TITLE

Effects of acute or chronic heat exposure, exercise and dehydration on plasma cortisol, IL-6 and CRP levels in trained males

RUNNING TITLE

Heat acclimation: Plasma Cortisol, Interleukin-6, and C-Reactive Protein

AUTHORS

Joseph T. Costello[1], Rebecca A. Rendell[1,2], Matthew Furber[3,4], Heather C. Massey[1], Michael J. Tipton[1], John S. Young[5], Jo Corbett[1]

AFFILIATION

[1] Extreme Environments Laboratory, Department of Sport and Exercise Science, University of Portsmouth, United Kingdom

[2] Department of Sport and Physical Activity, Bournemouth University, United Kingdom

[3] University of Hertfordshire, Division of Sport, Health and Exercise Science, College Lane, Hatfield, Hertfordshire, AL10 9AB, UK

[4] GlaxoSmithKline (GSK) Human Performance Lab, Unit 2 Brentside Executive Park, Great West Road, Brentford, Middlesex, TW8 9DA, UK

[5] School of Pharmacy and Biomedical Sciences, University of Portsmouth, Portsmouth, UK

CORRESPONDING AUTHOR

Dr Joseph T Costello, Ph.D.

Address: Department of Sport and Exercise Science, University of Portsmouth, PO1 2ER, United Kingdom.

Email: joe.costello@port.ac.uk

Phone: +44 23 9284 5366

Abstract

This study examined the acute and chronic effects of euhydrated and hypohydrated heat exposure, on biomarkers of stress and inflammation. Eight trained males [mean (SD) age: 21 (3) y; mass: 77.30 (4.88) kg; $\dot{V}O_{2max}$: 56.9 (7.2) $mL \cdot kg^{-1} \cdot min^{-1}$] undertook two heat acclimation programmes (balanced cross-over design), once drinking to maintain euhydration and once with restricted fluid-intake (permissive dehydration). Days 1, 6, and 11 were 60 min euhydrated exercise-heat stress tests (40 °C; 50 % RH, 35% peak power output), days 2–5 and 7–10 were 90 min, isothermal-strain (target rectal temperature: 38.5 °C) exercise-heat sessions. Plasma was obtained pre- and post- exercise on day 1, 2, and 11 and analysed for cortisol, interleukin-6 (IL-6), and C-reactive protein (CRP). Cortisol and CRP were also assessed on day 6. IL-6 was elevated following the initial (acute) 90 minute isothermal heat strain exercise-heat exposure (day 2) with permissive dehydration ((pre exercise: 1.0 $pg \cdot mL^{-1}$ [0.9], post-exercise: 1.8 $pg \cdot mL^{-1}$ [1.0], P = 0.032) and when euhydrated (pre-exercise: 1.0 $pg \cdot mL^{-1}$ [1.4], post-exercise: 1.6 $pg \cdot mL^{-1}$ [2.1], P = 0.048). Plasma cortisol levels were also elevated but only during permissive dehydration (P = 0.032). Body mass loss was strongly correlated with Δcortisol (r = -0.688, P = 0.003). Although there was a trend for post-exercise cortisol to be decreased following both heat acclimation programmes (chronic effects), there were no within or between intervention differences in IL-6 or CRP. In conclusion, acute exercise in the heat increased IL-6 and cortisol only when fluid-intake is restricted. There were no chronic effects of either intervention on biomarkers of inflammation as evidenced by IL-6 and CRP returning to basal level at the end of heat acclimation.

Keywords

Thermoregulation, stress, extreme environments, acclimatization, acclimation,

Highlights

- Acute exercise in the heat increases IL-6 regardless of hydration status
- Acute exercise in the heat increases cortisol only when fluid-intake is restricted
- This cortisol response was strongly correlated with whole body sweat loss
- Cortisol, IL-6 and CRP were not augmented after heat acclimation

1. Introduction

Heat acclimation improves perceptions of thermal comfort and submaximal, as well as maximal, aerobic exercise performance in warm-hot conditions [34,37,42] and possibly cool environments [12,31,38]. The performance and perceptual benefits associated with heat acclimation are achieved via an earlier onset of sweating, plasma volume expansion, and alterations in fluid-electrolyte balance which ultimately lead to an attenuated rise in body core temperature and lower cardiac frequency during rest and exercise [12,22,37,41]. Consequently, various heat acclimation protocols are employed in both occupational and sporting settings in an attempt to minimise the physiological challenges encountered during prolonged exercise in the heat [30].

