Eur J Appl Physiol
DOI 10.1007/s00421-011-1989-x

ORIGINAL ARTICLE

Heart rate variability and baroreceptor sensitivity following exercise-induced hyperthermia in endurance trained men

Rachel G. Armstrong · Saif Ahmad · Andrew J. Seely · Glen P. Kenny

Received: 27 September 2010 / Accepted: 28 April 2011

Abstract We evaluated the effect of exercise-induced hyperthermia (EIH) on autonomic nervous system (ANS) function in the early (<80 min) and late (24 and 48 h) stages of recovery. Eight males underwent three repeated 6 min 70° head-up tilts (HUT1, HUT2 and HUT3), each separated by 10-min supine rest in a non-exercise/non-heat stress control state (NHS). On a separate day, three 6 min 70° HUT were performed following EIH (esophageal temperature ≥40°C) and repeated after 24 and 48 h of recovery. Heart rate, stroke volume (SV), mean arterial pressure and cardiac output ($\dot{Q}$) were evaluated during the last min prior to a change in posture. Responses to 70° HUT were compared to the same challenge performed without prior exercise and under a NHS condition. Relative to NHS, $\dot{Q}$ was maintained during the repeated HUT's following EIH, despite significant reductions in SV and sustained elevations in esophageal temperature ($p < 0.05$). The preserved $\dot{Q}$ appears to be due to increased HR (HUT1: NRS = 76 ± 3 beats min^{-1}, EIH = 126 ± 6 beats min^{-1}) stemming from modulation of the ANS toward sympathetic dominance. Parasympathetic withdrawal was evidenced by a reduction in root mean squared successive difference (i.e., HUT1: NHS = 66 ± 12 ms, EIH = 9 ± 1 ms) of heart rate variability and paralleled by a reduction in baroreceptor sensitivity for all HUT's following EIH ($p < 0.05$). Despite significant modulation in ANS activity, Q is maintained and participants do not become orthostatic intolerant/syncopal during the short-term recovery period following EIH. Normal ANS and cardiovascular function is restored following 24 h of recovery.

Keywords Postural stress · Exercise · Heart rate variability · Heat stress

Introduction

It is well documented that the autonomic nervous system (ANS) plays a key role in the regulation of cardiovascular function during and following a dynamic bout of exercise (Brenner et al. 1997; Iellamo 2001; Parekh and Lee 2005). Heart rate variability (HRV), which represents the time difference between repeated heart beats (Flouris and Cheung 2009), and baroreceptor sensitivity (BRS), which represents the amount of change in heart rate attributable to changes in systolic blood pressure (Ogoh et al. 2005), can be used as a reflection of the cardiorespiratory control system providing information regarding the balance between sympathetic and parasympathetic function of the ANS (van Ravenswaaij-Arts et al. 1993). By performing an intermittent orthostatic challenge of 70° head-up tilt we induced changes in baroreceptor loading status, invoking a compensatory cardiovascular reflex response (Rowell et al. 1973) isolating the effects of a severe hyperthermic episode on ANS function.

Independent factors such as exercise (Armstrong et al. 2010; Brenner et al. 1997; Parekh and Lee 2005), passive heat exposure (Brenner et al. 1997, 1998) and/or orthostatic

Communicated by Narihiko Kondo.

R. G. Armstrong · G. P. Kenny (✉)
Human and Environmental Physiology Research Unit, Faculty of Health Sciences, School of Human Kinetics, University of Ottawa, 125 University, Montpetit Hall, Ottawa, ON K1N 6N5, Canada
e-mail: gkenny@uottawa.ca

S. Ahmad · A. J. Seely
Divisions of Thoracic Surgery and Critical Care Medicine, Ottawa Health Research Institute, Ottawa Hospital-General Campus, Ottawa, ON K1H 8L6, Canada

Published online: 17 May 2011

challenges (Butler et al. 1994; Westerhof et al. 2006) are known to affect ANS function. However, each of these factors has been shown to modulate resting ANS function in different ways. Specifically, exercise has been demonstrated to cause reductions in BRS (Loimaala et al. 2000; Niemela et al. 2008; Ogoh et al. 2005; Skrapari et al. 2007). Recently, we reported a similar pattern of response following exercise-induced hyperthermia (EIH) (i.e., esophageal temperature $\geq$40°C) with attenuations in BRS persisting for the 80-min recovery period (Armstrong et al. 2010). It remains unclear, however, if this reduction in BRS persists for an extended period and/or if this attenuation in BRS is paralleled by a concomitant modulation in HRV. To date, studies examining HRV immediately after acute endurance exercise ($\leq$45 min) demonstrate an attenuated cardiac vagal modulation or parasympathetic nervous system activity causing a decrease in HRV (Parekh and Lee 2005; Brenner et al. 1997). Furthermore, passive heat exposure resulting in an increase in core temperature has been demonstrated to induce a modest activation of the sympathetic nervous system and a withdrawal of the parasympathetic nervous system activity (Yamamoto et al. 2007; Brenner et al. 1997, 1998). Exercise in the heat (40°C) has been shown to cause the greatest disturbance in ANS function, compared to passive heating and/or exercise performed under thermoneutral conditions, as evidenced by a significantly greater activation of the sympathetic nervous system combined with parasympathetic withdrawal (Brenner et al. 1997). While a lack of research exists on the long-term recovery pattern of ANS function, investigators have reported attenuations in HRV (a decreased vagal modulation of the heart) for up to 24 h after exhaustive exercise regimens (Furlan et al. 1993; Bernardi et al. 1997; Hautala et al. 2001). The extent to which changes in the relative contribution of sympathetic and parasympathetic contribution persists into recovery remains to be elucidated especially under conditions of prolonged elevated thermal strain.

To the best of our knowledge, there have been no studies designed to examine the effects of EIH to levels associated with exertional heat stroke (a condition typically marked by an elevated core temperature of $\geq$40°C) (Armstrong et al. 2007; WHO 2007) upon autonomic response. The hyperthermia of exertional heart stroke (a core temperature equivalent of >40°C at time of collapse) is recognized as the factor having the greatest effect on central nervous system disturbances. Strenuous physical exercise in a hot environment also leads to a serious deficit of effective arterial blood volume, unless intense splanchnic vasoconstriction maintains cardiac output and blood pressure. While these levels of hyperthermia can involve significant impairment of central nervous system function and cardiovascular compensatory responses (Hubbard 1990), little is known about the consequences of these changes on the short and long recovery of autonomic nervous function. Moreover, while studies eliciting hyperthermia via exercise in the heat have generally supported a dominant central impairment of neuromuscular activation, the impact on visceral motor (involuntary) activity of the ANS during the recovery period remains unclear.

