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SHORT COMMUNICATION

Cerebrovascular and cardiovascular responses to the Valsalva manoeuvre during hyperthermia

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Abstract

Background: During hyperthermia, the perturbations in mean arterial blood pressure (MAP) produced by the Valsalva manoeuvre (VM) are more severe. However, whether these more severe VM-induced changes in MAP are translated to the cerebral circulation during hyperthermia is unclear.

Methods: Healthy participants ($n = 12$, 1 female, mean ± SD: age 24 ± 3 years) completed a 30 mmHg (mouth pressure) VM for 15 s whilst supine during normothermia and mild hyperthermia. Hyperthermia was induced passively using a liquid conditioning garment with core temperature measured via ingested temperature sensor. Middle cerebral artery blood velocity (MCAv) and MAP were recorded continuously during and post-VM. Tieck's autoregulatory index was calculated from the VM responses, with pulsatility index, an index of pulse velocity (pulse time) and mean MCAv ($MCAv_{mean}$) also calculated.

Results: Passive heating significantly raised core temperature from baseline (37.9 ± 0.2 vs. 37.1 ± 0.1°C at rest, $p < 0.01$). MAP during phases I through III of the VM was lower during hyperthermia (interaction effect $p < 0.01$). Although an interaction effect was observed for $MCAv_{mean}$ ($p = 0.02$), post-hoc differences indicated only phase IIa was lower during hyperthermia (55 ± 12 vs. 49.3 ± 8 cm s^{-1} for normothermia and hyperthermia, respectively, $p = 0.03$). Pulsatility index was increased 1-min post-VM in both conditions (0.71 ± 0.11 vs. 0.76 ± 0.11 for pre- and post-VM during normothermia, respectively, $p = 0.02$, and 0.86 ± 0.11 vs. 0.99 ± 0.09 for hyperthermia $p < 0.01$), although for pulse time only main effects of time ($p < 0.01$), and condition ($p < 0.01$) were apparent.

Conclusion: These data indicate that the cerebrovascular response to the VM is largely unchanged by mild hyperthermia.

KEYWORDS

blood pressure, cerebral autoregulation, cerebral blood flow, heat stress, middle cerebral artery blood velocity

1 | INTRODUCTION

During hyperthermia circulatory adjustments permit a fivefold increase in cutaneous blood volume (Crandall et al., 2008) and a 2.5-fold increase in cardiac output, although the latter is dependent on the duration and magnitude of hyperthermia (Crandall & Wilson, 2011). Hyperthermia also affects cerebral blood flow, albeit primarily due to the cerebral circulation being immensely sensitive to arterial carbon dioxide content (Ainslie et al., 2005). When the internal (core) temperature is elevated by >+1°C, hyperventilation-induced hypocapnia decreases cerebral blood flow (Brothers et al., 2009a; Nelson et al., 2011). Despite the acute reduction in cerebral blood flow during hyperthermia, the ability of the cerebral vasculature to counter changes in intraluminal pressure, termed cerebral autoregulation, appears unchanged as assessed during thigh cuff release (Low et al., 2009) and oscillatory lower body negative pressure (Brothers et al., 2009b). Interestingly, Low et al. (2009) reported improved autoregulatory capacity in the very low-frequency range (0.02–0.07 Hz) during spontaneous fluctuations in blood pressure when hyperthermic.

The Valsalva manoeuvre (VM) is a forced exhalation against a closed glottis that produces marked and phasic changes in blood pressure. During the strain, phase I (PI) is indicated by a transient increase in blood pressure. The sustained increase in thoracic pressure subsequently reduces atrial filling and blood pressure (phase IIa, PIIa) with a sympathetically mediated increase in heart rate (HR), facilitating recovery in blood pressure (phase IIb [PIIb]). When the strain is terminated, blood pressure declines (phase III [PIII]), with the reduction in thoracic pressure restoring atrial filling. The now increased cardiac output is then ejected into a vasoconstricted arterial tree mediating a rise and overshoot in blood pressure (Phase IV [PIV]) (Perry et al., 2014; Tiecks et al., 1995).

Due to the rapid and bidirectional perturbations in blood pressure, the VM has been used to evaluate cerebral autoregulation, and assess peripheral and cerebral autonomic function (Tiecks et al., 1995; Zhang et al., 2004). During mild hyperthermia (sublingual temperature +~0.8°C), Davis and Crandall (2010) reported a trend for a greater increase in mean arterial blood pressure (MAP) from PIIa to PIIb, although the absolute reductions in PIIa and PIIb MAP were greater during hyperthermia. However, Davis and Crandall (2010) did not report cerebral blood flow or a proxy (e.g., middle cerebral artery blood velocity, MCAv), so how these more pronounced VM-induced perturbations in MAP affect the cerebral circulation remain unknown. Thus, the current experiment aims to explore the cerebrovascular responses to rapid and bidirectional perturbations in MAP induced by the VM during concomitant mild hyperthermia in the supine position. We hypothesize that during hyperthermia the VM will produce greater perturbations in blood pressure, reflected in concurrent changes in MCAv. Specifically, lower MCAv from PIIa through PIII of the VM during hyperthermia.

