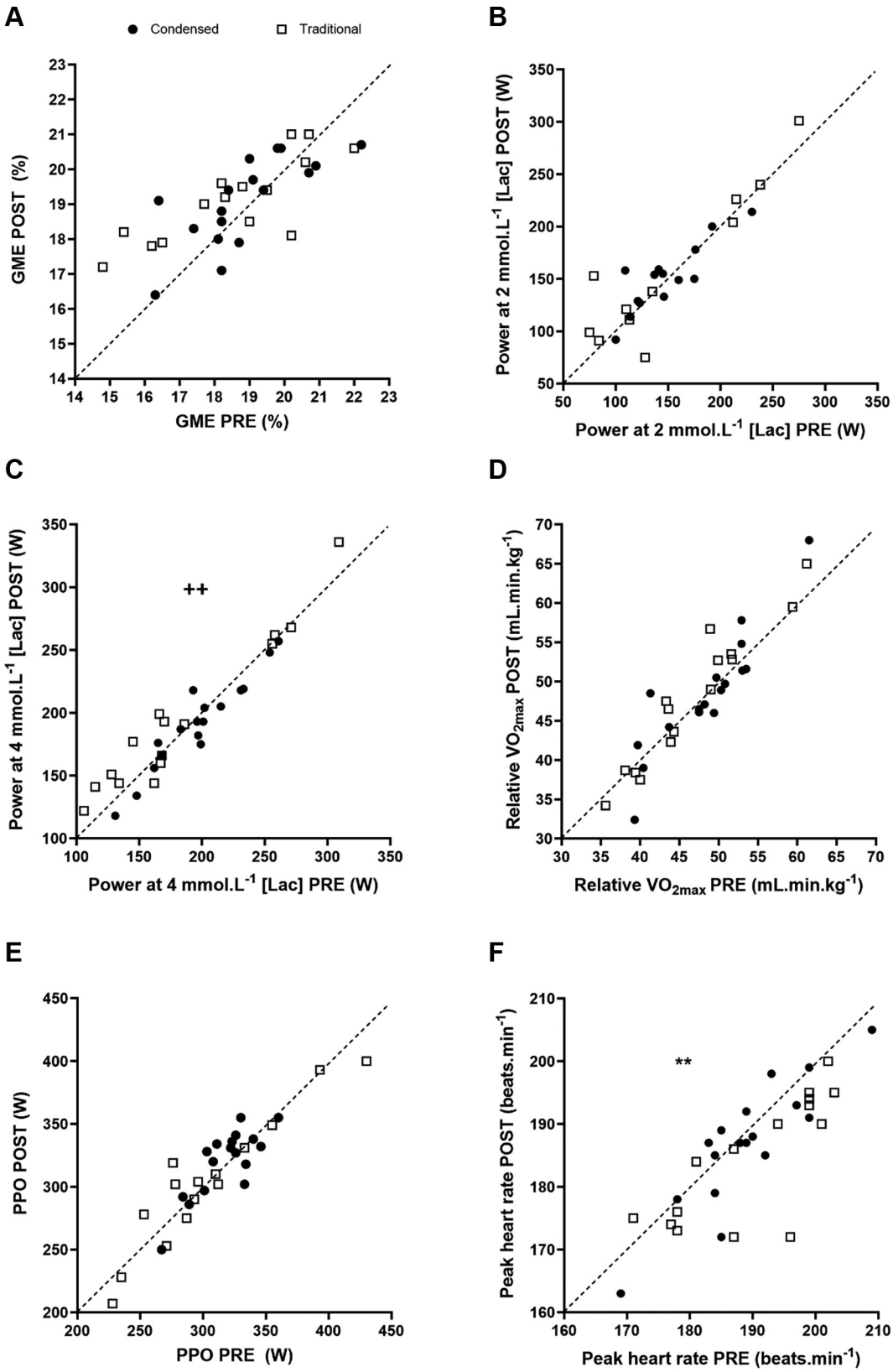

Figure 4. Individual data for gross mechanical efficiency (GME) (*A*), power at 2 (*B*) and 4 (*C*) mmol·L^{-1} blood lactate, maximum rate of oxygen uptake ($\dot{V}O_{2max}$; *D*), peak power output (*E*), and peak heart rate (*F*) from graded exercise tests before (pre) and after (post) undertaking a condensed or traditional heat acclimation (HA) intervention. Dashed line, line of identity; **effect of time $P < 0.010$; ++interaction effect $P < 0.010$.

Table 4. *Physiological responses to acute (10 min) hypoxia ($F_{I_{O_2}} = 0.15$) at rest and during exercise at 100 W before (pre) and after (post) either a condensed (n = 17) or traditional (n = 13) heat acclimation intervention*

	Condensed HA			Traditional HA			*P* Value		
	Pre	Post	Delta	Pre	Post	Delta	Time	Group	Interaction
Rest									
$\dot{V}_E$, L·min^{-1}	13.40 (3.05)	14.00 (4.00)	1.40 (2.35)	13.20 (5.85)	13.40 (2.35)	0.80 (3.20)	0.080	Pre = 0.711 Post = 0.967	0.483[a]
$\dot{V}_{O_2}$, L·min^{-1}	0.46 (0.08)	0.47 (0.13)	0.03 (0.10)	0.46 (0.14)	0.47 (0.13)	0.04 (0.11)	0.117	Pre = 0.650 Post = 1.000	0.934[a]
RER (ratio)	0.90 (0.11)	0.89 (0.06)	−0.01 (0.10)	0.88 (0.08)	0.88 (0.07)	−0.01 (0.12)	0.888	Pre = 0.902 Post = 0.934	0.805[a]
Heart rate, beats·min^{-1}	78 ± 10	77 ± 9	−1 ± 7	81 ± 13	77 ± 14	−4 ± 7	0.111	0.704	0.243
O_2 pulse, mL·beat^{-1}	5.9 (1.5)	6.0 (1.3)	0.5 (1.4)	5.9 (2.7)	6.0 (2.6)	0.5 (2.3)	**0.018**	Pre = 0.869 Post = 0.805	0.621[a]
Sp_{O_2}, %	95 ± 2	96 ± 2	1 ± 2	95 ± 2	95 ± 2	−0 ± 2	0.422	0.944	0.103
Exercise									
$\dot{V}_E$, L·min^{-1}	40.90 (5.60)	41.30 (7.10)	1.50 (4.00)	41.70 (6.70)	40.70 (5.90)	−0.20 (3.05)	0.120	Pre = 0.869 Post = 0.536	0.123[a]
$\dot{V}_{O_2}$, L·min^{-1}	1.68 ± 0.10	1.66 ± 0.09	−0.02 ± 0.08	1.70 ± 0.17	1.68 ± 0.16	−0.01 ± 0.06	0.177	0.667	0.736
RER (ratio)	0.93 ± 0.06	0.94 ± 0.06	0.00 ± 0.04	0.93 ± 0.04	0.93 ± 0.05	−0.00 ± 0.04	0.966	0.865	0.726
Heart rate, beats·min^{-1}	118 ± 13	115 ± 12	−3 ± 7	122 ± 18	117 ± 15	−5 ± 7	**0.004**	0.661	0.488
O_2 pulse, mL·beat^{-1}	14.3 ± 1.0	14.5 ± 1.2	0.2 ± 0.8	14.2 ± 2.4	14.7 ± 2.5	0.4 ± 0.7	**0.036**	0.938	0.469
Sp_{O_2}, %	90 ± 3	92 ± 2	2 ± 3	91 ± 3	92 ± 3	1 ± 3	**0.012**	0.697	0.315

Data are presented mean ± SD or median (IQR) for nonparametric data. *P* value = significance value from statistical analysis. HA, heat acclimation; RER, respiratory exchange ratio; Sp_{O_2}, peripheral capillary oxygen saturation; $\dot{V}_E$, minute ventilation; $\dot{V}_{O_2}$, rate of oxygen uptake. [a]Where data did not meet the assumption of normality, the interaction term was assessed by between group analysis of the delta value by Mann–Whitney *U* test. Bold typeface denotes statistically significant time, group, or interaction effect at stated *P* value.