Some benefits of heat acclimation, including improved cardiovascular stability, occur within the first few days [36,37]. The logistics, in relation to time and cost, associated with longer heat acclimation protocols may be difficult for many athletes and occupational personnel e.g. prior to competition or preceding military deployment. Therefore, the extent of adaptations from short- (≤7 heat exposures) and medium-term (8-14 heat exposures) heat acclimation programmes have recently received interest [9,42]. In an attempt to enhance the beneficial effect of shorter term heat acclimation Garett and colleagues [21] provided evidence that in contrast to traditional hydration guidance [3], restricting fluid intake (permissive dehydration) during a 5-day heat acclimation may provide a supplemental stimulus with some positive effects. Specifically, compared to a euhydrated heat acclimation programme, daily mild dehydration led to higher resting body mass, a tendency for a greater

expansion of plasma volume, a larger rise in resting forearm perfusion by way of higher vascular conductance, and a larger reduction in cardiac frequency during exercise [21]. However, the current literature base is contradictory and Neal et al [33] have recently reported that permissive dehydration during a medium term heat acclimation protocol did not positively affect the acquisition and decay of heat acclimation, or endurance performance parameters, although no negative effects were reported either.

Regardless of these inconsistent findings, short- and medium-term heat acclimation programmes are becoming increasingly popular in team sports and in various occupational settings [9,34,42]. However, few researchers have considered the potential negative side effects [26,42,47]. It is well established that strenuous endurance exercise results in an acute immune and stress response. Typical features of this response are alterations in cortisol [4,48], and the peripheral distribution pattern of leukocytes [35], and increases in cytokine concentration (e.g. interleukin-6 [IL-6]; [2,26]) as well as other inflammatory biomarkers such as C-reactive protein (CRP) [35].

Further, exercise in high ambient temperatures is known to exert a synergistic impact on the stress response to exercise [2,19,26]. The acute stress (e.g. cortisol) and inflammatory responses (e.g. cytokines) following exercise in hot temperatures exceed those seen in cooler conditions [39,45]. Despite reports suggesting that restricting fluid intake during acute exercise augments the plasma cortisol response [4,6,17,29] and cytokine production [25,26], the independent effects of hydration status on the stress and inflammatory responses to heat acclimation has received

little attention. The increased physical and psychological strain experienced during heat acclimation, combined with the possibility of inadequate recovery, may increase potential for minor illnesses [26,46] and ultimately impair subsequent exercise performance [42,47].

Accordingly, the primary aim of this study was to investigate the acute and chronic effects of 11-day euhydrated and dehydrated heat acclimation protocols on biomarkers of stress and inflammation. It was hypothesised that circulating levels of cortisol, IL-6, and CRP, after an initial (acute exposure) isothermal-strain exercise-heat session, would be elevated and that the permissive dehydration would exaggerate this response. Similarly, we hypothesised that resting and post-exercise levels of cortisol, IL-6 and CRP would be augmented at the end (chronic exposure) of the permissive dehydration heat acclimation protocol.

2. Methods

2.1. Participants

Eight un-acclimated, trained male athletes (>150 km cycling weekly) [mean (SD) age: 21 (3) years, body mass: 77.3 (4.9) kg, stature: 181 (5) cm, $\dot{V}O_{2max}$: 56.9 (7.2) $mL \cdot kg^{-1} \cdot min^{-1}$; peak power output: 338 (46) W] volunteered and provided written informed consent for the study, which was conducted in accordance with the Institution's ethics and governance committee and Declaration of Helsinki [2013]. Participants were all engaged in recreational endurance exercise (running, cycling, and triathlon) and free from any symptoms of illness, inflammation or soreness at the

start of the study. Participants were also instructed not to take any medication, including anti-inflammatories, for the duration of the experiment.