Therefore, the aim of this study was to examine the effect of EIH to levels associated with exertional heat stroke on ANS function in the early stages of recovery (<80 min). Further, we evaluated the residual effect of the hyperthermic episode on ANS function following 24 and 48 h of recovery. In order to evaluate the effect of an exercise-induced hyperthermic episode on ANS function, we performed an intermittent orthostatic challenge of 70° head-up tilt. In addition to inducing changes in baroreceptor loading status and invoking a compensatory cardiovascular reflex response (Rowell et al. 1973), orthostatic challenges are known to affect ANS function (Butler et al. 1994; Westerhof et al. 2006). Moreover, heat stress reduces the sensitivity of the spontaneous baroreflex control of HR during orthostasis (Kenny et al. 2010). Hence, by performing an intermittent orthostatic challenge following EIH and comparing responses during the same orthostatic challenge performed without prior exercise and under a non-heat stress (NHS) condition, it is possible to isolate the effects of a severe hyperthermic episode on ANS function by HRV. Responses were compared to the same challenge performed without prior exercise and under a NHS condition. We tested the hypothesis that EIH alters ANS function during the recovery period as measured by a reduction of HRV and decrease in BRS persisting for up to 24-h postexercise.

Methods

Participants

Following approval of the experimental protocol from the University of Ottawa Research Ethics Committee and obtaining written informed consent, eight healthy, non-smoking normotensive, male participants volunteered for the study. Mean (±SD) physical characteristics of the participants were: age (22 ± 3 years), height (177 ± 4 cm), weight (72.9 ± 5.7 kg), body surface area (1.89 ± 0.09 m^2), body fat (15 ± 5%), and $\dot{V}O_{2peak}$ (63 ± 7 ml O_2 kg^{-1} min^{-1}). Participants were college level athletes, comprised of runners, tri-athletes and cyclists who performed structured aerobic and resistance exercise $\geq$4 times/week for duration of $\geq$45 min. Body weight was measured prior to the preliminary screening session (72.9 ± 5.7 kg) and experimental testing on day 1(72.6 ± 5.5 kg), day 2 (before EIH: 73.1 ± 5.8 kg, after EIH: 71.9 ± 5.9 kg), day

3 (72.8 ± 6.0 kg) and day 4 (72.2 ± 5.5 kg). Physically active fit subjects were used for this study due to the fact that subjects were required to perform prolonged exercise in the heat until they achieved a core temperature of ≥40°C. Previous studies from our laboratory demonstrate that individuals with reduced levels of fitness and/or are not regularly exercising are unable to achieve this elevated state of hyperthermia (Proulx et al. 2006). Hence, we used young healthy subjects who were regularly engaged in physical activity at least four times per week.

Experimental protocol

All participants undertook one screening visit and four experimental sessions. During the screening visit, body adiposity and maximum oxygen consumption were measured. Body density was measured using the hydrostatic weighing technique and body fat percentage was then calculated using the Siri equation (1956). Peak oxygen consumption $\dot{V}O_{2peak}$ was determined by measuring expired oxygen (O_2) and carbon dioxide (CO_2) concentrations (AMETEK model S-3A/1 and CD 3A, Applied Electrochemistry, Pittsburgh, PA, USA) during a progressive treadmill running protocol. The $\dot{V}O_{2peak}$ data were used to select the submaximal workload for the experimental exercise phase of the study.

To control for seasonal acclimatization, all experimental trials were performed during the months of October to April. Average ambient air temperature in Ottawa, ON, Canada from October 2006 to April 2007 reached as low as −25°C in mid-to-late January and as high as 15°C in April. For those subjects involved in competitive sports, this period of time represented the off-season period. No laboratory acclimatization sessions were performed prior to the experimental trials. For each experimental trial, subjects were instructed to avoid physical activity and excessive stressors such as exposure to hot or cold temperatures, particularly during the period between awakening and experimentation and during transit from home to the laboratory. Trials were performed at the same time of day for each subject to avoid circadian variation in core and skin temperatures. Subjects were asked to fast at least 2 h prior to experimentation, and water ingestion was permitted ad libitum during this time to promote euhydration (body weight was not significantly different between the preliminary screening visit and any of the 4 experimental trials). However, water consumption was restricted at the start of the experimental trial. On arrival at the laboratory subjects, clothed in shorts and athletic shoes, were fitted with the appropriate instruments.

Each subject performed four experimental trials. During the first experimental session, subjects remained resting in the supine posture for 30 min in a NHS thermoneutral ambient temperature (T_{am} of 22°C) condition (NHS control). At the end of the baseline period, subjects were exposed to three consecutive 6 min 70° head-up tilts (HUT1, HUT2 and HUT3, respectively), each separated by a 10-min supine recovery (i.e., SUP1, SUP2 and SUP3, respectively). Three consecutive tilts were evaluated since adaptive effects of repeated tilting have been demonstrated in previous literature by the fifth head-up tilt (Berry et al. 2006). During the second visit, subjects remained resting in the supine posture for 30 min on a tilt-table. At the end of the baseline resting period, subjects entered a temperature controlled chamber maintained at a T_{am} of 42°C where they were rendered hyperthermic by performing treadmill running at ∼65% of their predetermined $\dot{V}O_{2peak}$ until esophageal temperature reached 40.0°C (24 ± 5 min) (EIH). Immediately following the cessation of exercise, the subjects were transferred back to a NHS thermoneutral ambient condition (T_{am} of 22°C) where they remained seated in an upright posture for ∼15 min. This was done to ensure that esophageal temperature achieved a stable elevated value paralleled by a reduction in skin perfusion and sweating to resting baseline values prior to the start of the postural stress (Kenny et al. 2007, 2010). They were then placed on a tilt-table in a supine posture for 15 min and subsequently exposed to three consecutive 6 min 70° HUT, each separated by 10 min of recovery in the supine posture. Participants were instructed to breathe spontaneously throughout the experimental procedure with no attempt to control the depth or frequency of the respiratory pattern. The Finometer is sensitive to changes in body weight and therefore weight was entered at two time points on day 2. Body weight was first entered into the Finometer prior to EIH. The second measurement of body weight was entered following EIH where there was a measured reduction in body weight. The new body mass was entered into the Finometer to ensure that accurate hemodynamic measurements were captured during the recovery period.

The third and fourth experimental sessions were conducted in a NHS condition (T_{am} of 22°C) at 24 and 48 h following the EIH trial. The experimental design was the same as the first experimental session described above.

Measurements

Esophageal temperature (T_{es}) was measured by placing a pediatric thermocouple probe of approximately 2 mm in diameter (Mon-a-therm Nasopharyngeal Temperature Probe, Mallinckrodt Medical, St-Louis, MO, USA) through the participant's nostril while they were asked to sip water

through a straw. The location of the probe tip in the esophagus was estimated to be at the level of the eighth and ninth thoracic vertebrae.