Deacclimation following CHA and THA

To assess deacclimation, a subset of 20 participants (CHA = 12; THA = 8) undertook an additional HST 22 days after completing their final HA session (Supplemental Table S4). For each of the thermal variables (e.g., resting, exercise, and peak T_{rec}, $\bar{T}_{sk}$, and $\bar{T}_b$, with the exception of resting T_{sk}, there was no main effect of time or HA group and no interaction effect. Together this indicates that that the thermal benefits gained during each intervention were well maintained over the deacclimation period, irrespective of group. However, main effects of time were evident for WBSR, skin blood flow, and thermal comfort, which were each decreased from the post HA HST to the deacclimation HST, with no between-groups or interaction effect for these parameters, although there was a trend ($P = 0.051$) toward an interaction effect for WBSR indicative of a greater decay rate in THA than CHA. A follow-up analysis comparing the pre-HA HST to the decay HST indicated that despite some evidence for decay, WBSR remained higher at the end of the deacclimation period than before the HA intervention [main effect of time ($F_{1,17} = 13.061$, $P = 0.002$); group and interaction effects both $P > 0.050$], whereas skin blood flow and thermal comfort did not differ from the pre-HA HST. Between-groups differences were also observed for the Δ plasma volume and Δ blood volume during the deacclimation period, which was reduced in CHA compared with THA. A follow-up analysis of the Δ plasma volume and Δ blood volume from the pre-HA HST to the deacclimation HST indicated that, over this time period, the between-groups difference in Δ plasma volume (CHA = 0.4 ± 6.2% vs. THA = 6.6 ± 7.8%; $t_{18} = -1.979$, $P = 0.063$) and Δ blood volume (CHA = 0.6 ± 4.1% vs. THA = 4.7 ± 4.9%; $t_{18} = -2.023$, $P = 0.058$) were not significantly different.

DISCUSSION

This study sought to determine, for the first time, whether a novel 2-day "condensed" HA intervention (i.e., CHA) could elicit the hallmark thermophysiological changes that characterize the heat adapted phenotype, and whether these adaptations were different from those occurring with a "traditional" once-daily HA intervention (i.e., THA). Our data showed: *1)* hallmark thermophysiological adaptations to heat, including reduced resting (e.g., Δ resting T_{rec}: CHA = −0.14 ± 0.21°C; THA = −0.35 ± 0.29°C) and exercising thermal strain (e.g,. Δ peak T_{rec}: CHA = −0.28 ± 0.26°C; THA = −0.36 ± 0.17°C), reduced sweat electrolyte content and increased WBSR (Δ WBSR: CHA = +0.21 ± 0.10 L·h^{-1}; THA = +0.34 ± 0.11 L·h^{-1}), expanded PV (Δ PV: CHA = +7.5 ± 7.9%; THA = +5.1 ± 7.2%), reduced cardiovascular (e.g., Δ peak heart rate: CHA = −8 ± 8 beats·min^{-1}; THA = −7 ± 13 beats·min^{-1}) and renal strain, lower serum heat shock protein 70, and improvements in thermal comfort and sensation, can be achieved within 2 days; *2)* with the exception of resting T_{rec}, resting $\bar{T}_b$, average exercising $\bar{T}_b$ and WBSR, the thermophysiological adaptations elicited by CHA did not differ from those elicited by THA, although some indices of inflammatory, gastrointestinal, and renal stress response were greater during CHA; *3)* both HA interventions elicited hypoxic cross-tolerance, which was most evident during hypoxic exercise, as indicated by a reduced heart rate and an increased O_2 pulse and Sp_{O_2}, whereas with the exception of an increased power at LT following THA, the interventions did not improve temperate exercise performance parameters; *4)* data from a subset of participants indicated that following a 22-day deacclimation period, the majority of thermophysiological responses did not differ from the post-HA time point, with the exception of skin blood flow,

thermal comfort, and WBSR, which decayed across both groups, although the latter remained above preintervention levels.

The present study, which used a pseudo-passive (i.e., minimal exercise component) controlled hyperthermia technique to elicit a target T_{rec} of ~38.5°C (57, 69), was designed to deliver a similar thermophysiological stimulus, irrespective of the differing frequency of application. Our data, which demonstrated, for both groups, a T_{rec} over the final 45 min of each HA session in accordance with the target T_{rec}, as well as a similar session average T_{rec} and time to target T_{rec}, indicate that this was effectively achieved. This approach also elicited a similar cardiovascular strain in both HA interventions, albeit that mean heart rate was relatively lower (~120 beats·min^{-1} vs. ~140–170 beats·min^{-1}) than previous studies that utilized an active (i.e., exercise) approach to controlled hyperthermia rather than our pseudo-passive approach (25, 57, 70). This reduced cardiovascular strain was by design and was intended to minimize the confounding influence of exercise and a potential "training effect" that may have been evident in other studies (43), while also supporting high completion rates.

Despite this close control, we did observe some between-groups differences in indices of thermophysiological strain during the HA intervention, but these were not unexpected. Specifically, we observed an elevated starting T_{rec} and reduced WBSR for the CHA group compared with THA, as well as a slightly higher RPE with CHA. The higher starting T_{rec} in CHA likely results from the combination of circadian effects on T_{rec} (71), which would not have been evident in THA, as well as the ~60 min recovery period between HA sessions not enabling a return to baseline for *sessions 2–4* and *5–8*. However, the principal of controlled hyperthermia does not rely on a specific ΔT_c, but rather the maintenance of a fixed thermal forcing function at a defined target T_c (~38.5°C) (69, 72), and it was not practically feasible, nor desirable, to actively cool participants undertaking CHA. Given that the body mass change over the course of each CHA day was only −1.2 ± 0.9%, the lower WBSR over the course of the CHA intervention likely results from the combined effects of hidromeiosis, leading to reduced sweating after the initial daily session in CHA (73, 74), as well as a progressive increase in the daily sweating rate in THA as a consequence of adaptation. Although the between-groups difference in mean RPE was relatively modest and, at a group-level, the total number of HA sessions completed by individuals did not differ, it is notable that 82% of participants completed all eight HA sessions in CHA compared with 100% of participants in THA. Similarly, two participants did not reach the lower-bound target T_{rec} in all of the HA sessions in CHA, but this was not evident for any participants in THA.

Aligned to the greater perceived exertion during CHA, greater increases in plasma IL-6 (at HA4), plasma LBP (at HA8), and serum creatinine were also evident in CHA, indicating a greater inflammatory response, gastrointestinal leakage of lipopolysaccharide, and renal stress. The median increases in IL-6 and LBP in THA were in keeping with values previously presented for exercise heat stress (75–78). Similarly, although the *stage 1* AKI threshold was reached by two participants in CHA at HA4 and three participants in CHA at HA8, these rates are lower than have previously been reported during heat stress (79), possibly due to the reduced exercise component in the present study, and it has been suggested that the serum creatinine changes represent a normal physiological response to conserve fluid during heat stress that reflects neural, hormonal, and/or hemodynamic responses upstream of the kidneys (80). Our data are generally consistent with this interpretation, with no significant time, group, or interaction effects evident over the course of the HA intervention for our plasma and urine biomarkers markers of renal insult, with the exception of a smaller change in urine KIM-1 level during CHA. Moreover, comparison of the pre HST1 and pre HTS2 data demonstrated that serum creatinine (CHA: $t_{16} = -0.463$, $P = 0.650$), plasma LBP (CHA: $t_{15} = -0.638$, $P = 0.533$), and urine KIM-1 (THA: $t_{11} = 1.560$, $P = 0.147$) had returned to baseline levels after the intervention period indicating that these effects were transient. Plasma IL-6 remained slightly elevated following CHA ($Z = -2.72$, $P = 0.023$), but this difference was small [2.2 (6.6) pg·mL^{-1}] and did not persist when comparing the post HST1 and post HST2 data ($Z = -0.398$, $P = 0.691$).

