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4 1 **Inter-individual variation in the adaptive response to heat acclimation**

5 2 **Running Head:** variability in heat acclimation response

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10 4 **Original Investigation**

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62 **ABSTRACT**  
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64 **Aim:** To investigate inter-individual variance in adaptive responses to heat acclimation (HA).  
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66 **Methods:** 17 males ( $VO_{2max}=58.8(8.4)$  ml·kg<sup>-1</sup>·min<sup>-1</sup>) undertook 10-days (exercise + heat-  
67 stress [40°C, 50%RH]) HA. Adaptation was assessed by heat stress tests (HST; 60–minutes  
68 cycling, 35% peak power output) pre- and post-HA. **Results:** Inter-individual variability was  
69 evident in adaptive responses e.g. mean(range) reduction in end-exercise  $T_{re}=-0.70(-0.20$  to -  
70 1.32)°C, but, in the main, the variance in adaptation was unrelated across indices (thermal,  
71 sudomotor, cardiovascular, haematological), indicating independence between adaptation  
72 indices. Variance in adaptive responses was not correlated with aerobic **capacity**, history of  
73 previous HA, or the accrued thermal-dose. Some responses to the initial HST were related to  
74 the subsequent adaptations e.g.  $\Delta T_{sk}$  during the initial HST and the reduction in **the** within  
75 HST  $\Delta T_{re}$  after HA ( $r=-0.676$ ), but responses to the initial HST may also have been influenced  
76 by HST design e.g.  $\Delta T_{re}$  correlated with metabolic heat production ( $r=0.609$ ). Metabolic heat  
77 production also correlated with the reduction in the within HST  $\Delta T_{re}$  after HA ( $r=-0.514$ ).  
78  
79 **Summary:** HA indices are mainly independent; ‘low’, or ‘high’, responders on one **index** do  
80 not necessarily demonstrate similar response across other indices. Variance in HA responses  
81 was not related to aerobic **capacity**, previous HA, or thermal-dose. Thermo-physiological  
82 responses to a HST might identify individuals who will benefit from HA. However, some initial  
83 responses are influenced by HST design, which may also affect the scope for demonstrating  
84 adaptation. **Conclusion:** Variance in the HA response remains largely unaccounted for and future  
85 studies should identify factors contributing to this variance.  
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109 **KEYWORDS:** Acclimatization; adaptation; thermal; responders; non-responders  
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121 51 **HIGHLIGHTS**  
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- 123 52 • Although we demonstrated pronounced inter-participant variance in the adaptive  
124 response to heat, this was not explained by factors that have putatively been suggested  
125 to influence this response, such as maximal aerobic capacity, previous heat acclimation,  
126 or the thermal ‘dose’ accrued during the heat intervention.  
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133 56 • Classification of individuals as either ‘low’ or ‘high’ responders to heat may not be  
134 appropriate. Acclimation indices appear to be largely independent and individuals  
135 demonstrating a pronounced, or blunted, adaptive response on one index of acclimation  
136 do not necessarily demonstrate a similar response across other indices.  
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138 57  
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142 60 • Some of the thermo-physiological responses to an initial heat stress test undertaken  
143 before a programme of heat acclimation were related to the magnitude of subsequent  
144 adaptation, suggesting that this type of test may have utility in assessing baseline ‘heat-  
145 readiness’, as well as in identifying individuals who will most benefit from heat  
146 acclimation.  
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153 65 • Some of the initial responses may have been influenced by the heat stress test design,  
154 which could also affect the scope for demonstrating adaption, although most of the  
155 variance in the adaptive response remained unaccounted for.  
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## 1.0 INTRODUCTION

At the **cohort** level, the typical heat acclimation (HA) response is well characterised (for recent reviews see: Daanen *et al.*, 2018; Périard *et al.*, 2015; Tyler *et al.*, 2016). Broadly speaking, the heat-adapted phenotype is characterised by hypervolemia (Senay *et al.*, 1976), an increased sudomotor response (Nadel *et al.*, 1974), and reduced heart rate, **rectal temperature ( $T_{re}$ )**, and mean body temperature ( $\bar{T}_b$ ) during exercise at a given external work rate in the heat (Neal *et al.*, 2016b; Rendell *et al.*, 2017). However, whilst there is consistency between studies when the adaptive response to heat is viewed at the **cohort** level, where individual data are presented considerable heterogeneity is evident. For instance, Senay *et al.* (1976) demonstrated a typical group response for the plasma volume increase to a 10-day HA programme, yet the individual data show the final plasma volume expansion ranged from ~8 to 33%. In a related paper large variations in the reduction in exercise heart rate (~-2 to -32 beats·minute<sup>-1</sup>) and  $T_{re}$  (~-0.3 to -1.2°C) were evident following the same 10-day HA programme (Wyndham *et al.*, 1976). Heterogeneity has also been demonstrated in the sudomotor adaptation (**sweating rate**) following HA (Mitchell *et al.*, 1976). These observations are consistent with later work by Racinais *et al.* (2012) who also noted high inter-individual variation in the adaptive response to a 6-day heat acclimatization programme (*e.g.* change in ( $\Delta$ ) plasma volume of -10 to +20%) with apparent ‘responders’ and ‘non-responders’; similar findings were also reported by Racinais *et al.* (2014) following a 2-week acclimatization intervention. Although the variability reported by Racinais *et al.*, (2012 and 2014) might **be** attributable to the greater complexity of natural acclimatization compared to laboratory protocols (Edholm, 1966), recent research using a standard 10-day laboratory HA **intervention** also demonstrated a broad spectrum of adaptive responses to HA (Neal *et al.*, 2016b; Rendell *et al.*, 2017). Interestingly, it is unknown whether the response profile is consistent across HA indices, that is, whether individuals who have **a pronounced, or conversely low, adaptive response** for a given **index** of HA, demonstrate the

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93 same response across the range of HA indices. However, cardiovascular changes can occur in  
94 the absence of significant alterations in plasma volume (Garrett *et al.*, 2009; Neal *et al.*, 2016a)  
95 and reductions in  $T_{re}$  and  $\bar{T}_b$  post-HA have also been reported without plasma volume changes  
96 (Neal *et al.*, 2016a), whereas the plateau in the  $T_{re}$  adaptation during HA may precede  
97 pronounced sudomotor adaptation (Périard *et al.*, 2015). Given the apparent independence  
98 between some aspects of the HA response, it might be anticipated that the magnitude of  
99 response is specific to the HA index.

