The Role of High-Intensity Interval Training (HIIT) on Cardiac Autonomic Function in Physically Inactive Males

by

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Abstract:

Purpose: Cardiac autonomic dysfunction and physical inactivity are associated with increased risk of cardiovascular disease. Short duration high intensity interval training (HIIT) has been shown to improve aerobic capacity; however, adaptations of the cardiac autonomic system are less clear. Therefore, the aim of the present study was to assess cardiac autonomic adaptations to HIIT.

Methods: In a randomised crossover controlled trial, 40 physically inactive males (aged 21±1.7 years) completed 2-weeks of HIIT and control period. The HIIT protocol consisted of 3 x 30-second maximal cycle ergometer sprints against a resistance of 7.5% body weight, interspersed with 2-minutes of active recovery. In total, 6-sessions were performed. Cardiac autonomic function was measured using a plethysmographic device (Task Force® Monitor). Total spectral density (PSD) and associated low-frequency (LF) and high-frequency (HF) power spectral components were recorded in absolute (ms^2) and normalised units (nu).

Results: Each participant completed 18-maximal cycle ergometer sprints over a 2-week period. The HIIT intervention produced significant improvements in HR (62.2±8.6 to 57.7±8.3 $b \cdot min^{-1}$; $p<0.001$), HRV (R-R PSD ln) (3.53±0.27 to 3.67±0.26; $p<0.005$), R-R HF (ln) (2.96±0.37 to 3.05±0.33; $p<0.005$) and R-R LF/HF ratio (2.00±1.04 to 1.47±0.77; $p<0.001$) compared to the control period. The present study also produced statistically significant improvements in peak VO_2 ($ml \cdot min^{-1}$) (3535.6±487.9 to 3744.6±581.7 $ml \cdot min^{-1}$; $p<0.001$), peak VO_2 ($ml \cdot min^{-1} \cdot kg^{-1}$) (43.17±5.2 to 45.29±5.2 $ml \cdot min^{-1} \cdot kg^{-1}$; $p<0.001$), systolic blood pressure (116.1±4.9 to 111.3±8.8 mmHg; $p<0.001$) and rate pressure product (7385.6±1177.5 to 6387.8±908.7 mmHg; $p<0.001$) post HIIT compared to the control period.

Conclusion: A short-term programme of HIIT was associated with a significant increase in cardiac autonomic modulation, demonstrated by a residual increase in cardiac vagal activity. HIIT also produced significant improvements in functional capacity and reductions in systolic blood pressure.

Chapter 1: Introduction

It is well known that physical inactivity is associated with an accelerated decline in heath and has been identified as the 4th leading cause of mortality globally (WHO, 2010). Physical inactivity increases the incidence of numerous chronic diseases such as, coronary artery disease (CAD) (Myers et al., 2015), cancer (Torre et al., 2015), diabetes (Gill and Cooper, 2008) and obesity (Fogelholm, 2010). At present, CAD is the leading cause of mortality in the UK (Townsend, Bhatnagar et al., 2015). A greater understanding of the responses of novel risk factors associated with CAD may help to provide greater insight into the prevention and attenuation of this major health concern.

The autonomic nervous system (ANS) is responsible for the beat-to-beat regulation of the cardiovascular system (CVS) for maintenance of homeostasis (Sztajzel, 2004). Research has demonstrated that cardiac autonomic dysfunction is a known risk factor for cardiovascular disease (CVD) (Lahiri et al., 2008). This has stimulated an interest on the impact cardiac autonomic function has in predicting outcome and in response to physical activity (PA) (Kiviniemi et al., 2015). Heart rate variability (HRV) is a valid non-invasive method used to assess autonomic modulation, providing information on the relative contribution of parasympathetic and sympathetic modulation to maintain homeostasis (Thayer et al., 2010). Cardiovascular disease is characterised by attenuated parasympathetic activity and heightened sympathetic activity (Lahiri et al., 2008). Autonomic dysfunction, expressed as decreased HRV indicates an increased risk of cardiovascular morbidity in healthy subjects (Hautala et al., 2009) as well as patient populations (Kiviniemi et al., 2007).

Exercise has been identified as cardio-protective, providing healthy changes in autonomic dynamics through increased parasympathetic activity and attenuated sympathetic activity

(Goldsmith et al., 2000). These training induced autonomic changes decrease resting heart rate (HR) and increase HRV (Carter et al., 2003) which has been shown to reduce the incidence of CVD.

Despite the well-established benefits of exercise, it remains difficult to adhere to current PA guidelines. The current PA guidelines suggest an adult should aim to be active daily and meet 150-minutes of exercise per week of moderate-intensity, more specifically '30 minutes on at least 5 days per week' (Townsend, Wickramasinghe et al., 2015). A recent meta-analysis (Woodcock et al., 2011) studied the impact of moderate PA on all-cause mortality and demonstrated that 30-minutes of moderate-intensity exercise five times per week reduced all-cause mortality by 19% versus no activity. Comparable health benefits are known to be achievable through 75-minutes of vigorous-intensity over the duration of a week (Baker et al., 2015). However, current guidelines are not evidence based (Weed, 2016) and adherence to this volume of PA is poor with lack of time the most commonly cited barrier to meeting exercise participation guidelines (Gibala, Little et al., 2012). It is interesting to note that guidelines do not consider the potential utility of intermittent exercise such as HIIT, despite evidence suggesting low volume, high intensity exercise can confer equal to or superior health benefits to current physical activity recommendations (Fletcher et al., 2001).

High-intensity interval training has become an accepted and practicable method to improve cardiovascular health with a reduced time commitment (Sculthorpe et al., 2017). A systematic review and meta-analysis (Ramos et al., 2015) reporting the impact of HIIT in comparison to moderate-intensity continuous training (MICT) identified HIIT as a more effective strategy to improve vascular function than MICT, perhaps due to its tendency to positively influence traditional CVD risk factors. Furthermore, HIIT has been shown to produce significantly greater increases in aerobic capacity, metabolic and vascular health

compared to MICT (Astorino et al., 2012). Moderate-intensity continuous training has been shown to improve autonomic modulation of the heart; however, adaptations of the cardiac autonomic nervous system following HIIT are less clear.

1.0. Physical activity/ inactivity

1.0.1. Physical activity

A physically active lifestyle and higher levels of aerobic fitness are widely accepted as factors that improve a number of health outcomes including; HRV, resting HR, peak VO2 and blood pressure (BP) (Cornelissen et al., 2011). Regular exercise significantly impacts cardiorespiratory fitness and it is strongly recommended in both primary and secondary prevention of cardio-metabolic diseases (Swift et al., 2013). The protective influence of exercise on the heart to counter damaging cardiac events is believed to be the result of adjusted influences by the ANS, for example, HR and HRV (Grant et al., 2012). However, it is suggested the effects of exercise upon the cardiovascular autonomic regulation are dependent upon the frequency, intensity and duration of the exercise itself (Wilson et al., 2015).

Aerobic exercise has been suggested to protect the heart against harmful cardiac events by increasing cardiac vagal modulation of HR and also by decreasing sympathetic outflow (Hautala et al., 2009). Depressed high frequency (HF) power of HRV is associated with impaired parasympathetic activity, which is related to increased risk of CVD (Buchheit and Grinde, 2006).

1.0.2. Physical inactivity

Physical inactivity has been described as the greatest public health threat of the 21st century and directly contributes to 1 in 6 deaths (Blair, 2009). A physically inactive lifestyle is associated with CVD and premature morbidity and mortality (Coombs et al., 2015; Phillips et al., 2015). A systematic review and meta-analysis of 33 studies identified that regular PA was associated with a 35% reduced risk of CVD mortality and a 33% reduced risk of all-cause mortality compared to those who were physically inactive (Maddison et al., 2015). Despite the positive benefits of regular PA, many individuals are not meeting PA guidelines (Grant et al., 2012) which are 150-minutes of exercise per week of moderate-intensity. A common theme amongst the literature for physical inactivity is time constraints alongside everyday lifestyle such as; education, work and childcare (Sequeira et al., 2011).

A meta-analysis (Sattelmair et al., 2011) identified a dose-response relationship between PA (MICT) and CAD risk. The evidence reported individuals who met the recommended PA guidelines of 150-minutes per week had a 14% lower risk of CAD compared to individuals who were physically inactive. However, it was reported that individuals who were PA at half the recommended physical activity guidelines (75-minutes per week) had the same 14% lower risk of CAD compared to no PA. These findings question current recommendations and provide evidence that shorter duration exercise provides equal CAD risk reduction.

High intensity interval training has been described as 'more motivating' compared to traditional MICT which has been describe as 'quite boring' (Bartlett et al., 2011). Given the well documented association between physical inactivity and adverse health outcomes, the role of developing strategies that promote the adoption of a physically active lifestyle is central to the improvement of overall health (Myers et al., 2015).

In relation to the recommended PA guidelines, long term adherence to exercise programs is often less than 50% at 6 months (Bartlett et al., 2011). In a study by Gibala et al., (2006), sixteen healthy, physically active men completed either a high volume endurance training (ET) or sprint interval training (SIT) programme, performing six training sessions over a two week period. Training volume differed; each session consisted of either four to six repeats of 30-seconds 'all out' cycling with 4 minutes of recovery (SIT) or 90-120 minutes of continuous cycling (ET). Training time commitment over two weeks was 2.5 hours for SIT and 10.5 hours for ET. The novel findings reported no difference between groups of six sessions of either low volume sit or high volume ET which induced similar improvements in muscle oxidative capacity, muscle buffering capacity and exercise performance. These findings are consistent with previous research that has shown an increase in muscle oxidative capacity after a similar SIT protocol of six sessions over two weeks (Burgomaster et al., 2005). Given the large difference in training volume, these data demonstrate that SIT is a time-efficient strategy to induce adaptations and exercise performance that are comparable to traditional ET.