Previous research has shown that when HA is defined solely by the number of daily exposures, ≤5 consecutive daily heat exposures typically results in an incomplete adaptation profile relative to longer HA interventions (15, 19, 20, 23–31), but these studies have not attempted to account for the lower total thermal dose accumulated over the shorter timescale. Our data indicate that CHA resulted in an array of adaptations consistent with the heat adapted phenotype, with the magnitude of many of the adaptations not different from those elicited by THA. In the main, the reduction in indices of peak thermal strain, as indicated by peak T_{rec} (CHA = −0.28°C vs. THA = −0.36°C), peak $\bar{T}_{sk}$ (CHA = −0.46°C vs. THA = −0.47°C), and peak $\bar{T}_b$ (CHA = −0.31°C vs. THA = −0.39°C) during the HST, was similar between the groups and in keeping with the magnitude of reduction reported by others. For example, for males undertaking 5–10 days of once daily HA (accumulating a total heat exposure of 643 ± 282 min vs. 600 min in the present study), reductions in peak T_c of approximately −0.3 to −0.4°C (25, 30, 58, 81–83), peak $\bar{T}_{sk}$ of approximately −0.4°C (25, 58, 83), and peak $\bar{T}_b$ of −0.4°C (58) have been reported. Thus, for these acclimation indices, the frequency of heat exposure may be less important than the total thermal dose administered. In contrast, for some resting indices of thermal strain [resting T_{rec} (CHA = −0.14°C vs. THA = −0.35°C); resting $\bar{T}_b$ (CHA = −0.11°C vs. THA = −0.33°C)], the magnitude of adaptation was less with CHA than THA. In a meta-analysis, Tyler et al. (84) reported a mean reduction in resting T_c of 0.17°C for both short term (4–7 days) and medium term (8–14 days) interventions, which was evaluated as being physiologically important and is broadly consistent with the reduction in resting T_{rec} seen with the 2-day CHA program. However, others have reported larger reductions in resting T_{rec} with 10–12 days of controlled-hyperthermia HA [−0.38°C (25); −0.38°C (30); −0.26°C (85)], including with a passive controlled-hyperthermia HA approach [−0.30°C (69)], that are more similar to the reduction in resting T_{rec} elicited by the THA intervention.

Although changes in sweating are often the slowest adaptations to fully manifest (7, 84, 86), our data indicate that both HA interventions significantly increased WBSR (CHA = +0.21 L·h^{-1} vs. THA = +0.34 L·h^{-1}). This equated to a +20% increase in WBSR over the 2-day CHA, which was fourfold greater than the mean increase (+5%) previously reported in a meta-analysis of studies using 4–7 days of daily HA (84) and suggests that CHA may accelerate sweating adaptation. Nevertheless, the increase in WBSR with CHA was less pronounced than with THA, possibly due to a lower WBSR during the HA sessions eliciting less sweat gland "training," or possibly as a result of differences in the time course of different components of sudomotor adaptation; it has been suggested that central modifications occur more rapidly than peripheral modifications, such as sweat gland hypertrophy and increased cholinergic sensitivity (7, 87). Moreover, sweat production is not the same as sweat evaporation, with acclimatization often resulting in the production of excess sweat (i.e., nonevaporated), which contributes little to evaporative heat loss (88). The similar magnitude of reduction in peak thermal strain during the postintervention HSTs, despite between-groups differences in WBSR, suggests that evaporative efficiency was improved to a greater extent with CHA than THA. This assertion is partially supported by the trend ($P = 0.051$) toward a larger reduction in sweat sodium content with CHA (CHA = −23 mmol·L^{-1} vs. THA = −8 mmol·L^{-1}), which would enhance evaporative heat loss for a given skin temperature (89). In addition, the lack of difference in local (back) sweat rate (see Table 4), which is consistent with the concept of site specific sudomotor adaptation (7), could have resulted in similar group increases in the percentage of wet skin surface area for evaporation, despite the between-groups differences in WBSR.

We demonstrated expanded PV and reduced average exercising and end-exercise heart rate during the post HA HST, with no differences between interventions. Given that cardiovascular adaptations are believed to manifest quickly (4–5 days) during HA (90, 91), it is perhaps unsurprising that cardiovascular stability was improved with CHA, with the observed increases in PV in keeping with previous literature examining short [5 days (21, 70, 92)] and medium term [10 days (25, 70)] controlled hyperthermia HA. In contrast, the reductions in average and peak exercise heart rate were slightly lower than previously reported, with meta-analysis indicating a 12 beats·min^{-1} reduction in average heart rate and 16 beats·min^{-1} reduction in "time-matched" heart rate with ≥4 days of HA (84). This difference is likely explained by the lower cardiovascular strain elicited by our "pseudo-passive" approach compared with the higher cardiovascular strain elicited by "active" HA interventions; the exercise component of active HA may account for ∼30% of the reduction in heart rate following an "active" HA program (46).

The reduced thermophysiological strain in both HA interventions likely underpinned the perceptual benefits apparent in both conditions, which included a lower thermal sensation, higher thermal comfort and a trend toward a reduction in RPE, which was not different between the groups. These perceptual measures are implicated in behavioral thermoregulation and the control of exercise work rate during heat stress (93), but further research is required to establish if the perceptual adaptations in the present study translate into performance benefit during exercise in the heat. In addition, time effects were evident for the within HST Δ serum HSP70 concentration and Δ serum creatinine, both of which were lower post-HA. Increases in serum HSP70 are associated with the achievement of a minimal T_{rec} level of 38.5°C (94), with the post intervention HST consistent with a mean peak T_{rec} of ∼38.2°C and in keeping with the post HA reductions in serum HSP concentration shown previously (26, 95). The reduction in the Δ serum creatinine post HA indicates superior renal function following the HA interventions, as has been demonstrated previously (79). Given that the reduction in Δ serum creatinine within HSTs was similar across groups, whereas renal strain was higher during the CHA intervention than THA intervention, we speculate that this effect is likely a consequence of improved renal perfusion post-HA due to the (similar) reduction in thermophysiological strain, rather than a renal adaptation per se.