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101 Understanding the basis for heterogeneity in the HA response has important practical utility  
102 for the screening and identification of individuals who will most benefit from undertaking HA,  
103 in optimising the HA process, and in identifying those individuals best suited to performing in  
104 a hot environment or those at increased risk of an adverse response e.g. poor heat tolerance  
105 (Epstein, 1990). The need to increase understanding of the factors underpinning the inter-  
106 individual variability in the HA response was highlighted as a priority in a 2012 International  
107 Olympic Committee consensus statement (Bergeron *et al.*, 2012), yet little subsequent progress  
108 has been made. Historic work suggests that a dose-response relationship between heat exposure  
109 and the magnitude of the adaptive response underpins some of the variability in the HA  
110 response (Fox *et al.*, 1963; Lind & Bass, 1963) although there may be a ceiling-effect for  
111 thermal ‘dose’ given that elevating  $T_{re}$  beyond 38.5°C during a HA intervention does not confer  
112 any additional benefit (Gibson *et al.*, 2015). Moreover, there is some evidence to suggest that  
113 individuals with a high maximal aerobic capacity ( $VO_{2max}$ ) may be partially heat acclimated  
114 (Ravanelli *et al.*, 2018; Shvartz *et al.*, 1977), probably by virtue of some of their training  
115 adaption (e.g. hypervolemia) as well as through the high thermal-strain that can be elicited  
116 through their habitual exercise at high absolute exercise intensities under temperate conditions  
117 (Ely *et al.*, 2009). Similarly, individuals with a high  $VO_{2max}$  may acclimate more rapidly than

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298 118 individual with a lower  $\text{VO}_{2\text{max}}$  (Pandolf *et al.*, 1977), whereas meta-analytic data suggests that  
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300 119 the process of re-acclimation is more rapid than initial HA (Daanen *et al.*, 2018) and animal  
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302 120 models have provided evidence of a HA memory, at least in terms of cytoprotection (Horowitz,  
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304 121 2016). Finally, whilst the roles of  $\text{VO}_{2\text{max}}$  and anthropometric factors have historically been  
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306 122 emphasised in explaining the thermophysiological responses to exercise in the heat, recent  
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308 123 work has demonstrated that the metabolic heat production ( $H_{\text{prod}}$ ) explained the largest amount  
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310 124 of the inter-individual variance in the  $\Delta T_{\text{re}}$  whereas the evaporative requirement for heat  
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312 125 balance ( $E_{\text{req}}$ ) explained the largest amount of variance in sweating rate (Cramer and Jay, 2015).  
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314 126 However, there has, historically, been no attempt to standardise these parameters in protocols  
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316 127 for assessing HA (*e.g.* Garrett *et al.*, 2009; Gibson *et al.*, 2015; Neal *et al.*, 2016ab; Pandolf *et*  
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318 128 *al.*, 1977; Rendell *et al.*, 2017; Senay *et al.*, 1976; Shvartz *et al.*, 1977) raising the possibility  
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320 129 that the design of the heat stress test (HST) might contribute to the variance observed in the  
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322 130 response to the initial baseline assessment of acclimation state. Likewise, it might be  
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324 131 anticipated that a large increase in  $T_{\text{re}}$  during the HST prior to HA, which might be influenced  
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326 132 by  $H_{\text{prod}}$  rather than acclimation state *per se*, could provide the greatest scope for demonstrating  
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328 133 an adaptive response thereafter.  
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334 135 Accordingly, the primary aim of the present study was to examine the putative factors  
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336 136 underpinning the observed variance in the adaptive response to a standard HA intervention.  
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338 137 We hypothesised that  $\text{VO}_{2\text{max}}$ , a history of previous HA, the thermal dosage experience during  
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340 138 the HA intervention, and the baseline response to a standard HST), would be significant  
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342 139 contributors to the variance in the HA response. We also investigated the extent to which the  
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344 140 inter-individual variability in the magnitude of adaptive response to heat was consistent across  
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346 141 adaption indices, that is, whether individuals who have a pronounced, or conversely low,  
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348 142 adaptive response on one index of HA demonstrate a similar response across other indices of  
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357 143 HA, or whether the magnitude of adaptive response is specific to the **index** of adaption. Based  
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359 144 upon the apparent independence between some indices of HA we hypothesised that the  
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361 145 response profile would be non-uniform. Finally, we investigated the factors influencing the  
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363 146 thermo-physiological responses to the initial HST, and whether this influenced the subsequent  
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365 147 adaptive response to a HA **intervention**. Our hypothesis was that the highest  $T_{re}$  and whole-  
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367 148 body sweating rates (WBSR) in the initial HST would be observed in those individuals with  
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369 149 the highest  $H_{prod}$  and  $E_{req}$ , respectively, and that these high baseline responses would provide  
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371 150 greater scope for evidencing adaptation.  
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## 376 152 **2.0 METHODS**

### 378 153 **2.1 Participants**

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381 154 **Seventeen** trained males participated (Mean(SD) age: 22(5) years; height: 1.81(0.05) m; mass:  
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383 155 74.4(6.3) kg; body surface area (BSA, Dubois and Dubois, 1916) 1.94(0.10) m<sup>2</sup>;  $VO_{2max}$ :  
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385 156 58.8(8.4) mL·kg<sup>-1</sup>·min<sup>-1</sup>). These data were pooled from previously published studies (Neal *et*  
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387 157 *al.*, 2016b; Rendell *et al.*, 2017). The studies received ethical approval from the Universities  
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389 158 Science Faculty ethics committee and were conducted in accordance with the Declaration of  
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391 159 Helsinki (2013). All participants completed a health history questionnaire and provided written  
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393 160 informed consent.  
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### 398 162 **2.2 Experimental design**

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400 163 A within-participant repeated-measures design was employed. All participants undertook a  
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402 164 preliminary graded exercise test (GXT) under temperate ambient conditions (target ambient  
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404 165 conditions: 22°C; 50%RH) in the seven day period prior to commencing the HA **intervention**.  
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406 166 Thereafter, participants undertook 11 consecutive days of exercise-heat exposures (target  
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408 167 ambient conditions: 40°C; 50%RH). The first, sixth and eleventh day consisted of a  
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416 168 standardised exercise HST for assessing the HA responses; the other days consisted of exercise-  
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418 169 heat exposures using the controlled **hyperthermia** (CH) approach. Nine of the participants had  
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421 170 previously undertaken a heat acclimation programme (3 to 18 months washout).  
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### 424 172 **2.3 Experimental procedures**

#### 425 173 **2.3.1 Graded Exercise Test**

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429 174 Participants initially cycled (Excalibur, Lode, The Netherlands) at 85-110 W, dependent upon  
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431 175 the estimated fitness of the participant. After 20 minutes work-rate was incremented by 25 W  
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433 176 every 3 minutes until fingertip capillary blood lactate concentration [Lac] was  $\geq 4$  mmol·L<sup>-1</sup>  
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435 177 (Biosen C-line, EKF Diagnostic, Cardiff, UK). Thereafter, following a five-minute recovery  
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437 178 period, the participant cycled at 100 W for five minutes, before work-rate was increased by 25  
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439 179 W·min<sup>-1</sup> until volitional exhaustion.  $\text{VO}_{2\text{max}}$  was defined as the highest 15 s  $\text{VO}_2$ .  
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#### 443 181 **2.3.2 Exercise-Heat Stress Test**

