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Age alters cardiac autonomic modulations during and following exercise-induced heat stress in females

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ABSTRACT
The aim of this study was to examine the effect of natural ageing on heart rate variability during and following exercise-induced heat stress in females. Eleven young (~24 years) and 13 older (~51 years), habitually active females completed an experimental session consisting of baseline rest, moderate intensity intermittent exercise (four 15-min bouts separated by 15-min recovery) and 1-hour of final recovery in a hot and dry (35°C, 20% relative humidity) environment. Respiratory and heart rate recordings were continuously logged with 10-min periods analysed at the end of: baseline rest; each of the exercise and recovery bouts; and during the 1-hour final recovery period. Comparisons over time during exercise and recovery, and between groups were conducted via two-way repeated-measures ANCOVAs with rest values as the covariate. During baseline rest, older females exhibited lower heart rate variability compared to young females with similar levels of respiration and most (~71-79%) heart rate variability measures during repeated exercise and recovery. However, older females exhibited heart rate variability metrics suggestive of greater parasympathetic modulation (greater long axis of Poincare plot, cardiac vagal index; lower low-high frequency ratio) during repeated exercise with lower indices during the latter stage of prolonged recovery (less very low frequency component, Largest Lyapunov Exponent; greater cardiac sympathetic index). The current study documented several unique, age-dependent differences in heart rate variability, independent of respiration, during and following exercise-induced heat stress for females that may assist in the detection of normal heat-induced adaptations as well as individuals vulnerable to heat stress.

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Introduction

During normal ageing, changes in resting cardiac autonomic control occur as the balance between the activities of the sympathetic and parasympathetic nervous systems are altered [1]. More specifically, ageing leads to increased sympathetic activity and attenuated parasympathetic activity [2]. These age-induced alterations can be measured by heart rate variability, a non-invasive and well-established method for the assessment of cardiac autonomic control [3]. Reduced heart rate variability was strongly associated with cardiovascular and all-cause mortality [4] with ageing, characterized by reductions in heart rate variability, potentially contributing to the increased risk for cardiovascular disease and greater mortality [5,6].

Reductions in resting heart rate variability with advancing age have been observed in both males and females [6–9] with distinct differences in the activities of the sympathetic and parasympathetic branches noted between sexes [10,11]. For example, women of all ages exhibited lower sympathetic and greater parasympathetic activities compared to men [10]. Furthermore, Umetani et al. [11] reported that women aged less than 50 years exhibited higher heart rate variability compared to men with these sex differences absent at ages greater than 50 years [11,12].

The decline in cardiac autonomic control with natural ageing has been examined primarily during short-term rest or over a 24-hour period [6–8] with less known about the impact of age on heart rate

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variability during and/or following stressful conditions such as performing exercise, especially in the heat. During exercise, altered cardiac autonomic control has been demonstrated with a predominance of sympathetic activity during exercise, particularly with increasing exercise intensity, and a gradual reactivation of parasympathetic activity during recovery [13,14]. Similar reductions in cardiac autonomic (heart rate variability) responses have been reported with exposure to heat stress in males and females [5,15–18]. Brenner and colleagues [17] reported a reduction in resting parasympathetic tone and an increase in sympathetic tone during exercise in hot conditions (40°C, 30% relative humidity) that remained consistent between repeated bouts of 30-min cycling (50% maximum rate of oxygen consumption, $\dot{V}O_{2max}$). Recently, Carrillo et al. [5] examined heart rate variability prior to and during a prolonged 3-hour exposure to a high heat stress condition (i.e., 44°C, simulating an exposure to an extreme heat event) noting that relatively healthy older adults (63 years) experienced an attenuated sympathetic response relative to their younger (23 years) counterparts. Specifically, older adults exhibited less heart rate variability at rest and a diminished sympathetic response during heat stress which was suggested to possibly contribute to poorer thermoregulatory function experienced by the older adults [5]. Reductions in heart rate variability may provide insights into systemic autonomic control and thermoregulation given the coupling between human cardiac activity and sympathetic outflow to muscle and skin [19,20], and with sudomotor and cutaneous activity during whole-body heating and cooling [19,21].

While ageing impacts on cardiac autonomic control, it has also been recently identified as a key modulator of thermoregulation with impairments in whole-body heat dissipation observed from those aged greater than 40 years [22,23]. Anderson and Kenney [24] demonstrated that older females (52-62 years) exhibited greater body core temperatures which were associated with lower whole-body (as estimated by changes in body mass) and local sweating responses compared to younger females (20-30 years) during a 2-hour low intensity walk in the heat. This was reinforced by Larose et al. [25] who reported age-related reductions in whole-body evaporative heat loss (as measured by a whole-body direct calorimeter) during short duration (15-min), moderate intensity, intermittent exercise bouts. These impairments were maintained despite a progressively greater heat storage in older (~51 years) versus younger (~24 years) females [25]. Further, this age difference was reported to be dependent on the level of heat stress as defined by the combined metabolic and environmental heat load with older females demonstrating reduced whole-body heat loss at low-to-moderate heat loads (i.e. ≥325W, equivalent to ~47-63% of $\dot{V}O_{2max}$) with the magnitude of difference exacerbated with greater elevations in the level of thermal stress [26].