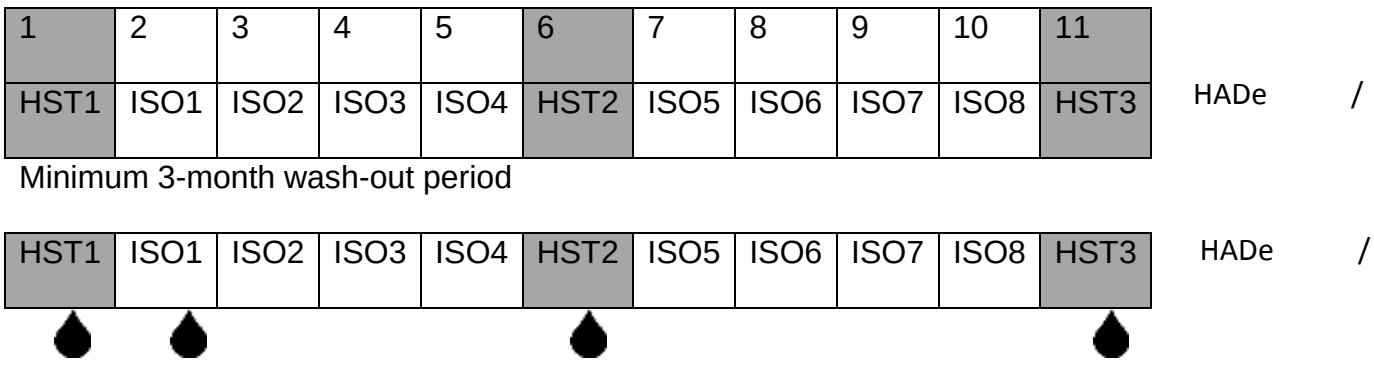
2.2. Experimental design

This study was part of a larger project investigating effects of heat acclimation on performance variables in trained cyclists, and the experimental design has been described in detail elsewhere [33]. Briefly, a within-participant, balanced cross-over design (with three months washout) was employed, with participants undertaking both control [euhydrated heat acclimation (HAEu)] and intervention [permissive dehydration (HADe)] HA programmes (target ambient conditions: 40°C; 50% RH). Four participants completed the HAEu first. Each HA programme lasted 11-days and consisted of three bouts of exercise at a fixed external work rate [heat stress test (HST)], undertaken on day 1 (HSTpre), day 6, and day 11 (HSTpost).. The HST was completed on a CompuTrainer cycle ergometer (RacerMate Inc., Seattle, Washington, USA) for 60 min at 35% of peak power output. During the HSTs 1.25 L of 3.6 % carbohydrate-electrolyte solution (drink temperature 20 °C) was ingested to replace fluid losses, divided into five boluses (0.25 L) and consumed immediately prior to commencing exercise and every 15 min thereafter.

HSTs were interspersed with eight (days 2–5 and 7–10) isothermal strain exercise-heat exposures (ISO). The ISO consisted of cycling (RacerMate Inc., Seattle, WA, USA), at a work rate eliciting a rating of perceived exertion (RPE; [5]) of 15 (anchored by the word ‘Hard’) until rectal temperature reached 38.3 °C, at which point external power output was adjusted as appropriate to maintain the target rectal

temperature of 38.5 °C. Each ISO lasted a total of 90 minutes. Rectal temperature was recorded using a thermistor (Grant Instruments, Cambridge, UK) self-inserted 15 cm beyond the anal sphincter. Nude body mass (dry) was measured pre- and post-each test session (Industrial Electronic Weight Indicator, Modell 10, Ohaus Corporation, Parsippany, NJ, USA). As previously described [33], during the HAEu intervention all participants consumed 0.25 L of 3.6 % carbohydrate-electrolyte fluid (Science in Sport, Nelson, UK) every 15 min, including immediately before and after each ISO (total fluid consumed = 1.75 L); drink temperature was 20 °C. After exercise, participants were encouraged to drink *ad libitum* to ensure similar hydration for the following day. Permissive dehydration was achieved by restricting fluid intake during exercise [21] and no fluid was provided in the HADe during each ISO, or for 10 min after. Thereafter, participants consumed 1.75 L of the same beverage and were encouraged to drink *ad libitum* to ensure adequate hydration for the following day. Blood was sampled at a similar time of day for all participants to limit diurnal variation.

Figure 1. Graphical presentation of the study protocol



denotes blood sampling before and after exercise in the heat, isothermal heat strain (ISO), heat stress test (HST), euhydrated heat acclimation (HAEu), permissive dehydration heat acclimation (HADe).

2.3. Blood sampling procedure

Immediately before and after exercise on day 1, 2, 6, and 11 a 10 mL venous blood samples was obtained (K2 EDTA blood collection tubes, Beckton Dickson & Company, Plymouth, UK) from the antecubital vein following 10 min of seated rest. Haemoglobin concentration (201^{+} HemoCue, Sweden) and haematocrit (Hawksley, Lancing, UK) were measured in triplicate. These values were used to estimate plasma volume changes using the method of Dill and Costill [13]. Whole blood samples were centrifuged (1500g for 15min at 4 °C, Heraeus^{TM} Multifuge^{TM} 3 S-R, ThermoElectron Corporation, Germany) and the resultant plasma stored at −80 °C. IL-6 (Promo Kine, PromoCell, Sickingenstrasse, 69126 Heidelberg, Germany; Sigma Aldrich, St Louis, MO 63103 USA), CRP (RayBiotech, Inc., Norcross, GA 30092, USA) and cortisol (Sigma-Aldrich, St Louis, MO 63103 USA) were measured in plasma using commercially available quantitative human enzyme linked immunosorbent assays (ELISA) kits. Manufacturer instructions were followed for high sensitivity for each of the kits and repeated freeze-thaw cycles of plasma were minimized. Intra-assay coefficient of variations for IL-6 was 6.8% (acute: Promokine) and 19.6% (chronic: Sigma-Aldrich), and 5.8% and 4.0% for CRP and Cortisol respectively. Minimum detectable plasma concentrations were 0.92 $pg \cdot mL^{-1}$ for IL-6, 34 $pg \cdot mL^{-1}$ for CRP, and 26.3 $ng \cdot mL^{-1}$ for Cortisol. All analytes were corrected for changes in plasma volume before statistical analysis.