Previous research suggests that HA can attenuate physiological strain during exposure to a hypoxic environment (40, 41) and also confer ergogenic benefit under temperate conditions (43). Our data indicate that both HA conditions increased resting and exercise O_2 pulse, reduced exercise heart rate and increased exercise Sp_{O_2}. These data are in accordance with previous research showing similar benefits after three or more days of HA (85, 96–99) but demonstrate for the first time that hypoxic cross-tolerance can be obtained with a 2-day CHA intervention. The range of cross-tolerance benefits was more pronounced when exercise was superimposed on the hypoxic stressor, a finding that is consistent with others (97). The precise mechanisms by which HA confers hypoxic cross-tolerance remain to be elucidated, although it has been suggested that adaptations occurring with HA can affect autonomic control through effects on central command, cardiopulmonary and arterial baroreflexes, and carotid chemoreflexes (91), each of which could contribute to a lowering of heart rate and an increased O_2 pulse, whereas a lower T_b would result in a leftward shift in the oxyhemoglobin dissociation curve and a higher Sp_{O_2} (99). In contrast, with the exception of an increase in the power output eliciting a [Lac] of 4 mmol·L^{-1} with THA, we found limited evidence of beneficial effect of HA on indices of temperate exercise performance with neither group significantly improving $\dot{V}O_{2max}$ or PPO during the GXT. The evidence supporting the benefits of HA on temperate endurance exercise indices is equivocal (45, 100). However, in contrast to the majority of previous studies (see Ref. 45), the present study minimized the exercise component of HA, thereby negating any potential training effects of the interventions. In addition, the timing of assessment after HA may determine whether any beneficial effect is observed (101) and we cannot exclude the possibility that different results would have been evident with a different period between the HA intervention and the subsequent GXT; such an effect might be particularly important with CHA where a longer recovery period may be necessary following the condensed stressor.

The reductions in thermal strain with both interventions were well-maintained over a 22-day deacclimation period, with no time, group, or interaction effects on resting or exercising (average and peak) indices of T_{rec}, and

$\bar{T}_b$, and exercising $\bar{T}_{sk}$. The extant literature on the decay in indices of thermal strain are contradictory. For example, Williams et al. (47) reported a 50% loss in T_{rec} adaptation over a 3-wk deacclimation period, with a meta-regression analysis suggesting that peak T_c decays at a rate of 2.6% per deacclimation day (50), although the decay in T_{rec} was less pronounced when the daily heat exposure duration was increased. In contrast, following a 9-day HA intervention, Pandolf et al. (49) reported little change (0%–18%) in T_{rec} or heart rate (2%–29%) over deacclimation periods of 3–18 days. Similarly, Weller et al. (15) reported that the reduction in resting and peak T_{rec} induced by a 10-day HA intervention was maintained over 12- and 26-day deacclimation periods, with peak $\bar{T}_{sk}$ adaptations maintained over a 12-day deacclimation period and only modest changes over the 26-day period, and "minimal" changes in heart rate over both time scales. The reasons for these discrepancies are unclear, but our data extend these observations by demonstrating that when a large-daily thermal dose is delivered on two consecutive days, the reductions in thermal and cardiovascular strain are well-maintained for up to 22 days. There was, however, evidence of a decay in WBSR with both groups, with a trend toward a larger reduction with THA (interaction effect $P = 0.051$). Others have also identified a dissociation between the rate of decay in WBSR and the decay in indices of thermal strain (25, 50) but our data also indicate that local (back) sweat rate was unaffected and that WBSR remained above the pre-exercise baseline levels; together this appears to have resulted in sufficient sweat evaporation to maintain the reduction in thermal strain over the decay period. Our data also indicate contraction of PV expansion in CHA, but not THA, but this did not appear to affect the reduction in cardiovascular strain during the HST, which was maintained in both groups. This is in contrast with the 2.3% loss in heart rate adaptations per decay day (50), or 90% loss over 3 wk reported previously (47), but is in keeping with the data of others (15, 49), and suggests the plasma volume changes do not underpin the retention of cardiovascular adaptations, which might be accounted for by the lower thermal strain and a diminished skin blood flow requirement.

The present study was not without limitations. Although within-participant crossover designs are typically stronger, evidence of re-acclimation and heat acclimation "memory" (15, 50, 102), and the potential confounders that may occur with prolonged washout periods (e.g., seasonal acclimatization status, training status and anthropometric factors, participant drop-out) mean that in the context of the present study, a between-groups design was most appropriate. For practical reasons, we did not include a third group performing one HA session per day for only 2 days, but numerous studies have shown incomplete adaptation over longer time scales (15, 19, 20, 23–31), and our design enabled us to examine our research question (i.e., whether the adaptations elicited by delivering a large thermal "dose"' over a condensed timescale differed from those elicited when a similar thermal "dose" was administered over a longer time scale). Our findings are only applicable to young, healthy males under the conditions studied. Previous research with once-daily HA suggests that that females may adapt over a slower timescale than males and future research should examine the efficacy of CHA in this cohort (81), whereas our peripheral blood flow data cannot be extrapolated to nonglabrous skin given the lack of active vasodilation at our assessment site (thumb). In addition, we cannot exclude that our results may have differed in less-humid environments supporting greater evaporation of produced sweat, where the between-groups differences in sweating rate may have translated into more pronounced differences in thermal profile. Likewise, although the elevated inflammation, gastrointestinal leakage, and renal stress with CHA was modest and transient, this may not be the case if an individual were to repeatedly use this type of intervention. It should also be noted that, although there was no group-level difference in the magnitude of postintervention reduction in peak T_{rec} and $\bar{T}_b$, one individual showed a pronounced elevation in peak T_{rec} and $\bar{T}_b$ following CHA, which might indicate a maladaptive response to this intervention. Related to this point, the time elapsed between the intervention and the assessment of efficacy may influence the changes detected (101), presumably by influencing the balance of residual fatigue with adaptation benefits; we cannot exclude the possibility that this differed between our groups, or that our post intervention assessments missed the optimal adaptation period.

In conclusion: *1)* compared with THA, the CHA intervention was associated with greater increases in some markers of inflammation and gastrointestinal leakage as well as elevated renal stress, but differences were generally modest and transient; *2)* CHA elicited an array of thermophysiological adaptations to heat stress that, for many aspects, did not differ from that acquired when a similar thermal dose was provided over a longer timescale; *3)* both CHA and THA improved aspects of hypoxic tolerance, with this effect more pronounced during hypoxic exercise than hypoxic rest, whereas benefits during temperate normoxic exercise were limited; *4)* reductions in thermal strain were well maintained over a 22-day decay period, although there was deacclimation in cutaneous blood flow, plasma and blood volume (in CHA), thermal comfort and WBSR. Together these novel data suggest that CHA might represent a viable option for time-restricted individuals preparing for exposure to hot conditions (e.g., military personnel, firefighters, athletes, individuals preparing for heat wave) and possibly high-altitude environments.

DATA AVAILABILITY

The source data are available to verified researchers upon request by contacting the corresponding author.

SUPPLEMENTAL MATERIAL

Supplemental Tables S1–S4: https://doi.org/10.17029/dce31fad-bf8f-4fc1-ba7d-0740968e0661.

ACKNOWLEDGMENTS

We acknowledge the valuable pilot work of Jennifer Wright, Liam Colley, and Jim House; the laboratory technical support by Danny White and Harry Mayes; the guidance provided by Nicola Armstrong, Graham White, Katrina Hinde, and Daniel Piccolo; and the MSc students who assisted in the laboratory.

GRANTS

This project was supported by grants from the Defence Science and Technology Laboratory.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

AUTHOR CONTRIBUTIONS

C.E.S., J.T.C., M.J.T., E.F.W., A.A.M.G., J.S.Y., B.J.L., F.A.M., and J.C. conceived and designed research; C.E.S., J.T.C., and J.C. performed experiments; C.E.S., J.T.C., M.J.T., E.F.W., A.A.M.G., J.S.Y., B.J.L., T.B.W., and J.C. analyzed data; C.E.S., J.T.C., M.J.T., E.F.W., A.A.M.G., J.S.Y., B.J.L., T.B.W., F.A.M., and J.C. interpreted results of experiments; C.E.S., J.T.C., A.A.M.G., J.S.Y., and J.C. prepared figures; C.E.S., J.T.C., M.J.T., E.F.W., and J.C. drafted manuscript; C.E.S., J.T.C., M.J.T., E.F.W., A.A.M.G., J.S.Y., B.J.L., T.B.W., F.A.M., and J.C. edited and revised manuscript; C.E.S., J.T.C., M.J.T., E.F.W., A.A.M.G., J.S.Y., B.J.L., T.B.W., F.A.M., and J.C. approved final version of manuscript.

