Investigating the Effects of High-Intensity Interval Training on Baroreflex Sensitivity

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ABSTRACT

Cardiovagal baroreflex sensitivity (cvBRS) is known to be influenced by endurance exercise. In fact, endurance exercisers typically display a greater cvBRS compared to sedentary controls. Despite the merits of endurance training, adherence to exercise is a problem for many individuals. High-intensity interval training (HIIT) protocols generally involve less time and work completed while imparting similar cardiovascular responses compared to endurance training. To our current knowledge, the findings of HIIT and cvBRS have been equivocal. This study investigated the effects of 12-weeks of HIIT on cvBRS and the relationship between cvBRS and measures of arterial stiffness in 16 young, healthy males. Following HIIT, cvBRS appeared to be unchanged along with most measures of arterial stiffness (carotid to femoral pulse wave velocity, common carotid artery (CCA) distensibility, and compliance); however, CCA intima-media thickness (IMT) significantly improved. Systolic blood pressure, a major determinant of cvBRS, was unchanged, while resting heart rate appeared to improve following 12-weeks of HIIT. Therefore, these findings suggest that in this sample, 12-weeks of HIIT does not appear to influence cvBRS.

KEY WORDS: cardiovagal baroreflex sensitivity, arterial stiffness, blood pressure regulation, high-intensity interval training, cardiovascular system

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ABBREVIATIONS

AMS	*Artery Management System*
ANOVA	*analysis of variance*
ANS	*autonomic nervous system*
ATRAMI	*autonomic tone and reflexes after MI*
B-mode	*brightness mode*
BMI	*body mass index*
BP	*blood pressure*
BRS	*baroreflex sensitivity*
CAD	*coronary artery disease*
CCA	*common carotid artery*
CSEP	*Canadian Society for Exercise Physiology*
cvBRS	*cardiovagal baroreflex sensitivity*
CVD	*cardiovascular disease*
d_{max}	*maximal diameter*
d_{min}	*minimal diameter*
DBP	*diastolic blood pressure*
DICOM	*Digital Imaging and Communications in Medicine*
ECG	*electrocardiogram*
FFT	*fast Fourier transform*
FM	*fat mass*
HBP	*high blood pressure*
HF	*high frequency*
HIIT	*high-intensity interval training*
hr	*hour*
HR	*heart rate*
HR_{max}	*heart rate maximum*
HR_{peak}	*heart rate peak*
HRV	*heart rate variability*
Hz	*Hertz*
ICC	*intraclass correlation coefficient*
IMT	*intima-media thickness*
kg	*kilogram*
LD	*lumen diameter*
LF	*low frequency*
LM	*lean mass*
MAP	*mean arterial (blood) pressure*
MI	*MI*
min	*minute*
ml/kg/min	*millilitres per kilogram per minute*
mM	*millimolar*
mmHg	*millimetres of Mercury*
ms	*millisecond*
PP	*pulse pressure*

PPO	*peak power output*
PTT	*pulse transit time*
PWV	*pulse wave velocity*
RER	*respiratory exchange ratio*
RHR	*resting heart rate*
RRI	*R-R interval*
SBP	*systolic blood pressure*
SLR	*simple linear regression*
SV	*stroke volume*
VO_2	*volume of oxygen consumption*
VO_2max	*maximal volume of oxygen consumption*
VO_2peak	*peak volume of oxygen consumption*
W	*Watt*

CHAPTER I: INTRODUCTION

1.1. PREAMBLE

Baroreceptors are stretch-sensitive mechanoreceptors that modulate sympathetic and parasympathetic (vagal) activity. Arterial baroreceptors, which are located in the aortic arch and carotid sinus, respond to acute changes in vessel distension caused by changes in blood pressure (BP) on a beat-by-beat basis (La Rovere et al. 2008). This pathway, known as the arterial baroreflex, regulates BP by adjusting cardiac vagal and sympathetic outflow. Therefore, arterial pressure is a highly regulated cardiovascular variable (Colombari et al. 2001) and the arterial baroreflex is an important determinant of cardiovascular neural regulation (La Rovere et al. 2011).

The cardiovagal baroreflex is one arm of the arterial baroreflex that elicits reflexive alterations in R-R interval (RRI) in response to changes in BP. The sensitivity of the cardiovagal baroreflex (cardiovagal baroreflex sensitivity; cvBRS) is a measure of autonomic nervous system (ANS) function, and is defined as the change in RRI (ms) per unit change in BP (mmHg) (Swenne 2013). More specifically, cvBRS is determined as the slope of the linear portion of the sigmoidal relationship between RRI and BP (Parlow et al. 1995, Zamir et al. 2014). cvBRS is therefore a measure of how efficient the cardiac baroreflex is in modulating heart rate (HR). cvBRS has been implicated in many cardiovascular diseases (CVD). A reduced cvBRS, for example, is associated with an increased risk of cardiac mortality and sudden cardiac death in post myocardial infarction

(MI) and heart failure patients (Maestri et al. 1998, La Rovere et al. 2001). As well, cvBRS is reduced in those with hypertension (Lage et al. 1993), diabetes mellitus (Frattola et al. 1997), obesity (Chobanian et al. 2003), and older adults (Madden et al. 2010). Similarly, arterial stiffness has been linked to CVD (Benetos et al. 2002, Laurent et al. 2006), hypertension (Guimarães et al. 2010), diabetes (Vlachopoulos et al. 2010), obesity (Nordstrand et al. 2011, Strasser et al. 2015) and has been shown to also increase with age (Benetos et al. 2002, O'Rourke et al. 2002, Vlachopoulos et al. 2010, Adji et al. 2011). In fact, a mechanistic link between cvBRS and arterial stiffness has been explored (Lipman et al. 2002). Lipman et al. (2002) observed that cvBRS and carotid artery distensibility, a measure of arterial elasticity and the inverse of arterial stiffness, demonstrates a strong inverse relationship regardless of age. In fact, the data from Lipman et al. (2002) demonstrates that a relationship between increased arterial stiffness and decreased cvBRS exists even in healthy middle-aged individuals, suggesting that vascular stiffening exerts a large influence on cvBRS.

Several factors, such as endurance exercise, have been shown to augment cvBRS (Halliwill et al. 1996, Monahan et al. 2000, Madden et al. 2010). Studies have addressed the beneficial impact of regular endurance exercise on ANS function. For instance, habitual rowers display a greater cvBRS compared to sedentary controls (Cook et al. 2006). Regular endurance exercise as an intervention has been shown to attenuate age-related reductions in cvBRS (Monahan et al. 2000, 2001), as well as partially restore the loss of cvBRS in healthy but previously sedentary middle-aged and older men (Monahan et al.

2000). Likewise, three months of regular vigorous endurance training demonstrated an increase in cvBRS in older adults with type 2 diabetes, hypertension, and hypercholesterolemia (Madden et al. 2010). Yet, despite the merits of endurance training, not many individuals have the time or motivation to partake in long endurance training sessions. Hence, high-intensity interval training (HIIT) may be regarded as an alternate, more time efficient strategy.

HIIT is defined as short, repeated bursts of vigorous exercise at an intensity greater than the anaerobic threshold (Laursen and Jenkins 2002) separated by periods of rest or low-intensity exercise (Gibala et al. 2012, Gillen et al. 2013). This type of training has consistently demonstrated similar improvements or changes in physiological responses as endurance training (Burgomaster et al. 2005, Gibala et al. 2006, Rakobowchuk et al. 2008, 2009, Little et al. 2010, Hood et al. 2011, Tjønna et al. 2013, Gillen et al. 2013, Gillen and Gibala 2014, Skelly et al. 2014) such as improved peripheral vascular structure and function in healthy men and women (Rakobowchuk et al. 2008, 2009), reduced arterial stiffness in hypertensive patients (Guimarães et al. 2010), favourable changes in body composition and muscle oxidative capacity in overweight and obese women (Gillen et al. 2013), and decreased resting HR in MI patients (Moholdt et al. 2012). HIIT doesn't appear to influence BP (Ciolac et al. 2010); however, ANS function by measure of heart rate variability (HRV) in MI patients has been shown to be improved (Munk et al. 2010). Nevertheless, ANS function by measure of cvBRS is equivocal (La Rovere et al. 2008) and this may be due to both the time of measurement and the measurement technique used.

The importance of measuring cvBRS in response to HIIT is its ability to reflect changes in cardiovascular health (La Rovere et al. 2008), combined with the merits of HIIT in terms of time efficiency. The current Canadian physical activity guidelines suggest that an adult aged 18 – 64 years should accumulate at least 150 minutes of moderate-intensity physical activity per week, in bouts of 10 minutes or more (Tremblay et al. 2011). However, a recent study evaluating public awareness of the Canadian physical activity guidelines for adults was reported to be as low as 12.9% (Dale et al. 2016). Despite the limitations in sample size and underrepresentation of males, the percentage of awareness was attributed to a lack of knowledge transfer and dissemination of the guidelines. Thus, in addition to one of the most cited barriers to exercise being a 'lack of time' (Trost et al. 2002), another barrier to exercise appears to be the lack of awareness of the current guidelines.

Despite a lack of time or awareness of guidelines, a growing body of evidence suggests that HIIT may be the most effective strategy for improving fitness and health (Gillen and Gibala 2014). Furthermore, the physiological benefits of HIIT are numerous and comparable to traditional moderate-intensity endurance exercise (Burgomaster et al. 2005, Gibala et al. 2006, Rakobowchuk et al. 2008, 2009, Little et al. 2010, Hood et al. 2011, Tjønna et al. 2013, Gillen et al. 2013, Skelly et al. 2014). It is speculated that the high-intensity requirements of this type of training can stimulate the same changes induced by slower, more traditional endurance exercise training, in a shorter time span (Gillen and Gibala

2014). Thus, because ANS function plays a key role in cardiovascular regulation, investigating the merits of HIIT on cvBRS is warranted.

1.2. RATIONALE

Traditional endurance exercise training has many benefits with regards to improving fitness (Nalcakan 2014), reducing CVD risk (Donnelly et al. 2009), BP regulation (Cornelissen and Fagard 2005), and modulating ANS function (Carter et al. 2003). However, adherence to exercise is a problem for many individuals (Allen and Morey 2010). Given that HIIT protocols generally involve less time and work compared to traditional endurance training, examining whether a more time efficient exercise has beneficial effects on ANS function is viable.

1.3. OBJECTIVE

The purpose of this investigation was to determine whether there are favourable improvements in ANS function by measuring cvBRS in response to a 12-week HIIT stimulus. ANS function was assessed by cvBRS in a group of young, healthy males independent of BP and body composition indices. Furthermore, cvBRS was investigated non-invasively using transfer function analysis.

1.4. HYPOTHESIS

First, we hypothesized that cvBRS will improve following 12-weeks of HIIT independent of changes in BP and body composition indices. Second, we hypothesized that improvements in cvBRS will be concordant with improvements in central arterial stiffness.

CHAPTER II: LITERATURE REVIEW

2.1. PHYSIOLOGY OF THE BAROREFLEX

2.1.1. ANATOMY OF THE ARTERIAL BAROREFLEX

The largest branch extending from the arch of the aorta, the arteria innominata or innominate artery, gives rise to the right common carotid artery (CCA), which lies behind the right sternoclavicular articulation (Gray 2000). The highest point of the arch of the aorta gives rise to the left CCA, which is longer and deeper relative to the right CCA. Each vessel passes obliquely upwards from behind the sternoclavicular articulation to the upper border of the thyroid cartilage, beyond which, the CCAs split into the external and internal carotid arteries. It is at the origin of the internal carotid arteries where the carotid sinus is found, the location of numerous sensory components of the baroreflex known as arterial baroreceptors. These sensory components are also located in the heart, aortic arch, great veins and blood vessels of the lungs (Fadel and Raven 2012).

The arterial baroreflex is crucial in maintaining homeostasis through neural regulation of the cardiovascular system (La Rovere et al. 2011, 2013) Small branches of cranial nerve X, the vagus nerve, transmit afferent signals from the aortic baroreceptors, while the Hering nerve (a branch of cranial nerve IX, the glossopharyngeal nerve) transmits carotid baroreceptor afferent signals. Although the aortic and carotid baroreceptor afferent signals originate and travel using different cranial nerves, both converge within the nucleus tractus solitarius of the

medulla oblongata in the brainstem (Fadel and Raven 2012), the primary site of cardiorespiratory reflex integration (Colombari et al. 2001).

The neural signals that regulate the baroreflex can be classified into two groups: (1) afferent signals, nerve impulses that travel *toward* the central nervous system from sensory organs or receptors; and (2) efferent signals, nerve impulses that travel *away* from the central nervous system to effector organs or receptors. Baroreceptors regulate sympathetic and vagal neural activity through afferent signaling achieved through conformational changes. It is for this reason that baroreceptors are often grouped together within the class of mechanoreceptors known as stretch receptors, as their stimulation is a result of distortion. Arterial wall deformation manifested from arterial pressure changes result in baroreceptor stimulation, altering both sympathetic and vagal activity that act to adjust cardiovascular parameters such as HR, contractility, and vascular resistance (La Rovere et al. 2011). As a result, the arterial baroreceptors primarily function as a feedback loop, reflexively responding to beat-by-beat changes in BP (Tzeng 2012).

Cardiovascular adjustments are necessary in order to maintain mean arterial blood pressure (MAP). The interplay between the sympathetic and vagal nervous systems allow for appropriate changes to be made in order to regulate MAP. For instance, with a rise in BP, the baroreceptors are stretched increasing the rate of afferent signaling, which results in a reflex-mediated decrease in sympathetic nerve activity and an increase in vagal activity. This translates into a reduction in HR and vascular dilation to reduce BP. Conversely, with a drop in

BP, the baroreceptors decrease the rate of afferent signaling. As a result, there is a reflex-mediated increase in sympathetic nerve activity and decrease in vagal activity. Therefore, there is an increase in HR and vascular constriction to raise BP. This rapid reflex mechanism is done in accordance to maintain MAP and offers protection to the heart against arrhythmias (Swenne 2013).

2.2. CARDIOVAGAL BAROREFLEX SENSITIVITY

Cardiovagal baroreflex sensitivity (cvBRS) is a measure of ANS function and is defined as the change in interbeat interval, or RRI (ms), per unit change in BP (mmHg) (Swenne 2013). cvBRS is an integrated measure of the ability of the baroreflex to control HR on a beat-by-beat basis through vagal activity (La Rovere et al. 2008). It can be further separated into a mechanical and neural component. The mechanical component can be described as the transduction of arterial pressure into barosensory stretch, thereby activating the baroreceptors (Hunt et al. 2001). In contrast, the neural component can be described as the transduction of barosensory stretch into autonomic outflow, thereby modulating vagal activity to the heart (Hunt et al. 2001). In this way, integrated cvBRS is quantified as each unit change in RRI per unit change in BP.

The Oxford and modified Oxford techniques have been previously employed to measure cvBRS through pharmacologically-induced perturbations in BP. Intravenous doses of vasopressor agents, substances that evoke a change in BP through vasoconstriction and/or vasodilation, allow for a linear relationship between systolic blood pressure (SBP) and RRI to be plotted, the slope representing cvBRS (La Rovere et al. 2008). However, as these techniques are

invasive and involve the administration of vasoactive drugs like sodium nitroprusside and phenylephrine hydrochloride, it will not be considered as a suitable method of cvBRS measurement for this study. Therefore, a noninvasive spontaneous measurement of cvBRS using spectral analysis will be explored.

Unlike the invasive Oxford and modified Oxford techniques, noninvasive spontaneous methods rely on spontaneously occurring fluctuation in SBP and RRI to measure cvBRS. One such method is the spectral method, which uses transfer function to exploit the assumption that parallel oscillations in SBP and RRI are mediated by the cardiac baroreflex (Diaz and Taylor 2006). Beat-by-beat BP and RRI are usually collected for a period of five minutes and converted from a time to frequency domain measurement using the Fast Fourier Transform (FFT). FFT separates the signals into both low frequency (LF; 0.04 – 0.15 Hz) and high frequency (HF; 0.15 – 0.40 Hz) spectra. cvBRS is computed as the average transfer function gain between the spectra of SBP and RRI in the LF range, which reflects baroreflex modulation (Bonyhay et al. 2013). Furthermore, only SBP and RRI oscillations that have a coherence of 0.5 or greater are selected to ensure reliability (Saul et al. 1991).

2.2.1. THE VALUE OF CARDIOVAGAL BAROREFLEX SENSITIVITY

A key study in the determination of the prognostic value of cvBRS was the multicenter Autonomic Tone and Reflexes After MI (ATRAMI) study. The objective was to provide a prognostic predictive value of cvBRS for cardiac mortality in post-MI patients within whom left-ventricular ejection fraction and ventricular arrhythmias were known (La Rovere et al. 1998). The ATRAMI

research team revealed that a low cvBRS (<3.0 ms/mmHg) contributes to a high risk of cardiac mortality after a MI. More specifically, a low or impaired cvBRS was associated with an altered autonomic balance characterized by high sympathetic activity (sympathetic overdrive) and low vagal activity, a coupling often termed sympathetic predominance. In fact, an impaired cvBRS is common in many CVD and related risk-factor states (La Rovere et al. 2008). For instance, physical inactivity/deconditioning (Hughson and Shoemaker 2015), adult obesity (Chobanian et al. 2003), dyslipidemia (Grigoropoulou et al. 2014), metabolic syndrome (Thorp and Schlaich 2015), type 2 diabetes (Frattola et al. 1997, Madden et al. 2010, Grigoropoulou et al. 2014), hypertension (Lage et al. 1993, Madden et al. 2010), and hypercholesterolemia (Madden et al. 2010), all have been shown to display impaired cvBRS. Therefore, reducing sympathetic predominance overdrive and improving the protective vagal flow is favourable.

The most important correlates of cvBRS have been determined to be age and BP (La Rovere et al. 2008). In addition, arterial stiffening is an important determinant as it is related to BRS (Lipman et al. 2002), as well as increasing SBP, pulse pressure (PP) and decreasing diastolic blood pressure (DBP) in our ageing community (O'Rourke et al. 2002). As such, the loss of arterial elasticity and associated increase in arterial stiffness is regarded as the main determinant of BRS reduction with age (La Rovere et al. 2008). Furthermore, the ATRAMI study determined that as age increases, vagal activity decreases and cvBRS was a powerful indicator of cardiac mortality below the age of 65 (Schwartz and La Rovere 1998). In relation to this thesis, although our population is young, healthy

and without a previous MI, the ATRAMI study supports our use of cvBRS as a powerful marker of ANS function.

2.3. BAROREFLEX DYNAMICS DURING EXERCISE

Endurance exercise is identified as any activity that elevates HR to 60 – 80% of maximum, for at least 20 minutes in duration (Carter et al. 2003). Various physiological systems govern the response to endurance exercise and can be categorized into neural and local factors. Neural factors include: (1) central command, (2) the muscle metaboreflex (exercise pressor reflex), and (3) the arterial baroreflex. Local factors include the endogenous chemical factors involved in peripheral vasoconstriction and vasodilation, namely acetylcholine and norepinephrine.

Central command involves the activation of regions in the brain responsible for skeletal muscle motor unit recruitment. At the same time, the medulla is responsible for changes in the balance of sympathetic and vagal efferent activity which dictates increases in HR, myocardial contractility and peripheral vasoconstriction at the onset of exercise (Iellamo 2001, Carter et al. 2003). The muscle metaboreflex, or exercise pressor reflex, involves the afferent neural signals sent to the medulla resulting from the contracting skeletal muscle via stretch (mechanoreceptors) and metabolic by-products (chemoreceptors) (Carter et al. 2003). The arterial baroreflex involves the rapid reflex adjustment of arterial BP via baroreceptor signaling to maintain homeostasis. Examination of central command, the muscle metaboreflex, and local factors fall outside the scope of this proposal. Therefore, we will only focus on the arterial baroreflex;

however, as the other mechanisms are highly related, they will be mentioned as needed.

During exercise, the dynamics of the baroreflex loop are puzzling. There is a complex interplay between central command and the muscle metaboreflex (Fadel and Raven 2012). It is well known that HR and BP increase in parallel at the onset of dynamic exercise. However, this is in contradiction to the negative feedback system characteristic of the arterial baroreflex. Mancia et al. (1978) suggested that the arterial baroreflex was "switched off" during exercise in order to elicit the appropriate neural and cardiovascular responses (Mancia et al. 1978). However, we now know that the baroreflex functions normally during exercise as it does during rest. In fact, as described in a recent review (Fadel and Raven 2012), the baroreflex is considered to "reset" as shown in exercising dogs and leg cycling in humans. The cvBRS has been found to shift upward and rightward during exercise, which allows the baroreflex to operate normally and efficiently at progressively increasing BPs during exercise (Fadel et al. 2003, Raven et al. 2006) and is achieved primarily through vagal withdrawal rather than an increase in sympathetic activity (Ogoh et al. 2005). Thus, if cvBRS was measured during exercise, it would appear that the sensitivity is unchanged compared to rest.