2.4. Statistical analyses

The distribution of data was assessed using descriptive methods (skewness, outliers, and distribution plots) and inferential statistics (Shapiro–Wilk test). Acute body mass loss on day 2 and chronic body mass losses (average of HADe and HAEu sessions) were analysed using separate paired sample t-tests. The acute and chronic effects of exercising in a dehydrated state on plasma IL-6, CRP, and cortisol was analysed non-parametrically using a Friedman analysis of variance. Post-hoc analysis using a one-sided Wilcoxon signed rank test and a Bonferroni correction was employed where appropriate. Spearman correlations were used to determine relationships between the change in IL-6, CRP, and cortisol and the within session change in nude body mass. Correlation coefficients were considered as strong (≥ 0.60), moderate (0.40 to 0.59), and weak (0.2–0.39) [10]. All statistical analyses were performed using SPSS (Statistical Package for the Social Sciences), version 22.0 (SPSS Inc, Chicago, IL, USA). Statistical significance was accepted at $P < 0.05$, and a statistical trend defined as $P < 0.10$. All data are expressed as means (SD) for parametric data and medians (interquartile range [IQR]) for non-parametric data.

3. Results

3.1. Body mass changes

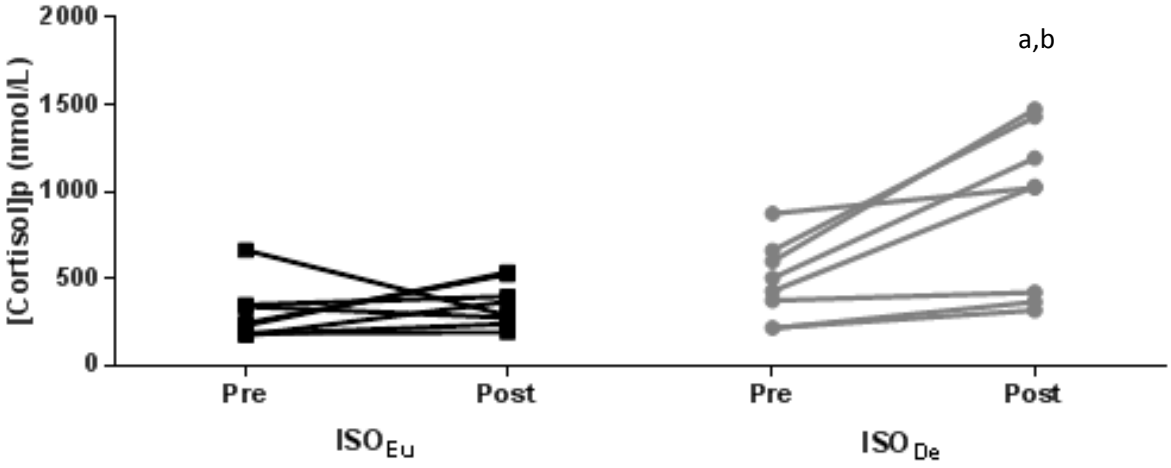
Acute body mass loss was greater in HADe [mean (SD), -2.35 (0.89) %] compared to the HAEu [-0.26 (0.81) %] condition after the first isothermal heat strain exercise bout ($P < 0.001$; for more information see [33]). A main effect for the influence of intervention on mean session body weight loss indicted that chronic hypohydration was achieved during HADe and euhydration was maintained after the HAEu sessions (mean body mass loss −2.71 (0.82) % vs. −0.56 (0.73) %, $P < 0.001$, for more information see [33]).

3.2. Acute effects of hydration status when exercising in the heat

Cortisol, IL-6 and CRP were similar at rest (pre-exercise) before the first ISO intervention (all $P > 0.05$). IL-6 was increased after exercise when dehydrated (pre exercise: 1.0 $pg \cdot mL^{-1}$ [0.9], post-exercise: 1.8 $pg \cdot mL^{-1}$ [1.0], $P = 0.032$) and when euhydrated (pre-exercise: 1.0 $pg \cdot mL^{-1}$ [1.4], post-exercise: 1.6 $pg \cdot mL^{-1}$ [2.1], $P = 0.048$). No differences (all $P > 0.05$) between HADe and HAEu in IL-6 were observed. Neither exercise, nor hydration status altered CRP (pre HADe exercise: 10.5 $mg \cdot L^{-1}$ [15.9], pre HAEu exercise: 10.9 [16.4], post HADe exercise: 9.5 [21.6], post HAEu exercise: 10.9 [15.6]; all $P > 0.05$). In comparison to pre-exercise, cortisol was elevated post-exercise when dehydrated (pre exercise: median 473.7 $nmol \cdot L^{-1}$ [IQR 388.6], post exercise: 1113.0 $nmol \cdot L^{-1}$ [983.1], $P = 0.016$, Figure 2), but not when fluid was provided (pre exercise: 237.4 $nmol \cdot L^{-1}$ [165.0], post exercise: 335.7 $nmol \cdot L^{-1}$ [294.1], $P = 0.624$). Similarly, immediately after exercise, the plasma cortisol concentration was significantly higher in HADe than in HAEu ($P = 0.016$).