2 | METHODS

2.1 | Participants and ethical approval

Twelve healthy participants (1 female, mean ± SD: age 24 ± 3 years; body mass 75 ± 13 kg; height 180 ± 8 cm) provided written consent and participated in the study. The female participant completed the trial in the early follicular phase. All participants were not taking any medication and had no history of disease. All procedures were approved by the Massey University Human Ethics Committee (SOA 20/46) and conducted in accordance with the latest version of the Declaration of Helsinki.

2.2 | Study design

All participants visited the temperature-controlled laboratory twice. The first visit consisted of a full familiarization. The middle cerebral artery was insonated as described below (see Section 2.4). Participants then practiced a 15 s end-inspiratory VM at a mouth pressure of 30 mmHg whilst supine. The supine position was adopted to reduce the risk of syncope during PIII of the VM, especially during hyperthermia. Mouth pressure and duration were selected to enable comparisons with existing data during hyperthermia (Davis & Crandall, 2010) and generate clearly discernible phases of the VM (Perry et al., 2014). Mouth pressure was measured via transducer and displayed in real time to the participant. The second laboratory visit was the experimental trial, which occurred <1-week following familiarization. Participants arrived having abstained from caffeine for ≥12 h, and exercise and alcohol consumption for ≥24 h. Participants were also instructed to consume 500 mL of water the night before and 500 mL 4 h before the experiment to ensure euhydration, and remove the confounding influence of dehydration on cerebrovascular responses (Perry et al., 2016). Euhydration was confirmed by urine specific gravity (<1.020) 30 min before the start of the trial (mean ± SD 1.013 ± 0.006).

2.3 | Experimental design

Participants arrived at the laboratory having consumed a temperature sensor 4 h prior for the measurement of core temperature (T_{core}—intestinal). Following the confirmation of hydration status, nude body weight was measured. Temperature thermistors were placed on the calf, thigh, chest and forearm. Participants then donned a liquid conditioning garment (LCG). Participants then lay supine for instrumentation. Following 20 min of rest, baseline data were collected for 5 min, with the mean of the last 2 min of this period representing normothermic baseline. Following baseline participants performed an end-inspiratory (normal tidal breath) VM at a mouth pressure of 30 mmHg for 15 s. Except for the 20 min rest, this

process was repeated at T_{core} + 1°C, typically where reductions in resting MCAv are reported. The +1°C rise in T_{core} was calculated from the nadir value obtained following the onset of passive heating.

2.4 | Measurements

2.4.1 | Cardiorespiratory variables

HR was measured using a three-lead electrocardiogram (ECG, Lead II; ADInstruments). Noninvasive beat-to-beat arterial blood pressure was measured by finger photoplethysmography (Finometer MIDI; Finapres Medical Systems). The cuff was placed on the index finger of the left hand and referenced to the level of the heart. The finometer was corrected against a calibrated automated sphygmomanometer (Sure Signs VM4; Philips Medical Systems). Unilateral MCAv (right side) was measured using transcranial Doppler ultrasonography (Doppler-BoxX, DWL; Compumedics). Blood velocity in the M1 segment of the middle cerebral artery was measured using a 2 MHz probe fixed over the temporal window fixed in position via an adjustable headband. The M1 segment was identified using search techniques described elsewhere (Aaslid et al., 1982; Willie et al., 2011). The partial pressure of end-tidal carbon dioxide ($P_{ET}CO_2$) was measured using a breath-by-breath online gas analyser (Model ML206; ADInstruments) and collected continuously using a nasal cannula.

2.5 | Hydration status

Hydration status was assessed by measuring urine specific gravity with a handheld refractometer (PAL-10s Refractometer; ATAGO), by the same experienced operator.

2.6 | Body temperatures

T_{core} was indexed via ingestion of a calibrated single-use temperature sensor (accurate to 0.1°C; CorTemp, HQInc.) and transmitted to a wireless handheld data logger (CorTemp) in real time. Mean skin temperature (T_{skin}) was measured using calibrated skin thermistors (accurate to 0.2°C; Grant Instrument Ltd.) secured in place using surgical tape (3M Healthcare) and the weighted mean was calculated as previously described (Ramanathan, 1964). T_{skin} data were displayed continuously in real time using TracerDaq software (Measurement Computing Corporation).

2.7 | Passive heating

An LCG (CORETECH TUBEsuit, Delta Temax Inc.) was used to manipulate T_{skin}. The two-piece LCG covered the trunk, arms and legs and has a high density of polymer tubing sewn into its construction. All participants wore cycle shorts underneath to ensure maximal contact of the tubing with the skin. To further minimize heat loss, participants were covered with an aluminium foil blanket. A heated water bath (Grant Instruments Ltd. Accurate to 0.1°C), with inbuilt pump (flow rate: 1.9 L min^{-1}) perfused the LCG. For heating, the initial water temperature was 55°C and adjusted to participant tolerance. When approaching the target T_{core}, and during the experimental measures (baseline and VM), the foil blanket was removed and the water bath temperature was decreased to 36°C to limit the rise in T_{core} as previously described (Brothers et al., 2009b; Low et al., 2009; Perry & Mündel, 2021).

