Effects of High-Intensity Intermittent Exercise on Fat Loss, Cardiovascular, and Autonomic Function

Mehrdad Heydari

A thesis submitted for the degree of

Doctor of Philosophy

at

School of Medical Sciences

Faculty of Medicine

University of New South Wales

May 2013

Sydney, Australia

COPYRIGHT STATEMENT

AUTHENTICITY STATEMENT

_I certify that the Library deposit digital copy is a direct equivalent of the final officially approved version of my thesis. No emendation of content has occurred and if there are any minor variations in formatting, they are the result of the conversion to digital format.‘

Signed ……..... Date …….....

ORIGINALITY STATEMENT

I hereby declare that this submission is my own work and to the best of my knowledge it contains no materials previously published or written by another person, or substantial proportions of material which have been accepted for the award of any other degree or diploma at UNSW or any other educational institution, except where due acknowledgement is made in the thesis. Any contribution made to the research by others, with whom I have worked at UNSW or elsewhere, is explicitly acknowledged in the thesis. I also declare that the intellectual content of this thesis is the product of my own work, except to the extent that assistance from others in the project's design and conception or in style, presentation and linguistic expression is acknowledged.'

Signed …… Date ……

PREFACE

The main chapters of this thesis have been reproduced from papers that have been published or are under peer-review. The citations to these papers are provided at the start of chapters two to five. At the time of writing, chapter two had not yet been published but was submitted for peer-review to the Journal of Sports Sciences. Content of chapters two to five appear as published but minor alterations have been made to the format of the papers; this includes the placement of tables and figures. References style was also changed to be consistent throughout the thesis.

DEDICATED TO:

My father, for his encouragement and support

My mother, for her endless and unconditional love

and

My wife Leila and my beautiful daughters Rose and Hannah who came into my life mid-journey and brought with them love and happiness

AKNOWLEDGMENTS

I have been fortunate to have the intellectual supervision, mentoring, and guidance of Associate Professor Stephen Boutcher and am always grateful for his patience and continued support which made it possible to bring this journey to fruition. I would also like to acknowledge the assistance that I obtained from my co-supervisor Dr Yati Boutcher.

I would like to express my appreciation to those who generously contributed to my research, particularly Judith Freund, at St. Vincent‘s hospital who assisted with DEXA and CT scans and ILP medical students for their help with data collection.

Finally, I would like to take this opportunity to sincerely thank the study participants who graciously gave up their time to participate in this research and also my office friends Daniel and Rahman for their help and creating a warm and friendly environment.

PUBLICATIONS

- **M. Heydari**, J. Freund, and S. H. Boutcher. The effect of high-intensity intermittent exercise intervention on fat loss in overweight young males. *Journal of Obesity*. 2012; doi:10.1155/2012/480467.
- **M. Heydari**, Y. N. Boutcher and S. H. Boutcher. High-intensity intermittent exercise and cardiovascular and autonomic function. *Clinical Autonomic Research*. 2013; 23(1): 57-65, doi:10.1007/s10286-012-0179-1. This article has been selected as a *paper of the month* by The Research Committee, School of Medical Sciences (SoMS), UNSW, December 2012. http://medicalsciences.med.unsw.edu.au/staff/research-support/paper-month (Access date: 12/02/2013)
- **M. Heydari**, Y. N. Boutcher and S. H. Boutcher. The effects of high-intensity intermittent exercise training on cardiovascular response to mental and physical challenge. *International Journal of Psychophysiology.* 2013; 87(2): 141-146, doi: 10.1016/j.ijpsycho.2012.11.013.
- **M. Heydari** and S. H. Boutcher. Rating of perceived exertion after 12 weeks of high-intensity intermittent sprinting. *Perceptual and Motor Skills,* 2013; 116(1): 1-12, doi: 10.2466/06.15.29.PMS.116.1.
- **M. Heydari**, J. Freund, and S. H. Boutcher. Visceral fat mass of overweight males following 12 weeks of high-intensity intermittent exercise (Abstract). *Medicine and Science in Sports and Exercise*. 2011; 43(5): 905, doi: 10.1249/01.
- **M. Heydari**, J. Freund, and S. H. Boutcher. Aerobic fitness and abdominal fat mass of overweight males following 12 weeks of high-intensity intermittent

exercise (Abstract). *Obesity Research and Clinical Practice*. 2010; 4(Suppl 1): S41, doi: 10.1016/j.orcp.2010.09.083.

- A. A. Khaki, A. Khaki, **M. Heydari**, and L. Gholizadeh. A description of gender differences in angiographic findings in a single-center Iranian hospital. *Journal of Vascular Nursing*. 2010; 28(1): 11-3.
- L. Gholizadeh, P. M. Davidson, **M. Heydari**, and Y. Salamonson. Heart disease and depression: is culture a factor? *Journal of Trans Cultural Nursing*, in press.
- **M. Heydari**, D. Ghareman and S. H. Boutcher. Metabolic response of trained and untrained males during acute high-intensity intermittent exercise. *Journal of Sports Sciences*, under review.
- **M. Heydari**, J. Freund, Y. N. Boutcher and S. H. Boutcher. Visceral fat accumulation and metabolic risk factors of westernized overweight young males of Asian and European descent. *Nutrition, Metabolism and Cardiovascular Diseases*, under review.
- S. H. Boutcher, F. K.C. Hui, **M. Heydari**, S. L. Dunn, and J. Freund. Comparison of bioelectrical impedance and dual energy x-ray absorptiometry assessment of body composition change after an exercise intervention. *Journal of Sports Sciences*, under review.
- L. Gholizadeh, P. M. Davidson, **M. Heydari**, Y. Salamonson, and D. Hare. Cross cultural comparison of the Cardiac Depression Scale. *Journal of Psychosocial Nursing,* under review.
- L. Gholizadeh, Y. Salamonson, **M. Heydari**, and P. M. Davidson. Casual attributions of Middle Eastern women hospitalized for coronary heart disease: an observational study. *International Journal of Research in Nursing*, under review.

CONFERENCE PRESENTATIONS

- **M. Heydari**, Y. N. Boutcher and S. H. Boutcher. The effects of high-intensity intermittent exercise on cardiovascular and autonomic reactivity. 22nd *Australasian Psychophysiology Conference and Annual General Meeting of the Society (ASP),* Sydney, Australia. Oral presentation, 2012.
- **M. Heydari,** Sprint to fight fat. The University of New South Wales media release. http://newsroom.unsw.edu.au/news/health/sprint-fight-fat. (Access date: 29/06/2012)
- **M. Heydari**, Y. N. Boutcher and S. H. Boutcher. The effects of 12 weeks of high-intensity intermittent exercise on resting cardiovascular and autonomic function. *The Australian Cardiovascular Health and Rehabilitation Association (ACRA)*, Brisbane, Australia. Moderate poster presentation, 2012.
- L. Gholizadeh, P. M. Davidson, and **M. Heydari**. The interplay of heart disease, depression and culture. *The Australian Cardiovascular Health and Rehabilitation Association (ACRA)*, Brisbane, Australia. Moderate poster presentation, 2012.
- **M. Heydari**, J. Freund, and S. H. Boutcher. Visceral fat mass of overweight males following 12 weeks of high-intensity intermittent exercise. *American College of Sports Medicine (ACSM) Annual meeting*, Denver, Colorado, USA. Poster presentation, 2011.
- L. Gholizadeh, **M. Heydari**, and P. M. Davidson. The importance of specification of risk target when assessing patients‘ causal attributions for coronary heart disease. *The Asia Pacific Conference on Metabolic Syndrome (APCMS).* Sydney, Australia. Poster presentation, 2011.

- **M. Heydari**, J. Freund, and S. H. Boutcher. Aerobic fitness and visceral fat mass of overweight males following 12 weeks of high-intensity intermittent exercise. *Australian and New Zealand Obesity Society's Annual Meeting (ANZOS)*, Sydney, Australia. Oral presentation, 2010.
- **M. Heydari**, J. Lane, and S. H. Boutcher. The relationship between aerobic fitness and metabolic syndrome markers in sedentary young males. *The 1st International and 3rd Iranian Congress of Endocrine & Metabolism Updates*, Isfahan, Iran, Poster presentation, 2010.
- **M. Heydari**, C. Tran, J. Freund, S. H. Boutcher. Association between regional adiposity distribution and insulin resistance in young overweight males. *The 1st International and 3rd Iranian Congress of Endocrine & Metabolism Updates*, Isfahan, Iran, Poster presentation, 2010.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

ABBREVIATIONS

ABS: Australian Bureau of statistic
ACh: Acetylcholine
ACTH: Adrenocorticotropic Hormone
AIx: Augmentation Index
ANP: Atrial Natriuretic Peptide
ANS: Autonomic Nervous System
BA: Brachial Artery
BEI: Baroreceptor Effectiveness Index
BMI: Body Mass Index
BP: Blood Pressure
BRS: Baroreflex Senstivity
CAD: Coronary Artery Disease
CHD: Coronary Heart Disease
CO: Cardiac Output
COP: Cardiac Output Program
COPD: Chronic Obstructive Pulmonary Disease
CPWV: Central Pulse Wave Velocity
CRH: Corticotrophine Releasing Hormone
CS: Citrate Synthase
CT: Computed Tomography
CVD: Cardiovascular Disease
DBP: Diastolic Blood Pressure
DEXA: Dual-Energy X-Ray Absorbtiometry
eNOS: endothelial Nitric Oxide Synthase
EPOC: Excess Post-exercise Oxygen Consumption
FBF: Forearm Blood Flow
FFA: Free Fatty Acid
FFM: Free Fat Mass
FM: Fat Mass
FMD: Flow-Mediated Dilation
FVR: Forearm Vascular Resistance
GH: Growth Hormone
HC: Hip Circumference
HDL-C: High-Density Lipoprotein Cholesterol
HF: Heart Failure

HF: High Frequency
HI: Heater Index
HIIE: High-Intensity Intermittent Exercise
HPA: Hypothalamic Pituitary Adrenal
HPV: Heart Period Variability
HR: Heart Rate
HU: Hounsfield Unit
ICG: Impedance Cardiography
LDF: Laser Doppler Flowmetry
LDL-C: Low-Density Lipoprotein Cholesterol
LF: Low Frequency
LVET: Left Ventricle Ejection Time
MAP: Mean Arterial Pressure
MRI: Magnetic Resonance Imaging
MS: Multiple Sclerosis
NO: Nitric Oxide
PAR-Q: Physical Activity Readiness-Questionarie
PEP: Pre-Ejection Period
PORH: Post-Occlusion Reactive Hyperemia
PPWV: Peripheral Pulse Wave Velocity
PWV: Pulse Wave Velocity
RER: Respiratory Exchange Ratio
RH: Reactive Hyperemia
RMR: Resting Metabolic Rate
RPE: Ratings of Perceived Exertion
RPP: Rate Pressure Product
RQ: Respiratory Quotient
SBP: Systolic Blood Pressure
StO2: Tissue Oxygen Saturation
SV: Stroke Volume
TC: Total Cholesterol
TiVi: Tissue Viability Imager
TP: Total Power
VLDL-C: Very Low-Density Lipoprotein Cholesterol
VLF: Very Low Frequency
WC: Waist Circumference
WHO: World Health Organisation

ABSTRACT

This thesis consists of a series of publications that address public health questions in the field of exercise physiology. The thesis aimed to investigate the effects of high-intensity intermittent exercise (HIIE) on fat metabolism, fat loss, and cardiovascular and autonomic function and is composed of two studies. Study I used a comparative research design to compare the metabolic response to acute HIIE of trained and untrained young males. Males completed 20 min of HIIE consisting of 8-sec fast pedalling at 65% of maximum workload followed by 12-sec of slow pedalling at 25% of maximum workload. Blood lipids, glucose, lactate, and catecholamine response of two groups was compared. Study II used a randomised controlled trial to examine the effects of 12 weeks of HIIE training on abdominal, visceral, total body fat mass, and fat free mass of young males. Cardiovascular and autonomic response to HIIE at rest and during mental and physical challenge was also investigated. Males completed 20 min of interval sprinting, 3 times per week, for 12 weeks.

Study I found that trained compared to untrained males recorded similar response to acute HIIE. Fat oxidation rate increased significantly in both groups after acute exercise with no difference between groups. Glycerol level was significantly elevated for both groups during exercise. Lactate concentration also increased in both groups during HIIE, however, was higher for untrained males. Furthermore, both groups showed significant increases in epinephrine and norepinephrine during HIIE.

In Study II aerobic fitness improved for the exercise group who, compared to controls, showed greater total fat, abdominal, trunk, and visceral adiposity fat loss and greater increase in fat free mass. The exercise group also recorded a significant

reduction in heart rate accompanied by increased stroke volume at rest and during mental and physical challenge. Forearm vasodilatory capacity and forearm blood flow of the exercise group increased during the first two min of Stroop although remained unchanged at rest. Also, arterial stiffness, heart period variability and baroreflex sensitivity increased significantly at rest and during Stroop.

It is concluded that acute HIIE training generated similar metabolic responses for both trained and untrained males. Twelve weeks of chronic HIIE had positive effects on body composition, and cardiovascular and autonomic function of overweight males at rest and during mental and physical challenge.

Introduction

Rationale

Obesity has been associated with serious health complications such as hypertension, type 2 diabetes, and cardiovascular disease (Lavie, Milani, & Ventura, 2009; Zalesin, Franklin, Miller, Peterson, & McCullough, 2011). The rate of obesity is increasing dramatically in developed and developing countries among both men and women. According to a prediction by the World Health Organisation, by 2015 approximately 3 billion adults will be overweight or obese internationally (Australian Institute of Health and Welfare, 2012). In parallel with international trends, obesity is a challenge for the health care system of Australia, with one in four Australian adults (25%) and one in twelve Australian children (8%) being obese in 2007-08 (Australian Institute of Health and Welfare, 2012). In the United States, more than one-third of adults and almost 17% of youth were obese in 2009-2010 (Ogden, Carroll, Kit, & Flegal, 2012).

There is evidence that body fat loss has great potential for promoting general health and preventing the complications associated with metabolic syndrome and type 2 diabetes (Church, 2011). Diet and exercise are the main strategies underpinning the majority of fat loss regimens, however, traditional aerobic exercise fails to result in substantial weight loss (Wu, Gao, Chen, & Van Dam, 2009). Furthermore, the effects of diet interventions on maintaining weight loss and lean body mass in long term are negligible and many individuals put the weight back on within five years (Wadden, 1993).

Therefore, other types of exercise modalities such as high-intensity intermittent exercise (HIIE) have been suggested to have the potential to result in greater body fat

loss (Christmass, Dawson, & Arthur, 1999). HIIE has the potential to maintain or improve lean body mass while decreasing excessive fat mass (Boutcher, 2011). HIIE typically consists of repeated bouts of intense exercise (6 sec to 4 min) followed by light bouts of exercise or complete rest (Boutcher, 2011). Compared to steady state exercise, HIIE has been shown to be more effective in reducing body fat mass (Trapp, Chisholm, Freund, & Boutcher, 2008). Acute HIIE has also been shown to result in significant increases in epinephrine and norepinephrine levels during exercise (Trapp, Chisholm, & Boutcher, 2007). Catecholamines are responsible for lipolysis and fat release from subcutaneous and intra muscular fat stores (Issekutz, 1978).

Exercise has also been shown to have beneficial effects on cardiovascular and autonomic body responses (Miller, Balady, & Fletcher, 1997; Rosenwinkel, Bloomfield, Arwady, & Goldsmith, 2001). However, the majority of these studies have focused on steady state aerobic training such as regular running and cycling and the outcome measures examined have been mainly induced resting heart rate and blood pressure (BP) (Wilmore et al., 2001). Vascular adaptations to aerobic exercises have included limb blood flow, limb vasodilatory capacity, and arterial stiffness. Limb blood flow and vasodilatory capacity, indicants of the ability of the arterioles to dilate, have been enhanced by aerobic training in exercising (Martin, Kohrt, Malley, Korte, & Stoltz, 1990) and non exercising muscles (Silber, McLaughlin, & Sinoway, 1991). Autonomic adaptations to aerobic exercise have been assessed by changes in vagal influence on the heart and arterial baroreflex sensitivity (BRS). The vagal influence on the heart, as measured by heart period variability (HPV), has been shown to increase after steady state endurance exercise training (Tulppo et al., 2003). The cardiac, vascular, and autonomic responses to other forms of chronic exercise,

such as HIIE, however, have not been examined. Therefore, Study II evaluated the effects of HIIE on various cardiovascular, metabolic, and autonomic variables.

The human body system is constantly challenged by a wide range of stimuli including physical and psychological stressors. Smoking, obesity, diabetes, physical inactivity, and family history are traditionally known risk factors which predict about 50% of the variance of a cardiovascular event (WHO, 2011). Other risk factors, such as psychological stress have also been linked to development of cardiovascular disease (Chida & Steptoe, 2010). Both acute and chronic steady state aerobic exercise (e.g., cycling, jogging, and swimming) have been shown to reduce cardiovascular reactivity (Blumenthal et al., 1991; Boutcher & Hamer, 2006; Georgiades et al., 2000). Participation in steady state aerobic exercise has also been shown to decrease cardiovascular reactivity to mental challenge in hypertensive and Type A patients, with initially elevated cardiovascular reactivity to mental challenge (Boutcher & Hamer, 2006), yet the cardiovascular health benefits of HIIE training on mental challenge are undetermined. Furthermore, the main focus of previous studies has been on examining HR and BP response to mental challenge during exercise and relatively less attention has been devoted to other aspects of cardiovascular responses such as skeletal muscle blood flow, arterial stiffness, and baroreceptor sensitivity during mental stress. It is not clear whether autonomic control of the heart, as determined by BRS and arterial stiffness, under mental and physical challenge is influenced by HIIE training. Therefore, Study II aimed to examine the effects of HIIE on multiple measures of cardiovascular and autonomic reactivity during mental and physical challenge.

Aims

The specific aims are to examine:

1. the acute effect of high-intensity interval exercise on metabolic response in trained and untrained males.
2. the chronic effect of 12 weeks of HIIE on body fat and fat free mass in overweight males.
3. the chronic effect of 12 weeks of HIIE on cardiovascular and autonomic function in overweight males during rest.
4. the chronic effect of 12 weeks of HIIE on cardiovascular and autonomic function in overweight males during mental and physical challenge.

Hypotheses

It is hypothesized that:

1. glycerol and catecholamins will be significantly increased during acute HIIE regardless of aerobic fitness level.
2. 12 weeks of HIIE will result in significant body composition change of young healthy overweight males.
3. 12 weeks of HIIE will result in a significant reduction in visceral fat of young healthy overweight males.
4. 12 weeks of HIIE will result in a significant increase in fat free mass of young healthy overweight males.
5. 12 weeks of HIIE will result in a significant improvement in resting cardiovascular and autonomic function of young healthy overweight males.

