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Spontaneously hypertensive rats have greater impairments in regulating abdominal temperature than brain cortex temperature following physical exercise

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ABSTRACT

This study aimed to evaluate the changes in brain (T_{brain}) and abdominal (T_{abd}) temperatures in spontaneously hypertensive rats (SHRs) following fatiguing exercise. Male normotensive Wistar rats (NWRs) and SHRs were used at 16 weeks of age. Their arterial pressure was measured by tail plethysmography prior to the experiments to confirm the hypertensive status of the SHRs. Then, the rats underwent implantation of an abdominal temperature sensor to measure T_{abd} and a guide cannula in the frontal cortex to enable the insertion of a thermistor to measure T_{brain}. After a familiarization period, each animal was subjected to incremental speed exercises until fatigue in either a temperate (25 °C) or warm (32 °C) environment, followed by a 60-min post-exercise period at the same temperature at which they exercised. T_{brain}, T_{abd} and tail-skin temperature (T_{skin}) were measured every min throughout the experiments. SHRs exhibited higher T_{abd} values than NWRs, and these higher values were transiently and persistently observed at 25 °C and 32 °C, respectively. For example, at 32 °C, T_{abd} was 0.84 °C higher in SHRs at the 25th min (large effect size). In contrast, regardless of the ambient temperature, SHRs exhibited similar T_{brain} values as NWRs, indicating preserved T_{brain} regulation following exercise in hypertensive rats. SHRs presented higher T_{skin} during the last half of the post-exercise period at 25 °C, whereas no inter-group differences were observed at 32 °C. In conclusion, the present results highlight that SHRs, an animal model that mimics uncontrolled essential hypertension in humans, exhibited greater impairments in regulating T_{abd} than T_{brain} during the post-exercise period.

1. Introduction

The core body temperature of mammals is tightly controlled within narrow limits by a precise, well-coordinated balance between the rates of heat production and heat loss (Wanner et al., 2015; Webb, 1995). This precise control is observed, for example, in freely moving rats, which present small fluctuations in core temperature when exposed to a wide range of ambient temperatures (Yang and Gordon, 1996). However, some particular conditions cause the rats' core temperature to deviate from these narrow limits; these conditions include the development of a systemic inflammatory response (Wanner et al., 2017) and performance of a physical exercise session (Wanner et al., 2015).

The increase in core temperature observed during the early moments of physical exercise results from a temporary imbalance between the above-mentioned rates, with the rate of heat production increasing faster than the rate of cutaneous heat loss (Gleeson, 1998; Webb, 1995). As physical exercise continues, heat loss mechanisms are then activated, and a steady-state core temperature is observed when exertion is

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performed under conditions of compensable heat stress (Gleeson, 1998; Sawka et al., 2011; Webb, 1995). Nevertheless, the core temperature will not reach a plateau when mammals are subjected to vigorous exercise or to exercise in warm/hot environments, which represent conditions of uncompensable heat stress (Sawka et al., 2011; Wanner et al., 2015). High values of core temperature, such as those achieved under the latter conditions (Cheung and Sleivert, 2004; Drummond et al., 2016; Kunstetter et al., 2014; Pires et al., 2013), may trigger a systemic inflammatory response and thus represent a risk to health (Bouchama and Knochel, 2002; Pires et al., 2017), even after exercise has been terminated (i.e., during the recovery period).

Recovery from exercise brings physiological systems back to levels commonly observed in resting conditions, thereby allowing an organism to safely perform another exercise bout. In the context of physical training, recovery is an important component of the overall exercise regimen and is a paramount requirement for performance and continued improvement (Bishop et al., 2008). In general, the post-exercise recovery of physiological parameters is a biphasic process, with an initial rapid phase lasting from seconds to a few minutes followed by a slower second phase lasting from a few minutes to hours (Gaesser and Brooks, 1984). With exercise cessation, metabolic rate and the resulting heat production are rapidly reduced (Gaesser and Brooks, 1984; Webb, 1995), whereas the reduction in cutaneous heat loss is slower (Primola-Gomes et al., 2007), thus favouring the dissipation of body heat and restoration of the resting thermal balance. The duration of the core temperature recovery during the post-exercise period is influenced by several factors, such as the ambient temperature (Kenny et al., 1997) and intensity of prior exercises (Kenny et al., 1997).