Much of our understanding of age-related changes in cardiac autonomic control and heat tolerance have been based on studies conducted in males with resting parasympathetic activity suppressed and sympathetic activity enhanced acutely during heat stress [15,27]. Very little is known about heart rate variability changes in ageing females during heat stress with reductions in whole-body heat loss potentially exposing older females to a greater risk of developing heat-related injuries, reduced heart rate variability and increased risk of cardiac instability or events [28–30]. Since heat loss capacity differs markedly between men and women [31,32], it is important to examine females separately to evaluate the independent effect of aging. In this context, examining the impact of age on heart rate variability during heat stress will advance our understanding of the age-related changes in cardiovascular function in women that may contribute to altered thermoregulatory function in older women. Therefore, the aim of the current study was to examine the effect of age on heart rate variability during and following exercise-induced heat stress in young (~24 years) and older (~51 years) females. In line with our prior results where older adults demonstrated less heart rate variability at rest and a diminished sympathetic response during heat stress [5], it was hypothesised that older females would demonstrate reduced heart rate variability and autonomic responses during intermittent exercise and recovery in the heat compared to young females.

Methods

This study was part of a larger investigation, the main results of which have been published previously [25].

Since detailed information concerning the study population and design appeared in the original publication, we provided brief summaries below.

Participants

Eleven young habitually active (Young, 24.3 ± 3.6 years, 1.66 ± 0.04 m, 64.8 ± 14.1 kg) and 13 older active (Older, 51.3 ± 7.5 years, 1.65 ± 0.04 m, 68.0 ± 10.4 kg) females, matched for aerobic capacity and body surface area [25], volunteered for this study. All provided written informed consent in line with a protocol approved by the University of Ottawa Research Ethics Committee.

Procedures

Participants completed an experimental session within a whole-body air calorimeter (a device that records very precise measurements of heat dissipated by the human body) regulated at 35°C and 20% relative humidity. They remained upright and seated for a 30-min baseline-resting period (Rest). Thereafter, they performed four 15-min bouts of cycling exercise (Ex1, Ex2, Ex3, and Ex4) at a constant rate of metabolic heat production equal to 300 W, each separated by 15-min recovery (Rec1, Rec2 and Rec3) periods and a final recovery period of 60-min (immediate 15-min, Rec4; final 15-min, Rec60) [25]. A fixed rate of heat production was employed to maintain a similar thermal drive for sweat production. All sessions were conducted with participants being similarly dressed (i.e. shorts, sports bra, and sandals), following the consumption of a light breakfast (minimum of 3 hours pre-session), and without alcohol, caffeine, intense exercise, and/or thermal stimuli for the preceding 24 hours.

Heart rate variability analysis

During the experimental session, heart rate was continuously recorded via a 3 channel DigiTrak XT Holter Monitor (Philips, Andover, MA, USA) at a sampling frequency of 175 Hz and uploaded via manufacturer's software for later analysis. All heart rate recordings (i.e. RR-intervals) were exported to a dedicated software program (CIMVA v3.7, Ottawa Hospital Research Institute – Dynamical Analysis Laboratory, Ottawa, Canada) for the analysis of heart rate variability [33]. The RR interval time series from all participants were automatically cleaned by removing artefacts (e.g. outside of physiological limits) and abnormal beats (e.g. atrial fibrillation, ectopics). Recordings were analysed for heart rate variability as 5-minute moving windows with an incremental step size of 30 seconds as described previously [34]. These 5-minute windows were averaged to determine stable 10-minute recordings at the end of each of the following time periods: Rest, Ex1, Rec1, Ex2, Rec2, Ex3, Rec3, Ex4, Rec4 and Rec60. A set of 56 heart rate variability measures (Table 1) was examined for each 10-minute recording.

Given the complexity of presenting results for all 56 indices, the most commonly described indices in past studies [34,35] were chosen to be presented currently and included the following: heart rate, coefficient of variation, short and long axes of Poincaré plot (SD1, SD2 respectively), very low (VLF, 0.003-0.04 Hz), low (LF, 0.04-0.15 Hz) and high (HF, 0.15-0.4 Hz) frequency components, LF/HF ratio, short-term ($\alpha 1$) and long-term ($\alpha 2$) fractal scaling exponents via Detrended Fluctuation Analysis, Largest Lyapunov Exponent (LLE), Shannon Entropy (shannEn), Cardiac Sympathetic Index (CSI) and Cardiac Vagal Index (CVI) [33]. These indices represented a variety of statistical, time- and frequency-domain, and non-linear or complexity measures.

Respiratory analysis

Respiratory variables including respiratory rate, tidal volume, ventilatory rate and rate of oxygen consumption ($\dot{V}O_2$) were continuously monitored via indirect calorimetry, as previously described [25].

Statistical analysis

The normal distribution of variables was confirmed via the Kolmogorov-Smirnov test with a Lilliefors Significance correction with data transformed via natural logarithm when this assumption was violated (i.e. LF, HF). Comparisons between groups at Rest were conducted via independent t-tests. As differences at Rest existed for some variables, comparisons over time and between groups during intermittent exercise (i.e. Ex1, Ex2, Ex3, Ex4) and during the recovery periods (i.e. Rec1, Rec2, Rec3, Rec4, Rec60) were conducted via 2-way repeated-

Table 1. Heart rate variability measures examined in the current study [33].