Body mass loss was significantly correlated with ΔCortisol (r = -0.688, P = 0.003), but not ΔIL-6 (r = -0.321, P = 0.226) or ΔCRP (r = -0.074, P = 0.787). ΔCortisol was positively correlated to ΔIL-6 (r = 0.500, P = 0.049). No other statistically significant differences or correlations were observed.

Figure 2. Effects of isothermal strain exercise-heat exposure with (ISO_{Eu}) and without (ISO_{De}) fluid replacement on plasma cortisol, C-reactive protein, and interleukin-6 responses (n = 8). Each line represents one participant. [a] significantly different to pre exercise in ISO_{De} ($P < 0.05$), [b] significantly different to post-exercise in ISO_{Eu} ($P < 0.05$)


a,b
[Cortisol]p (nmol/L)
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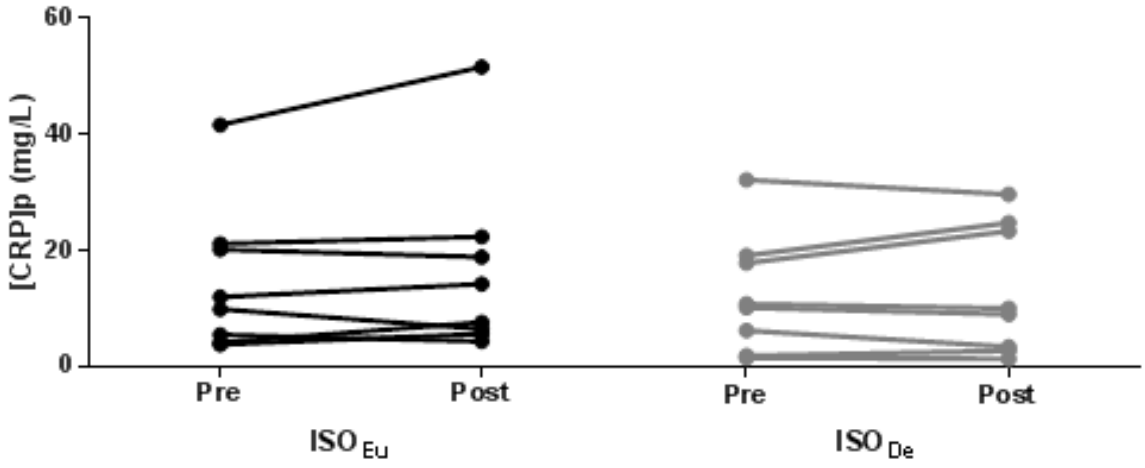
[CRP]p (mg/L)
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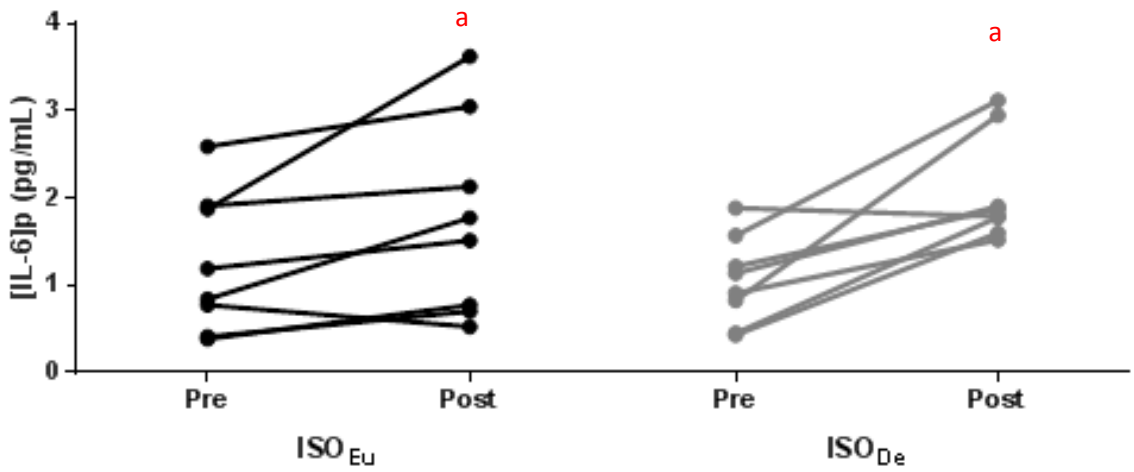
a
a
[IL-6]p (pg/mL)
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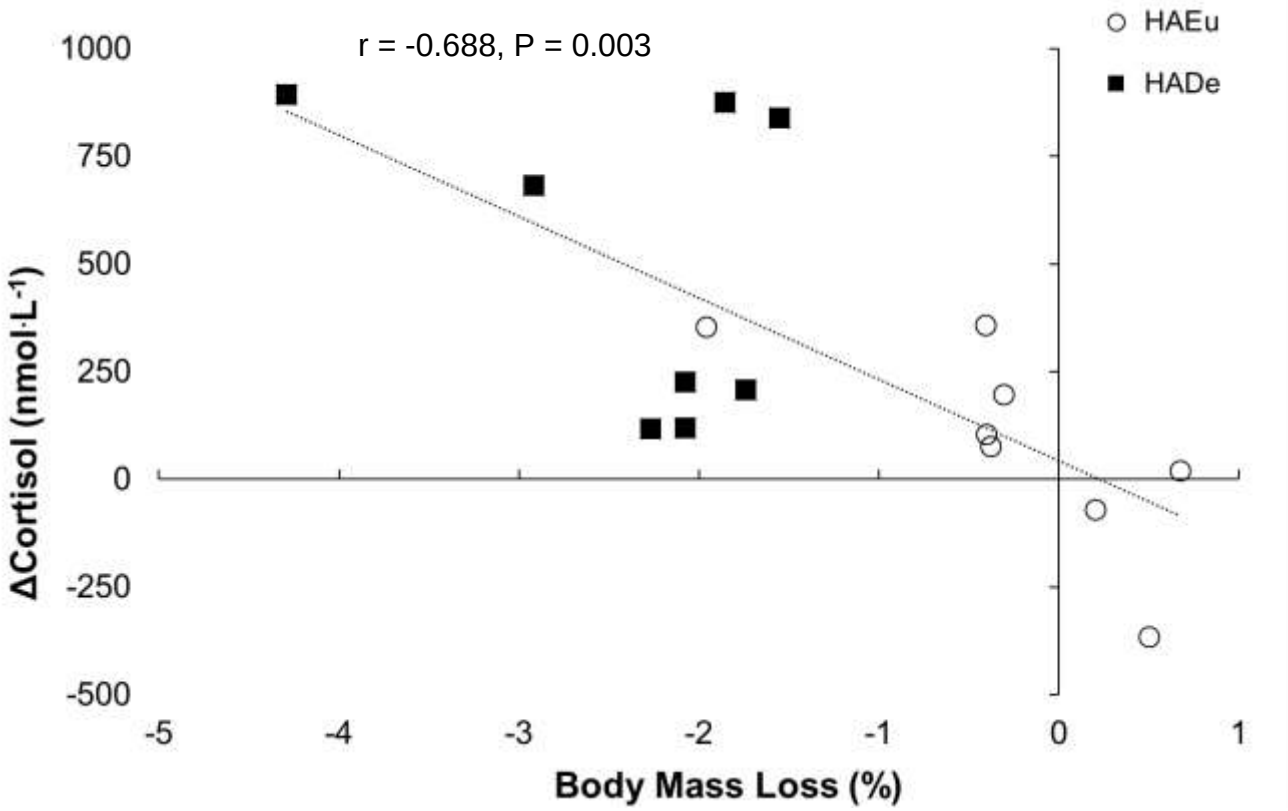
Figure 3. Correlations between post-exercise body mass loss and change in plasma cortisol (n = 8). Euhydrated heat acclimation (HAEu), permissive dehydration heat acclimation (HADe).



3.3. Chronic effects of euhydrated and hypohydrated heat acclimation protocol

No difference in plasma cortisol, IL-6 or CRP were observed pre- or post-exercise during the HST before the heat acclimation interventions (all $P > 0.05$, Table 1). Although the Friedman test indicated a significant difference in IL-6 ($P < 0.026$), no post-hoc differences were observed. Similarly, no differences ($P = 0.114$) in CRP were observed between HADe and HAEu. There was a trend for post exercise cortisol to be lower after 6- and 11-days of HA ($P < 0.1$); however there were no differences between HADe and HAEu.

Table 1: Effects of euhydrated and hypohydrated heat acclimation protocols on plasma cortisol, interleukin-6 and C-reactive protein (median [IQR], n = 8).