6. 12 weeks of HIIE will result in a significant change in cardiovascular and autonomic function of young healthy overweight males in response to mental and physical stressors.

Chapter 1: Literature Review

Introduction

This literature review firstly provides an overview of obesity and its related risk factors. Next the effects of exercise and diet on health and fat loss are discussed. The effects of different exercise modalities, in particular high-intensity intermittent exercise (HIIE), on physiological factors and fat and fat free mass are then summarized. Then the effects of HIIE on cardiovascular and autonomic measures are described. Finally, psychometric and psychophysiological effects of HIIE are discussed.

Obesity Overview

Westernized countries normally have a high obesity prevalence. The rate of obesity is also rapidly being increased in developing countries (Speiser et al., 2005). According to the World Health Organization (WHO) obesity has more than doubled since 1980 and is continuing to increase which make obesity and overweight consequences a major health concern. Obesity is an abnormal or excessive fat accumulation that adversely affects health and increases mortality (González-Castejón & Rodriguez-Casado, 2011). Body mass index (BMI) is an age-independent and unisex indicator to assess whether an individual is obese. It is a reasonable indicator of health risk and is calculated by dividing body weight in kilograms by the square of height in meters. Table 1.1 shows a BMI classification, which is consistent across age, fat distribution pattern, and certain ethnicities. This BMI classification was originally established by WHO, however, a new classification for Asian

populations has been recently recommended with a cut-off point of 23 kg/m^2 (WHO, 2004).

Table 1.1. The International classification of obesity based on BMI

Classification	BMI (kg/m^2)	
	Principal cut-off points	**Additional cut-off points**
Underweight	**<18.50**	**<18.50**
Severe thinness	<16.00	<16.00
Moderate thinness	16.00 - 16.99	16.00 - 16.99
Mild thinness	17.00 - 18.49	17.00 - 18.49
Normal range	**18.50 - 24.99**	**18.50 - 22.99**
		23.00 - 24.99
Overweight	**≥25.00**	**≥25.00**
Pre-obese	25.00 - 29.99	25.00 - 27.49
		27.50 - 29.99
Obese	**≥30.00**	**≥30.00**
Obese class I	30.00 - 34.99	30.00 - 32.49
		32.50 - 34.99
Obese class II	35.00 - 39.99	35.00 - 37.49
		37.50 - 39.99
Obese class III	≥40.00	≥40.00

Source: World Health Organisation, Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. Lancet, 2004.363(9403), 157-163.

Based on a report from the Australian Bureau of Statistics (ABS), the proportion of overweight or obese men progressively increased from 45% in 1989-1990 to 52% in 1995, 58% in 2001, and 62% in 2004-2005 (ABS, 2008). The rate of women classified as overweight or obese also steadily increased from 32% in 1989-1990, to 37% in 1995, 42% in 2001, and 45% in 2004-2005 (ABS, 2008). Men have a higher rate of obesity (62%) than women (45%) and the rate of being overweight is also much higher in males (43%) compared to females (28%) (ABS, 2008). It appears that men are getting overweight or obese at earlier age than women; 45 versus 48 years (ABS, 2008). Unfortunately, the rate of obesity and its related costs are also on the increase. In Australia, the number of adults being overweight or obese has increased from 4.6 million people in 1989-1990 to 5.4 million in 1995, 6.6

million in 2001, and 7.4 million in 2004-2005 and the cost of obesity associated illnesses exceeded $21 billion in 2005 (ABS, 2008). Obesity also has increased in the United States by 47.8%, rising from 23% to 34%, among adults aged 20 years and over between 1988-94 and 2005-08. Obesity also increased by 54.5% in children aged 6–11 years, from 11% to 17% and in adolescents aged 12–19 years by 63.6%, from 11% to 18% during the same period (Centers for Disease Control and Prevention, CDC, 2010). According to a recent national health and nutrition examination survey by the U.S. Department of Health and Human Services, over 78 million adults (35.7%) and about 12.5 million children and adolescents (16.9%) were obese in 2009-2010 (Ogden, Carroll, Kit, & Flegal, 2012).

Obesity among children is also on the rise and it causes major health related problems. Children with obesity are more likely to become obese adults (Epstein, Wing, & Valoski, 1985) and the chance of having obesity related health issues such as cardiovascular disease and type 2 diabetes is higher among obese children (DiPietro, Mossberg, & Stunkard, 1994; Mahoney et al., 1996). Also childhood obesity has a significant economic impact. It has been estimated that the cost of health issues related to obesity in children and adults exceeded $58 billion in 2008 in Australia (ABS, 2009). The rate of childhood obesity from 1995 to 2007 in Australia is presented in Figure 1.1. This rate has increased from 21% in 1995 to 25% in 2007-2008. Currently at least one quarter (about 600,000) of children aged between 5 and17 are overweight or obese in Australia (ABS, 2009).

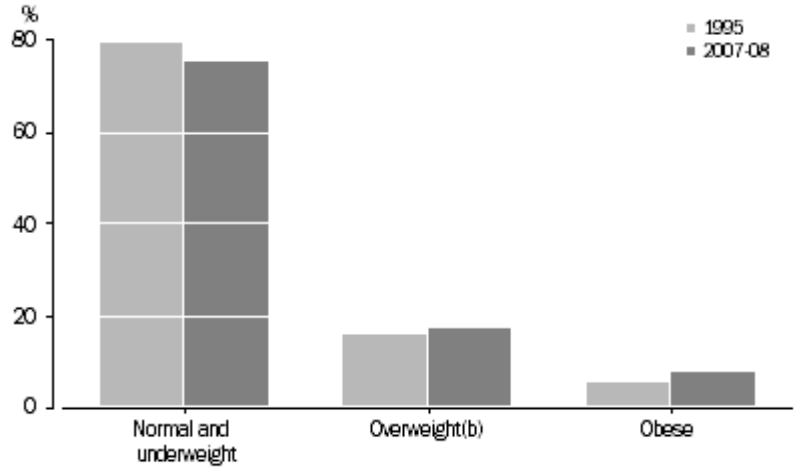

Figure 1.1. Children's obesity rate based on BMI 1995, 2007-08

Source: Australian Bureau of Statistic (ABS). (2009), Australian Social Trends. Retrieved 11 January 2012 from http://www.abs.gov.au/AUSSTATS/abs@.nsf/Lookup/4102.0Main+Features20Sep+2009

Lack of physical activity is one of the major causes of obesity in children. The Australian Bureau of Statistics has reported the findings of a survey conducted in 2006 which revealed that 37% (about 974,000) of Australian children were not taking part in any organised sport. The rate was higher among girls (42%) compared to boys (31%). Also children aged between 5 to 8 years were least likely to participate in a organised sport (ABS, 2009). Figure 1.2 shows this trend.

Body fat increases with ageing mostly because of a change in lifestyle and a decline in physical activity. Young adults are more likely to get involved in moderate to vigorous physical activity (ABS, 2009); for example 35% of men and 30% of women at the age of 18-24 years are overweight and obese but by the age of 35-44 years the rate of being overweight and obese increase to more than 70% in men and more than 40% in women (ABS, 2009).

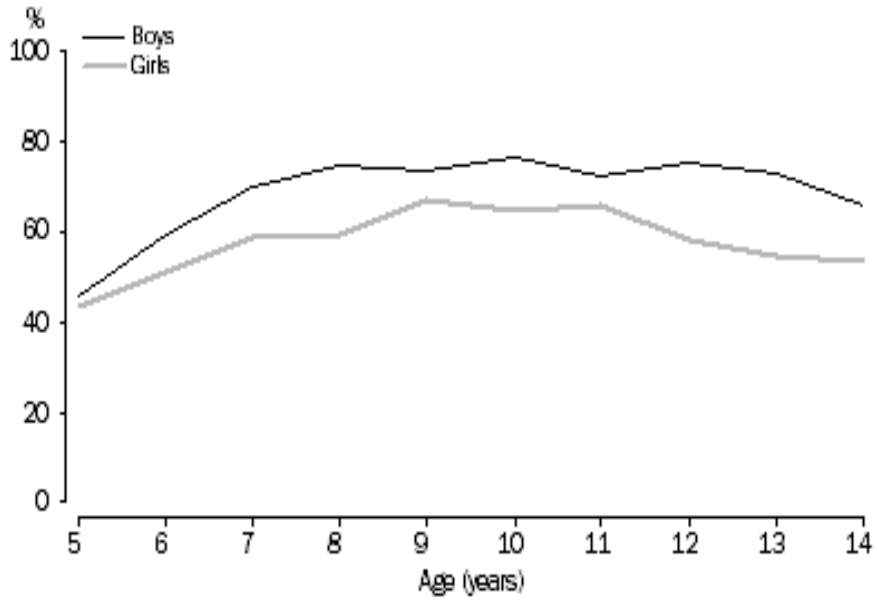

Figure 1.2. Children's participation in organised sport, Australia, April 2006

Source: ABS. (2009). Children's Participation in Cultural and Leisure Activities, Australia. Retrieved 12 December 2012 from http://www.abs.gov.au/AUSSTATS/abs@.nsf/allprimarymainfeatures/D93ED0B65019B0E7CA25765C0019B8BF?opendocument

Causes of Obesity

There are many factors that cause or contribute to obesity. Some of these factors are inherited and others are the result of a poor lifestyle. Figure 1.3 indicates some potential causes of obesity. Some of the factors cannot be changed, however, factors such as dietary habits and amount of physical activity can be improved. Having healthy eating and taking part in regular physical activity can prevent obesity and overweight.

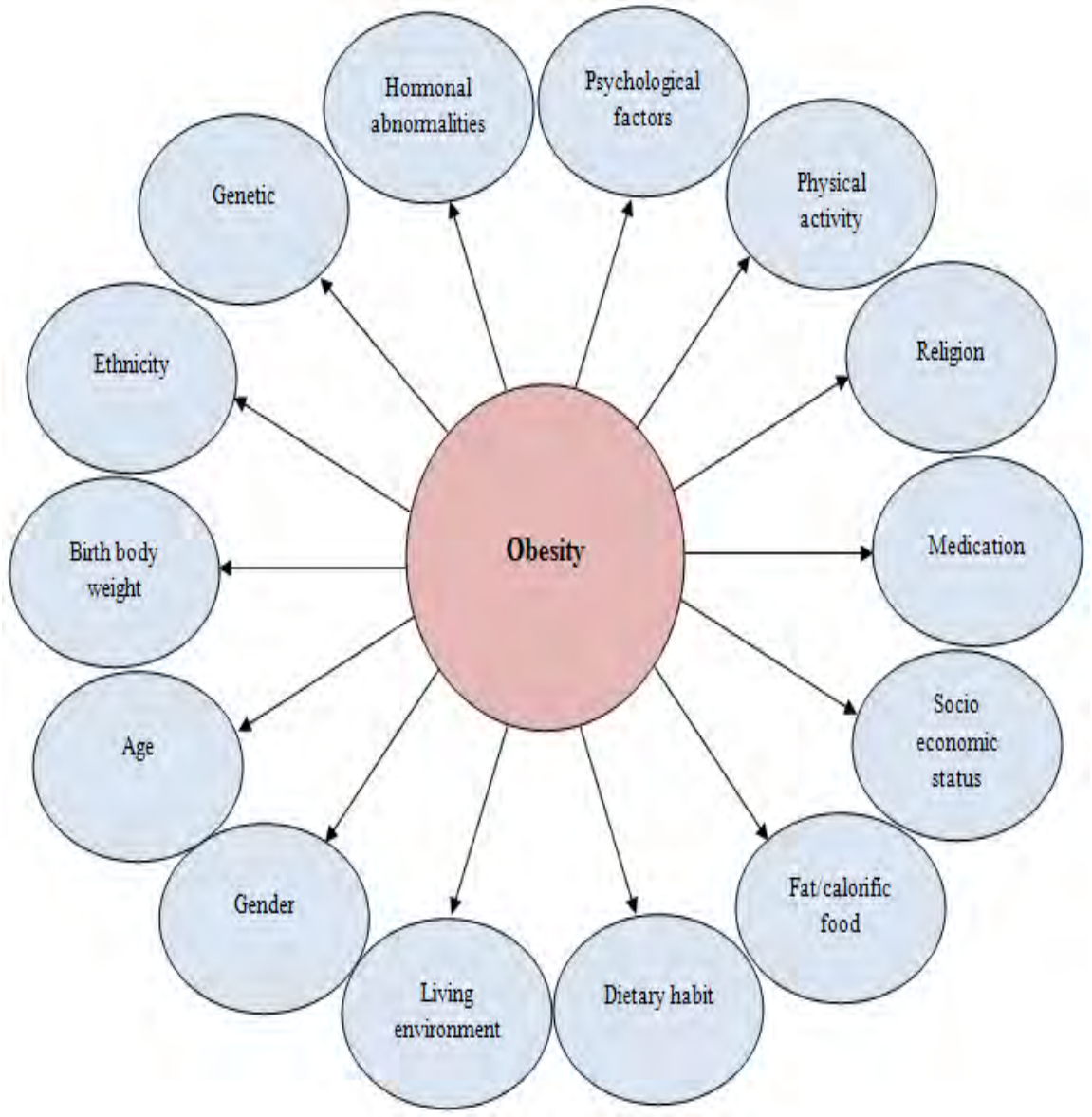

Figure 1.3. Potential causes of obesity

Typically obesity occurs if a long term imbalance exists between energy intake and energy expenditure (Hill & Wyatt, 2005). Figure 1.4 illustrates that in the condition of energy balance, body fat is maintained, but in order to lose fat either a decline in energy intake or a rise in energy expenditure must occur. However, a number of individual factors such as genetic, medical, behavioural and physiological variables may affect the ability to lose fat (Boutcher & Dunn, 2009).

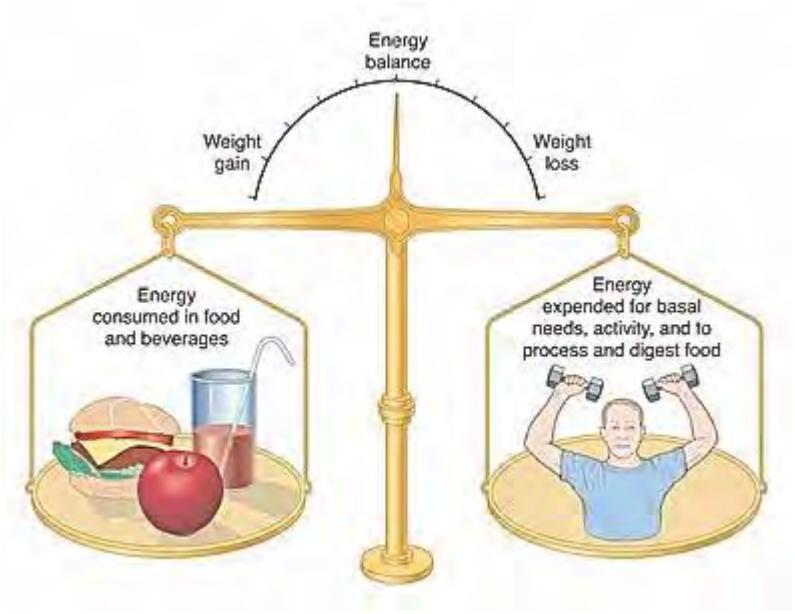

Figure 1.4. Energy balance

The Role of Adipose Tissue

Adipocytes are the main cellular part of fat tissue and have an essential role in providing energy during starvation periods. Adipocytes are also involved in thermogenesis and in the support and insulation of internal organs such as kidney and heart (Trayhurn & Beattie, 2001). Furthermore, adipocytes act as the main energy depository in the form of triglyceride and as the endocrine organ to regulate homeostasis by releasing critical hormones such as adiponectin (Trayhurn & Wood, 2004, 2005).

Obesity has major implications for health and longevity (Speiser et al., 2005). It is associated with elevated blood pressure, serum lipids and type 2 diabetes (Bordenave et al., 2008), risk of cardiovascular disease (CVD) (Lavie et al., 2009; Zalesin et al., 2011), and some kinds of cancer (Dulloo, 2011). Excessive abdominal and visceral fat are important risk factors for cardiovascular health (Stunkard, 1996) and insulin resistance (Racette, Evans, Weiss, Hagberg, & Holloszy, 2006).

Abdominal obesity also is an indicator of metabolic syndrome (Church, 2011) and visceral adipose tissue is a good predictor of cardiovascular health and metabolic syndrome (Kissebah et al., 1982).

Fat oxidation among obese individuals is impaired even after a period of fat loss program (Ranneries et al., 1998) and regaining of weight is more likely to occur. Therefore, it seems to be essential to improve fat oxidation rate in order to prevent and reduce obesity and it is feasible that many obesity related complications can be improved through visceral fat loss.

Weight Loss

Losing fat in the obese individual is an important factor from a health perspective in order to prevent obesity related disorders (Sørensen, Rissanen, Korkeila, & Kaprio, 2005). Losing 5 to 10% of body weight substantially reduces health risk (Donnelly et al., 2004). For example, complications associated with type 2 diabetes can be prevented through weight loss, healthy diet and regular exercise (Church, 2011). Weight loss also has been shown to increase work productivity and quality of life (Ross et al., 2009), however, losing weight is not easy and needs motivation and determination to be engaged in physical activity and to resist over eating (Elfhag & Rössner, 2005). Although reducing energy intake typically leads to weight loss, the majority of dieters regain their lost weight within a period of time (Kramer, Jeffery, Forster, & Snell, 1989; Skender et al., 1996). It seems that a decrease in resting metabolic rate (RMR), mostly because of a decrease in muscle mass and an increase in metabolic efficiency, are the main factors responsible for weight regain after diet-only weight loss programs (Dulloo, 1993, 2007; Major, Doucet, Trayhurn, Astrup, & Tremblay, 2007).

In the majority of weight loss programs, physical activity and diet are the main components. Theoretically, a decrease in energy intake and an increase in energy expenditure results in weight loss and burning of stored fat. An increased RMR due to muscle mass gain and reduced respiratory quotient (RQ) after exercise training show that utilizing fat is facilitated by regular physical activity (Byrne & Wilmore, 2001; Lemmer et al., 2001). In most diet-based weight loss programs, a decline in muscle mass and consequently a decreased RMR, seems to be inevitable (Frey-Hewitt, Vranizan, Dreon, & Wood, 1990). Thus, exercise programs which sustain or increase fat free mass are preferable.

Exercise and its Health Benefits

Regular exercise is associated with various health benefits such as reduced risk of hypertension, stroke, onset of type 2 diabetes, colon and breast cancer (Kim et al., 2006; Lindström et al., 2006), depression, metabolic syndrome (U. S. Department of Health and Human Services, 2008), and an improvement in blood glucose levels (Marwick et al., 2009). These health benefits may occur without a significant change in weight or diet (Ross et al., 2000; Slentz et al., 2004). Cardiorespiratory fitness also is an important factor in preventing CVD (Sallis, Patterson, Buono, & Nader, 1988). Even among type 2 diabetic patients, higher level of fitness was associated with reduced risk of CVD (Church, LaMonte, Barlow, & Blair, 2005).