2.8 | Data analysis

2.8.1 | Calculations

Cerebrovascular conductance index (CVCi) was calculated via the equation $MCAv_{mean}$/MAP and the Gosling pulsatility index (Pi) for MCAv was calculated as systolic MCAv (SMCAv)—diastolic MCAv (DMCAv)/$MCAv_{mean}$. Post-VM Pi was averaged for 1 min following PIV of the VM. For variables of interest ($MCAv_{mean}$ and MAP) the absolute change from baseline, and relative change from baseline were determined for VM.

An index of pulse wave velocity, described herein as pulse time, was calculated by measuring the time from the R wave in lead II to the foot of the systolic wave of the MCAv waveform and calculating the average across 10 cardiac cycles. Pulse time was calculated immediately preceding the VM and 1 min post-VM.

2.9 | Autoregulatory index (AI)

Tieck's AI method was used to assess dynamic cerebral autoregulation during PII and PIV of the VM using the following equations:

PII:

$$AI - II = \frac{MCAv_{mean}\ (PIIb - PIIa)/MCAv_{mean}(PIIa)}{MAP(PIIb - PIIa)/MAP(PIIa)}.$$

PIV:

$$AI - IV = \frac{MCAv_{mean}\ (PIV)/MCAv_{mean}(PI)}{MAP(PIV)/MAP(PI)}.$$

Values that are greater than 1.00 indicate that autoregulation is present, while values less than 1.00 indicate that autoregulation is absent (Tiecks et al., 1995).

2.10 | Data acquisition

All data were collected continuously (except for mouth pressure) using an analogue to digital converter (PowerLab, ADInstruments), sampled at 1000 Hz and interfaced with a computer. Data were analysed using LabChart software (v8.1.16 ADInstruments).

2.11 | Statistical analysis

Dependent variables immediately preceding and during the VM were analysed using a two-way repeated measures analysis of variance (ANOVA) (phase × condition, 2 × 6 for absolute variables, 2 × 5 for changes from the previous phase). Pi and pulse time were compared pre- and post-VM in each condition using a two-way ANOVA (time × condition, 2 × 2). Resting hemodynamic variables and AI were analysed using paired *t* tests. Post-hoc pairwise comparisons were used to isolate main effects. Effect sizes were estimated using partial eta squared (partial η^2, two-way ANOVA interaction effect only), with large effect sizes identified as >0.14, medium 0.06–0.14 and small <0.06 (Cohen, 2013).

3 | RESULTS

Participant's baseline responses to hyperthermia are detailed in Table 1, which include the expected increase in HR, T_{core} and T_{skin}. Blood pressure and $MCAv_{mean}$ were unchanged, although the latter showed a small nonsignificant reduction, presumably due to the trend for a reduction in $P_{ET}CO_2$ at baseline (see Table 1).

3.1 | Responses to the VM

The typical responses to the VM are presented in Figure 1, with the average hemodynamic responses to the VM detailed in Figure 2 and the change from the previous VM phase in Figure 3. Post-hoc analyses revealed that MAP was lower during hyperthermia than in normothermia from PIIa through PIII of the VM (PIIa 87 ± 7 vs. 75 ± 12 mmHg for normothermia and hyperthermia respectively, $p \le 0.01$; PIIb 99 ± 12 vs. 85 ± 19, $p = 0.01$; 84 ± 11 vs. 72 ± 19, $p = 0.02$; also see Figure 2). However, MCAv was only significantly lower during hyperthermia during PIIa (55 ± 12 vs. 49 ± 8 cm s^{-1}, $p \le 0.03$; also see Figure 2). Additional post-hoc analyses of the absolute change from previous VM phase for MAP and MCAv indicated the magnitude of change for both metrics was greatest during hyperthermia in PIIa (MCAv −5 ± 5 vs. −12 ± 8 cm s^{-1}, $p = 0.05$ and MAP −14 ± 5 vs. −26 ± 10 mmHg, $p \le 0.01$) and PIV (MCAv 10 ± 7 vs. 20 ± 15 cm s^{-1}, $p = 0.04$ and MAP 11 ± 8 vs. 28 ± 21 mmHg, $p \le 0.01$; also see Figure 3).

HR, Pi and pulse time pre- and post-VM are presented in Figure 4. When analysing the percentage change in pulse time from pre-VM to 1-min post-VM there was no significant difference between normothermic and hyperthermic conditions (−2.2 ± 2.6 and −4.3 ± 4.9% respectively, $p = 0.26$). Similarly, the percentage change from baseline to post-VM Pi was not different (8.2 ± 10.3 and 11.9 ± 12.3%, $p = 0.35$). Tieck's Autoregulation index (Tiecks et al., 1995) during the VM was unchanged by hyperthermia during PII (0.8 ± 0.6 vs. 1.5 ± 1.16, $p = 0.10$) and PIV (1.3 ± 0.13 vs. 1.4 ± 0.20, $p = 0.27$).