444 182 Participants cycled on a calibrated CompuTrainer cycle ergometer (RacerMate Inc., Seattle,  
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446 183 Washington, USA) for 60 minutes at 35% of the GXT peak power. All HSTs were completed  
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448 184 at the same time of day, within-participant.  
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#### 453 186 **2.3.3 Controlled Hyperthermia**

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455 187 Participants self-selected their initial work rate on the Computrainer cycle ergometer in order  
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457 188 to elicit a target rating of perceived exertion (RPE [Borg, 1982]) of 15. This was maintained  
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459 189 until  $T_{\text{re}}=38.3^\circ\text{C}$ , at which point external power output and convective cooling ( $\sim 2\text{-}3$  m·s<sup>-1</sup>)  
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461 190 were adjusted as appropriate to maintain the target  $T_{\text{re}}$  ( $38.5\text{-}38.7^\circ\text{C}$ ). Convective cooling was  
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463 191 manipulated to facilitate the exercise component and provide some perceptual benefit, whilst  
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465 192 maintaining a high mean skin temperature. The total exercise-heat exposure was 90-minutes  
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475 193 per session. The time each individual spent with a  $T_{re} > 38.5^{\circ}\text{C}$  during the CH sessions was used  
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477 194 as an index of the thermal ‘dose’ accrued during the HA **intervention** as used previously  
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479 195 (Zurawlew *et al.*, 2016).  
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## 483 484 197 **2.4 General procedures**

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486 198 Participants wore the same clothes (shorts, undergarments, shoes) each day, abstained from  
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488 199 alcohol throughout the experimental period and caffeine for 12 hours before exercise, and were  
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490 200 instructed to consume a similar diet before each test and drink 500 mL of water 2 hours before  
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492 201 every attendance. Participants were instructed to maintain their normal high-intensity training  
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494 202 (except 24 hours before HSTs or GXTs) and replace an equivalent duration of low/moderate  
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496 203 training with that completed in the laboratory to maintain usual training volume. To estimate  
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498 204 WBSR, nude body mass was measured immediately before and after every exercise session  
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500 205 (Industrial Electronic Weight Indicator, Model I10, Ohaus Corporation, Parsippany, New  
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502 206 Jersey, USA), having adjusted for fluid consumption. During HST and controlled hyperthermia  
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504 207 sessions 250 mL boluses of 3.6% carbohydrate solution (drink temperature  $20^{\circ}\text{C}$ ) were  
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506 208 ingested, immediately prior to commencing exercise and every 15 minutes thereafter. After  
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508 209 every exercise session, participants were encouraged to drink *ad libitum* to ensure similar  
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510 210 hydration for each of the following days.  
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515 212 Ambient conditions were measured by a **wet-bulb globe temperature** (WBGT) logger (Squirrel  
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517 213 1000, Grant Instruments, Cambridge, UK),  $T_{re}$  by a thermistor (Grant Instruments, Cambridge,  
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519 214 UK) self-inserted approximately 15 cm beyond the anal sphincter and cardiac frequency ( $f_c$ ) by  
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521 215 short range telemetry (Polar RS800, Polar Elector, Kempele, Finland). Participants were  
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523 216 withdrawn from a session if  $T_{re} > 40^{\circ}\text{C}$ . During HSTs and GXTs, skin temperature ( $T_{sk}$ ) was  
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525 217 measured using thermistors on the chest, biceps, thigh and calf (Grant Instruments, Cambridge,  
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534 218 UK). During HSTs expired gases (Douglas bag method) were measured at 15 minute intervals.

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536 219  $\text{VO}_2$  was measured breath-by-breath throughout the GXTs (Quark B2, COSMED, Rome, Italy).

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541 221 Before and after HSTs 10 mL venous blood samples were obtained from the antecubital vein

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543 222 for the triplicate measurement of haemoglobin concentration [Hb] (201+ HemoCue, Sweden)

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545 223 and haematocrit (Hct) (Hawksley, England). Blood volume changes were determined

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547 224 according to Dill and Costill (1974).

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## 550 551 226 **2.5 Data analysis**

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553 227 Mean skin ( $T_{\text{sk}}$ ) calculated according to Ramanathan (1964) with  $T_{\text{b}}$  calculated using a two-

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555 228 compartment model (Jay *et al.*, 2007).  $H_{\text{prod}}$  was calculated according to ISO 8896 (Malchaire,

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557 229 2004). The rate of dry heat exchange ( $H_{\text{dry}}$ ) was calculated as:

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$$H_{\text{dry}} = C + R \text{ (W/m}^2\text{)}$$

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$$C = h_c (T_{\text{sk}} - T_a) \text{ (W/m}^2\text{)}$$

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563 232 
$$R = h_r (T_{\text{sk}} - T_r) \text{ (W/m}^2\text{)}$$

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565 233 C and R represent convective and radiant heat exchange, respectively,  $T_a$  and  $T_{\text{sk}}$  denote

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567 234 ambient and mean skin temperatures ( $^{\circ}\text{C}$ ), respectively,  $T_r$  is the mean radiant temperature ( $^{\circ}\text{C}$ ),

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569 235 assumed to the equivalent to ambient temperature in the laboratory setting,  $h_c$  is the convective

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571 236 heat transfer coefficient, and  $h_r$  is the radiant heat transfer coefficient:

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$$h_c = 8.3 v^{0.6} \text{ (W}\cdot\text{m}^{-2}\cdot\text{K}^{-1}\text{)}$$

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575 238 
$$h_r = 4\varepsilon\sigma (BSA_r/BSA) ((T_{\text{sk}} + T_r) / 2 + 273.15)^3 \text{ (W}\cdot\text{m}^{-2}\cdot\text{K}^{-1}\text{)}$$

576  
577 239 Where:  $v$  is air velocity ( $\text{m}\cdot\text{s}^{-1}$ ),  $\varepsilon$  is skin emissivity (0.95),  $\sigma$  is the Stefan-Boltzmann constant

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579 240 ( $5.67\cdot 10^{-8} \text{ W}\cdot\text{m}^{-2}\cdot\text{K}^{-4}$ ), and  $BSA_r/BSA$  is the non-dimensional effective radiant surface area

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581 241 for a seated individual valued at 0.70.

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243 Respiratory heat exchange ( $H_{\text{resp}}$ ) was calculated as:

$$E_{\text{res}} + C_{\text{res}} = 0.0173(H_{\text{prod}})(5.87 - P_a) + 0.0014(H_{\text{prod}})(34 - T_a) \text{ (W/m}^2\text{)}$$

245 Where:  $E_{\text{res}}$  and  $C_{\text{res}}$  are evaporative and convective heat loss from the respiratory tract,  
246 respectively, and  $P_a$  is the ambient vapor pressure (kPa).