Measure	Definition
Statistical	
HR	Heart rate
CV	Coefficient of variation (based on intervals)
formF	Form factor
SymDce_2	Symbolic dynamics: modified conditional entropy, non-uniform case
SymDfw_2	Symbolic dynamics: forbidden words, non-uniform case
SymDse_2	Symbolic dynamics: Shannon entropy, non-uniform case
SymDp0_2	Symbolic dynamics: percentage of 0 variations sequences, non-uniform case
SymDp1_2	Symbolic dynamics: percentage of 1 variations sequences, non-uniform case
SymDp2_2	Symbolic dynamics: percentage of 2 variations sequences, non-uniform case
Geometric	
FGR	Finite growth rates
gcount	Grid transformation feature: grid count
SD1	Poincaré plot SD1
SD2	Poincaré plot SD2
CSI	Poincaré plot cardiac sympathetic index = SD2 / SD1
CVI	Poincaré plot cardiac vagal index = $\log_{10}$(16 x SD1 x SD2)
dlmax	Recurrence quantification analysis: maximum diagonal line
vlmax	Recurrence quantification analysis: maximum vertical line
pDpR	Recurrence quantification analysis: determinism/ recurrences
pD	Recurrence quantification analysis: percentage of determinism
pL	Recurrence quantification analysis: percentage of laminarity
pR	Recurrence quantification analysis: percentage of recurrences
sedl	Recurrence quantification analysis: Shannon entropy of the diagonals
sevl	Recurrence quantification analysis: Shannon entropy of the vertical lines
Informational	
aFdP	Allan factor distance from a Poisson distribution
fFdP	Fano factor distance from a Poisson distribution
sgridAND	Grid transformation feature: AND similarity index
sgridTAU	Grid transformation feature: time delay similarity index
sgridWGT	Grid transformation feature: weighted similarity index
IoV	Index of variability distance from a Poisson distribution
KLPE	Kullback-Leibler permutation entropy
MSE	Multiscale entropy
ARerr	Predictive feature: error from an Autoregressive model
QSE	Quadratic Sample Entropy
shannEn	Shannon entropy
histSI	Similarity index of the distributions
Energetic	
LFHF_ratio	Low frequency – high frequency ratio
LFpower	Low frequency power
HFpower	High frequency power
Complexity	Hjorthparameters: complexity
AsymI	Multiscale time irreversibility asymmetry index
PSeo	Plotkin and Swamy energy operator average energy
Teo	Teager energy operator average energy
VLFpower	Very low frequency power
Invariant	
cDim	Correlation dimension exponent
dfa_alpha1	Detrended fluctuation analysis: $\alpha1$
dfa_alpha2	Detrended fluctuation analysis: $\alpha2$
dfa_auc	Detrended fluctuation analysis: area under the curve
eScaleE	Embedding scaling exponent
LLE	Largest Lyapunov exponent
Multifractal_c1	Multifractal spectrum cumulant of the first order
Multifractal_c2	Multifractal spectrum cumulant of the second order
slopeLS	Power Law (based on frequency) slope
y_intLS	Power Law (based on frequency) y intercept
SDLEalpha	Scale dependent Lyapunov exponent slope
SDLEmean	Scale dependent Lyapunov exponent mean value
Hurst	Hurst Exponent

measures ANCOVA with Rest levels as a covariate. Post-hoc comparisons were conducted via Tukey's HSD when significant effects were identified via the ANCOVA. All values are presented as mean ± SD with analyses conducted using the Statistical Package for the Social Sciences (Version 22; IBM Corp., Armonk, NY, USA) and an alpha level of 0.05.

Results

Pre-exercise rest

At Rest, the Older group exhibited significantly lower values compared to the Young group for CV, SD1, SD2, HF, LLE, shannEn and CVI (Table 2). In contrast, the Older group presented with greater values of $\alpha1$ compared to the Young group (Table 2). All respiratory variables were similar between groups (Table 2).

Table 2. Respiratory and heart rate variability measures during rest for Young (n = 11) and Older (n = 13) females.

	Young (n = 11)	Older (n = 13)
Respiratory measures		
Respiratory rate (breaths/min)	17.5 ± 1.9	16.0 ± 2.9
Tidal volume (L)	0.56 ± 0.16	0.65 ± 0.22
Ventilatory rate (L/min)	9.3 ± 2.5	9.6 ± 1.7
$\dot{V}O_2$ (ml/kg/min)	4.3 ± 1.0	4.0 ± 0.6
Heart rate variability measures		
HR (bpm)	76.2 ± 12.2	73.7 ± 11.2
CV (%)	8.2 ± 2.3	5.2 ± 1.6**
SD1 (ms)	36.3 ± 20.8	17.9 ± 8.1*
SD2 (ms)	85.3 ± 27.6	59.5 ± 22.9*
VLF (ms^2)	243 ± 93	275 ± 103
LF (ms^2)	167 ± 67	168 ± 89
HF (ms^2)	149 ± 67	90 ± 47*
LF/HF	1.39 ± 0.79	2.54 ± 2.03
$\alpha1$	1.01 ± 0.22	1.23 ± 0.20*
$\alpha2$	0.93 ± 0.14	0.96 ± 0.19
LLE	1.13 ± 0.22	0.91 ± 0.23*
shannEn	5.46 ± 0.38	4.91 ± 0.56*
CSI	2.66 ± 0.82	3.66 ± 1.60
CVI	−1.38 ± 0.32	−1.85 ± 0.37**

$\dot{V}O_2$ = rate of oxygen consumption; Heart rate variability measures as defined in Table 1.
*p<0.05, **p<0.01 vs. Young.

Table 3. Respiratory and heart rate variability measures during intermittent exercise for Young (n = 11) and Older (n = 13) females.