TABLE 1 Baseline values during normo- and hyperthermia.

	Normothermia	Hyperthermia	*p* Value
$MCAv_{mean}$ (cm s^{-1})	61 ± 11	59 ± 12	0.45
MAP (mm Hg)	80 ± 6	81 ± 9	0.60
HR (beats min^{-1})	62 ± 12	88 ± 12	<0.01
CVCi (cm s^{-1} $mmHg^{-1}$)	0.77 ± 0.18	0.74 ± 0.18	0.42
Pi	0.76 ± 0.12	0.89 ± 0.10	<0.01
$P_{ET}CO_2$ (mmHg)	40 ± 4	37 ± 5	0.08
Mean skin temperature (°C)	33.2 ± 0.8	37.2 ± 0.8	<0.01
Core temperature (°C)	37.1 ± 0.1	37.9 ± 0.2	<0.01

Note: Data are means ± SD.

Abbreviations: CVCi, cerebrovascular conductance index; HR, heart rate; MAP, mean arterial blood pressure; $MCAv_{mean}$, mean middle cerebral artery blood velocity; $P_{ET}CO_2$, partial pressure of end-tidal carbon dioxide; Pi, pulsatility index; PP, pulse pressure.

4 | DISCUSSION

We investigated the haemodynamic response to the VM during normothermia and hyperthermia. Our main findings are (1) hyperthermia reduces PIIa $MCAv_{mean}$. However, despite lower PIIb and PIII MAP when hyperthermic, $MCAv_{mean}$ was comparable between hyperthermia and normothermia. (2) Pi was increased by the VM with the change post-VM persisting irrespective of T_{core}. (3) pulse time (proxy for pulse velocity) was reduced post-VM with the percentage decrease consistent across conditions. Collectively, these data are inconsistent with our hypothesis and indicate that during hyperthermia the cerebrovascular response to a supine VM is largely similar to normothermic conditions despite greater variations in MAP.

The more pronounced PIIa reduction in MAP during hyperthermia, which is in agreement with others (Davis & Crandall, 2010; Yamazaki et al., 2003), occurs concurrent to lowered $MCAv_{mean}$. It has been hypothesized (Davis & Crandall, 2010) that the hyperthermia-induced peripheral blood shift underpins the greater PIIa MAP reductions, as more pronounced PII perturbations in MAP occur when thoracic blood volume is reduced (Stewart et al., 2004). Whilst the PIIa $MCAv_{mean}$ reduction is more pronounced during hyperthermia in the current study, $MCAv_{mean}$ rapidly recovers in PIIb so that no differences are apparent between conditions for the remaining phases, despite lowered MAP during PIIb and PIII whilst hyperthermic. Although $P_{ET}CO_2$ was not statistically different between conditions, the cerebral vasculature is immensely sensitive to perturbations in the partial pressure of arterial carbon dioxide (Ainslie et al., 2005) and small changes in $P_{ET}CO_2$ may impact $MCAv_{mean}$. Thus, potentially explaining the lower, albeit not-statistically significant, $MCAv_{mean}$ at rest during hyperthermia. Despite this, and that hypocapnia improves cerebral autoregulation (Aaslid et al., 1989), there were no differences in PI $MCAv_{mean}$