Fat oxidation rate may be increased by regular physical activity during exercise and rest (Henriksson, 1977; Treuth, Hunter, Weinsier, & Kell, 1995). Thus, long term physical activity is beneficial for weight control as it can switch substrate usage towards fat oxidation. Endurance exercise enhances lipid metabolism and reduces

glucose metabolism by activating certain molecular pathways and cellular adaptations (Brun, Romain, & Mercier, 2011).

Exercise

Regular physical activity is a well known intervention for managing weight and preventing obesity (Jakicic & Otto, 2005, 2006). Exercise has three main effects on obese patients: helping to avoid weight gain, improving stabilization after slimming, and reducing obesity-related comorbidities (Brun et al., 2011). Exercise at a moderate intensity between 150 and 250 minutes weekly may be suitable for controlling weight but it seems to be insufficient for losing body fat unless physical activity is accompanied with diet restriction (Brun et al., 2011). Consequently, it appears that there is a dose-response relationship between exercise and body fat reduction. It has also been recommended that exercise duration is more important than exercise intensity for inducing weight loss (Brun et al., 2011). However, the amount of actual fat loss after participating in aerobic exercise typically is much less than expected and outcomes are usually disappointing (Wu et al., 2009). HIIE seems to be more effective in reducing fat when compared to steady state exercise (Boutcher, 2011).

Exercise training, even without weight loss, is associated with a significant reduction in abdominal visceral fat (Lee et al., 2005). Whether exercise intensity is important for reducing visceral fat is not clear, although it was shown that high-intensity exercise training, compared to low-intensity exercise training was more effective in reducing abdominal visceral fat (Irving et al., 2008) mostly because of producing greater negative energy balance and secretion of lipolytic hormones such as growth hormone and epinephrine (Pritzlaff et al., 2000; Pritzlaff et al., 1999).

However, Slentz et al. (2005) suggested that in the isocaloric condition low volume moderate-intensity and low volume high-intensity exercise training were equally effective in preventing significant increases in abdominal visceral fat in previously sedentary, overweight adults. Kuk et al. (2007a) in a review suggested that a moderate amount of exercise (~150-200 min/wk) with less than 1500 kcal/wk energy expenditure is associated with modest (5-10%) visceral fat reductions, whereas energy expenditure of 3500-4500 kcal/wk (~ 450 min/wk) is associated with greater (~ 30%) visceral fat reductions, Figure 1.5.

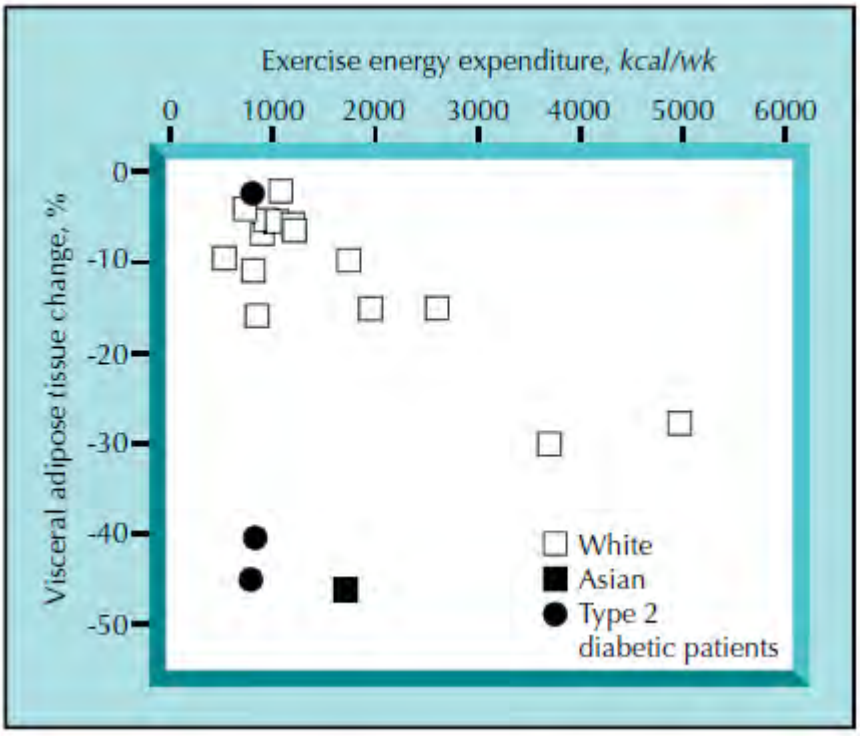

Figure 1.5. Dose response relationship between net reductions in visceral adipose tissue as compared with control and weekly exercise energy expenditure.

Source: Kuk, J. L., Janiszewski, P. M., & Ross, R. (2007a). Exercise, visceral adipose tissue, and metabolic risk. Current Cardiovascular Risk Reports, 1(3), 254-264.

Physical activity can result in fat loss because of negative energy balance and shifts in substrate utilization from carbohydrate to fat during rest and exercise (Barwell, Malkova, Leggate, & Gill, 2009). Fat loss may occur even without a

change in RMR. It has been suggested that those participants with the largest shift towards fat utilization had the greatest fat loss (Barwell et al., 2009). It has also been suggested that individuals with a higher rate of fat oxidation seems to be protected from fat gain (Barwell et al., 2009).

Fat and Carbohydrate Oxidation during Rest and Exercise

Resting metabolic rate is the required amount of energy to maintain post absorptive homeostatic function during rest and it accounts from 60% to 75% of total energy expenditure (Donnelly et al., 2004). Diet-induced thermogenesis and physical activity are responsible for the remaining 20% to 30% of entire energy expenditure (Melzer, 2011). Some factors affecting RMR include age, gender, stress, hormonal level, and lean muscle mass (Arciero, Goran, & Poehlman, 1993). For the individual consuming a normal diet (e.g., 35% fat, 12% protein, and 53% carbohydrate) energy source can be measured in the resting condition by evaluating the ratio of oxygen consumption (O_2) and carbon dioxide production (CO_2) through indirect calorimetery (Melzer, 2011). Respiratory quotient (RQ) is the ratio of CO_2 and O_2 and varies between 0.69, which indicates 100% fat oxidation, and 1.0 which indicates 100% carbohydrate oxidation for energy production (Melzer, 2011). A RQ equal to 0.82 is the average resting RQ at which fat oxidation contributes more than half of the total energy expenditure (Melzer, 2011).

The proportion of substrate utilization during exercise is different in the fasting and fed conditions. Carbohydrate (plasma glucose and muscle glycogen) and fat (intramuscular triglycerides and plasma fatty acids) are the major sources of energy during physical activity (Melzer, 2011). The dominant source of energy is typically determined by the exercise intensity and volume (Melzer, 2011). The main source of

energy during rest and exercise with an intensity of less than 25% of $\dot{V}O_{2max}$ is fat (Romijn et al., 1993). When exercise intensity increases, carbohydrate oxidation also increases, whereas fat contribution decreases (Romijn et al., 1993). However, fat oxidation does not stop completely. For example, at higher exercise intensities (e.g., 60% $\dot{V}O_{2max}$ or more), fat oxidation gradually increases when exercise volume increases (Romijn et al., 1993). Fat_{max} is the maximum point of fat oxidation (Brun et al., 2011) and it seems to occur because of shifting energy source to fat and muscle glycogen depletion (Ahlborg, Felig, Hagenfeldt, Hendler, & Wahren, 1974; Bergman & Brooks, 1999). This muscle glycogen depletion normally happens after a long exercise session (Thomson, Green, & Houston, 1979). When 30% to 40% of muscle glycogen stores are depleted, the source of energy typically switches to fat (Kirwan et al., 1988). But muscles tends to use carbohydrate as the main source of energy when exercise intensity increases and fat oxidation even may shut down if intensity exceeds 85-90% of $\dot{V}O_{2max}$ (Brun et al., 2011).

Steady State versus HIIE

Fat oxidation rate increases during steady state exercise. The highest point of lipid oxidation rate at an optimal intensity is called fat_{max} (Nordby, Saltin, & Helge, 2006). Fat_{max} can differ from 0.4 to 1 g of fat per minute. Glycogen depletion occurs after one hour of continuous low intensity steady state exercise and is accompanied by an increase in fat oxidation. It has been reported that 300 minutes of steady state exercise per week for 12 weeks significantly decreased body mass and body fat, however, triglyceride, blood lipids, adiponectin and HOMA-IR (a measure of insulin resistance) were unchanged (Yoshimura et al., 2011).

It has been shown that fat oxidation rate increases after 10 weeks of training at fat_{max} intensity but body mass, resting free fatty acids (FFA), and fasting glucose and insulin levels were unchanged. This increase in lipid oxidation rate was more likely due to an increase in citrate synthesis (CS) activity (Bordenave et al., 2008). In another study body weight or body composition were unchanged after 50 to 60 min of steady state exercise, three times per week, for 12 weeks (van Aggel-Leijssen, Saris, Wagenmakers, Hul, & van Baak, 2001). Thus, long duration, frequently repeated steady state exercise only results in a small decline in body fat (Wu et al., 2009). For example, Barwell et al. (2009) have shown that even long exercise sessions up to 60 min, 5 times per week for 7 weeks, resulted in less than a kilogram of fat loss.

High-intensity intermittent exercise (HIIE) is an alternative training modality which results in enhanced muscle glycogen storage and muscle oxidative and buffering capacity (Gibala et al., 2006). In general three forms of HIIE protocols exist which vary in exercise and recovery periods including the 30-second Wingate test. The length of both the sprint and recovery period used in past research has typically varied from 6 sec to 4 min. HIIE has been shown to be an effective and time efficient exercise training approach for losing fat in both males and females (Boutcher, 2011). Also it seems that HIIE, compared to steady state exercise, is more enjoyable at the same average heart rate and energy expenditure (Bartlett et al., 2011). HIIE does not have a common definition but generally it consists of intense and relatively short bouts of physical activity. The intensity reached during this type of exercise is often maximum or close to maximum (Boutcher, 2011). The format of HIIE training may differ based on participant‘s fitness and health status from a few seconds to a few minutes exercise followed by low intensity exercise or rest. This

type of exercise can be performed on a treadmill or outdoors but the most common modality is the bicycle ergometer due to its safety and stability.

It has been shown that HIIE increases $\dot{V}O_{2max}$ significantly (Coker, Williams, Kortebein, Sullivan, & Evans, 2009; Tanisho & Hirakawa, 2009) which is similar to that achieved with regular aerobic exercise (Trapp et al., 2008). Some of the benefits and advantages of HIIE include a significant increase in anaerobic power (Tanisho & Hirakawa, 2009) and a decrease in abdominal visceral fat (Coker et al., 2009) whereas steady state exercise has a smaller effect. Furthermore, HIIE is short in duration and can be more enjoyable. Thus it might be suitable for overweight individuals with limited time and tolerance for physical activity.

The effects of HIIE on aerobic fitness, body weight, muscular and physical adaptations have been investigated in a number of studies (Gibala et al., 2006; McKay, Paterson, & Kowalchuk, 2009). In a study by McKay et al. (2009), an HIIE group trained at 120% of their $\dot{V}O_{2max}$ and a steady state exercise group trained at 65% of their $\dot{V}O_{2max}$ but the increase in $\dot{V}O_{2max}$ and exercise performance and the decrease in body weight were similar in both groups considering that the time of training for HIIE group was one-tenth that of the steady state group. In another study 16 weeks of HIIE training resulted in a significant reduction in weight, BMI, waist circumference, fasting glucose, systolic and diastolic blood pressure, and a significant improve in insulin sensitivity, high-density lipoprotein cholesterol (HDL-C), adiponectin levels, and $\dot{V}O_{2max}$. Fasting glucose, insulin sensitivity, HDL-C and adiponectin did not change after steady state exercise (Tjønna et al., 2008).

It has been reported that muscle glycogen reduces after HIIE (MacDougall, Ward, & Sutton, 1977). Also performance level during HIIE improves after having

carbohydrate drinks (Nicholas, Williams, Lakomy, Phillips, & Nowitz, 1995). Thus, it seems that carbohydrates are the major source of energy during HIIE. But it appears that fat oxidation rate increases during the post exercise period (EPOC). It has been suggested that EPOC fat oxidation after HIIE may be equal to fat oxidation amount during steady state exercise (Brun et al., 2011). HIIE may be a time efficient and economical type of exercise for losing fat. It is also a unique form of exercise that employs both aerobic and anaerobic pathways leading to muscle adaptations which increase fat oxidation during and after exercise (Talanian, Galloway, Heigenhauser, Bonen, & Spriet, 2007). Also It has been shown that HIIE can activate muscle mitochondrial enzymes resulting in a decrease in carbohydrate oxidation and an increase in fat oxidation (Talanian et al., 2007). These adaptations include an increase in muscle oxidative capacity (Gibala & McGee, 2008), an increase in resting glycogen content, a decrease in glycogen utilization rate, and decreased lactate production during exercise (Gibala et al., 2006).

Cardiovascular Response to HIIE

Regular physical activity has positive effects on cardiovascular health. A strong correlation between fitness level and many aspects of cardiovascular health has been shown in previous research. For example, Keteyian et al. (2008) has reported that maximal $\dot{V}O_2$ was a strong predictor of all-cause mortality, in which the risk of death (15%) decreased by only a 1 $ml \cdot kg^{-1} \cdot min^{-1}$ increase in $\dot{V}O_{2max}$. The risk of CVD may decrease in women and older men by performing low intensity and high volume exercise but it has been suggested that higher intensity exercise is needed for middle-aged men to produce the same results (Wisløff, Ellingsen, & Kemi, 2009). It has also been shown that moderate intensity exercise is associated with reduced

coronary heart disease (CHD) regardless of exercise duration or the amount of consumed calorie (Tanasescu et al., 2002).

Heart rate (HR) can determine the intensity of the training. In HIIE heart rate increases during the sprint and decreases during the recovery phase (Boutcher, 2011). The HR elevation depends on the length of the sprint and recovery phase. In one study HR was increased to 170 bpm after one bout of Wingate test (Weinstein, Bediz, Dotan, & Falk, 1998). In a study conducted by Bracken et al. (2009), HR was increased to 142 bpm after the first bout and reached 173 bpm after 10 bouts. Each bout consisted of a 6-sec sprint followed by 30 sec of recovery. A previous study in our laboratory showed that 20 min of HIIE on a stationary bike (8-sec sprint followed by a 12-s light pedalling) increased the HR to 150 bmp in 5 minutes and 170 bpm towards the end of exercise. In this protocol HR had a small drop of 3 to 5 bpm during the 12-sec recovery phase (Trapp et al., 2007). In animal model studies, the size of the heart and substrate utilization changed after HIIE training. For example, Hafstad et al. (2011) showed a 10% increase in the ratio of heart weight to body weight. In this study a 36% increase in glucose oxidation and a decrease in fatty acid oxidation rate resulted in a change in cardiac substrate utilization. Cardiac maximal mitochondrial respiratory capacity also increased after HIIE training.

In a study conducted by Gormley et al. (2008), resting HR and BP did not improve after 6 weeks of near maximal intensity in the form of HIIE . However, in other previous studies HIIE was effective in reducing resting BP. For example, systolic and diastolic BP were decreased by 10 and 6 mmHg after HIIE training (Tjønna et al., 2008). It has been suggested that this amount of reduction in BP can prevent 30-40% of the premature deaths occurring from stroke (Lewington et al.,

2002). Guimarães et al. (2010) have also shown that both steady state and interval exercise are beneficial for BP control but arterial stiffness was only reduced after HIIE training among hypertensive individuals.

Blood Lactate Response to HIIE

Blood lactate level increases in response to high-intensity exercise and it is an indicator of a shift in substrate and metabolism pathway to glycolisis. Blood lactate increases up to 16 $mmol \cdot l^{-1}$ after 8 minutes of recovery in a Wingate test (Özturk & Gokce, 1998). Lactate concentration gradually increases with shorter bouts of HIIE (Boutcher, 2011). Trapp et al. (2007) observed that lactate level increased to 2-4 $mmol \cdot l^{-1}$ and 4-5 $mmol \cdot l^{-1}$ after 5 and 15 minutes of HIIE respectively. It seems that fitness level of the participants and the duration of both sprint and recovery are important determinators of lactate production. For example, in the same study lactate concentration was higher after longer 12-sec compared to 8-sec sprint. Lactate level was also higher (7-8 $mmol \cdot l^{-1}$) among trained individuals compared to untrained (Trapp et al., 2007). Thus, it appears that even short periods of recovery after a sprint are important for the reduction of post exercise lactate level. Weston et al. (1996) reported an increase in skeletal muscle buffering capacity after 2 weeks of HIIE among trained cyclists. The HIIE protocol in this study consisted of 6-8 bouts of cycling for 5 minutes at 80% of peak power output separated by a 1-min recovery time.

Aerobic Power Response to HIIE

Both steady state aerobic exercise and HIIE can increase aerobic power significantly but it seems that HIIE is a more effective and efficient approach.

Gormley et al. (2008) have reported that after 6 weeks of training with various intensities, the biggest improvement in $\dot{V}O_{2max}$ was achieved with near maximal intensity exercise (20.6% increase), followed by a 14.3% increase with vigorous intensity, and a 10% increase with moderate intensity. This result was in agreement with other research suggesting that HIIE is more effective for improving $\dot{V}O_{2max}$ (Braith, Pollock, Lowenthal, Graves, & Limacher, 1994; Gutin et al., 2002; Irving et al., 2009; O'Donovan et al., 2005; Tjønna et al., 2008).

Possible mechanisms underlying $\dot{V}O_{2max}$ improvement after HIIE exercise include changes in muscle mitochondrial oxidative capacity and increased cardiac efficiency. Little et al. (2011) investigated the changes in the exercising muscles after high-intensity interval training consisting of four bouts of 30-sec all-out cycling separated by four minutes rest. In this study protein content of the main regulator of mitochondrial biogenesis, peroxisome proliferator-activated receptor ɣ coactivator (PGC)-1α, was increased by 66% 3 hours post exercise recovery. Protein content of the mitochondrial enzymes such as citrate synthase (CS), cytochrome *c* oxidase (COX II), and COX IV were also increased 30%, 29%, and 30% respectively at 24 hours recovery. After 3 hours post exercise mRNA expression of PGC-1α increased by almost 750% and maximal activity of CS was increased by 14% in 24 hours post exercise. Also the maximal activity of citrate synthase was increased by 14% when measured 24 hours following exercise. Similar results were found by Hood et al. (2011) using HIIE training. Protein contents of CS, COX II, and COX IV increased by 31%, 16%, and 39% respectively after training. Glucose transporter (GLUT4) and PGC-1α protein content were also increased by 260% and 56% after training.