	Ex1	Ex2	Ex3	Ex4
Respiratory measures				
Respiratory rate (breaths/min)				
Young	26.3 ± 4.7	27.8 ± 5.1	28.1 ± 5.2	29.7 ± 5.9
Older	22.5 ± 3.1	24.0 ± 3.8	24.7 ± 4.0	25.4 ± 4.6
Tidal volume (L)				
Young	1.19 ± 0.16	1.13 ± 0.16	1.13 ± 0.14	1.08 ± 0.14
Older	1.33 ± 0.24	1.24 ± 0.23	1.25 ± 0.20	1.22 ± 0.19
Ventilatory rate (L/min)				
Young	29.8 ± 4.1	30.1 ± 3.3	30.3 ± 3.5	30.7 ± 3.8
Older	28.8 ± 2.2	28.6 ± 2.8	29.7 ± 2.4	29.6 ± 2.4
$\dot{V}O_2$ (L/min)				
Young	17.5 ± 3.1	17.3 ± 3.1	17.6 ± 3.2	17.6 ± 3.3
Older	16.1 ± 2.4	15.9 ± 2.8	16.6 ± 2.6	16.6 ± 2.5
Heart rate variability measures				
$\alpha 1$				
Young	0.82 ± 0.28	0.77 ± 0.25	0.83 ± 0.30	0.84 ± 0.33
Older	0.80 ± 0.18	0.78 ± 0.21	0.75 ± 0.25	0.72 ± 0.27
$\alpha 2$				
Young	1.06 ± 0.16	1.08 ± 0.13	1.02 ± 0.13	1.00 ± 0.18
Older	1.04 ± 0.23	1.06 ± 0.24	1.02 ± 0.28	1.05 ± 0.26
LLE				
Young	1.54 ± 0.18	1.58 ± 0.16	1.56 ± 0.18	1.56 ± 0.22
Older	1.56 ± 0.16	1.55 ± 0.19	1.59 ± 0.13	1.59 ± 0.16
shannEn				
Young	3.31 ± 0.33	3.16 ± 0.51	3.15 ± 0.53	3.20 ± 0.52
Older	3.66 ± 0.43	3.51 ± 0.42	3.43 ± 0.55	3.40 ± 0.69
CSI				
Young	2.27 ± 0.74	2.06 ± 0.58	2.16 ± 0.84	2.18 ± 0.84
Older	2.22 ± 0.77	2.10 ± 0.75	1.97 ± 0.59	1.96 ± 0.71
CVI				
Young	−2.70 ± 0.20	−2.78 ± 0.30	−2.79 ± 0.29	−2.76 ± 0.27
Older	−2.50 ± 0.31	−2.59 ± 0.32	−2.62 ± 0.37	−2.64 ± 0.42

$\dot{V}O_2$ = rate of oxygen consumption; Heart rate variability measures as defined in Table 1.

Intermittent exercise

During intermittent exercise, most heart rate variability measures were similar between bouts and groups (Table 3, Figure 1), except for SD2, shannEn and CVI, which were significantly lower for Young compared to Older females (SD2, 15.9 ± 5.1 vs. 19.1 ± 7.4, $P<0.05$; shannEn, 3.20 ± 0.47 vs. 3.50 ± 0.52, $P<0.05$; CVI, -2.76 ± 0.26 vs. -2.59 ± 0.35, $P<0.05$). Overall, the LF/HF ratio during intermittent exercise was greater for Young compared to Older females (2.45 ± 1.66 vs. 1.35 ± 0.82, $P<0.05$). All respiratory variables were similar between bouts and groups (Table 3).

Recovery

Most heart rate variability measures were similar between recovery periods (Figure 2, Table 4) except for CV and shannEn which were significantly greater after an extended recovery period (i.e. after 60-min; Rec60) as compared to the earlier stage of the prolonged recovery period (i.e. 15-min; Rec4) (CV, 6.5 ± 1.9 vs 5.9 ± 2.2%, $P<0.05$; shannEn, 5.05 ± 0.48 vs. 4.89 ± 0.61, $P<0.05$). The Young females exhibited lower values of VLF across all recovery bouts compared to the Older group (main effect, 275 ± 81 vs. 332 ± 71, $P<0.05$) with this difference most evident during Rec4 (Figure 2). Group differences were also noted for LLE and CSI with the Young group exhibiting greater LLE and lower CSI values compared to the Older group at Rec4 and Rec60 (Table 4). Older females also displayed a lower LLE and greater CSI at Rec60 compared to the earlier recovery bouts (Table 4). For respiratory variables, a main effect for time was identified with tidal volume during Rec1 and Rec2 greater than that for Rec4 (0.61 ± 0.20 and 0.60 ± 0.18 vs. 0.56 ± 0.14 L, $P<0.05$), and Rec1 and Rec3 greater than that for Rec60 (0.61 ± 0.20 and 0.60 ± 0.17 vs. 0.57 ± 0.16 L, $P<0.05$). There were no group or interaction effects for any respiratory variable (Table 4).

Discussion

The current study demonstrated for the first time that compared to young females, older females exhibited less (CV, SD1, SD2, HF, LLE, shannEn, CVI) heart rate variability at baseline rest, similar to greater (SD2, shannEn, CVI) heart rate variability measures during