REFERENCES

1. **Sawka MN**, **Leon LR**, **Montain SJ**, **Sonna LA.** Integrated physiological mechanisms of exercise performance, adaptation, and maladaptation to heat stress. *Compr Physiol* 1: 1883–1928, 2011. doi:10.1002/cphy.c100082.
2. **Parsons IT**, **Stacey MJ**, **Woods DR.** Heat adaptation in military personnel: mitigating risk, maximizing performance. *Front Physiol* 10: 1485, 2019. doi:10.3389/fphys.2019.01485.
3. **Périard JD**, **Eijsvogels TMH**, **Daanen HAM.** Exercise under heat stress: thermoregulation, hydration, performance implications, and mitigation strategies. *Physiol Rev* 101: 1873–1979, 2021. doi:10.1152/physrev.00038.2020.
4. **Cheuvront SN**, **Kenefick RW**, **Montain SJ**, **Sawka MN.** Mechanisms of aerobic performance impairment with heat stress and dehydration. *J Appl Physiol (1985)* 109: 1989–1995, 2010. doi:10.1152/japplphysiol.00367.2010.
5. **Wallace RF**, **Kriebel D**, **Punnett L**, **Wegman DH**, **Wenger CB**, **Gardner JW**, **Gonzalez RR.** The effects of continuous hot weather training on risk of exertional heat illness. *Med Sci Sports Exerc* 37: 84–90, 2005. doi:10.1249/01.mss.0000150018.90213.
6. **International Union of Physiological Sciences Thermal Commission.** Glossary of terms for thermal physiology. *Jpn J Physiol* 51: 245–280, 2001.
7. **Patterson MJ**, **Stocks JM**, **Taylor NA.** Humid heat acclimation does not elicit a preferential sweat redistribution toward the limbs. *Am J Physiol Regul Integr Comp Physiol* 286: R512–R518, 2004. doi:10.1152/ajpregu.00359.2003.
8. **Roberts MF**, **Wenger CB**, **Stolwijk JA**, **Nadel ER.** Skin blood flow and sweating changes following exercise training and heat acclimation. *J Appl Physiol Respir Environ Exerc Physiol* 43: 133–137, 1977. doi:10.1152/jappl.1977.43.1.133.
9. **Nadel ER**, **Pandolf KB**, **Roberts MF**, **Stolwijk JA.** Mechanisms of thermal acclimation to exercise and heat. *J Appl Physiol* 37: 515–520, 1974. doi:10.1152/jappl.1974.37.4.515.
10. **Bean WB**, **Eichna LW.** Performance in relation to environmental temperature. Reactions of normal young men to simulated desert environment. *Fed Proc* 2: 144–158, 1943.
11. **Eichna LW**, **Park CR**, **Nelson N**, **Horvath SM**, **Palmes ED.** Thermal regulation during acclimatization in a hot, dry (desert type) environment. *Am J Physiol* 163: 585–597, 1950. doi:10.1152/ajplegacy.1950.163.3.585.
12. **Armstrong LE**, **Casa DJ**, **Millard-Stafford M**, **Moran DS**, **Pyne SW**, **Roberts WO**; **American College of Sports Medicine.** Exertional heat illness during training and competition. *Med Sci Sports Exerc* 39: 556–572, 2007. doi:10.1249/MSS.0b013e31802fa199.
13. **Racinais S**, **Alonso JM**, **Coutts AJ**, **Flouris AD**, **Girard O**, **González-Alonso J**, **Hausswirth C**, **Jay O**, **Lee JK**, **Mitchell N**, **Nassis GP**, **Nybo L**, **Pluim BM**, **Roelands B**, **Sawka MN**, **Wingo J**, **Périard JD.** Consensus recommendations on training and competing in the heat. *Br J Sports Med* 49: 1164–1173, 2015. doi:10.1136/bjsports-2015-094915.
14. **Pandolf KB.** Time course of heat acclimation and its decay. *Int J Sports Med* 19, *Suppl* 2: S157–S160, 1998. doi:10.1055/s-2007-971985.
15. **Weller AS**, **Linnane DM**, **Jonkman AG**, **Daanen HA.** Quantification of the decay and re-induction of heat acclimation in dry-heat following 12 and 26 days without exposure to heat stress. *Eur J Appl Physiol* 102: 57–66, 2007. doi:10.1007/s00421-007-0563-z.
16. **Périard JD**, **Racinais S**, **Sawka MN.** Adaptations and mechanisms of human heat acclimation: Applications for competitive athletes and sports. *Scand J Med Sci Sports* 25, *Suppl* 1: 20–38, 2015. doi:10.1111/sms.12408.
17. **Joint Service Publication 375.** Chapter 41 Annex E. (Online). https://assets.publishing.service.gov.uk/media/6216303ae90e0710acb254e2/JSP_375_Chapter_41_Annex_E_Acclimatisation_-_V1.1_January_2022.pdf. [2 Feb 2024].
18. **Périard JD**, **Racinais S**, **Timpka T**, **Dahlström Ö**, **Spreco A**, **Jacobsson J**, **Bargoria V**, **Halje K**, **Alonso JM.** Strategies and factors associated with preparing for competing in the heat: a cohort study at the 2015 IAAF World Athletics Championships. *Br J Sports Med* 51: 264–270, 2017. doi:10.1136/bjsports-2016-096579.
19. **Sunderland C**, **Morris JG**, **Nevill ME.** A heat acclimation protocol for team sports. *Br J Sports Med* 42: 327–333, 2008 [Erratum in *Br J Sports Med* 43: 764, 2009]. doi:10.1136/bjsm.2007.034207.
20. **Petersen CJ**, **Portus MR**, **Pyne DB**, **Dawson BT**, **Cramer MN**, **Kellett AD.** Partial heat acclimation in cricketers using a 4-day high intensity cycling protocol. *Int J Sports Physiol Perform* 5: 535–545, 2010. doi:10.1123/ijspp.5.4.535.
21. **Garrett AT**, **Creasy R**, **Rehrer NJ**, **Patterson MJ**, **Cotter JD.** Effectiveness of short-term heat acclimation for highly trained athletes. *Eur J Appl Physiol* 112: 1827–1837, 2012. doi:10.1007/s00421-011-2153-3.
22. **Neal RA**, **Corbett J**, **Massey HC**, **Tipton MJ.** Effect of short-term heat acclimation with permissive dehydration on thermoregulation and temperate exercise performance. *Scand J Med Sci Sports* 26: 875–884, 2016. doi:10.1111/sms.12526.
23. **Kelly M**, **Gastin PB**, **Dwyer DB**, **Sostaric S**, **Snow RJ.** Short duration heat acclimation in Australian football players. *J Sports Sci Med* 15: 118–125, 2016.
24. **Convertino VA**, **Greenleaf JE**, **Bernauer EM.** Role of thermal and exercise factors in the mechanism of hypervolemia. *J Appl Physiol Respir Environ Exerc Physiol* 48: 657–664, 1980. doi:10.1152/jappl.1980.48.4.657.
25. **Neal RA**, **Massey HC**, **Tipton MJ**, **Young JS**, **Corbett J.** Effect of permissive dehydration on induction and decay of heat acclimation, and temperate exercise performance. *Front Physiol* 7: 564, 2016. doi:10.3389/fphys.2016.00564.
26. **Lee BJ**, **Thake CD.** Heat and hypoxic acclimation increase monocyte heat shock protein 72 but do not attenuate inflammation following hypoxic exercise. *Front Physiol* 8: 811, 2017. doi:10.3389/fphys.2017.00811.
27. **Buono MH**, **Kolding M**, **Leslie E**, **Moreno D**, **Norwood S**, **Ordille A**, **Weller R.** Heat acclimation causes a linear decrease in sweat sodium ion concentration. *J Therm Biol* 71: 237–240, 2018. doi:10.1016/j.jtherbio.2017.12.001.
28. **Kirby NV**, **Lucas SJE**, **Lucas RAI.** Nine-, but not four-days heat acclimation improves self-paced endurance performance in females. *Front Physiol* 10: 539, 2019. doi:10.3389/fphys.2019.00539.
29. **Klous L**, **De Ruiter C**, **Alkemade P**, **Daanen H**, **Gerrett N.** Sweat rate and sweat composition during heat acclimation. *J Therm Biol* 93: 102697, 2020. doi:10.1016/j.jtherbio.2020.102697.
30. **Moss JN**, **Bayne FM**, **Castelli F**, **Naughton MR**, **Reeve TC**, **Trangmar SJ**, **Mackenzie RWA**, **Tyler CJ.** Short-term isothermic heat acclimation elicits beneficial adaptations but medium-term elicits a more complete adaptation. *Eur J Appl Physiol* 120: 243–254, 2020. doi:10.1007/s00421-019-04269-5.
31. **Saillant MM**, **Charkoudian N**, **Salgado RM.** Individual variability in achievement of short-term heat acclimation during a fixed intensity protocol. *J Therm Biol* 110: 103373, 2022. doi:10.1016/j.jtherbio.2022.103373.