The benefits of HIIT are of considerable interest as physiological adaptations appear to occur with considerably less exercise time commitment than traditional exercise guidelines (Little et al., 2011). The reduced time commitment may have the potential to improve adherence (Shiraev et al., 2012). Therefore, HIIT may be a decisive factor between physical inactivity (exercise adoption) and PA (exercise adherence) towards reducing the relative risk in all-cause mortality.

1.1. Cardiac autonomic function and cardiovascular health

The cardiovascular system (CVS) is instrumental in the body's ability to maintain homeostasis and plays a vital role in health and disease prevention (Levick, 2010). A greater

aerobic capacity and physical fitness is associated with reduced all-cause mortality (Perk et al., 2012) and improved autonomic modulation via functional and structural adaptations in the CVS (Kiviniemi et al., 2014). As exercise is initiated and its intensity increases, there is increasing oxygen demand to the working muscles. To meet these requirements, the sympathetic nervous system is activated, which causes an increase in myocardial inotropy, lusitropy, chronotropy and dromotropy, which together augment stroke volume and cardiac output, as well as an increasing peripheral arteriovenous oxygen difference (Fletcher et al., 2013).

The ANS plays a central role in cardiovascular regulation, an imbalance between sympathetic and parasympathetic nervous activity results in cardiac autonomic dysfunction, which is an independent risk factor for CVD (Soares-Miranda et al., 2012). Therefore, the ANS plays an important role in maintaining cardiovascular homeostasis (Goldstein et al., 2011). There is a dynamic relative balance between the sympathetic nervous system and parasympathetic nervous system in a healthy heart. Parasympathetic input from vagal tone contributes largely to the maintenance of resting HR (Coote et al., 2010). The average resting HR in adults is approximately 72 $b \cdot min^{-1}$, with a reference range of 50-90 (Freeman, Dewey et al., 2006). A healthy resting HR represents the effect of the neural output of the parasympathetic (vagus) nerves which slows HR down, whereas the sympathetic nerves accelerate it. At rest, both the sympathetic and parasympathetic nerves are active with the vagal effects dominant. Therefore, HR reflects the relative activity of the sympathetic and parasympathetic nervous systems.

During rest and exercise, the ANS mediates changes in arterial blood pressure (ABP), HR and peripheral vascular tone to facilitate regional and systemic circulatory regulation (Freeman, 2006).Baroreceptor reflex sensitivity (BRS) has also been shown to be a useful indices of vagal activity (Thayer et al., 2010) and predictor of mortality (La Rovere et al., 1998). At rest, an increase in BP causes the baroreflex to reduce sympathetic outflow and increase parasympathetic tone, having a cardio-protective effect (Swenne, 2013).

An acute bout of exercise elicits a number of physiological responses, whereas accumulated bouts of acute exercise produce more permanent chronic adaptations that may be termed the exercise training response (Cornelissen et al., 2011). The results from a meta-analysis (Sandercock et al., 2005) show a significant dose-response relationship between exercise and improved cardiac autonomic modulation, measured non-invasively via HRV.

Research has reported changes in HR are primarily due to alterations in the ANS. The immediate response of the CVS during acute exercise is an increase in HR due to the reduced cardiac vagal modulation of HR and increased sympathetic activity (Fletcher et al., 2013). After chronic exercise, autonomic balance is altered toward parasympathetic predominance due to increased vagal modulation of HR and due to a decreased sympathetic activity (Hautala et al., 2009).

Kiviniemi et al., (2014) assessed cardiac autonomic function following HIIT. Twenty-six, healthy middle age physically inactive men were randomised into either a HIIT or MICT group, performing six training sessions over a two week period. HIIT consisted of four to six repeats of 30 seconds ‘all out’ cycling with 4 minutes of recovery (HIIT) and MICT consisted of 40-60 minutes of continuous cycling (MICT). The study reported a significant increase ($p<0.001$) in LF power (a non-invasive marker of sympathetic modulation) in the R-R interval

during 24-hour ambulatory measurements following two weeks HIIT, when compared to the MICT group. Athlough 24-hour HF power (a non-invasive marker of parasympathetic modulation) increased more following HIIT, the reported findings were not significant. There was also no significant training effect or training-group interactions observed in the mean 24-hour HR or LF/HF ratio. These findings offer some insight into the physiological changes of cardiac autonomic modulation following HIIT when compared to MICT. LF power includes both cardiac sympathetic and vagal effects which are determined by vagal modulation and baroreflex. This suggests that the increase in LF power is possibly due to an increase in vagal and/or baroreflex-mediated modulation without major changes in sympathovagal balance.

1.2. Exercise training and cardiac autonomic function

1.2.1. Moderate- intensity continuous training (MICT)

Aerobic exercise training (AET) in the form of MICT is considered the most effective approach and preferable lifestyle modification to improve cardiorespiratory fitness safely and it is highly recommended within exercise prescription both in health and disease populations (Azevedo and Dos Santos, 2014).

AET is most commonly performed at a moderate-intensity which represents 3 to <6 METs, allowing the participant to perform a prolonged training session of upto 45-60 minutes (Thompson et al., 2003). The American College of Sports Medicine (ACSM) classify moderate intensity as 64%-76% of maximal HR and 46%-63% of peak aerobic capacity (VO_2 peak) (Gillen and Gibala, 2013).

Research findings indicate that by taking part in regular PA, the physiological response to exercise can play a vital role in altering cardiac autonomic function (Hautala et al., 2003). Tulppo et al., (2003) examined the effects of AET on HR dynamics in fifty-five healthy, yet physically inactive men. The training period was eight weeks, including six 30-minute sessions a week for the moderate volume training group and six 60-minute sessions a week for the high volume training group at an intensity of 70-80% of maximum HR. The reported findings were measured over a 24-hour period.

The study identified a significantly ($p<0.001$) similar reduction in HR following both moderate (baseline 70±7 decreasing to 64±8 $b \cdot min^{-1}$) and high volume (baseline 67±5 decreasing to 60±6 $b \cdot min^{-1}$) training groups. A significant ($p<0.001$) and similar increase in HF power (ln ms^2) was reported following both moderate (baseline 6.19±1.02 increasing to 6.76±0.96) and high volume (baseline 6.61±1.01 increasing to 7.12±0.92) training groups. LF power (ln ms^2) also showed a significant ($p<0.001$) and similar increase following both moderate (baseline 7.42±0.56 increasing to 7.75±0.59) and high volume (baseline 7.62±0.57 increasing to 7.89±0.63) training groups. LF/HF ratio identified a significant ($p<0.01$) and similar reduction following both moderate (baseline 4.1±2.4 decreasing to 3.1±1.5) and high volume (baseline 3.1±1.6 decreasing to 2.4±1.1) training groups. These findings demonstrate AET in a physically inactive population resulted in altered autonomic regulation of HR towards vagal dominance. The evidence suggests a moderate training volume is sufficient to induce these beneficial effects.

Research suggests long-term adherence to AET can be challenging in many population groups due to the extended time commitment and/or the physical challenge to perform continuous aerobic exercise (Kessler et al., 2012). Therefore, current PA guidelines may be a factor in physical inactivity. The utility of vigorous intensity activity needs further exploration.

1.2.2. High-Intensity Interval Training (HIIT)

High-intensity interval training (HIIT) is performed at a vigorous-intensity with physical exertion corresponding to ≥6 METs (Thompson et al., 2003). The ACSM classify vigorous intensity as 77%-95% of maximal HR and 64%-90% of maximal oxygen uptake (Garber et al., 2011). HIIT is performed at (85-95% of peak HR) and consists of alternating periods of intensive aerobic exercise with periods of active low-intensity recovery (Guiraud et al., 2012; Weston, Taylor et al., 2014).

Recent studies have revealed the potential of as little as three HIIT sessions per week, involving ≤10 minutes of intense exercise within a time commitment of ≤30 minutes per session, including warm-up, recovery between intervals and cool down (Gillen and Gibala, 2013). A systematic review and meta-analysis (Sloth, Sloth et al., 2013) identified the most commonly used training protocol for HIIT consists of repeated wingate based sessions of 30-seconds all out cycling sprints performed three times per week, with training volume per session varying from three to seven bouts, interspersed by 2 to 5 minutes of active recovery. Due to the early research findings, HIIT may be an effective and practical method to improve aerobic fitness and health, yet requiring less time (Kiviniemi et al., 2014).

The vigorous-intensity of a HIIT session is known to challenge the metabolic system. HIIT is characterised by the product of high levels of catecholamines, intense sympathetic activity and enhanced anaerobic metabolism which are known to delay post-exercise vagal reactivation due to slower removal of metabolites that are accumulated during exercise (Oliveira et al., 2013). Amongst research HIIT has shown a superior effect on HR, autonomic and metabolic reactivity, maximal oxygen uptake, endothelial function and lactate levels in healthy subjects (Guiraud et al, 2013).