As evidenced by epidemiological studies conducted in the United States of America and Europe, the incidence of heat-related illness is higher in hypertensive subjects than in normotensive subjects during heat waves (Argaud et al., 2007; Ellis, 1972). Therefore, hypertensive subjects are likely at an increased health risk under conditions when their core temperature reaches high levels, such as during exercise in the heat and the subsequent post-exercise period. However, according to a recent study, subjects with essential hypertension under pharmacological management exhibit greater evaporative heat loss and faster body cooling than normotensive subjects during recovery from moderate-intensity exercise performed in a hot environment (Fonseca et al., 2015). Notably, post-exercise thermoregulation in hypertensive individuals whose blood pressure is not controlled by anti-hypertensive drugs has not been investigated.

The spontaneously hypertensive rat (SHR) has been extensively used as an animal model of human essential hypertension (Trippodo and Frohlich, 1981) and is a suitable model to investigate the effects of non-treated arterial hypertension on post-exercise thermoregulation. SHRs have greater physiological responses after central cholinergic stimulation (da Fonseca et al., 2018) or when subjected to stressful conditions (Lawler et al., 1985), including physical exercise, where they exhibit greater increases in abdominal (T_{abd}) (Campos et al., 2014; Drummond et al., 2016) and brain (T_{brain}) temperatures (Drummond et al., 2016) resulting from higher metabolic heat production and lower cutaneous heat loss than normotensive rats (Campos et al., 2014; Drummond et al., 2016). These greater physiological responses in SHRs are often maintained during the ensuing recovery from these stressful conditions (Hajós and Engberg, 1986; Lawler et al., 1985). Therefore, we hypothesized that SHRs would present attenuated cutaneous heat loss and slower recovery of both the T_{abd} and T_{brain} after treadmill running because of their increased peripheral resistance (Trippodo and Frohlich, 1981), sympathetic hyperactivity (Judy et al., 1976) and endothelial dysfunction (Kerr et al., 1999) compared with normotensive rats. In fact, we expected the recovery of SHRs to be even slower in response to environmental heat stress, a situation in which dry heat loss to the environment is limited. Thus, this study aimed to evaluate the effects of arterial hypertension on the changes in the T_{brain} and T_{abd} following exercise in two environmental conditions (i.e., at an ambient temperature of 25 °C or 32 °C).

2. Materials and methods

2.1. Animals

Sixteen-week-old male SHRs (n = 8) and normotensive Wistar rats (NWRs; n = 8) were housed in cages under a 14/10-h light/dark cycle in a temperature-controlled room (24 °C). This light/dark cycle was chosen to mimic the daylight duration during summer in the city of Belo Horizonte (19°55′14″ South and 43°56′16″ West, where the experiments were performed). Initially, four animals were housed in each standard polypropylene cage. After surgery, the rats were housed individually. Standard rat chow (Nuvilab®; Nuvital Nutrientes, Colombo - PR, Brazil) and tap water were available *ad libitum*. The SHR group had a lower body mass than the NWR group at the time of the experiments (321 ± 12 g vs. 371 ± 19 g, $p < 0.05$). Considering that the development of hypertension in SHRs depends on age rather than on body mass, the two groups were age-matched (Campos et al., 2014; Drummond et al., 2016; Hom et al., 2007).

The sample size calculation was performed as proposed by Armitage et al. (2002). Our previous study (Campos et al., 2014) was used as a data source. More specifically, we used the T_{abd} in rats subjected to treadmill running; these data presented a standard deviation of 0.59 °C when the greatest difference in the T_{abd} during exercise at distinct ambient temperatures was observed. The following parameters were adopted for calculation: i-a significance level of 5%, ii-a power of 80% for the statistical tests; iii-a difference of 0.87 °C between groups to be detected. This calculation indicated that 8 rats per experimental group were required to detect the expected difference; this recommendation was then followed. The experimental protocol was approved by the Ethics Commission on Animal Use of the Universidade Federal de Viçosa (protocol 58/2012) and was conducted in accordance with the regulations provided by the National Council for the Control of Animal Experimentation (CONCEA/Brazil).

At the beginning of the experiments, systolic (SAP) and diastolic arterial pressure were measured by tail-cuff plethysmography (model LE5001; Panlab, Barcelona, Spain) to confirm hypertension in the SHRs. All SHRs had an SAP ≥150 mmHg and were therefore considered hypertensive (Okamoto and Aoki, 1963).

2.2. Surgical procedures

The surgical procedures for the implantation of a guide cannula in the brain cortex and a temperature sensor in the abdomen were previously described (Drummond et al., 2016). The rats were allowed 5 days to recover from surgery prior to familiarization with running on the treadmill (Drummond et al., 2016). This recovery period was sufficient for the rats to recover and regain their presurgical body mass.