Heart rate (HR) was monitored using a Polar coded transmitter, recorded continuously and stored with a Polar Advantage interface and Polar Precision Performance software (Polar Electro Oy, Finland). Beat-to-beat blood pressure (MAP) was recorded using finger photoplethysmography (Finometer® PRO; Finapres Medical Systems, Amsterdam, The Netherlands) with resting values verified by manual auscultation of the brachial artery. A cuff of appropriate size was placed on the middle finger of the non-dominant hand of the patient, which in turn was maintained at heart level. Hand height was corrected to heart level using a hydrostatic height correction system. This system measures the relative vertical position of the hand and heart to compensate for any difference. The Finometer device (sampling rate 200 Hz) uses a volume clamp method (Penaz 1975) to capture beat-to-beat (continuous) values of blood pressure and pulse rate in the finger artery. It has been shown to track acute changes in blood pressure and is strongly correlated to intra-arterial radial pressure (Parati et al. 1989). From the blood pressure waveform, stroke volume (SV) and cardiac output ($\dot{Q}$) were calculated using the Modelflow method (BeatScope 1.1a software; Finapres Medical Systems, Amsterdam, The Netherlands) which incorporates sex, age, height and mass data. This method provides a reliable estimate of rapid changes in SV and $\dot{Q}$ in healthy humans at rest, during exercise (Sugawara et al. 2003) and during 70° HUT (Jellema et al. 1996). Total peripheral resistance (TPR) was calculated as MAP/$\dot{Q}$.

Baroreflex sensitivity (BRS) was measured non-invasively using a Finometer device (sampling rate 200 Hz) (Finometer® PRO; Finapres Medical Systems, Amsterdam, The Netherlands). Baroreflex sensitivity was calculated as previously described (Westerhof et al. 2006) and it expresses the change in interbeat interval for a simultaneously occurring change in blood pressure. The Beatfast software (BeatScope 1.1a; Finapres Medical Systems, Amsterdam, The Netherlands) was used to determine beat-to-beat variables, interbeat interval and systolic, diastolic, and mean arterial pressures. Systolic blood pressure and interbeat interval were used to calculate BRS in ms $mmHg^{-1}$ (Westerhof et al. 2006).

RR interval data were collected in milliseconds (ms) using a 5-lead electrocardiogram (ECG) Holter monitor (Philips Zymed DigiTrak Plus Recorder, Andover, MA, USA) which sampled ECG data at 175 Hz. To characterize the ANS function, multi-parameter HRV analysis was performed on RR interval time series employing the continuous individualized variability analysis (CIMVA) software (Ahmad et al. 2009; Seely and Macklem 2004). The time domain measures of HRV that were computed included mean RR interval, standard deviation (SDNN) of RR intervals, and root mean squared successive difference (RMSSD) of RR intervals. We characterized the frequency domain measures of HRV using the fast Fourier transform (FFT) whereby we measured the low frequency (Westerhof et al. 2006) (0.04–0.15 Hz), high frequency (HF) (0.18–0.4 Hz), and low to high frequency ratio (LF/HF) components of the RR interval time series. The beat-by-beat data sets were converted to equidistant time series prior to applying the FFT in order to calculate spectral powers. We computed the Fourier LF and HF components in normalized units [LFnu = LF/(LF + HF) and HFnu = HF/(LF + HF)] which is the recommended analysis set forth by the Task Force (1996) for accurate assessment of ANS activity. The LF component is reported to reflect both sympathetic and vagal modulation whereas the HF component appears to be the result of vagal modulation. Moreover, the LF/HF component has been proposed as a measure of the cardiac sympathovagal balance (Parekh and Lee 2005; Seely and Macklem 2004).

A Teeter Hang Ups F5000 inversion table was used to manipulate posture. The angle of the tilt was measured using a Unitek Magnetic Polycast Protractor.

Statistical analyses

A two-way repeated measures ANOVA was used to analyze the absolute and relative (%) change from the non-exercise/NHS condition (i.e., NHS) in BRS, HRV (mean, SD, RMSSD, LF/HF, HFnu, LFnu), HR, MAP, TPR, SV, $\dot{Q}$, and T_{es} using the repeatable factors of treatment day (levels: NHS, EIH, 24 and 48 h), and postural stress [levels: HUT1, HUT2, and HUT3) or (SUP1, SUP2, and SUP3)]. Pair-wise comparisons were performed using paired sample *t* tests (Tables 1, 2, 3, 4). For BRS, values were averaged over the last 2 min of each postural position and HRV time and frequency domain values were averaged over the entire duration of each period. The last minute before postural manipulation was used for analysis of the remaining hemodynamic variables (Table 4). Relative change (%) for each of the successive orthostatic challenges (levels: pre-tilt-HUT1, SUP1-HUT2, SUP2-HUT3) was defined as follows (prior supine position − head-up tilt response)/(prior supine position) × 100) for HRV parameters (BRS, LF/HF, HF and LF) (Figs. 1, 2). It is important to note that for the calculation of the relative change (%) following EIH (i.e., pre-tilt-HUT1); pre-tilt represents a 15-min supine position maintained following exercise and prior to HUT1. This period of time was used in order to evaluate the true response to postural stress

following exercise. Since no exercise was performed prior to HUT1 during the NHS, 24 and 48 h conditions, supine represents the final 15 min of the 30-min baseline resting period. The level of significance was set at 0.05 and the alpha level was adjusted during multiple comparisons so as to maintain the rate of type I error at 5% during Holm–Bonferroni post hoc analysis. Based on previous publications with data similar to the present study (Berry et al. 2006; Gagnon et al. 2008), it was established that a minimum of seven subjects would be required to have appropriate statistical power ($\beta = 0.9$ and $\alpha = 0.05$). All analyses were performed using the statistical software package SPSS 17.0 for Windows (SPSS Inc., Chicago, IL, USA).

Results

There were no significant differences between treatment days for absolute baseline values of BRS, time and frequency domain measures of HRV, HR, MAP, TPR, SV, $\dot{Q}$ and T_{es} during baseline supine resting (Tables 1, 2, 3, 4). Participants lost an average of 1.2 ± 0.4 kg following EIH ($p < 0.05$). All participants re-gained the lost weight as there were no observed significant differences between body weight measurements on day 1 (72.6 ± 5.5 kg) and at 24 (72.8 ± 6.0 kg) and 48 h (72.2 ± 5.5 kg) post-EIH.

