Left ventricular mechanical, cardiac autonomic and metabolic responses to a single session of high intensity interval training.

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Abstract

Purpose: High intensity interval training (HIIT) produces significant health benefits. However, the acute physiological responses to HIIT are poorly understood. Therefore, we aimed to measure the acute cardiac autonomic, haemodynamic, metabolic and left ventricular mechanical responses to a single HIIT session.

Methods: Fifty young, healthy participants completed a single HIIT session, comprising of three 30-second maximal exercise intervals on a cycle ergometer, interspersed with 2-minutes active recovery. Cardiac autonomics, haemodynamics and metabolic variables were measured pre, during and post HIIT. Conventional and speckle tracking echocardiography was used to record standard and tissue doppler measures of left ventricular (LV) structure, function and mechanics pre and post HIIT.

Results: Following a single HIIT session, there was significant post-exercise systolic hypotension (126±13mmHg to 111±10mmHg $p<0.05$), parallel to a significant reduction in total peripheral resistance (1640±365dyne·s·cm^5 to 639±177dyne·s·cm^5, $p<0.001$) and significant increases in baroreceptor reflex sensitivity and baroreceptor effectiveness index (9.2±11ms·mmHg^{-1} to 24.8±16.7ms·mmHg^{-1} and 41.8±28 to 68.8±16.2, respectively) during recovery compared to baseline. There was also a significant increase in the low to high frequency heart rate variability ratio in recovery (0.7±0.48 to 1.7±1, $p<0.001$) and significant improvements in left ventricular global longitudinal strain (-18.3±1.2% to -29.2±2.3%, $p<0.001$), and myocardial twist mechanics (1.27±0.72º·cm^{-1} to 1.98±0.72º·cm^{-1}, $p=0.028$) post HIIT compared to baseline.

Conclusion: A single HIIT session is associated with acute improvements in autonomic modulation, haemodynamic cardiovascular control and left ventricular function, structure and

mechanics. The acute responses to HIIT provide crucial mechanistic information, which may have significant acute and chronic clinical implications.

Key Words: High intensity interval training, cardiac autonomics, metabolism, cardiac mechanics.

Abbreviations:
Baroreceptor Effectiveness Index (BEI)
Baroreceptor sensitivity (BRS)
Blood pressure (BP)
Diastolic blood pressure (dBP)
End diastolic volume (EDV)
Heart Rate (HR)
Heart rate variability (HRV)
High Frequency (HF)
High intensity interval training (HIIT)
Left Ventricle (LV)
Low Frequency (LF)
Moderate intensity continuous training (MICT)
Respiratory exchange ratio (RER)
Stroke Volume (SV)
Systolic blood pressure (sBP)
Task Force Monitor (TFM)
Total peripheral resistance (TPR)

Introduction

Physical inactivity is associated with the progression of numerous chronic health conditions, which increases the risk of all-cause mortality (Ekelund et al. 2016). It is well-established that achieving the current physical activity guidelines improves health outcomes (World Health Organization 2015). Despite this, physical inactivity remains detrimentally high at an estimated 27.5% globally (Guthold et al. 2018) and adherence to physical activity guidelines may be as low as 5% when measured objectively (Troiano et al. 2008).

Behavioural psychology research has identified motivation and perceived lack of time as the most common barriers to physical activity, which are therefore targeted areas for behaviour change (Herazo-Beltrán et al. 2017). One proposed approach is to increase exercise efficiency through a reduction in duration while attempting to maintain similar health benefits. High-intensity interval training (HIIT) is an exercise modality, which supports this approach through its combination of practicality and efficacy. HIIT is a convenient, time-efficient form of exercise which typically involves short bouts of high intensity work separated with appropriate active recovery periods. HIIT has seen significant empirical success in improving health measures with multiple meta-analyses supporting its role in weight loss, aerobic capacity and cardiometabolic health; as well as promoting positive psychological responses, which have implications for adherence (Batacan et al. 2017; Oliveira et al. 2018; Roy et al. 2018; Cao et al. 2019).