32. **Gibson OR**, **James CA**, **Mee JA**, **Willmott AGB**, **Turner G**, **Hayes M**, **Maxwell NS.** Heat alleviation strategies for athletic performance: a review and practitioner guidelines. *Temperature (Austin)* 7: 3–36, 2020. doi:10.1080/23328940.2019.1666624.
33. **Armstrong LE**, **VanHeest JL.** The unknown mechanism of the overtraining syndrome: clues from depression and psychoneuroimmunology. *Sports Med* 32: 185–209, 2002. doi:10.2165/00007256-200232030-00003.
34. **Lambert GP.** Role of gastrointestinal permeability in exertional heatstroke. *Exerc Sport Sci Rev* 32: 185–190, 2004. doi:10.1097/00003677-200410000-00011.
35. **Starkie RL**, **Hargreaves M**, **Rolland J**, **Febbraio MA.** Heat stress, cytokines, and the immune response to exercise. *Brain Behav Immun* 19: 404–412, 2005. doi:10.1016/j.bbi.2005.03.005.
36. **Donham BP**, **Frankfurt SB**, **Cartier RA**, **O'Hara SM**, **Sieg VC.** Low incidence of death and renal failure in United States military service members hospitalized with exertional heat stroke: a retrospective cohort study. *Mil Med* 185: 362–367, 2020. doi:10.1093/milmed/usz214.
37. **Notley SR**, **Meade RD**, **D'Souza AW**, **Friesen BJ**, **Kenny GP.** Heat loss is impaired in older men on the day after prolonged work in the heat. *Med Sci Sports Exerc* 50: 1859–1867, 2018. doi:10.1249/MSS.0000000000001643.
38. **Pryor RR**, **Pryor JL**, **Vandermark LW**, **Adams EL**, **Brodeur RM**, **Armstrong LE**, **Lee EC**, **Maresh CM**, **Anderson JM**, **Casa DJ.** Exacerbated heat strain during consecutive days of repeated exercise sessions in heat. *J Sci Med Sport* 22: 1084–1089, 2019. doi:10.1016/j.jsams.2019.06.00.
39. **Tipton M.** A case for combined environmental stressor studies. *Extrem Physiol Med* 1: 7, 2012. doi:10.1186/2046-7648-1-7.
40. **Gibson OR**, **Taylor L**, **Watt PW**, **Maxwell NS.** Cross-adaptation: heat and cold adaptation to improve physiological and cellular responses to hypoxia. *Sports Med* 47: 1751–1768, 2017. doi:10.1007/s40279-017-0717-z.
41. **Sotiridis A**, **Debevec T**, **Geladas N**, **Mekjavic IB.** Cross-adaptation between heat and hypoxia: mechanistic insights into aerobic exercise performance. *Am J Physiol Regul Integr Comp Physiol* 323: R661–R669, 2022. doi:10.1152/ajpregu.00339.2021.
42. **Lorenzo S**, **Halliwill JR**, **Sawka MN**, **Minson CT.** Heat acclimation improves exercise performance. *J Appl Physiol (1985)* 109: 1140–1147, 2010. doi:10.1152/japplphysiol.00495.2010.
43. **Corbett J**, **Neal RA**, **Lunt HC**, **Tipton MJ.** Adaption to heat and exercise performance under cooler conditions: a new hot topic. *Sports Med* 44: 1323–1331, 2014. doi:10.1007/s40279-014-0212-8.
44. **Sotiridis A**, **Debevec T**, **Ciuha U**, **Eiken O**, **Mekjavic IB.** Heat acclimation does not affect maximal aerobic power in thermoneutral normoxic or hypoxic conditions. *Exp Physiol* 104: 345–358, 2019. doi:10.1113/EP087268.
45. **Waldron M**, **Fowler R**, **Heffernan S**, **Tallent J**, **Kilduff L**, **Jeffries O.** Effects of heat acclimation and acclimatisation on maximal aerobic capacity compared to exercise alone in both thermoneutral and hot environments: a meta-analysis and meta-regression. *Sports Med* 51: 1509–1525, 2021. doi:10.1007/s40279-021-01445-6.
46. **Corbett J**, **Massey HC**, **Costello JT**, **Tipton MJ**, **Neal RA.** The effect of medium-term heat acclimation on endurance performance in a temperate environment. *Eur J Sport Sci* 22: 190–199, 2022. doi:10.1080/17461391.2020.1856935.
47. **Williams CG**, **Wyndham CH**, **Morrison JF.** Rate of loss of acclimatization in summer and winter. *J Appl Physiol* 22: 21–26, 1967. doi:10.1152/jappl.1967.22.1.21.
48. **Givoni B**, **Goldman RF.** Predicting effects of heat acclimatization on heart rate and rectal temperature. *J Appl Physiol* 35: 875–879, 1973. doi:10.1152/jappl.1973.35.6.875.
49. **Pandolf KB**, **Burse RL**, **Goldman RF.** Role of physical fitness in heat acclimatisation, decay and reinduction. *Ergonomics* 20: 399–408, 1977. doi:10.1080/00140137708931642.
50. **Daanen HAM**, **Racinais S**, **Périard JD.** Heat acclimation decay and re-induction: a systematic review and meta-analysis. *Sports Med* 48: 409–430, 2018. doi:10.1007/s40279-017-0808-x.
51. **Marshall HC**, **Campbell SA**, **Roberts CW**, **Nimmo MA.** Human physiological and heat shock protein 72 adaptations during the initial phase of humid-heat acclimation. *J Therm Biol* 32: 341–348, 2007. doi:10.1016/j.jtherbio.2007.04.003.