Effect of EIH on ANS and cardiovascular function: early stages of recovery

There was a main effect of treatment day (NHS vs. EIH) on BRS (Table 1), HR, SV, T_{es} (Table 4) and time domain measures (mean, SDNN, RMSSD) of HRV (Table 2) during all HUT ($p < 0.05$) and SUP ($p < 0.05$) recovery postures. The reduction in absolute values of BRS, SV, and time domain measures of HRV following EIH were offset by significant increases in HR. The changes in frequency domain measures of HRV in normalized units (Table 3) were affected by the treatment day (NHS vs. EIH) for each of the successive HUT and SUP postures with the exception of SUP2 and HUT3. The significant reduction in RMSSD, an index thought to be directly related to the parasympathetic nervous system, combined with a time domain reduction in SDNN and mean RR interval following EIH is the central finding in this study demonstrating the modulation of ANS function toward sympathetic dominance and parasympathetic withdrawal. Furthermore, we show that the relative change (%) in HF and LF/HF ratio were significantly reduced during the first postural transition (i.e., pre-tilt supine rest to HUT1) but not different during the final two transitions following EIH as compared to NHS (Fig. 2). No significant difference in the relative change (%) in BRS and LF was observed between treatment days (NHS vs. EIH) for any of the successive 70° head-up tilt challenges (Fig. 1). This modulation in ANS function preserved $\dot{Q}$ throughout recovery such that $\dot{Q}$ was significantly increased ($p < 0.05$) during SUP1 following EIH as compared to NHS. Similarly, the changes in TPR were affected by treatment day (NHS vs. EIH); such that TPR was significantly reduced ($p < 0.05$) during SUP1 following EIH compared to NHS. There was a main effect of treatment day on MAP; such that MAP was significantly reduced following EIH compared to NHS during SUP2 ($p < 0.05$).

Effect of EIH on ANS and cardiovascular function: 24 and 48 h of recovery

No differences in absolute values of HR, TPR, SV, $\dot{Q}$, T_{es}, BRS, time (mean RR, SDNN, RMSSD) and frequency domain measures of HRV during repeated 70° head-up tilt challenges performed 24 and 48 h following EIH compared to NHS (Tables 1, 2, 3, 4). The time domain HRV reduction in RMSSD, SDNN and mean RR interval were restored following 24 h of recovery, demonstrating re-established parasympathetic activity. However, a significantly elevated MAP was measured following 24 h

Table 1 Mean (±SE) absolute values of baroreceptor sensitivity during repeated 70° head-up tilts performed under a non-heat stress state and in the early and late stages (24 and 48 h) of recovery following exercise-induced hyperthermia

Variable	Day	Experimental trial	Pre-tilt supine rest	Postexercise supine	Posture					
					HUT1	SUP1	HUT2	SUP2	HUT3	SUP3
BRS (ms mmHg^{-1})	1	NHS	20.6 (4.7)		8.1 (1.6)	20.1 (2.5)	8.9 (1.5)	21.4 (4.1)	9.0 (1.4)	23.0 (3.5)
	2	EIH	19.2 (2.6)	4.2 (0.4)	1.9 (0.3)[a]	9.0 (1.8)[a]	3.9 (0.4)[a]	10.1 (2.0)[a]	3.4 (0.5)[a]	16.8 (3.7)[a]
	3	24 h	19.8 (2.1)		8.6 (1.5)	22.7 (3.9)	9.7 (1.3)	22.1 (2.8)	9.2 (1.6)	20.6 (1.5)
	4	48 h	23.7 (4.6)		9.4 (1.8)	21.4 (2.2)	9.3 (1.8)	21.3 (2.1)	10.3 (1.7)	23.8 (2.4)

24 and 48 h indicate responses measured 24 and 48 hours after EIH, respectively

EIH Exercise-induced hyperthermia

[a] Difference from the non-exercise/non-heat stress control condition (NHS) ($p < 0.05$)

Table 2 Mean (±SE) cardiovascular responses measured using time domain HRV analysis during repeated 70° head-up tilts performed under a non-heat stress state and in the early and late stages (24 and 48 h) of recovery following exercise-induced hyperthermia

Variable	Day	Experimental trial	Pre-tilt supine rest	Postexercise supine	Posture					
					HUT1	SUP1	HUT2	SUP2	HUT3	SUP3
Mean (ms)	1	NHS	1,040 (49)		937 (38)	941 (35)	956 (37)	964 (40)	958 (33)	1,003 (36)
	2	EIH	1,007 (40)	581 (17)	558 (25)[a]	638 (19)[a]	614 (33)[a]	688 (22)[a]	644 (34)[a]	732 (30)[a]
	3	24 h	1,059 (62)		928 (49)	966 (42)	977 (61)	998 (43)	967 (58)	1,006 (44)
	4	48 h	1,059 (57)		938 (47)	931 (38)	966 (55)	1,001 (40)	950 (52)	1,030 (41)
SD (ms)	1	NHS	99 (12)		142 (12)	154 (18)	153 (13)	157 (16)	152 (13)	161 (14)
	2	EIH	99 (13)	29 (4)	46 (4)[a]	63 (9)[a]	69 (10)[a]	86 (18)[a]	83 (14)[a]	102 (20)[a]
	3	24 h	95 (11)		130 (13)	160 (23)	152 (21)	162 (24)	150 (19)	149 (24)
	4	48 h	105 (13)		148 (19)	171 (24)	171 (17)	186 (26)	168 (18)	191 (25)
RMSSD (ms)	1	NHS	86 (17)		66 (12)	76 (14)	71 (11)	78 (11)	70 (11)	83 (12)
	2	EIH	77 (15)	8 (1)	9 (1)[a]	19 (4)[a]	18 (4)[a]	35 (11)[a]	30 (9)[a]	43 (10)[a]
	3	24 h	74 (14)		61 (12)	73 (11)	71 (12)	75 (11)	69 (11)	74 (11)
	4	48 h	76 (13)		68 (13)	71 (10)	75 (13)	82 (10)	67 (12)	87 (10)

24 and 48 h indicate responses measured 24 and 48 h after EIH, respectively

EIH Exercise-induced hyperthermia, *SD* standard deviation of RR intervals, *RMSSD* root mean squared standard deviation of RR intervals

[a] Difference from the non-exercise/non-heat stress control condition (NHS) ($p < 0.05$)

Table 3 Mean (±SE) cardiovascular responses measured using frequency domain measures of HRV using the fast Fourier transform (FFT) during repeated 70° head-up tilts performed under a non-heat stress state and in the early and late stages (24 and 48 h) of recovery following exercise-induced hyperthermia