Lipids Response to HIIE

It has been shown that glycerol, glucose, and free fatty acid (FFA) levels changed in response to seven sessions of HIIE. β-hydroxyacyl-CoA dehydrogenase (β-HAD) activity and CS maximal activity also increased (Talanian et al., 2007). During HIIE with trained participants, glycerol increased at an earlier stage than the untrained indicating the utilization of fat in these subjects (Trapp et al., 2007).

CHD has an inverse correlation with high-density lipoprotein cholesterol (HDL-C) (Musa, Adeniran, Dikko, & Sayers, 2009). An increase in HDL-C and a decrease in low-density lipoprotein cholesterol (LDL-C) are also important factors in dyslipidaemia treatment (Lira et al., 2009). It has been reported that HDL-C level increased by regular HIIE training but did not change with steady state exercise (Tjønna et al., 2008). Total cholesterol (TC) and TC/HDL ratio also decreased with regular HIIE (Musa et al., 2009).

It appears that intensity may play an important role in the blood lipid response to exercise. Cornelissen et al. (2009) reported a significant decrease in triglyceride after high-intensity training but not lower intensity training. TC, HDL-C, LDL-C, and TC/HDL ratio did not change after either type of training. An acute bout of HIIE has a positive effect on blood lipids. It has been shown that cholesterol and LDL-C decreased after high-intensity exercise (Lira et al., 2009). Tsekouras et al. (2008) also reported a significant reduction in very low-density lipoprotein (VLDL) after two months HIIE (4 bouts of 4 min at 90% $\dot{V}O_{2max}$ followed by 4 min at 60% of $\dot{V}O_{2max}$ three times per week) training. Thus, HIIE can positively alter blood lipid profile and should be considered as a potential strategy for improving lipoprotein metabolism.

Insulin and Fasting Glucose Response to HIIE

Fasting glucose and insulin response to regular aerobic exercise is inconsistent in previous studies. The use of differing exercise intensities might be one of the reasons underlying this inconsistency. In a study by Tjonna et al. (2008) fasting glucose decreased and insulin sensitivity increased after high-intensity aerobic exercise whereas moderate intensity exercise did not change fasting glucose and insulin sensitivity. HIIE training has been shown to have a positive effect on fasting glucose and insulin. Trapp et al. (2008) used HIIE training for 15 weeks in premenopausal women and reported a significant decrease in fasting insulin. HIIE as short as six sessions in two weeks decreased insulin level by 16% and improved insulin sensitivity by 35% but fasting glucose level remained unchanged (Hood, Little, Tarnopolsky, Myslik, & Gibala, 2011). HIIE might have a positive effect on individuals with metabolic abnormality by reducing fasting blood glucose and insulin (Tjønna et al., 2008). For example, Little et al. (2011) found a significant reduction in average 24-hour glucose level in type 2 diabetes patients after 2 weeks of HIIE (10 bouts of 60-sec cycling at ~90% maximal HR separated by 60-sec rest) training. It seems that there is a strong negative correlation between training intensity and insulin response. The mechanism behind this is not clear but changes in muscle mitochondrial capacity might be an important factor (Hood et al., 2011).

Hormonal Response to HIIE

HIIE generates a significant hormonal response. This response to HIIE mostly depends on training protocol, participants‘ fitness level, and exercise background. Hormonal response to HIIE is an important factor in substrate utilization and long term adaptation. For example, growth hormone (GH) plays an important role in

metabolism and homeostasis. Studies have shown that acute aerobic exercise amplifies the GH release during and immediately after exercise in both men and women (Pritzlaff, et al., 1999; Wideman et al., 1999), although GH concentration increase from baseline was higher for men compared with women (Bunt, Boileau, Bahr, & Nelson, 1986; Wideman et al., 2000). Also higher GH concentration has been reported with higher exercise intensity and there is a linear relationship between GH release and exercise intensity (Pritzlaff-Roy et al., 2002). Although it seems that GH secretion is less responsive to chronic endurance training (Deuschle et al., 1998; Hartman et al., 2000) serum GH concentration was increased by 2-fold in a study conducted by Weltman et al. (1992) using young females participants. It has been shown that there is an association between visceral obesity and reduced GH secretion (Vahl et al., 1997). Treatment by GH reduced visceral fat mass, TC, LDL-C, and enhanced insulin sensitivity (Franco et al., 2005). It has been reported that GH pulse amplitude and area under the curve increased in obese adults after HIIE training (Irving et al., 2009). Nevill et al. (1996) conducted a study with endurance and sprint runners and found an increase in GH after 30 sec of sprint running. Although GH response to 30-sec sprints was higher among sprint trained than endurance trained athletes there was no significant difference between two groups. Gray et al. (1993) also reported that GH increased by 2000% after an intense interval running.

Chronic exercise training also creates a number of hormonal changes that maybe implicated in the stress response. The pathways of these changes are depicted in Figure 1.6. Stress activates corticotrophin-releasing hormone (CRH) and adrenocorticotropic hormone (ACTH) which leads to cortisol increase. This increase in cortisol level can result in visceral fat accumulation through different pathways. Cortisol increases insulin levels and both of these hormones are lypolisis inhibitors

that result in metabolic abnormalities (Björntorp & Rosmond, 2000). An increase in leptin level (Nieuwenhuizen & Rutters, 2008) and positive energy balance also increase fat storage.

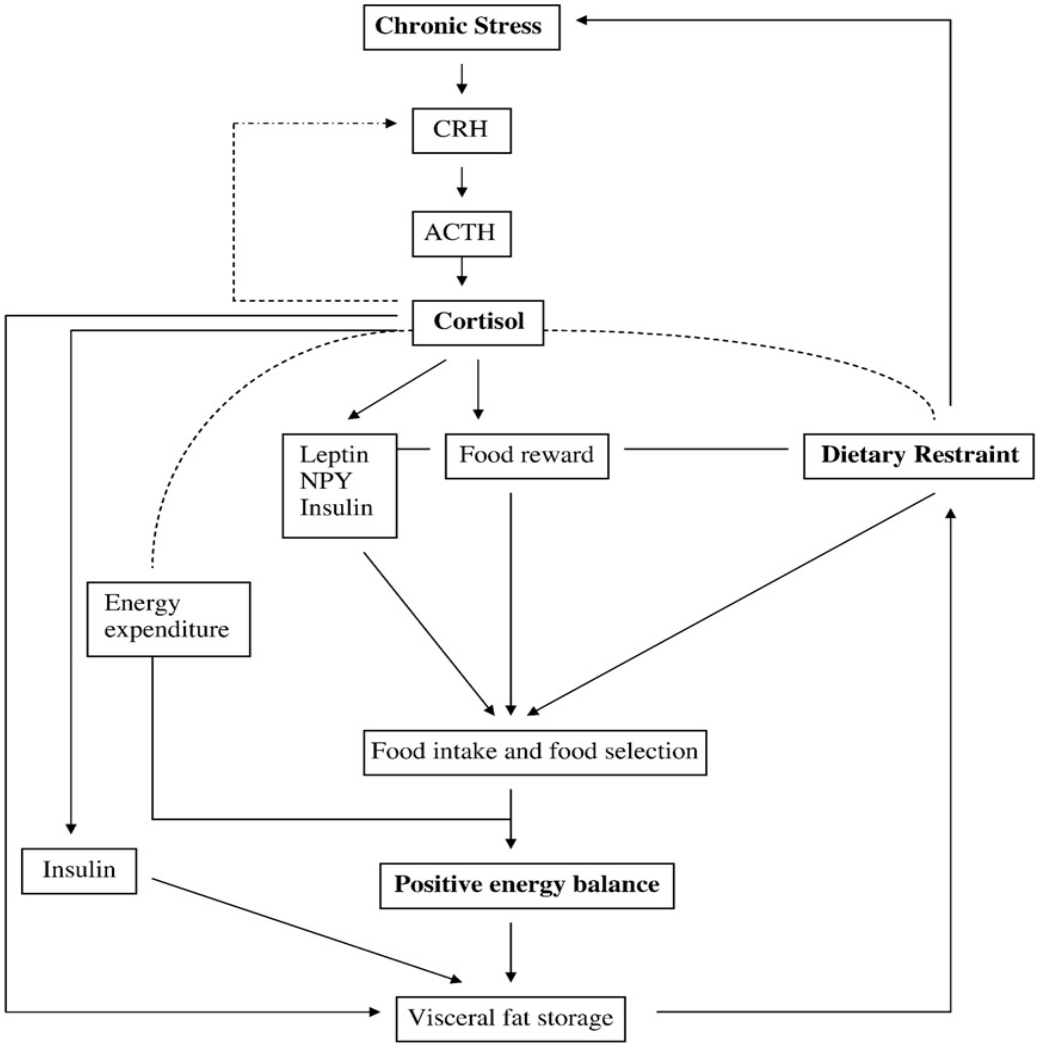

Figure 1.6. An overview of the effect of chronic stress on visceral fat accumulation pathways

Source: Nieuwenhuizen, A. G., & Rutters, F. (2008). The hypothalamic-pituitary-adrenal-axis in the regulation of energy balance. Physiology and Behavior, 94(2), 169-177.

Research examining the acute and chronic response of cortisol to HIIE is scarce. Wahl et al. (2003) found a significant increase in cortisol after HIIE (4 bouts of 30-sec all-out exercise interspersed by 5-min rest) training. Also it has been shown that 10 min of high-intensity exercise bouts resulted in an elevation in cortisol, GH,

ACTH, and catecholamines (de Vries, Bernards, de Rooij, & Koppeschaar, 2000). Leptin is produced by white adipose tissue and has an important role in body weight regulation (Venner, Lyon, & Doyle-Baker, 2006). The level of circulating leptin is relative to adipose tissue mass (Watts, Jones, Davis, & Green, 2005; Wilding, 2001). Obese individuals have been shown to have an increased level of leptin (Dyck, 2005; Kougias et al., 2005; McMurray & Hackney, 2005; Meier, 1996) and leptin resistance (Blaak et al., 2006). Figure 1.6 illustrates the leptin production regulated by numerous factors (Wilding, 2001).

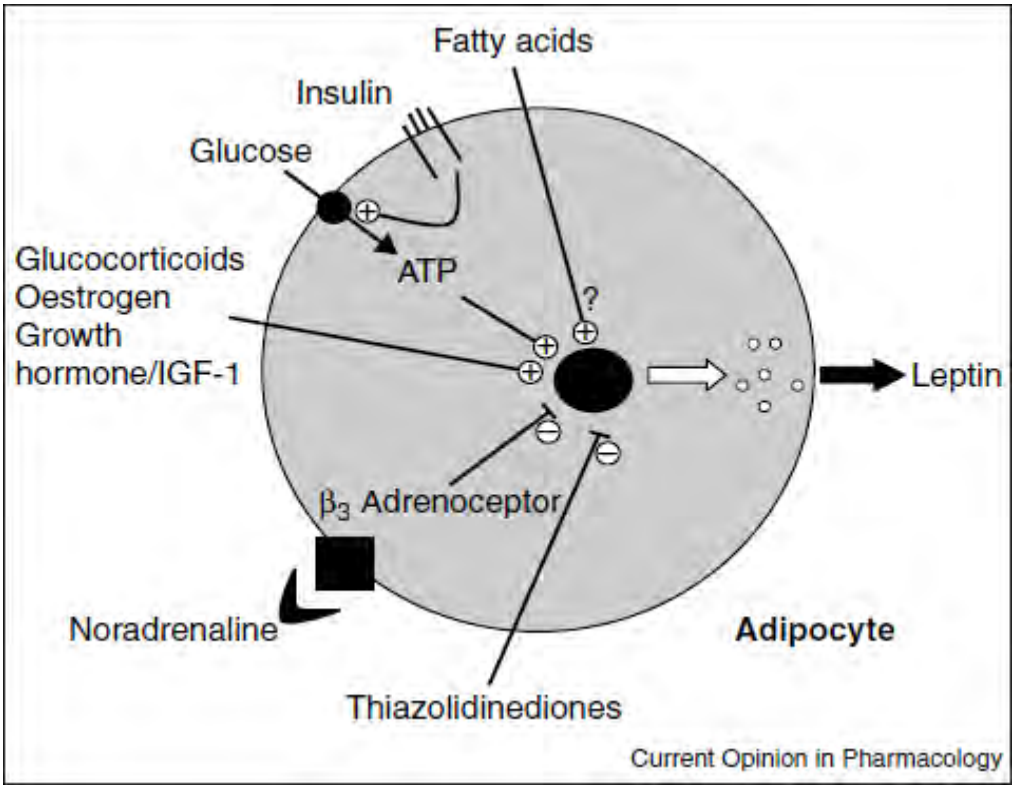

Figure 1.7. Factors influencing lepton production

Source: Wilding, J. P. H. (2001). Leptin and the control of obesity. Current Opinion in Pharmacology, 1(6), 656-661.

Based on HIIE type and participants‘ characteristics, leptin response to HIIE may also vary (Kraemer et al., 2003; Weltman et al., 2000). Kraemer et al. (2003) found that leptin and testosterone levels significantly increased after HIIE in well

trained male runners whereas Trapp et al. (2008) showed a reduced leptin concentration after HIIE in overweight females.

It has been shown that HIIE has an increasing effect on catecholamines (Trapp et al., 2007). It seems that catecholamines, especially norepinephrine, are involved in fat metabolism and fat release from intramuscular and subcutaneous fat depots (Issekutz, 1978). There are more β-adrenergic receptors in abdominal fat store than subcutaneous fat store (Rebuffé-Scrive, Andersson, Olbe, & Björntorp, 1989) suggesting that HIIE may be important for controlling abdominal obesity (Boutcher, 2011). Talanian et al. (2007) reported an increase in epinephrine among active females after 4-min high-intensity cycling, however, epinephrine concentration declined after 2-min of rest due to degradation but the level of epinephrine was six fold higher than baseline after 10 bouts of cycling at the same intensity. This change in epinephrine level was accompanied by an enhanced glycerol concentration indicating an increase in fat oxidation rate.

Christmass et al. (1999) found a significant increase in plasma norepinephrine after both short (6-sec sprint, 9-sec recovery) and long (24-sec sprint, 36-sec recovery) HIIE protocols. Trapp et al. (2007) also reported an increase in epinephrine and norepinehprine after two types of HIIE protocols (8 sec/12 sec and 12 sec/18 sec), in trained and untrained women. These results are in agreement with the findings of Bracken et al. (2009) who showed a 6.3 fold increase in epinephrine after 10 bouts of 6 sec/30 sec sprint in men. It has been shown that catecholamine response to HIIE is much greater compared to steady state exercise (Zouhal, Jacob, Delamarche, & Gratas-Delamarche, 2008).

Fat Free Mass Response to HIIE

The effect of HIIE on fat free mass (FFM) has not been extensively examined. FFM is composed of all nonfat tissues in the body. One study using dual-energy X-ray absoptiometry (DEXA) found that trunk muscle mass was significantly increased in young females by 0.6 kg after 15 weeks of HIIE, (Trapp et al., 2008) whereas another study using magnetic resonance imaging (MRI) showed a significant increase in thigh muscle cross sectional area of older males and females after HIIE (Boudou, Sobngwi, Mauvais-Jarvis, Vexiau, & Gautier, 2003). The 1.2 kg increase in total FFM found after HIIE confirms the ability of this type of exercise to increase FFM (Heydari, Freund, & Boutcher, 2012; see Chapter 3). However, the length of this 12-week intervention was 3 weeks less than that conducted by Trapp et al. (2008) that used females as participants. As exercise HRs and relative exercise intensity of the two trials were similar it appears that males responded with a similar decrease in total fat but a greater increase in FFM after HIIE. FFM increase in the trunk after HIIE was 0.7 kg for males and 0.4 kg for females, whereas in the legs was 0.4 kg for males and 0.1 kg for females. Thus, males compared to females recorded greater increases in FFM in their trunk and legs. This characteristic may be important for fat loss programs as it has been shown that muscle mass is typically decreased after dietary restriction (Saris, 1993) and is typically unchanged after aerobic exercise training (Stiegler & Cunliffe, 2006). The significant increase in leg FFM may also reflect important metabolic adaptations resulting in enhanced insulin sensitivity (Burgomaster, Hughes, Heigenhauser, Bradwell, & Gibala, 2005).

Fat Loss Response to HIIE

Regular physical activity is crucial to maintain a normal body weight and to avoid obesity and its complications. It seems that steady state exercise causes a small change in fat metabolism and total body fat. However HIIE is a time efficient and more effective method for losing fat mass (Wu et al., 2009). The mechanisms underlying the beneficial effect of HIIE and why it is superior to steady state exercise in losing fat are not fully understood and require more research. A number of different metabolic pathways and hormonal response are probably involved. Furthermore, HIIE can change the substrate utilization in favour of fat oxidation which results in fat loss. Talanian et al. (2007) found a significant increase in fat oxidation and a decrease in carbohydrate utilization after only seven sessions of HIIE.

Some studies have compared the fat loss effect of both HIIE and steady state exercise trainings. Trapp et al. (2008) compared steady state exercise (40 min cycling at 60% $\dot{V}O_{2max}$) with HIIE (20 min of 8-sec sprint, 12-sec recovery on the bike) after 15 weeks of training in young overweight females. Aerobic fitness improved in both groups but only the HIIE group reduced body mass, total fat mass, trunk fat, and fasting insulin levels. Irving et al. (2009) have shown a decrease in total body fat along with abdominal and subcutaneous fat mass after 16 weeks of HIIE, however, exercise at low intensity failed to reduce abdominal and subcutaneous fat. Other studies have also showing similar results. For example, Tremblay et al. (1994) found greater subcutaneous fat reduction in a HIIE group but not in a steady state group after 24 weeks of training.

It has been shown that visceral fat is an independent predictor of all cause mortality (Kuk et al., 2006). HIIE is thought to be a time and cost effective exercise modality for fat loss, particularly visceral and abdominal fat. Trapp et al. (2008) found a significant reduction in abdominal fat (0.15 kg) after 15 weeks of HIIE. In this context Boudou et al. (2003) reported a 44% reduction in abdominal fat along with a 48% increase in insulin sensitivity without a change in body weight in type 2 diabetic patients after 8 weeks of HIIE exercise. Similar findings were found by Mourier et al. (1997) who showed that visceral and subcutaneous adipose tissue decreased by 48% and 18% respectively. Interestingly, there was no body weight change but insulin sensitivity increased by 46%.

Over all, results show that HIIE is a successful method for reducing total body mass as well as visceral and abdominal fat. It seems that participants who possess greater abdominal and visceral fat show more reduction after regular HIIE exercise (Boutcher, 2011). More research is needed to identify the exact mechanisms behind the HIIE effects on visceral and abdominal fat but increases in oxidative capacity and catecholamine levels are possibly involved. The major HIIE effects are summarized in Table 1.2.