Mechanistically, much of the reported benefits of HIIT are associated with chronic peripheral adaptations regarding mitochondrial content, capillary density, insulin sensitivity, glycaemic control, and vascular health (MacInnis and Gibala 2017). Our current understanding of any

104 myocardial adaptations associated with HIIT is based upon the work of O'Driscoll et
105 al.,(O'Driscoll et al. 2018) who reported significant improvements in left ventricular function
106 and mechanics, as well as a significant increase in cardiac autonomic modulation following a
107 2-week HIIT intervention. Whilst the training effects of HIIT have been previously
108 documented, the acute responses are not well characterised and may provide important
109 mechanistic information for the chronic adaptations reported following HIIT.

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111 To our knowledge, no study to date has attempted to measure the combined cardiac autonomic,
112 continuous haemodynamic, metabolic and myocardial functional, structural and mechanical
113 responses to HIIT. With the combination of these measurements, the aim of this study is to
114 clearly establish the acute physiological responses to a single session of HIIT in a cohort of
115 physically inactive adults. We hypothesize acute improvements in cardiac autonomic and
116 haemodynamic modulation, and myocardial mechanics following HIIT.

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Methodology

Ethical Approval

This research was approved by the Canterbury Christ Church University Ethics Committee and conformed to the Declaration of Helsinki principles (Ref: 17/SAS/47F). All participants completed and signed informed consent before testing.

Participant characteristics

Fifty (25 male and 25 female) young, healthy participants were recruited. All participants (age 22.87 ± 2.58 years; height 171.3 ± 9.5 cm; weight 73.8 ± 14.9 kg; BMI 25.24 ± 4.47 kg/m^2) had blood pressure within the normal range, were taking no medication, had no history of cardiac or metabolic disease, and with a normal clinical cardiovascular examination and 12-lead electrocardiogram. All participants were physically inactive, as defined by not meeting the current global physical activity guidelines (World Health Organization 2010).

Experimental procedures

Participants were required to visit the laboratory on a single occasion after fasting for 8 hours and refraining from alcohol and caffeine consumption for 24-hours prior to testing. On arrival, the participants height and weight were measured using a SECA 213 stadiometer and SECA 700 mechanical column scales (SECA GmbH & Co., Hamburg, Germany) respectively. Resting blood pressure (BP) was measured according to the current guidelines (Whelton et al. 2018) using an automated oscillometric blood pressure monitor (Dinamap Pro 200 Critikon; GE Medical Systems, Freiburg, Germany).

149 ***Cardiac autonomic and Haemodynamic assessment***

150 Cardiac autonomic and haemodynamic variables were measured using the Task Force
151 Monitor (TFM) which is a validated non-invasive beat-to-beat monitoring system providing
152 automatic calculations of all outputs. The TFM continuously recorded heart rate and stroke
153 volume through a six-channel electrocardiogram and impedance cardiography respectively.
154 The impedance cardiography functioned via an electrode strip located at the nape of the neck
155 and two electrodes on the torso in line with the xiphoid process. With the recording of these
156 two values (HR and SV), cardiac output was automatically calculated. Additionally, total
157 peripheral resistance was calculated in accordance with Ohm's law. Continuous systolic,
158 diastolic and mean blood pressure (sBP, dBP and mBP) measurements were obtained via the
159 use of the vascular unloading technique at the proximal limb of the index or middle finger.
160 These recordings were automatically corrected to oscillometric BP values obtained at the
161 brachial artery of the opposite arm. With the sBP and heart rate recordings, the TFM
162 calculated continuous rate pressure product measurements.

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164 Through power spectral analysis and an autoregressive model, cardiac autonomic variables
165 were obtained via assessment of the amplitude of R-R intervals and oscillating fluctuations in
166 frequency (Akselrod et al. 1981). Using the TFM automatic QRS algorithm, high and low
167 frequency parameters of heart rate variability were calculated and automatically expressed in
168 both absolute (ms^2) and normalised units (nu) (Pan and Tompkins 1985)·(Li et al. 1995). As
169 separate mechanistic measures, baroreceptor sensitivity and baroreflex effectiveness index
170 were recorded via the sequence method which relies on the linear regression of continuous
171 changes in sBP and the lengthening or shortening of the R-R interval (Taylor et al. 2017).

From all regressions, a mean slope of BRS was calculated and only sections with correlation coefficients of r> 0.95 were analysed.