The most recent hypothesis describes that the resetting of the baroreflex acts to restrain the BP response to exercise (Fadel and Raven 2012). Resetting occurs in an intensity-dependent manner by buffering the progressive increases in sympathetic nervous system activation resulting from the activation of both central command and muscle metaboreflexes, in order to maintain baroreflex

function (Fadel and Raven 2012).The significance of maintaining baroreflex function is seen quite clearly in pathology. For example, an impaired arterial baroreflex cannot maintain the appropriate neural and cardiovascular responses required by exercise, often resulting in an augmented BP response. This results in insufficient buffering of sympathetic nervous system activation, leading to uncontrolled vasoconstriction in the exercising skeletal muscle, limiting perfusion requirements, and likely causing the onset of muscle ischemia (Joyner 2006).

The arterial baroreflex also operates differently in response to exercise intensity. High-intensity endurance exercise shifts the autonomic balance towards sympathetic predominance from vagal predominance (Iellamo et al. 2002). This may seem counterintuitive, as sympathetic predominance is associated with detrimental and negative cardiovascular conditions; however, this phenomenon appears to be beneficial for endurance athletes who are training towards a peak performance. In one particular study, Iellamo et al. (2002) examined the autonomic profile of world class rowers over nine months before a world championship event. Measurements were collected over four time points: baseline, three months (75% training load), six months (75% training load), and nine months (100% training load), which was 20 days before the world championship event. Progressive bradycardia was seen as training load increased from baseline to 75% training load (months three and six of training) (56 beats/min, vs. 50 beats/min, $p < 0.01$), concordant with an increase in HF-RRI variability, and a decrease in LF-RRI variability and LF-HF ratio. Likewise,

cvBRS increased from baseline to 75% training load (26.3 ms/mm Hg vs. 32 ms/mm Hg), however this was nonsignificant.

At nine months (100% training load) opposite effects were observed. There was a relative increase in HR compared to baseline (56 beats/min vs. 61 beats/min, $p < 0.01$), concordant with a significant decrease in HF-HRV, and an increase in LF-HRV and LF-HF ratio compared to baseline. cvBRS also significantly decreased at 100% training load compared to baseline (15.5 ms/mmHg vs. 26.3 ms/mmHg, $p < 0.01$). Therefore, at 100% training load, a shift towards sympathetic predominance was seen as cvBRS was significantly reduced concordant with changes in HRV and HR. The apparent switch from vagal to sympathetic predominance in high-performance athletes was a unique finding with regards to exercise and ANS function. In fact, the negative connotation associated with sympathovagal imbalance may be simply a transient high-intensity exercise training adaptation. In fact, Iellamo et al. (2002) suggested that this phenomenon reflects an optimal state for increasing athletic performance.

2.3.1. ENDURANCE EXERCISE TRAINING & PHYSIOLOGICAL ADAPTATIONS

Physiological adaptations to endurance training have been well established and include increased total body maximal oxygen consumption (VO_2max) (Karlsson et al. 1974, Rowell 1974, Henriksson and Reitman 1977, Hoppeler et al. 1985, Shi et al. 1995, Amano et al. 2001, Moriguchi et al. 2005), improved maximal sustainable power output and work capacity (Karlsson et al. 1974, Gollnick and Saltin 1982, Hoppeler et al. 1985), increased capillary density

(Brodal et al. 1977, Hoppeler et al. 1985) and capillary-to-muscle fibre ratio (Hoppeler et al. 1985), increased mitochondrial density and volume of mitochondria per volume of muscle fibre (Hoppeler et al. 1973, 1985), increased skeletal muscle oxidative enzyme activity (Kiessling et al. 1974, Henriksson and Reitman 1977), improved fat metabolism (greater fat oxidation) (Karlsson et al. 1974, Henriksson and Reitman 1977), and improved muscle glycogen sparing attributes (reduced muscle glycogen utilization, depletion and lactate production) (Karlsson et al. 1974, Henriksson and Reitman 1977). Long-term endurance training has also been known to induce positive changes in body mass and body mass management (Houmard et al. 1993, Amano et al. 2001, Donnelly et al. 2009), improved glucose transporter type 4 (Houmard et al. 1993) and insulin action (Houmard et al. 1993, Duncan et al. 2003, Bradley et al. 2008), an improved lipoprotein profile (Moriguchi et al. 2005), as well as improved endothelial function in individuals with a high-risk for CVD (Lavrencic et al. 2000, Green et al. 2004, Vona et al. 2004). Improved endothelial function has also been reported in post-menopausal women (Swift et al. 2012) and hypertensive individuals (Moriguchi et al. 2005) following endurance training.

2.3.1.1. ENDURANCE TRAINING AND CARDIOVAGAL BAROREFLEX ADAPTATIONS

Two of the most prominent findings with endurance training in respect to ANS function is the increase in vagal activity and decrease in sympathetic activity to the heart at rest (Carter et al. 2003), as well as the reduction in resting HR (training-induced bradycardia) (Yamamoto et al. 2001). In fact, Yamamoto et al.

(2001) reported a reduction in resting HR as high as 28% (68.1 ± 3.7 to 53.2 ± 2.8, $p < 0.05$) in response to a six week endurance training program when compared to sedentary controls. In addition, the measurement of HRV suggested enhanced cardiovagal activity. Yamamoto et al. (2001) speculated that the cardiovagal improvement contributed to the observed training-induced bradycardia; however, findings from Scott et al. (2004) suggested that enhanced cardiovagal activity does not explain training-induced bradycardia alone, even in endurance trained athletes (Scott et al. 2004). Despite the presence of bradycardia in athletes compared to controls, Scott et al. (2004) determined that HRV was similar between groups, suggesting that any training-induced bradycardia is likely due to intrinsic HR adaptations.

During a single bout of endurance exercise, Raczak and colleagues (2005) found that mild exercise (defined as 30 minutes of treadmill exercise training at 65% maximum HR) increased cvBRS measured by transfer function analysis post-exercise (11.8 ± 6.1 to 16 ± 7.8 ms/mm Hg, $p = 0.034$). cvBRS measured by an intravenous bolus of phenylephrine also increased post-exercise (16 ± 8.8 to 21.9 ± 9.3 ms/mm Hg, $p = 0.022$). These findings suggest that even a single short session of mild/moderate-intensity exercise can improve baroreflex function in a group of young healthy, sedentary males. Furthermore, this study was unique in that there was a significant increase in both the invasive (phenylephrine) and noninvasive (spectral) methods of measuring cvBRS. Utilization of both techniques allowed for the investigation of BRS under different physiologic

conditions. The positive change in cvBRS was attributed to an increase in vagal tone (Raczak et al. 2005).

Likewise, Halliwill et al. (1996) found that immediately following a single bout of moderate-intensity exercise (60 minutes of cycling at 60% VO_2peak), cvBRS was augmented (4.7 ± 0.7 to 6.1 ± 0.9 ms/mmHg, $p < 0.05$). However, despite the attribution to increases in vagal tone reported by Raczak et al. (2005), Halliwill et al. (1996) observed that MAP was reduced for up to 75 minutes (86 ± 2 to 81 ± 2 mmHg, $p < 0.05$) while HR stayed elevated for up to 30 minutes post-exercise ($p < 0.05$). Stroke volume (SV) and spectral analysis of tonic cardiac vagal control revealed no changes. As well, because HR was elevated and estimated vagal tone was unchanged, it was speculated that sympathetic activity remained elevated. The post-exercise increase in plasma norepinephrine (253 ± 23 to 1591 ± 262 pg/ml, $p < 0.05$) along with a consistent SV, despite an increased HR, provides further support. These results suggest that the augmented baroreflex response may be working against the induction of post-exercise hypotension (Halliwill et al. 1996).

Hart et al. (2010) reported similar findings in BP, despite both the intensity (low) and modality of exercise (rowing) being different. Post-exercise (four hours of ergometer rowing at 10 – 15% below the individuals lactate threshold), left ventricular systolic and diastolic function decreased. Correspondingly, MAP was reduced (98 ± 4 to 86 ± 4 mmHg, $p < 0.05$), while HR remained elevated (60 ± 2 to 81 ± 1 beats/min, $p < 0.05$) and cvBRS did not change. Therefore, it appears that differing intensities and duration of exercise

need to be investigated as intensity may influence the acute response of cvBRS to exercise. Both Raczak et al. (2005) and Halliwill et al. (1996) observed increases in sensitivity following a single bout of moderate-intensity endurance exercise, whereas Hart et al. (2010), who utilized an exercise protocol that was largely low-intensity, showed no change in cvBRS.

The effects of regular low- versus high-intensity endurance exercise training in sedentary middle-aged males (aged 35 – 55 years) over a period of five months has been investigated (Loimaala et al. 2000). Low-intensity exercise was described as walking or jogging four to six times per week at a HR corresponding to 55%VO_2max. High-intensity exercise was described as jogging four to six times per week at a HR corresponding to 75%VO_2max. In contrast, the control group had no supervised exercise sessions during the intervention and was allowed a maximum of two exercise sessions per week. Following the exercise intervention, HR decreased significantly from pre- to post-exercise only in the high-intensity group (-6 beats/min). VO_2max also significantly increased only in the high-intensity group compared to the control group (+2.4 ml/kg/min). There were non-significant changes in measures of cvBRS and HRV in all three groups (control, low-intensity and high-intensity groups). These results suggest that, despite an improvement in fitness, five months of endurance training at either a low- or high-intensity did not have a significant effect on cardiac autonomic function. However, in light of the lack of significance, changes in BRS and HRV were trending toward higher values in the high-intensity group compared to

controls, further suggesting that intensity may influence how cvBRS responds to exercise.

Compared to Loimaala et al. (2000), Monahan et al. (2000) conducted a two-part study to observe the effects of regular endurance exercise in age-associated declines in cvBRS. In the first cross-sectional study, cvBRS was not associated with physical activity status among young men, but was similar between the young and middle-aged men in the moderate exercise and endurance-trained groups. In contrast, when compared to their age-matched sedentary peers, middle-aged and older men who were either endurance trained or regularly participated in moderate-intensity endurance exercise, displayed a greater cvBRS ($p < 0.05$). These findings suggest that cvBRS is maintained in middle-aged and older men who regularly participate in moderate-intensity endurance exercise. In the second study, a three-month endurance exercise intervention in 13 middle-aged and older men (56 ± 1 years) resulted in an increase in cvBRS of ~25% (7.9 ± 0.8 to 9.8 ± 0.9 ms/mm Hg, $p < 0.05$), a reflection that the exercise prescription was effective in attenuating the age-related decline in cvBRS. Taken together, these two studies demonstrate that regular endurance exercise training can improve cvBRS in previously sedentary middle-aged and older men (Monahan et al. 2000).

In support of Monahan et al. 2000, long-term endurance training has been associated with increases in vagal activity and decreases in sympathetic activity. Sympathetic and vagal activities were favourably altered in response to 12-weeks of endurance training in 18 middle-aged obese men and women who trained three

times per week for 30 minutes per session (Amano et al. 2001). Similarly, a cross-sectional sample of 80 young/middle-aged males and females displayed augmented vagal and reduced sympathetic indicators in the trained (defined as being physically active for <45 min/day at least 5 days/week) versus untrained group (Gregoire et al. 1996). In eight young men, eight months of endurance training (45 minutes of walking/jogging, four times per week, at HR ~1% below their anaerobic threshold) significantly decreased resting HR and increased vagal tone (Shi et al. 1995). The difference in resting HR was abolished with a selective vagal blockade (atropine), as well as combined vagal and β_1-receptor blockade (atropine and metoprolol). In contrast, the difference remained apparent with β_1-receptor blockade only (Shi et al. 1995). The results of Shi and colleagues (1995) suggest that eight months of endurance training increases the dominance of vagal control of HR.

Finally, ANS adaptations from long-term endurance training was investigated between athletes and non-athletes in response to a dynamic exhaustive exercise test (Shin et al. 1995). Both groups displayed attenuated LF and HF spectral markers of HRV during exercise. However, in the athlete group (endurance training for a period longer than three years), the lower resting and rapid recovery of HR post-exercise was attributed to their relatively higher HRV compared to non-athletes. Therefore, the enhanced vagal activity was a result of adaptive neural changes produced by long-term endurance training.

2.4. ARTERIAL STIFFNESS

Arterial stiffness is a general term that describes the changes in the mechanical properties of the arterial tree and its elasticity. Specifically, arterial stiffness refers to the decreased capacity of a vessel to distend in response to increases in pressure or volume. Pathologically, arterial stiffness is one of the earliest detectable signs of changes within the structural and cellular components of the vessel wall, resulting in functional changes (Cavalcante et al. 2011).

Arterial stiffening occurs naturally within the arterial tree, and increases with increasing age (Lee and Oh 2010). In fact, within young, healthy individuals, there is a certain degree of heterogeneity of stiffness. As PP's are amplified throughout the arterial tree, a natural stiffness gradient is created, which results in more elastic central arteries and stiffer peripheral arteries (Koelwyn et al. 2012). However, despite the presence of a natural gradient in young, healthy individuals, age-related arterial stiffening tends to affect the central arteries more (aorta and carotid) while sparing peripheral arteries. The amplification of stiffness in the central arteries with age is largely attributed to changes in the balance of elastin and collagen, the structural proteins in the vascular wall (Zieman et al. 2005).

Elastin fibers are predominantly located within the intimal and medial layers of the arterial wall. The two layers are separated from each other by fenestrated elastin fibres of the internal elastic lamina (Kohn 2015). The media is composed of vascular smooth muscle cells, collagen fibres, a mucopolysaccharide viscoelastic gel, along with the presence of elastin (Stary et al. 1992). In contrast to the intimal and medial layers, the adventitia, the outermost layer of the arterial

wall, is composed mainly of circumferentially arranged collagen fibrils intermixed with elastin, surrounded by loose but supportive connective tissue (Kohn 2015). As such, there are distinct layer-specific properties present in the arterial wall, with differing load-bearing properties, and different mechanical properties with varying levels of deformation (Kohn 2015). For example, at low levels of deformation, elastin dominates the mechanics, whereas at higher levels, elastin displays significantly less load-bearing capabilities (Schriefl et al. 2012). The load bearing is shifted towards the high tensile strength of collagen intermixed with elastin, which serves to allow for both distension, but also protection against rupture (Kohn 2015).

A balance of elastin and collagen maintain the integrity of the vascular wall through dynamic processes of production and degradation (Zieman et al. 2005). When this balance is offset, elastin content tends to diminish while collagen is overproduced (Johnson et al. 2001), which may contribute to the development and progression of vascular stiffness (Zieman et al. 2005). Arterial stiffening is thought to occur by the fragmentation of elastin and accumulation of collagen in the medial and adventitial layers of the artery wall (Zieman et al. 2005). In this way, the artery becomes more rigid and is less likely to distend. Central artery stiffening is also associated with increased luminal pressure, inflammation, hypertension, as well as extrinsic factors including hormones, salt, and glucose regulation (Zieman et al. 2005).

Since arterial stiffness is associated with a myriad of CVDs (Benetos et al. 2002, O'Rourke et al. 2002, Laurent et al. 2006, Guimarães et al. 2010,

Vlachopoulos et al. 2010, Adji et al. 2011, Nordstrand et al. 2011, Strasser et al. 2015), several surrogate markers and estimations have been designed and implemented which include invasive methods, such as intravascular ultrasound, as well as non-invasive methods such as surface ultrasound imaging and pulse wave velocity (PWV). In regards to non-invasive methods, ultrasonography is a common tool utilized in the assessment of local arterial wall elasticity (Koelwyn et al. 2012). The elasticity can be gauged by calculating arterial compliance, the change in arterial cross-sectional area for a given change in PP, and arterial distensibility, which is arterial compliance normalized to diastolic diameter. In regards to PWV, applanation tonometry is a technique used to non-invasively assess local PP waveforms with a high fidelity strain gauge transducer to approximate regional arterial stiffness (Koelwyn et al. 2012). Measurement of PWV with applanation tonometry is measured as the physical distance between the common carotid artery and femoral artery measurement sites divided by the pulse transit time, defined as the time delay between the arrival of the pulse wave between the two arterial sites (Koelwyn et al. 2012). Carotid to femoral (aortic) PWV is currently considered the gold standard for the non-invasive measurement of arterial stiffness.

2.4.1. VALUE OF ARTERIAL STIFFNESS

Arterial aging is a degenerative process primarily caused by the fragmentation of elastin fibres (Nichols and O'Rourke 2005). Although arteries stiffen naturally with age (Tanaka et al. 2000), there is a significant relationship between ageing, increased BP (Wang et al. 2010), and CVD (Benetos et al. 2002).

Indeed, the progressive stiffening of arteries over a lifetime impart crippling effects on cardiac metabolism and function (Nichols and O'Rourke 2005). As such, age is often considered a primary risk factor for CVD (Benetos et al. 2002). Causes of normal age-related arterial stiffening include changes in collagen and elastin, the structural proteins of the arterial wall (Kohn 2015). As elastin fibres become fragmented, they shift their load-bearing capacity onto the stiffer collagen fibres, which is thought to increase arterial stiffness (Kohn 2015). Fragmentation of elastin has been attributed to the exposure of pulsatile wall stress over a lifetime (Greenwald 2007). Taken together, the structural change incurred over the vascular tree is known as arterial remodeling.

Overweight and obesity are known independent risk factors for CVD morbidity and mortality (Chobanian et al. 2003), atherosclerosis-related diseases including coronary artery disease (CAD), MI, and stroke (Barton et al. 2012). Additionally, overweight and obesity are considered risk factors in accelerated, premature vascular aging (Barton et al. 2012). Arterial stiffness and its relationship to measures of whole-body fat and visceral obesity appear to be strong in obese middle-aged adults (Strasser et al. 2015). For example, after adjusting for age and sex, Strasser and colleagues (2015) found a significant positive association between carotid to femoral PWV, body mass index (BMI) ($p = 0.005$), waist circumference ($p < 0.0001$), and visceral fat mass ($p < 0.0005$) (Strasser et al. 2015). Likewise, distensibility has also been observed to be altered with obesity status (Moore et al. 2013). Moore et al. (2013) conducted a study to examine indices of arterial elasticity in highly obese, middle-aged males and

females. Compared to age- and sex-matched non-obese controls, carotid IMT and distensibility were significantly increased ($p < 0.0002$) and reduced ($p < 0.05$), respectively. Moreover, both carotid IMT and distensibility were significantly correlated with age, SBP, BMI, and waist-to-hip ratio. The findings of Moore et al. (2013) reveal that changes in both carotid IMT and distensibility correspond well with traditional cardiovascular risk factors, which further strengthens the parameters of arterial stiffness as early markers for CVD development.

There is no question that arterial stiffness and increased BP are highly linked. SBP, DBP, and MAP have been shown to be significantly correlated with carotid to femoral PWV in both individuals with and without at least one risk factor for CVD (Amar et al. 2001). BP has also been linked to arterial distensibility. Laurent and colleagues (1994) found that carotid artery distensibility decreased as BP increased in both hypertensive subjects and age- and sex-matched controls (Laurent et al. 1994). Furthermore, increased BP has been noted to be a major determinant of increases in carotid IMT (Puato et al. 2008). Thus, it is clear that BP is a major determinant of arterial stiffness and thickness in the central vessels (O'Rourke 1990).

2.5. ARTERIAL STIFFNESS, BRS, AND ENDURANCE TRAINING

2.5.1. ARTERIAL STIFFNESS & BRS

Arterial stiffness and cvBRS are highly linked, as activation of the baroreceptor-reflex loop is a function of arterial deformation. Baroreflex function is therefore linked to the mechanical properties of vessels at which they are found.

For instance, in order to increase afferent firing of signals from the baroreceptors to the cardiovascular centres in the brain, deformation of the baroreceptor-harbouring vessels must occur. In a way, baroreceptors sense the changes in BP indirectly, by that of wall deformation of barosensitive vessels. Ultimately, changes in afferent signaling transmitted to the central nervous system trigger the appropriate adjustments to buffer or oppose the change in BP in order to maintain homeostasis (Lanfranchi and Somers 2002). Loss of distensibility, or stiffening of barosensitive vessels, has been suggested to limit stretch and relaxation, which affects BP modulation (Mattace-Raso et al. 2007). Therefore, many factors can influence the structural and mechanical determinants of stiffness, all of which directly influence arterial deformation. It would be plausible that anything that results in changes in deformation of a baroreceptor-harbouring vessel would alter the baroreflex loop. Thus, arterial health, and in particular arterial stiffness, is irrefutably a large component of baroreflex function.