Recent evidence has begun to emerge demonstrating the efficacy and safety of HIIT (Arena et al., 2013). A recent meta-analysis on patients with lifestyle induced chronic diseases (Weston, Wisloff and Coombes, 2014) examined the potential health benefits of performing HIIT as an alternative to MICT. There was a 19.4% improvement in VO_2 peak in nine of the ten studies, for HIIT (baseline 22.5 mL/kg/min increasing to 27.9 mL/kg/min) compared to a 10.3% increase in VO_2 peak following MICT (baseline 22.6 mL/kg/min increasing to 25.2 mL/kg/min). The mean difference was statistically significant ($p<0.001$) between groups. The study also reported greater improvements in systolic and diastolic blood pressure, increased maximal rate of calcium ions (Ca^{2+}) reuptake, increased availability of nitric oxide and increase in cardiac function. Another meta-analysis (Barlow et al., 2012) highlighted that with each 1 metabolic equivalents (METs) (3.5 mL/kg/min) improvement in aerobic capacity, there is a 13% to 15% reduction in all-cause mortality and cardiovascular events, respectively. Indeed, the protective role of PA occurs even in the presence of established CVD risk factors. Therefore, the greater improvement in cardiorespiratory fitness following HIIT may provide greater health protection.

HIIT appears to be well tolerated and a safe training method, the varied protocol can be easily adapted to include longer/ shorter intervals and longer/shorter recovery periods (active or passive) specific to the needs of the individual (Millar et al., 2009). Literature suggests it is the accumulated time engaged in the high-intensity intervals that determines the physiological benefits (Kemi and Wisloff, 2010). The underlying physiologic concept behind HIIT is that the metabolic rate is raised for a brief period that is considerably higher than that for a moderate-intensity programme; therefore, this permits a longer duration of a given training period to be spent at a higher percentage of VO_2 peak (Arena et al., 2013).

A 30-second Wingate test is sufficiently long enough to allow for developing the maximal glycolytic power and short enough for maximal effort to be exerted until the end of the bout (Micklewright et al., 2006). The alternating periods of reduced intensity between the loaded cycle are designed such that the cardiopulmonary system does not fully recover to near resting levels, whilst permitting the subject enough recovery to be able to repeat the next bout of high-intensity exercise (Kessler et al., 2012). Andersen et al., (2000) also reported the relative intensity and not the duration of cycling is of more importance in relation to all-cause mortality in healthy subjects. Therefore it can be suggested exercise intensity or increased exposure to vigorous-intensity exercise may be the most critical aspect of a training programme necessary for improving changes in cardiac autonomic function.

It has been widely documented that HIIT has shown numerous clinical benefits in both healthy and diseased populations (Shiraev and Barclay, 2012). Evidence based research has demonstrated the effects of acute and chronic HIIT protocols on cardiac autonomic function in different population groups. Two acute studies of single sessions with a range of 10-18 participants examined the effects of HIIT on cardiac autonomic profile in a young, healthy male population (Millar et al., 2009) and a population of chronic disease patients (Guiraud et al., 2013). The findings demonstrate a single session of HIIT can alter cardiac autonomic control, leading to significant improvements of HR and HRV in different populations.

In addition, a chronic study of twelve weeks with a total of thirty-eight physically inactive participants investigating the effects of HIIT on cardiovascular and autonomic function in a young, healthy male population (Heydari, Boutcher et al., 2013) has demonstrated significant improvements in cardiac, vascular and autonomic function after long-term adherence to HIIT programmes.

Heydari, Boutcher et al., (2013) reported significant ($p<0.05$) reductions in resting HR following HIIT (baseline 67.4±9.7 reducing to 61.2±8.9 $b \cdot min^{-1}$) when compared to the control group (baseline 68.9±7.7 increasing to 70.4±6.7 $b \cdot min^{-1}$), respectively. The improvements in resting HR identified are similar to the results of numerous longitudinal aerobic exercise studies that have documented exercise-induced bradycardia. The mechanism that causes bradycardia is unclear, however it is considered to reflect a combination of reduced intrinsic HR, decreased sympathetic tone and enhanced parasympathetic tone.

Heydari, Boutcher et al., (2013) reported a significant ($p<0.05$) increase in HF power ($ln\ ms^2$) (baseline 6.9±1.4 increasing to 7.2±1.1) compared to the control group (baseline 7.1±1.0 decreasing to 6.8±1.1). In addition, LF power ($ln\ ms^2$) identified a significant increase ($p<0.05$) (baseline 7.3±0.8 increasing to 7.7±0.8) when compared to the control group (baseline 7.1±0.7 decreasing to 7.0±0.9).These findings therefore indicate an increased parasympathetic influence and/ or inhibition of sympathetic activity which is beneficial to cardiovascular health.

Heydari, Boutcher et al., (2013) reported a significant ($p<0.05$) increase in SV (baseline 77.2±24.9 increasing to 90.4±26.3 ml) compared to the control group (baseline 75.6±18.9 decreasing to 70.2±20.9 ml). Research suggests HIIT decreases the metabolic rate on the heart at rest causing an increase to SV. Increased myocardial contractility could possibly explain an increase in SV, although increased end-diastolic volume appears to be the more likely mechanism responsible. Also reported were significant ($p<0.05$) reductions in SBP and DBP following HIIT (baseline 119.6±9.9 decreasing to 115.5±9.7 mmHg) and (baseline 63.7±7.3 decreasing to 59.2±7.5 mmHg) compared to the control group (baseline 117.4±13.4 increasing to 121.7±12.8 mmHg) and (baseline 62.2±7.0 increasing to 65.8±6.6 mmHg), respectively.

It could be suggested that low volume, high-intensity activity causes an increase in cellular and peripheral vascular stress. A significant ($p<0.05$) increase in baroreflex sensitivity was also reported following HIIT when compared to the control group. The improvements in baroreflex sensitivity can possibly explain the reduction in resting blood pressure following HIIT. However, research suggests a possible mechanism influencing resting blood pressure include an increase in endothelial NO synthase and prostaglandin release which can influence vasodilatory adaptations.

HIIT may contribute to the aerobic adaptation of the circulatory system as it is forced to generate a greater amount of blood supply at a very high rate with a decreasing anaerobic contribution. Alternatively, a number of studies have shown vascular function improvement of upper-limb following lower-limb exercise in healthy subjects in both conduit arteries.

Furthermore, a significant ($p<0.05$) improvement in VO_2 max ($ml \cdot min^{-1} \cdot kg^{-1}$) was also reported following HIIT (baseline 34.2±4.4 increasing to 39.4±3.5 $ml \cdot min^{-1} \cdot kg^{-1}$) when compared to the control group (29.0±5.0 increasing to 30.4±5.5 $ml \cdot min^{-1} \cdot kg^{-1}$). The underlying mechanisms responsible for an increase in aerobic capacity following HIIT are unclear; however it could involve an increase in SV by enhanced cardiac contractility, enhanced mitochondrial oxidative capacity and/or increased skeletal muscle capacity.

The literature reviewed has shown how chronic HIIT programmes can produce physiological and autonomic changes in different populations. Research has also shown how acute single sessions can alter cardiac autonomic control, yet there has been no research to examine the effects of a short-term HIIT intervention over a two week period on cardiac autonomic function in young, physically inactive males.

1.3. Rationale

It has been documented that a HIIT programme offers similar cardiovascular protective adaptations that can reduce the risk of numerous chronic diseases as a MICT programme, but with less of a time commitment. Several exercise intervention studies have focussed on the secondary preventions of future adverse health conditions. However, recent NHS guidelines have highlighted the importance of primary prevention interventions as a prophylactic strategy to reduce the risk of developing adverse chronic diseases (The Kings Fund, 2015). Current evidence supports HIIT as an effective intervention which improves traditional and novel risk factors for CVD. Therefore, the aim of this study is to perform a randomised cross over controlled study, investigating effects short term HIIT has on cardiac autonomic function in physically inactive males.

1.4. Hypothesis

Null hypothesis (H_0): There will not be a statistically significant difference in cardiac autonomic function measured via HRV in participants completing a programme of HIIT compared to a control period.

Alternative hypothesis (H_1): There will be a statistically significant difference in cardiac autonomic function measured via HRV in participants completing a programme of HIIT compared to a control period.

Chapter 2: Method

2.0. Participant information

Forty healthy, physically inactive male students from Canterbury Christ Church University volunteered to participate in the study (mean age 21.7±1.7 years, weight 82.61±11.5kg, height 179.86±5.4m and BMI 25.5±3.03kg/m^2). Recruitment and interest in the study developed from posters and word of mouth. The study was approved by Canterbury Christ Church University Ethics Committee. Inclusion criteria were as follows; participants must be male, physically inactive and non-smokers. Prior to testing, each participant received written information explaining the full extent of the study. Prior to any assessments, each participant provided written informed consent and completed a physical activity readiness questionnaire (PAR-Q).

2.1. Equipment

Prior to each assessment, a single baseline measurement of height (m) was recorded using a stadiometer (Model 220, Seca Gmbh, Hamburg, Germany) and mass (kg) recorded using the mechanical counterbalanced weighting scale (Model 761, Seca Gmbh, Hamburg, Germany).

Heart rate variability and BP was measured non-invasively using the Task Force® Monitor (TFM) (CNSystems, Medizintechnik AG, 2010, Version 2.2.22.2). The TFM was used for the continuous non-invasive beat-to-beat monitoring and real-time calculation of all autonomic and haemodynamic parameters using power spectral analysis. All of the data was recorded at a set frequency of 1000Hz and 16-bit resolution. The TFM enables the continuous measurement of BP by the use of the vascular unloading technique and beat to beat stroke

volume measurement with impedance cardiography. A 6-channel ECG is included for R-R interval determination and the beat to beat values are used for the real-time calculation of HRV by an autoregressive model.