Intervention stages were used to distinguish and separate specific periods of measurement for appropriate data organisation. Using the intervention marks, cardiac autonomic and haemodynamic measurements were continuously recorded during a 5-minute pre-exercise rest period, which is presented as baseline. Recording then proceeded during the three separate 30-second exercise periods which correspond to HIIT 1, HIIT 2 and HIIT 3, and the 2-minute rest periods in between each exercise interval were also recorded. Finally, a 5-minute recovery period was recorded immediately post-exercise with the participant in a supine position.

Metabolic measures

Gas exchange measures were acquired using the Oxycon Pro (Jaeger, Wurzburg, Germany) online gas analyser. Prior to testing, calibration of the gas cylinder was performed to appropriate concentrations (15% O2; 5% CO2). Additionally, flow was calibrated using a 3-L syringe (Cosmed, Rome, Italy). Participants were appropriately fitted with a Hans Rudolph mask, with an attached pneumotach flowmeter for measurement. Continuous recording of breath-by-breath gas analysis data was achieved throughout each intervention period.

Conventional echocardiographic image acquisition

Transthoracic echocardiography was performed pre and immediately post HIIT, following methodology previously detailed (O'Driscoll et al. 2018). All images were acquired using a Vivid-q ultrasound system (GE Healthcare, Milwaukee, Wisconsin) with a 1.5-3.6 MHz

phased array transducer (M4S-RS Matrix cardiac ultrasound probe). All participants were measured in the left lateral decubitus position by one consistent sonographer. Cardiac measurements were recorded in accordance with the current guidelines (Lang et al. 2015) and stored for offline analysis using commercial software with the results averaged (EchoPAC, V.113.0.x, GE Healthcare). Images were captured in the parasternal short and long-axis and apical 2-, 3-, and 4-chamber views. Interventricular septal and posterior wall thickness, fractional shortening and left ventricle (LV) internal dimensions were measured, and relative wall thickness was calculated as (2 LV posterior wall thickness)/LV internal diameter. LV ejection fraction was determined via the modified biplane Simpson's rule. Pulsed-wave Doppler measures were acquired to assess transmitral early (E) and late (A) diastolic-filling velocities from the apical 4-chamber view, with the sample volume placed at the tips of the mitral valve. Isovolumic relaxation time was measured from the start of aortic valve closure to mitral valve opening. Tissue Doppler imaging was captured at the lateral and septal mitral annulus to assess peak longitudinal (S'), peak early diastolic (E'), and peak late diastolic (A') velocities, with values averaged. LV filling pressure was estimated from the mitral E/E= ratios (Ommen et al. 2000). Total peripheral resistance was calculated through Ohm's law. Stroke volume was derived from LV end diastolic and LV end systolic volumes, with cardiac output achieved as the product of heart rate and stroke volume.

Myocardial Mechanics

Speckle-tracking imaging was utilised pre and post HIIT to achieve the LV global longitudinal and time-derivative strain rate from the apical 2-, 3-, and 4-chamber views. The average value of peak systolic longitudinal strain and peak systolic strain rate from all three views was calculated as global strain and strain rate. Peak global strain rate during early and

late diastole and their ratio as indices of diastolic function was calculated as proposed in previous work (Wang et al. 2007). The parasternal short axis view from the LV base, level with the mitral valve (mitral valve leaflets on view) and apex (circular LV cavity with no papillary muscle visible) was used to acquire the LV radial and circumferential strain and strain rate, and LV rotation and rotational velocity; again as previously applied (Leitman et al. 2004; Notomi et al. 2005; van Dalen et al. 2008; Weiner et al. 2010). For effective speckle-tracking analysis, the highest quality images were used for tracing the endocardium and a full-thickness myocardial region of interest was selected. All images were reviewed to validate quality and those that did not achieve the required optimisation and standardization were excluded. Images were optimized for scan depth and sector width to obtain high frame rates (>60 Hz) and kept constant throughout each examination. The endocardial trace line and/or region-of-interest width was readjusted to ensure an adequate tracking score. Raw frame-by-frame rotation and rotation-rate data was normalized to the percentage duration of systole and diastole using cubic-spline interpolation to allow for between and within subjects comparison as basal and apical rotation are not acquired from the same cardiac cycle (GraphPad Prism 6 Software, La Jolla, CA) (Stembridge et al. 2014). LV twist and untwist parameters were acquired via subtraction of the basal data from the apical data at each time point, with LV torsion defined as LV twist per unit length and calculated by dividing the total twist by LV diastolic length (Stembridge et al. 2014). The sonographer's reproducibility of speckle-tracking indices has been reported in previous work (O'Driscoll et al. 2017, 2018).