Measures of arterial stiffness have been shown to have a strong relationship with cvBRS (Bonyhay et al. 1996, Monahan et al. 2000, 2001, Steinback et al. 2005, Cook et al. 2006). Steinback and colleagues (2005) found that rapid changes in the mechanical properties of the carotid artery elicited by head-up tilt, in particular reductions in carotid artery diameter and carotid artery distensibility, coincide with reductions in cvBRS. Correspondingly, a reduction in maximal carotid artery distensibility following head-up tilt correlated with a reduction in cvBRS ($r = 0.75$, $p < 0.05$).

To further emphasize the importance of arterial stiffness and its relationship to cvBRS, Bonyhay and colleagues (1996) found cvBRS, measured using the invasive Oxford method, to be significantly associated with carotid artery distensibility ($r = 0.78$, $p < 0.001$). In fact, 61% of the variance in cvBRS was explained by the inter-individual variability of carotid artery distensibility. These results suggest that cvBRS is directly related to carotid artery distensibility.

Likewise, cvBRS determined from the noninvasive Valsalva maneuver method has also been found to be significantly related to carotid artery compliance ($r = 0.71$, $p < 0.001$) (Monahan et al., 2001). Among the correlates of percent body fat, DBP, resting HR, and VO_2max, carotid artery compliance was the strongest independent correlate of cvBRS, explaining 51% of the variance, while resting HR accounted for an additional 20% of variance. When carotid artery compliance was accounted for in the relationship between cvBRS and age, age only explained 14% of the variance in cvBRS. When the influence of age was removed from the relationship between cvBRS and carotid artery compliance, the model remained significant ($r = 0.44$, $p < 0.05$). Similarly, Monahan et al. (2001) found carotid artery compliance to be the strongest independent correlate of cvBRS, explaining 36% of the variance ($p < 0.01$) in middle-aged healthy males and females. When the influence of DBP and HR were controlled for, the relationship between cvBRS and carotid artery compliance remained significant ($r = 0.45$, $p < 0.05$). Therefore, these results suggest that cvBRS is strongly related to carotid artery compliance, which is both a function of carotid distensibility and a measure of arterial stiffness.

Higher carotid artery compliance has also been associated with a greater cvBRS in rowers compared to sedentary controls ($r = 0.54$, $p < 0.005$) (Cook et al. 2006). The results of Cook et al. (2006) suggest that habitual exercise has a positive impact on both cvBRS and arterial stiffness.

2.5.2. ARTERIAL STIFFNESS & ENDURANCE TRAINING

Regular moderate-intensity endurance exercise is known to increase central artery elasticity in recreationally active and endurance trained middle-aged and older men (Tanaka et al. 2000, Sugawara et al. 2006) and young, healthy untrained males and females (Rakobowchuk et al. 2008). In post-menopausal women, 12-weeks of moderate- and high-intensity physical activity favourably improved carotid arterial stiffness measured by β-stiffness index (moderate-intensity: 13.5 ± 4.4 to 9.5 ± 4.2, $p < 0.05$; vigorous intensity: 12.3 ± 4.6 to 8.2 ± 3.6, $p < 0,05$), a clinically-used marker of stiffness derived from regional diameters similar to distensibility (Sugawara et al. 2006). The β-stiffness index was also significantly associated with the duration of physical activity (moderate: $r = -0.25$, $p < 0.05$; vigorous: $r = -0.27$, $p < 0.01$) after adjusting for age, height, BMI, and MAP, indicating that the effects of moderate- and high-intensity physical activity do not differ from each other.

Tanaka and colleagues (2000) demonstrated that regular low- to moderate-intensity endurance exercise attenuates age-related increases in central arterial stiffness (carotid artery compliance) in healthy middle-aged and older men (Tanaka et al. 2000). Likewise, high-volume moderate-intensity endurance training has also been shown to improve arterial health by improving peripheral

artery distensibility and endothelial function, a surrogate measure of vascular health in both young, healthy males and females (Rakobowchuk et al. 2008). However in contrast to Tanaka et al. (2000), Rakobowchuk and colleagues found that carotid artery distensibility remained unchanged ($p = 0.29$) (Rakobowchuk et al. 2008). This conflicting finding may possibly be explained by the differences in measurement (carotid artery compliance, an absolute measure, versus carotid artery distensibility, a normalized measure), the sample characteristics, and the modality of exercise. For the latter, Rakobowchuk et al. (2008) utilized a cycling protocol whereas Tanaka et al. (2000) utilized a walking/jogging protocol.

In contrast to the aforementioned positive effects of endurance exercise on a number of arterial stiffness indices, two long-term investigations, the Atherosclerosis Risk in Communities (ARIC) (Schmitz et al. 2001) and the Swiss Cohort Study on Air Pollution and Lung and Heart Diseases in Adults (SAPALDIA) 3 (Caviezel et al. 2015), revealed findings that physical activity and carotid artery distensibility do not necessarily demonstrate a strong association. In a population of males and females aged 45 – 64 years and free of CVD, carotid artery distensibility was not associated with work physical activity ($p = 0.58$), sport physical activity ($p = 0.17$), or leisure physical activity ($p = 0.45$), which all constitute non-vigorous (low- to moderate-intensity) regular physical activity (Schmitz et al. 2001). In previous ARIC publications, regular physical activity was defined as reporting a given sport activity for at least 1 hr/wk for 10 or more months of the past year, while vigorous physical activity was defined as those with an intensity greater than 5 metabolic equivalents (Schmitz et al. 2001).

Likewise, in an a population of males and females aged 50 – 81 years also free of CVD, no association of self-reported physical activity with carotid artery distensibility was observed with moderate-intensity physical activity ($p = 0.45$) and total physical activity ($p = 0.08$) (Caviezel et al. 2015).

In a more clinical population where carotid artery distensibility is known to be significantly reduced, it was unchanged following 16-weeks of endurance training in elderly males with heart failure and preserved ejection fraction compared to controls (Kitzman et al. 2013). The endurance training involved with this study consisted of walking on a track, ergometer cycling, and isolated arm ergometry, for one hour, three times per week at low- to moderate-intensity (<70% heart rate reserve). VO_2max increased substantially from baseline (14.2 ± 2.8 vs. 15.8 ± 3.3 ml/kg/min, $p = 0.0001$) despite the lack of improvement in arterial stiffness, suggesting that physical fitness improvements were largely from microvascular and skeletal muscle adaptations, and not due to improvements in cardiac output and large artery function.

It is possible that for noticeable improvements in carotid artery distensibility, higher intensity exercise rather than low- to moderate-intensity exercise may likely need to be utilized. In fact, while both the ARIC (Schmitz et al. 2001) and SAPALDIA 3 (Caviezel et al. 2015) cohort studies reported a lack of significance between physical activity and carotid artery distensibility, a systematic break down of intensity revealed that carotid artery distensibility was positively associated with only high intensity physical activity.

In the Amsterdam Growth and Health Longitudinal Study, a younger, healthy cohort were examined at eight time points between the ages of 13 and 36 years (van de Laar et al. 2010). Across the age group, participants in the lowest carotid artery stiffness tertile accrued, on average, 25.3 and 31.9 min/wk more high-intensity physical activity compared to participants in the intermediate and highest tertiles, respectively (van de Laar et al. 2010). Multivariate regression analysis revealed that more time spent in habitual physical activity, particularly high-intensity, was favourably associated with all cardiovascular risk factors (MAP, skinfold ratio, total-to-high-density lipoprotein cholesterol ratio, resting HR, sex, height), even after adjusting for lifestyle risk factors (i.e. alcohol consumption, smoking behaviour, and total energy intake). The main results of the Amsterdam Growth and Health Longitudinal Study identified that high-intensity physical activity imparts the greatest beneficial impact on not only carotid artery distensibility, but other measures of carotid artery stiffness as well (van de Laar et al. 2010).

2.5.3. RELATIONSHIP BETWEEN ARTERIAL STIFFNESS, ENDURANCE TRAINING, & BRS

As mentioned, cvBRS is strongly associated with central artery elasticity in healthy, sedentary males (Monahan et al. 2001, Cook et al. 2006). Age is also associated with declines in cvBRS (Bristow et al. 1969, Monahan et al. 2000), but these reductions can be attenuated with regular endurance exercise (Monahan et al. 2000). Monahan et al. (2001) revealed that improvements in cvBRS are strongly associated with corresponding increases in carotid artery compliance

following an endurance exercise intervention, where cvBRS increased 27% (7.8 ± 0.8 to 9.9 ± 0.9 ms/mmHg, $p < 0.01$), and carotid artery compliance increased 29% (1.07 ± 0.09 to 1.38 ± 0.12 × 10^{-2} mm^2/mmHg, $p < 0.01$). These results indicate that reduced central artery elasticity has an important mechanistic role in the age-associated reduction in cvBRS. Thus, interventions that could potentially decrease the stiffness of large elastic arteries may be effective in attenuating age-related reductions in cvBRS. However, given the findings of Schmitz et al. (2001) and Caviezel et al. (2015), it is unclear whether the moderate-intensity endurance training protocol used by Monahan et al. (2001) could improve carotid artery distensibility. Therefore, investigating the relationship between higher intensity endurance exercise on carotid artery distensibility is warranted.

2.5.4. THE ROLE OF EXERCISE INTENSITY

The findings with ANS function, arterial stiffness, and endurance training are mixed, especially when considering the role of exercise intensity. For instance, cvBRS has been observed to improve in younger, healthy individuals (Raczak et al. 2005), and in middle-aged and older sedentary men who partake in a three month moderate-intensity exercise program (Monahan et al. 2000). In contrast, cvBRS did not appear to be improved in sedentary middle-aged men following either a low or high intensity five month endurance training program (Loimaala et al. 2000). However, in the five month endurance training study led by Loimaala et al. (2000), high intensity was defined as 75% VO_2max, despite high-intensity being defined by the American College of Sports Medicine as exercise between 80 to 85% of heart rate max. It is possible that the prescribed

intensity was not enough of a stimulus to exert significant changes in cvBRS; however, this would not explain the findings by Monahan et al. (2000) who reported favourable changes in cvBRS with moderate-intensity exercise. Loimaala et al. (2000) does suggest that the lack of improvement in ANS function could be due to the lack of randomization and differences in measurement protocols.

Results with elite athletes and differing training intensities have also been interesting in terms of sympathetic predominance (Iellamo et al. 2002). Sympathetic predominance has been reported in recreational marathon runners (Manzi et al. 2009). In the studies by Halliwill et al. (1996) and Hart et al. (2010), the effect of a single bout of moderate- and low-intensity exercise, respectively, may not have been a strong enough stimulus to induce a change in cardiovagal tone. In fact, autonomic adaptations have been revealed to have a dose-response relationship in athletes (Manzi et al. 2009). Therefore, it is worth investigating the effects that a combination of high-intensity over more than a single bout may have on cvBRS.

2.6. HIGH-INTENSITY INTERVAL TRAINING

High-intensity interval training (HIIT) is identified by short, repeated bursts of vigorous exercise at an intensity greater than the anaerobic threshold (Laursen and Jenkins 2002) separated by periods of rest or low-intensity exercise (Gibala et al. 2012, Gillen et al. 2013). Low-volume HIIT is characterized as training sessions that are relatively brief. Intense exercise makes up ≤10 minutes within a ≤30 minute training session, including a warm-up, recovery periods, and cool-down (Gillen et al. 2013).

2.6.1. PURPOSE OF HIIT

The purpose of HIIT is two-fold: (1) improve performance, by repeatedly stressing the physiological systems beyond that which is actually required for a specific endurance exercise (Laursen and Jenkins 2002); and (2) improve health, by eliciting favourable changes in physiological and health-related markers comparable to that of traditional endurance exercise (Gibala et al. 2012). Therein the advantage of HIIT becomes apparent—physiological changes that rival endurance training despite the drastic reduction in time commitment and volume.

2.6.2. RATIONALE FOR HIIT

HIIT protocols generally involve less time and work compared to traditional endurance training while evoking similar physiological responses (Burgomaster et al. 2005, Gibala et al. 2006, Rakobowchuk et al. 2008, 2009, Little et al. 2010, Hood et al. 2011, Tjønna et al. 2013, Gillen et al. 2013, Gillen and Gibala 2014, Skelly et al. 2014). However, limited studies have examined how a more time efficient exercise affects cvBRS.

To our present knowledge, only seven studies have looked at the effects of high-intensity exercise on ANS function (Cottin, Médigue, & Papelier, 2008; Currie, Rosen, Millar, Mckelvie, & Macdonald, 2013c; Heydari, Boutcher, & Boutcher, 2013a, 2013b; Pichot et al., 2000, 2005; Stuckey et al., 2012); however, only three specifically measured cvBRS and are within the realm of low-volume HIIT or sprint interval training protocols (Heydari et al., 2013a, 2013b; Stuckey et al., 2012). Of these three, two were long-term exercise prescriptions, which lasted

12-weeks (Heydari et al. 2013a, 2013b). Therefore, examining the long-term effects of HIIT on cvBRS warrants further investigation.

2.6.3. GENERAL PHYSIOLOGICAL ADAPTION OF HIIT

The physiological adaptations following HIIT include improved VO_2max (Gibala et al. 2006, Rakobowchuk et al. 2008, Tjønna et al. 2013), increased skeletal muscle oxidative capacity (Burgomaster et al. 2005, Gibala et al. 2006, Little et al. 2010, Hood et al. 2011), increased resting muscle glycogen content (Burgomaster et al. 2005, Gibala et al. 2006, Little et al. 2010), increased total glucose transporter type 4 content (Little et al. 2010, Hood et al. 2011), improved insulin sensitivity (Hood et al. 2011), and improved peripheral vascular structure and function (Rakobowchuk et al. 2008, 2009), in healthy men and women. Interval training has been examined in a population of overweight and obese women, revealing favourable changes in body composition and muscle oxidative capacity (Gillen et al. 2013). Furthermore, HIIT has been recently revealed to elicit a similar 24-hour energy expenditure post-exercise compared to moderate-intensity endurance exercise, despite having a lower energy expenditure during exercise (Skelly et al. 2014).

The merits of HIIT have also been explored in athletes. Notably, for athletes that are already well-trained, HIIT can substantiate further increases in endurance performance (Laursen and Jenkins 2002). In well-trained cyclists, six to seven weeks of HIIT sessions every third day (a total of 12 sessions) significantly improved peak power output and 40 km time trial performance (Westgarth-Taylor et al. 1997). In well-trained middle distance runners, four

weeks of HIIT (8 x 2 – 3 min at VO_2max running speed), two times per week, resulted in significant improvements in 3000 m running performance (Smith et al. 2003). Four weeks of HIIT, two times per week, produced faster times in constant distance trials, power production over the constant distance trials, and relative VO_2peak in young, healthy rowers (Driller et al. 2009). As such, with well-documented improvements in performance, it is no surprise that HIIT is typically an integral component of athletic training programs (Gibala and Jones 2013).

2.6.4. ACUTE ARTERIAL & BRS ADAPTATIONS FOLLOWING HIIT

The acute effects of HIIT on carotid artery distensibility appear to be similar to those seen in resistance exercise training (Rakobowchuk et al. 2009). One hour following either a single bout or four bouts of Wingate testing, carotid artery distensibility was transiently reduced. Comparatively, this same repeated Wingate testing design elicited an increase in popliteal artery distensibility, revealing that sprint interval training, a form of HIIT, has differential effects on local artery distensibility (Rakobowchuk et al. 2009). Likewise, the transient reduction in carotid artery distensibility is concordant with the observed increase in carotid to femoral PWV ($p < 0.001$), and the transient increase in popliteal artery distensibility is concordant with the decrease in exercised lower limb PWV ($p < 0.001$) (Rakobowchuk et al. 2009).

Cottin et al. (2008) used spectral methods to analyze autonomic control of HR and BP. Low frequency SBP (LF-SBP) variability reflects sympathetic activity, whereas high frequency (HF-SBP) variability reflects the mechanical effect of breathing on SBP (Kohl et al. 1999). LF-HRV reflects both sympathetic

and vagal activity, whereas HF-HRV reflects only vagal activity. During high-intensity exercise, there was a decrease in LF-BRS and the maintenance of HF-BRS when ventilatory thresholds were exceeded. Cottin et al. (2008) hypothesized that HF-BRS would progressively decrease as exercise load increased from ventilatory threshold one (moderate-intensity exercise) to ventilatory threshold two (high-intensity exercise). However, this study revealed that, despite vagal withdrawal due to high-intensity exercise, there were increases in both HF-SBP variability and HF-HRV when ventilatory threshold two was exceeded, which allowed the gain in HF-BRS to be maintained while the LF components decreased. Cottin et al. (2008) speculate that when the second ventilatory threshold was exceeded, HF-SBP variability likely increased due to exercise-induced hyperpnea, which increased the respiratory modulations of BP. Likewise, HF-HRV likely increased in a non-neural pathway via mechanoelectric feedback, the mechanical effect of breathing and stretching of the sinus node (Kohl et al. 1999). Thus, SBP variations driven by mechanoelectric feedback to provide a baroreflex response should be taken with caution.

Autonomic recovery following sprint interval exercise, measured by HRV, BP variability, and cvBRS, was assessed in 10 young, healthy, recreationally active males (Stuckey et al. 2012). Following both single and multiple Wingate tests, HRV and BP variability indices indicated a decrease in vagal tone that returned to resting levels two hours post-exercise. Comparatively, cvBRS remained depressed even after two hours of recovery, but only following multiple and not a single Wingate test. In response to a standing orthostatic challenge,

cvBRS remained depressed following both the single and multiple Wingate tests. The results of Stuckey et al. (2012) support the notion that autonomic balance is not fully recovered within two hours of passive recovery following sprint interval exercise. It was speculated that an augmented metaboreflex may have a greater role in BP control post-exercise and that metabolites may be responsible for attenuating cvBRS.

2.6.5. CHRONIC ARTERIAL & BRS ADAPTATIONS FOLLOWING HIIT

Pichot et al. (2000) assessed ANS function using HRV in seven middle-distance runners during their usual four-week training cycle to monitor physical performance and fatigue. A typical training cycle in this particular group of athletes consisted of three weeks of high-intensity training sessions (6 – 10 sessions per week) and one week of low-intensity training sessions. HR was monitored weekly using an ambulatory Holter monitor one hour after both a high- and low-intensity training session. Findings from Pichot et al. (2000) indicate that there was a progressive decrease in HRV with the three weeks of high-intensity training, displaying a tendency of lower vagal and higher sympathetic drive. During the recovery week however, there was an increase in HRV associated with a relative increase in vagal activity and decrease in sympathetic drive. Despite the merits of this study, ANS function was assessed during periods of high- and low-intensity exercise, and not necessarily HIIT. Furthermore, Pichot et al. 2000 assessed ANS function using HRV, and not cvBRS. However, the results of Pichot et al. (2000) support the findings of Iellamo et al. (2002), where a progressive transition into a state of sympathetic predominance was seen with

higher intensity training. In another study by Pichot et al. (2005), ANS activity was assessed by HRV and cvBRS before and after a 14 week intensive cycling intervention in elderly men. LF- and HF-HRV increased, while LF/HF ratio decreased. cvBRS also improved following the intervention (7.0 ± 1.8 to 9.8 ± 2.1 ms/mmHg, $p < 0.01$), demonstrating an increase in vagal activity in response to 14-weeks of endurance training. However, similar to a previous study by Pichot et al. (2000), although the exercise prescription was high-intensity, the 40 minute sessions, four times per week, consisting of four minutes of moderate-intensity cycling and one minute of high-intensity sprinting, would not be considered a low-volume HIIT protocol.

Currie and colleagues (2013c) investigated the effects of 12-weeks of moderate-intensity endurance exercise and low-volume HIIT on measures of HR recovery and HRV in older males with documented CAD. Following the training protocol, neither group (endurance vs. HIIT) displayed differences in HR recovery 1-minute or 2-minutes post-exercise. One of the main mechanisms of HR recovery improvements following exercise is improved vagal modulation; however, there was no apparent change in HRV in either group. The lack of change in HR recovery was attributed to the high pre-training HR recovery values in the sample, which were comparable to values reported in healthy individuals. Similarly, the lack of change in HRV was attributed to the lower risk CAD status, normative cardiac autonomic function of the sample, time from post-CAD event, and small sample size. As Currie et al. (2013c) noted, the sample of CAD patients began the exercise training 140 – 171 days (5 – 6 months) after their CAD event,

it is likely that the time between the cardiac event and the training program was too long and therefore, the patients were less likely to experience improvements with training.