2.3. Incremental speed exercise and post-exercise period

After the familiarization period, each animal was subjected to two incremental, fatiguing exercise protocols followed by a 60-min post-exercise period in either a temperate (25 °C) or warm environment (32 °C). The order of the experimental trials was randomized and balanced. The tail-skin temperature (T_{skin}), T_{abd} and T_{brain} were measured before, during and after the exercise session. The temperature values measured before (resting values) and during the post-exercise period are reported in the present study; the temperature values measured during exercise have already been reported in an earlier study (Drummond et al., 2016). All experiments were performed between 0700 and 1300 h, and an interval of at least 48 h was provided between trials.

On the day of the experiments, the thermocouple (model 409B; Yellow Spring Instruments, Yellow Springs - Ohio, USA) was fixed to the

tail of the rats with adhesive tape, and a thermistor was inserted into the brain cortex through the guide cannula. Then, the rats were subjected to an incremental speed exercise on a custom-made treadmill (Gaustec, Nova Lima - MG, Brazil). The initial speed was set to 10 m min^{-1} and increased at increments of 1 m min^{-1} every 3 min until volitional fatigue occurred (Primola-Gomes et al., 2009). The electrical stimulation was set to 0.2 mA throughout the exercise period. The exercise was performed until fatigue, which was defined as the point at which the animals were no longer able to keep pace with the treadmill for 10 s (Campos et al., 2014).

2.4. Control of environmental temperature during exercise and post-exercise periods

During the exercise and post-exercise periods, the dry ambient temperature inside the treadmill was controlled at 25 °C and 32 °C. Importantly, in a given experimental trial, the ambient temperature was the same for the exercise and post-exercise periods. During the experiments performed at 25 °C, the ambient temperature was controlled with air conditioning (Komeco, Palhoça - SC, Brazil). The temperature of 25 °C corresponds to the low end of the thermoneutral zone of rats resting on a treadmill, as evidenced by a heat loss index (Romanovsky et al., 2002) ranging from 0.20 to 0.25 under these experimental conditions (Malheiros-Lima et al., 2018). During the experiments performed at 32 °C, two electric heaters (Britânia, Curitiba - PR, Brazil) were positioned at the same level, with one in front of and the other behind the treadmill belt.

2.5. Histological analysis

After the experiments, the rats were deeply anaesthetized with i.p. injections of ketamine and xylazine (120 and 15 mg/kg body mass, respectively). Rats were perfused with 100 mL of heparinized (10 $U.mL^{-1}$) phosphate-buffered saline (PBS) through the ascending aorta (right atrium cut) followed by 400 mL of cold 4% paraformaldehyde (Sigma-Aldrich, St. Louis - MO, USA) in PBS using a peristaltic metering pump (Milan Equipamentos Científicos, Colombo - PR, Brazil) constantly set to a flow rate of 10 mL min^{-1}. The brains were removed, post-fixed with paraformaldehyde for 48 h at 4 °C and transferred to a 30% sucrose solution at 4 °C for 48 h. The brains were then cut on a cryostat (Leica Microsystems, Wetzlar, Germany) into 50-μm sections and stored at 4 °C in a 0.9% saline solution until being mounted on glass slides. The brain slices were stained with 0.5% cresyl violet and examined under a light microscope. The positions of the thermistor tips were confirmed by comparing the sites of the brain lesions to the neural substrates described in the Paxinos and Watson atlas (Paxinos and Watson, 2007). No difference was observed in the positioning of the cannula between the groups (Drummond et al., 2016); therefore, the different T_{brain} responses observed in the SHRs during the post-exercise period resulted from hypertension *per se* and not from the positioning of the thermistor tips.

2.6. Measurements and calculations

Both the T_{brain} and T_{abd} were measured as indices of the core body temperature (IUPS, 2001), although we recognize that these two temperatures do not respond in a similar way (particularly regarding their time course) to several arousing stimuli (Kiyatkin, 2007) and physical exercise (Hasegawa et al., 2008). T_{brain} was measured using a thermistor (Beta Therm Corp., Shrewsbury - MA, USA) that was inserted through the guide cannula into the right frontal cortex. The thermistor had a diameter of 0.53 mm and was connected to equipment that measured changes in resistance (model 289 FVF; Fluke, Everett - WA, USA). The resistance values (ohm) were converted into temperature values using the Steinhart-Hart equation. Temperature was measured in this brain area because perceived exertion in humans cycling at different ambient temperatures is strongly correlated with frequency changes in the electroencephalogram obtained over the frontal cortex (Nybo and Nielsen, 2001). T_{abd} was measured by telemetry using a temperature sensor (G2 E-Mitter, model ER4000; Mini-Mitter, Bend - OR, USA) implanted in the abdominal cavity. T_{skin} was measured using a thermocouple fixed to the right lateral surface 1 cm from the base of the tail. The close proximity to the base of the tail enabled more sensitive measurements of changes in skin temperature that occurred as a function of changes in local blood flow (Young and Dawson, 1982). The ambient temperature was measured by two thermocouples taped to the ceiling of the treadmill chamber: one was placed in the front end, whereas the other was placed at the rear end of the treadmill belt, close to the stimulating grid.