Exercise protocol

The HIIT exercise protocol consisted of a single Wingate session, characterised by three 30-second periods of maximal intensity cycling. Using a WATT bike pro (Nottingham, England),

the exercise periods were loaded with 7.5% of the participants body mass and separated with 2-minutes of unloaded active recovery. Consistent and enthusiastic verbal encouragement was given during the exercise periods for intensity maintenance. Each participant performed a 2-minute warm up with no active recovery post-exercise. Cardiac autonomic, haemodynamic and metabolic parameters were recorded continuously for 5-mins at baseline, during the 3-HIIT intervals and 5-minutes immediately post HIIT for the recovery period in the supine position. Cardiac imaging was performed at baseline and immediately following HIIT in the recovery period.

Statistical analysis

All continuous variables are presented as mean ± standard deviation. Data analysis was performed using statistical package for social sciences (SPSS 26 release version for Windows; SPSS Inc., Chicago, IL). A one-way repeated measures ANOVA was performed with a Bonferroni post-hoc test to identify statistically significant differences. Correlation analyses was performed to ascertain any associations between BRS and BEI with LF and HF HRV parameters. Data was reported as statistically significant when $p<0.05$.

Results

All fifty participants successfully completed the single HIIT session with no adverse events reported.

Haemodynamics

Figure 1 presents the haemodynamic responses throughout each stage of the HIIT session. There was a significant increase in sBP from baseline (126±13 mmHg) compared to HIIT 1 (152±38mmHg, $p<0.001$), HIIT 2 (154±19mmHg, $p<0.001$) and HIIT 3 (152±35mmHg, $p<0.001$), with a significant decrease in recovery post HIIT (111±10mmHg, $p<0.001$), which was significantly lower than baseline ($p<0.05$). mBP significantly increased from baseline (88±8mmHg) to HIIT 1 (111±36mmHg, $p<0.001$), HIIT 2 (109±24mmHg, $p<0.05$) and HIIT 3 (108±34mmHg, $p<0.05$), and significantly decreased in recovery post HIIT (76±8 mmHg). dBP significantly increased from baseline (69±8mmHg) to HIIT 1 (93±35mmHg, $p<0.001$), HIIT 2 (89±24.8mmHg, $p<0.05$) and HIIT 3 (92±30mmHg, $p<0.001$), and significantly decreased post exercise in recovery post HIIT (59±9mmHg, $p<0.001$).

Heart rate significantly increased from baseline (69±10b·min^{-1}) to HIIT 1 (148±17b·min^{-1}, $p<0.001$), HIIT 2 (157±16b·min^{-1}, $p<0.001$), HIIT 3 (160±18b·min^{-1}, $p<0.001$) and significantly decreased in recovery post HIIT (100±12b·min^{-1}, $p<0.001$) when compared to HIIT 3, but remained significantly elevated post HIIT when compared to baseline ($p<0.001$). Stroke volume significantly increased from baseline (65.7±11.1ml) to HIIT 1 (97.6±24.4ml, $p<0.001$), HIIT 2 (102.2±25.8ml, $p<0.001$), HIIT 3 (102.2±23.3ml, $p<0.001$) and recovery post HIIT (103.8±32.2ml, $p<0.001$). As a result of these responses, cardiac output significant

increase from baseline (4.49±0.98L·min^{-1}) to HIIT 1 (14.29±3.52L·min^{-1}, p<0.001), HIIT 2 (15.86±3.48L·min^{-1}, p<0.001), HIIT 3 (16.18±3.57L·min^{-1}, p<0.001) followed by a significant decrease post exercise in recovery (10.28±3.17L·min^{-1}, p<0.001) when compared to HIIT 3, but remained significantly elevated post HIIT when compared to baseline (p<0.001).