Low-volume HIIT and the effects on arterial health have been investigated with interesting results (Currie 2013a). Despite the significant improvements in VO_2max, resting hemodynamic indices, and absolute endothelial function, carotid artery distensibility remained unchanged following 12-weeks of either endurance training or HIIT in a CAD sample, although this is not a surprise since there were no training-induced changes in carotid artery pulse pressure or carotid artery lumen diameter (Currie 2013a). The lack of findings in arterial elasticity is supported by Rakobowchuk et al. (2008) who also observed no changes in carotid artery distensibility following six weeks of sprint interval training in young, healthy males and females. As both these studies employ protocols of higher intensity, intensity itself does not appear to be a major influence on carotid artery distensibility. For instance, the protocol employed by Rakobowchuk et al. (2008) is of lower volume but higher intensity compared to Currie (2013a), yet both observed no changes in carotid artery distensibility. Therefore, further research is required to elucidate the amount of volume required to elicit such changes at near maximal to supramaximal intensities, as it appears that 12-weeks of HIIT or six weeks of sprint interval training does not affect arterial elasticity.

Heydari et al. (2013a) investigated the effects of 12-weeks of high-intensity exercise on ANS function in young overweight/obese males. Participants in the intervention group performed HIIT three times per week for 12-weeks at a

workload of 80 – 90% maximal HR. After the intervention, resting HR was reduced (67.4 ± 9.7 to 61.2 ± 8.9 beats/min, $p < 0.05$) while SV increased (77.2 ± 24.9 to 90.4 ± 26.3 ml, $p < 0.05$) in the intervention group compared to the control group. SBP, DBP, and MAP were significantly improved (119.6 ± 9.9 to 115.5 ± 9.7; 63.7 ± 7.3 to 59.2 ± 7.5; 83.1 ± 8.2 to 78.7 ± 8.0 mmHg, $p < 0.05$, respectively) in the intervention group compared to the control group. Carotid to femoral PWV was significantly reduced in the intervention group compared to the control group. Additionally, HRV increased in both the LF and HF components in the intervention group, and cvBRS significantly increased by 12%. Hence, the overall, findings of Heydari and colleagues (2013a) demonstrated improvements in cardiac, vascular, and ANS function following a 12 week HIIT intervention. The observed improvement in arterial stiffness replicates results from previous investigations (Tanaka et al. 2000, Sugawara et al. 2006). Likewise, the increase in cvBRS is supported by similar findings by Monahan et al. (2000), although the exercise modality was different. Lastly, Heydari and colleagues (2013b) also investigated cvBRS following a 12 week HIIT exercise intervention in young healthy males. As expected, resting HR and BP decreased, and SV improved following the intervention. cvBRS also significantly increased (18.3±2.9 vs. 23.8±3.8 ms/mmHg, $p < 0.05$), while arterial stiffness, measured by augmentation index, significantly decreased in the intervention group (8.2±2.9 vs. 5.1±2.7%, $p < 0.05$) compared to controls. It is generally understood that with increases in arterial stiffness, there is disengagement of the stretch-sensitive baroreceptors (Lipman et al. 2002), and in this way, the decrease in arterial stiffness and

seemingly concordant increase in cvBRS would appear to be related. However, an association was not apparent for either group . While cvBRS is known to be highly influenced by vascular stiffness (Lipman et al. 2002), the results of Heydari et al. (2013b) would suggest that the increase in cvBRS following a 12 week HIIT intervention was not influenced by a decrease in arterial stiffness.

While there is merit in the two investigations led by Heydari et al. (2013a, 2013b), the HIIT protocol utilized is questionable. Both studies defined HIIT as 20 minutes of eight seconds of sprinting at 80 – 90% of age-predicted HR maximum followed by 12 seconds of rest. While another study has employed a similar protocol (Trapp et al. 2008), the majority of HIIT protocols vary between low-volume HIIT and sprint interval training protocols where the intervals are upwards of one minute long (Gillen and Gibala 2014). In addition, in both studies by Heydari et al. (2013a & 2013b), cvBRS was determined using the sequence method. Although this method has been shown to be both valid and reproducible, this method should be taken with caution as it may inherently miss measuring part of the sympathetic component of the baroreflex (Swenne 2013).

2.6.6. APPLICATION OF HIIT IN CLINICAL & AGEING POPULATIONS

The merits of HIIT have recently been extended into many diverse clinical populations. 12-weeks of HIIT, three times per week, has been shown to decrease HR, increase SV, and increase cvBRS both at rest and during a cognitive challenge (Stroop task) in young, overweight males (Heydari et al. 2013b). 10-weeks of HIIT, three times per week, has been shown to improve VO_2max and

reduce BP and fasting glucose levels, in middle-aged, healthy and previously inactive males (Tjønna et al. 2013). Six weeks of HIIT, three times per week, improved body composition, as evidenced by increases in abdominal and leg region fat-free mass, and muscle oxidative capacity, as evidenced by the maximal activities of citrate synthase and ß-hydroxyacyl-CoA from muscle biopsies, in young, overweight and obese women (Gillen et al. 2013). Compared to moderate-intensity endurance exercise, Currie and colleagues (2013b) revealed that HIIT elicits similar improvements in peak exercise capacities and brachial artery endothelial function, a noninvasive surrogate of coronary artery endothelial function, in a CAD population. Finally, although clinically a "healthy" group of individuals, 14-weeks of high-volume HIIT, four times per week, elicited greater vagal predominance in active, elderly men, enhancing HRV and cvBRS (Pichot et al. 2005).

2.6.7. CURRENT EXERCISE RECOMMENDATIONS

An impaired cvBRS increases the risk of stroke and CVD morbidity and mortality. In addition, post-MI patients with a low cvBRS are more likely to die from fatal arrhythmias (La Rovere et al. 1998). As described earlier, reductions in cvBRS can be attenuated with regular endurance exercise (Monahan et al. 2000). There is no doubt that traditional endurance exercise has a positive impact on CVD. For instance, three months of endurance training in subjects with multiple cardiac risk factors (greater than 65 years of age, type II diabetes, hypertension, and dyslipidemia) increased cvBRS without any significant changes in anthropometrics (Madden et al. 2010). However, traditional endurance exercise

training is undoubtedly time demanding. Even though endurance exercise training reduces all-cause cardiovascular mortality by modifying the traditional CVD risk factors (Taylor et al. 2004), participation and adherence rates remain low, even within cardiac rehabilitation patients (Barbour and Miller 2008).

The American College of Sports Medicine currently recommends an exercise prescription of 30 – 60 min/day (150 min/wk) of moderate-intensity endurance exercise ≥ 5 days/wk, or 20 – 60 min/day (75 min/wk) of high-intensity endurance physical activity ≥ 3 – 5 days/wk (Garber et al. 2011). In comparison, the guidelines initiated jointly by the Canadian Society for Exercise Physiology and ParticipACTION recommend that adults aged 18 – 64 years should accumulate ≥ 150 min/wk of moderate to vigorous intensity endurance physical activity in bouts of 10 min or more (Tremblay et al. 2011), further supporting the notion of shorter duration, but higher intensity endurance physical activity. Despite the current recommendations, adherence to an exercise program is challenging for many people (Allen and Morey 2010). Specifically, a 'lack of time' remains the most commonly cited barrier to exercise (Trost et al. 2002). One major advantage of HIIT compared to traditional endurance exercise is the associated time efficiency. As well, because HIIT has been shown to elicit similar physiological adaptations compared with traditional endurance exercise training, implementing HIIT as a training program is becoming increasingly popular.

CHAPTER III: METHODS

3.1. STUDY PARTICIPANTS

Sixteen young, healthy, non-smoking, normotensive males (23.8±3.0 years, 18 – 28 years) gave informed written consent to participate in this study. Participants were excluded if they had any cardiovascular conditions, a BMI < 18.5 kg/m^2 (underweight) or ≥ 30 kg/m^2 (obese), currently involved in a rigorous training program (training more than three times per week at high-intensity), were allergic to dairy/soy products, and/or if they had a baseline VO_2peak ≥ 56 mL/kg/min, as a VO2max greater than 56 mL/kg/min is indicative of a highly-fit individual. Further improvements in variables of interest may not be as apparent with a group of highly trained individuals. The study was performed in accordance with the Helsinki Declaration on the use of human subjects and met the ethical standards of the Brock University Research Ethics Board, receiving approval (Appendix A).

3.2. EXPERIMENTAL DESIGN

Participants reported to the Human Hemodynamics Laboratory at Brock University to participate in the experimental protocol. Prior to the experimental protocol, participants were invited to attend a familiarization session, which included a description of the experimental details, protocol, benefits, and risks. At this time, participants filled out the medical history questionnaire (Appendix B), in addition to reviewing and signing the informed consent form (Appendix C). Participants were also asked to complete a three day food diary (Appendix D) in

the days leading up to their first testing session. They were instructed to eat similar meals before all future testing sessions. This was to control for within-subject meal intake prior to testing sessions. Testing occurred at the same time each day for each participant, after a minimum of a four hour fast. Participants refrained from light exercise, and consuming alcohol and caffeine for a minimum of 12 hours prior to testing, and heavy exercise for at least 24 hours. On the day of testing, participants voided their bladder prior to data collection to prevent the effect of bladder distension on arterial BP (Fagius and Karhuvaara 1989). Participants wore athletic attire for the duration of the experimental protocol. When finished, participants were provided with a standard meal replacement drink (Ensure, Abbott Nutrition Canada, Saint-Laurent, Québec, Canada), which they were instructed to consume one to two hours prior to all training (HIIT) sessions. This was to control for between-subject meal intake prior to training sessions and the acute effects of diet (Rakobowchuk et al. 2008).

3.2.1. TESTING SESSIONS

Testing sessions occurred at three time points over the duration of the protocol: week 0, baseline (PRE); week 6, midpoint (MID); and week 12, endpoint (POST). Midpoint and endpoint were scheduled 24 – 48 hours after the previous HIIT session to ensure the participant had recovered from training. First, basic anthropometric measures were collected prior to autonomic and vascular data collection (Appendix E). Participants were then placed in the supine position, instrumented and then rested for 15 minutes in order to achieve a resting state. Three manual BP measurements were then taken followed by 10 minutes of beat-

by-beat HR and BP collection for autonomic evaluation. Subsequently, carotid artery ultrasonography and tonometry were conducted for vascular evaluation. Three manual BP measurements were taken post-data collection to ensure baseline BP values. Autonomic and vascular evaluation in our lab has been described previously (Klassen et al. 2016), and is highlighted in 3.3.2. and 3.3.3.

Second, participants underwent body composition testing by way of air displacement plethysmography to determine lean mass (LM), percent LM (%LM), fat mass (FM), and percent FM (%FM). Third, participants completed a VO_2max test to determine measures of cardiorespiratory fitness and training loads for the HIIT sessions. Following VO_2max testing, participants were monitored until sufficient rest was achieved, and subsequent HIIT sessions were scheduled to take place in the most consistent manner as possible.

3.2.2. HIIT SESSIONS

For each HIIT session, participants were reminded to refrain from heavy exercise for at least 24 hours prior, and to consume the standard meal replacement drink one to two hours prior. HIIT sessions were divided into two blocks differentiated by volume (low-volume, block A; high-volume, block B) and each spanning six weeks, with a frequency of two sessions per week. Therefore, there were 12 sessions per block, or 24 training sessions for the entire study. This protocol was modeled after several investigations incorporating HIIT (Little et al. 2010, Hood et al. 2011, Currie et al. 2013a). HR was continuously monitored in order to ensure that the participants were exposed to a maximal stimulus (Appendix F). The blocks were divided as follows:

Block A, Low-Volume: 240 min or 4 hr = 60 min/week = 30 min/session

- 3 min warm-up at 30 W
- 10x60 sec bouts at 90%HR_{max}
    - 75 sec active rest at 45 W between each bout
- 5 min cool-down at 30 W

With completion of block A, two more intervals were added to ensure a maximal stimulus and observe any training effects.

Block B, High-Volume: 272 min or 4.5 hr = 68 min/week = 34 min/session

- 3 min warm-up at 30 W
- 12x60 sec bouts at 90%HR_{max}
    - 75 sec active rest at 45 W between each bout
- 5 min cool-down at 30 W

3.3. EXPERIMENTAL MEASURES

3.3.1. ANTHROPOMETRIC & BODY COMPOSITION MEASURES

Standing height was measured in centimetres (cm) with a stadiometer (STAT 7X, Ellard Instrumentation Ltd., Monroe, WA, USA) and body mass was measured in kilograms (kg) with a digital scale (BWB-800S, Tanita Corporation, Tokyo, Japan). BMI was calculated as body mass (kg) divided by height squared (m^2). Hip and waist circumference (cm) were measured with an inelastic measuring tape. Hip circumference was measured at the largest part of the

buttocks below the iliac crest. Waist circumference was measured at the level of the umbilicus. Waist/hip ratio was calculated by dividing the waist circumference by the hip circumference.

Body composition was measured using the BOD POD® (BODPOD, *Gold Standard*, Life Measurement Inc., Concord, CA, USA), which uses air displacement plethysmography, to determine both absolute and percent fat mass and lean mass. Participants were seated in the chamber and a minimum of two volume measurements were conducted. A third volume measurement was performed if the difference between the previous measures was greater than 150 mL. Participants were required to wear tight-fitting active wear in order to ensure a valid measurement.

3.3.2. BAROREFLEX SENSITIVITY MEASUREMENT

3.3.2.1. BEAT-BY-BEAT RRI & BP MEASUREMENTS

A single lead electrocardiogram (ECG) was used to obtain RRI, the time between successive heartbeats. Continuous non-invasive BP was measured at the left middle finger using the Nexfin® monitoring system (BMEYE Monitor Series, BMEYE, Amsterdam, The Netherlands). After 15 minutes of rest in the supine position, the first of two sets of manual BP measurements was taken using a manual sphygmomanometer on the upper arm and a stethoscope placed over the right brachial artery for auscultation. This measure was done in triplicate, where the first recording was used as a calibration measure. Average BP (SBP and DBP) was considered the average of the second and third recordings and MAP (1/3 SBP

+ 2/3 DBP) was calculated from these values. The manual BP recordings also served as a reference point for the beat-by-beat BP data collection from the Nexfin® monitoring system, where the continuous finger BP measurements were adjusted to the average manual brachial SBP and DBP, as described previously (O'Leary et al. 2005). Continuous BP and RRI were recorded for a 10 minute period. Both BP and RRI were sampled at a rate of 1000 Hz to provide a resolution of one millisecond using the online data analyses and acquisition systems, PowerLab® and LabChart® (Version 7, ADInstruments Inc., Colorado Springs, CO, USA). Average resting HR [RHR (bpm) = RRI (seconds/60)] was calculated for the first minute of the 10 minute data collection.

3.3.2.2. CARDIOVAGAL BAROREFLEX SENSITIVITY ANALYSIS

The continuous BP and HR data were inspected for ectopic beats, as they have been shown to markedly affect cvBRS (Pinna et al. 2005). The cleanest five minute segment was used in the calculation of cvBRS.

MATLAB® numerical computation and visualization software (Version R2012b, MathWorks, Natick, MA, USA) was used to interpolate and resample the data at mean cardiac frequency in order to obtain an equal interval between samples (Pinna et al. 2004). A low-pass Butterworth filter (0.95 Hz) was used and the data was detrended to remove any linear trends. FFT was used with the Welch method and a Hanning window set to one-fourth of the signal length with a one-half overlap. Spectral analysis was used to delineate SBP and RRI into LF (0.05 – 0.15 Hz) and HF (0.15 – 0.40 Hz) bands (Robbe et al. 1987). As described by Robbe et al. 1987, LF variations relate to changes in vasomotor tone, and are

considered a marker of both vagal and sympathetic modulation. HF variations are mainly attributed to respiratory activity, which is considered vagal modulation (Robbe et al. 1987). The mean transfer function gain of SBP to RRI was used to determine cvBRS (ms/mmHg) for the LF region using a coherence ≥ 0.5 (Persson et al. 2001).

3.3.3. ARTERIAL MEASUREMENTS

3.3.3.1. COMMON CAROTID ARTERY

Following continuous data collection, ultrasonography was performed on the right CCA (1 – 2 cm proximal to the carotid bifurcation), using B-mode ultrasound (Vivid q, General Electric Medical Systems, The Netherlands) and a 12 MHz linear array vascular transducer to obtain distensibility, compliance, diameter, and thickness measures. Three, two-dimensional B-mode images were recorded for approximately five heartbeats. Ultrasound movie clips were digitally stored in Digital Imaging and Communications in Medicine (DICOM) format for further offline analysis using a semi-automated edge-tracking system, Artery Management System (AMS, Chalmers University of Technology, Göteborg, Sweden).

Measurements of carotid intima-media thickness (IMT), minimal and maximal diameters were determined from the five best quality heartbeats by the same investigator. Carotid lumen diameter (LD) was measured as the distance between the leading edge of the near-wall adventitia-media interface and the leading edge of the far-wall lumen-media interface. True LD is defined as the

distance between the leading edge of the near-wall intima-lumen interface and the leading edge of the far-wall lumen-intima interface. However, the presence of a clear near-wall intima-lumen was inconsistent between participants. Therefore, our measurements of LD included the bright white of the near-wall intima-media complex instead of the intima-lumen interface, which may overestimate the true LD. Far-wall IMT was determined as the distance between the far-wall leading edge of the lumen-intima interface and the leading edge of the intima-media interface.

Distensibility, which is the relative change in arterial diameter for a given pressure change, was be determined using the equation (O'Rourke et al. 2002):

$$Distensibility = [\Pi(d_{max}/2)^2 - \Pi(d_{min}/2)^2] / \Pi(d_{min}/2)^2 \times PP$$

where d_{max} is the maximal diameter, d_{min} is the minimal diameter and PP is the corresponding pulse pressure. The numerator of the equation simplifies to represent the change in arterial cross-sectional area between systole and diastole, whereas the denominator represents arterial cross-sectional area during diastole multiplied by the average PP.

Compliance, which is the absolute change in arterial diameter with a given pressure, was determined from the equation (O'Rourke et al. 2002):

$$Compliance = [\Pi(d_{max}/2)^2 - \Pi(d_{min}/2)^2] / PP$$

Local PP measurements were collected from the left CCA immediately following ultrasonography using applanation tonometry. Since pressures collected with this technique are sensitive to hold-down pressure, absolute carotid artery BP

measurements were calibrated to the adjusted left middle finger BP values (Kelly and Fitchett 1992). A minimum of ten beats was used to calculate average PP.

3.3.3.2. PULSE WAVE VELOCITY

Following ultrasonography, PWV was used to estimate central artery stiffness. PWV is the current gold standard for the non-invasive measurement of arterial stiffness. PWV was assessed using applanation tonometry with a hand-held tonometer (model SPT-301, Millar Instruments Inc., Houston, TX, USA). The tonometer was calibrated with an external device using a two-point calibration system. This noninvasive pressure sensor was placed over the left CCA and the left femoral artery. The time delay (PTT, pulse transit time) between proximal and distal pulse waves were calculated. The distances between the sternal notch to the left CCA and left femoral artery were measured as segment lengths in meters (m). The PWV estimate is determined from the equation (O'Rourke et al. 2002):

$$PWV = D / \Delta t$$

where D is the distance (segment length) between measurement sites, and Δt is the pulse transit time (PTT). Carotid and femoral artery tonometry were not performed simultaneously; therefore, the R-wave of the ECG was used as the initiation point of the pulse wave. To calculate carotid and femoral PTTs (ms), the time at the minimum point immediately prior to the upstroke of the pressure wave was subtracted from the time at the R-wave of the ECG. The PWV estimate was calculated by averaging a total of 15 – 20 heartbeats. .

3.3.4. CARDIORESPIRATORY FITNESS MEASUREMENTS

3.3.4.1. VO_2MAX TESTING

Cardiorespiratory fitness was assessed using a stationary electronically-braked cycle ergometer (Lode® Excalibur, Version 5.3.1, Lode B.V., Groningen, The Netherlands), The VO_2max test consisted of a five minute warm-up at 100 watts (W), after which the workload increased by one watt every two seconds until volitional fatigue or the pedal cadence dropped below 40 revolutions per minute. The values obtained during this test were used to determine the estimated workload in watts for 90 - 100% peak power output (PPO) to be used for each interval in the HIIT sessions. Cardiorespiratory fitness testing and HIIT workload estimates were based on a previous protocol utilizing HIIT (Currie et al. 2013a). Criteria exist with maximal graded exercise testing that indicate whether or not an individual has reached their VO_2max:

1. Plateau in VO_2 curve,
2. Blood lactate ≥ 8 mM,
3. Respiratory exchange ratio (RER) ≥ 1.10,
4. Age-predicted maximum HR (HR_{max}) = 220 – age

The individuals needed only to meet one of three criteria, VO_2 plateau, RER ≥ 1.10, or age-predicted HR_{max}, as blood lactate testing was not conducted. The three listed criteria are regarded as sufficient for assessing cardiorespiratory fitness (Mier et al. 2012).