Variable	Day	Experimental trial	Pre-tilt supine rest	Postexercise supine	Posture					
					HUT1	SUP1	HUT2	SUP2	HUT3	SUP3
FFT LFnu	1	NHS	67 (5)		71 (4)	70 (4)	71 (3)	70 (3)	72 (2)	68 (3)
	2	EIH	69 (4)	81 (0.1)	81 (0.1)[a]	81 (0.5)[a]	81 (0.6)[a]	75 (3)	77 (3)	74 (3)[a]
	3	24 h	69 (4)		72 (3)	70 (2)	71 (3)	70 (3)	71 (3)	68 (3)
	4	48 h	69 (4)		72 (3)	71 (3)	71 (3)	69 (3)	73 (3)	68 (4)
FFT HFnu	1	NHS	33 (5)		29 (4)	30 (4)	29 (3)	30 (3)	28 (2)	32 (3)
	2	EIH	31 (4)	19 (0.1)	19 (0.1)[a]	19 (0.5)[a]	19 (0.6)[a]	25 (3)	23 (3)	26 (3)[a]
	3	24 h	31 (4)		28 (3)	30 (2)	29 (3)	30 (3)	28 (3)	32 (3)
	4	48 h	31 (4)		28 (3)	29 (3)	29 (3)	31 (3)	27 (3)	32 (4)
FFT LF/HF	1	NHS	2.45 (0.36)		2.81 (0.35)	2.76 (0.32)	2.81 (0.32)	2.70 (0.34)	2.91 (0.30)	2.40 (0.33)
	2	EIH	2.52 (0.32)	4.37 (0.03)	4.37 (0.03)[a]	4.23 (0.15)[a]	4.27 (0.15)[a]	3.50 (0.39)	3.70 (0.37)	3.16 (0.32)[a]
	3	24 h	2.67 (0.44)		2.92 (0.32)	2.62 (0.29)	2.80 (0.38)	2.62 (0.33)	2.79 (0.38)	2.46 (0.31)
	4	48 h	2.59 (0.34)		2.96 (0.43)	2.77 (0.36)	2.76 (0.38)	2.47 (0.33)	3.00 (0.39)	2.54 (0.44)

24 and 48 h indicate responses measured after 24 and 48 h after EIH, respectively

EIH Exercise-induced hyperthermia

[a] Difference from the non-exercise/non-heat stress control condition (NHS) ($p < 0.05$)

recovery compared to NHS during HUT1, HUT2, SUP2 and HUT3 ($p < 0.05$), respectively (Table 4).

Discussion

A key finding of this study is that despite the significant reduction in SV and sustained increase in esophageal temperature following EIH, modulation of ANS activity toward sympathetic dominance and withdrawal of parasympathetic tone, maintains cardiac output during a repeated postural challenge in endurance trained men. This finding is supported by the fact that there was a significant increase in heart rate, secondary to a decrease in time domain HRV measurements of RMSSD, an index thought to be directly related to the parasympathetic nervous

Table 4 Mean (±SE) hemodynamic and thermoregulatory responses during repeated 70° head-up tilts performed in the early and late stages (24 and 48 h) of recovery following exercise-induced hyperthermia

Variable	Day	Experimental trial	Pre-tilt supine rest	Postexercise supine	Posture					
					HUT1	SUP1	HUT2	SUP2	HUT3	SUP3
HR (beats min^{-1})	1	NHS	58 (3)		76 (3)	58 (3)	75 (4)	58 (3)	75 (4)	55 (3)
	2	EIH	61 (3)	98 (3)	126 (6)[a]	86 (4)[a]	116 (6)[a]	82 (4)[a]	111 (6)[a]	73 (6)[a]
	3	24 h	59 (4)		77 (6)	57 (4)	74 (6)	57 (4)	75 (6)	57 (4)
	4	48 h	57 (3)		80 (5)	56 (3)	77 (6)	56 (3)	78 (5)	54(3)
MAP (mmHg)	1	NHS	90 (3)		95 (4)	94 (3)	97 (3)	92 (3)	97 (4)	92 (3)
	2	EIH	86 (2)	79 (4)	91 (3)	87 (4)	92 (3)	86 (4)[a]	98 (5)	88 (4)
	3	24 h	90 (3)		102 (4)[a]	96 (3)	104 (4)[a]	99 (3)[a]	105 (5)[a]	97 (3)
	4	48 h	84 (4)		96 (4)	91 (4)	96 (3)	90 (3)	98 (4)	91 (4)
TPR (mmHg l^{-1} min)	1	NHS	15.9 (0.7)		16.3 (1.4)	15.9 (0.6)	17.2 (1.4)	16.1 (0.8)	17.7 (1.5)	16.8 (0.9)
	2	EIH	14.6 (1.0)	12.2 (0.5)	15.5 (1.0)	13.6 (0.8)[a]	16.8 (1.0)	14.1 (1.0)	17.7 (1.0)	14.6 (1.5)
	3	24 h	16.6 (0.9)		17.3 (1.2)	16.6 (0.9)	19.1 (1.1)	16.9 (0.8)	18.7 (1.5)	17.0 (1.0)
	4	48 h	16.3 (1.5)		17.0 (1.6)	16.0 (1.1)	16.1 (0.9)	16.0 (1.0)	17.4 (1.3)	17.2 (1.2)
SV (ml)	1	NHS	102 (6)		80 (5)	99 (8)	77 (6)	99 (7)	75 (7)	102 (7)
	2	EIH	99 (4)	68 (4)	48 (3)[a]	76 (5)[a]	51 (3)[a]	79 (5)[a]	52 (4)[a]	86 (3)[a]
	3	24 h	96 (6)		81 (6)	101 (7)	76 (4)	102 (7)	79 (5)	103 (7)
	4	48 h	96 (6)		74 (5)	103 (7)	82 (7)	103 (7)	76 (4)	102 (8)
$\dot{Q}$ ($l\ min^{-1}$)	1	NHS	6.0 (0.3)		6.0 (0.4)	6.0 (0.3)	5.8 (0.4)	5.8 (0.4)	5.6 (0.3)	5.6 (0.4)
	2	EIH	6.1 (0.4)	6.6 (0.3)	6.0 (0.3)	6.4 (0.3)[a]	5.6 (0.2)	6.2 (0.3)	5.6 (0.2)	6.3 (0.4)
	3	24 h	5.5 (0.3)		6.1 (0.4)	5.9 (0.3)	5.5 (0.3)	5.9 (0.3)	5.8 (0.4)	5.9 (0.4)
	4	48 h	5.5 (0.5)		5.8 (0.4)	5.8 (0.3)	6.1 (0.4)	5.7 (0.4)	5.7 (0.4)	5.5 (0.4)
T_{es} (°C)	1	NHS	36.9 (0.1)		36.9 (0.1)	36.8 (0.1)	36.9 (0.1)	36.8 (0.1)	36.9 (0.1)	36.8 (0.1)
	2	EIH	36.9 (0.1)	37.6 (0.05)	37.6 (0.1)[a]	37.4 (0.1)[a]	37.5 (0.1)[a]	37.3 (0.1)[a]	37.3 (0.1)[a]	37.1 (0.1)[a]
	3	24 h	36.7 (0.2)		36.7 (0.2)	36.6 (0.2)	36.7 (0.2)	36.7 (0.2)	36.7 (0.2)	36.6 (0.2)
	4	48 h	36.8 (0.1)		36.9 (0.1)	36.8 (0.1)	36.9 (0.1)	36.8 (0.1)	36.9 (0.1)	36.8 (0.1)