Rate pressure product significantly increased from baseline (8642±1414) to HIIT 1 (22541±6308, p<0.001), HIIT 2 (24202±4142, p<0.001) and HIIT 3 (23983±6225, p<0.001), with a significant decrease in recovery post HIIT (11054±1798, p<0.001). Total peripheral resistance significantly decreased from baseline (1640±365dyne·s·cm^5) to HIIT 1 (638±231dyne·s·cm^5, p<0.001), HIIT 2 (576±158dyne·s·cm^5, p<0.001), HIIT 3 (586±213dyne·s·cm^5, p<0.001) and in recovery post HIIT (639±177dyne·s·cm^5, p<0.001).

Cardiac autonomic and metabolic parameters

As presented in Figure 2A, there was a significant decrease in HRV expressed as R-R power spectral density from baseline (3101.7±3571.6m^2) to HIIT 1 (927.2±934.6m^2, p<0.001), HIIT 2 (565±1194.9m^2 p<0.001), HIIT 3 (381.6±521.7m^2, p<0.001) and in recovery post HIIT (578.1±1317.9m^2, p<0.001). Figure 2B shows a significant decrease in low frequency (normalized units) from baseline (47.7±15.5%) compared to HIIT 1 (38±13.7, p<0.05), HIIT 2 (35.5±11.3, p<0.001) and HIIT 3 (32.3±11.5%, p<0.001), with a paradoxical significant increase in recovery post HIIT (62.3±15.5%), which was significantly greater than baseline and HIIT 3 (both p<0.001). Accordingly, high frequency (normalized units) significantly increased from baseline (52.3±15.5%) to HIIT 1 (62.2±13.2%, p<0.05), HIIT 2 (64.5±11.3%, p<0.001) and HIIT 3 (67.7±11.5%, p<0.001), with a significant decrease in recovery post HIIT (37.7±15.5%), which was significantly lower than baseline and HIIT 3 (both p<0.001). As a

result of these inverse changes, there was no significant change in low frequency/high frequency (LF/HF) ratio from baseline (1±0.59) to HIIT 1 (0.9±0.43) and HIIT 2 (0.85±0.45), with a significant decrease from baseline to HIIT 3 (0.7±0.48, $p<0.05$). However, there was a significant increase in recovery post HIIT, which was significantly greater than baseline (1.7±1, $p<0.001$) (Figure 2C). The absolute frequency domain responses are shown in Table 1.

As shown in Figure 2D, there was no significant change in BRS from baseline (9.2±11ms·mmHg^{-1}) compared to HIIT 1 (7.1±7.4ms·mmHg^{-1}), HIIT 2 (9±11.3ms·mmHg^{-1}) and HIIT 3 (6.7±9.3ms·mmHg^{-1}). However, there was a significant increase in recovery post HIIT (24.8±16.7ms·mmHg^{-1}) from HIIT 3, which was significantly greater than baseline (both $p<0.001$). Figure 2D also shows no significant difference in BEI from baseline (41.8±28) to HIIT 1 (41±22.2), but a significant decrease from baseline to HIIT 2 (24.3±23.5, $p<0.05$) and HIIT 3 (16.2±17.3, $p<0.001$); followed by a significant increase post exercise in recovery (68.8±16.2) from HIIT 3, which was also significantly greater than baseline (both $p<0.001$).

Correlation analyses demonstrated a significant assocation between BRS and LF (r. = 0.7; $p<0.001$) and BRS and HF (r. = 0.66; $p<0.001$), during HIIT 1; BRS and LF (r. = 0.86; $p<0.001$) and BRS and HF (r. = 0.93; $p<0.001$) during HIIT 2, and BEI and LF (r. = 0.5; $p=0.004$) and BEI and HF (r. = 0.59; $p=0.001$) during HIIT 3. In recovery, there was a significant correlation between the LF/HF ratio and BRS (r. = -0.4; $p=0.014$).

As illustrated in Table 1, aerobic capacity ($\dot{V}O_2$), carbon dioxide production ($\dot{V}CO_2$) and breathing frequency (L·min^{-1}) significantly increased from baseline compared to all 3 HIIT

335 stages and recovery post HIIT (all $p<0.05$). Minute ventilation ($\dot{V}_E$) and a-vO_2 difference
336 ($mLO_2 \cdot 100mL^{-1}$) both significantly increased from baseline compared to the 3 HIIT stages (all
337 $p<0.001$), with a significant decrease from HIIT 3 to recovery post HIIT ($p<0.001$). Respiratory
338 exchange ratio (RER) significantly increased from baseline compared to HIIT 1 ($p<0.001$),
339 HIIT 2 stages ($p<0.001$) and recovery ($p<0.05$), but there was no significant difference between
340 HIIT 3 and recovery post HIIT ($p<0.001$).