248 The rate of evaporation required for heat balance ( $E_{\text{req}}$ ) was expressed as:

$$E_{\text{req}} = H_{\text{prod}} - H_{\text{dry}} - H_{\text{resp}} \text{ (W/m}^2\text{)}$$

251 The maximum rate of evaporation to the environment ( $E_{\text{max}}$ ) was determined by:

$$E_{\text{max}} = h_e (P_{\text{sk,s}} - P_a) \text{ (W/m}^2\text{)}$$

253 where  $h_e$  is the evaporative heat transfer coefficient, calculated as the product of  $h_c$  and the  
254 Lewis relation coefficient (16.5 K/kPa), and  $P_{\text{sk,s}} - P_a$  is the skin-air vapor pressure gradient

256 The value of  $P_{\text{sk,s}}$  was calculated based on  $T_{\text{sk}}$  using Antoine's equation:

$$P_{\text{sk,s}} = 10 \cdot \exp [18.956 - 4.030.18/(T_{\text{sk}} + 235)] \text{ (kPa)}$$

259 As per convention, heat balance parameters were calculated in  $\text{W/m}^2$ ; however, these values  
260 are expressed in W or  $\text{W/kg}^{-1}$  where appropriate.

## 262 2.6 Statistical Analysis

263 Heat acclimation was assessed using the data obtained from the pre vs. post HA HSTs  
264 conducted on day 1 and day 11 of the HA **intervention**. A range of indices were used to assess  
265 HA including: thermal (end-exercise  $T_{\text{re}}$  and  $T_{\text{b}}$ , the within HST  $\Delta T_{\text{re}}$  and  $\Delta T_{\text{b}}$ ),  
266 cardiovascular (average exercise heart rate), sudomotor (WBSR), and haematological ( $\Delta$  blood  
267 volume). Data are expressed as mean(SD) unless otherwise stated. **To identify the factors**

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268 influencing the thermo-physiological responses to the initial HST we used an approach similar  
269 to that described by Cramer and Jay (2015). Statistical analyses were undertaken using SPSS  
270 (IBM Version. 22, IBM, New York, New York, USA) with alpha set *a priori* as  $\leq 0.05$ . Strength  
271 of relationship between variables was assessed using Pearson's product-moment correlation.

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<b>Pre HA</b>	<b>Post HA</b>	<b>Pre-post HA</b>
Mean(SD)	Mean(SD)	<b>change</b>
min:max	min:max	Mean(SD)
		min:max

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272 Correlation coefficients were considered as strong ( $\geq 0.60$ ), moderate (0.40 to 0.59), and weak  
273 (0.20 to 0.39) (Cohen, 1998). Within-individuals differences were assessed by paired samples  
274 t-test. Between-individuals differences were assessed by independent samples t-tests.

275  
276 **3.0 RESULTS**

277 At the cohort level, a clear adaptive response was evident following the HA programme, as  
278 evidenced by significant reductions in the mean(SD) end-exercise  $T_{re}$  and  $T_{\square b}$ , a reduced  
279 within HST  $\Delta T_{re}$  and  $\Delta T_{\square b}$ , a lower average exercise heart rate, increased WBSR and  
280 pronounced hypervolemia. However, inspection of the individual responses revealed notable  
281 inter-participant variation in the range of adaptive responses (Table 1).

<b>End exercise <math>T_{re}</math> (°C)</b>	38.79(0.43) 38.18:39.74	38.09(0.40)*** 36.98:38.71	-0.70 (0.34) -0.20:-1.32
<b><math>\Delta T_{re}</math> (°C)</b>	1.53(0.53) 0.78:2.34	1.23(0.44)** 0.37:2.17	-0.30(0.32) 0.47:-0.71
<b>End Exercise <math>T_{\square_b}</math> (°C)</b>	38.65(0.46) 38.02:39.65	37.86(0.35)*** 37.15:38.62	-0.79(0.29) -0.35:-1.25
<b><math>\Delta T_{\square_b}</math> (°C)<sup>a</sup></b>	1.51(0.45) 0.82:2.16	1.13(0.33)*** 0.50:1.71	-0.38(0.27) 0.27:-0.79
<b>Whole body sweat rate (L·hr<sup>-1</sup>)</b>	1.45(0.33) 1.09:2.22	1.79(0.49)*** 1.15:2.89	0.34(0.29) 0.02:1.03
<b>Blood volume (%)</b>	100.0(0.0) 100.0:100.0	106.5(2.8)*** 102.0:112.9	6.5(2.8) 2.0:12.9
<b>Average heart rate (beats·minute<sup>-1</sup>)<sup>a</sup></b>	150(11) 135:174	129(8)*** 120:144	-21(5) -12:-29

**Table 1:** Effect of heat acclimation (HA) on thermophysiological indices measured during a standard heat stress test undertaken before and after heat acclimation (n=17, except <sup>a</sup> where n=16).

Significant difference from pre HA is denoted by: \*\* = P < 0.01; \*\*\* = P < 0.001.

The inter-participant range for  $VO_{2max}$ , expressed in absolute terms, was 3.49 to 5.05 L·min<sup>-1</sup>. Absolute  $VO_{2max}$  was not related to the magnitude of reduction in end-exercise  $T_{re}$  (P = 0.930) or  $T_{\square_b}$ , (P = 0.785), the reduction in the within HST  $\Delta T_{re}$  (P = 0.722) or  $\Delta T_{\square_b}$  (P = 0.714), the increase in WBSR (P = 0.405) or blood volume (P = 0.410) or the reduction in average heart rate (P = 0.086) following the HA intervention. The inter-participant range for  $VO_{2max}$ , expressed in relative terms was 45.2 to 74.6 mL·kg<sup>-1</sup>·min<sup>-1</sup>. The individual relative  $VO_{2max}$  was not related to the magnitude of reduction in end-exercise  $T_{re}$  (P = 0.947) or  $T_{\square_b}$  (P = 0.686) the reduction in the within HST  $\Delta T_{re}$  (P = 0.852) or  $\Delta T_{\square_b}$  (P = 0.868), the increase in WBSR (P =