Despite the effectiveness of measuring cardiorespiratory fitness with a VO_2max test, many individuals fail to reach their true max (Howley et al. 1995,

Mier et al. 2012), and instead reached a VO_2peak. The incidence of a true VO_2 plateau has been reported as low as 20% (Mier et al. 2012). Therefore, data reported reflect VO_2peak.

The training status of the individual was confirmed as a result of the VO_2peak test. Training status was based on normative data for males aged 20 – 29 (Heywood 2006). The categories are stratified as follows:

Sedentary, VO_2max < 45 ml/kg/min;

Recreationally active, VO_2max = 45 to 55 ml/kg/min;

Trained, VO_2max = 56 to 60 ml/kg/min;

Highly-trained, VO_2max > 60 ml/kg/min;

where only those individuals who stratify into the sedentary and recreationally active category were considered for further testing.

3.3.4.2. HIGH-INTENSITY INTERVAL TRAINING

All HIIT sessions were performed on the Lode® Excalibur cycle ergometer and HR monitored. The training session included a standardized three minute warm-up and a five minute cool down at 30 W. The PPO at VO_2peak provided an estimate as to the cycling wattage used during the HIIT sessions; however, the primary indicator of intensity was achieved through continuous HR monitoring with a chest strap and a corresponding wristwatch (Timex® Personal Heart Rate Monitor, Model M593, Timex Corporation, Middlebury, CT, USA). Participants exercised at or above 90%HR_{max} for each interval. Thus, the wattage for each interval was adjusted slightly from the PPO at VO_2peak in order to ensure that the participants were exercising at the prescribed intensity. A member

of the research team supervised all exercise training sessions to ensure the usage of proper techniques and correct intensity.

3.4. STATISTICAL METHODS

Sixteen participants were recruited; however, a total sample size of 14 participants was used for analysis, as there was one drop-out and one exclusion due to the presence of ectopic beats at baseline. Analyses were completed using SAS (Version 9.4, SAS Institute Inc., Cary, NC, USA). The level of significance for all measures was set to $\alpha = 0.05$. Data are reported in tables as means and standard deviations. Data are presented in figures as means and standard errors.

A one-way repeated measures ANOVA was used to determine a training effect (PRE-, MID-, POST-training) for all dependent variables (Table 1). Significant differences were followed up with Holm-Bonferroni post-hoc testing to determine at which timepoints the differences occurred.

A Pearson correlation analysis was used to determine which variables (baseline and change variables) were significantly associated with PRE to POST change in cvBRS (ΔcvBRS). A Spearman correlation was used with variables that did not reach normality at baseline (height, waist-hip ratio, and DBP). ΔcvBRS was analyzed using simple linear regression models while adjusting for covariates which included baseline cvBRS, baseline compliance, change in compliance, change in distensibility, change in carotid PP, and change in IMT.

CHAPTER IV: RESULTS

4.1. EFFECT OF TRAINING

4.1.1. PARTICIPANT COMPLIANCE & TRAINING INTENSITY

Participants attended two supervised training sessions per week for the duration of the protocol. Training session compliance was 100%, as were the PRE-, MID-, and POST-training testing sessions. Care was taken during each training session to adjust the workload based on the previous VO_2max test PPO, in order to elicit the target HR of 90%. An average HR was taken after each training session to ensure the participant completed the workout at the appropriate intensity.

4.1.2. EFFECT OF TRAINING ON DEMOGRAPHIC AND BODY COMPOSITION VARIABLES

Repeated measures ANOVA data for the effects of training are presented in Table 1. Following the training program, body mass and BMI significantly increased. Post-hoc analysis revealed that POST-training body mass was significantly higher compared to PRE-training; while, no significant differences for BMI were found at any time point. Absolute and percent measures of fat mass and lean mass, along with hip circumference, waist circumference, and waist/hip ratio remained unchanged.

TABLE 1. PRE-, MID-, and POST-testing data.

Variable	PRE	n	MID	n	POST	n	p
Body Composition Data							
Body Mass, kg	78.9 (7.8)	14	79.4 (7.8)	14	79.8 (7.7)*	14	0.004
BMI, kg/m^2	24.1 (2.5)	14	24.3 (2.5)	14	24.3 (2.5)	14	0.026
Lean Mass, kg	70.0 (6.5)	14	69.6 (6.1)	14	70.4 (6.6)	14	0.190
Fat Mass, kg	8.71 (3.9)	14	9.58 (3.6)	14	9.25 (4.2)	14	0.218
Percent Lean Mass, %	89.1 (4.5)	14	88.1 (3.8)	14	88.6 (4.9)	14	0.281
Percent Fat Mass, %	10.9 (4.5)	14	11.9 (3.8)	14	11.4 (4.9)	14	0.281
Hip Circumference, cm	98.6 (5.4)	14	98.4 (5.8)	14	98.4 (5.6)	14	0.904
Waist Circumference, cm	84.2 (6.6)	14	84.2 (6.6)	14	84.8 (6.8)	14	0.133
Waist-Hip Ratio	0.85 (0.04)	14	0.85 (0.04)	14	0.86 (0.04)	14	0.145
Cardiorespiratory Fitness Data							
Absolute VO_2peak, mL/min	3638 (545)	14	4068 (447)*	14	4099 (455)*	12	0.002
Relative VO_2peak, mL/kg/min	46.3 (6.7)	14	51.6 (6.5)*	14	51.2 (5.8)*	12	0.004
Peak HR, bpm	195 (6)	14	195 (8)	13	195 (9)	13	0.842
RER	1.23 (0.06)	14	1.28 (0.19)	14	1.21 (0.06)	12	0.349
PPO, W	327 (39)	14	355 (37)*	14	360 (31)*	13	<0.001
Resting Blood Pressure and Heart Rate Data							
RHR, bpm	60 (8)	13	56 (10)	14	57 (9)	11	0.042
SBP, mm Hg	121 (7)	14	120 (9)	14	117 (8)	14	0.083
DBP, mm Hg	73 (8)	14	70 (7)*	14	67 (5)*	14	0.001
MAP, mm Hg	89 (6)	14	86 (7)*	14	84 (5)*	14	<0.001
Arterial Structure and Function Data							
Carotid PP, mm Hg	50 (10)	14	53 (8)	13	51 (9)	14	0.569
Compliance, mm^2/mm Hg	0.14 (0.04)	14	0.12 (0.03)	13	0.13 (0.04)	14	0.061
Distensibility, mm Hg^{-1}	0.0052 (0.0015)	14	0.0043 (0.0011)	13	0.0044 (0.0010)	14	0.042
Carotid LDmax, mm	6.64 (0.49)	14	6.65 (0.35)	14	6.61 (0.44)	14	0.870
Carotid LDmin, mm	5.94 (0.48)	14	6.01 (0.32)	14	5.97 (0.40)	14	0.670
IMT, mm	0.44 (0.09)	14	0.40 (0.08)*	14	0.36 (0.09)*†	14	<0.001
PWV, m/s	6.15 (0.73)	14	5.51 (0.41)*	14	5.84 (0.78)	14	0.008
Autonomic Function Data							
cvBRS, ms/mm Hg	16.5 (7.0)	12	14.4 (6.6)	13	15.6 (7.4)	11	0.758

BMI, body mass index; VO_2, oxygen consumption; HR, heart rate; RER, respiratory exchange ratio; PPO, peak power output; RHR, resting heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; PWV; carotid to femoral pulse wave velocity; PP, pulse pressure; LD, lumen diameter; IMT, intima media thickness; cvBRS, cardiovagal baroreflex sensitivity; RRI, R-R interval. A one-way repeated measures ANOVA was used with Holm-Bonferroni pairwise multiple comparison corrections for PRE-, MID-, and POST-means.
* indicates $p < 0.05$ v. PRE.
† indicates $p < 0.05$ v. MID.

4.1.3. EFFECT OF TRAINING ON CARDIORESPIRATORY FITNESS

Two participants POST-training have missing VO_2max and RER data due to one drop-out and another one had technical difficulty. Therefore, means are calculated for n = 14, 14, and 12 participants at PRE-, MID-, and POST-training, respectively (Table 1). Sample sizes for peak HR at PRE-, MID-, and POST-training are 14, 13, and 13, respectively. At MID-training, there were issues with

the heart rate monitor, and at POST-training, the missing value is due to the drop-out. For PPO data, sample sizes at PRE-, MID-, and POST-training are 14, 14, and 13, respectively. The missing value at POST-training is also due to the drop-out.

Absolute VO_2peak increased following 12-weeks of HIIT (3638 ± 545 v. 4099 ± 455 mL/min, $p = 0.002$). Likewise, relative VO_2peak increased (46.3 ± 6.7 v. 51.2 ± 5.8 mL/kg/min, $p = 0.004$). PPO also increased following 12-weeks of HIIT (327 ± 39 v. 360 ± 31 W, $p < 0.001$). Absolute VO_2peak, relative VO_2peak, and PPO were significantly greater at MID- compared to PRE-training; however, no further changes were observed from MID- to POST-training. Peak HR and RER remained unchanged following training. The effect of 12-weeks of HIIT on absolute and relative VO_2peak is displayed in Figure 1.

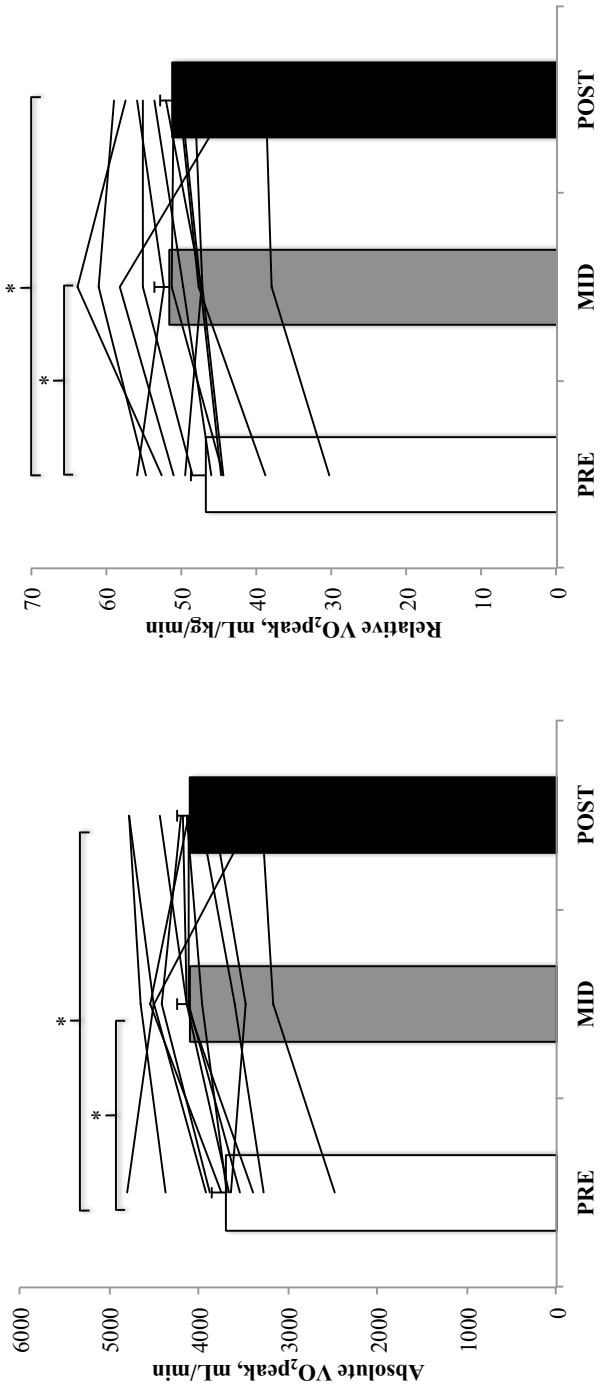

Figure 1. Absolute (left) and relative (right) VO_2peak mean responses (bars) and individual responses (lines), PRE- (white), MID- (grey), and POST-training (black). VO_2, oxygen consumption. Only complete PRE-, MID-, and POST-training data are shown (n = 12).
* indicates $p < 0.05$.

4.1.4. EFFECT OF TRAINING ON RESTING HR AND BP

DBP decreased following 12-weeks of HIIT (73 ± 8 v. 67 ± 5 mm Hg, $p = 0.001$), along with MAP (89 ± 6 v. 84 ± 5 mm Hg, $p < 0.001$). Improvements in DBP and MAP were seen at MID- compared to PRE-training; however, no further change was observed from MID- to POST-training. A resting HR (RHR) ANOVA found significant changes; however, post-hoc analysis revealed no actual differences between any timepoints. SBP remained unchanged. Sample sizes for RHR at PRE-, MID-, and POST-training were 13, 14, and 11, respectively. This is due to the number of artifacts or unuseable segments of resting beat-by-beat HR collection since our RHR was derived from RRI.

4.1.5. EFFECT OF TRAINING ON ARTERIAL STRUCTURE AND FUNCTION AND cvBRS

Data is complete for maximal and minimal diameters (LD), IMT, and PWV; however, sample sizes for PRE-, MID-, and POST-training for carotid PP, compliance, and distensibility were 14, 13, and 14, respectively. The difference at MID-training was due to the unusable carotid PP data in determining average carotid PP, compliance, and distensibility. For cvBRS, samples sizes were 12, 13, and 11, for PRE-, MID-, and POST-training, respectively. This was due to the lack of a clean five minute segment of beat-by-beat HR and BP data to be analyzed.

Most measures of carotid artery structure and function (PP, compliance, and LD) remained unchanged following 12-weeks of HIIT. IMT decreased

following the training program (0.44 ± 0.09 v. 0.36 ± 0.09 mm, $p < 0.001$). Initial improvements were seen at MID-training (0.44 ± 0.09 v. 0.40 ± 0.08 mm, $p < 0.05$) and further improvements were seen at POST-training (0.40 ± 0.08 v. 0.36 ± 0.09 mm, $p < 0.05$). An overall time effect was found for distensibility; however, post-hoc analysis revealed no significant differences between any timepoints. The effects of 12-weeks of HIIT on IMT are displayed in Figure 2. Distensibility and compliance are displayed in Figure 3.

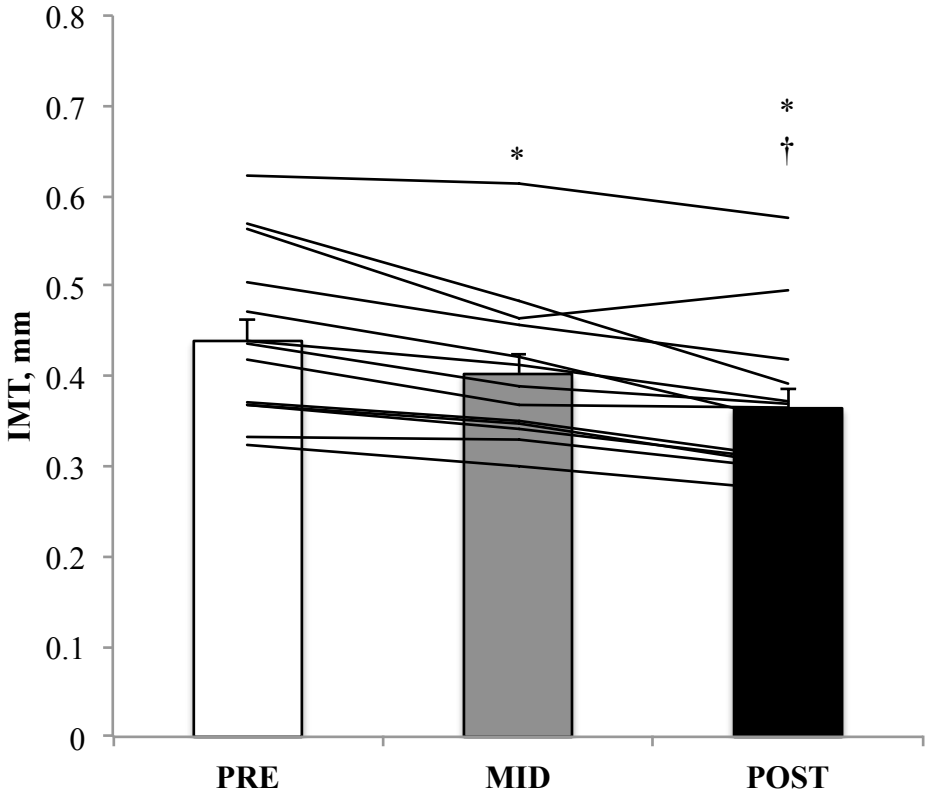

Figure 2. IMT means (bars) and individual responses (lines), PRE- (white), MID- (grey), and POST-training (black). IMT, intima media thickness.
* indicates $p < 0.05$.

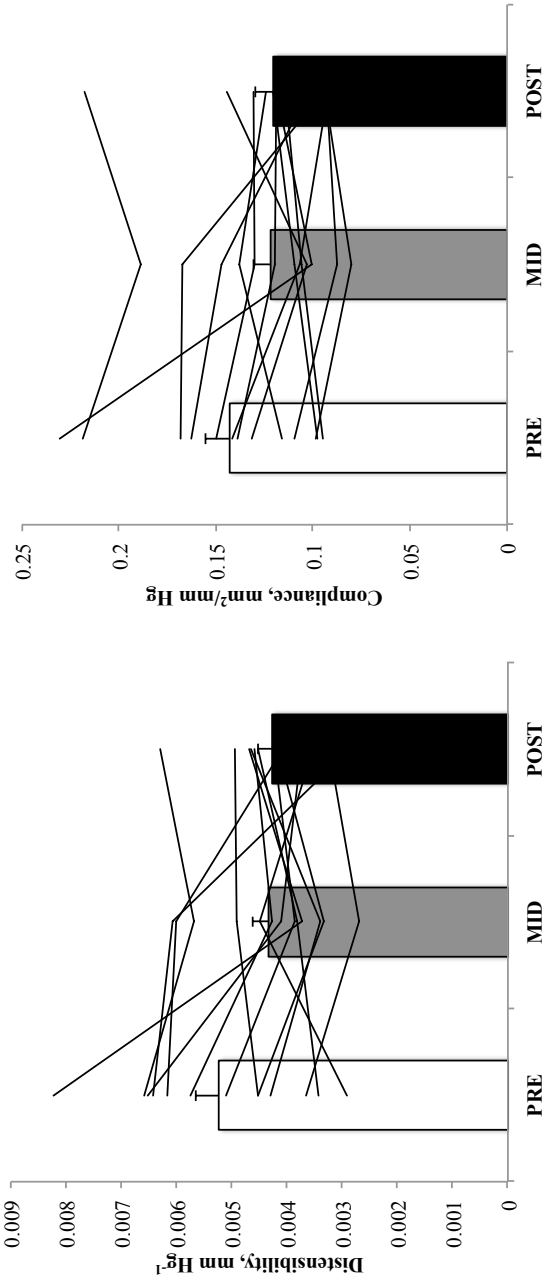

Figure 3. Distensibility (left) and compliance (right) mean responses (bars) and individual responses (lines), PRE- (white), MID- (grey), and POST-training (black). Only complete PRE-, MID-, and POST-training data are shown (n = 13). There was an overall significant effect for time ($p = 0.042$); however, post-hoc testing revealed no differences between timepoints.

PWV remained unchanged following 12-weeks of HIIT. Interestingly, PWV improved from PRE- to MID-training (6.15 ± 0.73 v. 5.51 ± 0.41 m/s, $p < 0.05$); however, PWV returned to PRE-training levels at POST-training. The effect of 12-weeks of HIIT on PWV is displayed in Figure 4.