341

342 ***Cardiac structure and function***

343 Baseline and post HIIT echocardiographic structural, functional and LV tissue doppler
344 parameters are presented in Table 2. There was a significant decrease in LV internal diameter
345 systole ($p=0.002$) and left ventricular end-diastolic posterior wall thickness ($p=0.037$).
346 Separately, there were significant decreases in both Peak E/A ratio ($p<0.001$), isovolumetric
347 relaxation time ($p=0.032$), and a significant increase in Peak A velocity ($p=0.001$). There were
348 also several significant changes in global LV systolic function, with significant decreases in
349 LV end-diastolic volume ($p=0.033$), LV end-systolic volume ($p=0.004$), and significant
350 increases in LV ejection fraction ($p=0.002$), fractional shortening ($p=0.006$) and lateral and
351 septal peak S' (both $p=0.001$). There were no significant changes in estimated LV filling
352 pressures from pre to post HIIT.

353

354 ***Left ventricular mechanics***

355 Pre and Post HIIT myocardial mechanics are displayed in Table 3. Peak global longitudinal
356 strain ($p<0.001$), strain rate ($p=0.001$) and global longitudinal strain rate in early diastole
357 ($p=0.004$) significantly increased in recovery immediately following HIIT. There was a

significant increase in basal systolic ($p=0.001$) and diastolic ($p=0.001$) rotational velocity, and significant decreases in basal radial strain ($p=0.009$) and strain rate ($p<0.001$), but no significant change in basal rotation, circumferential strain or strain rate. Apical rotation ($p=0.025$) and apical systolic ($p<0.001$) and diastolic ($p=0.016$) rotational velocity all significantly increased, as well as significant increases in apical circumferential strain ($p=0.003$) and strain rate ($p<0.001$), but no significant change in apical radial strain or strain rate. These mechanical changes produced significant increases in all LV twist parameters, including LV twist ($p=0.034$), systolic twist velocity ($p=0.001$), untwist velocity ($p=0.001$) and LV torsion ($p=0.028$).

Discussion

As the first study to investigate the combined physiological responses to a single HIIT session, we found significant improvements in cardiac autonomic modulation and haemodynamic regulation, as well as improvements in LV systolic and diastolic function and cardiac mechanics. As illustrated in Figure 3, the physiological responses following HIIT occur through a complex interplay of numerous mechanistic pathways, some of which are not conclusively understood.

Cardiac autonomics

This is the first study to investigate the acute cardiac autonomic, haemodynamic, metabolic and myocardial responses to a single HIIT session. HIIT induced a significant step wise reduction in HRV and associated absolute low and high frequency domains. A greater proportion of the HRV frequency remained in the HF domain, which is supported by the HFnu response and significant reduction in LF/HF ratio. During recovery post HIIT, all absolute HRV parameters remained significantly depressed compared to baseline; however, there was a significant increase in the proportion of HRV within the LF domain, represented by LFnu, which is supported by the significant increase in LF/HF ratio and indicates a relative sympathetic predominance in recovery. These responses are similar to those reported following aerobic exercise (Kaikkonen et al. 2008); however, they are opposite to those previously reported following isometric exercise (Taylor et al. 2017). Compared to baseline, our results demonstrate a decline in BRS and significant reduction in BEI during HIIT. This suggests active resetting of the baroreceptors, which is associated with increasing HR and BP, and is similar to responses reported during other forms of exercise (Hartwich et al. 2011). However,

of mechanistic importance, BRS and BEI significantly increased in recovery immediately post HIIT, which was significantly greater than baseline. The 2.7- and 1.7-fold increase in BRS and BEI, respectively, is similar to that reported following alternative short duration exercise (Taylor et al. 2017), which may be associated with the BP responses seen in the recovery period following HIIT. However, these results are in contrast to responses following both aerobic and dynamic resistance training, which commonly produce a post-exercise reduction in baroreceptor reflex modulation (Somers et al. 1985; Niemelä et al. 2008).