	Euyhydrated Protocol (HAEu)						Dehydrated Protocol (HADe)					
	Pre Heat Acclimation		Mid Heat Acclimation		Post Heat Acclimation		Pre Heat Acclimation		Mid Heat Acclimation		Post Heat Acclimation	
	Pre Ex	Post Ex	Pre Ex	Post Ex	Pre Ex	Post Ex	Pre Ex	Post Ex	Pre Ex	Post Ex	Pre Ex	Post Ex
Cortisol ($nmol \cdot L^{-1}$)	114.0 [102.0]	150.8 [106.0]	80.8 [55.2]	71.6 [44.4]	92.5 [64.0]	77.4 [44.4]	100.0 [69.0]	133.0 [140.2]	91.6 [48.2]	62.7 [48.3]	94.5 [88.6]	56.3 [32.2]
IL-6 ($pg \cdot mL^{-1}$)	52.1 [3.7]	57.8 [15.2]	-	-	45.9 [13.9]	50.1 [14.8]	52.0 [10.4]	53.3 [8.9]	-	-	46.9 [9.9]	53.4 [8.9]
CRP ($mg \cdot L^{-1}$)	12.5 [23.5]	11.8 [17.3]	2.9 [4.1]	2.5 [3.8]	3.4 [12.0]	4.0 [8.5]	11.1 [25.0]	9.9 [32.0]	1.6 [4.8]	2.3 [3.7]	4.6 [5.0]	3.9 [8.4]

4. Discussion

This study investigated acute and chronic effects on biomarkers of stress and inflammation of an 11-day heat acclimation programme, with and without permissive dehydration. In partial support our first hypothesis plasma IL-6 was elevated following the initial 90 min isothermal strain exercise-heat exposure with permissive dehydration and when fluid was provided. Plasma cortisol was also elevated following the initial 90 min isothermal strain exercise-heat exposure with permissive dehydration but not when fluid was provided. This change in cortisol was negatively correlated with the magnitude of whole body sweat loss. Contrary to our second hypothesis, resting levels of cortisol, IL-6, and CRP were not significantly augmented after 11-days of heat exposure.

Circulating levels of cortisol are regulated by the hypothalamic–pituitary–adrenal axis and by a neuroendocrine feedback circuit that can be activated by physiological stimuli such as stress and exercise [11]. As expected, we observed a ~2-fold increase in cortisol levels following the initial 90 min isothermal strain exercise-heat exposure in HADe, but not when hydration was maintained (Figures 2 and 3). This increase is similar to that seen in other research [8,28,32] examining hormonal responses during exercise-induced dehydration in the heat, when average body water loss was ≥2 %. The exact physiological mechanism(s) responsible for these increases is not known; however, González-Alonso *et al* [24] suggested that the superimposition of dehydration on hyperthermia during exercise in the heat leads to an inability to maintain cardiac output and blood pressure, making the dehydrated athlete less able to cope with hyperthermia. Interestingly, no post-exercise (in the heat) increases in cortisol were observed in the same condition when hydrated

(Figure 1), or indeed during the first HST pre-acclimation where the participants in both the HADe and the HAEu interventions were euhydrated (Table 1). These data lend support to earlier work by Armstrong *et al* [1] and Ganio *et al* [20] who reported that cortisol remained unaltered following exercise-induced dehydration, eliciting an average body mass loss was 1.3 % and 1.6 % respectively, i.e. a smaller reduction in body mass than in the present study. By employing a balanced within participant methodological design, and since other factors known to affect hormone changes (i.e. circadian rhythm, environmental temperature, prior exercise, and nutrition; [14]) were minimised, we can be confident that these changes are primarily attributable to the mild, transient level of hypohydration (~2.5 % body mass loss). Together these data also suggest there is a threshold effect of body mass loss (~2 %), via exercise-induced dehydration, on plasma cortisol (Figure 3).

Although the plasma concentration of several other cytokines may be affected by exercise, IL-6 increases more dramatically than any other cytokine [16]. In the current study, IL-6 was augmented (~2-fold) after exercise, in both protocols following the initial isothermal strain exercise-heat exposure (Figure 2). These IL-6 data are similar to [16], or less than [25,26], those previously reported in similar studies. Guy *et al* [25] have recently reported that the greatest acute pre- to post-exercise change in IL-6 following exercise in the heat was ~4-fold. In the current study participants completed cycling at an RPE of 15 until a target rectal temperature of 38.3 °C (~ 40-min), at which point external power output was adjusted as appropriate to maintain the target rectal temperature (38.5 °C). This is compared to Guy and colleagues [25] who employed a protocol consisting of 10-min cycling at 50 %, 60 % and 70 % $\dot{V}O_{2max}$ followed by a 5-km time trial. As over 50% of the variation

in plasma IL-6 increase can be explained by the duration and intensity of exercise [16], these differences are likely attributable to the methodological differences. Plasma CRP remained unchanged following the initial ISO heat exposure in both the HADe and the HAEu interventions (Figure 2). Although, relatively small increases in plasma levels of IL-6 induce anti-inflammatory cytokines and CRP [23,40], it is likely that the modest increases in IL-6 following exercise are responsible for these CRP data immediately post-exercise.