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770 305 0.252) or blood volume (P = 0.381), or the reduction in average heart rate (P = 0.089) following  
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772 306 the HA intervention.  
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777 308 Nine of the participants had undergone a prior HA **intervention** before participating in the  
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779 309 present study. Independent samples t-test indicated that prior experience of heat acclimation  
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781 310 did not affect the reduction in end-exercise  $T_{re}$  (prior heat exposure =  $-0.32(0.34)^{\circ}\text{C}$  vs. no prior  
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783 311 exposure =  $-0.40(0.19)^{\circ}\text{C}$ , P = 0.555) or  $T_{\square_b}$  (prior heat exposure =  $-0.83(0.25)^{\circ}\text{C}$  vs. no prior  
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785 312 exposure =  $-0.74(0.33)^{\circ}\text{C}$ , P = 0.566), the reduction in the within HST  $\Delta T_{re}$  (prior heat  
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787 313 exposure =  $-0.39(0.22)^{\circ}\text{C}$  vs. no prior exposure =  $-0.19(0.39)^{\circ}\text{C}$ , P = 0.194) or  $\Delta T_{\square_b}$  (prior  
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789 314 heat exposure =  $-0.39(0.19)^{\circ}\text{C}$  vs. no prior exposure =  $-0.38(0.36)^{\circ}\text{C}$ , P = 0.980), increase in  
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791 315 WBSR (prior heat exposure =  $0.25(0.18) \text{ L}\cdot\text{hr}^{-1}$  vs. no prior exposure =  $0.45(0.36) \text{ L}\cdot\text{hr}^{-1}$ , P =  
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793 316  $0.158$ ) and blood volume (prior heat exposure =  $6.9(3.1)\%$  vs. no prior exposure =  $6.1(2.6)\%$ ,  
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795 317 P = 0.581) or the reduction in average exercise heart rate (prior heat exposure =  $-15(8)$   
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797 318  $\text{beats}\cdot\text{min}^{-1}$  vs. no prior exposure =  $-11(6) \text{ beats}\cdot\text{min}^{-1}$ , P = 0.264).  
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802 320 The total time individual spent in CH sessions with a  $T_{re} > 38.5^{\circ}\text{C}$  was  $456(64)$  minutes (range  
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804 321  $326:552$  minutes). Total time spent with a  $T_{re} > 38.5^{\circ}\text{C}$  was not significantly correlated with  
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806 322 any of the adaption indices. Likewise, the average external work rate sustained during each CH  
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808 323 session, expressed either in absolute ( $101(16) \text{ W}$ , range  $69:130 \text{ W}$ ) or relative terms  
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810 324 ( $1.37(0.28) \text{ W}\cdot\text{kg}^{-1}$ , range  $0.86:1.99 \text{ W}\cdot\text{kg}^{-1}$ ) was not correlated with the reduction in the end-  
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812 325 exercise  $T_{re}$  (P = 0.986, P = 0.939, respectively), end-exercise  $T_{\square_b}$  (P = 0.489, P = 0.888,  
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814 326 respectively), the within session  $\Delta T_{re}$  (P = 0.614, P = 0.981, respectively),  $\Delta T_{\square_b}$  (P = 0.718, P  
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816 327 = 0.620, respectively),  $\Delta$ blood volume (P = 0.726, P = 0.344, respectively) and the reduction  
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818 328 in average exercise heart rate (P = 0.077, P = 0.068, respectively). However, there was a  
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820 329 significant moderate negative relationship between the average absolute power sustained in  
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829 330 each CH session and the increase in WBSR ( $r = -0.530$ ,  $P = 0.029$ ), but the relative power  
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831 331 sustained in each CH session was not significantly related to WBSR ( $P = 0.054$ ).  
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836 333 The baseline responses to the pre-HA HST were correlated with a number of the adaption  
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838 334 indices (Figure 1 a-f). The reduction in end-exercise  $T_{re}$  following HA was correlated with the  
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840 335 pre-HA HST end-exercise  $T_{re}$  ( $r = -0.490$ ,  $P = 0.046$ ) and the baseline [Hb] ( $r = 0.550$ ,  $P =$   
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842 336  $0.022$ ). The reduction in the within session  $\Delta T_{re}$  following HA was correlated with the end  
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844 337 exercise  $T_{sk}$  ( $r = -0.529$ ,  $P = 0.029$ ),  $\Delta T_{sk}$  ( $r = -0.676$ ,  $P = 0.004$ ) and  $\Delta T_b$  ( $r = -0.526$ ,  $P =$   
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846 338  $0.036$ ) in the pre-HA HST. The reduction in end-exercise  $T_b$  following HA was correlated  
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848 339 with end-exercise  $T_{re}$  ( $r = -0.638$ ,  $p = 0.006$ ),  $T_{sk}$  ( $r = -0.527$ ,  $P = 0.030$ ),  $T_b$  ( $r = -0.646$ ,  $P =$   
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850 340  $0.005$ ) and the within session  $\Delta T_{re}$  ( $r = -0.660$ ,  $P = 0.004$ ),  $\Delta T_{sk}$  ( $r = -0.573$ ,  $P = 0.020$ ) and  
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852 341  $\Delta T_b$  ( $r = -0.706$ ,  $P = 0.002$ ) in the pre-HA HST. The reduction in the within session  $\Delta T_b$   
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854 342 following HA was correlated with the end-exercise  $T_{sk}$  ( $r = -0.679$ ,  $P = 0.004$ ) and  $T_b$  ( $r = -$   
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856 343  $0.600$ ,  $P = 0.014$ ) and the  $\Delta T_{re}$  ( $r = -0.514$ ,  $P = 0.042$ ),  $\Delta T_{sk}$  ( $r = -0.827$ ,  $P < 0.001$ ),  $\Delta T_b$  ( $r =$   
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858 344  $-0.697$ ,  $P = 0.003$ ), in the pre-HA HST. The increase in WBSR following HA was correlated  
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860 345 with the average exercise  $T_{sk}$  in the pre-HA HST ( $r = -0.565$ ,  $P = 0.018$ ), whereas the decrease  
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862 346 in average exercise heart rate following HA was correlated with the average ( $r = -0.713$ ,  $P =$   
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864 347  $0.002$ ) and end-exercise ( $r = -0.757$ ,  $P = 0.001$ ) heart rate in the pre-HA HST. The increase in  
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866 348 blood volume following HA was not related to any of the variables measured in the pre-HA  
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868 349 HST.  
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874 351 To examine the specificity of the adaptive response *i.e.* whether those having a pronounced, or  
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876 352 more limited, response for one adaption index also demonstrated a similar response for other  
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878 353 indices of HA, correlation analysis were performed between the thermal indices of adaption  
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880 354 (end-exercise  $T_{re}$  and  $T_b$ , within HST  $\Delta T_{re}$  and  $\Delta T_b$ ) and the thermoregulatory (WBSR),  
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888 355 haematological ( $\Delta$  blood volume) and cardiovascular (average exercise heart rate) indices of  
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890 356 adaption. This analysis indicated that the magnitude of increase in WBSR following HA was  
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892 357 moderately related to the magnitude of the reduction in the within HST  $\Delta T_{re}$  ( $r = 0.487$ ,  $P =$   
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894 358  $0.048$ ), but there were no other significant relationships between the indices of adaption.  
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899 360 **Our analysis of the factors influencing the thermo-physiological responses to the initial HST**  
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901 361 **(figure 2 a-d) demonstrated that the absolute  $H_{prod}$  (596(56) W, range 509:738 W) was strongly**  
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903 362 **correlated with the within HST  $\Delta T_{re}$  ( $r = 0.609$ ,  $P = 0.009$ ) and moderately correlated with the**  
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905 363 **within HST session  $\Delta T_{\square_b}$  ( $r = 0.523$ ,  $P = 0.038$ ) and WBSR ( $r = 0.525$ ,  $P = 0.030$ ). The relative**  
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907 364  **$H_{prod}$  ( $8.1(0.9) W \cdot kg^{-1}$ , range  $6.7:10.2 W \cdot kg^{-1}$ ) was moderately correlated with the end exercise**  
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909 365  **$T_{re}$  ( $r = 0.508$ ,  $P = 0.037$ ) and the within HST  $\Delta T_{re}$  ( $r = 0.584$ ,  $P = 0.014$ ).  $E_{req}$  ( $r = 0.685$ ,  $P =$   
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911 366  $0.002$ ) and  $E_{req}/E_{max}$  ( $r = 0.669$ ,  $P = 0.003$ ) were strongly correlated with WBSR. Thereafter,**  
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913 367 **we investigated whether those variables identified as being significantly related to our indices**  
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915 368 **of acclimation in the initial HST were also related to the subsequent magnitude of adaptive**  
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917 369 **response for that parameter. This analysis demonstrated a moderate negative correlation**  
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919 370 **between the reduction in the within session  $\Delta T_{re}$  following the HA **intervention** and the absolute**  
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921 371  **$H_{prod}$  in the initial HST ( $r = -0.514$ ,  $P = 0.035$ ), but there were no further significant correlations.**  
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#### 924 372 925 926 373 **4.0 DISCUSSION**