Functional capacity was measured using the Cosmed Quark CPET (Quark CPET 10.0e), which records values for expired gas exchange. The incremental exercise test to exhaustion was conducted using an SRM Ergometer with intergrated SRM Training System (SRM, Julich, Germany). Before testing, the gas cylinder was calibrated to gases of known concentration (O_2, 15%; CO_2, 5%) and set to 5-bar. Before each exercise test, a three-litre syringe was used to calibrate flow (Cosmed, Rome, Italy). Expired volume was measured using a Hans Rudolph pneumotach flowmeter connected via a Hans Rudolph Mask and Headgear. Breath-by-breath pulmonary gas-exchange data was collected continuously during the incremental tests and averaged over consecutive 10-second periods.

The HIIT intervention was performed using a Wattbike trainer (Nottingham, England). All of the wattbikes are computer operated with a polar view software (Wattbike Expert Software v 2.50.42), allowing participant specific calculations of exercise resistance for the prescribed HIIT programme.

2.2. Study protocol

All participants were required for a total duration of twelve weeks. Upon completion of the familiarisation test, participants were randomly assigned into either a HIIT (n:20) or control (n:20) training group.

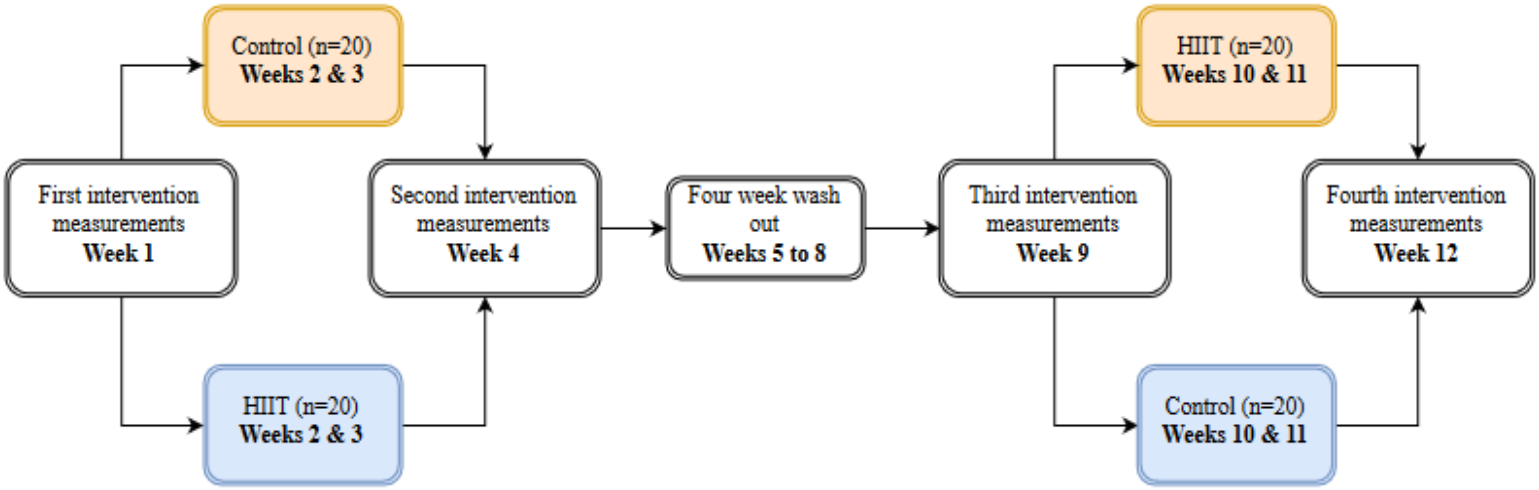

Figure 2.1. Study design

All participants were informed that they could withdraw from the study at any point. In an attempt to minimise any potential exercise or diet-induced variability, the HIIT group were particularly encouraged to maintain normal daily living activities with only the addition of HIIT and the control group were encouraged to maintain their normal daily living activities and abstain from any structured out of the ordinary exercise training. Participants were instructed to avoid eating 4 hours before each test with only the intake of water. Participants were also instructed to abstain from caffeine and alcohol intake 24 hours prior to each test. Dietary habits were confirmed prior to testing by dietary recall and verbal communication.

2.3. Testing

Each participant first completed a familiarisation incremental exercise test to exhaustion on the SRM ergometer. Research suggests the SRM system has become a well-known training tool in both amateur and professional cyclists. The SRM system has been used as a reference system to validate other ergometers as its power output measurements appear valid and reliable (Bertucci et al., 2005).

Each participant completed a 2-minute warm-up on the SRM ergometer, then performed an incremental exercise test to exhaustion keeping a self-selected pedal cadence between 70-80r·min^{-1}. The saddle and handle bar height configuration was recorded and reproduced in subsequent tests. In this study, each participant began at 50 watts resistance, thereafter a ramp protocol was introduced where the intensity increased by 20W·min^{-1} for every 1 minute. This protocol was similar to that of (Bailey et al., 2009) who used a pedal cadence between 70-90r·min-1 and increased resistance at a rate of 25W·min^{-1}. Research suggests functional capacity can be accurately determined with the use of ramp protocols in which small increments in work rate occur at intervals of 30 to 60 seconds. It is suggested a protocol should be tailored to yield a fatigue-limited exercise duration of ≈10 minutes and <12 minutes (Myers et al., 1991); a short duration and high sensitivity is advantageous for measuring anaerobic threshold (Wasserman et al., 1973).

All participants underwent the test until volitional exhaustion or until preferred cadence could not be maintained >60r·min^{-1}. On completion, all participants were advised to cool down sufficiently. All participants were unaware of the exercise time and work rate increment. Participants were verbally encouraged to ensure a maximal effort was achieved.

For the first week of testing, all forty participants were allocated a day and one hour time slot and visited the laboratory for pre-intervention measurements of HRV and BP on the TFM. A strength of the TFM is that all haemodynamic parameters are detected on a beat-to-beat basis and monitored in real time (Fortin et al., 1998). The TFM has provided valid evidence detailing correct and reliable haemodynamic data (Fortin et al., 2001). The TFM does not only facilitate the diagnosis of all kind of haemodynamic disturbances, it has also proved to be a valuable device for the investigation of pharmacological interventions (Sztajzel, 2004).

Prior to any testing, height and weight was recorded for data entry. For short-term recordings on HRV, a standard method (Kleiger et al., 2005) was performed where each participant was positioned in the supine position on a bed for the standard duration of 15-minutes rest, after 15-minutes a continuous measurement was recorded for 5-minutes. Heart rate variability was measured via a 6-channel ECG; four Ambu Bluesensor T electrodes (size large) were positioned in the correct anatomical position on the participant's upper torso and lower abdomen and connected to the appropriate colour coded wires. All testing was homogenous throughout; each participant's bicep circumference was measured and recorded for the specificity size of the pneumatic Dura-cuf (CNSystems) (Adult 23-33cm or Large Adult 31-40cm). Connected to the TFM, the pneumatic Dura-cuf (CNsystems) specific to the individual participant's bicep circumference was positioned on the upper right arm for alternate measurements of oscillometric BP. Alternate measurements of beat-to-beat BP were recorded via the left index finger by the use of the vascular unloading technique. This was automatically collaborated to oscillometric BP measure at the arm using a Medium Volar. Throughout the TFM recordings, complete silence was demanded in order to remove any environmental variables and the lights were turned off to ensure participants were in a maximal resting state. On completion of this test, the measurements were then recorded (as shown in figure 2.2).

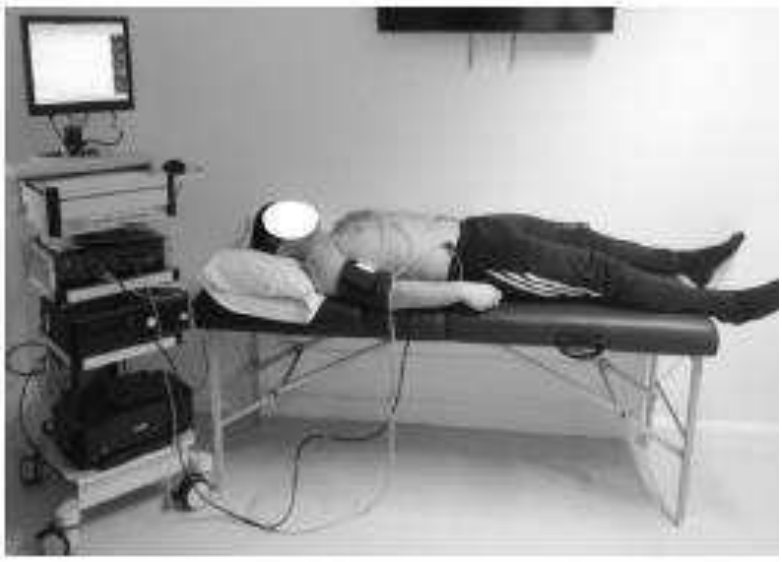

Figure 2.2. A participant completing a resting measure on the Task Force® Monitor.

Following the recordings on the TFM, an incremental exercise test to exhaustion on the SRM ergometer was conducted using the same protocol as previously mentioned during the familiarisation exercise test and a recording of functional capacity was measured via the Cosmed Quark. On completion of this test, the measurements were then recorded (as shown in figure 2.3). The Douglas bag system remains the gold standard for gas exchange measurement, however, this method has been replaced by an automated metabolic gas analysis system. A validation study of the Cosmed Quark CPET (Nieman et al., 2013) indicates that the CPET mixing chamber system provides valid, accurate metabolic measurements that compare closely with the Douglas bag system.