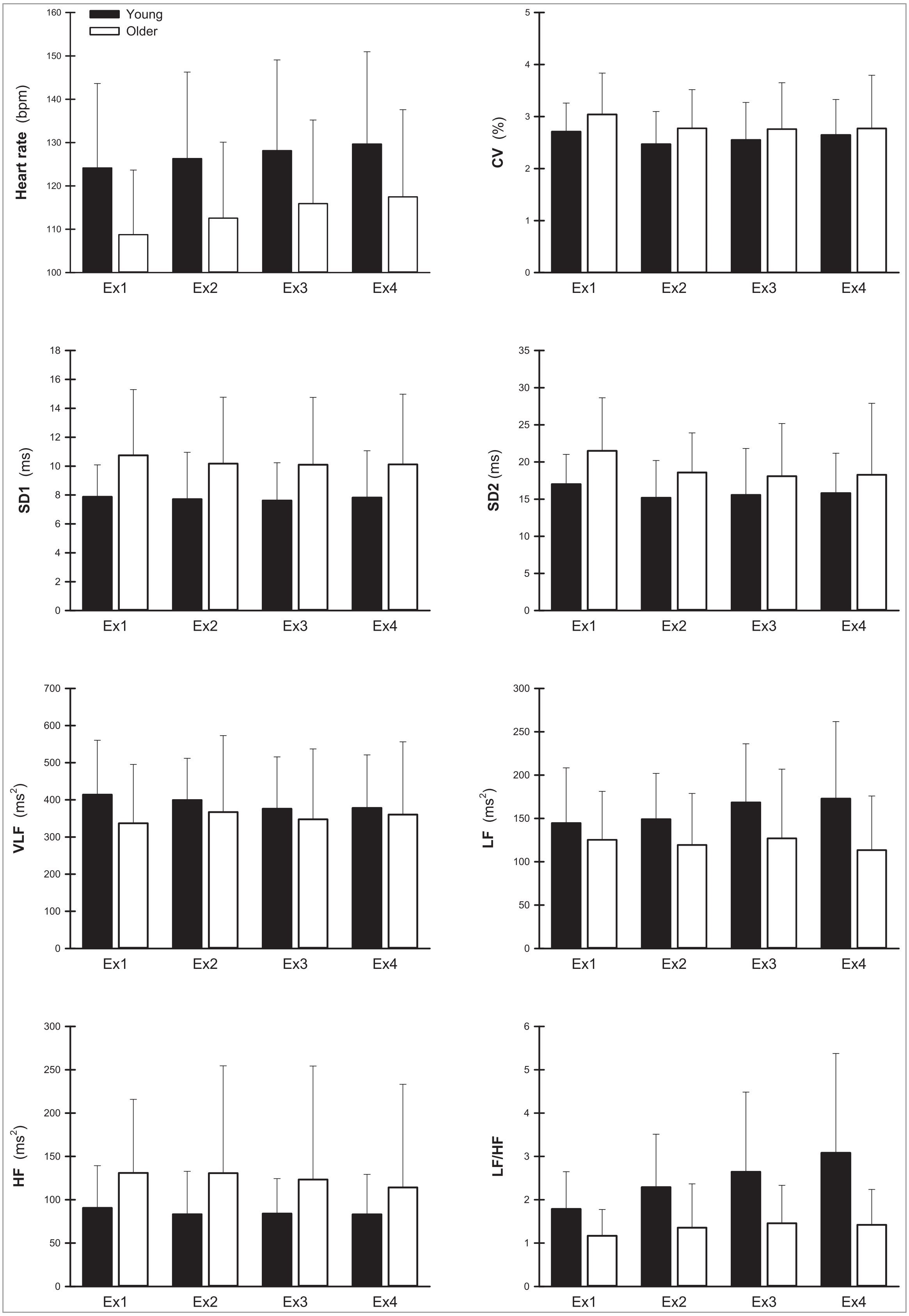

Figure 1. Heart rate variability measures during each 15-min bout of cycling exercise (Ex1, Ex2, Ex3, Ex4) for Young (n = 11) and Older (n = 13) females. Heart rate variability measures as defined in Table 1.