2.7. Statistical analysis

The Shapiro-Wilk test was used to test all variables for normal distributions; these tests were performed on temperature data measured at fatigue, which corresponded to the moment zero in our analyses. Because all data were normally distributed, they are presented as the means ± S.E.M. We used mixed-design ANOVAs to compare the curves for T_{brain}, T_{abd}, and T_{skin}, with the effect of rat strain (SHRs vs. NWRs) representing a between-groups analysis and the effects of ambient temperature (25 °C vs. 32 °C) and post-exercise time points (every minute for 60 min) representing within-groups analyses. Whenever applicable, these ANOVAs were followed by *post hoc* tests: Student's t-test (LSD) or the Scott-Knott test. The areas under the curve (AUCs) for body temperature were compared between groups and environments using mixed-design two-way ANOVAs followed by the Tukey *post hoc* test. The AUCs for these body temperatures were calculated using the trapezoidal rule. The significance level was set to 5%.

The Cohen's d effect size (ES) was calculated to assess the magnitude of the differences in data between experimental groups. The ES was calculated by subtracting the mean value for one group from the mean value of the group it was being compared to. The result was then divided by a combined standard deviation for the data. The ES values were classified as trivial (ES < 0.2), small (ES 0.2–0.6), medium (ES 0.6–1.2) or large (ES ≥ 1.2) (Hopkins et al., 2009). The limits of the 95% confidence interval (CI) were calculated according to the equation described by Fritz et al. (2012).

3. Results

Immediately before the beginning of exercise at 25 °C (Fig. 1), the SHRs showed a higher T_{abd} than the NWRs (37.32 ± 0.10 °C vs. 36.81 ± 0.09 °C, $p < 0.05$; $d = 1.75$, 95% CI: 0.60 to 2.90), whereas no inter-group differences were observed in T_{brain} and T_{skin}. Similar responses were observed before exercise initiation at 32 °C, with the SHRs showing higher T_{abd} than the NWRs (37.41 ± 0.11 °C vs. 37.00 ± 0.10 °C, $p < 0.05$; $d = 2.24$, 95% CI: 0.99 to 3.49) but no changes in T_{brain} and T_{skin}. The increased pre-exercise T_{abd} observed in SHRs can be classified as a large effect induced by hypertension.

As previously published (Drummond et al., 2016), SHRs subjected to exercise exhibited higher thresholds for triggering increases in T_{skin}, as well as greater increases in T_{brain} and T_{abd} during incremental exercises at 25 °C and 32 °C than NWRs. Indeed, these greater increases persisted until the moment when rats fatigued, which represents the start of the post-exercise period. At fatigue, T_{skin} was reduced in SHRs at 25 °C but unchanged at 32 °C. Despite modifying exercise thermoregulation, hypertension did not influence the time to fatigue in either environment (Drummond et al., 2016).

The mixed-design ANOVAs that compared the body temperature curves after physical exertion revealed the existence of a triple interaction among rat strain, ambient temperature and time points for T_{brain} ($F = 1.39$; $p < 0.05$) and T_{skin} ($F = 5.93$; $p < 0.001$), but not for T_{abd} ($F = 0.35$; $p > 0.05$). However, significant main effects of rat strain