Figure 2.3. A participant completing an incremental exercise test to exhaustion.

On week four, all forty participants were allocated a select day and one hour time slot. Participants visited the laboratory for post-intervention measurements of HRV on the TFM followed by an incremental exercise test to exhaustion on the SRM ergometer recording functional capacity measurements via the Cosmed Quark. The HIIT group post-intervention measurements were recorded 72-hours after the final training session. These performance

measurements were identical in all respects to the initial testing phase. On completion of these tests, the measurements were then recorded.

Research suggests a detraining period between two to four weeks of physical inactivity is sufficient to reverse physiological and performance adaptations (Mujika and Padilla, 2000). During week five to eight, a four-week washout period was completed to reverse any training effects. The study design then crossed over and all forty participants from week nine to twelve completed the alternate group. The protocol for both the HIIT and control group was replicated the same as week one to four. At the end of twelve weeks, the data recorded for both groups represents HIIT (n: 40) and control (n: 40).

2.4. Training intervention

Two weeks was chosen for HIIT as research has demonstrated this duration as sufficient to enhance physiological adaptations. A systematic review and meta-analysis (Sloth, Sloth et al., 2013) identified the most commonly performed HIIT protocol, which included 30-seconds all out maximal sprint, three times per week consisting of three to seven bouts with 2 to 5 minutes active recovery. An adaptation of this protocol was performed in this study. Research suggests that power outputs, cadence and physiological variables from a 30-second all-out maximal sprint performed on the wattbike are highly reproducible (Driller et al., 2013).The validity and reliability of the wattbike (Hopker et al., 2010) suggest it is an acceptable training tool for both trained and untrained populations and sufficiently accurate to track performance changes over time.

On the second and third week, twenty control participants were at rest and twenty HIIT participants were divided into two groups of ten (group cycle) for the duration of HIIT protocol (as shown in figure 2.4). The training was conducted at a frequency of three times per week, consisting of three bouts of 30-seconds all out maximal sprints with a 2-minute active recovery period of unloaded cycle for a period of two weeks. At the start of each session, weight (kg) was recorded for data entry. All three wingate sessions per week for the two allocated groups were completed at the same time of day. Research suggests HIIT may require initial supervision in untrained and high risk individuals (Kessler et al., 2012); therefore all HIIT sessions were supervised. All twenty participants in the HIIT group completed a 5-minute warm up then proceeded into three bouts of 30-seconds all-out maximal sprints on a wattbike trainer, cycling against a resistance and air brake resistance in relation to 0.075kg/kg body mass (Astorino et al., 2012) (which was determined from the input of each participant's weight into the wattbike software). Each interval was separated by a 2-minute active recovery (unloaded cycle). On completion of the third repetition, a 5-minute cool-down period was performed. Strong verbal encouragement was provided during exercise, participants were unaware of the time remaining in each 30-second sprint. All participants in the control group during the second and third week were at rest. There was 100% adherence to HIIT sessions in both groups.

Figure 2.4. A HIIT group completing x3 30-second maximal sprints on a wattbike trainer.

2.5. Data Analysis

Continuous variables are expressed as mean ± standard deviation. A two-way repeated measures ANOVA was performed with a Bonferroni post hoc test, for comparison of outcome measures between and within groups. Spectral measures of HRV were positively skewed and therefore log transformed (ln) prior to analysis. All data were analysed using the statistical package for social sciences (SPSS 22 release version for Windows; SPSS Inc., Chicago IL, USA).

Chapter 3: Results

3.0. Cardiac autonomic parameters

There was a significant reduction in HR (62.2±8.6 to 57.7±8.3 $b \cdot min^{-1}$; $p<0.001$) in the HIIT group and no significant change (64.7±10.6 to 64.3±10.8 $b \cdot min^{-1}$; $p=0.479$) during the control period. There was a significant difference ($p=0.011$) in HR between conditions (see figure 3.1A). As shown in figure 3.1B, there was a significant increase in HVR expressed as R-R PSD (ln) (3.53±0.27 to 3.67±0.26; $p<0.005$) in the HIIT group and no significant change (3.51±0.24 to 3.51±0.25; $p=0.532$) during the control period. There was a significant difference ($p=0.04$) in R-R PSD (ln) between conditions.

As shown in figure 3.1C, there was a significant reduction in R-R LFnu (%) (61.4±11.5 to 57.6±11.6; $p<0.001$) in the HIIT group and no significant change (59.6±11.8 to 59.5±12.5; $p=0.583$) during the control period. There was no significant difference ($p=0.389$) in R-R LFnu (%) between conditions. There was a significant increase in R-R HFnu (%) (38.6±11.5 to 42.4±11.6; $p<0.001$) in the HIIT group and no significant change (40.4±11.8 to 40.5±12.5; $p=0.583$) during the control period. There was no significant difference ($p=0.389$) in R-R HFnu (%) between conditions (as shown in figure 3.1D).

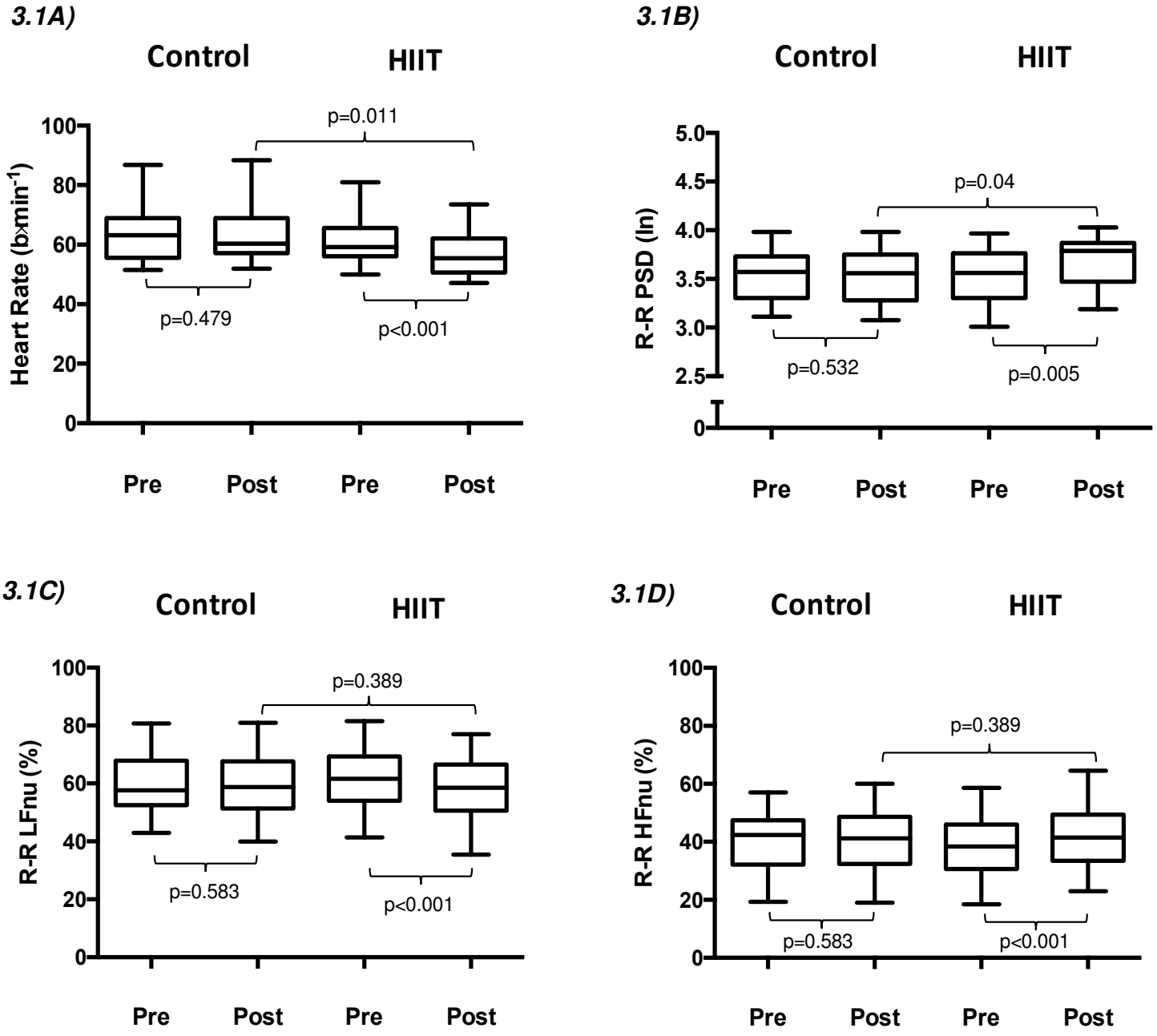

Figure 3.1. Changes in heart rate (A), heart rate variability (R-R PSD ln) (B), normalised units low-frequency (R-R LFnu %) (C), and normalised units high-frequency (R-R HFnu %) (D).

As shown in figure 3.2A, there was no significant change in R-R LF (ln) (3.17±0.25 to 3.19±0.23; p=0.102) in the HIIT group and no significant change (3.17±0.20 to 3.16±0.21; p=0.12) during the control period. There was no significant difference (p=0.625) in R-R LF (ln) between conditions. As shown in figure 3.2B, there was a significant increase in R-R HF (ln) (2.96±0.37 to 3.05±0.33; p<0.005) in the HIIT group and no significant change (2.99±0.34 to 2.97±0.37; p=0.162) during the control period. There was a significant difference (p=0.048) in R-R HF (ln) between conditions. There was a significant reduction in R-R LF/HF ratio (2.00±1.04 to 1.47±0.77; p<0.001) in the HIIT group and no significant change (1.90±0.97 to 1.92±1.01; p=0.661) during the control period. There was a significant difference (p=0.007) in R-R LF/HF ratio between conditions (as shown in figure 3.2C).