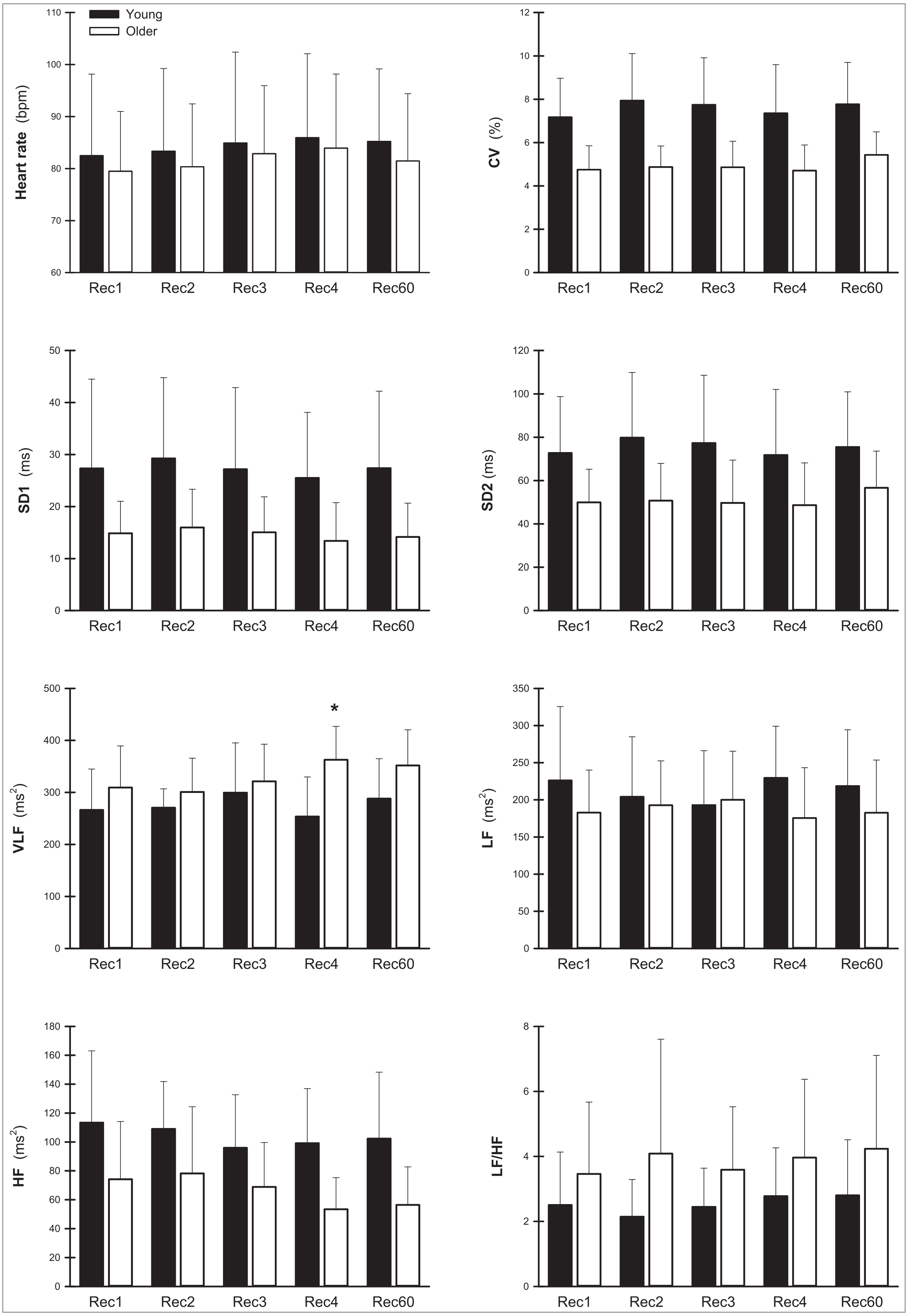

Figure 2. Heart rate variability measures during each 15-min recovery (Rec1, Rec2, Rec3) period and the final 60-min recovery period (immediate 15-min, Rec4; final 15-min, Rec60). Heart rate variability measures as defined in Table 1. *p<0.05 vs. Young.

Table 4. Respiratory and heart rate variability measures during recovery from intermittent exercise for Young (n = 11) and Older (n = 13) females.

	Rec1	Rec2	Rec3	Rec4	Rec60
Respiratory measures					
Respiratory rate (breaths/min)					
Young	18.7 ± 2.6	18.7 ± 2.7	18.9 ± 2.8	19.6 ± 2.4	19.1 ± 3.3
Older	17.5 ± 3.0	18.0 ± 3.2	17.9 ± 3.2	18.3 ± 2.8	17.4 ± 3.0
Tidal volume (L)					
Young	0.59 ± 0.15	0.59 ± 0.14	0.58 ± 0.15	0.54 ± 0.11	0.53 ± 0.13
Older	0.64 ± 0.24	0.61 ± 0.21	0.63 ± 0.19	0.57 ± 0.17	0.61 ± 0.18
Ventilatory rate (L/min)					
Young	10.3 ± 2.1	10.2 ± 1.8	10.1 ± 1.8	10.0 ± 1.5	9.4 ± 1.5
Older	10.1 ± 1.5	10.1 ± 1.7	10.4 ± 1.6	9.8 ± 2.4	9.6 ± 2.1
$\dot{V}O_2$ (L/min)					
Young	4.6 ± 0.9	4.6 ± 0.8	4.5 ± 0.7	4.5 ± 0.6	4.3 ± 0.6
Older	4.0 ± 0.5	4.1 ± 0.6	4.2 ± 0.6	4.1 ± 0.9	4.0 ± 0.6
Heart rate variability measures					
$\alpha 1$					
Young	1.17 ± 0.22	1.12 ± 0.24	1.12 ± 0.23	1.15 ± 0.19	1.17 ± 0.23
Older	1.30 ± 0.18	1.30 ± 0.21	1.30 ± 0.20	1.32 ± 0.14	1.39 ± 0.20
$\alpha 2$					
Young	0.91 ± 0.16	0.95 ± 0.16	0.97 ± 0.18	0.88 ± 0.17	0.95 ± 0.14
Older	0.98 ± 0.11	0.96 ± 0.08	0.97 ± 0.10	1.05 ± 0.14	1.01 ± 0.13
LLE					
Young	1.13 ± 0.15	1.11 ± 0.28	1.11 ± 0.27	1.13 ± 0.30	1.10 ± 0.23
Older	0.94 ± 0.17*	0.99 ± 0.26	1.00 ± 0.24	0.94 ± 0.19*	0.77 ± 0.20*abcd
shannEn					
Young	5.23 ± 0.54	5.31 ± 0.56	5.26 ± 0.58	5.19 ± 0.54	5.27 ± 0.49
Older	4.71 ± 0.42	4.74 ± 0.41	4.68 ± 0.49	4.64 ± 0.57	4.87 ± 0.39
CSI					
Young	3.07 ± 0.93	2.97 ± 0.90	3.20 ± 1.29	3.02 ± 1.11	3.07 ± 0.85
Older	3.64 ± 0.98	3.52 ± 1.10	3.58 ± 1.08	3.83 ± 0.76*	4.31 ± 1.07*abc
CVI					
Young	−1.60 ± 0.42	−1.52 ± 0.39	−1.57 ± 0.39	−1.62 ± 0.37	−1.56 ± 0.37
Older	−1.99 ± 0.31	−1.95 ± 0.31	−2.00 ± 0.34	−2.07 ± 0.38	−1.95 ± 0.29

$\dot{V}O_2$ = rate of oxygen consumption; Heart rate variability measures as defined in Table 1.
*$p<0.05$ vs. Young.
[a] $p<0.05$ vs. Rec1, [b] $p<0.05$ vs. Rec2, [c] $p<0.05$ vs. Rec3, [d] $p<0.05$ vs. Rec4

repeated exercise bouts and similar to less (VLF, LLE) heart rate variability during prolonged recovery in the heat. These heart rate variability responses represented important and unique adjustments in cardiac autonomic modulations for older females during moderate intensity intermittent exercise and recovery that may also contribute to age-dependent changes in thermoregulatory function.