Table 1.2. Effect of high-intensity intermittent exercise on subcutaneous and abdominal fat, body mass, waist circumference, and $\dot{V}O_{2max}$

Study	Subcutaneous fat (kg)	Abdominal fat (kg)	Body mass	Waist Cir (cm)	Type of HIIE	Length of intervention	$\dot{V}O_{2max}$	Insulin sensitivity	Type of measurement for abdo fat
Boudou et al. (2003)	⇩18%	⇩.5 kg (44%)	⇩1.7kg (2%)	#	2 min/ 3 min	18 weeks	#	⇧58%	MRI
Burgomaster et al. (2008)	#	#	⇩1.0kg (5%)	#	Wingate	6 weeks	⇧4%	#	#
Dunn (2009)	⇩1.6 kg (5%)	⇩.5 kg (6%)	⇩1.4kg (2%)	⇩3.5 cm (4%)	8 sec/12 sec	12 weeks	⇧14%	⇧24%	DEXA
Helgerud et al. (2007)	#	#	⇩.8kg (1%)	#	15 sec/15 sec	8 weeks	⇧6%	#	#
Helgerud et al. (2007)	#	#	⇩1.5kg (2%)	#	4 min/4 min	8 weeks	⇧8%	#	#
Mourier et al. (1997)	⇩18%	⇩48%	⇔	#	SSE-/ 2/3 min	10 weeks	⇧41%	⇧46%	MRI
Perry, Heigenhauser, Bonen & Spriet (2008)	#	#	#	#	Wingate	2 weeks	⇧9%	#	#
Tjønna et al. (2008)	#	#	⇩2.3kg (2.5%)	⇩5.0 cm (5%)	4 min/3 min	16 weeks	⇧35%	⇧24%	#
Tjønna et al. (2009)	⇩5%	⇩8%	⇧.1kg (.03%)	⇩7.2 cm (7%)	4 min/3 min	12 weeks	⇧10%	⇧33%	DEXA
Trapp et al. (2008)	⇩2.5 kg (12%)	⇩.15 kg (9.5%)	⇩2.5kg (5%)	#	8 sec/12 sec	15 weeks	⇧24%	⇧33%	DEXA
Tremblay, Simoneau, & Bouchard (1994)	⇩9%	⇩9%	⇩.01kg (.01%)	#	30 sec/ 3 min	24 weeks	⇧20%	#	Skinfold
Warburton et al. (2005)	#	#	⇩3.0kg (4%)	#	2 min/2 min	16 weeks	⇧15%	#	#
Whyte, Gill, & Cathcart (2010)	#	#	⇩1.0kg (.1%)	⇩2.4 cm (2%)	Wingate	2 weeks	⇧9%	⇧25%	#

Note. ⇧Indicates increased; ⇩Indicates decreased; ⇔Indicates no change; #not recorded

Visceral Fat Response to HIIE

Visceral adipose tissue is a strong independent predictor of glucose tolerance (Brochu et al., 2000), insulin resistance (Després et al., 1995; Fox et al., 2007; Ross, Aru, Freeman, Hudson, & Janssen, 2002), dyslipidemia (Kanaley et al., 2001; Nguyen-Duy, Nichaman, Church, Blair, & Ross, 2003), incidence of cardiovascular disease (Fujimoto et al., 1999; Nakamura et al., 1994), myocardial infarction (Nicklas et al., 2004), hypertension (Hayashi et al., 2004; Rhéaume et al., 2009), metabolic syndrome (Després, 2006), type 2 diabetes (Boyko, Fujimoto, Leonetti, & Newell-Morris, 2000; Bray et al., 2008), and all-cause mortality (Kuk et al., 2006). Mourier et al. (1997) showed a significant reduction in visceral fat, measured by MRI, following an exercise regimen consisting of steady state exercise and HIIE for 8 weeks. These findings also add to the results of studies that have shown that aerobic training interventions decrease visceral adipose tissue (Ohkawara, Tanaka, Miyachi, Ishikawa-Takata, & Tabata, 2007). It has been shown that with a similar BMI, individuals with high levels of aerobic fitness, compared with individuals with low levels of aerobic fitness, have lower amount of visceral adiposity (Wong et al., 2004).

Whether there is a sex difference in response to visceral fat loss is unclear. It seems that men, compared with women, show greater visceral fat reductions (Donnelly et al., 2003; Poehlman, Dvorak, DeNino, Brochu, & Ades, 2000; Wilmore et al., 1999), however, men have greater exercise capacity which leads to higher energy expenditure and consequently they may lose more visceral fat.

The relationship between WC, hip circumference (HC), BMI, and visceral fat is important from a clinical health perspective. It has been shown that visceral

adipose tissue is negatively associated with HC, thigh circumference, and BMI after controlling for WC but only HC remains negatively associated with visceral adipose tissue after control for WC and age (Kuk, Janiszewski, & Ross, 2007b).

As visceral compared to overall obesity is more strongly associated with cardiovascular disease risk (Kuk et al., 2006), the ability of HIIE to reduce visceral fat may have positive health implications. For example, it was shown that reduction in visceral fat was associated with improvement in glucose and lipid metabolism (Ross, et al., 2000). Further, Okauchi et al. (2007) found that a reduction in visceral fat lowered risk of atherosclerotic cardiovascular disease. Interestingly, Ohkawara et al. (2007) estimated the optimal dose of aerobic exercise necessary to significantly reduce visceral fat and concluded that 3,780 kcal expended per week was needed. As an exercise session (e.g., cycling on a stationary cycle ergometer) lasting around an hour at a moderate exercise intensity expends about 520-550 kcal then to reach an optimal exercise caloric expenditure of 3,780 kcal per week an individual would have to perform approximately seven one-hour exercise sessions per week. In contrast, participants in Study II, described in Chapter 3, exercised for only one hour per week. Also Donnelly et al. (2003) conducted a 16-month, 5 hours of aerobic exercise per week program with overweight young males and recorded a 23% decrease in visceral fat. Thus, it appears HIIE can bring about significant decreases in visceral fat (17% reduction) with programs that are both significantly shorter in length (e.g., 16 months versus 3 months) and have less exercise commitment per week (5 hours versus 1 hour) (Heydari et al., 2012; see Chapter 3).

Although visceral fat reduction can be accompanied by total weight loss, some studies have shown visceral fat loss with no or a small decrease in body mass. Johnson et al. (2009) found a visceral fat reduction in obese men and women after 4

weeks of cycling training at an intensity of 50-70 % of $\dot{V}O_{2max}$ was accompanied with no weight loss. This was also supported by prior research showing visceral fat reduction with minimal weight loss (Ross et al., 2004; Slentz et al., 2005).

In a recent meta-analysis, it was shown that aerobic exercise training is effective in reducing visceral adipose tissue in overweight or obese people, whereas resistance training dose not significantly induce visceral fat loss, however, there is an association between exercise volume and visceral adipose tissue modification. This dose response relationship leads to a greater amount of energy expenditure and fat loss. In a combination of both aerobic and progressive resistance training, it seems that aerobic component of training play a central role in visceral adipose tissue modification (Ismail, Keating, Baker, & Johnson, 2012). Our study (Heydari et al., 21012, see Chapter 3) appears to be the first to examine the effects of 20-min bouts of HIIE on visceral fat of young males.

Heart Period Variability Response to HIIE

Heart period variability is a sensitive index of vagal control of the heart which reflects rhythmic variations in HR at the frequency of respiration. HPV analysis is a non invasive method to investigate the autonomic regulation of the heart. Low HPV is associated with a number of cardiac events such as sudden cardiac death, heart failure, diabetes, hypertension, asymptomatic left ventricular dysfunction, and myocardial infarction. It has been shown that cardiac autonomic balance was improved by regular exercise training (Rowell, 1986).

The effect of endurance training on HPV, however, is inconclusive. Some longitudinal studies, from 6 weeks to 5 years, have found an increase in HPV in healthy participants with low, moderate and high-intensity endurance training

(Amano, Kanda, Ue, & Moritani, 2001; Carter, Banister, & Blaber, 2003; Jurca, Church, Morss, Jordan, & Earnest, 2004; Kiviniemi et al., 2006; Lee, Wood, & Welsch, 2003; Leicht, Allen, & Hoey, 2003; Levy et al., 1998; Melanson & Freedson, 2001; Mourot, Bouhaddi, Perrey, Rouillon, & Regnard, 2004; Schuit et al., 1999; Tulppo, et al., 2003). However, other studies showed no change in HPV after endurance training (Catai et al., 2002; Loimaala, Huikuri, Oja, Pasanen, & Vuori, 2000; Martinmäki, Häkkinen, Mikkola, & Rusko, 2008; Uusitalo, Laitinen, Väisänen, Länsimies, & Rauramaa, 2004). These conflicting results could be a result of using different training protocols, (duration, frequency, intensity and participant's characteristics) or different techniques for measuring HPV.

With regard to intense training Levy et al. (1998) showed an increase in HPV after 6 months of intense training in both old and young males, however, Catai et al. (2002), Loimaala et al. (2000), and Uusitalo et al. (2004) did not find any change in HPV. It has been found that young people had a better response to endurance training compared to their middle-aged counterparts (Carter et al., 2003). A significant effect of exercise training on resting HF power and RR interval has been found in a meta-analysis and the greater change in RR interval has been shown in younger participants and also in longer interventions lasting over 12 weeks (Sandercock, Bromley, & Brodie, 2005).

Sloan et al. (2009) showed that autonomic control of the heart was enhanced after 12 weeks of endurance exercise in sedentary healthy young males but HPV did not improve in females or in the resistance training group. Madden et al. (2006) also found similar results when comparing aerobic endurance and resistance training after 6 months in older women. Strength training with moderate to high intensity has

shown no effect on HPV change in young and older adults (Cooke & Carter, 2005; Karavirta et al., 2009).

Despite the advantages of HIIE in improving aerobic power most of the studies investigating the effects of exercise training on HPV have used continuous endurance training. Only two studies have looked at HPV using interval training in older active males and coronary artery disease (CAD) populations and results showed an increase in HPV after interval training (Munk, Butt, & Larsen, 2010; Pichot et al., 2005). Whether high-intensity interval exercise has an effect on HPV in overweight young males is unknown. The effects of exercise on HPV are summarized in Table 1.3.

Table 1.3. Effect of exercise on heart period variability

Study	Male/ Female	Age	No. of subjects	Intensity	Type of exercise	Length of intervention	HPV
Amano et al. (2001)	M/F	40s	18	Moderate	cycling 20 min 3 times/w	12 weeks	⇧
				Moderate		12 weeks	⇔
Carter et al. (2003)	M/F	19-21 40-45	24	High	running 45-60 min 4 times/w	12 weeks	⇧
Catai et al. (2002)	M	21 53	17	70-85% of HR peak	walking and/or jogging 40 min 3 times/w	12 weeks	⇧
Cooke & Carter (2005)	M/F	21	21	High	Resistance 3times/w	8 weeks	⇔
Cornelissen, Verheyden, Aubert, & Fagard (2009)	M/F	55	36	Low and High	walking/ jogging/cycling 50 min 3 times/w	30 weeks	⇔
Currie, Thomas, & Goodman (2009)	M	25	14	65% of VO_{2max}	cycling 2 hrs/day	6 days	⇔
Dougherty, Glenny, & Kudenchuk (2008)*	M/F	55	10	60-80% of HR max	walking/ cycling 1 hour 3 times/w	8 weeks	⇧
Iwasaki, Zhang, Zuckerman, & Levine (2003)	M/F	29	11	Moderate and High	walking and jogging/running 30-45 min 3-4 times/w in the first 3 mon	1year	⇧
Jurca et al. (2004)	F	57	88	Moderate	walking/cycling 44 min 3-4 times/w	8 weeks	⇧
Kakiyama et al. (2005)	M	21	10	70% of VO_{2max}	cycling 30 min 3-4 times/w	8 weeks	⇔
Karavirta et al. (2009)	M	40-67	93	Moderate	cycling 30-60 min 2 times/w and resistance training	21 weeks	⇔
Kiviniemi et al. (2006)	M	26	17	70-80% of HR max	walking and jogging 30-60 min 6 times/w	8 weeks	⇧
Lee et al. (2003)	M	23	24	High 80-85% of VO_{2max}	cycling 40 min 4 times/w	2 weeks	⇧

Table 1.3. Effect of exercise on heart period variability (continued)

Study	Male/ Female	Age	No. of subjects	Intensity	Type of exercise	Length of intervention	HPV
Loimaala et al. (2000)	M	45-47	83	Low:55% of VO_{2max} High:75%	walking/ jogging 30 min, 4-6 times/w	20 weeks	⇔
Madden et al. (2006)	F	70	45	High	endurance exe 5 times/w and resistance training	24 weeks	⇧endurance ⇔resistance
Martinmäki et al. (2008)	M	36.8	11	Low to High	cycling 15 min 2 times/w	14 weeks	⇔
Melanson & Freedson (2001)	M	25-45	11	80% HR max	cycling 30 min 3 times/w 4-6 times/w	16 weeks	⇧
Mourot et al. (2004)	M	18-22	8	#	cycling, 3 times/w	6 weeks	⇧
Munk et al. (2010)*	M/F	58	20	#	HIIE	24 weeks	⇧
Pichot et al. (2005)	M	73.5	11	65-85% of HRmax	cycling interval exe 45 min.4 times/w. 9*5min bouts. (4min at 65%HRmax +1 min at 85%)	14 weeks	⇧
Schuit et al. (1999)	M/F	67	51	Moderate	different kinds of exe 45 min 3times/w	24 weeks	⇧
Sloan et al. (2009)	M/F	18-45	149	70% HR max	running/cycling 45-60 min/ resistance training, 3-4 times/w	12 weeks	⇧endurance ⇔resistance
Tulppo et al. (2003)	M	35	55	#	walking and jogging 30/60 min 6 times/w	8 weeks	⇧
Uusitalo et al. (2004)	M	53-63	89	#	walking/jogging/swimming/cycling 45-60 min 3-5 times/w	5 years	⇔
Verheyden, Eijnde, Beckers, Vanhees, & Aubert (2006)	M	55-75	37	65-80% of HR Res	cycling /walking/ jogging 75 min 10 times/4 weeks	1 year	⇔
Yamamoto, Miyachi, Saitoh, Yoshioka & Onodera (2001)	M	22	12	80% of VO_{2max}	cycling 40 min 4 times/w	6 weeks	⇧

Note. ⇧Indicates increased; ⇩Indicates decreased; ⇔Indicates no change; *study has been done on cardiac patients; #not recorded.

Baroreflex Response to HIIE

Arterial baroreflex is an important physiological mechanism which controls the homeostasis of BP in the short and long-term period (Persson, 2005; Schachter, 1997). The homeostatic influence of the baroreflex is of crucial importance to cardiovascular flexibility and its inhibition during challenging situations is an integral part of the autonomic response to stressful conditions, supporting adaptive reactions in the organism–environment interactions (Reyes Del Paso, González, & Hernández, 2004; Reyes Del Paso, González, Hernández, Duschek, & Gutiérrez, 2009; Yasumasu, Reyes Del Paso, Takahara, & Nakashima, 2006).

Changes in the sensitivity of baroreceptor reflex may have diagnostic and prognostic value in some populations like patients with hypertension, myocardial infarction, heart failure, and diabetes (Parati, Di Rienzo, & Mancia, 2000). Reduced arterial BRS has been reported in hypertensives (Gribbin, Pickering, Sleight, & Peto, 1971; Krontorádová et al., 2008; Parmer, Cervenka, & Stone, 1992) and chronic obstructive pulmonary disease (COPD) patients (Costes et al., 2004). This low sensitivity of arterial baroreflex is associated with impaired regulation of arterial BP (Shi et al., 2000) and higher cardiovascular event risk (Mancia, Grassi, Giannattasio, & Seravalle, 1999; Robinson, Dawson, Eames, Panerai, & Potter, 2003).

Overweight and obese people also have a reduced cardiovagal BRS especially those with elevated abdominal visceral fat (Alvarez, Beske, Ballard, & Davy, 2002; Beske, Alvarez, Ballard, & Davy, 2002; Gordon, Scott, & Levine, 1997; Grassi et al., 1995; Grassi et al., 2000; Honzíková et al., 2006; Hubert, Feinleib, McNamara, & Castelli, 1983; Kriketos et al., 2001; Lazarova et al., 2009).

The effects of different types of exercise training on autonomic function (ANS) have been investigated in a number of studies. Evidence shows that BRS increases after intense aerobic exercise (Madden, Lockhart, Potter, & Cuff, 2010; Martín-Vázquez & Reyes del Paso, 2010). As opposed to intense aerobic exercise, mild to moderate aerobic exercise, such as walking or jogging did not improve the BRS in middle-aged healthy sedentary males (Loimaala et al., 2000). Endurance training also favourably increases BRS (Cooke et al., 2002; Costes et al., 2004; Gardenghi et al., 2007; Grassi, Seravalle, Calhoun, & Mancia, 1994; Iellamo, Legramante, Massaro, Raimondi, & Galante, 2000; Iwasaki et al., 2003; Komine, Sugawara, Hayashi, Yoshizawa, & Yokoi, 2009; Krieger, Da Silva, & NegrÃO, 2001; La Rovere, Bersano, Gnemmi, Specchia, & Schwartz, 2002; Laterza et al., 2007; McDonald, Sanfilippo, & Savard, 1993; Monahan et al., 2000; Monahan, Tanaka, Dinenno, & Seals, 2001; O'Sullivan & Bell, 2000; Somers, Conway, Johnston, & Sleight, 1991). A study using patients with myocardial infarction showed significant improvement in BRS after 6 weeks of leg ergometer training (Leitch et al., 1997).

Several studies showed an increase in BRS after aerobic exercise and a decrease following resistance training (Collier et al., 2008; Gulli, Cevese, Cappelletto, Gasparini, & Schena, 2003; Monahan, et al., 2000; Shin, Minamitani, Onishi, Yamazaki, & Lee, 1995; Ueno & Moritani, 2003). In a recent study using rats, BRS was reduced after 10 weeks of resistance exercise compared to sedentary or aerobic training groups (Silveira et al., 2011).

It has been shown that exercise also improves the BRS through weight loss. There is evidence that 5-10% weight loss significantly increased resting BRS (Alvarez, Davy, Ballard, Beske, & Davy, 2005). Whether high-intensity interval

training improves the autonomic function and baroreflex responses in overweight young men, however, is unknown.

Arterial Stiffness Response to HIIE

Arterial stiffness is a risk factor for cardiovascular disease morbidity and mortality (Laurent et al., 2001) including heart failure, myocardial infarction as well as stoke, renal disease, and dementia (Safar, Levy, & Struijker-Boudier, 2003). Reduction in buffering function of the large arteries (e.g., aorta) due to arterial stiffness leads to an increase in left ventricular hypertrophy, systolic BP, and coronary ischemia (Rajkumar, Cameron, Christophidis, Jennings, & Dart, 1997). Some of the causes and locations of arterial stiffness are illustrated in Figure 1.8.