The cardiac autonomic results are of interest, since the improved BRS and BEI and increased LF and LF/HF ratio immediately post-HIIT is contradictory, compared to previous research. Cote et al., (2015) reported similar results with a significant increase in LF/HF post HIIT, but reported a significant decrease in BRS. Despite methodological differences, such as timing of post exercise measures (30-mins vs immediately post HIIT), the mechanistic underpinning of this post-exercise sympathetic dominance accompanied by an increase in baroreflex functioning is unclear and certainly requires future research. Although is not always the case, the withdrawal of sympathetic autonomic activity may often occur following such maximal exercise, which in combination with venous pooling, can result in reduced cerebral blood flow and consequently induce vasovagal post-exercise syncope. Since our HRV results indicate the contrary, one mechanistic hypothesis is a sympathetic response induced as a direct preventative mechanism of this common syncope; as supported through previous work identifying increases in LF/HF and normalised LF power during orthostasis, especially in young cohorts homogenous to the present study (Kawaguchi et al.; Sato et al. 2007). Conversely, perhaps such a response is not a result of complex neural-physiological mechanistic interactions, but rather reflects methodological complications with the application of HRV indices. Specifically, research from Goldstein et al., (Goldstein et al. 2011) suggested that the LF parameter of HRV

provides an index of baroreflex function rather than sympathetic tone based on various lines of evidence (Goldstein et al. 2011). As an example, LF power has often been shown not to increase during exercise (as exhibited in our findings), despite evident increases in cardiac and extracardiac sympathetic outflows (Warren et al. 1997; Goldstein et al. 2011). Furthermore, patients following bilateral thoracic sympathectomies have normal baroreflex function and LF power, despite partial cardiac sympathetic denervation (Moak et al. 2005). Since this hypothesis appears to align well with our findings, perhaps the HRV results are actually representing the changes in baroreflex function as opposed to sympathetic tone. Our correlation analysis supports this concept.

Haemodynamics

Compared to baseline, HIIT induced a significant increase in sBP, mBP and dBP, which remained relatively stable over each interval. During post exercise recovery, there was a significant decrease in sBP, which was significantly lower than baseline. This is similar to previously reported acute evidence (Cote et al. 2015), while generally aligning with the training effects typically observed (O'Driscoll et al. 2018). Since cardiac output remained elevated post-HIIT, this reduction can be directly attributed to changes in peripheral vascular resistance, as supported by the significant reductions in TPR, which remained in the recovery period. HIIT has been linked to the promotion of greater sheer stress-induced nitric oxide bioavailability through an increased flow mediated dilation response compared to lower intensity modalities (Ramírez-Vélez et al. 2019). This increase in endothelial derived-nitric oxide may act on vascular smooth muscle cells to induce vasodilation through increasing cyclic guanosine monophosphate production via the activation of soluble guanylate cyclase; thus explaining the reduced TPR and hypotension (MacInnis and Gibala 2017). In addition, the arterial baroreflex

453 is a fundamental regulator of short and long-term BP with compelling evidence for its role in
454 post exercise hypotension.

455

456 **Myocardial responses**

457 Our results show significant acute cardiac responses to HIIT with improved LV function and
458 cardiac mechanics. Specifically, we found significant improvements in peak global LV
459 longitudinal strain and strain rate, which were not observed following a 2-week HIIT
460 intervention (O'Driscoll et al. 2018). Global longitudinal strain and strain rate, have been
461 proposed as strong indicators of measuring myocardial function; thus, the results from the
462 present study may provide important clinical implications (Karlsen et al. 2019). Additionally,
463 we found significant reductions in LV end-diastolic posterior wall thickness and end-systolic
464 internal diameter. These parameters independently provide implications regarding structural
465 health and clinical outcomes; and thus, although these changes are not always observed in
466 chronic interventions, these acute responses may be of clinical importance (Quiñones et al.
467 2000; O'Driscoll et al. 2018).