52. **McIntyre RD**, **Zurawlew MJ**, **Oliver SJ**, **Cox AT**, **Mee JA**, **Walsh NP.** A comparison of heat acclimation by post-exercise hot water immersion and exercise in the heat. *J Sci Med Sport* 24: 729–734, 2021. doi:10.1016/j.jsams.2021.05.008.
53. **Durnin JV**, **Womersley J.** Body fat assessed from total body density and its estimation from skinfold thickness: measurements on 481 men and women aged from 16 to 72 years. *Br J Nutr* 32: 77–97, 1974. doi:10.1079/bjn19740060.
54. **Dervis S**, **Coombs GB**, **Chaseling GK**, **Filingeri D**, **Smoljanic J**, **Jay O.** A comparison of thermoregulatory responses to exercise between mass-matched groups with large differences in body fat. *J Appl Physiol (1985)* 120: 615–623, 2016. doi:10.1152/japplphysiol.00906.2015.
55. **Cramer MN**, **Jay O.** Explained variance in the thermoregulatory responses to exercise: the independent roles of biophysical and fitness/fatness-related factors. *J Appl Physiol (1985)* 119: 982–989, 2015. doi:10.1152/japplphysiol.00281.2015.
56. **Bain AR**, **Jay O.** Does summer in a humid continental climate elicit an acclimatization of human thermoregulatory responses? *Eur J Appl Physiol* 111: 1197–1205, 2011. doi:10.1007/s00421-010-1743-9.
57. **Gibson OR**, **Mee JA**, **Tuttle JA**, **Taylor L**, **Watt PW**, **Maxwell NS.** Isothermic and fixed intensity heat acclimation methods induce similar heat adaptation following short and long-term timescales. *J Therm Biol* 49-50: 55–65, 2015. doi:10.1016/j.jtherbio.2015.02.005.
58. **Rendell RA**, **Prout J**, **Costello JT**, **Massey HC**, **Tipton MJ**, **Young JS**, **Corbett J.** Effects of 10 days of separate heat and hypoxic exposure on heat acclimation and temperate exercise performance. *Am J Physiol Regul Integr Comp Physiol* 313: R191–R201, 2017. doi:10.1152/ajpregu.00103.2017.
59. **Cramer MN**, **Jay O.** Biophysical aspects of human thermoregulation during heat stress. *Auton Neurosci* 196: 3–13, 2016. doi:10.1016/j.autneu.2016.03.001.
60. **Lunt HC**, **Barwood MJ**, **Corbett J**, **Tipton MJ.** 'Cross-adaptation': habituation to short repeated cold-water immersions affects the response to acute hypoxia in humans. *J Physiol* 588: 3605–3613, 2010. doi:10.1113/jphysiol.2010.193458.
61. **Ramanathan NL.** A new weighting system for mean surface temperature of the human body. *J Appl Physiol* 19: 531–533, 1964. doi:10.1152/jappl.1964.19.3.531.
62. **Miller KC**, **Hughes LE**, **Long BC**, **Adams WM**, **Casa DJ.** Validity of core temperature measurements at 3 rectal depths during rest, exercise, cold-water immersion, and recovery. *J Athl Train* 52: 332–338, 2017. doi:10.4085/1062-6050-52.2.10.
63. **Jay O**, **Gariépy LM**, **Reardon FD**, **Webb P**, **Ducharme MB**, **Ramsay T**, **Kenny GP.** A three-compartment thermometry model for the improved estimation of changes in body heat content. *Am J Physiol Regul Integr Comp Physiol* 292: R167–75, 2007. doi:10.1152/ajpregu.00338.2006.
64. **Borg GA.** Psychophysical bases of perceived exertion. *Med Sci Sports Exer* 14: 377–381, 1982. doi:10.1249/00005768-198205000-00012.
65. **Dill DB**, **Costill DL.** Calculation of percentage changes in volumes of blood, plasma, and red cells in dehydration. *J Appl Physiol* 37: 247–248, 1974. doi:10.1152/jappl.1974.37.2.247.
66. **Ricci Z**, **Cruz DN**, **Ronco C.** Classification and staging of acute kidney injury: beyond the RIFLE and AKIN criteria. *Nat Rev Nephrol* 7: 201–208, 2011. doi:10.1038/nrneph.2011.14.
67. **Bongers CCWG**, **Alsady M**, **Nijenhuis T**, **Tulp ADM**, **Eijsvogels TMH**, **Deen PMT**, **Hopman MTE.** Impact of acute versus prolonged exercise and dehydration on kidney function and injury. *Physiol Rep* 6: e13734, 2018. doi:10.14814/phy2.13734.
68. **Goulet EDB**, **Asselin A**, **Gosselin J**, **Baker LB.** Measurement of sodium concentration in sweat samples: comparison of 5 analytical techniques. *Appl Physiol Nutr Metab* 42: 861–868, 2017. doi:10.1139/apnm-2017-0059.
69. **Fox RH**, **Goldsmith R**, **Kidd DJ**, **Lewis HE.** Acclimatization to heat in man by controlled elevation of body temperature. *J Physiol* 166: 530–547, 1963. doi:10.1113/jphysiol.1963.sp007121.
70. **Willmott AGB**, **Hayes M**, **James CA**, **Dekerle J**, **Gibson OR**, **Maxwell NS.** Once- and twice-daily heat acclimation confer similar heat adaptations, inflammatory responses and exercise tolerance improvements. *Physiol Rep* 6: e13936, 2018. doi:10.14814/phy2.13936.
71. **Edwards B**, **Waterhouse J**, **Reilly T**, **Atkinson G.** A comparison of the suitabilities of rectal, gut, and insulated axilla temperatures for