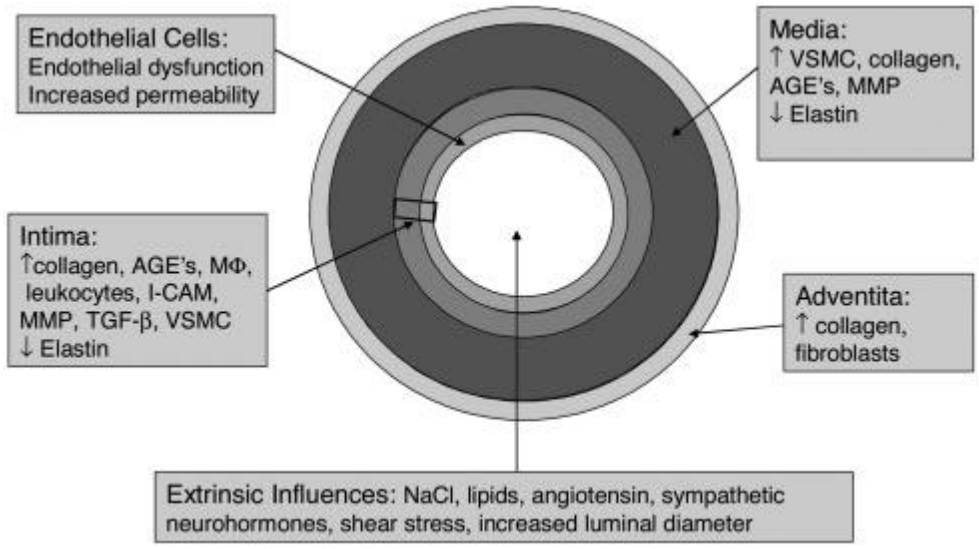

Figure 1.8. Summary of the multiple causes and locations of arterial stiffness

Source: Zieman, S. J., Melenovsky, V., & Kass, D. A. (2005). Mechanisms, pathophysiology, and therapy of arterial stiffness. Arteriosclerosis, Thrombosis, and Vascular Biology, 25(5), 932-943.

Commonly used non-invasive methods to assess arterial stiffness include: central and peripheral pulse wave velocity analysis (PWV), which are measured by applanation tonometry or photoplethysmography; Augmentation Index (AIx), which is based on pressure waveform; and MRI.

There are number of ways to lessen arterial stiffness including weight loss, reducing salt intake and alcohol consumption, and exercise. In this section the effects of different types of exercise on reducing arterial stiffness will be reviewed.

It has been shown that obese individuals typically possess an increase in arterial stiffness (Wildman, Mackey, Bostom, Thompson, & Sutton-Tyrrell, 2003) which is an early marker of vascular wall damage (van Popele et al., 2001). It was also reported that moderate weight loss was associated with artery elasticity improvement in obese participants (Goldberg, Boaz, Matas, Goldberg, & Shargorodsky, 2009). Sciacqua et al. (2003) found an improvement in forearm blood flow (FBF) respond to acetylcholine (ACh) after a combined weight loss and low intensity aerobic intervention in healthy obese participants. Although Tanaka et al. (2000) found a reduction in arterial stiffness after 3 months of endurance training with a moderate intensity in middle-aged men, the improvement in arterial compliance was not associated with changes in body mass, BP, adiposity, or $\dot{V}O_{2max}$. This is in agreement with prior research. Balkestein et al. (1999) found no change in compliance and distensibility of large arteries in an isobaric condition after 3 months of energy restricted diet which resulted in significant weight loss and lowered BP. Those arterial wall properties improved at operating pressure but not during the isobaric condition suggesting an indirect effect of weight loss through a decrease in BP. Balkestein et al. (1999) also found that adding a low intensity physical activity to this program did not improve arterial wall properties. The principal of applanation tonometery is illustrated in Figure 1.9.

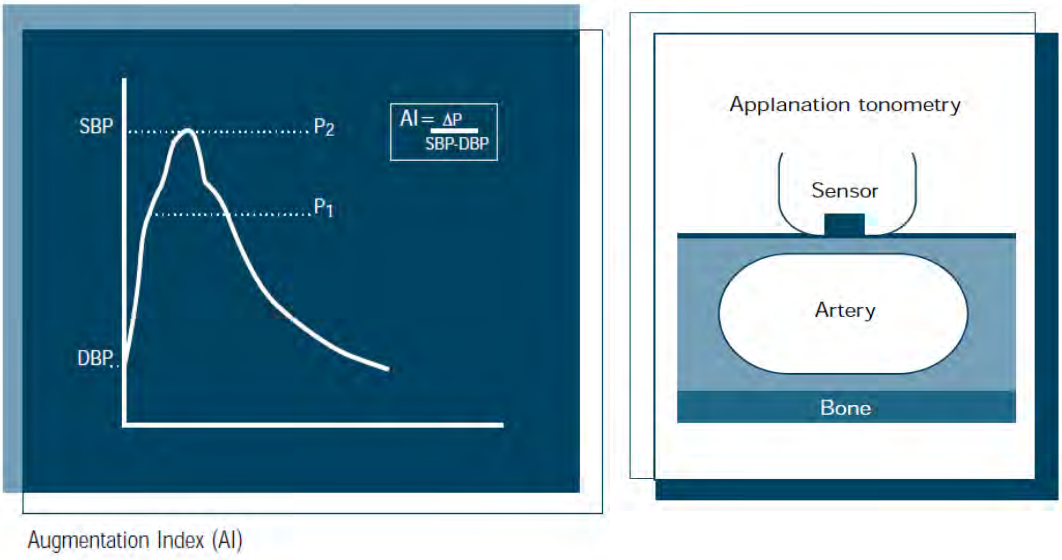

Figure 1.9. The principle of applanation tonometery[1]

Source: Clinical Cardiovascular Advisory Group. (n.d). A clinical guide pulse wave analysis Retrieved 18 January 2013, from www.atcormedical.com.

In another study using postmenopausal women with elevated BP, two groups of participants, sodium restricted and exercise, were compared. Central pulse wave velocity (CPWV), peripheral pulse wave velocity (PPWV), and AIx were unchanged after 13 weeks of aerobic training, whereas CPWV and AIx improved in a sodium-restricted group (Seals et al., 2001). This result is most likely due to the reduced systolic BP and pulse pressure in the sodium-restricted group.

Data on the effects of exercise on arterial stiffness are sparse. It seems that having a highly active lifestyle reduces central arterial stiffness in both males and females. It has been reported that older active males and females showed a 26 to 30% lower level of aortic PWV and 36 to 50 % lower level of carotid AIx respectively, compared to sedentary counterparts (Tanaka, DeSouza, & Seals, 1998; Vaitkevicius et al., 1993). The reliability and reproducibility of AIx and PWV to determine arterial stiffness have been demonstrated (Papaioannou et al., 2004; Salvi et al.,

[1] The artery is partially compressed against a hard structure. The small sensor (0.5 mm in diameter) detects the force on the artery wall.

2008; Wilkinson et al., 1998). An example of a central pressure wave form is illustrated in Figure 1.10.

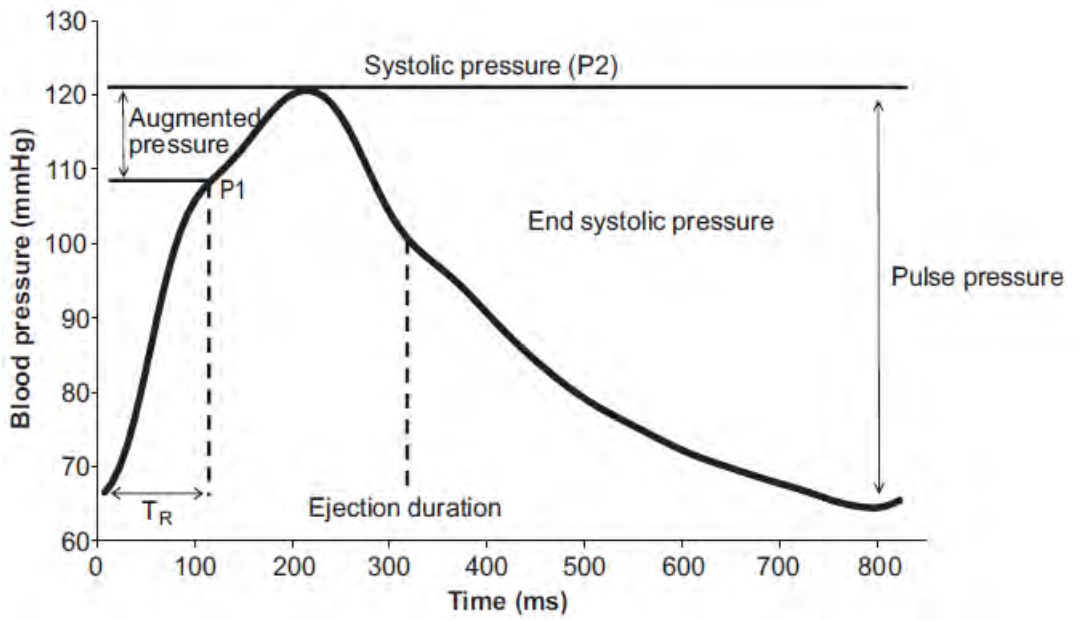

Figure 1.10. Diagram of central pressure waveform[2]

Source: Sharman, J. E., Davies, J. E., Jenkins, C., & Marwick, T. H. (2009). Augmentation index, left ventricular contractility, and wave reflection. Hypertension, 54(5), 1099-1105.

Regular aerobic training has been shown to be an effective way to improve arterial compliance in healthy young (Cameron & Dart, 1994; Kakiyama et al., 2005), elderly (Moreau, Donato, Seals, DeSouza, & Tanaka, 2003; Tanaka et al., 2000), congestive heart failure (Parnell, Holst, & Kaye, 2002), and diabetes patients (Madden, Lockhart, Cuff, Potter, & Meneilly, 2009; Yokoyama et al., 2004). The decreased arterial compliance can be improved by even several weeks of regular exercise training in healthy middle-aged adults (Collier et al., 2008) and participants with coronary artery disease (Edwards, Schofield, Magyari, Nichols, & Braith, 2004). Although in a recent study, arterial stiffness determined by PWV and AIx

[2] T_R: timing of the reflected pressure wave; P1: first systolic peaks; P2: second systolic peak

normalized to a rate of 75 $b \cdot min^{-1}$ (AIx@75 HR) showed no change after 8 weeks of endurance training in postmenopausal women (Sugawara et al., 2012). This is in line with the findings of Ferrier et al. (2001) on systolic hypertensives. They found no change in CPWV and PPWV after 8 weeks of moderate intensity cycling in elevated BP participants. Overall, most studies using aerobic or endurance training such as cycling, walking, and running which involve large muscle group have shown changes in arterial haemodynamics and systemic arterial shear stress.

Contrary to aerobic endurance exercise, moderate or high-intensity resistance training increases arterial stiffness in both acute and long term response to training in healthy young men and women (Collier et al., 2008; Fahs, Heffernan, & Fernhall, 2009; Kawano, Tanaka, & Miyachi, 2006; Miyachi et al., 2004; Yoon et al., 2010). But Yoshizama et al. (2009) found no change in central and peripheral arterial stiffness after 12 weeks of resistance training in women (Yoshizawa et al., 2009). Okamato et al. (2009a) have shown an increase in peripheral arterial stiffness with upper resistance training but no change with lower resistance training. In another study by Okomato et al. (2009b) peripheral arterial stiffness was reduced after 10 weeks of home-based resistance training in women. In a cross sectional study the whole body arterial stiffness was higher in strength-trained athletes compared to the age-matched sedentary controls (Bertovic et al., 1999).

In a combination of resistance and endurance training, carotid arterial compliance was unchanged after 16 weeks of training (Kawano et al., 2006), whereas McGavock et al. (2004) have shown an increased in large artery compliance after 10 weeks of combined training with similar exercise intensities for both studies.

Some training studies have shown arterial stiffness changes in central arteries, such as the aorta or carotid arteries (Hayashi, Sugawara, Komine, Maeda, & Yokoi,

2005; Tanaka et al., 2000; Yoshizawa et al., 2009), whereas peripheral arterial stiffness showed no improvement after exercise training (Hayashi et al., 2005; Yoshizawa et al., 2009).

In terms of intensity, Sugawara et al. (2004) found a lowered arterial stiffness after 12 weeks of aerobic exercise with both low, 40% of HR reserve, and moderate, 70% of HR reserve, intensity in women suggesting no intensity effect, whereas Goto et al. (2003) showed an augmented endothelium-dependent vasodilation with moderate intensity, 50% of $VO_{2\ max}$ but not low (25%) and high (75 %) intensity in young healthy males. It has been shown that exercise as short as 6 days of intense endurance training can improve central and peripheral arterial stiffness measured by PWV but not AIx in healthy young males (Currie et al., 2009). It may be difficult to improve normal endothelial function in healthy individuals with low to moderate intensity exercise, whereas more intense training may enhance greater vasodilator improvements via oxidative stress and different shear stress pattern (Green, Spence, Halliwill, Cable, & Thijssen, 2011).

In a comparison between acute interval and constant exercise, Tordi et al. (2010) found a greater response for vascular adaptations (lower PWV) by intermittent exercise in lower limb with relatively moderate intensity matched for both types of exercise. Also in an acute response to HIIE, Rakobowchuk et al. (2009) found a decrease in central arterial distensibility and an increase in peripheral arterial distensibility during the recovery period, whereas Kingwell et al. (1997) showed an increase in both central and peripheral arterial compliances after acute moderate intensity exercise.

Greater adaptations in interval training might be related to greater stimulus of pulsatile stretch determined by fluctuation in arterial pressure and shear stress

determined by blood flow (Hodis & Zamir, 2009). Larger cardiac output (CO) fluctuations during interval exercise may modulates vascular shear stress and result in a higher endothelium-derived nitric oxide (NO) and other substances (Green, Maiorana, O'Driscoll, & Taylor, 2004). NO is a vasodilator and exerts its effect on vascular smooth muscle. In addition, some other vasodilators such as atrial natriuretic peptide (ANP) may release more in interval training than constant exercise. This is because of higher intra-atrial pressure and lower mediastinal pressure during this type of exercise (Schmitt et al., 2004).

It has been shown that low volume of HIIE could provide similar improvements in peripheral arterial distensibility and endothelial function as with high volume endurance training in healthy young participants (Rakobowchuk et al., 2008) indicating the effectiveness and time efficiency nature of HIIE compared to steady state exercise training. However, in a recent study using the same HIIE protocol, Whyte et al. (2010) did not find any change in arterial stiffness over 6 sessions of HIIE during two weeks of training.

The inconsistency among these intervention results and variability in the outcomes might be due to using various exercise protocols with different frequency, intensity, and exercise duration as well as training modality. Applying different measurement techniques in assessing arterial stiffness may also have contributed to this discordance.

To date no study has investigated the effects of long term high-intensity intermittent training on arterial stiffness in young overweight males. The arterial stiffness improvement determined by PWV and AIx75 in the Chapter 3 study might be due to either an indirect effect of weight loss and reduced BP or an enhanced contractile state of vascular smooth muscle. Other possible mechanisms which

underlie these mostly functional changes are a decrease in the release of neurohormonal vasoconstrictions and declined efferent sympathetic tone as well as an enhanced release of NO stimulated by an increased endothelial mechanical signalling including pulsatile flow and stretch (Green et al., 2005).

Whether the structural parts of the vessels determined by compliance coefficient, distensibility coefficient, and diameter have changed after HIIE needs to be further investigated. The exercise effects on arterial stiffness are summarized in Table 1.4.[3]

[3] Distensibility and compliance are important vessel wall properties. Distensibility is the ability of a vessel to stretch and is related to elastic properties of the arterial wall, and compliance is the ability of a vessel to stretch and hold volume and reflects the buffering function of the artery. Distensibility is defined as the compliance divided by the arterial volume.

Table 1.4. Effect of exercise on arterial stiffness

Study	Male/ Female	Age	No. of subjects	Intensity	Type of exercise	Length of study	Result
Cameron & Dart (1994)	M	18-32	13	75% of $VO_{2\ max}$	cycling 30 min 3 times/w	4 weeks	Arterial compliance⇧
Collier et al. (2008)	M/F	48	30	65% of $VO_{2\ max}$ and 10RM	running 3 times/w resistance 3 times/w	4 weeks	CPWV & PPWV ⇧ in resistance but ⇩in aerobic training
Currie et al. (2009)	M	25	14	65% of $VO_{2\ max}$	cycling 2 hrs/day	6 days	CPWV & PPWV⇩but AIx75⇔
Ferrier et al. (2001)[d]	M/F	64	20	65% of HR max	cycling 40 min 3 times/w	8 weeks	CPWV & PPWV⇔
Goldberg et al. (2009)[a]	M/F	55.3	37	mod	cycling /walking / jogging 60 min 4 times/w + diet	24 weeks	Artery elasticity improved
Goto et al. (2003)	M	21	26	25/50/75% of $VO_{2\ max}$	cycling 30min 5-7times/w	12 weeks	Endothelium-dependent vasodilation⇧ in 50%
Hayashi et al. (2005)	M	31-64	17	75% of HR max	walking/ jogging 45 min 3-4 times/w	16 weeks	CPWV⇩but PPWV⇔
Kakiyama et al. (2005)	M	21	10	70% of VO2 max	cycling 30 min 3-4 times/w	8 weeks	CPWV⇩but AIx75⇔
Kawano et al. (2006)	M	21	39	50% of 1RM	resistance 3 times/w resistance & endurance	16 weeks	Carotid arterial compliance ⇩ in resistance but ⇔ in resistance &endurance
Madden et al. (2009)[b]	M/F	65-83	36	60-75% of HR max	running /cycling 60 min 3 imes/w	12 weeks	PWV⇩
McGavock et al. (2004)[b]	F	59	28	65-75% of HR Res 50-65% of 1RM	cycling 30-55min and resistance 3 times/w	10 weeks	Large arteriy compliance⇧
Miyachi et al. (2004)	M	20-38	28	80% of 1RM	resistance 3 times/w	16 weeks	Carotid arterial compliance ⇩
Moreau et al. (2003)	F	58	11	65-80% of HR max	Walking 40-45 min 4-5 times/w	12 weeks	Carotid arterial compliance ⇧

Table 1.4. Effect of exercise on arterial stiffness (continued)

Study	Male/ Female	Age	No. of subjects	Intensity	Type of exercise	Length of study	Result
Moreau et al. (2003)	F	58	11	65-80% of HR max	Walking 40-45 min 4-5 times/w	12 weeks	Carotid arterial compliance ⇧
Okamoto, Masuhara, & Ikuta (2009b)	M/F	20.1	30	80% of 1RM	resistance 2 times/w	10 weeks	PPWV⇧ in upper resistance training PPWV⇔ in lower resistance training
Okamoto, Masuhara, & Ikuta (2009a)	F	42-55	12	#	resistance 40 min 2times/w	10 weeks	PPWV⇩
Parnell et al. (2002)[c]	M/F	17-70	21	50-60% of HR max	cycling /walking/weights 30min 3times/w to 60 min 5-7 times/w	8 weeks	arterial compliance ⇧ but CPWV & PPWV & AIx⇔
Rakobowchuk et al. (2008)	M/F	23.3	20	HIIE: Wingate Endurance: 65 % of VO_{2max}	HIIE:4-6 30 sec 3/w Endurance: cycling at 40-60 min 5 times /w	6 weeks	Peripheral artery distensibility and endothelium-dependent vasodilation⇧ but carotid artery distensibility⇔
Seals et al. (2001)	F	>50	35	65-80% of HR max	walking 40-45 min 5-7 times/w	13 weeks	CPWV, PPWV& AIx75⇔
Sugawara et al. (2012)	F	59-61	45	60-75% of HR max	cycling 25-45 min 3-6 times/w	8 weeks	PWV⇔ AIx75⇔
Sugawara, Inoue, Hayashi, Yokoi, & Kono (2004)	F	52-66	15	Low: 40% of HR Res High: 70% of HR Res	cycling 3-5 times/w	12 weeks	Central arterial compliance ⇧
Tanaka et al. (2000)	M	53	20	70-75% of HR max	walking/ jogging 40-45 min 4-6 times/w	12 weeks	Central arterial compliance ⇧
Thijssen, De Groot, Smits, & Hopman (2007)	M	70	8	65-85% of HR Res	cycling 20 min 3 times/w	8 weeks	Peripheral vasuculture improved but central arterial compliance ⇔

Table 1.4. Effect of exercise on arterial stiffness (continued)

Study	Male/ Female	Age	No. of subjects	Intensity	Type of exercise	Length of study	Result
Whyte et al. (2010)[a]	M	32.1	10	HIIE: Wingate	HIIE:4-6 30 sec 3/w	2 weeks	PWV⇔
Wijnen et al. (1993)	M	22-44	19	75% of $VO_{2\ max}$	cycling 45 min 3 times/w	6 weeks	Central & peripheral arterial compliance & distensibility⇔
Yokoyama et al. (2004)[b]	M/F	53	23	40-60% of HR max	cycling /walking 40 min 5 times/w	3 weeks	Central & Peripheral arterial stiffness ⇩
Yoshizawa et al. (2009)	F	32-59	35	60-70% of $VO_{2\ max}$ 60% of 1RM	cycling 30 min 2 times/w resistance 2 times/w	12 weeks	Resistance: CPWV & PPWV⇔ Aerobic: CPWV⇩ but PPWV⇔

Note. ⇧Indicates increased; ⇩Indicates decreased; ⇔Indicates no change; study has been done on [a]overweight and obese patients, [b]diabetic patients, [c]cardiac patients, [d]hypertensive patients; #not recorded; CPWV: central pulse wave velocity, PPWV: peripheral pulse wave velocity, AIx: augmentation index.