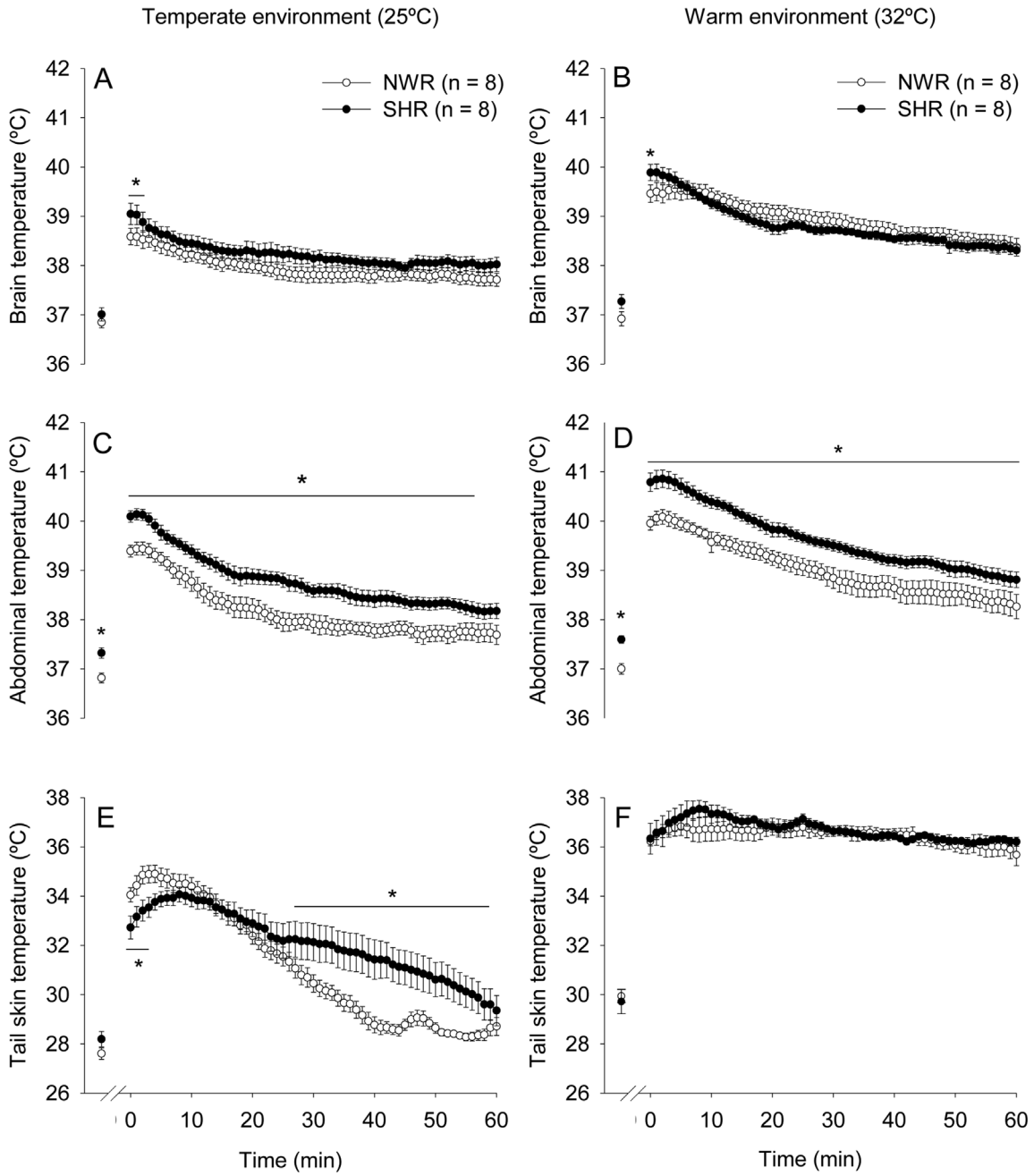

Fig. 1. Brain (panels A and B), abdominal (panels C and D) and tail-skin (panels E and F) temperatures in SHRs and NWRs following exercise at 25 °C (panels A, C and E) or at 32 °C (panels B, D and F). Data are presented as the means ± S.E.M. *$p < 0.05$ compared with the NWR group in the same environment. The symbols before the break in the x-axis represent the pre-exercise temperature values.

(F = 21.69; $p < 0.001$), ambient temperature (F = 38.53; $p < 0.001$) and time points (F = 183.16; $p < 0.001$), and a significant interaction between ambient and time (F = 3.27; $p < 0.001$) were observed for T_{abd}. More specific comparisons are presented in the following three paragraphs.