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928 374 Our findings demonstrate that the individual-variation in the adaptive responses to the 10-day  
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930 375 HA **intervention** was not related to baseline  $VO_{2max}$ , previous exposure to a HA **intervention**,  
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932 376 or the thermal ‘dose’ accrued during the HA **intervention**. In addition, there was limited  
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934 377 evidence for strong relationships between the various indices of acclimation, indicating that the  
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936 378 characterising of individuals as ‘high’, or ‘low’, responders to HA should be done so with  
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938 379 reference to specific indices of HA, rather than as a ‘global’ classification. Importantly, some  
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947 380 of the thermo-physiological responses during the initial HST were related to the magnitude of  
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949 381 subsequent adaptive responses to the HA **intervention**, which suggests that some of these  
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951 382 baseline responses may be useful in estimating the potential benefits that an individual may  
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953 383 obtain from HA. However, we urge some caution, because the  $T_{re}$  and WBSR responses during  
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955 384 the initial HST were also related to the inter-**participant** differences in  $H_{prod}$  and  $E_{req}$ , indicating  
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957 385 that the design of the HST may also influence some of these initial thermo-physiological  
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959 386 responses. Moreover, the inter-**participant** differences in  $H_{prod}$  during the initial HST were also  
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961 387 related to the reduction in the within session  $\Delta T_{re}$  following HA, indicating that the design of  
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963 388 the HST may have influenced the scope for demonstrating adaption subsequently.  
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969 390 It has often been suggested that the adaptive response to heat is augmented in those with a high  
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971 391 **VO<sub>2max</sub>** (e.g. Armstrong and Maresh, 1991; Casadio *et al.*, 2017), although closer inspection of  
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973 392 the extant literature suggests that this assertion is based on a limited number of observations  
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975 393 (Pandolf *et al.*, 1977). Likewise, it has been proposed that individuals with a high **VO<sub>2max</sub>** are  
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977 394 partially heat acclimated compared to those with lower **VO<sub>2max</sub>** (e.g. Aoyagi *et al.*, 1997;  
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979 395 Shvartz *et al.*, 1977). However, the present study has shown that baseline **VO<sub>2max</sub>** (absolute or  
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981 396 relative) was not related to the initial thermo-physiological responses to exercise in the heat,  
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983 397 nor to the magnitude of the adaptive responses following the HA **intervention**. The reasons for  
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985 398 these discrepant findings are unclear, although at the genomic level, transcriptome profile data  
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987 399 from rodent models has shown that heat and exercise each induce specific transcriptional  
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989 400 programmes (Kodesh *et al.*, 2011). Alternatively because, both the baseline **VO<sub>2max</sub>** and the  
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991 401 adaptive response of **VO<sub>2max</sub>** to training have a considerable genetic component (Bouchard *et*  
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993 402 *al.*, 2011a,b) the use of **VO<sub>2max</sub>** as surrogate of training level and by extension the extent to  
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995 403 which elevated thermal strain is encountered through habitual training will, at best, provide a  
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997 404 crude estimate. **Future studies investigating this topic should consider analyses of in-depth**  
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405 training data, rather than relying on measurement of  $VO_{2max}$  as a surrogate of training level.

406 Importantly, our observations have practical relevance; irrespective of baseline  $VO_{2max}$ ,  
407 individuals required to exercise in high ambient temperatures should consider undertaking a  
408 HA intervention and those with a high  $VO_{2max}$  should not consider themselves partially heat-  
409 acclimated. Indeed, the belief that a  $VO_{2max}$  confers some HA may, in part, explain the recent  
410 report that only 15% of athletes at the 2015 Athletics world Championship employed an HA  
411 programme prior to competition (Périard *et al.*, 2017).

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413 We also hypothesised that individuals who had undergone prior HA might demonstrate an  
414 augmented acclimatory response. However, our analyses indicated that there were no  
415 significant differences in the adaptive response of those individuals who had undertaken a prior  
416 HA intervention. This finding is somewhat at odds with data showing that the magnitude of  
417 some aspects of the acclimation response are increased with re-acclimation (Saat *et al.*, 2005).  
418 Indeed, a recent meta-analysis concluded that the process of re-acclimation to heat was faster  
419 than the initial acclimation, at least in terms of reduction in deep body temperature and  
420 cardiovascular adaptations (Daanen *et al.*, 2018). Likewise, data from rodent studies has  
421 demonstrated the presence of a cellular cytoprotective acclimation memory (Horowitz, 2016),  
422 although the relevance of these observations for the whole-organism acclimation response is  
423 not yet clear. Indeed, we were not able to measure aspects of cellular tolerance in the present  
424 study and so cannot draw comparisons with Horowitz *et al.* (2016), whilst closer inspection of  
425 the meta-analytic data indicates that in many of the primary studies the re-acclimation process  
426 took place after a relatively short decay (*e.g.* Saat *et al.*, 2005) and some of the effects are  
427 likely due to a baseline influence caused by retention of some of the initial adaptation to HA.  
428 Importantly, our data indicate that the baseline HST responses of those who had undergone

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429 prior HA were not different from those who were undertaking HA for the first time suggesting  
430 that the elapsed period between the acclimation was sufficient to enable full decay.