Vascular Adaptation Response to HIIE

Arterial function assessment and improvement are crucial for cardiovascular health. Cardiovascular disease and multiple sclerosis (MS) can be predicted by assessing endothelial dysfunction (Bonetti et al., 2004; Gokce, Keaney, et al., 2002; Ranadive et al., 2012; Rubinshtein et al., 2010) as subclinical markers of atherosclerosis and CVD such as arterial dysfunction are present before clinical symptoms (Agewall, 2003). The hypothesized response of arteries to increased flow and shear stress following varying durations of exercise training are described in Figure 1.11.

Endothelial function plays an important role in arterial stiffness although it is not the only contributor. Numerous studies have investigated endothelial function by using invasive and non-invasive approaches. Non-invasive methods include brachial artery (BA) flow-mediated vasodilation, pulse wave velocity analysis and augmentation index, finger plethysmography (EndoPAT), and measuring the biochemical markers of endothelial dysfunction. Non-invasive techniques assessing endothelial function can represent the coronary vascular function because of the systemic nature of endothelial dysfunction (Arrebola-Moreno, Laclaustra, & Kaski, 2012).

Studies investigating the effects of exercise on arterial adaptation have shown inconsistent results. Different adaptations may have been induced based on the time-course of the training program. Short term exercise training enhances NO bioactivity resulting in arterial functional improvement involving phenotype alteration of endothelial cells and vascular smooth muscle but structural adaptations more likely happen after longitudinal training due to an increase in arterial diameter,

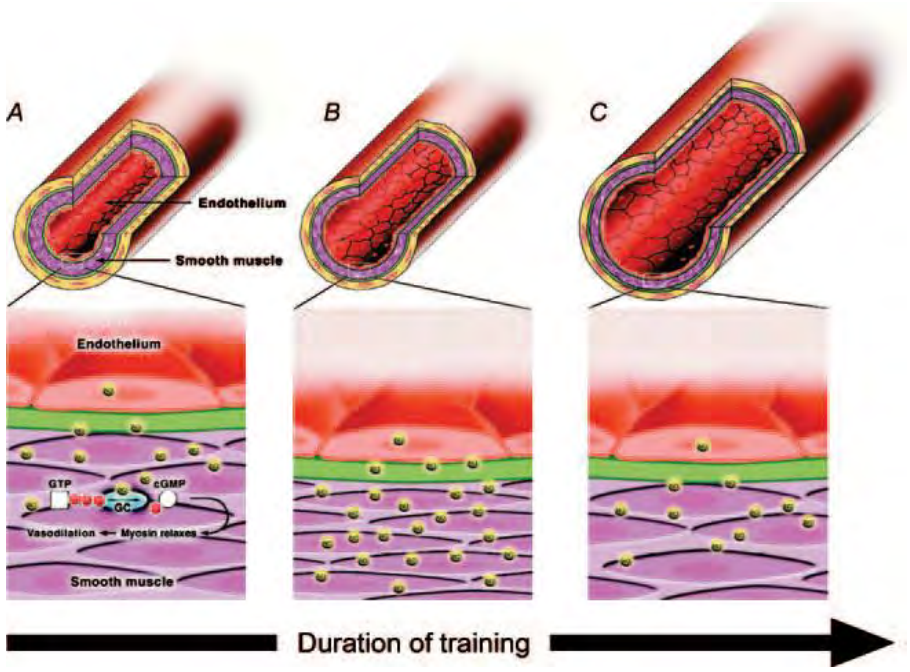

Figure 1.11. Hypothesized response of arteries to increased flow and shear stress following varying durations of exercise training[4]

Source: Maiorana, A., Driscoll, G., Taylor, R., & Green, D. (2003). Exercise and the nitric oxide vasodilator system. Sports Medicine, 33(14), 1013-1035.

angiogenesis, and remodelling. Artery remodelling, after extended exercise program, may suppress functional adaptation and NO will typically return to a normal level. Tinken et al. (2008) have assessed the time course of change in endothelial function and vasodilatory capacity in the brachial artery during 8 weeks of lower limb exercise training and found that endothelial function peaked after 2 weeks of training but returned to baseline levels after 8 weeks of training, whereas vasodilatory response to reactive hyperemia continuously increased throughout the

[4] (**a**) In untrained vessel baseline endothelial release of NO diffuses to smooth muscle and activates GC leading to production of cyclic GMP. Cyclic GMP opens calcium channel causing smooth muscle relaxation and vessel vasodilation. Localised fluctuations in release of NO act to homeostatically regulate wall shear. (**b**) In vessel following medium-term exercise training acute increase in shear stress, associated with repetitive exposure to increased flow during bouts of exercise, stimulates increased endothelial NO production and consequent vasodilation. Up-regulation of the NO-dilator system, including eNOS expression, occurs to buffer increased shear stress. (**c**) In vessel following long-term exercise training structural adaptation occurs, possibly partly due to NO-mediated changes in smooth muscle cells, resulting in chronic increase in vessel calibre which normalise shear stress. NO function returns towards baseline levels. **eNOS:** endothelial nitric oxide synthase; **GC:** guanylate cyclase; **GMP:** guanosine monophosphate; **GTP:** guanosine triphosphate; **NO:** nitric oxide

training period, showing remodelling adaptation. Similar results was found by Pullin et al. (2004) who showed that endothelial function assessed by FMD of BA reached a peak on day 6 of exercise training but returned to baseline on day 9. The hypothesized response of vascular adaptation to exercise following varying durations of exercise training are described in Figure 1.12.

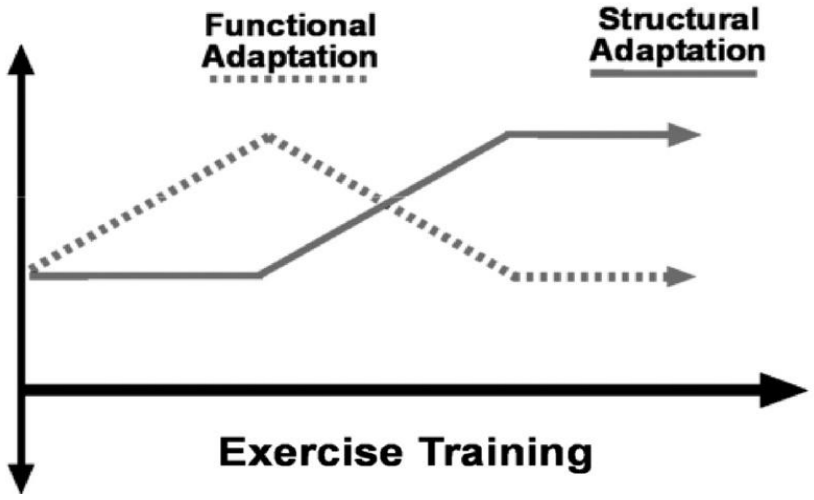

Figure 1.12. Vascular adaptation to exercise training[5]

Source: Green, D. J. (2009). Exercise training as vascular medicine: Direct impacts on the vasculature in humans. Exercise and Sport Sciences Reviews, 37(4), 196-202

Regular exercise may induce a systemic effect on endothelial function through a shear stress-independent mechanism (i.e., hormonal factors and circumference stretch) and also alterations in the shear profile such as waveforms (Padilla et al., 2011). Some prior research has indicated the systemic influence of exercise on the vasoculture (Green et al., 2004; Green, O'Driscoll, Joyner, & Cable, 2008; Green et al., 2011; Jasperse & Laughlin, 2006; Thijssen et al., 2010). However, Thijssen et al. (2007) found no vascular adaptation in non-trained areas after 8 weeks of cycling in older males. Thus, upper limb vascular adaptation after lower limb training is

[5] Exercise training is initially associated with rapid changes in artery function, including the bioavailability of endothelium-derived nitric oxide (NO). This functional change is eventually superseded by arterial remodelling.

unclear. Results of studies examining the impact of lower limb exercise training on upper limb vascular function in humans are shown in Table 1.5.

Table 1.5. Studies of the impact of lower limb exercise training on upper limb vascular function in humans

Healthy subjects:		**Hypertension:**		**Diabetes:**	
Kingwell, Sherrard, Jennings, & Dart (1997)	⇧	Higashi et al. (1999)	⇧	Maiorana, O'Driscoll, Cheetham et al. (2001)	⇧
Higashi et al. (1999)	⇧	Moriguchi et al. (2005)	⇧	Lavrencic, Salobir, & Keber (2000)	⇧
DeSouza et al. (2000)	⇧	Westhoff et al. (2007)	⇧	Fuchsjäger-Mayrl et al. (2002)	⇧
Goto et al. (2003)	⇧⇔*	**CHF:**		Xiang & Wang (2004)	⇧
Pullin et al. (2004)	⇧	Maiorana et al. (2000)	⇧	**CAD:**	
Maiorana, O'Driscoll, Dembo, et al. (2001)	⇔	Linke et al. (2001)	⇧	Walsh, Bilsborough et al. (2003)	⇧
Thijssen et al. (2007)	⇔	Belardinelli, Capestro, Misiani, Scipione, & Georgiou (2006)	⇧	Edwards et al. (2004)	⇧
Moriguchi et al. (2005)	⇔	Wisloff et al. (2007)	⇧	Gokce Vita et al. (2002)	⇔
Bergholm et al. (1999)	⇩	Demopoulos et al. (1997)	⇔	Motohiro et al. (2005)	⇔
Hypercholesterolaemic:		Dziekan et al. (1998)	⇔	**Peripheral artery disease:**	
Lewis, Dart, Chin-Dusting, & Kingwell (1999)	⇧	Kobayashi et al. (2003)	⇔	Andreozzi, Leone, Laudani, Deinite, & Martini (2007)	⇧
Walsh et al. (2003)	⇧				

Note. ⇧Indicates enhanced upper limb vascular function following predominantly lower limb exercise training intervention, ⇔indicates no change, ⇩indicates reduced function. *Goto found enhanced function with moderate intensity training, but no change with low- or high-intensity training.

A number of studies have shown vascular function improvement of the upper limb following lower limb exercise in healthy participants in both conduit (e.g. brachial and radial; Clarkson et al., 1999; Pullin et al., 2004; Tinken, Thijssen, Black, Cable, & Green, 2008) and resistance arteries (e.g., forearm arteries; DeSouza et al., 2000; Goto et al., 2003; Kingwell, Sherrard et al., 1997), whereas other studies have indicated no change (Maiorana, O'Driscoll, Dembo et al., 2001; Moriguchi et al., 2005; Østergård et al., 2006; Thijssen et al., 2007) and one study even showed a decrease (Bergholm et al., 1999) in vascular function.

It should be noted that the beneficial effects of lower limb exercise on endothelial function of nonworking limbs are more obvious in pre existing cardiovascular risk factors or diseased populations (Green et al., 2004; Maiorana, Driscoll, Taylor, & Green, 2003; Moyna & Thompson, 2004; Thijssen et al., 2010). For example, Moriguchi et al. (2005) found an improved flow-mediated dilatation in brachial artery function, after 12 weeks of cycling at an intensity of 50% of $\dot{V}O_{2max}$ for 60 min, twice a week, in hypertensive participants but were unable to show this result in normotensives. The vessel diameter was not changed in either group after 12 weeks of aerobic exercise training.

Similar results were found by Higashi et al. (1999) after 12 weeks of aerobic training at an intensity of 52% of $\dot{V}O_{2max}$ in hypertensive individuals. Furthermore, it has been suggested that endothelial functional adaptation may occur in older sedentary participants but not in healthy young individuals (DeSouza et al., 2000). Thus, it might be difficult to see an improvement in endothelial function after lower limb training in healthy young individuals. The proposed mechanisms by which exercise training may alter endothelial cell phenotype and function beyond the active muscle beds are described in Figure 1.13.

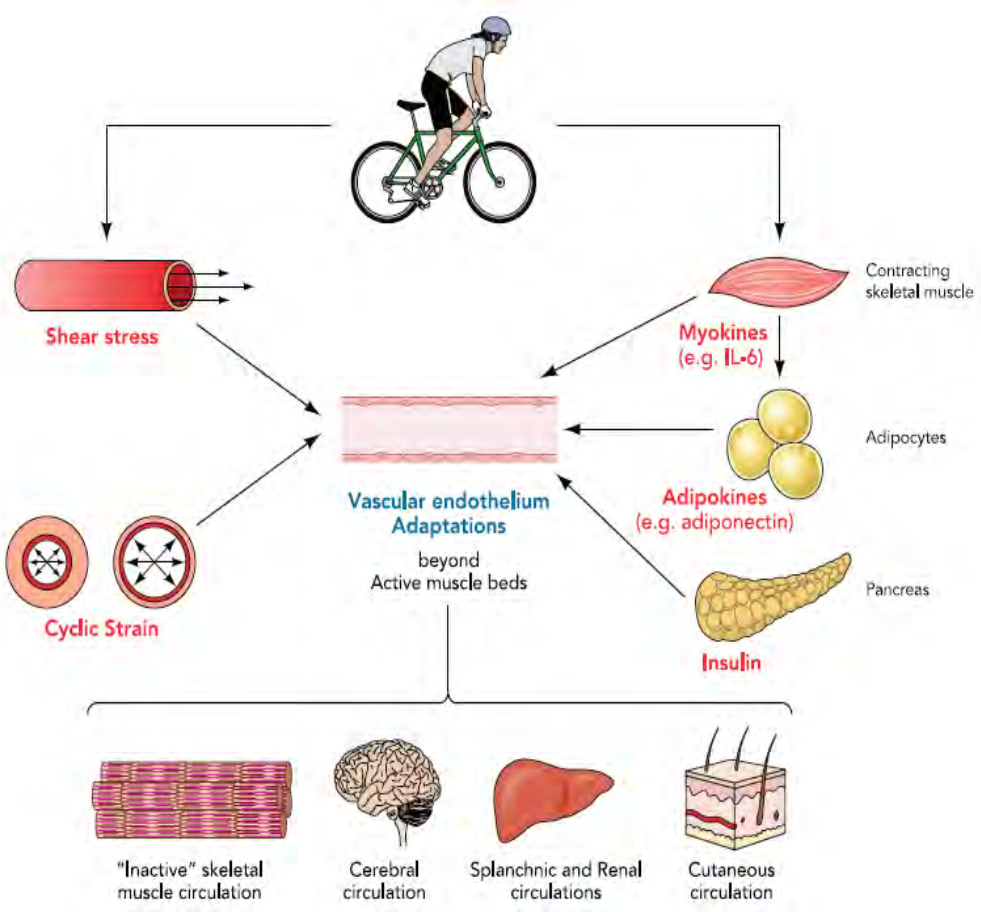

Figure 1.13. Proposed mechanisms by which exercise training may alter endothelial cell phenotype and function beyond the active muscle beds[6]

Source: Padilla, J., Simmons, G. H., Bender, S. B., Arce-Esquivel, A. A., Whyte, J. J., & Laughlin, M. H. (2011). Vascular effects of exercise: Endothelial adaptations beyond active muscle beds. Physiology, 26(3), 132-145.

The mechanisms underlying this phenomenon have not been fully elucidated. The endothelial adaptation in conduit arteries may be attributed to increased shear rate, whereas it is unclear in resistance arteries (Green et al., 2011). Other possible mechanisms in forearm vasodilatory functional adaptation include an increase in

[6] During a bout of exercise, endothelial gene expression can be regulated by changes in the magnitude and profiles of shear stress and cyclic strain as well as by circulating factors such as myokines released from contracting skeletal muscle. Exercise training may also restore/maintain normal phenotype of adipocytes resulting in a healthier adipokine release, thereby signaling expression of healthy endothelial cell genes. In addition, exercise training may exert a systemic effect on endothelial phenotype and function in part through sensitizing the endothelium to the beneficial effects of insulin.

endothelial NO synthase (eNOS) and prostaglandin release and a decline in free radical-mediated NO degradation and sympathetic vasoconstrictor tone (Niebauer & Cooke, 1996). Studies investigating the resistance vessel adaptation in the upper limb (FBF) following lower limb exercise in healthy individuals have used aerobic continuous exercise for their training protocol (Bergholm et al., 1999; DeSouza et al., 2000; Goto et al., 2003; Kingwell, Berry, Cameron, Jennings, & Dart, 1997; Maiorana, O'Driscoll, Dembo et al., 2001; Thijssen et al., 2007). Most of these researches have used ACh as endothelium-dependent vasodilator and measured forearm blood flow response to ACh infusion. This increase in forearm blood flow response to ACh after exercise training may be explained by endothelial adaptation related to cutaneous circulation (Green et al., 2011). In healthy individuals ACh promotes NO production from the vessel leading to vasodilation, however, in individuals with endothelial dysfunction ACh has a direct vasoconstrictor effect on endothelial smooth muscles in the absence of NO release (muscarinic effect) (Arrebola-Moreno et al., 2012).