468

469 A single HIIT session elicited significant improvements in LV twist, systolic twist velocity,
470 untwist velocity and torsion. In addition to providing prognostic implications, increased LV
471 twist enhances potential energy during the ejection phase with recoil of this systolic
472 deformation and release of elastic energy contributing to pressure decay, enhancing LV
473 diastolic suction and thus filling (Sengupta et al. 2008; O'Driscoll et al. 2017). Despite this
474 increase in diastolic function, LV end-diastolic volume (EDV) decreased post HIIT, potentially
475 as a consequence of the sustained elevation in heart rate and a pooling-induced decrease in
476 venous return. This post HIIT reduction in EDV combined with the increased stroke volume

resulted in a greater ejection fraction. It may be postulated that increases in stroke volume and ejection fraction post HIIT are attributed to the LV mechanical and functional improvements, as supported through the enhancements of contractility parameters such as end-systolic internal diameter and fractional shortening. These observed LV mechanical changes may be explained via the same mechanistic pathway responsible for decreased peripheral vascular resistance, which induced post HIIT systolic hypotension, resulting in a decreased afterload and thus improved LV systolic function. This mechanistic explanation is supported through the significant increases in systolic tissue doppler parameters and the non-significant decreases in LV filling pressures post HIIT; as well as being endorsed in the chronic HIIT literature (O'Driscoll et al. 2018).

Metabolic responses

Interest in HIIT interventions has been predominantly based upon its ability to produce significant improvements in aerobic capacity, comparable to that observed following traditional moderate-intensity continuous training (MICT), despite being an anaerobic modality in nature (Milanović et al. 2015; MacInnis and Gibala 2017). While the acute results of the present study support this anaerobic predominance, there also appears to be some aerobic contribution to HIIT, particularly in the final interval, with a respiratory exchange ratio (RER) below the threshold of 1, predominantly facilitated by an increase in oxygen uptake. This transfer in primary energy metabolism towards the later stages of the HIIT session highlights the potential to manipulate acute programme variables (such as exercise bout duration) of this modality to favour either aerobic or anaerobic metabolic pathways and may be an important mechanism for improvements in aerobic capacity (MacInnis and Gibala 2017). This response however, may reflect anaerobic endurance and/or fatigue.

Limitations

Our study investigated healthy and young participants and therefore may have limited application to ageing and clinical populations, suggesting the need for future research using participants from specific demographics. The primary limitation of this study lies within the application of HRV measurement in this setting. Indeed, the short duration of recording and changes in respiration induced via acute maximal exercise may affect HRV recordings and is a limitation regarding interpretation. However, given the novelty of this study, we considered cardiac autonomic measurements integral to provide a comprehensive non-invasive assessment of the combined physiological responses to HIIT. Further, these results should be interpreted in the context of the short-duration HIIT protocol employed, and thus the relative applicability of these findings to differing HIIT protocols of longer durations is unknown. Finally, cycle wattage was not recorded during HIIT and as such, we are unable to report on power output at each stage of HIIT.

Conclusion

A single HIIT session is associated with significant improvements in cardiac autonomic modulation and haemodynamic regulation, as well as improvements in LV systolic and diastolic function, mechanics and cardiac remodelling. In general, the acute responses detailed support the established chronic adaptations following a programme of HIIT, which may have independent clinical implications.

Declarations

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Conflict of Interest: There are no conflicts of interest.

Ethics Approval: This research was approved by the Canterbury Christ Church University Ethics Committee and conformed to the Declaration of Helsinki principles (Ref: 17/SAS/47F).

Data Availability: The sharing of data in an open-access repository was not included in our participants consent. Thus, in accordance with standard ethical practice, data may only be available on request from the corresponding author.

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686 **Figure legends**

687

688 Figure 1: Hemodynamic responses to high intensity interval training. Values are presented as
689 mean±SEM. A) systolic, mean and diastolic blood pressure responses. B) heart rate and rate
690 pressure product responses. C) total peripheral resistance response. D) stroke volume and
691 cardiac output responses. *p<0.05, **p<0.001 between baseline and all stages. §§p<0.001
692 between HIIT 3 and recovery.

693

694 Figure 2: Autonomic responses to high intensity interval training. Values are presented as
695 mean±SEM. A) R-R power spectral density (heart rate variability) response. B) R-R
696 normalized units low-frequency and high-frequency responses. C) R-R LF:HF ratio response.
697 D) baroreceptor reflex sensitivity and baroreceptor effectiveness index response *p<0.05,
698 **p<0.001 between baseline and all stages. §§p<0.001 between HIIT 3 and recovery.

699

700 Figure 3: Central illustration of the acute mechanistic responses to HIIT.