During the post-exercise period at 25 °C, T_{brain}, T_{abd} and T_{skin} decreased over time in the NWR and SHR groups. SHRs only showed higher T_{brain} values than the NWRs in the first 2 min (38.87 ± 0.20 °C vs. 38.52 ± 0.18 °C, at the 2nd min, $p < 0.05$; $d = 0.65$, 95% CI: −0.36 to 1.66) and higher T_{abd} from the 1st until the 56th min (38.79 ± 0.14 °C vs. 37.95 ± 0.19 °C, at the 25th min, $p < 0.05$; $d = 1.78$, 95% CI: 0.62 to 2.94). In addition, the SHRs exhibited lower T_{skin} than the NWRs from the 1st until the 3rd min (33.54 ± 0.40 °C vs. 34.89 ± 0.35 °C, at the 3rd min, $p < 0.05$; $d = 1.25$, 95% CI: 0.18 to 2.32) but higher T_{skin} from the 27th until the 58th min of the post-exercise period (31.42 ± 0.79 °C vs. 28.77 ± 0.32 °C, at the 40th min, $p < 0.05$; $d = 1.54$, 95% CI: 0.42 to 2.66). Despite the transient and moderate increase in T_{brain}, all temperature changes induced by hypertension at 25 °C were considered large.

During the post-exercise period at 32 °C, T_{brain} and T_{abd}, but not T_{skin}, decreased over time in the NWR and SHR groups; T_{skin} remained at high levels ranging from 36 to 38 °C. No differences were observed in T_{brain} (NWR: 38.37 ± 0.18 °C vs. SHR: 38.30 ± 0.11 °C, at the 60th min, $p > 0.05$; $d = 0.14$, 95% CI: −0.84 to 1.12) and T_{skin} (NWR: 35.67 ± 0.44 °C vs. SHR: 36.21 ± 0.18 °C, at the 60th min, $p > 0.05$; $d = 0.57$, 95% CI: −0.43 to 1.57) between SHRs and NWRs. In contrast, T_{abd} remained higher in SHRs than in NWRs throughout the 60-min period following exercise cessation (39.50 ± 0.11 °C vs.

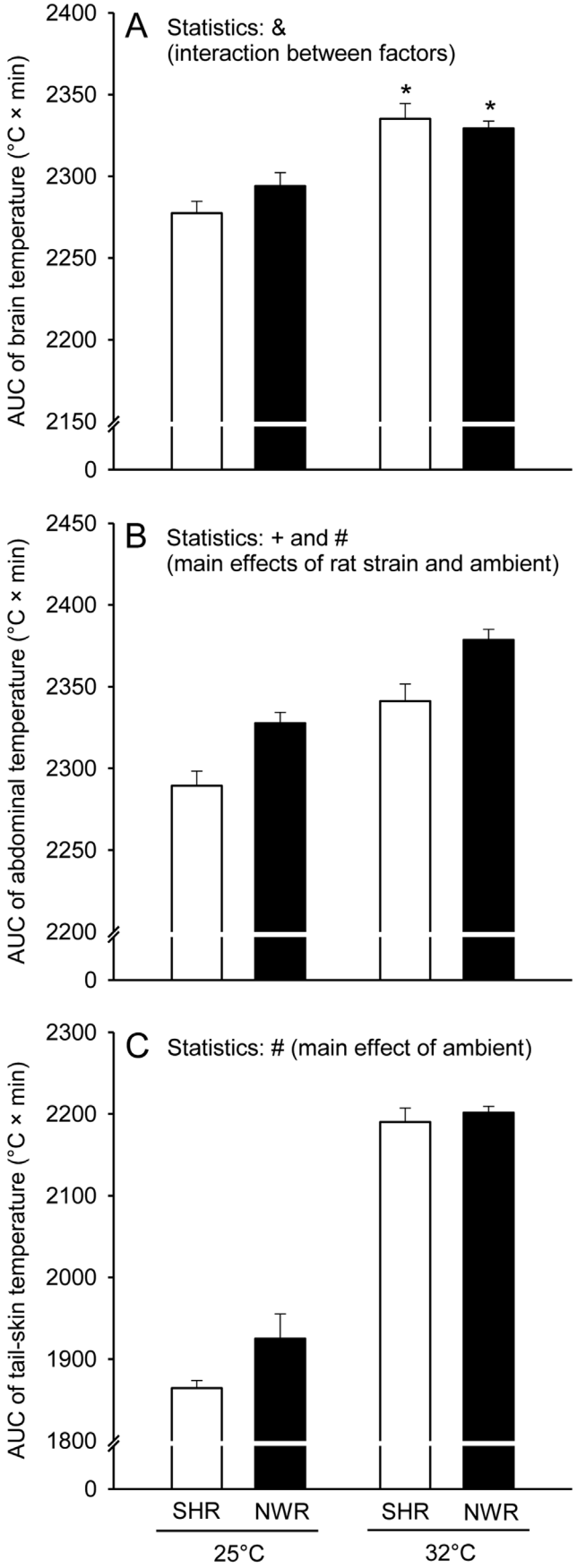

Fig. 2. AUCs for the three body temperatures evaluated after exercise in both environments: brain cortex temperature (T_{brain}; panel C); abdominal temperature (T_{abd}; panel B) and tail-skin temperature (T_{skin}; panel C). Data are presented as the means ± S.E.M. + denotes a significant major effect of rat strain ($p < 0.05$ when comparing SHRs vs. NWRs), # denotes a significant major effect of ambient temperature ($p < 0.05$ when comparing 25 °C vs. 32 °C); & denotes a significant interaction between the two factors ($p < 0.05$); * denotes a significant difference from the 25 °C trial within a given rat strain ($p < 0.05$)..