Resting response

The Older females exhibited smaller resting values of most heart rate variability measures indicating less parasympathetic modulation and complexity of heart rate control. Age-induced reductions in heart rate variability have been previously reported in participants resting in thermoneutral conditions [5,8,12,36]. Elderly females (60-70 years) were reported to exhibit impaired vagal modulations compared to middle-aged females (40-50 years) [36]. Recently, Carrillo et al. [5] reported that older males and females (∼63 years), albeit primarily males (5 out of 25 were older females), exhibited less resting heart rate variability compared to younger (∼23 years, 2 out of 20 were young females) counterparts in thermoneutral conditions, prior to heat stress. The current study extends upon this by demonstrating that this same relationship between age and heart rate variability occurs during resting heat stress, a response which we confirm to occur in females. We showed that older females exhibited less heart rate variability and parasympathetic modulations compared to young females, most likely as a result of an age-induced reduction in cardiac acetylcholine response to stimulation [37] and reduced muscarinic receptor activity [38].

Exercise response

As expected, exercise in the heat resulted in changes of most heart rate variability measures compared to resting values, a response previously reported for young adults [17,39]. The current study though is the first, to our knowledge, to document this exercise and heat response for heart rate variability in an older, uniquely female population. During intermittent cycling exercise, all heart rate variability measures were similar between bouts with the majority (~71%) of these exercise measures comparable between groups. This similarity indicated a like degree of cardiac autonomic modulations during exercise-induced heat stress and between groups, and was evident despite the significant heart rate variability differences noted between groups at rest. While comparisons with other studies of heart rate variability during exercise and heat in older adults was difficult due to the unique population and methodology studied, Carillo et al. [5] recently reported that the majority (56-60%) of the heart rate variability measures for older adults were significantly different to those exhibited by young adults throughout 3 hours of passive heat stress. However, these authors [5] suggested that when differences in resting heart rate variability values were considered (i.e. change from rest), older adults experienced a smaller heart rate variability change and weak sympathetic response to a passive heat stress while young adults underwent a greater heart rate variability change and sympathetic activation. In the current study, the initial resting heart rate variability values were included as a covariate for analyses that resulted in very few heart rate variability differences noted between groups during the exercise bouts. These results indicated that older females actually had similar cardiac autonomic modulations to younger females during exercise in the heat, a result not previously reported in similar studies of heart rate variability during heat stress. Subsequently, age differences for heart rate variability during heat stress reported previously may be related primarily to the initial heart rate variability levels, then age per se. Further, differences in type of heat stress (passive vs. exercise-induced) and sex (male vs. female) should also be considered in future studies to clarify the role of normal ageing on heart rate variability during heat stress.

The current study did identify a few between-group heart rate variability differences, after accounting for the initial resting levels. Specifically, greater SD2, shannEn and CVI, and lower LF/HF were noted for the older compared to younger females during repeated exercise in the heat. Importantly, these differences were independent of respiration [40,41] and indicated greater cardiac parasympathetic modulations and heart rate complexity in older females. A similar result of a lower LF/HF during passive heat was reported for older males and females compared to younger adults [5] that supports greater parasympathetic modulations during heat stress in older adults. As previously reported, older females maintained a similar to greater cardiac parasympathetic modulation despite any potential differences in whole-body heat dissipation and therefore level of hyperthermia, as defined by the amount of heat stored in the body [25]. Compared to young adults, older adults were reported to dissipate less heat which in some cases led to a greater body heat storage [23–25]. These age-induced alterations were suggested to potentially be linked with abnormal autonomic activation [5] as sustained sympathetic activity has been reported during exercise in the heat, particularly for older adults [16,42]. In contrast, the current study identified similar to greater cardiac parasympathetic modulation during exercise in the heat for older compared to young females of comparable fitness. This altered autonomic control likely contributed to changes in baroreflex activity [18,21], and potentially less sympathetic modulation, impaired sudomotor capacity [24] and a resultant greater heat storage for older females [24,25]. Less blood volume for older compared to young females [43] was unlikely to contribute to this altered baroreflex activity with reduced blood volume likely to enhance sympathetic modulations, a result not seen for older habitually active females during exercise in the current study. Compared to young females, a greater parasympathetic modulation for older females may occur with this result potentially leading to a similar or lower risk of cardiac instability and arrhythmia [28–30] during exercise and heat stress. None of the current older females exhibited a cardiac abnormality with lower heart rate variability values for this population during similar stress potentially indicating an abnormal cardiac autonomic response to exercise-induced heat stress that remains to be examined.

The current results of similar to enhanced parasympathetic modulations for older females during heat stress were in contrast to those of Carillo et al. [5] with differences in study populations (i.e. as noted above, participants were primarily males) and type of heat stress (passive vs. exercise-induced heat stress) making comparisons difficult, despite similar heart rate variability analyses. Of note was that both studies examined a range of heart rate variability measures with most studies of heart rate variability and age focussing on traditional linear measures [6,7,9]. The current study identified unique and possibly sensitive measures of heart rate variability during heat stress in older females. Future studies are encouraged to examine further the impact of age on heart rate variability during heat stress and the most appropriate heart rate variability measures to examine autonomic activity and heat-induced cardiovascular control and risk.