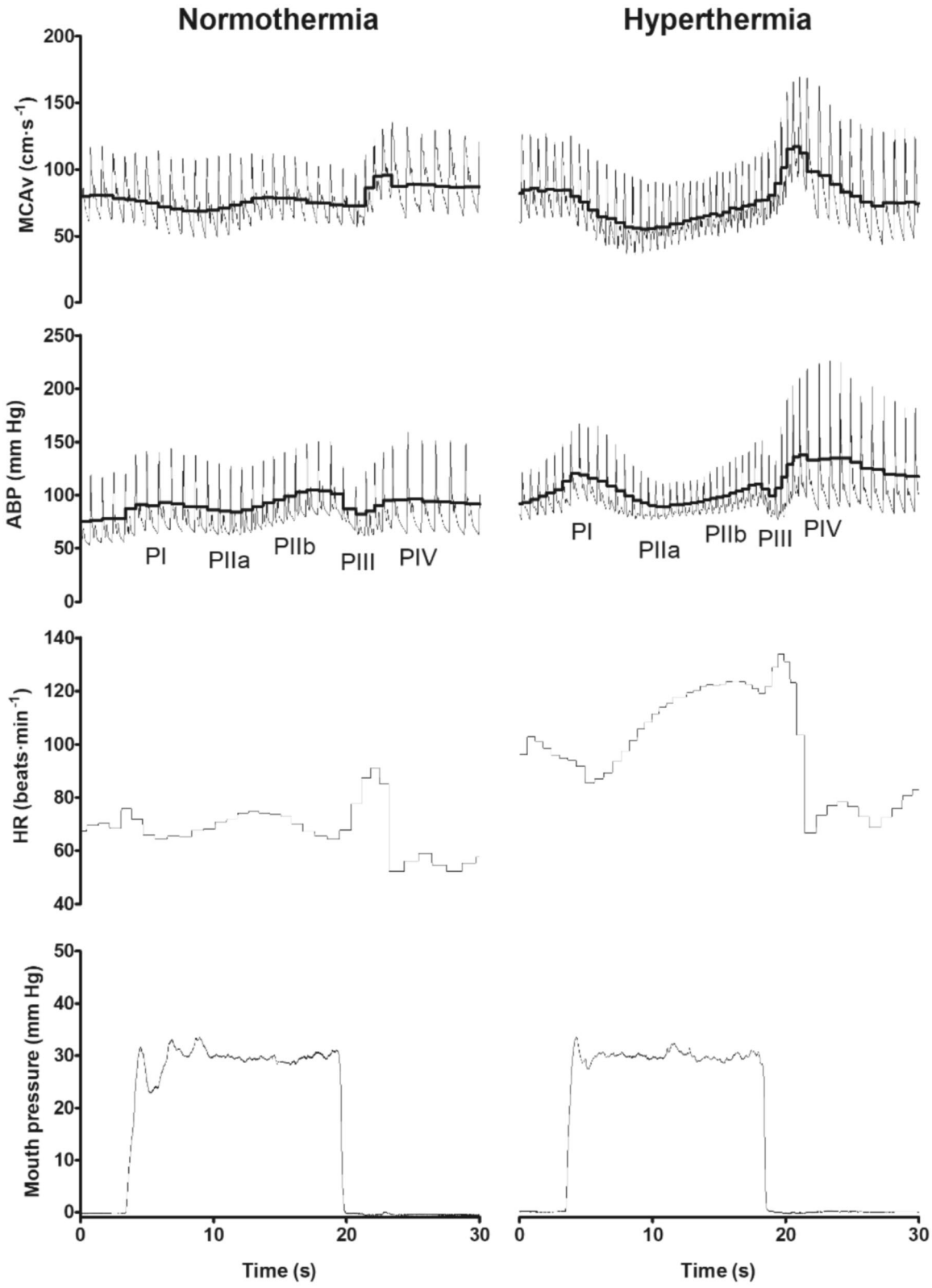

FIGURE 1 Typical responses to the Valsalva manoeuvre in a single participant whilst normothermia (left column) and during hyperthermia. The thick black line in the MCAv and ABP traces represent the mean MCAv and mean arterial blood pressure, respectively. ABP, arterial blood pressure; HR, heart rate; MCAv, middle cerebral artery blood velocity; PI, Valsalva manoeuvre phase I; PIIa, phase IIa; PIIb, phase IIb; PIII, phase III; PIV, phase IV.