38.84 ± 0.21 °C, at the 30th min, $p < 0.05$; $d = 1.40$, 95% CI: 0.31 to 2.49). This inter-group difference in T_{abd} at 32 °C can be classified as a large increase caused by hypertension.

As expected, ambient temperature influenced body temperatures during the post-exercise period. In the NWRs, T_{brain} was higher during the entire post-exercise period, whereas it was higher in the SHRs from the 1st until the 48th min. T_{abd} and T_{skin} were also higher at 32 °C than at 25 °C in the two groups throughout the 60-min period following exercise cessation.

AUCs were calculated for each temperature analysed to examine the overall response of body temperatures during the 60-min period following exercise (Fig. 2). A significant effect of ambient temperature was observed on T_{brain}, T_{abd} and T_{skin} ($F > 80.76$ and $p < 0.001$ for the three analyses), and AUCs were always higher at 32 °C than at 25 °C. Only the analysis of T_{abd} data showed a significant effect of rat strain ($F = 13.83$, $p < 0.01$), with higher AUCs recorded for SHRs than NWRs. In contrast, the analyses of T_{brain} and T_{skin} did not reveal a significant effect of rat strain ($F = 0.31$, $p = 0.589$ and $F = 3.61$, 0.078, respectively). Moreover, no significant interactions between factors were observed for T_{abd} ($F = 0.01$, $p = 0.948$) and T_{skin} ($F = 1.91$, $p = 0.189$). Although a significant interaction was reported for T_{brain} ($F = 5.75$, $p < 0.05$), the *post hoc* analysis revealed higher AUCs at 32 °C than at 25 °C for each of the two strains tested, thereby reinforcing the influence of environmental conditions on the post-exercise brain temperature.

4. Discussion

In the present study, the control of body temperature was evaluated in SHRs following a fatiguing exercise in a temperate (25 °C) or warm environment (32 °C). Our main finding was that SHRs subjected to an incremental speed exercise exhibited impaired recovery of T_{abd} during the post-exercise period, regardless of the environmental conditions. Additionally, SHRs subjected to exercise exhibited normal recovery of T_{brain} similar to normotensive rats during the post-exercise period in both environments. Based on these results, SHRs efficiently regulate T_{brain} but not T_{abd} following a fatiguing exercise.

Before discussing the present findings that involve thermoregulation following exercise, brief comments on treadmill running-induced changes in body temperatures are necessary. Regardless of the environment, SHRs exhibited greater increases in T_{abd} resulting from higher metabolic heat production and delayed cutaneous heat loss than normotensive rats (Campos et al., 2014; Drummond et al., 2016); SHRs also exhibited exaggerated exercise-induced increases in T_{brain}. Notably, T_{brain} and T_{abd} are regulated by different mechanisms. Because heat exchange through the skull with the surroundings is very limited, brain heat is mainly dissipated through cerebral blood flow (CBF) (Nybo et al., 2002). In addition, CBF is inversely correlated with systemic blood pressure levels (Fujishima et al., 1995). Therefore, a reduced CBF in SHRs may underlie the greater increase in T_{brain} during exercise.

In addition, T_{brain} always increased to less of an extent than T_{abd} during exercise in both strains in either environment. This attenuated increase in the T_{brain} of running rats is usually observed when temperature is measured in the brain cortex (Drummond et al., 2016) but not in the thalamus (Damasceno et al., 2015) or hypothalamus (Fonseca

et al., 2014) and is consistent with the theory of selective brain cooling that would protect the brain from thermal damage when T_{brain} values are high (Lim and Mackinnon, 2006). Although the existence of selective brain cooling in rats is controversial, the most accepted theory proposes that cool blood draining from the nose and head skin cools the brain tissue under conditions of hyperthermia (Caputa, 2004; Caputa et al., 1996). Ventilation seems to play a role in selective brain cooling at least in humans, as evidenced by the fact that arterial blood is directed to the brain tissue after cooling in the upper respiratory tract. Interestingly, patients have been reported to reduce their intracranial temperature when asked to breathe vigorously for 3 min with inhalation through the nose and exhalation through the mouth (Mariak et al., 1999).