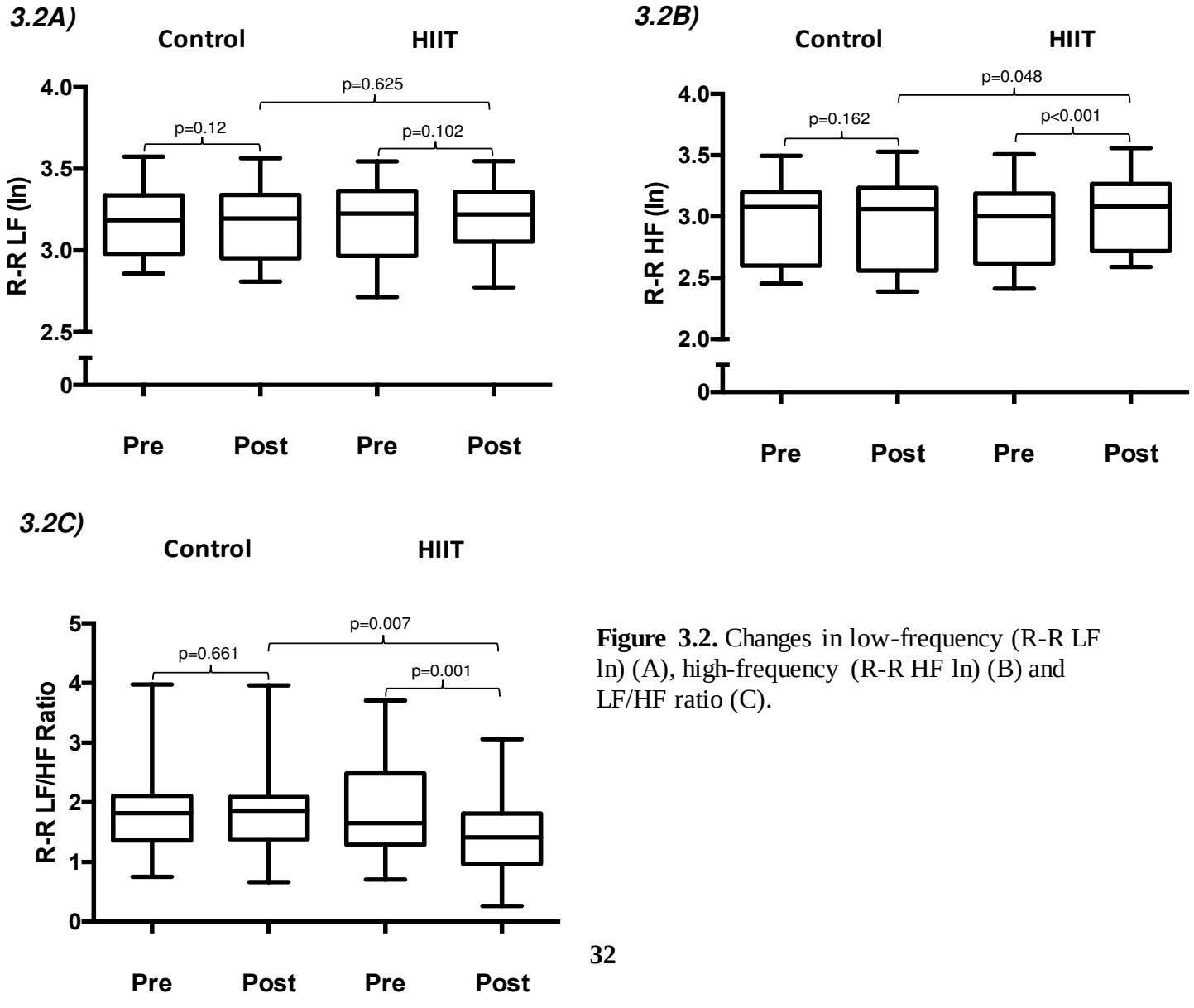

Figure 3.2. Changes in low-frequency (R-R LF ln) (A), high-frequency (R-R HF ln) (B) and LF/HF ratio (C).

3.1. Haemodynamic parameters

There was a significant reduction in SBP (116.1±4.9 to 111.3±8.8 mmHg; p<0.001) in the HIIT group and no significant change (115.9±4.9 to 115.6±4.6 mmHg; p=0.837) during the control period. There was a significant difference (p<0.001) in sBP between conditions. There was a significant reduction in RPP (7385.6±1177.5 to 6387.8±908.7 mmHg; p<0.001) in the HIIT group and no significant change (7450.5±1156.3 to 7202.7±1060.3; p=0.415) during the control period. There was a significant difference (p=0.001) in RPP between conditions. As shown in table 3.1, there were no significant differences in MBP or DBP within or between conditions.

Table 3.1 displays changes in haemodynamic parameters following HIIT and control period

Table 3.1.	**HIIT period (n=40)**			**Control period (n=40)**			
Variable	Pre-HIIT	Post-HIIT	P-value within group	Pre-Control	Post-Control	P-value within group	P-value between groups
Haemodynamic parameters							
SBP (mmHg)	116.1 ± 4.9	111.3 ± 8.8	<0.001	115.9 ± 4.9	115.6 ± 4.6	0.837	<0.001
MBP (mmHg)	85 ± 6.1	81.5 ± 5	0.029	84.3 ± 5.9	83.7 ± 5.2	0.721	0.022
DBP (mmHg)	67.6 ± 6.7	64.8 ± 6.1	0.038	67.1 ± 6.2	66.4 ± 6.4	0.72	0.124
RPP (mmHg)	7385.6 ± 1177.5	6387.8 ± 908.7	<0.001	7450.5 ± 1156.3	7202.7 ± 1060.3	0.415	0.001

Note: mmHg = Millimeter of mercury; SBP = Systolic blood pressure; MBP = Mean blood pressure; DBP = Diastolic Blood Pressure; RPP = Rate Pressure Product.

3.2. Functional capacity

There was a significant increase in peak VO_2 ($ml \cdot min^{-1}$) (3535.6±487.9 to 3744.6±581.7 $ml \cdot min^{-1}$; p<0.001) in the HIIT group and no significant change (3522.4±466.5 to 3531.8±536.1 $ml \cdot min^{-1}$; p=0.942) during the control period. There was a significant difference (p=0.013) in peak VO_2 ($ml \cdot min^{-1}$) between conditions. There was a significant increase in peak VO_2 ($ml \cdot min^{-1} \cdot kg^{-1}$) (43.17±5.2 to 45.29±5.2 $ml \cdot min^{-1} \cdot kg^{-1}$; p<0.001) in the HIIT group and no significant change (43.4±5.2 to 42.9±5.4 $ml \cdot min^{-1} \cdot kg^{-1}$; p=0.732) during the control period. There was a significant difference (p=0.011) in peak VO_2 ($ml \cdot min^{-1} \cdot kg^{-1}$) between conditions. As shown in table 3.2, there were no significant differences in V_E (ml/min) and V_E/VCO_2 Slope within or between conditions.

Table 3.2 displays changes in cardiorespiratory parameters following HIIT and control period

Table 3.2.	**HIIT period (n=40)**			**Control period (n=40)**			
Variable	Pre-HIIT	Post-HIIT	P-value within group	Pre-Control	Post-Control	P-value within group	P-value between groups
Cardiorespiratory parameters							
Peak VO_2 ($ml \cdot min^{-1}$)	3535.6 ± 487.9	3744.6 ± 581.7	<0.001	3522.4 ± 466.5	3531.8 ± 536.1	0.942	0.013
Peak VO_2 ($ml \cdot min^{-1} \cdot kg^{-1}$)	43.17 ± 5.2	45.29 ± 5.2	<0.001	43.4 ± 5.2	42.9 ± 5.4	0.732	0.011
V_E (ml/min)	112.9 ± 24.8	131.7 ± 29.4	0.009	112.3 ± 22.2	118.9 ± 26.6	0.292	0.007
V_E/VCO_2 Slope	29.5 ± 4.4	31.9 ± 4.4	0.034	29.8 ± 8.5	31.1 ± 8.4	0.126	0.545

Note: ExT = VO_2 = Oxygen uptake; V_E = Minute ventilation; VCO_2 = Volume of Carbon Dioxide.

Chapter 4: Discussion

4.0. Summary of results

This is the first study to assess changes in cardiac autonomic modulation following a two-week HIIT protocol in a large sample size of physically inactive male participants. This randomised cross over controlled trial demonstrated that HIIT significantly improved cardiac autonomic function compared to a control condition. Accordingly, the null hypothesis is rejected. Overwhelming evidence indicates that regular physical activity in the form of both acute and chronic exercise can reduce the severity and occurrence of diseases related to unhealthy lifestyles. In addition to the improvement in cardiac autonomic function, HIIT significantly improved haemodynamic and cardiorespiratory parameters when compared to a control period. An increase in HRV and aerobic capacity and reduced arterial BP has been associated with an improved survival benefit (Routledge et al., 2010). Findings from the present study offer new and consistent research which demonstrates the response of HIIT on these health markers in a physically inactive male population. These findings offer further understanding of the role of HIIT and the potential it could have on PA guidelines and primary health care.