24 and 48 h indicate responses measured 24 and 48 h after EIH, respectively

EIH Exercise-induced hyperthermia, *HR* heart rate, *MAP* mean arterial pressure, *TPR* total peripheral resistance, *SV* stroke volume, $\dot{Q}$ cardiac output

[a] Difference from the non-exercise/non-heat stress control condition (NHS) ($p < 0.05$)

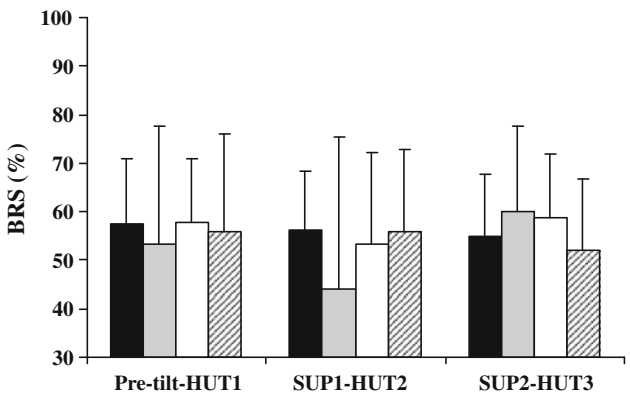

Fig. 1 Percent change (±SD) in baroreceptor sensitivity (BRS) from the supine position prior to each head-up tilt challenge was evaluated during the non-exercise/non-heat stress condition (*black bars*) and during the early (*gray bars*) and late stages [24 h (*white bars*) and 48 h (*stripped bars*)] of recovery following exercise-induced hyperthermia

system, and SDNN, during the early stages of recovery (<80 min) following EIH as compared to NHS. Further, in contrast to our hypothesis we show that the cardiovascular and thermoregulatory responses to a repeated 70° head-up tilt challenge performed at 24- and 48-h postexercise were not significantly different from those responses measured during the NHS control trial, since RMSSD, SDNN and mean RR interval were restored following 24 h of recovery. A novel finding of this study was that a greater relative change in mean arterial pressure was observed during repeated orthostatic challenges following 24 h of recovery as compared to the NHS control condition.

Effect of EIH on ANS and cardiovascular function: early stages of recovery

Though comprehensive reports have been conducted to examine autonomic regulation following exercise (Iellamo

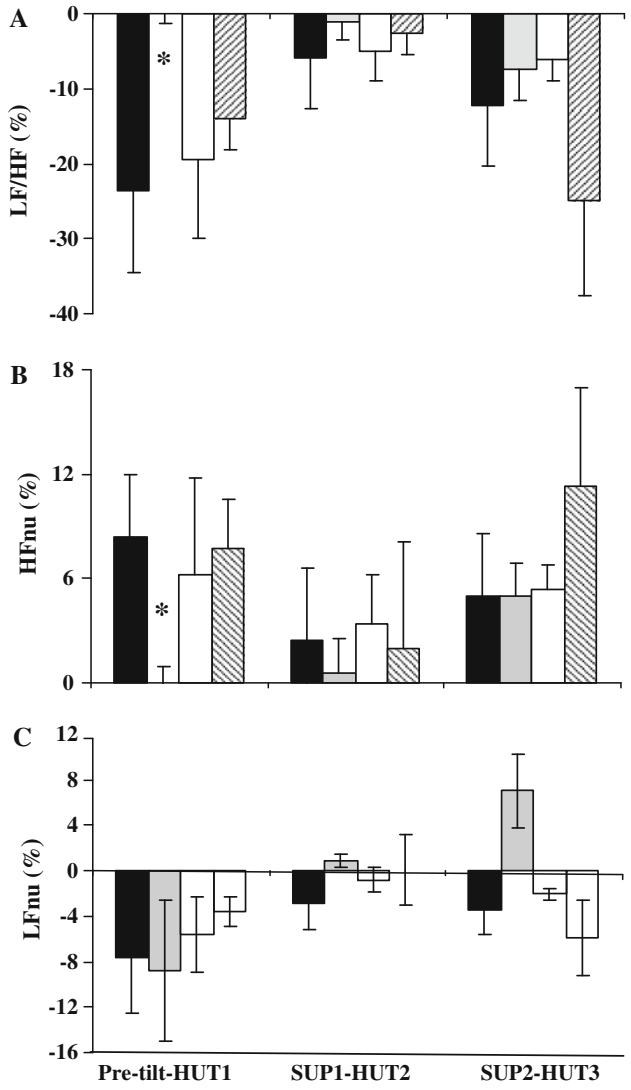

Fig. 2 Relative change (%) = [prior supine position head-up tilt response/prior supine position × 100] in heart rate variability measured by **a** LF/HF, **b** HFnu, **c** LFnu was evaluated from the supine position prior to each head-up tilt challenge during the non-exercise/non-heat stress condition (*black bars*), during the early [<80 min (*gray bars*)] and late stages [24 h (*white bars*) and 48 h (*stripped bars*)] of recovery following exercise-induced hyperthermia. *Asterisk* denotes difference between non-heat stress control and during the early stages of recovery following exercise-induced hyperthermia ($p < 0.05$)

2001; Parekh and Lee 2005; Terziotti et al. 2001; Brenner et al. 1997, 1998; Furlan et al. 1993; Bernardi et al. 1997; Hautala et al. 2001), few studies to date have examined this response following exercise performed in the heat (Brenner et al. 1997) on physically active men. Brenner et al. (1997) demonstrated a withdrawal of parasympathetic and enhancement of sympathetic activity during recovery from exercise performed in thermoneutral (23°C) and hot (40°C) ambient conditions. However, they showed that the greatest contribution of sympathetic drive was measured following exercise in the heat when end-exercise core temperature increased by 1.3°C above resting levels as compared to exercise in thermoneutral conditions (increase of 0.8°C).

In the present study, we show that following an exercise-induced heat stress, resulting in an esophageal temperature increase of ~3.3°C above baseline resting, the ANS contributes to the preserved cardiac output during a repeated orthostatic stress. Past research findings have shown that following a single bout of dynamic exercise, a prolonged period of postexercise hypotension occurs as a result of a persistent reduction in peripheral vascular resistance that is not completely offset by increases in cardiac output (Halliwill 2001). By introducing repeated postural challenges (i.e., 70° head-up tilts) during the recovery period, we were able to demonstrate that cardiac output was maintained, secondary to increases in heart rate, despite significant reductions in SV (Table 4). The reduction in SV following the EIH is likely due to a decreased venous return. It is plausible that the decreased venous return in our study was to some extent associated with the progressive reduction in central blood volume as a result of the dehydration experienced during the exercise performed in the heat (average loss of body weight ~1.2 kg). We show, however, that the reduction in venous return appears to be compensated by a marked sympathetically mediated tachycardia such that cardiac output is maintained near normal resting levels.