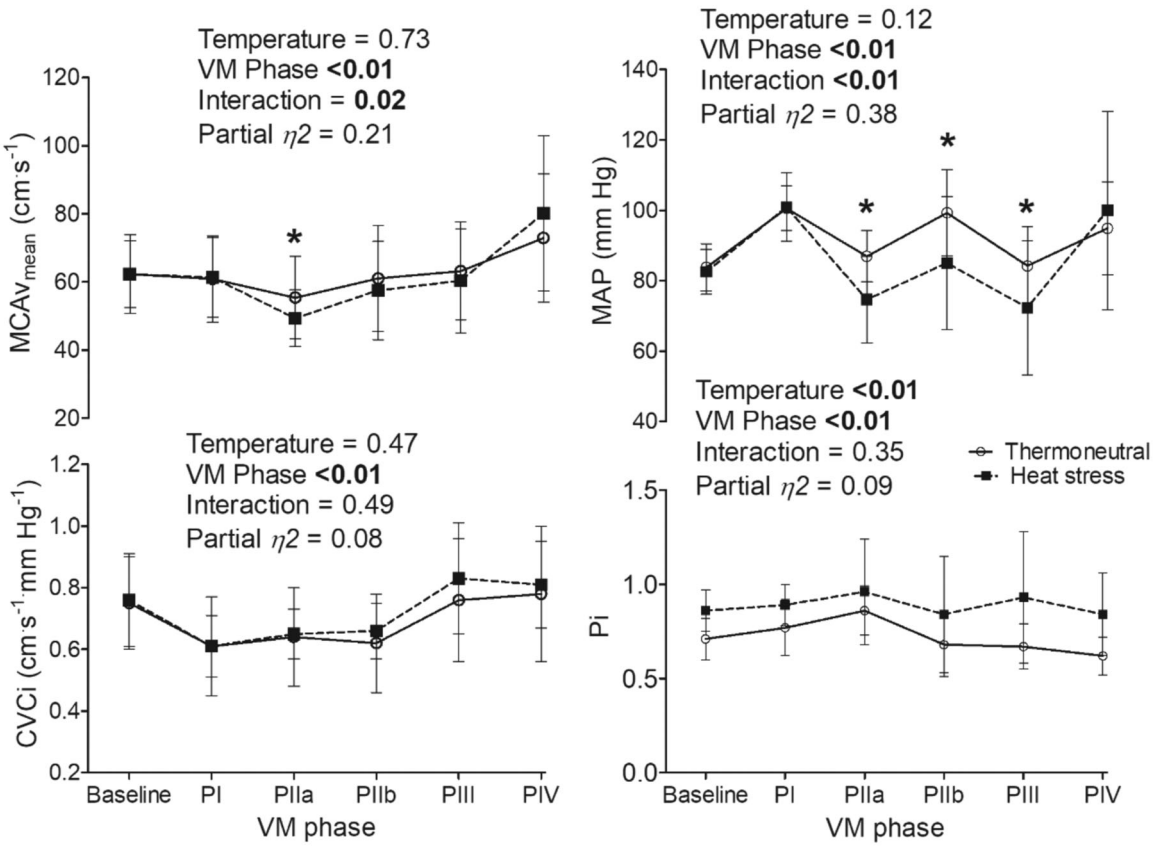

FIGURE 2 VM haemodynamics. *, Significant difference between normothermia and hyperthermia within VM phase ($p < 0.03$). Baseline represents data immediately before VM. Data are means ± SD. CVCi, cerebrovascular conductance index; MAP, mean arterial blood pressure; $MCAv_{mean}$, mean middle cerebral artery blood velocity; Pi, pulsatility index; PI, Valsalva manoeuvre phase I; PIIa, phase IIa; PIIb, phase IIb; PIII, phase III; PIV, phase IV; VM, Valsalva manoeuvre.

(i.e., initial haemodynamic challenge) between conditions in response to a similar MAP and change in MAP from baseline. Therefore, the effect of the slightly lowered $P_{ET}CO_2$ during hyperthermia in the current experiment appears negligible at VM onset.

We report no change in Tiecks (Tiecks et al., 1995) AI during PII or PIV. Despite lower absolute blood pressures when hyperthermic, particularly during the later phases of the VM (e.g., PIIb), $MCAv_{mean}$ was not different from normothermia, suggesting effective autoregulation across conditions. Interestingly, when data are reported as the absolute change from the previous VM phase a greater ΔMAP was apparent during hyperthermia in PIIb and PIV (decrease and increase respectively), coinciding with concurrent differences in $\Delta MCAv_{mean}$ (Figure 3). Transfer function analysis of cerebral autoregulation during hyperthermia has revealed improvements during very low frequency (i.e., 0.03 Hz) forced (Brothers et al., 2009b) and spontaneous fluctuations (Low et al., 2009) in MAP, with no changes observed in the low (0.07–0.20 Hz) and high-frequency ranges (>0.20 Hz). Considering that our metrics of autoregulation were unchanged by hyperthermia, and VM intensity was standardized, these data support previous findings that the rate of change in MAP, rather than the absolute MAP, primarily drives the MCAv response during changes in blood pressure (Tzeng et al., 2011). However, this assumes that a mouth pressure of 30 mmHg produces identical elevations in intracranial pressure across both conditions.

The regulation of cerebral blood flow is complex, with many regulators acting simultaneously during a given stressor (e.g., during the VM). Despite controversy surrounding the role of the autonomic nervous system in cerebral blood flow regulation, it appears that the autonomic nervous system may complement cerebral autoregulation to maintain cerebral perfusion during the VM (Zhang et al., 2004). We show that Pi and pulse time were modified by the VM, and the change in Pi and pulse time 1-min post-VM was similar between conditions. We propose that these observed changes are due to a maintenance of post-VM sympathetic vasoconstriction in central and/or intracranial arteries. As reviewed by Nardone et al. (2020), there is growing evidence that sympathetic activation can increase central arterial stiffness, particularly in men. The combination of the baroreflex response to PIIa and PIII hypotension, and the elevations in intracranial pressure (Greenfield et al., 1984; Schmidt et al., 2018), elevate peripheral sympathetic activity. Importantly, peripheral adrenergic vasoconstrictor responsiveness is maintained during hyperthermia (Keller et al., 2010). Whilst in the current study acute changes in Pi and pulse time (maker of arterial stiffness) were evident 1 min post-VM, further research is required to identify for the time course of these changes and their impact on arterial function.