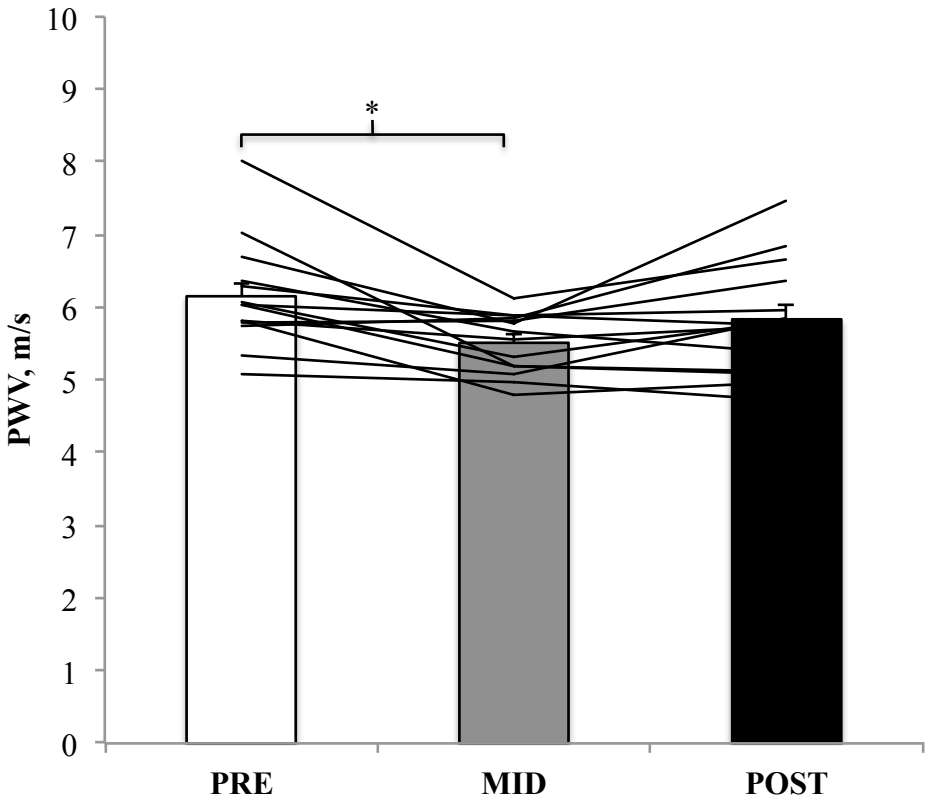

Figure 4. PWV mean responses (bars) and individual responses (lines), PRE- (white), MID- (grey), and POST-training (black). PWV, carotid to femoral pulse wave velocity.
* indicates $p < 0.05$.

As for cvBRS, two participants at PRE-training, one participant at MID-training, and an additional three participants at POST-training did not have a consistently clean five-minute segment for autonomic data analysis. Therefore, cvBRS was calculated for n = 12, 13, and 11 participants at PRE-, MID-, and

POST-training, respectively (Table 1). A one-way ANOVA determined that cvBRS remained unchanged following 12-weeks of HIIT (Figure 5).

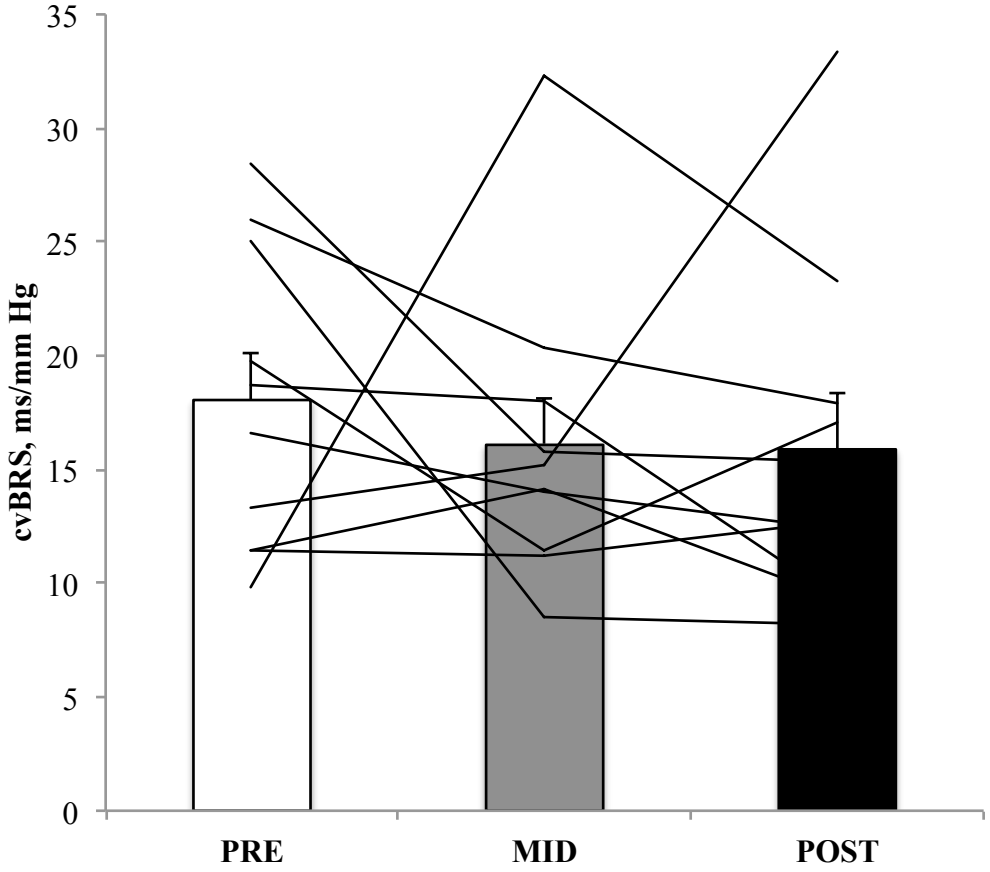

Figure 5. cvBRS mean responses (bars) and individual responses (lines), PRE- (white), MID- (grey), and POST-training (black). cvBRS, cardiovagal baroreflex sensitivity. Only complete PRE-, MID-, and POST-training data are shown (n = 10).

4.2. ΔcvBRS CORRELATIONS AND REGRESSION

Due to missing cvBRS data, 10 participants with complete PRE- and POST-training paired data were utilized for correlations and linear regression analyses.

4.2.1. CORRELATES AT BASELINE

PRE-to-POST ΔcvBRS was negatively correlated with compliance ($r = -0.73$, $p = 0.016$). Distensibility showed a negative correlation with ΔcvBRS, although this was non-significant ($r = -0.62$, $p = 0.057$). Likewise, negative correlations were observed with carotid LDmax ($r = -0.62$, $p = 0.054$), and LDmin ($r = -0.62$, $p = 0.054$), although these also were non-significant. As expected, ΔcvBRS was significantly correlated with baseline cvBRS ($r = -0.76$, $p = 0.011$). Bivariate correlates of ΔcvBRS with baseline variables are reported in Table 2.

TABLE 2. Baseline correlates of change in cvBRS.

Variable	r	p
Demographic Data		
Age, yr	-0.15	0.684
Height, cm	0.09	0.815†
Body Composition Data		
Body Mass, kg	-0.32	0.367
BMI, kg/m^2	-0.36	0.309
Lean Mass, kg	-0.30	0.407
Fat Mass, kg	-0.12	0.738
Percent Lean Mass, %	0.11	0.760
Percent Fat Mass, %	-0.11	0.760
Hip Circumference, cm	0.08	0.829
Waist Circumference, cm	-0.02	0.958
Waist-Hip Ratio	0.08	0.829†
Cardiorespiratory Fitness Data		
Absolute VO_2peak, mL/min	-0.26	0.462
Relative VO_2peak, mL/kg/min	-0.07	0.856
Peak HR, bpm	0.42	0.224
RER	0.03	0.934
PPO, W	-0.13	0.715
Resting Heart Rate and Blood Pressure Data		
RHR, bpm	0.38	0.284
SBP, mm Hg	-0.18	0.628
DBP, mm Hg	0.04	0.907†
MAP, mm Hg	-0.09	0.804
Arterial Structure and Function Data		
Carotid PP, mm Hg	0.55	0.097
Compliance, mm^2/mm Hg	-0.73*	0.016
Distensibility, mm Hg^{-1}	-0.62	0.057
Carotid LDmax, mm	-0.62	0.054
Carotid LDmin, mm	-0.62	0.054
IMT, mm	0.42	0.224
PWV, m/s	-0.22	0.538
Autonomic Function Data		
cvBRS, ms/mmHg	-0.76*	0.011

BMI, body mass index; VO_2, oxygen consumption; HR, heart rate; RER, respiratory exchange ratio; PPO, peak power output; RHR, resting heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; PWV; carotid to femoral pulse wave velocity; PP, pulse pressure; LD, lumen diameter; IMT, intima media thickness; cvBRS, cardiovagal baroreflex sensitivity; RRI, R-R interval.
* indicates $p < 0.05$.
† indicates Spearman correlation coefficient.

4.2.2. CORRELATES WITH CHANGE VARIABLES

ΔcvBRS was correlated with the PRE-to-POST changes in compliance ($r = 0.68$, $p = 0.031$), distensibility ($r = 0.65$, $p = 0.043$), carotid PP ($r = -0.69$, $p = 0.024$), and IMT ($r = -0.74$, $p = 0.014$). ΔcvBRS did not significantly correlate with PRE-to-POST changes in BP variables (SBP, DBP, MAP) or body composition indices (body mass, BMI, lean mass, fat mass, percent body fat, percent lean mass, hip circumference, waist circumference, waist/hip ratio). Pearson correlations of ΔcvBRS with change variables are reported in Table 3.

TABLE 3. Correlates of change in cvBRS with PRE-to-POST change variables.

Variable	r	p
Body Composition Data		
ΔBody Mass, kg	0.08	0.825
ΔBMI, kg/m^2	0.2	0.586
ΔLean Mass, kg	-0.08	0.816
ΔFat Mass, kg	0.12	0.737
ΔPercent Lean Mass, %	-0.13	0.716
ΔPercent Fat Mass, %	0.13	0.716
ΔHip Circumference, cm	0.23	0.525
ΔWaist Circumference, cm	-0.27	0.455
ΔWaist-Hip Ratio	-0.13	0.726
Cardiorespiratory Fitness Data		
ΔAbsolute VO_2peak, mL/min	0.17	0.657
ΔRelative VO_2peak, mL/kg/min	0.17	0.651
ΔPeak HR, bpm	0.20	0.577
ΔRER	0.22	0.563
ΔPPO, W	-0.14	0.698
Resting Heart Rate and Blood Pressure Data		
ΔRHR, bpm	-0.59	0.068
ΔSBP, mm Hg	0.19	0.610
ΔDBP, mm Hg	0.15	0.672
ΔMAP, mm Hg	0.20	0.579
Arterial Structure and Function Data		
ΔCarotid PP, mm Hg	-0.69*	0.024
ΔCompliance, mm^2/mm Hg	0.68*	0.031
ΔDistensibility, mm Hg^{-1}	0.65*	0.043
ΔCarotid LDmax, mm	0.08	0.823
ΔCarotid LDmin, mm	0.21	0.562
ΔIMT, mm	-0.74*	0.014
ΔPWV, m/s	0.19	0.593

BMI, body mass index; VO_2, oxygen consumption; HR, heart rate; RER, respiratory exchange ratio; PPO, peak power output; RHR, resting heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; PP, pulse pressure; LD, lumen diameter; IMT, intima media thickness; PWV; carotid to femoral pulse wave velocity; cvBRS, cardiovagal baroreflex sensitivity.
* indicates $p < 0.05$.

4.2.3. ANALYSIS OF ΔcvBRS

Simple linear regression was used to model the different covariates with ΔcvBRS. The covariates included were baseline cvBRS, compliance, change in compliance and change in distensibility. Regression analysis is reported in Table 4.

Model 1

Model 1 includes ΔcvBRS and baseline cvBRS. While adjusting for baseline cvBRS, ΔcvBRS was significant ($F_{1, 9} = 10.94$, $r = 0.58$, $p = 0.011$). This model explained 57% of the change in cvBRS.

Model 2

Model 2 includes ΔcvBRS and baseline compliance. The influence of baseline compliance on ΔcvBRS was significant ($p = 0.016$). Therefore, ΔcvBRS explained by baseline compliance following 12-weeks of HIIT was significant ($F_{1, 9} = 9.33$, $r = 0.54$, $p = 0.016$), and this model explained 54% of the change in cvBRS.

Model 3

Model 3 includes ΔcvBRS and PRE-to-POST change in compliance. The effect of change in compliance on ΔcvBRS was significant ($p = 0.031$). Therefore, ΔcvBRS explained by the change in compliance was significant ($F_{1, 9} = 6.83$, $r = 0.46$, $p = 0.0309$), and this model explained 46% of the change in cvBRS.

Model 4

Model 4 includes ΔcvBRS and PRE-to-POST change in distensibility. The influence of change in distensibility on ΔcvBRS was significant ($p = 0.043$). As well, this model explained 42% of the change in cvBRS. ($F_{1, 9} = 5.81$, $r = 0.42$, $p = 0.043$).

Model 5

Model 5 includes ΔcvBRS and PRE-to-POST change in PP. The influence of change in PP on ΔcvBRS was significant ($p = 0.025$). As well, this model explained 49% of the change in cvBRS. ($F_{1, 9} = 7.64$, $r = 0.49$, $p = 0.025$).

Model 6

Model 6 includes ΔcvBRS and PRE-to-POST change in IMT. The influence of change in IMT on ΔcvBRS was significant ($p = 0.014$). As well, this model explained 55% of the change in cvBRS. ($F_{1, 9} = 9.95$, $r = 0.55$, $p = 0.014$).

TABLE 4. Simple linear regression modelling with change in cvBRS.

Variable	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6
Intercept	21.2 (7.5)	25.3 (9.4)	2.25 (3.8)	2.52 (3.5)	-0.81 (2.8)	-28.4 (8.7)
cvBRS, ms/mm Hg	-1.30 (0.39)*	-				
Compliance, mm^2/mm Hg	-	-198.74 (65.0)*	-	-	-	-
ΔCompliance, mm^2/mm Hg	-	-	177.17 (67.8)*	-	-	-
ΔDistensibility, mm Hg^{-1}	-	-	-	4621.41 (1917.5)*	-	-
ΔCarotid PP, mm Hg	-	-	-	-	-0.58 (0.2)*	-
ΔIMT, mm	-	-	-	-	-	-388.40 (123.1)*
n	10	10	10	10	10	10
r	0.58	0.54	0.46	0.42	0.49	0.55
p Model	0.011	0.016	0.031	0.043	0.025	0.014

Data expressed as $\beta_{unstandardized}$ (± SE). Simple linear regression was performed.

* indicates $p < 0.05$.

CHAPTER V: DISCUSSION

5.1. EFFECT OF HIIT ON cvBRS

First, we sought out to investigate if cvBRS would be improved following 12-weeks of HIIT independent of changes in BP and body composition indices. Overall, cvBRS remained unchanged following the 12-weeks of HIIT. Second, we sought out to investigate whether any change in cvBRS would be concordant with changes in arterial stiffness (PWV, distensibility, compliance, IMT). We determined that the change in cvBRS, although not significant, was highly related to corresponding changes in distensibility, compliance, and IMT. As expected, the change in cvBRS was highly explained by baseline cvBRS. Interestingly, the change in cvBRS was also related to baseline compliance, a measure of absolute arterial elasticity, and the 12-week change in PP.

Previous investigations of cvBRS with HIIT demonstrate opposing results. Heydari et al. (2013a) observed a 23% increase in cvBRS in the intervention group. The sample consisted of young, sedentary males. Despite the similar age group (24.4 ± 4.7 years), the sample of Heydari et al. (2013a) reported a higher baseline body mass (89.2 ± 2.9 kg), BMI (28.4 ± 0.6 kg/m^2), and waist circumference (93.5 ± 1.6 cm) compared to our sample. It was noted that of the 17 participants in the intervention group of Heydari et al. (2013a), 12 were overweight and five were obese. In contrast, only four of our participants were overweight (BMI 25.0 – 29.9 kg/m^2). Heydari et al. (2013a) also reported a much lower baseline relative VO_2peak (33.9 ± 1.1 mL/kg/min) compared to the current study. Furthermore, there were significant improvements in body mass, BMI,

waist circumference, RHR, SBP, and cardiorespiratory fitness in Heydari et al. (2013a), whereas in the current sample, only cardiorespiratory fitness and MAP improved.

Given the significant changes reported by Heydari et al. (2013a), it is likely that the improvement in cvBRS was attributed to changes in RHR, SBP, body composition, and cardiorespiratory fitness. The absence of changes in the majority of the aforementioned variables, all determinants of cvBRS, may explain why no changes in ANS function following the HIIT protocol were observed.

Currie and colleagues (2013b) demonstrated similar autonomic findings, but with HRV, a measure related to cvBRS. Following 12-weeks of HIIT, there was no apparent change in HRV in older males with documented CAD. This finding was attributed to their already normative cardiac autonomic function. HRV measures beat-by-beat cardiac autonomic function and is reflective of vagal activity, not dissimilar to cvBRS. Hence, the lack of change in HRV following a similar training protocol is comparable to our current findings.

With the current protocol, cvBRS remained unchanged despite significant improvements in RRI. Since SBP is a major determinant of baroreflex function, the lack of change in SBP may likely be the reason that no change in cvBRS was observed with this protocol. In the time course of changes in cardiac autonomic function, RRI lengthens (or shortens) in response to an increase (or decrease) in SBP. Despite the reduction in RRI, it appears that SBP may be a stronger determinant of cvBRS.

The timing of testing days may also be a factor in the lack of change in cvBRS. It is possible that the timing of test days, although scheduled 24 – 48 hours following a HIIT session, may not have been enough time for the nervous system to fully recover. In fact, autonomic recovery following sprint interval exercise is known to be reduced (Stuckey et al. 2012). Although the aforementioned sprint interval exercise consisted of one or four Wingate tests, perhaps the relative intensity and volume of our protocol elicits longer periods of reduced autonomic function, which could be reflected in our results. In fact, transient reductions and shifts in autonomic function are known to occur following bouts of high intensity rowing (Iellamo et al. 2002). Although we did not test the relative contributions of sympathetic and vagal control of cardiac function (sympathovagal balance), autonomic balance is known to shift towards sympathetic predominance with higher intensity exercise (Iellamo et al. 2002). Hence, if MID- or POST-testing occurred during a period where autonomic balance is shifted towards sympathetic predominance, cvBRS would not be enhanced.

5.2. EFFECT OF HIIT ON ARTERIAL STIFFNESS

5.2.1. PULSE WAVE VELOCITY, COMPLIANCE, AND DISTENSIBILITY

HIIT has been shown to have a positive effect on central artery stiffness (Heydari et al. 2013a). However, the current study demonstrates that 12-weeks of HIIT had no effect. Interestingly, PWV improved with the first six weeks of

training, but returned to baseline levels at 12-weeks. This suggests that further improvements in arterial stiffness are not observed with additional volume.

Carotid artery compliance, as well as the corresponding PP and LD measures, also remained unchanged following 12-weeks of HIIT. As for distensibility, there was a significant effect for time; however, caution should be taken when interpreting these results, as post-hoc analysis did not reveal significant differences between time points.

To our current knowledge, there are limited studies that have explored the effects of HIIT on measures of arterial elasticity and diameters. Our findings are consistent with what has been observed following an acute bout of HIIT in a healthy population of men and women (Rakobowchuk et al. 2009), as well as following 12-weeks of HIIT in a CAD sample (Currie 2013a). In fact, lack of alterations in central artery elasticity following endurance training appear to be common in a young, healthy population (Tanaka et al. 2000). Rakobowchuk and colleagues (2008) did not find an improvement in CCA distensibility following six weeks of either sprint interval or endurance training and noted that due to the healthy baseline status of their participants, further room for improvement was largely limited (Rakobowchuk et al. 2008). We believe this is also the case with our sample. Additionally, changes in arterial diameter, a component of compliance and distensibility, is known to occur more extensively in peripheral sites in response to blood flow and shear stress (Black et al. 2016). Peripheral, but not central, vascular changes have been observed following acute (Rakobowchuk et al. 2009) and six weeks of HIIT (Rakobowchuk et al. 2008). The acute training

in Rakobowchuk et al. 2009 consisted of either one single Wingate test, or four Wingate tests, each separated by 4.5 minutes. In contrast, Rakobowchuk et al. (2013) reported improvements in both carotid artery stiffness and HRV following six weeks of both moderate and heavy interval training. Moderate was defined as repeated cycles of 10 seconds of work, 20 seconds recovery at 120% of pre-training VO_2peak; and heavy was defined as repeated cycles of 30 seconds of work, 60 seconds of recovery, also at 120% of pre-training VO_2peak. All participants completed 30 (week 1 – 2), 35 (week 3 – 4), and 40 (week 5 – 6) minutes of exercise. These opposing results could be due to the fact that their participants were more sedentary (lower VO_2peak), the training protocol was different (shorter work cycles and higher work intensity), and β-stiffness was used as the measure of stiffness. β-stiffness index is a regional measure of arterial stiffness similar to PWV; however, it is BP independent and is thought to reflect structural wall changes without the influence of distending pressure (Hayashi et al. 1980, Wohlfahrt et al. 2013, Lim et al. 2016).