The contribution of the ANS to maintaining cardiac output following EIH is further supported by our HRV and BRS results. Time domain measures of HRV, specifically reductions in RMSSD and SDNN, support parasympathetic withdrawal following EIH (Table 2). Our findings are consistent with previous reports demonstrating an increase in vagal withdrawal and sympathetic dominance following exercise (Iellamo 2001; Parekh and Lee 2005; Terziotti et al. 2001). Furthermore, the relative change in frequency domain measures of HRV is consistent with a modulation of ANS activity; such that during the early stages of exercise recovery (i.e., postural transition from pre-tilt supine rest to HUT1) the magnitude of change is suppressed as evidenced by a significant decrease in HF power and LF/HF ratio (Fig. 2). Our work therefore extends upon previous findings by demonstrating that the modulation in HRV is maintained during an orthostatic challenge performed under a marked elevated state of hyperthermia and dehydration.

Reductions in central blood volume, and therefore cardiac filling, result in the activation of baroreceptors (i.e., baroreceptor unloading), resulting in increased sympathetic and decreased parasympathetic outflow (Berry et al. 2006; Niemela et al. 2008). Our findings are consistent with previous observations that conducted exercise in

thermoneutral conditions (Niemela et al. 2008; Ogoh et al. 2005) such that we show that reductions in BRS following EIH from 19 ± 3 ms $mmHg^{-1}$ at baseline to 1.9 ± 0.3 ms $mmHg^{-1}$ during HUT1 (Table 1). This attenuation in BRS persisted throughout the ~80-min recovery period which was paralleled by a reduced cardiac vagal responsiveness and/or parasympathetic outflow (Table 1). The activation of baroreceptors as a consequence of reductions in venous return during the postexercise period is supported by our relative change results which demonstrated no significant difference between the non-exercise/NHS control condition and the early recovery period following EIH (Fig. 1). This compensatory reflex appears to restore cardiac output and blood pressure by increasing heart rate and vascular resistance (Table 4).

Effect of EIH on ANS and cardiovascular function: 24 and 48 h of recovery

The modulation of BRS and HRV observed following EIH did not persist beyond 24 h. We show that the pattern of response of BRS and HRV following 24 and 48 h was similar to that measured during the NHS control condition (Figs. 1, 2). Specifically, RMSSD and SDNN of HRV as well as HF, LF and LF/HF ratio were not significantly different from NHS indicating that sympathovagal balance was restored to normal levels 24 h following the EIH (Fig. 2). Our findings, however, are in disagreement with previous reports suggesting that attenuations in HRV, as evidenced by a decreased vagal modulation of the heart, occur for as long as 24 h following prolonged exhaustive exercise (duration of exercise ~4 to 6 h) (Bernardi et al. 1997; Furlan et al. 1993; Hautala et al. 2001) conducted under thermoneutral ambient conditions. In the present study, it is possible that despite the large increase in esophageal temperature (i.e., average increase of 3.3°C), the duration of exercise was insufficient (~25 min) to elicit a sustained modulation in ANS function lasting 24 h. Further studies are required to evaluate this response for shorter recovery intervals (i.e., <24 h).

A novel observation of this study was the elevation in mean arterial pressure measured during the repeated postural challenge performed following 24 h of recovery (Table 4). This response was paralleled by a slight increase in TPR following 24 h of recovery. Orthostatic hypertension has previously been classified by an increase in blood pressure upon assumption of upright posture (Fessel and Robertson 2006) by either an increase in diastolic blood pressure from <90 to ≥90 mmHg, an increase in systolic blood pressure from <140 to ≥140 mmHg or an overall increase in systolic blood pressure by at least 20 mmHg (Fessel and Robertson 2006). Based on further evaluation of our systolic blood pressure and diastolic blood pressure response we show that the increase in mean arterial pressure was the product of both an increase in systolic and diastolic blood pressure. For example at the final HUT (i.e., HUT3), systolic and diastolic blood pressure averaged 139 ± 7 and 89 ± 3 mmHg, respectively. Noteworthy, our systolic and diastolic blood pressure results meet the cut-off values for clinical diagnosis of orthostatic hypertension. The significantly greater change in mean arterial pressure cannot be explained by changes in BRS and/or HRV as these values were restored to baseline resting values. Therefore, other factors likely contributed to increases in arterial blood pressure following 24 h of recovery. It is plausible that exercise in the heat caused significant dehydration (average loss of body weight ~1.2 kg) and plasma hyperosmolarity (Bartholomew et al. 2005; Nybo 2008).

Limitations

Heart rate variability indices (particularly high-frequency power) are to a large extent influenced by breathing pattern and it is usually recommended to control the frequency of breathing and tidal volume in HRV studies. We did not attempt to control for the effects of respiration. Therefore, the focus of this manuscript is on time domain measures of HRV, specifically changes in RMSSD which are directly related to the parasympathetic nervous system. Frequency domain measures of HRV are used as a secondary measure to support our conclusion regarding withdrawal of parasympathetic activity following EIH.

Conclusion

We conclude that modulation of the ANS is an important contributing factor in the maintenance of cardiac output in early stages (<80 min) following EIH. The withdrawal of parasympathetic activity, evidenced by a reduction in RMSSD and SDNN of time domain HRV, and shift toward greater sympathetic drive that occurs during this period, results in a reflex tachycardia which helps to compensate for the reduction in venous return (and therefore cardiac filling). We show, however, that ANS activity and baroreflex sensitivity is restored following 24 h of recovery.

Acknowledgments This research was supported by the Natural Sciences and Engineering Research Council (RGPIN-298159-2004 and RGPIN-298159-2009) and Leaders Opportunity Fund from the Canada Foundation for Innovation (grants held by Dr. Glen Kenny). Ms. Rachel Armstrong was supported by a Natural Sciences and Engineering Research Council Canada Graduate Scholarship. Dr. Glen Kenny was supported by a University of Ottawa Research Chair.

Conflict of interest Ms. R. Armstrong has no conflicts of interest to disclose. Mr. Saif Ahmad has no conflicts of interest to disclose.

Dr. A. Seely founded Therapeutic Monitoring Systems in order to commercialize patented Continuous Individualized Monitoring Variability Analysis (CIMVA) technology, with the objective of delivering variability-directed clinical decision support to improve quality and efficiency of care. Dr. G. Kenny has no conflicts of interest to disclose.