The interplay between inflammatory and cortisol responses modulates an appropriate response to a stressor [48,49], or indeed combined stressors (i.e. heat, hypohydration, and exercise). Repeated bouts of exercise in the heat, over the course of several days, have been shown to result in augmented cortisol [48] and cytokine [49] levels. Contrary to studies of increased training volume or intensity [7], no within or between intervention changes in resting pre-exercise cortisol concentrations were observed in the current study (Table 1). This is probably reflective of the training status (average $\dot{V}O_{2max}$: >55 $mL \cdot kg^{-1} \cdot min^{-1}$) of the participants in the current study. However, there was a consistent trend ($P < 0.1$) for cortisol to be reduced post exercise after 6- and 11-days post heat acclimation, in both the HAEu and the HADe interventions. As elevated levels of cortisol may alter risk-taking behaviours [44], these observations regarding heat acclimation interventions may be useful in occupational, military and sporting contexts, where reductions in the stress hormone responses to subsequent heat exposures is desired.

As cortisol has a long half-life in the blood and is often thought to represent the body's long-term response to stress [7], it is somewhat counterintuitive that reduced

levels of post-exercise cortisol were observed. There are three plausible explanations for these observations. Firstly, it is well established that the circadian clock modulates a near-24-hour rhythm in plasma cortisol [50]. This circadian rhythm in plasma cortisol shows high levels in the morning near habitual wake time in humans and declines across the biological day [50]. The post-exercise plasma samples were collected ~2 hours after the resting sample in the current study. These potential circadian related reductions in cortisol were possibly masked by the initial psychophysiological stress response associated with the first HST and only became visible during the final HST after the HADe. Secondly, a similar decrease in the exercise-induced response of cortisol has previously been observed after 8-weeks of strength training [27] and after 7-weeks of volleyball training [15] suggesting that training reduces the catabolic response to the same pre-training exercise stimulus/stress. This reduced catabolic response was likely augmented following heat acclimation where the participants were acclimated, both physiologically and perceptually, to the exercise-induced heat stress. Finally, an increase in circulating cortisol levels are typically only visible after exercise if the intensity is equivalent >60 % of the maximal oxygen consumption for more than 20-mins [15,43]. Therefore, it is possible that the HST used in this study (35 % $\dot{V}O_{2max}$ for 60-mins) was not of sufficient intensity, and/or duration, to elicit short or long-term elevations in resting or post exercise cortisol in these trained participants.

Prolonged elevation of inflammatory cytokines may signify cumulative fatigue, overtraining, sleep debt, or a neuroinflammatory response [26,51]. Few studies have investigated the effects of heat acclimation on biomarkers of inflammation. Guy *et al* [26] recently examined the impact of a short-term heat acclimation intervention,

which consisted of seven sessions over 18 non-consecutive days, and reported that IL-6 returned to basal concentration prior to each HST. Although both HADe and HAEu were adequate to elicit several thermoregulatory, cardiovascular, and performance benefits [see 33], the current findings also suggest that there were no chronic inflammatory effects of 11-days of HADe and HAEu as evidenced by both IL-6 and CRP returning to basal levels before the final HST (Table 1). Therefore, trained athletes can use medium term heat acclimation, with or without permissive dehydration, during training programmes confident that immune system functionality will not be impaired.

The present study was not without limitation. Firstly, analysing a range of other pro-inflammatory cytokines (e.g. TNF-alpha, IL-8 and IL-15) and stress biomarkers (e.g. epinephrine, alpha amylase) would have provided further insight into hormonal and inflammatory effects of a short and medium-term heat acclimation intervention. Secondly, despite employing a cross-over study design, which is typically more powerful than a parallel-group design, it is possible that the small sample-size increased the potential for type II error. Nevertheless, we observed a number of key statistically significant effects in both IL-6 and cortisol. Finally, as we did not include a thermoneutral or cool comparison it is not possible to delineate the acute effects of exercise and heat exposure in the current study.

4. Conclusion

This is the first study to provide a detailed analysis of the hormonal and inflammatory response to a medium-term (11-day) heat acclimation intervention with euhydration and permissive dehydration in trained men. Our data demonstrate that, i) acute exercise in the heat increases IL-6 and ii) the stress hormone cortisol only when

fluid-intake was restricted. These increased concentrations of cortisol were strongly correlated with whole body sweat loss. Despite the inflammatory cytokine IL-6 transiently increasing following the initial isothermal-strain exercise-heat session in both programmes, there were no chronic inflammatory effects of either intervention as evidenced by IL-6 and CRP returning to basal level at the end of heat acclimation.

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Disclosure statement

The authors confirm there are no conflicts of interest.

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