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432 In the present study we used a controlled hyperthermia HA **intervention** in which work rate  
433 was adjusted in order to maintain a target  $T_{re}$  of 38.5°C-38.7°C on each day. In contrast to  
434 traditional approaches, which typically use the same daily work-rate (*e.g.* Lind and Bass 1963;  
435 Pandolf *et al.*, 1977; Senay *et al.*, 1976) and may, therefore, result in a diminishing thermal  
436 forcing-function over the HA **intervention**, this approach maintains the thermal forcing-  
437 function. Whilst our data indicate that the thermal ‘dose’ was well maintained over the course  
438 of the HA **intervention** (no time effect for time  $T_{re} > 38.5^{\circ}\text{C}$ ) there were notable inter-  
439 **participant** differences in the total time accumulated above this thermal threshold. Previous  
440 research suggests that the magnitude of adaptive response during HA is diminished when  $T_{re}$   
441 is  $< 38.5^{\circ}\text{C}$  (Fox *et al.*, 1963), but there is no additional benefit when  $T_{re}$  is raised to  $39.0^{\circ}\text{C}$   
442 (Gibson *et al.*, 2015). Likewise, Lind and Bass (1963) demonstrate that the adaptive response  
443 with  $1 \times 100$  min daily exercise-heat exposure was greater than  $2 \times 50$  minute daily exercise-  
444 heat exposures, which they attributed to the greater amount of time spent elevating tissue  
445 temperature with the multiple exposure protocol, whereas Fox *et al.*, (1963) demonstrated that  
446 the adaptive response was greatest in individuals spending the most time with a  $T_{re}$  of  $\sim 38.5^{\circ}\text{C}$ .  
447 In contrast, our data indicate that the indices of acclimation were not related to the time spent  
448 with a  $T_{re} > 38.5^{\circ}\text{C}$ . The reason for this apparently discrepant finding is not clear. However,  $T_{re}$   
449 may not be the most appropriate index of thermal strain and  $\bar{T}_b$  might represent a better index  
450 because it incorporates a measure of central and peripheral tissue temperature, which is  
451 important for HA (Regan *et al.*, 1996), whereas the thermoeffector stimulus may be more  
452 closely related to other parameters, such as  $E_{req}$  (Gagnon *et al.*, 2013).

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454 Inter-individual variability in the adaptive response to heat has led to the suggestion that  
455 individuals might be classified as ‘responders’ or ‘non-responders’ to heat (Racinais *et al.*,  
456 2012), as is the case with adaption to other stressors such as altitude (Chapman *et al.*, 1998),  
457 or exercise (Bouchard *et al.*, 2011b). However, in some instances this classification has been  
458 based upon a single reference parameter, such as plasma volume expansion (Racinais *et al.*,  
459 2012) and when a range of adaptation indices are presented it is unclear whether the response  
460 profile is consistent across indices (Racinais *et al.*, 2014). A moderate correlation was  
461 demonstrated between the increase in WBSR and the magnitude of the reduction in the within  
462 HST  $\Delta T_{re}$ , however, on the whole, the various aspects of the adaptive response were not  
463 correlated. Thus, the adaptive response to heat not only varies between individuals, but also  
464 between indices of adaptation. For example, the magnitude of blood volume expansion was not  
465 related to the changes in thermal indices of adaptation, WBSR, or exercise heart rate, thus an  
466 individual who demonstrates a high adaptive response for blood volume may demonstrate a  
467 low adaptive response for sudomotor, cardiovascular or thermal aspects of adaption. The basis  
468 for this between-indices variation is unknown, although independence between aspects of the  
469 adaptive response to heat has been demonstrated previously (Garrett *et al.*, 2009; Neal *et al.*,  
470 2016a; Périard *et al.*, 2015). Baseline differences might contribute to some of the variation.  
471 For instance, some individuals have a naturally-occurring high blood volume (Martino *et al.*,  
472 2002), which might limit the scope for hypervolemia, with less influence on other indices of  
473 adaptations. Alternatively, a low response for a given parameter may simply be a consequence  
474 of an insufficient stimulus for adaption for that parameter; recent studies examining  
475 heterogeneity in the training response have demonstrated that ‘non-responders’ to a standard  
476 exercise training programme demonstrate a training response when the exercise ‘dose’ in  
477 increased (Montero and Lundby, 2017).

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1183 479 Some of the physiological responses during the initial HST were related to the magnitude of  
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1185 480 subsequent adaptive response. For instance, the  $\Delta T_{\square_b}$  and  $\Delta T_{\square_{sk}}$  recorded in the pre-HA HST  
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1187 481 was related to the reduction in end-exercise  $T_{\square_b}$ , and the reduction in the within HST  $\Delta T_{re}$  and  
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1189 482  $\Delta T_{\square_b}$  following the HA **intervention**. Thus, a large increase in  $T_{\square_{sk}}$  or  $T_{\square_b}$  during a standard  
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1191 483 HST might be a useful index for assessing baseline HA status and in identifying those  
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1193 484 individuals who will most benefit from HA. Likewise, the reduction in end exercise  $T_{re}$  and  
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1195 485  $T_{\square_b}$  over the HA **intervention** was related to the end-exercise  $T_{re}$  in the pre-HA HST,  
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1197 486 indicating that individuals with the greatest end exercise  $T_{re}$  in the first HST also had the  
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1199 487 greatest reduction in end-exercise  $T_{re}$  in  $T_{\square_b}$  after HA **intervention**. However, we urge some  
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1201 488 caution with interpretation of this data. We hypothesised that the highest  $T_{re}$  and WBSR in the  
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1203 489 initial HST would be observed in individuals with the highest  $H_{prod}$  and  $E_{req}$ , respectively, and  
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1205 490 that these high baseline responses would provide greater scope for evidencing adaptation.  
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1207 491 Indeed, our analysis confirmed that  $H_{prod}$  (in W or  $W \cdot kg^{-1}$ ) was related to the  $T_{re}$  and  $T_{\square_b}$   
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1209 492 responses during the first HST, whereas the largest amount of variance in WBSR was explained  
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1211 493 by  $E_{req}$  and  $E_{req}/E_{max}$ . These finding are consistent with the Cramer and Jay (2015) and indicate  
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1213 494 that some of the response to the initial HST is determined by protocol design, rather than basal  
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1215 495 HA state. Whilst this was not unexpected, most studies of HA do not attempt to standardise  
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1217 496 heat production during the HST (*e.g.* Garrett *et al.*, 2009; Gibson *et al.*, 2015; Neal *et al.*,  
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1219 497 2016ab; Pandolf *et al.*, 1977; Rendell *et al.*, 2017; Senay *et al.*, 1976; Shvartz *et al.*, 1977)  
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1221 498 because it is typically assumed to be of little relevance for within-participants design so long  
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1223 499 as the same external work-rates are used post-HA. However, our analysis also demonstrated a  
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1225 500 moderate negative correlation between the reduction in the within HST  $\Delta T_{re}$  following HA and  
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1227 501 the absolute  $H_{prod}$  (W) in the initial HST, suggesting that the design of the initial HST may also  
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1229 502 affect the subsequent response. Although we acknowledge that correlation is not evidence of  
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1231 503 causality, we propose that this represents a potential baseline effect whereby those  
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1242 504 demonstrating low-baseline HST response (due to the low  $H_{\text{prod}}$ ) have less scope for evidencing  
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1244 505 an adaptive response. The precise design of any HST will depend upon the nature of the  
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1246 506 research question. However, future studies examining the variability in the adaptive response  
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1248 507 to HA should consider standardisation of  $H_{\text{prod}}$  when assessing basal acclimation status and the  
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1250 508 subsequent adaptive responses to a HA programme, particularly when there are differences in  
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1252 509 participant  $VO_{2\text{max}}$ . Importantly, none of the other adaptation indices were related to the HST  
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1254 510 design and the majority of the variance in the HA response remains unaccounted for;  
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1256 511 subsequent studies should examine the influence of genetic and epigenetic factors on the  
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1258 512 variability in the HA response.  
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## 1263 514 **5.0 Conclusion**