4.1. Adaptations and changes to cardiac autonomic parameters

The effects of HIIT on cardiac autonomic function are yet to be fully explored. Research has reported short-term HIIT increases parasympathetic activity and decreases sympathetic activity to the heart at rest (Besnier et al., 2017). The reported changes observed following two-weeks of HIIT in the present study are similar to existing research (Heydari, Boutcher et al., 2013), which has shown a positive relation between a reduced resting HR and an increase

in HRV. It has been suggested that HRV is increased when HR is controlled predominantly by parasympathetic activity (Lahiri et al, 2008).

A significant reduction in HR (-4.5 $b \cdot min^{-1}$; $p<0.001$) was observed in the present study following the HIIT intervention, which is an indicator of improved cardiovascular health. It is important to mention the study also demonstrated two-weeks HIIT can significantly ($p=0.011$) improve HR when compared to the control period. Previous research is consistent with similar reductions in HR ranging from 2 $b \cdot min^{-1}$ to 6.2 $b \cdot min^{-1}$ following chronic HIIT interventions (Guiraud et al., 2013; Heydari, Boutcher et al., 2013; Kiviniemi et al., 2014). However, several studies have reported no significant change in HR at baseline vs. post HIIT (Rakobowchuk et al., 2008; Astorino et al., 2012). It can be acknowledged that reductions in resting HR following HIIT interventions are frequent amongst literature, however the mechanisms underlying these reductions are complex and are yet to be fully understood (Gibala et al., 2006). Therefore it is somewhat hard to make generalisations.

A possible mechanism to explain a reduction in resting HR following HIIT is an increased SV. Following a twelve-week HIIT intervention, Heydari, Boutcher et al., (2013) observed a significant increase in SV (ml) (77.2±24.9 to 90.4±26.3; $p<0.05$). An increase in SV is likely to occur due to the increased ability to utilize the Frank-Starling mechanism. According to the Frank-Starling law, an increase in blood volume causes a direct increase in myocardial contractility and to maintain cardiac output, HR can decrease in response to a higher systolic volume. Although cardiac remodelling was not investigated in this study, a potential mechanism for improving SV and reducing HR is an increase in end diastolic volume.

Alternatively, the results in the present study have previously been associated with an increase in cardiac vagal modulation. There is a limited amount of research that explains the possible mechanisms responsible for improving cardiac vagal modulation, however angiotensin II and nitric oxide (NO) are potential mediators (Routledge et al., 2010). Further research is needed to clarify the possible role of NO in autonomic control as well as its potential influence on cardiac vagal tone.

An important finding in the study was a significant increase in HRV expressed as R-R PSD (ln) (+0.14; $p<0.005$) following HIIT and a significant ($p=0.04$) difference when compared to the control period. It can also be observed that the present study significantly improved R-R HF (ln) (a non-invasive marker of parasympathetic modulation) (+0.09; $p<0.005$) following HIIT and identified a significant ($p=0.048$) difference between groups. There was no significant change in R-R LF (ln) within or between groups (a non-invasive marker of sympathetic modulation) (+0.02; $p=0.102$) following HIIT. In comparison, Heydari, Boutcher et al., (2013) reported a significant ($p<0.05$) increase in HF power and LF power (ln ms^2) when compared to a control group. These findings indicate an increased parasympathetic influence and/or inhibition of sympathetic activity which is beneficial to cardiovascular health. The present study also significantly decreased R-R LF/HF ratio (-0.53; $p<0.001$) following HIIT and identified a significant ($p=0.007$) difference between the control period. The observed decrease in the LF/HF ratio may be a reflection of the significant increase in parasympathetic activity.

It is known that the R-R HF (ln) power is an established marker for cardiac vagal activity. However, the R-R LF (ln) power includes both cardiac sympathetic and vagal effects and a major part of it is determined by vagal modulation and baroreceptor reflex. This may explain the possible increase in R-R LF (ln) in the present study. The results reported are novel and contribute to the existing research outlining the possible benefits of short-term HIIT on cardiac autonomic function and the potential impact this mode of exercise may have on primary health care.

Previous findings in literature have identified an increase in baroreceptor sensitivity (BRS) following HIIT. Research has identified an increase in baroreceptor impulse frequency inhibits vasoconstrictor action and results in blood vessel vasodilation causing a subsequent reduction in BP. It is plausible to suggest that an increased HRV (R-R PSD ln) and increased parasympathetic tone (R-R-HF ln) observed in the present study may be the result of improved cardiovagal BRS. The significant reduction in arterial BP following HIIT supports this concept. An improvement in autonomic function and baroreflex activity are prevalent within HIIT research, indicating a greater sympathovagal balance (Goldstein et al, 2011). The exercise induced changes observed in the present study may offer a cardio-protective effect as well as reduce the incidence of CVD (Knight, 2012). Improvements in baroreflex sensitivity have also been shown to benefit cardiovascular health by reducing ventricular fibrillation, which in turn reduces mortality risk (La Rovere et al., 2001).

Of interest, prior research has demonstrated healthy individuals with a greater peak VO_2 have a significantly greater vagal modulation of HR (Tulppo et al., 2003). Indeed, aerobic capacity is the strongest independent predictor of mortality and a favourable aerobic capacity is associated with a reduced risk of chronic diseases (Lee et al., 2010). Individuals with high

levels of aerobic conditioning are recognised as having a lower resting HR and increased high-frequency HRV (Sandercock et al., 2006). In addition, Hautala et al., (2009) demonstrated participants with a greater functional capacity had a reduced LF/HF ratio and sympathetic nerve activity than individuals with a lower peak VO_2. It has been identified that an increase in aerobic capacity post HIIT is also associated with vagal influence on the heart (Boutcher et al. 2013). The increase in aerobic capacity following HIIT in this study support this concept.

In relation to current PA guidelines, the observed findings from the present study demonstrate significant improvements in HR and HRV can be achieved when completing physical activity of a lower training duration, which may reduce the risk of CVD. This study provides evidence to suggest that individuals who cite lack of motivation and time constraints could benefit from a training programme similar to the present study. The two-week HIIT intervention was a time efficient strategy to induce cardiac autonomic adaptations and exercise performance in a group exercise setting compared to a control period. The clinical importance of these findings in relation to health is significant as HR (Fox et al., 2007) and HRV (Thayer et al., 2010) are both independent predictors of poor health and as little as two weeks of HIIT evidenced in this study produced significant improvements in these markers.

The present study highlights the possibility for short-term HIIT programmes to be an effective strategy for primary health care. Research has found exercise drop-out rate following HIIT is less when compared to MICT (Heydari, Boutcher et al., 2013). An important finding in this study was complete adherence to the HIIT intervention, however this was over a short-term duration and it is unknown if adherence to long-term HIIT interventions would remain high. This present study provides important evidence with respect

to HIIT frequency (three days per week), low volume per session (3 x 30-seconds), low volume active recovery (2-minutes) and a short-term duration (two-weeks) in a young, physically inactive male population. The significant improvements identified in this study may suggest a need for current PA guidelines to adapt, allowing the potential for greater exercise adoption and adherence.

4.2. Adaptations and changes to haemodynamic parameters

The present two-week HIIT intervention identified a significant reduction in SBP (-4.8 mmHg; $p<0.001$) and a significant ($p<0.001$) difference between groups. In the present study, The HIIT group demonstrated a significant reduction in DBP (-2.8 mmHg; $p=0.038$) following two-weeks HIIT; however, there was no significant difference between groups. In comparison, Heydari, Boutcher et al., (2013) reported a significant reduction in SBP (-4.1 mmHg; $p<0.05$) and DBP (4.5 mmHg; $p<0.05$) following twelve weeks of HIIT. It is important to note a previous study reported no significant change in SBP or DBP following a short-term two-week HIIT intervention (Astorino et al., 2012). The findings in the present study offer new insight into the response of HIIT on BP. It is important to address the participants in this study were normotensive at baseline and this may have had an influence on the greater changes shown over the short-term intervention. However, reductions of this magnitude in a normotensive population, as seen in this study, may still have clinical significance, since a 2 mmHg reduction in BP is associated with a significant reduction in the risk of cardiovascular disease (Lewington et al., 2002).

Reductions in blood pressure and systemic vascular resistance as a result of HIIT can be a consequence of reduced autonomic nervous system activity (Fagard, 2006). Stimulation of

baroreceptors results in an increase in efferent cardiac parasympathetic activity and decreases in sympathetic activity due to its inability to stimulate the SA node (Triposkiadis et al., 2009). An increase in baroreceptor impulse frequency inhibits a vasoconstrictor action and results in blood vessel vasodilation (Gibala, Little et al., 2012). Arterial stiffness has been shown to be an independent predictor of CVD and all-cause mortality (Laurent et al., 2001). The attenuation of arterial stiffness has been attributed to the improvements in endothelial function (DeSouza et al., 2000) and reductions in sympathetic tone. It has been documented that an increased NO synthase release from the endothelium promotes vasodilation of the non-working muscle groups. Previous studies have shown a significantly greater increase in NO bioavailability following HIIT compared with a MICT protocol (Tjonna et al., 2008). An increase in NO bioavailability could be a possible mechanism to explain a subsequent reduction in BP following HIIT.

This present study also identified a significant reduction in RPP (-997.8 mmHg; $p<0.001$) following two-weeks HIIT and a significant ($p=0.001$) difference between the control period. Research suggests a combination of the significant reductions identified in the present study; SBP, HR and RPP indicate that the myocardial oxygen demand was significantly reduced (Fletcher et al., 2013). A reduced RPP has also been shown to mimic anti-ischaemic effects of beta blockers which is beneficial to CV health (Fletcher et al., 2013). The evidence in this study highlights the potential for HIIT as a non-pharmacological intervention for BP management when compared to a control period.