measurement of the circadian rhythm of core temperature in field studies. *Chronobiol Int* 19: 579–597, 2002. doi:10.1081/cbi-120004227.
72. **Taylor NA.** Human heat adaptation. *Compr Physiol* 4: 325–365, 2014. doi:10.1002/cphy.c130022.
73. **Peter J**, **Wyndham CH.** Activity of the human eccrine sweat gland during exercise in a hot humid environment before and after acclimatization. *J Physiol* 187: 583–594, 1966. doi:10.1113/jphysiol.1966.sp008110.
74. **Candas V**, **Libert JP**, **Vogt JJ.** Effect of hidromeiosis on sweat drippage during acclimation to humid heat. *Eur J Appl Physiol Occup Physiol* 44: 123–133, 1980. doi:10.1007/BF00421090.
75. **Costello JT**, **Rendell RA**, **Furber M**, **Massey HC**, **Tipton MJ**, **Young JS**, **Corbett J.** Effects of acute or chronic heat exposure, exercise and dehydration on plasma cortisol, IL-6 and CRP levels in trained males. *Cytokine* 110: 277–283, 2018. doi:10.1016/j.cyto.2018.01.018.
76. **Roca Rubio MF**, **Eriksson U**, **Brummer RJ**, **König J.** Sauna dehydration as a new physiological challenge model for intestinal barrier function. *Sci Rep* 11: 15514, 2021. doi:10.1038/s41598-021-94814-0.
77. **Wallett AM**, **Etxebarria N**, **Beard NA**, **Saunders PU**, **Welvaert M**, **Périard JD**, **McKune AJ**, **Pyne DB.** Running at increasing intensities in the heat induces transient gut perturbations. *Int J Sports Physiol Perform* 16: 704–710, 2021. doi:10.1123/ijspp.2019-0973.
78. **Lee BJ**, **Flood TR**, **Galan-Lopez N**, **McCormick JJ**, **King KE**, **Fujii N**, **Kenny GP.** Changes in surrogate markers of intestinal epithelial injury and microbial translocation in young and older men during prolonged occupational heat stress in temperate and hot conditions. *Eur J Appl Physiol* 124: 1049–1062, 2024. doi:10.1007/s00421-023-05329-7.
79. **Omassoli J**, **Hill NE**, **Woods DR**, **Delves SK**, **Fallowfield JL**, **Brett SJ**, **Wilson D**, **Corbett RW**, **Allsopp AJ**, **Stacey MJ.** Variation in renal responses to exercise in the heat with progressive acclimatisation. *J Sci Med Sport* 22: 1004–1009, 2019. doi:10.1016/j.jsams.2019.04.010.
80. **Schlader ZJ**, **Hostler D**, **Parker MD**, **Pryor RR**, **Lohr JW**, **Johnson BD**, **Chapman CL.** The potential for renal injury elicited by physical work in the heat. *Nutrients* 11: 2087, 2019. doi:10.3390/nu11092087.
81. **Mee JA**, **Gibson OR**, **Doust J**, **Maxwell NS.** A comparison of males and females' temporal patterning to short- and long-term heat acclimation. *Scand J Med Sci Sports* 25, *Suppl* 1: 250–258, 2015. doi:10.1111/sms.12417.
82. **Zurawlew MJ**, **Walsh NP**, **Fortes MB**, **Potter C.** Post-exercise hot water immersion induces heat acclimation and improves endurance exercise performance in the heat. *Scand J Med Sci Sports* 26: 745–754, 2016. doi:10.1111/sms.12638.
83. **Parsons IT**, **Snape D**, **Stacey MJ**, **Barlow M**, **O'Hara J**, **Gall N**, **Chowienczyk P**, **Wainwright B**, **Woods DR.** Improvements in orthostatic tolerance with exercise are augmented by heat acclimation: a randomised controlled trial. *Med Sci Sports Exerc* 56: 644–654, 2024. doi:10.1249/MSS.0000000000003355.
84. **Tyler CJ**, **Reeve T**, **Hodges GJ**, **Cheung SS.** The effects of heat adaptation on physiology, perception and exercise performance in the heat: a meta-analysis. *Sports Med* 46: 1699–1724, 2016 [Erratum in *Sports Med* 46: 1771, 2016]. doi:10.1007/s40279-016-0538-5.
85. **Lee BJ**, **Miller A**, **James RS**, **Thake CD.** Cross acclimation between heat and hypoxia: heat acclimation improves cellular tolerance and exercise performance in acute normobaric hypoxia. *Front Physiol* 7: 78, 2016. doi:10.3389/fphys.2016.00078.
86. **Cotter JD**, **Patterson MJ**, **Taylor NA.** Sweat distribution before and after repeated heat exposure. *Eur J Appl Physiol Occup Physiol* 76: 181–186, 1997. doi:10.1007/s004210050232.
87. **Sato K**, **Sato F.** Individual variations in structure and function of human eccrine sweat gland. *Am J Physiol* 245: R203–R208, 1983. doi:10.1152/ajpregu.1983.245.2.R203.
88. **Mitchell D**, **Senay LC**, **Wyndham CH**, **van Rensburg AJ**, **Rogers GG**, **Strydom NB.** Acclimatization in a hot, humid environment: energy exchange, body temperature, and sweating. *J Appl Physiol* 40: 768–778, 1976. doi:10.1152/jappl.1976.40.5.768.
89. **Gerrett N**, **Amano T**, **Inoue Y**, **Kondo N.** The sweat glands' maximum ion reabsorption rates following heat acclimation in healthy older adults. *Exp Physiol* 106: 302–315, 2021. doi:10.1113/EP088486.
90. **Senay LC**, **Mitchell D**, **Wyndham CH.** Acclimatization in a hot, humid environment: body fluid adjustments. *J Appl Physiol* 40: 786–796, 1976. doi:10.1152/jappl.1976.40.5.786.
91. **Périard JD**, **Travers GJS**, **Racinais S**, **Sawka MN.** Cardiovascular adaptations supporting human exercise-heat acclimation. *Auton Neurosci* 196: 52–62, 2016. doi:10.1016/j.autneu.2016.02.002.
92. **Tebeck ST**, **Buckley JD**, **Bellenger CR**, **Stanley J.** Differing physiological adaptations induced by dry and humid short-term heat acclimation. *Int J Sports Physiol Perform* 15: 133–140, 2020. doi:10.1123/ijspp.2018-0707.
93. **Flouris AD**, **Schlader ZJ.** Human behavioral thermoregulation during exercise in the heat. *Scand J Med Sci Sports* 25, *Suppl* 1: 52–64, 2015. doi:10.1111/sms.12349.
94. **Gibson OR**, **Dennis A**, **Parfitt T**, **Taylor L**, **Watt PW**, **Maxwell NS.** Extracellular Hsp72 concentration relates to a minimum endogenous criteria during acute exercise-heat exposure. *Cell Stress Chaperones* 19: 389–400, 2014. doi:10.1007/s12192-013-0468-1.
95. **Magalhães Fde C**, **Amorim FT**, **Passos RL**, **Fonseca MA**, **Oliveira KP**, **Lima MR**, **Guimarães JB**, **Ferreira-Júnior JB**, **Martini AR**, **Lima NR**, **Soares DD**, **Oliveira EM**, **Rodrigues LO.** Heat and exercise acclimation increases intracellular levels of Hsp72 and inhibits exercise-induced increase in intracellular and plasma Hsp72 in humans. *Cell Stress Chaperones* 15: 885–895, 2010. doi:10.1007/s12192-010-0197-7.
96. **Heled Y**, **Peled A**, **Yanovich R**, **Shargal E**, **Pilz-Burstein R**, **Epstein Y**, **Moran DS.** Heat acclimation and performance in hypoxic conditions. *Aviat Space Environ Med* 83: 649–653, 2012. doi:10.3357/asem.3241.2012.
97. **Gibson OR**, **Turner G**, **Tuttle JA**, **Taylor L**, **Watt PW**, **Maxwell NS.** Heat acclimation attenuates physiological strain and the HSP72, but not HSP90α, mRNA response to acute normobaric hypoxia. *J Appl Physiol (1985)* 119: 889–899, 2015. doi:10.1152/japplphysiol.00332.2015.
98. **Lee BJ**, **Mackenzie RW**, **Cox V**, **James RS**, **Thake CD.** Human monocyte heat shock protein 72 responses to acute hypoxic exercise after 3 days of exercise heat acclimation. *Biomed Res Int* 2015: 849809, 2015. doi:10.1155/2015/849809.
99. **White AC**, **Salgado RM**, **Schneider S**, **Loeppky AJ**, **Astorino AT**, **Mermier CM.** Does heat acclimation improve exercise capacity at altitude? A cross-tolerance model. *Int J Sports Med* 35: 975–981, 2014. doi:10.1055/s-0034-1368724.
100. **Borg DN**, **O'Brien JL.** Comment on "effects of heat acclimation and acclimatisation on maximal aerobic capacity compared to exercise alone in both thermoneutral and hot environments: a meta-analysis and meta-regression". *Sports Med* 52: 1715–1718, 2022. doi:10.1007/s40279-021-01611-w.
101. **Waldron M**, **Jeffries O**, **Tallent J**, **Patterson S**, **Nevola V.** The time course of adaptations in thermoneutral maximal oxygen consumption following heat acclimation. *Eur J Appl Physiol* 119: 2391–2399, 2019. doi:10.1007/s00421-019-04218-2.
102. **Tetievsky A**, **Assayag M**, **Ben-Hamo R**, **Efroni S**, **Cohen G**, **Abbas A**, **Horowitz M.** Heat acclimation memory: do the kinetics of the deacclimated transcriptome predispose to rapid reacclimation and cytoprotection? *J Appl Physiol (1985)* 117: 1262–1277, 2014. doi:10.1152/japplphysiol.00422.2014.