1265 515 At the cohort-level, there was clear evidence of HA following the 10-day HA intervention, but  
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1267 516 pronounced variation was evident at the individual-level. This inter-participant variation was  
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1269 517 not related to factors that have putatively been proposed to influence the adaptive response to  
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1271 518 heat, including  $VO_{2\text{max}}$ , a history of prior HA, and the thermal ‘dose’ accrued during the HA  
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1273 519 intervention. The magnitude of adaptive response is, in the main, specific to the index of  
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1275 520 adaption; individuals who demonstrate a high, or low, adaptive response on one index of HA  
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1277 521 do not automatically demonstrate a similar response across the spectrum of HA indices. Some  
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1279 522 of the thermo-physiological responses during the initial HST were related to the magnitude of  
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1281 523 subsequent adaptive response, indicating that the initial response to a standard HST may have  
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1283 524 utility in identifying those individuals who will obtain the greatest adaptations from HA.  
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1285 525 However, some of the initial thermo-physiological responses may also have been influenced  
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1287 526 by the design of the HST;  $\Delta T_{\text{re}}$  was strongly related to  $H_{\text{prod}}$  and WBSR was strongly related to  
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1289 527  $E_{\text{req}}$ . Moreover, the reduction in the within session  $\Delta T_{\text{re}}$  following HA was related to the  $H_{\text{prod}}$   
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1291 528 in the initial HST, indicating that the design of the HST may also have influenced the scope  
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529 for demonstrating adaption. Nevertheless, the substantial majority of the inter-individual  
530 variance in the adaptive response to heat remains unaccounted for and future studies should  
531 seek to increase understanding of the factors contributing to this variance.

532  
533 **6.0 ACKNOWLEDGMENTS**

534 We would like to acknowledge the assistance during data collection provided by Liam Colley,  
535 Megan Davies, Adrian Fautly, Bryony Kinchin, Geoff Long, Amanda Ward, Danny White and  
536 Jennifer Wright, as well as the guidance provided by Dr Victoria Downie.

537  
538 **7.0 FUNDING**

539 Rebecca Rendell was supported by a joint English Institute of Sport/University of Portsmouth  
540 research bursary. No funding was received in the preparation of this manuscript.

541  
542 **8.0 DECLARATION OF INTERESTS**

543 The authors have no conflicts of Interest to Declare

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545 **9.0 REFERENCES**

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696 **10 FIGURE CAPTIONS**

697 **Figure 1.** a) relationship between pre heat acclimation (HA) haemoglobin concentration and  
698 the reduction in end-exercise  $T_{re}$  following HA; b) relationship between  $\Delta T_{sk}$  in the pre HA  
699 Heat Stress Test (HST) and the reduction in the within HST  $\Delta T_{re}$  following HA; c) relationship  
700 between  $\Delta T_b$  in the pre HA HST and the reduction in the end-exercise  $T_b$  following HA; d)  
701 relationship between  $\Delta T_{sk}$  in the pre HA HST and the reduction in the within HST  $\Delta T_b$   
702 following HA; e) relationship between average exercise  $T_{sk}$  in the pre HA HST and the  
703 increase in whole body sweat rate following HA; f) relationship between end-exercise heart  
704 rate in the pre HA HST and the reduction in the average exercise heart rate following HA.

705  
706 **Figure 2.** Correlation coefficients for associations between thermoregulatory responses during  
707 the initial heat stress test and relevant independent variables: a) end exercise  $T_{re}$  ( $^{\circ}\text{C}$ ) = light  
708 grey bars,  $\Delta T_{re}$  ( $^{\circ}\text{C}$ ) = dark grey bars); b) end-exercise  $T_b$  ( $^{\circ}\text{C}$ ) = light grey bars),  $\Delta T_b$  ( $^{\circ}\text{C}$ )  
709 = dark grey bars; c) whole body sweat rate ( $\text{L}\cdot\text{hr}^{-1}$ ); d) average exercise heart rate ( $\text{beats}\cdot\text{min}^{-1}$ ). \*  $P < 0.05$ ; \*\* $P < 0.01$ . BSA = body surface area;  $\text{VO}_{2\text{max}}$  = maximum rate of oxygen uptake;  
710  $H_{\text{prod}}$  = heat production;  $E_{\text{req}}$  = evaporative requirement for heat balance;  $E_{\text{max}}$  = maximum rate  
711 of evaporation to the environment; ND = no denomination.  
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714 **11.0 AUTHOR BIOGRAPHIES**



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716 Dr Jo Corbett is an Associate Head in the Department of Sport and Exercise Science at the  
717 University of Portsmouth, UK. He is a member of the Extreme Environments Laboratory,  
718 where his research examines the effect of environmental stressors, alone and in combination,  
719 on human performance and health.

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721

722 Dr Rebecca Rendell (née Neal) completed her Ph.D. at the University of Portsmouth in 2017  
723 after receiving her Master's degree in Human and Applied Physiology from King's College  
724 London in 2013, and undergraduate degree in Sport and Exercise Science from the University  
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726 University and conducts research in the areas of exercise and extreme environmental  
727 physiology and sports performance.

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731 Dr Heather Massey is a senior lecturer in Sport Exercise and Health. Her research interests  
732 focus on human physiology in extreme environments. Primarily studying the effect  
733 combinations of environmental stressors (cross-adaptation), such as exposure to the cold and  
734 hypoxia, have on human thermoregulatory, vascular, respiratory and autonomic function.

735



736

737 Dr Joseph Costello is a Senior Lecturer in exercise physiology and a member of the Extreme  
738 Environments Laboratory at the University of Portsmouth, UK. His research interests are  
739 directed towards i) understanding the physiological effects of various stressors (e.g. exercise,  
740 extreme environments, clothing) on human performance and ii) establishing evidence-based  
741 practice in sport and exercise science through the publication of high quality systematic reviews  
742 and meta-analyses.

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745 Prof Mike Tipton is a professor of human & applied physiology with an interest in the  
746 physiological and pathophysiological response to extreme environments, and the selection,  
747 preparation and protection of those entering such environments

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