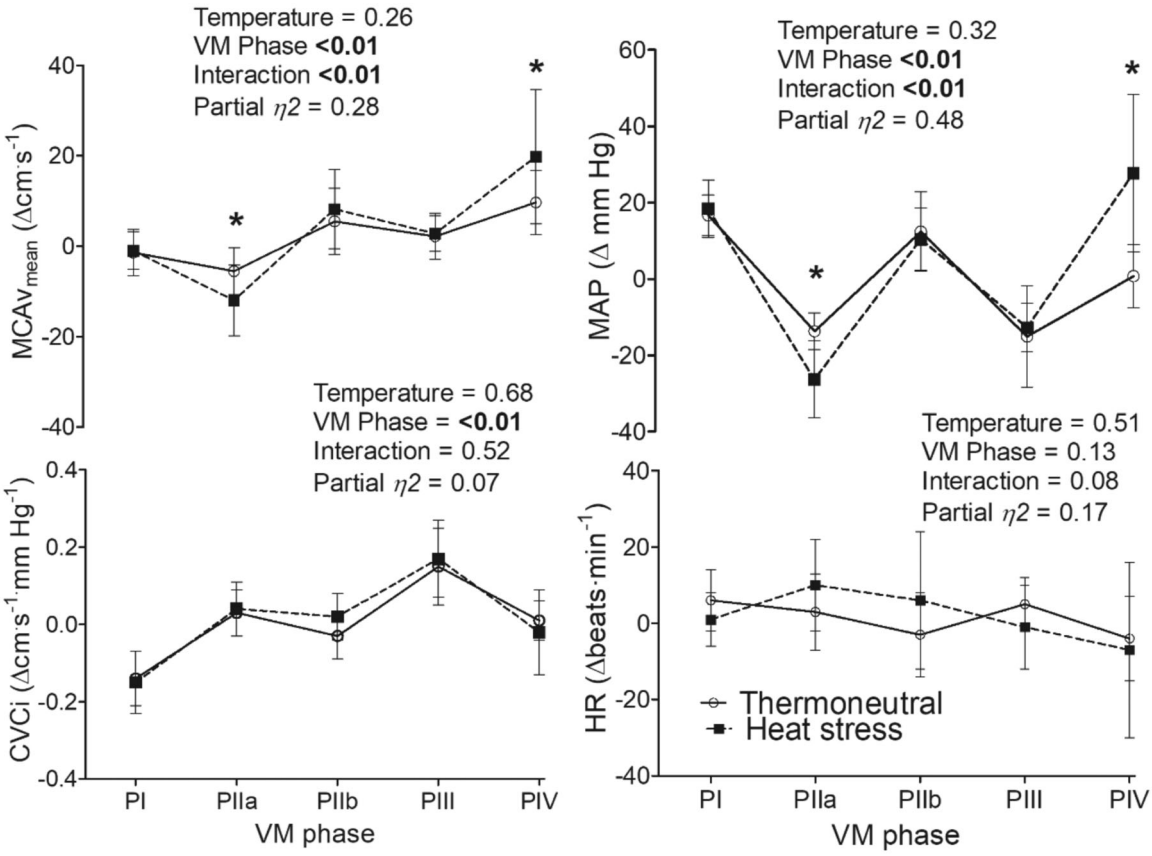

FIGURE 3 Absolute change from previous VM phase. *, Significant difference between normothermia and hyperthermia within VM phase ($p \leq 0.05$). Data are means ± SD. CVCi, cerebrovascular conductance index; HR, heart rate; MAP, mean arterial blood pressure; $MCAv_{mean}$, mean middle cerebral artery blood velocity; PI, Valsalva manoeuvre phase I; PIIa, phase IIa; PIIb, phase IIb; PIII, phase III; PIV, phase IV; VM, Valsalva manoeuvre.

4.1 | Perspectives

These data indicate that the cerebrovascular response to the VM is comparable between normothermia and mild hyperthermia. However, the VM in the current experiment was performed in the supine position. During normothermia, standing exacerbates the MAP and $MCAv_{mean}$ responses to the VM, with lower PIIa through PIII $MCAv_{mean}$ and lower MAP achieved (Pott et al., 2000). As we, and others (Davis & Crandall, 2010), have shown that mild hyperthermia reduces PIIa through PIII MAP, the reduction in MAP would be further exacerbated when standing, increasing the likelihood of syncope. Furthermore, as orthostatic tolerance is significantly reduced during hyperthermia (Schlader et al., 2016) the current findings may not apply to the standing position.

The pulse time findings of the current study demonstrate that the VM in isolation may alter arterial compliance. Exercise modalities that may employ the VM, such as resistance exercise, reduce carotid artery compliance (Miyachi et al., 2004) and increase cerebrovascular resistance (Thomas et al., 2021). Interestingly, meta analyses of arterial compliance and resistance exercise found that a reduction in arterial compliance was only associated with high-intensity training (Miyachi, 2013), classified as >70% of the one repetition maximum. As the VM is unavoidable at intensities >~80% of maximal voluntary contraction (MacDougall et al., 1992), it is plausible that the resistance training-induced reduction in central arterial compliance be due in part to the VM. It has been speculated that the acute reduction in central arterial compliance following resistance exercise is modulated by elevated sympathetic tone (DeVan et al., 2005), which is elevated during PIIb and PIV of the VM (Zhang et al., 2004). Therefore, it is plausible that the cardiovascular responses to the VM highlighted in the current study may underpin the resistance exercise-induced reduction in central arterial compliance.