5.2.2. CAROTID INTIMA-MEDIA THICKNESS

Of all the carotid artery structure and function variables, carotid IMT improved substantially from baseline to both MID- and POST-training. Measurement of IMT is a useful technique for identifying and quantifying subclinical vascular disease for the evaluation of CVD risk (Stein et al. 2008). In fact, an IMT increase of 0.1 mm has been shown to increase an individual's risk of MI and stroke by 10 – 15% and 13 – 18%, respectively (Lorenz et al. 2007). Our participants' IMT was within the normal range at all timepoints (Engelen et

al. 2013) with improvements of around 0.04 mm at each timepoint. While Rakobowchuk and colleagues (2013) found no changes in IMT following six weeks of either moderate- or high-intensity exercise in young, healthy men and women (Rakobowchuk et al. 2013), Currie (2013a) found improvements of a lesser magnitude in their sample of older (aged 62 ± 11 years) participants with CAD after 12-weeks of HIIT (Currie 2013a). Similar to Currie (2013a), we found no significant change in distensibility but significant improvements in IMT. Additional analysis revealed that the 12-week changes in distensibility and IMT were not correlated ($r = -0.33$, $p = 0.245$). Indeed, findings of a correlation between distensibility and IMT in the literature are inconsistent despite both being measures of arterial health (Alan et al. 2003, Doyon et al. 2013). However, both measures reflect different aspects of the arterial wall (distensibility, functional; IMT, structural), so the lack of a relationship between the two is not surprising. It appears that the impact of HIIT on arterial properties may differ by measurement index.

5.2.3. EFFECT OF ARTERIAL STIFFNESS ON cvBRS

In the findings of the current study there was no significant relationship between baseline and the 12-week change in cvBRS and change in PWV. The absence of a relationship is surprising, since arterial stiffness and cvBRS are known to be highly linked (Bonyhay et al., 1996; Cooke & Carter, 2005; K. D. Monahan et al., 2001). However, most studies that explore the relationship between cvBRS and arterial stiffness often utilize measures of local stiffness, which include carotid artery compliance and distensibility. This suggests that

changes in cvBRS may be attributed more to the local carotid artery changes rather than regional central PWV changes, which encompasses a much larger vasculature region.

Baseline distensibility was not observed to be significantly correlated with the overall change in cvBRS following 12-weeks of HIIT; however, it trended towards significance. A larger sample size would likely have improved the correlation and corresponding significance. In contrast, baseline compliance was significantly correlated with overall change in cvBRS. Similar findings between cvBRS and compliance have been demonstrated in other studies. Bonyhay and colleagues (1996), as well as Monahan et al. (2001) report a strong correlation between cvBRS and carotid artery compliance ($r = 0.78$, $p < 0.001$ and $r = 0.71$, $p < 0.001$, respectively). Likewise, Cook et al. (2005) found a moderate correlation ($r = 0.54$, $p < 0.005$). The results of the regression analysis suggest that the lower the baseline compliance, the greater the potential change in cvBRS.

Likewise, the change in compliance following 12-weeks of training was significantly correlated with the change in cvBRS, which further strengthens our findings with the relationship between carotid artery stiffness and ANS function. Interestingly, the change in distensibility was also significantly correlated with the change in cvBRS, even though baseline distensibility was not. The current findings are in contrast to those of Rakobowchuk and colleagues (2013) who reported that after six weeks of either moderate or high intensity interval training, changes in autonomic control (measured by HRV) were not related to arterial stiffness changes (Rakobowchuk et al. 2013).

The change in cvBRS was significantly explained by the 12-week change in PP. Such a finding is not a surprise since cvBRS and PP are known to be associated regardless of age and gender (Virtanen et al. 2004). Our univariate analysis is also supported by similar analyses done by Virtanen et al. (2004), who showed an inverse relationship exists between cvBRS and PP. Although analyses of cvBRS and PP individually revealed no differences as a result of training, the apparent significance in the regression model may be due to the underlying relationship between cvBRS and PP already.

Interestingly, the change in cvBRS was also highly correlated with the change in IMT. A relationship between cvBRS and IMT has been observed before. Specifically, a greater IMT in the carotid sinus has been associated with reduced cvBRS, even after controlling for factors that are known to influence cvBRS, such as age and BP (Gianaros et al. 2002). Notably, our findings are significant even though our measures of IMT were taken at the common carotid, an area which has a lesser density of baroreceptors compared to the carotid sinus. Physiologically, such a finding is not a surprise, since the baroreceptors rely on stretch of the arterial wall in order to be activated. Presumably, an increase in IMT would require a higher pressure to distend the vessel wall and activate the baroreceptors.

The change we observed PRE to POST in compliance and distensibility trended towards significance, while the PRE to POST change in IMT was significant. In contrast cvBRS did not significantly change following HIIT. Of interest, compliance, distensibility, IMT and cvBRS were linked based on

regression analysis. Overall, the findings from this study support those in the literature that have associated cvBRS with distensibility (Bonyhay et al. 1996), compliance (Cook et al. 2006), (Monahan et al. 2001) and IMT (Gianaros et al. 2002).

5.3. STRENGTHS & LIMITATIONS

To the best of our knowledge, this was the first study to assess the effects of HIIT on ANS function while simultaneously assessing BP, body composition, and arterial stiffness indices. This study is also one of the few studies to explore the effect of HIIT on carotid IMT. A particular strength of this study was that all participants completed the required training volume for the duration of the protocol. Therefore, participant compliance was 100%. Additionally, the target intensities were met with each training session, as HR was carefully monitored. The number of testing sessions was also a strength as we conducted PRE-, MID-, and POST-training data acquisition sessions. However, there are several limitations to be addressed.

First, the aim was to recruit a minimum of 20 males; however, due to logistical restraints, only 16 were recruited in time for the training protocol to begin. One participant dropped out prior to training, and another had several ectopic beats present during baseline testing, and therefore was excluded from the study. Hence, the total sample size was 14 participants. Several measures neared significance, therefore, having a larger sample size would likely have increased the statistical power (Appendix G). As well, having a larger sample size would have allowed us to complete more complex regression models, putting in several

variables into one model. However, although important, the regression models do not address the primary purpose of the study. The current sample was also fairly healthy according to measures of body composition and cardiorespiratory fitness. It is possible that the potential for any variable to improve was largely diminished by the healthy baseline status of the participants.

Second, the study did not include a control group. We had one group of participants who completed the HIIT training protocol. A control group that was not subjected to HIIT training may have provided more insight into the relationship between cvBRS and BP, body composition, and arterial stiffness indices. Additionally, a control group that completed a protocol designed to mimic the current Canadian physical activity guidelines for adults would provide us with the insight as to whether or not HIIT should be recommended as an alternative form of exercise. Despite the drastic reduction in training volume and time commitment, HIIT is also demanding, as noted by the exhaustion our participants displayed following each training session. In a bigger perspective, the time advantage of HIIT must be weighed against the training intensity and post-exercise exhaustion as compared to slower, low-intensity exercise.

Third, although the study was a 12-week HIIT protocol, two differing volumes were incorporated into the first and second halves of the study. The study design followed a similar short-term HIIT protocol (Little et al. 2010). In the first half, the participants exercised two times per week with 10 x 1 minute intervals at 90% of HR_{max} separated by 75 seconds of active rest. Total volume in the first half of the study (PRE-MID) was 240 minutes with 120 minutes of total HIIT

work. In the second half, two more intervals were added, with the same intensity and frequency. Total volume in the second half of the study (MID-POST) was 272 minutes, with 144 minutes of total HIIT work. One consideration would be to examine the effects of the differing volumes of exercise on measures of ANS function, resting BP and HR data, and carotid artery measures. Another consideration may be the effect of volume on rest and recovery. Although care was taken to ensure that testing dates only occurred 24 – 48 hours following the previous HIIT session, autonomic recovery was not monitored, and the additional volume could be impeding the collection of this data.

Finally, although the main outcome of our study was to assess the change in cvBRS with changes in BP, body composition and arterial stiffness, other complimentary measures of ANS function should be included such as HRV. Even though we found no changes in cvBRS with 12-weeks of HIIT, analysis of HRV may provide more insight as to whether or not the lack of change in cvBRS was due to the lack of change in the HRV indices.

CHAPTER VI: CONCLUSION

There is no question that traditional endurance exercise training imparts many benefits with regards to improving cardiorespiratory fitness, BP, arterial health, and ANS function. However, investigating the relationships between cardiorespiratory fitness, BP, arterial health, and ANS function with HIIT warrants attention. The purpose of this investigation was to determine whether there were favourable improvements in ANS function by measuring cvBRS in response to a HIIT protocol. This study found that cvBRS remained unchanged following 12-weeks of HIIT. Despite a reduction in RRI, it appears that SBP is a stronger determinant of cvBRS. However, significant improvements in carotid IMT were demonstrated, suggesting that arterial health improves. The current study also determined that changes in cvBRS were not related to changes in body mass or BMI, SBP, and regional central arterial stiffness (PWV); however, the PRE-to-POST change in cvBRS did track well with changes in distensibility, compliance and IMT, separately, as well as with baseline compliance suggesting that changes in cvBRS may be attributed more to local carotid artery stiffness rather than regional central PWV. Furthermore, the findings of the current study indicate that changes in cvBRS may be driven by baseline compliance. This suggests that baseline arterial stiffness plays an important role in ANS function and adaptation in response to HIIT. Overall, 12-weeks of HIIT did not alter cvBRS in our sample of young, healthy men.

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APPENDIX A

Brock University
Research Ethics Office
Tel: 905-688-5550 ext. 3035
Email: reb@brocku.ca

Bioscience Research Ethics Board

Certificate of Ethics Clearance for Human Participant Research

DATE: 3/5/2015

PRINCIPAL INVESTIGATOR: O'LEARY, Deborah - Health Sciences

CO-INVESTIGATOR: Andrea Josse

FILE: 14-147 - O'LEARY

TYPE: Masters Thesis/Project STUDENT: Austin Cameron
SUPERVISOR: Deborah O'Leary

TITLE: Investigating the Effects of High-Intensity Interval Training on Baroreflex Sensitivity

ETHICS CLEARANCE GRANTED

Type of Clearance: NEW Expiry Date: 3/31/2016

The Brock University Bioscience Research Ethics Board has reviewed the above named research proposal and considers the procedures, as described by the applicant, to conform to the University's ethical standards and the Tri-Council Policy Statement. Clearance granted from **3/5/2015** to **3/31/2016**.

The Tri-Council Policy Statement requires that ongoing research be monitored by, at a minimum, an annual report. Should your project extend beyond the expiry date, you are required to submit a Renewal form before 3/31/2016. Continued clearance is contingent on timely submission of reports.

To comply with the Tri-Council Policy Statement, you must also submit a final report upon completion of your project. All report forms can be found on the Research Ethics web page at http://www.brocku.ca/research/policies-and-forms/research-forms.

In addition, throughout your research, you must report promptly to the REB:

a) Changes increasing the risk to the participant(s) and/or affecting significantly the conduct of the study;
b) All adverse and/or unanticipated experiences or events that may have real or potential unfavourable implications for participants;
c) New information that may adversely affect the safety of the participants or the conduct of the study;
d) Any changes in your source of funding or new funding to a previously unfunded project.

We wish you success with your research.

Approved:

_____
Brian Roy, Chair
Bioscience Research Ethics Board

Note: Brock University is accountable for the research carried out in its own jurisdiction or under its auspices and may refuse certain research even though the REB has found it ethically acceptable.

If research participants are in the care of a health facility, at a school, or other institution or community organization, it is the responsibility of the Principal Investigator to ensure that the ethical guidelines and clearance of those facilities or institutions are obtained and filed with the REB prior to the initiation of research at that site.

APPENDIX B

SUBJECT SCREENING AND MEDICAL HISTORY QUESTIONNAIRE

Name: _____ Date: _____

Age: _____

Your responses to this questionnaire are confidential. If you answer "YES" to any of the following questions, please give additional details in the space provided and discuss the matter with one of the investigators. You may refuse to answer any of the following questions; however, participants may be subject to exclusion from the study based on their responses.

1. Are you currently taking any medication (including aspirin) or have you taken any medication in the last two days?	**YES**	**NO**
2. Have you taken any medication in the past six months?	**YES**	**NO**
3. Is there any medical conditions with which you have been diagnosed and are under the care of a physician (e.g. asthma, diabetes, hypertension, anorexia)?	**YES**	**NO**
4. Have you in the past, or are currently, experiencing any of the following: chest pains during exercise, dizziness or light headedness with exercise, irregular heart beat, high blood pressure or hypertension, high cholesterol, a heart murmur or defect, cardiovascular disease, heart problems of any kind, difficulty breathing, asthma or bronchitis, pneumonia or tuberculosis, diabetes, thyroid problems, other endocrine or hormonal problems, kidney stones, blood in your urine, other kidney problems, hernia, testicular problems, anaemia, blood clotting problems, other blood-related problems, digestive problems, hepatitis/jaundice, HIV/AIDS, severe skin problems, oral or dental problems or injuries, eating disorder/anorexia/bulimia, cancers or tumours, head injury, concussion, mild "bell ringers", burns or stings, numbness in your arms or legs, convulsions, seizures, or epilepsy, neurological disease or problems, severe headaches, hearing problems, eye injuries, vision problems, attention deficit/hyperactivity disorder, sleeping disorders, mental or emotional problems, problems with alcohol or drugs, broken bones, stress fractures or hairline cracks, dislocated joints, sprained joints, torn ligaments, torn cartilage, muscle/tendon injury, arthritis, painful or swollen joints, neck or upper back pain or injury, low back pain or injury, or any other significant medical problem?	**YES**	**NO**
5. If "yes" to any of the conditions listed in question 4, please describe below:		

6. Have you recently undergone a surgery or operation (within the past six months)?	**YES**	**NO**
7. If "yes" to question 6, please describe:		
8. Do you have a family history of any of the following: death before the age of 50, blood disorders or problems, sudden death during physical activity, arthritis, heart problems of any kind, cardiovascular disease including any coronary artery surgeries, diabetes, high blood pressure or hypertension, high cholesterol, chronic obstructive pulmonary disease, another other respiratory-related problems, other major medical problems?	**YES**	**NO**
9. If "yes" to question 8, please describe:		
10. Do you, or have you in the past, consumed any alcohol on a regular basis (i.e. daily, males ≤2 drinks/day, females ≤1 drink/day)?	**YES**	**NO**
11. Do you, or have you in the past, smoked on a regular basis (i.e. daily, ≤ 20 cigarettes/day)?	**YES**	**NO**
12. Are you, or have you in the past, engaged in any extreme diet?	**YES**	**NO**

13. Do you, or have you in the past, consumed any nutritional supplements (e.g. calcium, multi-vitamin, protein powders) on a regular basis (i.e. daily)?	**YES**	**NO**
14. Do you, or have you in the past, engaged in physical activity on a regular basis (i.e. 3-5 times per week)?	**YES**	**NO**
15. Are you aware of any allergies that include milk and soy ingredients?	**YES**	**NO**
16. Are you aware of any other allergies, drug reactions, or hypersensitivities?	**YES**	**NO**

17. If "yes" to question 16, please list ALL known allergies, drug reactions, and/or hypersensitivities.

APPENDIX C

INFORMATION AND CONSENT TO PARTICIPATE IN RESEARCH

Title: Investigating the Effects of High-Intensity Interval Training on Baroreflex Sensitivity

You are invited to participate in a research study being conducted by the investigators listed below. Any participant wishing to participate in this study is asked to complete this consent form. It is important that you read and understand the following explanation of the proposed study. This form outlines the purpose and testing procedures to be used in this study. It also describes your right to refuse to participate or withdraw from the study at any time, the time commitment and the potential risks and benefits, so that you can make an informed decision. For the tests, you will have to visit the Human Hemodynamics Laboratory (WH22, Brock University). This study is being conducted by researchers in the Faculty of Applied Health Sciences.

INVESTIGATORS:	**DEPARTMENT:**	**CONTACT:**
Dr. Deborah O'Leary	FAHS*, Brock University	(905) 688-5550 x4339
Austin J. Cameron	FAHS, Brock University	(905) 688-5550 x4593
Dr. Andrea Josse	FAHS, Brock University	(905) 688-5550 x3502

* FAHS = Faculty of Applied Health Sciences

I. PURPOSE:

The aim of the proposed study is to determine the physiological changes that occur concurrently within the cardiovascular and autonomic nervous systems following a high-intensity exercise training regime in young male adults. In order to examine the effects of high-intensity interval training (HIIT) on neural-vascular components, a cycling exercise training program will be prescribed with physiological assessments throughout the training.

II. DESCRIPTION OF THE TESTING PROCEDURES:

Inclusion/Exclusion Criteria
A "healthy" participant is one that is free of cardiovascular disease and does not partake in unhealthy behaviours such as excessive drinking. Cardiovascular exclusion criteria include the presence or history of coronary artery disease, which is defined as having at least one of the following: angiographically documented stenosis ≥ 50% in at least one major coronary artery; prior history of myocardial infarction, percutaneous coronary intervention, or coronary artery bypass graft surgery; positive exercise stress test determined by a positive nuclear scan, or symptoms of chest discomfort accompanied by electrocardiographic changes of > 1 mm horizontal or down-sloping ST segment depression.

Further exclusion criteria include smoking within three months, non-cardiac surgical procedure within two months, history of New York Heart Association class II-IV symptoms of heart failure (mild shortness of breath and/or angina with slight limitation during ordinary activity; marked limitation in activity due to symptoms; marked limitation in less-than-ordinary activities such as walking short

distances; severe limitations and experiences symptoms even during rest), documented valve stenosis, documented severe chronic obstructive pulmonary disease, symptomatic peripheral arterial disease, unstable angina, controlled and uncontrolled hypertension (resting diastolic blood pressure > 100 mm Hg), controlled and uncontrolled atrial arrhythmia or ventricular dysrhythmia, insulin-requiring diabetes mellitus, and any musculoskeletal abnormality that would limit exercise participation. Participants will also be excluded if they have a baseline VO2max ≥ 56 mL/kg/min, as a VO2max between 56 and 60 mL/kg/min is indicative of a well-trained status.

Exclusion criteria also include BMI cutoffs. According to Health Canada, the classifications of BMI are as follows:

Underweight	BMI < 18.5 kg/m^2
Normal Weight	BMI = 18.5 to 24.9 kg/m^2
Overweight	BMI = 24.9 to 29.9 kg/m^2
Obese	BMI > 30 kg/m^2

Participants will be excluded if they're BMI is under 18.5 kg/m^2 or over 29.9 kg/m^2. The upper limit is set to the overweight classification so as to compensate for the over-estimation of BMI. For example, a highly athletic male (minimal fat mass) who is 196 cm tall and 99 kg would have a BMI of 25.8 kg/m^2, classifying him as overweight despite his high lean mass status.

If a participant is allergic/intolerant/sensitive to dairy and/or soy, they will be excluded from the study. This is due to the contents of the meal replacement drink (Ensure) that will be provided before each training session (see below).

Inclusion criteria include being male between the ages of 18 and 30 who are sedentary, previously active, or recreationally active (VO2max < 56 mL/kg/min and not currently undertaking a rigorous exercise training program).

What is the time commitment?

If you agree to participate in this study, you will partake in a total of 28 sessions over 3.5 months, which is approximately 16.3 hours in total. On your first visit to the laboratory, you will be introduced to the laboratory environment and data collection procedures. Following this, an investigator will take you through the consent-process where you will be given an opportunity to ask questions before deciding whether or not you wish to participate. After which, a familiarization session will begin so that the participant understands the requirements of the study.

Upon receipt of informed consent, you will be scheduled to complete session 2 of 28, which includes a food diary, body composition analysis, baseline cardiovascular variable measurements (heart rate, blood pressure, pulse wave velocity, carotid and aortic imaging), and a maximal exercise test (VO_2max).

The next 26 visits to the laboratory will include completing each block of high-intensity interval training. Each block of training spans six weeks. Block A consists of 10x60 second intervals, and block B consists of 12x60 second intervals. At the end of block A (6 weeks), on a day separate to training, a food diary, measurements of heart rate, blood pressure, pulse wave velocity, carotid and aortic imaging will be completed. This will allow for sufficient rest after training.

Please note that food, exercise, and temperature may affect the results, so we will ask you not to eat 4 hours prior to exercising and testing, and not to exercise the day of testing. Heavy exercise and caffeine should be avoided 24 hours prior to any training session. A meal replacement drink will be provided and must be consumed at least 2 hours prior to exercise or testing. The meal replacement drink will be an Ensure® Original nutrition shake in milk chocolate, strawberry, or vanilla flavours. The nutrition drink comes from Ensure, Abbott Nutrition Canada, Saint-Laurent, Québec, Canada. One bottle is 8 fluid ounces (237 mL), 220 calories, 50 calories of which come from fat. Nutrition amounts per serving are as follows:

Fat	6 g	Sodium	190 mg
Saturated Fat	1 g	Potassium	390 mg
Trans Fat	0 g	Carbohydrate	33 g
Polyunsaturated Fat	3 g	Dietary Fiber	1 g
Monounsaturated Fat	2 g	Sugars	15 g
Cholesterol	5 mg	Protein	9 g

Vitamins and minerals, in amounts not specified, include: vitamin A, vitamin C, calcium, iron, vitamin D, vitamin E, vitamin K, thiamin, riboflavin, niacin, vitamin B6, folate, vitamin B12, biotin, pantothenic acid, phosphorus, iodine, magnesium, zinc, selenium, copper, manganese, chromium, molybdenum, chloride, and choline.