Post-exercise response

During recovery, most (79%) heart rate variability measures were similar between groups with older females exhibiting greater VLF and CSI, and reduced LLE compared to young females. These results again identified a few, unique heart rate variability differences independent of respiration [40,41] with older females exhibiting reduced parasympathetic and/or enhanced sympathetic modulations, and reduced cardiac chaotic behaviour during prolonged recovery. This difference was most evident at the end of the prolonged 60-min recovery period (~3 hours of accumulative heat stress and exercise). As stated previously, potential age-induced reductions in blood volume [43] may inhibit the baroreflex leading to reduced parasympathetic and/or enhanced sympathetic modulations. However, this mechanism was unlikely to account for the exercise and post-exercise results as different cardiac autonomic responses were observed for these stages. Further, changes in hydration and plasma volume levels were unlikely to contribute baroreflex and associated autonomic modulations as these levels were reported to be statistically similar between groups [25]. Interestingly, reduced parasympathetic and/or enhanced sympathetic modulations at post-exercise were evident for older compared to young females despite similar group changes in body heat content [25]. Previously older males and females were reported to exhibit a non-significantly greater rate of whole-body heat loss post-exercise [25,44] with this compensatory response likely resulting in an elevation in local sweat production and skin perfusion [45]. The current results provide further support that in older adults following exercise and heat stress, sympathetic modulations are augmented that enhances sudomotor capacity [24] and sweating [46,47] for heat loss.

Following a similar time (~3 hours) of passive heat stress, Carillo et al. [5] reported that LLE was greater for older compared to young adults despite a lower resting level. In the current study, LLE was also lower for older females compared to young females at rest but this difference was maintained during several of the recovery periods indicating low chaotic behaviour, possibly due to poorer parasympathetic modulation [48]. The parasympathetic nervous system has also been reported to contribute to the VLF component of heart rate variability [49], along with thermoregulatory factors [50]. Previously, we reported a restoration of the VLF and parasympathetic modulations post-exercise in the heat [35] with the current results providing further support that following exercise in the heat, parasympathetic reactivation occurs, albeit at a lower level for older females [7,8,12,36]. The impact of age on parasympathetic reactivation was evident despite both groups undertaking the same exercise workload (constant rate of metabolic heat production) and exhibiting similar levels of aerobic capacity. The current results have provided further support of the link between age-related disturbances in parasympathetic (via heart rate variability) and thermoregulatory function [42]. Enhancement of heart rate variability has been reported following heat acclimation in young adults [34] with inclusion of heat acclimation sessions possibly helping mitigate and circumvent age-related declines in autonomic reactivation. Future studies will clarify the impact of these regimes on heart rate variability responses during exercise and recovery in the heat for a range of populations.

Considerations

Despite novel findings of an age-dependent relationship with heart rate variability for females at rest, during exercise and recovery in the heat, several limitations should be noted. Firstly, a modest sample size of young and older females was examined. Larger studies may confirm further the current results and expand our current understanding of age-related impairments in cardiac autonomic activity during heat stress. Secondly, females were examined regardless of menstrual cycle phase as heart rate variability has been shown to be similar throughout the cycle [51]. However, others have reported that heart rate variability measures were influenced by the menstrual cycle [52,53] with further studies encouraged to consider cycle phase as well as menopausal status to minimise any potential impact of these factors on age-related differences in heart rate variability. Thirdly, our older females were matched with the young females for fitness and body composition with cardiac autonomic responses possibly worse for less fit individuals (i.e. lower than that observed in the current study) that remains to be confirmed. Fourthly, only female participants were examined currently due to the paucity of research with this population. Future studies may clarify whether the current age-dependent differences in heart rate variability during combined exercise and heat stress are also evident for males as sex differences in heart rate variability [10,11] and heat loss capacity [31,32] have been reported. Next, only indirect measures of cardiac autonomic modulation were examined due to their non-invasive ability and well-reported validity [3] with future studies utilising direct measure of autonomic activity expected to confirm the current results. Finally, a range of heart rate variability variables were examined with differences noted for only some of these. The optimal set of heart rate variability measures required to fully characterize cardiac autonomic control under all conditions is still uncertain with the physiological significance of some heart rate variability variables such as non-linear measures requiring further investigation.

In conclusion, the current study has identified age-dependent heart rate variability differences during repeated exercise and recovery that represents important adjustments in cardiac autonomic modulations that may contribute to the observed age-related deterioration in thermoregulatory function in older women. Identification of heart rate variability and its response during exercise and recovery in the heat may assist in the detection of normal heat-induced adaptations as well as individuals vulnerable to heat stress.

Disclosure of potential conflicts of interest

All authors, except A.S. and C.H., have no competing interests to declare. A.S. is a patent holder, Director and shareholder of Therapeutic Monitoring Systems (TMS) Inc., focused on commercialization of variability-derived clinical decision support tools developed in OHRI's Dynamical Analysis Laboratory. C. H. is a patent holder related to variability monitoring and physiological waveform analysis.

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Abbreviations

Ex1	cycling exercise bout 1
Ex2	cycling exercise bout 2
Ex3	cycling exercise bout 3
Ex4	cycling exercise bout 4
Rec1	recovery bout between Ex1 and Ex2
Rec2	recovery bout between Ex2 and Ex3
Rec3	recovery bout between Ex3 and Ex4
Rec4	initial 15-minutes of recovery following Ex4
Rec60	45–60 minutes of recovery following Ex4
$\dot{V}O_2$	rate of oxygen consumption
$\dot{V}O_{2max}$	maximum rate of oxygen consumption

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