The adequate control and management of BP is important for public health. Reductions in blood pressure lead to reduced myocardial workload and decrease the risk of subsequent cardiovascular events (Chobanian et al., 2003). The mechanisms responsible remain unclear;

however, improvements in endothelium-dependant responses, reductions in plasma renin activity, lower plasma noradrenaline and increased NO bioavailability are plausible explanations to the improvements seen at rest following exercise. However, a further understanding is needed to determine the physiological response of HIIT on haemodynamic parameters.

4.3. Adaptations and changes to cardiorespiratory parameters

This present study observed a significant increase in absolute peak VO_2 ($ml \cdot min^{-1}$) (+0.209; $p<0.001$) and relative peak VO_2 ($ml \cdot min^{-1} \cdot kg^{-1}$) (+2.12; $p<0.001$) following two weeks HIIT. There was a significant difference between the HIIT and control period, respectively. Existing research has identified similar improvements in comparison. Astorino et al., (2012) identified a significant improvement in peak VO_2 ($ml \cdot min^{-1} \cdot kg^{-1}$) (+2.40; $p<0.05$) following two-weeks HIIT. This evidence demonstrates consistency of findings, displaying significant cardiorespiratory changes after a short-term HIIT intervention. An increase in peak aerobic capacity as observed in the present study is associated with a lower risk of all-cause mortality and cardiovascular events. According to a dose-response analyses between cardiorespiratory fitness and cardiovascular events, a 1-MET increase of peak aerobic capacity (3.5 $ml \cdot min^{-1} \cdot kg^{-1}$) is associated with 13% and 15% reductions in risk of all-cause mortality and coronary heart disease (Kodama et al., 2009). The findings in the present study have clinical significance, however it is plausible to suggest that a longer duration of HIIT may confer greater improvements to peak aerobic capacity.

Research has demonstrated increased skeletal muscle oxidative capacity as reflected by the maximal activity of mitochondrial enzymes after as little as six sessions of HIIT over two

weeks (Burgomaster et al., 2005). This possible explanation together with increased central adaptations may be responsible for the improvements in peak VO_2, as demonstrated via the Fick principle where VO_2 is equal to Q x A-VO_2 max.

Moreover, research comparing six-weeks of HIIT with MICT that was designed according to current public health guidelines (Burgomaster et al. 2008; Rakobowchuk et al. 2008) found similar training-induced improvements in various markers of skeletal muscle and cardiovascular adaptation despite large differences in weekly training volume (~90% lower in the HIIT group) and time commitment (~67% lower in the HIIT group). In addition, other adaptations have been documented after several weeks of low-volume HIIT including an increased resting glycogen content, a reduced rate of glycogen utilization and lactate production during matched-work exercise, an increased capacity for whole-body and skeletal muscle lipid oxidation, enhanced peripheral vascular structure and function, improved exercise performance as measured by time-to-exhaustion and increased maximal oxygen uptake (Burgomaster et al. 2005, 2008; Gibala et al. 2006; Rakobowchuk et al. 2008).

It is therefore possible to stimulate rapid adaptations in skeletal muscle that are comparable to traditional endurance training with a relatively small dose of two weeks HIIT, providing the exercise stimulus is intense and applied in an intermittent manner (Gibala et al., 2006). The effect of HIIT on aerobic fitness is extraordinary given that the most intense component of the interval is completed anaerobically. The findings identified in the present study offer insight into the short-term effects of HIIT on cardiorespiratory changes and the possible benefits it has in relation to cardiac autonomic function.

4.4. Limitations

There are several limitations to the present study that warrant discussion. Previous research is limited and equivocal surrounding HIIT and HRV in a young, physically inactive male population which makes it somewhat difficult to make generalisations. With regards to the baseline measurements within the present study, the population was healthy, yet physically inactive. Regardless, HIIT still produced significant changes to cardiac autonomic function, peak aerobic fitness and systolic blood pressure. Thus future work in healthy participants should utilise this method in order to make comparisons and judgements on its clinical effect.

With respect to the population of the present study, it is plausible to suggest that stress, anxiety and lack of sleep from University assignments, exams, placement or student lifestyle could have had an effect on HR, HRV and BP throughout. In addition, there were no dietary recommendations or measurements of alcohol consumption throughout the duration of testing which could have possibly had an effect on results. In the present study, participants were instructed to maintain their normal daily living activities and abstain from any structured out of the ordinary exercise, however this was not measured or recorded.

The method design of a cross-over could have possibly made the participants become familiarised with exercise testing. Alternatively, the protocol design may have been a limitation where participants may not have been in a complete resting state prior to measurements on the TFM knowing that an incremental exercise test was following. Athlough this present study significantly improved parameters of cardiac autonomic function after two weeks; generalisations from this study cannot be made regarding the long term benefits of HIIT.

In the present study, high-intensity intervals were performed in a group cycle environment. This may have had an effect on exercise participation, engagement, improved adherence and enjoyment within the study as well as maximal exertion from participants. The cardiac autonomic responses to HIIT when performed in isolation are unknown.

The mechanisms responsible for the changes observed in the present study are complex and may not be the only explanation for the adaptations that occurred following HIIT. It is also plausible to suggest that the use of other non-invasive equipment such as echocardiography could be used to measure other potential adaptations. The use of the echocardiogram was unavailable for the present study as sufficient training and experience is required for accurate measures. The timing of post HIIT measurements may have had an effect on results in the study. Participants were tested 72-hours after their final HIIT session. It is unknown if this is the optimum timescale to perform post-testing. Further research is needed to identify the time response of physiological adaptations post HIIT to determine the recovery response.

The researcher acknowledges the limitations of a cross over design due to the potential carry over effect and bias. However, an advantage of a cross over design is that the individual serves as both conditions which could potentially reduce between-subject variability, allowing for a smaller effect size. In addition, a 4-week washout period was selected to ensure adequate time for participants to return to baseline. It is also important to note that a long duration washout period in the experiemental design can diminish the impact of carry over effects. Importantly, no significant difference within and between groups were seen between visit 1 and 3 of the study, indicating sufficient washout. In addition, each participant verbally confirmed that they maintained their usual habits during the study, with the exception of HIIT. It is also important to acknowledge that a 4-week washout period was

adequate for participants to lose the favourable physiological adaptations reported. The finding is in keeping with the training principle of reversibility and reiterates the requirements for a continued exercise stimulus in order to sustain the physiological improvements observed.

The researcher acknolwedges the limitations of not including a placebo in the study design which could provide further understanding to both positive and negative outcomes. It cannot be certain if physiological adaptations were wholly responsible for the results in the present study. However, incorporating a placebo with HIIT is very challenging, considering the aim of a placebo is to provide participants with an intervention, which tastes and feels the same as the tested intervention.

4.5. Conclusions

In the present study, the most important finding was that short-term HIIT induced significant changes in cardiac autonomic function. Given the lower training volume evident in the present study, the results suggest that HIIT is indeed a time-efficient strategy to induce significant changes in autonomic, haemodynamic and aerobic markers of health. This present study provides evidence based research which challenges the current recommended PA guidelines. Additional research is warranted to clarify the mechanisms responsible for these observed changes.

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Chapter 6: Appendices

Appendix 6.0.

Informed Consent

The full details of the test protocol have been explained to me. I am clear about what will be involved and I am aware of the purpose of the tests.

I know that I am not obliged to complete the tests. I am free to stop the test at any point and for any reason.

I understand that the results obtained will be kept confidential and will only be communicated to others such as my tutor if agreed in advance.

As far as I am aware, there is nothing that might prevent me from successfully completing the tests that have been outlined to me.

Signature of Participant: ……..

Signature of Sport Scientist: …….

Date: ……

Appendix 6.1.

Sport Science Health and Fitness Questionnaire.

Name: …….

Date of Birth: …… **Age: ……** **Sex: Male**

Please answer the following questions by ***circling*** the appropriate response and if necessary providing extra information in the spaces provided.

ANY INFORMATION CONTAINED HEREIN WILL BE TREATED AS CONFIDENTIAL

1. How would you describe your present level of fitness?

Untrained / Moderately trained / Trained / Highly trained

2. Average number of hours spent exercising **…….per wk**

3. How would you describe your present bodyweight?

Underweight / Ideal / Slightly overweight / Very overweight

4. How would you describe your smoking habits?

Non smoker / Previous smoker / Currently smoking

5. How would you describe your alcohol intake?

Never Drink / An occasional drink / A drink every day / More than one drink a day

(Note 1 drink = 1 unit)

6. Have you had to consult your doctor within the last six months? **Yes / No**

If you have answered **yes**, please give details:**……..**

7. Are you presently taking any form of medication? **Yes / No**

If you have answered **yes**, please give details: **……**

8. Do you suffer or have you ever suffered from any of the following?

a. Diabetes **Yes / No**

b. Asthma **Yes / No**

c. Epilepsy **Yes / No**

d. Bronchitis **Yes / No**

e. Any form of heart complaint **Yes / No**

f. Serious Back or Neck Injury **Yes / No**

g. High blood pressure **Yes / No**

9. Is there a history of heart complaint in your family? **Yes / No**

If you have answered **yes**, please give details: **……**

10. Do you have any allergies? **Yes / No**

If you have answered **yes**, please give details: **……**

11. Do you currently have any form of muscle or joint injury? **Yes / No**

If you have answered **yes**, please give details: **……**

12. Have you had to suspend your normal training/physical activity in the last two weeks? **Yes / No**

If you have answered **yes**, please give details: **……**