The findings yielded from post-exercise experiments partially corroborated our hypothesis, as hypertension only affected the recovery of T_{abd} (not T_{brain}) increased by previous treadmill running. At 25 °C, SHRs presented a reduction in T_{brain} similar to NWRs (Fig. 1A). However, T_{abd} remained higher in SHRs during most of the post-exercise period (Fig. 1C), except in the final minutes, when the temperature became similar in both groups. The lack of differences in T_{abd} at the end of the 60-min period probably reflects the greater cutaneous heat loss presented by hypertensive animals in the last half of the post-exercise period, as evidenced by high T_{skin} values that indicate tail-skin vasodilation (Fig. 1E). This augmented cutaneous heat loss in SHRs occurred despite the increased peripheral resistance reported in these rats and was likely driven by a thermal stimulus arising in the abdomens rather than in the brains of these rats.

At 32 °C, the differences in T_{brain} and T_{abd} between strains were similar to those recorded at 25 °C. The only exception was the higher T_{abd} values recorded in the SHRs until the end of the post-exercise period at 32 °C (Fig. 1D), probably due to the lack of inter-strain differences in T_{skin} (Fig. 1F) and, therefore, in tail-skin vasodilation, which is the primary heat loss mechanism in rats (Shellock and Rubin, 1984; Young and Dawson, 1982). In particular, in hot environments with a decreased thermal gradient between the skin and environment, saliva-spreading behaviour is an important adjunct thermolytic mechanism for core temperature regulation (Hainsworth and Stricker, 1971). Although this behaviour was not evaluated, the present data suggest that SHRs did not spread more saliva on the body surface following exercise because their T_{abd} (which depends on cutaneous heat loss) remained higher throughout the recording period.

Interestingly, the differences in T_{brain} between hypertensive and normotensive rats observed during treadmill running were not evident during the post-exercise period. The observation that T_{abd} remained elevated in SHRs for longer periods and the fast recovery of T_{brain}, which became similar to values recorded in NWRs within a few minutes, suggest that SHRs prioritize T_{brain} recovery following exercise. This result may be explained by a more pronounced post-exercise hypotension presented by hypertensive rats (Shyu and Thoren, 1986). Thus, considering that brain heat is mainly lost through CBF (Nybo et al., 2002), which is inversely correlated to systemic blood pressure levels (Fujishima et al., 1995), greater reductions in blood pressure levels might be associated with increased CBF and brain heat loss in hypertensive rats during the post-exercise period.

The fast T_{brain} recovery in SHRs may be particularly important because these rats present greater T_{brain} than NWRs at fatigue. According to *in vitro* studies, neuronal cells are some of the most heat-sensitive cells in the body and are characterized by a low upper-temperature limit tolerance in hyperthermic conditions and by a low proliferation potential (Dewhirst et al., 2003). In addition, acute physiological changes resulting from heat exposure (e.g., brain oedema) might be lethal to brain cells, even when few cells actually die from direct thermal injury (Dewhirst et al., 2003).

Our findings do not agree with a recent study that investigated post-exercise thermoregulation in hypertensive humans (Fonseca et al., 2015). In this study, subjects with essential hypertension displayed greater evaporative heat loss, leading to greater reductions in mean body temperature than normotensive subjects during recovery from moderate-intensity exercise performed in a hot environment. This result contradicts our findings, as none of the body temperatures measured in SHRs were lower than those measured in control rats following exercise in the heat. Notably, the subjects of the study by Fonseca and colleagues (Fonseca et al., 2015) were hypertensive individuals who received a combination of diuretics and angiotensin-converting enzyme inhibitors and showed well-controlled blood pressure levels. Therefore, the present results may be applicable to uncontrolled hypertensive subjects who exercise mainly in the heat and are likely at a greater risk of developing heat-related illnesses during the post-exercise period.

In conclusion, SHRs exhibit impaired recovery of T_{abd} during the post-exercise period. In particular, this recovery was more prolonged in the warm environment, which exacerbates the inability of SHRs to dissipate abdominal heat. Interestingly, regardless of the ambient temperature, T_{brain} regulation is preserved in SHRs following exercise. Based on our findings, uncontrolled arterial hypertension produces a greater impairment in T_{abd} regulation than in T_{brain} regulation during the post-exercise period.

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Declarations of interest

None.

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