Ingredients include: water, corn maltodextrin, sugar, milk protein concentrate, soy oil, soy protein isolate, sucromalt, cocoa powder (processed with alkali), and canola oil. Ingredients in less than 0.5% include the following: corn oil, magnesium phosphate, potassium citrate, cellulose gel, natural and artificial flavour, potassium chloride, sodium citrate, calcium phosphate, calcium carbonate, salt, choline chloride, ascorbic acid, cellulose gum, monoglycerides, soy lecithin, carrageenan, potassium hydroxide, liquid sucralose, ferric orthophosphate, dl-alpha-tocopheryl acetate, acesulfame potassium, zinc sulfate, niacinamide, manganese sulfate, calcium pantothenate, cupric sulfate, vitamin A palmitate, thiamine chloride hydrochloride, pyridoxine hydrochloride, riboflavin, folic acid, chromium chloride, biotin, sodium molybdate, sodium selenate, potassium iodide, cyanocobalamin, phylloquinone, and vitamin D3.

There are potential concerns with allergies as the drink does contain milk and soy ingredients. The Subject Screening and Medical History Questionnaire will address allergy screening.

For each training and data collection session, we will ask you to wear athletic attire. The following data collection procedures will be described in greater detail below:

1. Questionnaire
2. Body Composition and Anthropometry
3. Heart Rate
4. Blood Pressure
5. Carotid Artery and Aortic Ultrasound
6. Pulse Wave Velocity
7. VO_2max Test
8. Food Diary
9. High-Intensity Interval Training

1. **Questionnaire:** You will be asked to complete a questionnaire outlining your medical history and physical activities. Please be aware that the medical history questionnaire includes questions about drug use, alcohol use, and smoking. In all questionnaires, you may choose not to answer any question; however, you may be excluded from the study if any questions regarding current or past cardiovascular problems are not answered.
2. **Body Composition and Anthropometry:** Body muscle and fat mass will be measured while you sit in the BOD POD chamber. The BOD POD is an air displacement plethysmograph that uses whole-body densitometry to determine fat vs. lean mass. It is similar to the idea of under-water weighing in that it measures body mass (weight) and volume inside the chamber. BOD POD incorporates a built in window on the front of the chamber in the event of a claustrophobic event or for communication purposes as well as a safety button on the inside of the chamber for you to voluntarily exit on your own. During this assessment, you will be asked to relax and breathe normally. If you express any anxiety for confined spaces, body composition can also be measured using bioelectrical impedance analysis (BIA) and ultrasound using the BodyMetrix System. For BIA, a weak electrical current (800μA, 50kHz) passes from electrode plates that you stand on, to electrodes wands that you hold in your hands. This current is very low and one cannot feel it. There is no discomfort associated with this measurement. The BodyMetrix system uses ultrasound to measure fat thickness at the thigh and calculates body fat % and weight distribution. There is no discomfort associated with this measurement. With the BodyMetrix ultrasound device, body composition will be measured at three sites: thigh, chest, and waist. In addition, height, body mass, waist and hip circumference will be measured. Height will be measured using a stadiometer and body mass using a calibrated scale. Waist circumference will be measured using a standard, retractable, non-metallic tape measure placed around the waist at the level of the umbilicus. Hip circumference will be measured using the same tape measure across the largest part of the buttocks and below the iliac crest.
3. **Heart Rate:** Heart rate will be measured using six sensors placed on the skin of your chest. These electrodes are used to detect the electrical activity generated by the heart and are not used to transmit electrical signals into your body from the heart rate monitor. Heart rate will also be monitored during all exercise sessions using a comfortable chest strap and corresponding wristwatch.
4. **Blood Pressure:** Blood pressure will be monitored using a non-invasive method. After ten minutes of quiet rest, systolic and diastolic blood pressure will be measured manually using a sphygmomanometer and stethoscope at the brachial artery, like at the doctor's office. Following the manual blood pressure measurement, continuous beat-by-beat systolic and diastolic blood pressure will be collected non-invasively using a Nexfin, a small inflatable finger cuff placed on the middle finger on the left hand. This technique will allow us to continuously measure blood pressure throughout the protocol.
5. **Carotid Artery and Aortic Ultrasound**: Ultrasound will be performed with a small transducer in order to visualize the arteries of interest. This measurement requires a thin layer of gel to be applied to the skin. The measurement also involves the use of a pen like-device (a tonometer, described below in "*Pulse Wave Velocity*"), in order to measure pressure within the artery. Both the probe and tonometer will be pressed against the neck on opposite sides. It is a non-invasive procedure.
6. **Pulse Wave Velocity:** This is a measure of the speed of pressure waves between two different

points along the blood vessels. These waveforms are collected by a technique called "applanation tonometry", where a small pen-like device, the tonometer, is placed on the surface of the skin at the site of an artery. The tonometer detects pulses and converts them into waveforms. The waveforms are then used to calculate pulse wave velocity. Tonometry will be conducted at your carotid artery and sinus (neck), femoral artery (groin), and radial artery (wrist). A pulse oximeter will be place on your foot to measure dorsalis pedis artery waveforms. The values obtained from these measurements will allow for the calculation of central and peripheral pulse wave velocities.

7. **VO_2max Test:** The VO_2max test will take place on a stationary cycle ergometer. The test will consist of a 5 minute warm-up at 100 watts (W), after which the workload will increase by 1 W every 2 seconds until volitional fatigue or until the pedal cadence drops below 40 revolutions per minute (rpm) or drops 20 rpm over 5 seconds. The values obtained during this test will be used to estimate the workload (watts) for the HIIT sessions.
8. **Food Diary:** Prior to beginning the first session of training, you will need to record a minimum of three days of a food diary, in detail. This will be repeated at the end of each block and at the end of the study. In all, you will have to complete a pre, week 6, and week 12 (post) food diary. We also ask that you consume the same meal the night before the data collection sessions to ensure consistency.
9. **High-Intensity Interval Training:** Exercise training will make-up the largest portion of the study design. All exercise training sessions will be performed on a stationary cycle ergometer and will include a standardized 3-minute warm-up at 100 W and a 5-minute cool down at 30 W, with heart rate monitoring. All exercise-training sessions will be supervised by a member of the research team who will ensure that you are using proper techniques and exercising at the correct intensities. The exercise training will be divided into two blocks, each spanning six weeks, with a frequency of two sessions per week. Therefore, there will be 12 sessions per block, or 24 training sessions for the entire study. With completion of block A, more intervals (bouts) will be added. Each interval will meet a percent heart rate criterion—around 90%HRmax and the average HR for the training session should be 90%HRmax. The power output at VO2peak will give us an indication of the wattage settings during each HIIT session; however, this will be adjusted to ensure that you are exercising at 90%HRmax. After the final session of each block (weeks 6 and 12), in-lab testing will occur on a separate day. This is to ensure sufficient rest is met. A breakdown of the time commitment is shown below:

Time Commitment Breakdown of Training Sessions in Each Block

a) Familiarization Day 1: 30 minutes
- Protocol familiarization
- Food diary

b) Pre-Training Data Collection Day 2: 1.5 hr
- Body composition analysis
- Cardiovascular variable measurement
- VO2max test

c) Block A: 360 min or 6 hr = 60 min/week = 30 min/session
- 3 min warm-up at 30 W
- 10x60 sec bouts at 100% PPO
    - 75 sec active rest at 45 W between each bout

- 5 min cool-down at 30 W

d) Block B: 408 min or 6.8 hr = 68 min/week = 34 min/session

- 3 min warm-up at 30 W
- 12x60 sec bouts at 100% PPO
  - 75 sec active rest at 45 W between each bout
- 5 min cool-down at 30 W

e) Data Collection: weeks 6 and 12 = 3 hr = 1.5 hr/session

- Food diary
- Body composition analysis
- Cardiovascular variable measurement
- VO2max test

Time Commitment Breakdown for *Data Collection*

a) Body Composition Analysis: 10 minutes

- anthropometrics and/or BIA/Body Metrix = 5 min
- BOD POD analysis = 5 min

b) Vascular Analysis: 1 hour

- rest = 5 min
- manual blood pressure collection 1 = 10 min
- baseline beat-by-beat heart rate and blood pressure = 15 min
- ultrasonography = 15 min
- pulse wave velocity = 5 min
- manual blood pressure collection 2 = 10 min

c) VO2max test: 15 – 20 minutes

- warm-up = 5 min
- test = 6 – 7 min
- cool down = 5 min

Total Time Commitment: Approximately 16.3 hours

III. CONFIDENTIALITY:

Your participation will remain confidential. The personal data collected from this investigation will be kept secured on the premises of Brock University in the laboratory, and will not be accessed by anyone other than the listed investigators. Investigators will require disclosure of your name and contact information (phone, email), and therefore your participation is not completely anonymous during the conduct of the research. However, all participants will have their names removed from any data and assigned a unique anonymization code. The master list matching participants to the data will be password-protected and kept by Austin J. Cameron (student PI). All electronic data will be stored on password-protected computers and paper data in a locked filing cabinet. Following publication of the data, all personal identifiers will be confidentially destroyed, as well data will be destroyed 5 years following publication (electronic files will be deleted and paper data shredded), the allotted time required to keep scientific data post-publication. You should be aware that the results of this study will be made available to scientists through publication in a scientific journal, but your name and any personal data will not appear in compiling or publishing these results. Additionally, you will have

access to your own data as well as the group data when it becomes available, if you are interested.

IV. PARTICIPATION & WITHDRAWAL:

You can choose whether to participate in this study or not. If you are a Brock University student, your decision to participate, not participate, or withdraw, will in no way affect your academic standing at Brock University. You may also refuse to answer any questions posed to you during the study; however, you may be excluded from the study if some questions are not answered (i.e. any cardiovascular-related questions in the Subject Screening and Medical History Questionnaire). This is to ensure your safety. The investigators reserve the right to withdraw you from the study if they believe that it is necessary. In the event of a withdrawal from the study, compensation will still be given for any laboratory visits you are present for, as described in *VI. Remuneration*. As well, your participation or withdrawal will not affect your standing at Brock University either positively or negatively. Upon withdrawal, all of your associated data will be erased from computers and any paper documents shredded. If participants would like to withdraw, they can notify any of the investigators in person, by email, or by phone. Contact information is described in section *VIII. Inquiries.*

V. RISKS AND BENEFITS:

The only foreseeable risks involved in participation include:

a) In rare instances, possible skin irritation may occur from applying surface electrodes and/or conducting gel. This can be minimized by washing the skin and applying skin lotion.
b) Discomfort and tingling often occurs in the left middle finger where beat-by-beat blood pressure is taken. However this method is safe and poses no danger to the subject. Discomfort and tingling will subside within a few minutes after the testing is completed.
c) As with all exercise, there is a transient increase in the risk of cardiovascular complications; however, the risks associated with maximal exercise in a healthy population are low. In a sedentary young adult population without heart disease, the risk of cardiovascular event or complication is on the order of 1 in 400,000 – 800,000 hours of exercise[1]. Exercise is therefore considered very safe. Risks of muscle cramping and fatigue in your legs or buttocks are possible. These feelings should subside within a few days.
d) None of the procedures are diagnostic, however, if an unusually low or high result is attained for any of the measurements, reflecting a possible health-related problem, you will be alerted and advised to consult your physician. Only a physician can make a diagnosis.
e) Due to the nature of maximal graded exercise testing (VO2max test) and HIIT exercise, the risks of nausea and/or vomiting are increased. Prior to any exercise testing, we ask that you not eat for at least four hours prior and that you consume the Ensure meal replacement drink at least two hours prior to testing. This will ensure that digestion is complete, hence reducing the risk of nausea occurring during HIIT training. As well, if nausea and/or vomiting occurs, participants can choose to continue a training session at their own discretion or re-schedule for a later date. Fluids will be provided throughout the VO2max test and training sessions as well, and snacks will be made available at the end of each session.

[1]Myers 2003. Exercise and cardiovascular health. *Circulation*, 107:e2-e5.

VI. REMUNERATION:

To compensate you for your time, a $100 gift card redeemable at the Pen Centre will be provided upon completion of the study. If you choose to withdraw early, you will be compensated for your time. A minimum of 24 out of 28 sessions is required for full compensation. For anything less, compensation will be prorated to percentage-based attendance. For example, if you complete 15 sessions, you will receive (15/28)*$100 = $53. Prorated compensation will be provided if you withdraw/are withdrawn by researchers due to medical reasons.

Participation will allow you to become exposed to an interdisciplinary exercise physiology research protocol, contribute to the advancement of science, and gain knowledge about the function of your own body. You will also have the rare opportunity to see two-dimensional images of your carotid artery, sinus and aorta. All results will be provided to you in a final report at the completion of the study, upon request. You will *not* be given information regarding your data (i.e. body fat percentage, pulse wave velocity, etc.) at the time of testing, as the data still needs to be analyzed.

VII. RIGHTS OF RESEARCH PARTICIPANTS:

You will receive a signed copy of this ethics form. You may withdraw your consent to participate in this study at any time, and you may also discontinue participation at any time without penalty. In signing this consent form or in participating in this study you are not waiving any legal claims or remedies. This study has been reviewed and received clearance from the Brock University Research Ethics Board (file #). If you have any pertinent questions about your rights as a research participant, please contact the Brock University Research Ethics Officer (905 688-5550 ext. 3035, reb@brocku.ca)

VIII. INQUIRIES:

Please contact Dr. Deborah O'Leary (905-688-5550 x4339), Dr. Andrea Josse (905-688-5550 x3502), and/or Austin J. Cameron (905 688-5550 x4593) or email (ac13kk@brocku.ca) if you have any questions about the study.

Investigating the effects of Low-Volume High-Intensity Interval Training on Baroreflex Sensitivity

CONSENT STATEMENT

SIGNATURE OF RESEARCH PARTICIPANT

I HAVE READ AND UNDERSTAND THE ABOVE EXPLANATION OF THE PURPOSE AND PROCEDURES OF THE PROJECT. I HAVE ALSO RECEIVED A SIGNED COPY OF THE INFORMATION AND CONSENT FORM. MY QUESTIONS HAVE BEEN ANSWERED TO MY SATISFACTION AND I AGREE TO PARTICIPATE IN THIS STUDY.

_____
PRINTED NAME OF PARTICIPANT

_____ _____
SIGNATURE OF PARTICIPATNT DATE

_____
PRINTED NAME OF WITNESS

_____ _____
SIGNATURE OF WITNESS DATE

INVESTIGATOR

In my judgment the participant is voluntarily and knowingly giving informed consent and possesses the legal capacity to give informed consent and participate in this research study.

_____ _____
SIGNATURE OF INVESTIGATOR DATE

APPENDIX D

RECORD OF FOOD INTAKE

Name: _____ Date: _____

Day of Week (circle): Mon Tue Wed Thu Fri Sat Sun

Meal/Time	Food consumed	Amount (ml, grams, servings)	How it was prepared (baked, broiled)	Seasonings/ Toppings	Notes

APPENDIX E

Date: _____ Time (am/pm): _____

STUDENT (check for completeness)

SECTION 1: STUDENT INFORMATION		
Subject #: ____ ____ ____ ____ ____ ____ ____ ____ ____	**Name:**	
Gender: Male Female	**DOB:** __ __ / __ __ / __ __ __ __ (month) (day) (year)	**Age:** _____ **years** **Age:** _____ **months**
Height (cm): _____ **Sitting Height (cm):** _____	**Weight (kg):** _____ **Waist Circumference (cm)** _____ **Hip (cm)** _____	**BMI (kg/m^2)** _____

1. Consent (signed): _____
2. Medical Screening Questionnaire: _____
3. Have you had anything to eat or drink in the last 4 hours? _____. If yes, how long ago? _____
4. Did you participate in any exercise today? _____. If yes, how long ago? _____ . What type? _____. For how long? _____
5 Did you have any caffeine today? _____. If yes, how long ago? _____. What type? _____
6 Females. Currently on period? What day approx.?_____

SECTION 3 CONTINUED: BODY COMPOSITION MEASURES		
BODPOD Measurements		
Examiner:		
Lean Mass _____Kg Fat Mass _____Kg %BF_____ %FFM _____		
Body Volume _____ L Body Density _____ Kg/L Thoracic Gas Volume _____ L		
	HR _____	

SECTION 4: ARTERIAL MEASUREMENTS		
Blood Pressure - Manual		
	Systole (mmHg)	**Diastole (mmHg)**
Pre 1		
2		
3		
Post 1		
2		
3		

Distance Measurements	
Sternal notch to toe: **_____ cm**	Sternal notch to carotid: **_____ cm**
Sternal notch to sinus _____ cm	Sternal notch to femoral _____ cm
Sternal notch to radial artery _____ cm	Radial artery to finger_____ cm
Sternal notch to umbilicus _____ cm	Umbilicus to toe _____ cm

Notes for Cardiovascular Component

HIIT-BRS Ramp VO2max Protocol: 1W2S (AUSmx)

Subject ID: _____ **Date:** _____

fiO2 PRE: _____ **Correction Factor:** _____

fiO2 POST: _____

Stage	Time (Ramp/Actual)	Workload (Ramp/Actual)	HR	RPE
Warm-Up	5:00 (0)	100		
1	6:00 (1:00)	130		
2	7:00 (2:00)	160		
3	8:00 (3:00)	190		
4	9:00 (4:00)	210		
5	10:00 (5:00)	240		
6	11:00 (6:00)	270		
7	12:00 (7:00)	300		
8	13:00 (8:00)	330		
9	14:00 (9:00)	360		
10	15:00 (10:00)	390		

Recovery

1	1:00	50
2	2:00	50
3	3:00	50
4	4:00	50
5	5:00	50

*Actual: write down the time/watts they actually complete.
i.e. If the individual maxes out at 11:02, the workload would be 271 W.
**HR & RPE should be collected in the last 10 seconds of each minute.

Notes: _____

APPENDIX F

HIIT-BRS: HIIT Protocol

Subject ID: _____ **Date:** _____

Block: A B **Session:** ___ of 26

VO2peak DATA

Previous VO2max Date: _____

PPO: _____

HRmax: _____

90%HRmax: _____

Stage		Time (Interval/Total)	Workload (W)	HR (bpm)	RPE
Warm-Up		3:00 (0)	30		
	1	1:00 (4:00)			
Recovery		1:15 (5:15)	45		
	2	1:00 (6:15)			
Recovery		1:15 (7:30)	45		
	3	1:00 (8:30)			
Recovery		1:15 (9:45)	45		
	4	1:00 (10:45)			
Recovery		1:15 (12:00)	45		
	5	1:00 (13:00)			
Recovery		1:15 (14:15)	45		
	6	1:00 (15:15)			
Recovery		1:15 (16:30)	45		
	7	1:00 (17:30)			
Recovery		1:15 (18:45)	45		
	8	1:00 (19:45)			
Recovery		1:15 (21:00)	45		
	9	1:00 (22:00)			
Recovery		1:15 (23:15)	45		
	10	1:00 (24:15)			
Recovery		1:15 (25:30)	45		
	11	1:00 (26:30)			
Recovery		1:15 (27:45)	45		
	12	1:00 (28:45)			
Cool-Down		5:00 (33:45)	30		

Notes: _____

APPENDIX G

```
PROC POWER;
     PAIREDMEANS SIDES=2
          ALPHA = 0.05
          MEANDIFF = 0.9
          CORR = 0.5
          STDDEV = 7.2
          NPAIRS = .
          POWER = 0.1 TO 0.9 BY 0.1
          ;
RUN;
```

The POWER Procedure
Paired t Test for Mean Difference

Fixed Scenario Elements	
Distribution	Normal
Method	Exact
Number of Sides	2
Alpha	0.05
Mean Difference	0.9
Standard Deviation	7.2
Correlation	0.5
Null Difference	0

Computed N Pairs			
Index	Nominal Power	Actual Power	N Pairs
1	0.1	0.102	30
2	0.2	0.201	82
3	0.3	0.301	134
4	0.4	0.401	189
5	0.5	0.500	248
6	0.6	0.601	316
7	0.7	0.700	397
8	0.8	0.801	505
9	0.9	0.900	675