5 | LIMITATIONS

The measurement of MCAv using Transcranial Doppler ultrasonography provides a noninvasive proxy for cerebral blood flow. The excellent temporal resolution enables dynamic and continuous measurement. However, the accuracy of MCAv as a proxy for cerebral blood flow is dependent upon a stable arterial diameter. Others have shown that sympathetic activation induced by rhythmic handgrip exercise (Verbree et al., 2017) and moderate hypocapnia (Coverdale et al., 2014) produces vasoconstriction in the middle

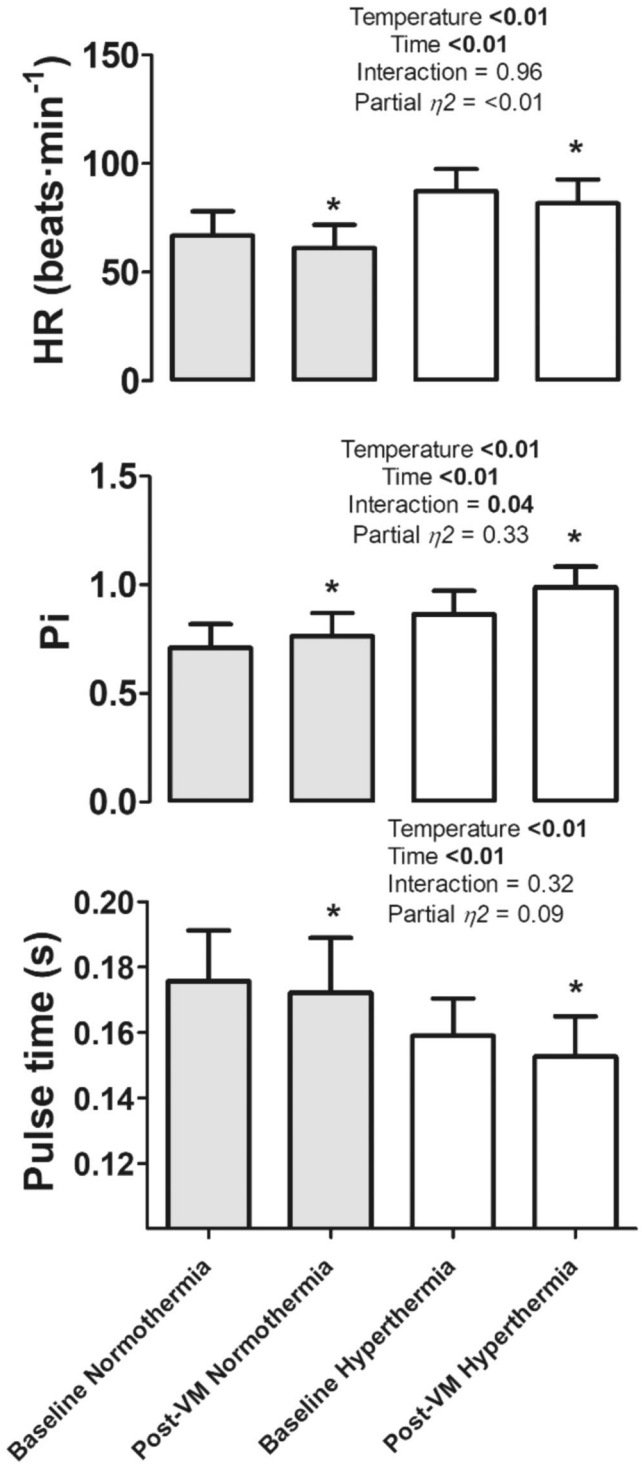

FIGURE 4 Heart rate (HR), pulsatility index (Pi) and pulse time changes in response to the Valsalva manoeuvre (VM). The post-VM timepoint refers to the 10 cardiac cycles 1 min after completion of the VM. Data are means ± SD. *, Significantly different from baseline within condition ($p < 0.017$).

cerebral artery. Whilst we demonstrate only minor changes in $P_{ET}CO_2$, vasoconstriction of the intracranial arteries may also occur in response to the elevated sympathetic nerve activity associated with hyperthermia and the VM. As such, it is possible that vasoconstriction of the middle cerebral artery may artificially elevate MCAv during hyperthermia and/or following the VM.

The current experiment utilized mild hyperthermia, with a modest ~0.8°C rise in T_{core} from the original baseline T_{core}. The rise in T_{core} achieved is comparable with existing data by Davis and Crandall (2010). More severe hyperthermia (e.g., T_{core} > +1.5°C), sufficient to significantly reduce resting $MCAv_{mean}$, may alter the haemodynamic response to the VM.

6 | CONCLUSION

These data indicate that the cerebrovascular response to the VM is largely unchanged during mild hyperthermia, despite the more severe perturbations in MAP. Irrespective of core temperature, the VM produces a profound hemodynamic challenge and the response to said challenge persists beyond the release of the strain.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study can be made available upon reasonable request to the corresponding author.

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