References

Ahmad S, Ramsay T, Huebsch L, Flanagan S, McDiarmid S, Batkin I, McIntyre L, Sundaresan SR, Maziak DE, Shamji FM, Hebert P, Fergusson D, Tinmouth A, Seely AJ (2009) Continuous multiparameter heart rate variability analysis heralds onset of sepsis in adults. PLoS One 4:e6642

Armstrong LE, Casa DJ, Millard-Strafford M, Moran DS, Pyne SW, Roberts WO (2007) Exertional heat illness during training and competition. Med Sci Sports Exerc 3:556–572

Armstrong RG, Seely AJ, Kilby D, Journeay SW, Kenny GP (2010) Cardiovascular and thermal responses to repeated head-up tilts following exercise-induced heat stress. Aviat Space Environ Med 81:646–653

Bartholomew K, O'Brien BJ, Gill ND (2005) Plasma volume expansion 24-hours post exercise: effect of doubling the volume of replacement fluid. J Sports Sci Med 4:179–184

Bernardi L, Passino C, Robergs R, Appenzeller O (1997) Acute and persistent effects of a 46-kilometer wilderness trail run at altitude: cardiovascular autonomic modulation and baroreflexes. Cardiovasc Res 34:273–280

Berry NM, Rickards CA, Newman DG (2006) Acute cardiovascular adaptation to 10 consecutive episodes of head-up tilt. Aviat Space Environ Med 77:494–499

Brenner IK, Thomas S, Shephard RJ (1997) Spectral analysis of heart rate variability during heat exposure and repeated exercise. Eur J Appl Physiol 76:145–156

Brenner IK, Thomas S, Shephard RJ (1998) Autonomic regulation of the circulation during exercise and heat exposure: inferences from heart rate variability. Sports Med 2:85–99

Butler GC, Yamamoto Y, Hughson RL (1994) Heart rate variability to monitor autonomic nervous system activity during orthostatic stress. J Clin Pharmacol 34:558–562

Fessel J, Robertson D (2006) Orthostatic hypertension: when pressor reflexes overcompensate. Nat Clin Pract Nephrol 2:424–431

Flouris AD, Cheung SS (2009) Influence of thermal balance on cold-induced vasodilation. J Appl Physiol 106:1264–1271

Furlan R, Piazza S, Dell'Orto S, Gentile E, Cerutti S, Pagani M, Malliani A (1993) Early and late effects of exercise and athletic training on neural mechanisms controlling heart rate. Cardiovasc Res 27:482–488

Gagnon D, Jay O, Reardon FD, Journeay WS, Kenny GP (2008) Hyperthermia modifies the nonthermal contribution to postexercise heat loss responses. Med Sci Sports Exerc 40:513–522

Halliwill JR (2001) Mechanisms and clinical implications of post-exercise hypotension in humans. Exerc Sport Sci Rev 29:65–70

Hautala A, Tulppo MP, Makikallio TH, Laukkanen R, Nissila S, Huikuri HV (2001) Changes in cardiac autonomic regulation after prolonged maximal exercise. Clin Physiol 21:238–245

Hubbard RW (1990) Heatstroke pathophysiology: the energy depletion model. Med Sci Sports Exerc 1:19–28

Iellamo F (2001) Neural mechanisms of cardiovascular regulation during exercise. Auton Neurosci 90:66–75

Jellema WT, Imholz BP, van Goudoever J, Wesseling KH, van Lieshout JJ (1996) Finger arterial versus intrabrachial pressure and continuous cardiac output during head-up tilt testing in healthy subjects. Clin Sci (Lond) 91:193–200

Kenny GP, Jay O, Journeay WS (2007) Disturbance of thermal homeostasis following dynamic exercise. Appl Physiol Nutr Metab 32:818–831

Kenny GP, Gagnon D, Shiff D, Armstrong R, Journeay WS, Kilby D (2010) Influence of nonthermal baroreceptor modulation of heat loss responses during uncompensable heat stress. Eur J Appl Physiol 108:541–548

Loimaala A, Huikuri H, Oja P, Pasanen M, Vuori I (2000) Controlled 5-mo aerobic training improves heart rate but not heart rate variability or baroreflex sensitivity. J Appl Physiol 89: 1825–1829

Niemela TH, Kiviniemi AM, Hautala AJ, Salmi JA, Linnamo V, Tulppo MP (2008) Recovery pattern of baroreflex sensitivity after exercise. Med Sci Sports Exerc 40:864–870

Nybo L (2008) Hyperthermia and fatigue. J Appl Physiol 104: 871–878

Ogoh S, Fisher JP, Dawson EA, White MJ, Secher NH, Raven PB (2005) Autonomic nervous system influence on arterial baroreflex control of heart rate during exercise in humans. J Physiol 566:599–611

Parati G, Casadei R, Groppelli A, Di Rienzo M, Mancia G (1989) Comparison of finger and intra-arterial blood pressure monitoring at rest and during laboratory testing. Hypertension 13: 647–655

Parekh A, Lee CM (2005) Heart rate variability after isocaloric exercise bouts of different intensities. Med Sci Sports Exerc 37:599–605

Penaz J (1975) Current photoelectric recording of blood flow through the finger. Cesk Fysiol 24:349–352

Proulx CI, Ducharme MB, Kenny GP (2006) Safe cooling limits from exercise-induced hyperthermia. Eur J Appl Physiol 96:434–445

Rowell LB, Wyss CR, Brengelmann GL (1973) Sustained human skin and muscle vasoconstriction with reduced baroreceptor activity. J Appl Physiol 34:639–643

Seely AJ, Macklem PT (2004) Complex systems and the technology of variability analysis. Crit Care 8:R367–R384

Siri WE (1956) The gross composition of the body. Adv Biol Med Phys 4:239–280

Skrapari I, Tentolouris N, Perrea D, Bakoyiannis C, Papazafiropoulou A, Katsilambros N (2007) Baroreflex sensitivity in obesity: relationship with cardiac autonomic nervous system activity. Obesity (Silver Spring) 15:1685–1693

Sugawara J, Tanabe T, Miyachi M, Yamamoto K, Takahashi K, Iemitsu M, Otsuki T, Homma S, Maeda S, Ajisaka R, Matsuda M (2003) Non-invasive assessment of cardiac output during exercise in healthy young humans: comparison between Modelflow method and Doppler echocardiography method. Acta Physiol Scand 179:361–366

Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology (1996) Heart rate variability. Standards of measurement, physiological interpretation, and clinical use. Eur Heart J 17:354–381

Terziotti P, Schena F, Gulli G, Cevese A (2001) Post-exercise recovery of autonomic cardiovascular control: a study by spectrum and cross-spectrum analysis in humans. Eur J Appl Physiol 84:187–194

Van Ravenswaaij-Arts CMA, Kollee LAA, Hopman JCW, Stoelinga GBA, Van Geijn HP (1993) Heart rate variability. Ann Intern Med 118:436–447

Westerhof BE, Gisolf J, Karemaker JM, Wesseling KH, Secher NH, van Lieshout JJ (2006) Time course analysis of baroreflex sensitivity during postural stress. Am J Physiol Heart Circ Physiol 291:H2864–H2874

World Health Organization (2007) International statistical classification of diseases and related health problems, 10th edn. World Health Organization Press, Switzerland

Yamamoto S, Iwamoto M, Inoue M, Harada N (2007) Evaluation of the effect of heat exposure on the autonomic nervous system by heart rate variability and urinary catecholamines. J Occup Health 49:199–204