Goto et al. (2003) showed an augmented endothelium-dependent vasodilation in the forearm with moderate intensity, 50% of $\dot{V}O_{2max}$ but not low (25%) and high (75 %) intensity cycling in young healthy males through increased NO production. In this study the oxidative stress indicator concentrations including plasma 8-OHdG and serum MDA-LDL increased after 12 weeks of high-intensity training but these researchers were unable to show an association between impaired endothelial function and increased oxidative stress (Goto et al., 2003). This indicates that high-intensity training may not result in endothelial dysfunction. Long time exercise with high-intensity may result in a decline in circulating antioxidants such as alpha-tocopherol and beta-carotene (Bergholm et al., 1999) and induce oxidative stress that

inactivates the NO bioavailability, however, augmented NO production due to an increase in exercise intensity (Matsumoto et al., 1994) may compensate for this impaired effect and result in a maintenance of endothelial function. A study with metabolic syndrome and type 2 diabetic patients showed an improvement in brachial artery endothelium dependent vasodilation assessed by reactive hyperaemia after 6 weeks of high-intensity (75-85% of HR max) aerobic training but not at low-intensity exercise (50-60% of HR max; Silva et al., 2012). A similar result was found by Green et al. (2005). In this study FBF significantly increased after moderate intensity (120 W) cycling, but was unchanged at lower exercise intensities (60 and 80 W). To date no study has used high-intensity interval training regimen to assess resting FBF. The effects of different stimuli (physical or chemical) on vascular endothelium are shown in Figure 1.14.

Increased blood flow along the vessel stimulates the endothelial to produce NO which rapidly directs to the smooth muscle cells and results in relaxation (Joannides et al., 1995). This is called endothelium-dependent flow-mediated dilatation (FMD). FMD, an endothelium-dependent function, has been evaluated noninvasively in a number of exercise based studies. The FMD of the brachial artery shows a mixed result after aerobic exercise training in healthy individuals. Pullin et al. (2004) have found an increase in FMD of BA after 4 weeks of cycling training in sedentary males. Clarkson et al. (1999) have shown similar findings after 10 weeks of aerobic and anaerobic training program in healthy young males, whereas Moriguchi et al. (2005) and Thijssen et al. (2007) were unable to show a change in FMD after 12 weeks and 8 weeks of cycling training in middle-aged and older males respectively. FMD of BA also did not change after 10 weeks of cycling training in healthy individuals at a relatively high intensity (70% of $\dot{V}O_{2max}$; Østergård et al., 2006).

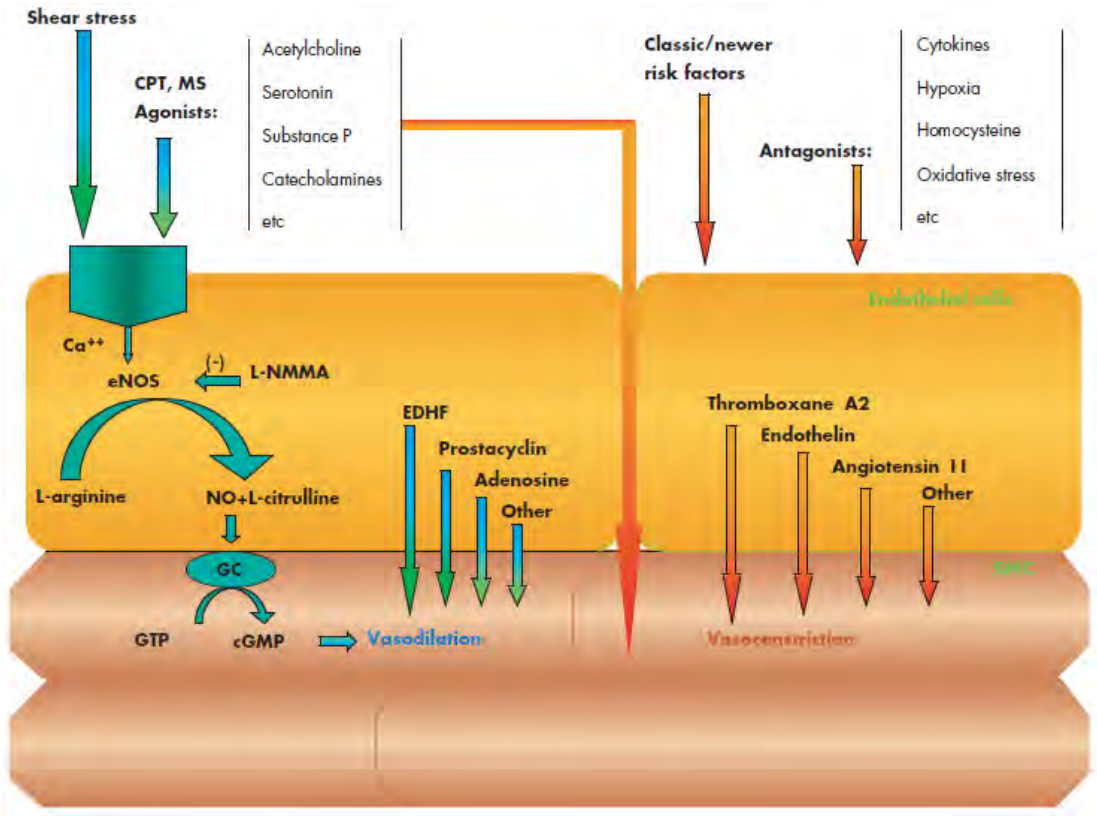

Figure 1.14. Effects of physical or chemical stimuli on vascular endothelium[7]

Source: Tousoulis, D., Antoniades, C., & Stefanadis, C. (2005). Evaluating endothelial function in humans: a guide to invasive and non-invasive techniques. Heart, 91(4), 553-558.

Vasodilatory Capacity Response to HIIE

Post-occlusion reactive hyperaemia (PORH), an index of endothelium-dependent vasodilation has been used as a clinical tool to assess endothelial function, microvascular function, and vasodilatory capacity in different populations such as type 2 diabetics (Yamamoto-Suganuma & Aso, 2009), peripheral vascular disease (Xuefeng et al., 2004), heart failure (van Langen, van Driel, Skotnicki, & Verheugt, 2001) and preeclampsia patients (Beinder & Schlembach, 2001), as well as healthy

[7] Stimuli leading to vasorelaxation in the presence of intact vascular endothelium (such as acetylcholine), produce vasoconstriction when acting directly on the underlying smooth muscle cells, in vascular areas with injured endothelium. CPT, cold pressor stress test; EDHF, endothelium derived hyperpolarising factor; eNOS, endothelial nitric oxide synthase; GC, guanyl cyclase; L-NMMA, NG-monomethyl-L-arginine; MS, mental stress; NO, nitric oxide; SMC, smooth muscle cell.

participants (Green, Cable, Fox, Rankin, & Taylor, 1994; Silber et al., 1991). The induced hypoxic condition during cuff inflation stimulates vasodilation of arterioles and also microvascular recruitment. This increased capacity of arterioles to restore blood can be identified after defilation and is a good predictor of intensive care unit death. In a recent study of 270 outpatients, it was shown that low reactive hyperemia (RH) was associated with higher cardiovascular adverse events during follow up (Rubinshtein et al., 2010).

Mechanisms involved in the reactive hyperemia include metabolic vasodilators, myogenic response, sensory nerves, and endothelial vasodilators (Cracowski, Minson, Salvat-Melis, & Halliwill, 2006). Of the latter mechanism, NO is not crucial for a hyperaemic response (Wong, Wilkins, Holowatz, & Minson, 2003; Zhao, Pergola, Roman, & Kellogg, 2004).

There are a few techniques to measure PORH including plethysmography (Acree et al., 2007; Faizi, Kornmo, & Agewall, 2009), ultrasound (Østergård et al., 2006; van Langen et al., 2001), laser doppler flowmetry (LDF) (Beinder & Schlembach, 2001; Hashimoto, 1993; Yamamoto-Suganuma & Aso, 2009) and tissue viability imager (TiVi) (Farnebo, Thorfinn, Henricson, & Tesselaar, 2010). Results from previous studies show variations. This variability in response to PORH may depend on the use of different techniques, cuff position, and duration of ischemia (between 1 and 10 min).

The effect of physical activity on vasodilatory capacity has been investigated in a number of studies and results have been inconsistent. Some studies have found no difference in forearm reactive hyperemia in trained and sedentary groups with either 3 or 5 min occlusion times (Boegli et al., 2003; Colberg, Stansberry, McNitt, & Vinik, 2002; Lenasi & Štrucl, 2010). In contrast, other studies have shown an

improvement in reactive hyperemia induced by exercise training (Rossi, Santoro, Maurizio, & Carpi, 2006). Boutcher and Boutcher (2005) found higher vasodilatory capacities in forearm and leg muscles in runners compared to untrained.

Ranadive et al. (2012) reported a difference in arterial functioning markers such as resting FBF, reactive hyperaemia of forearm vessels (peak FBF), and CPWV in patients with MS compared with control and physical activity was accounted for these differences. In this study it was also reported that physical activity was associated with peak FBF and CPWV but not resting FBF in MS patients indicating the importance role of physical activity in reducing the risk of CVD in this population (Ranadive et al., 2012). Vasodilatory capacity (arteriolar dilation) has been also reported to improve after long aerobic training in the exercising (Martin et al., 1990) and non exercising muscle (Silber et al., 1991). In this context, vasodilatory capacity assessed by peak FBF may increase after lower limb training. Silber et al. (1991) have shown a 50% increase in peak FBF after 4 weeks of cycyling training at an intensity of 70% $\dot{V}O_{2max}$ in healthy young individuals. Blood flow capacity can be increased by exercise training through capillarity increase, arterioles growth and remodelling, and also alteration in endothelial and smooth muscle phenotypes, plus changes in the control of vascular resistance (Laughlin & Roseguini, 2008).

The effect of exercise on vasodilatoy capacity may differ from blood flow response. It has been shown that only 4 weeks of handgrip exercise training can increase peak vasodilatory capacity determined by RH in young healthy males (Franke, Stephens, & Schmid, 1998; Green et al., 1994) without an increase in resting forearm blood flow. Higashi et al. (1999) examined the effect of 12 weeks of aerobic exercise on reactive hyperemia in hypertensive patients and found an

improvement in reactive hyperemia through the release of NO but baseline FBF remained unchanged.

It has been shown that obesity is associated with endothelial dysfunction both in men and women and young and old healthy adults (Acree et al., 2007; Perticone et al., 2001; Sciacqua et al., 2003). Acree et al. (2007) reported an impaired vascular reactivity, measured by reactive hyperaemia, in older obese men and women compared to normal weight group. A similar result was found by Weil et al. (2011) showing lower FBF respond in middle-aged overweight/obese males compared to a normal weight group and authors suggested that the greater impairment of endothelial vasodilation was not associated with abdominal obesity. Weil et al. (2011) also found no difference in FBF respond to ACh in overweight/obese individuals with or without abdominal adiposity. In contrast, Brook et al. (2001) have shown a blunted response to FMD in healthy overweight participants with higher visceral fat (waist to hip ratio ≥0.85) compared to those with lower visceral fat. It seems that visceral fat in particular has an adverse effect on vascular endothelial function.

Mayeur et al. (2011) have used different tests to assess reactive hyperaemia and recommended using the upper arm rather than the forearm and also using occlusion time until muscle tissue oxygen saturation (StO2) is decreased to 40% which is 4.4±1.3 min in young healthy males and females. This occlusion time (about 5 min) gives a lower minimal StO2 variability but higher recovery slope and sensitivity compare to 3 min of occlusion time. Faizi et al. (2009) also support the use of 5-min of occlusion in the finger plethysmography technique rather than 1.5, 3, or 8 min. In Study two the upper arm cuff with vascular occlusion time of 5 min has been utilised.

Rating of Perceived Exertion Response to HIIE

Rating of perceived exertion (RPE) has been used to prescribe exercise intensity in a variety of sporting activities and clinical settings (Ceci & Hassmen, 1991; Gearhart, Riechman, Lagally, Andrews, & Robertson, 2008; Stoudemire et al., 1996). The ability of RPE to regulate absolute and relative intensity has mainly been examined during aerobic exercise (Noble & Robertson, 1996; Robertson, 1982, 2004). Two models based on RPE have been developed to monitor increases in aerobic fitness after regular training (Robertson, 2004). The constant-level tracking model predicts that after exposure to aerobic training RPE will be decreased during post testing (Robertson, 2004). This model is supported by a number of studies that have shown that RPE is typically lower during a standardized exercise bout (e.g., a $\dot{V}O_{2max}$ test) that is repeated after aerobic training (Koseoglu et al., 1997; Nielsen et al., 1997). A second model is the constant RPE tracking model which suggests that after aerobic training the workload necessary to generate a similar RPE to that of the pretest will increase (Robertson, 2004). In support of the RPE tracking model absolute workloads have been shown to decrease after aerobic exercise training when adjusted to produce the same RPE recorded at pretest (Duncan & Howley, 1998; Noble & Robertson, 1996; Robertson, 2004).

It is likely that the physiological mediators underlying the generation of RPE during aerobic exercise are respiratory and metabolic in origin (Lagally et al., 2002). In contrast, mediators driving RPE during resistance exercise have been shown to be associated with peripheral skeletal muscles (Lagally et al., 2002). Thus, it is unclear if these RPE tracking models are applicable to resistance training. However, Gearhart et al. (2008) showed that at least for mid range RPEs the constant tracking model

was appropriate for resistance exercise. Whether these tracking models are appropriate for prescribing exercise intensity for high-intensity intermittent exercise (HIIE) is undetermined.

HIIE protocols vary but usually consist of all-out sprinting followed by low intensity exercise or rest. The length of both the sprint and recovery period has varied from 6 s to 4 min (Boutcher, 2011). Most commonly the sprints are performed on a stationary cycle ergometer at an intensity in excess of 90% of $\dot{V}O_{2max}$. The most utilized protocol in past research has been the Wingate test which consists of 30 s of all-out sprint with high resistance (Gibala & McGee, 2008), however, this protocol is extremely demanding. Thus, the Wingate protocol is likely to be unsuitable for most overweight, sedentary individuals interested in increasing fitness or losing body fat. Other less demanding HIIE protocols include an 8-sec cycle sprint followed by 12 sec of low intensity cycling for a period of 20 min (Trapp et al., 2008). Thus, instead of 4 to 6 sprints per session, as used in Wingate protocol studies, participants using the 8 sec/12 sec protocol sprint 60 times at a lower exercise intensity. This form of HIIE has been shown to be more effective for producing fat loss compared to steady state aerobic exercise (Trapp et al., 2008), however, the RPE response to fixed and variable workloads after HIIE training has not been examined.

Mental Challenge

Psychological stress is risk factor that contributes to cardiovascular disease development (Chida & Steptoe, 2010). Acute psychological stress increases sympathetic, cardiovascular, and hypothalamic pituitary adrenocortical (HPA) activity and reduces parasympathetic activity (Chrousos & Gold, 1992; McEwen, 1998). A large scale of these cardiovascular reactions due to exposure to acute

psychological stress increases the risk of the development of cardiovascular disease (Obrist, 1981). This is known as the reactivity hypothesis. High sympathetic activity during mental stress is a potential risk factor for a number of cardiovascular diseases including myocardial infarction (Deanfield et al., 1984; Rozanski et al., 1988), atherosclerosis (Rozanski, Blumenthal, & Kaplan, 1999; Yeung et al., 1991) and hypertension (Carroll, Ring, Hunt, Ford, & Macintyre, 2003; Carroll et al., 2001; Esler, Lambert, Brunner-La Rocca, Vaddadi, & Kaye, 2003), whereas low reactivity during acute stress shows an adaptive response and is a protective sign against cardiovascular disease. This is an important factor especially in the population at risk of cardiovascular disease such as obese population.

It has been argued that obesity, especially abdominal adiposity, is linked with physiological hyper-reactivity (Björntorp, 1991) and exaggerated cardiovascular reactions to stress (Davis, Twamley, Hamilton, & Swan, 1999; Waldstein, Burns, Toth, & Poehlman, 1999). Some studies have shown that obese individuals possess an elevated sympathetic rate during resting condition (Tentolouris, Liatis, & Katsilambros, 2006), whereas their sympathetic nervous system shows less response to stimulators. In a recent study by Phillips (2011), it was shown that obese individuals exhibited much smaller HR reactions to stress than non-obese individuals. Also, overweight and obese individuals have reduced BRS response to mental challenge (Honzíková et al., 2006; Lazarova et al., 2009). Similar to BRS the enhanced FBF response of lean participants to mental challenge is typically reduced in the overweight and obese (Agapitov, Correia, Sinkey, Dopp, & Haynes, 2002). The inability to vasodilate skeletal muscle during mental challenge results in increased systemic vascular resistance which is typically accompanied by an increase in BP (Seematter et al., 2000). It is likely that cardiovascular risks related to obesity

such as disturbance in cardiovascular reactivity during mental stress begins at relatively younger age in non-obese participants. Thus, it is clinically relevant to find a method for reducing the sympathetic response and lowering the cardiovascular reactivity during mental stress in young overweight populations which may be at higher risk of becoming obese in the future.

While exercise promotes cardiovascular health indirectly through improving other CVD risk factors, such as weight loss and decreased hypertension, numerous research studies have also shown the direct beneficiary effects of physical activity and physical fitness on various measures of cardiovascular health (Bucksch & Schlicht, 2006). Physical activity has a large impact on preventing cardiovascular disease (Hagberg, Park, & Brown, 2000; Jolliffe et al., 2001; Manson et al., 1999; Thompson et al., 2003) and improving the cardiovascular risk factor profiles, including increases in parasympathetic neural activity (Smith, Kukielka, & Billman, 2005; Tulppo et al., 2003) and reductions in blood pressure (Fagard, 2001; Hagberg et al., 2000). It has been proposed that aerobic training may also decrease physiological responsivity to stress (Boutcher & Hamer, 2006; Crews & Landers, 1987; Matthews, 1986; Plante & Karpowitz, 1987; van Doornen & de Geus, 1989). Ribeiro et al. (2005) demonstrated that a 4-month exercise/diet intervention conducted on obese children improved limb blood flow response to the Stroop task and decreased BP reactivity.

It has been shown that exercisers exhibit attenuated physiological reactivity to psychological stressors compared with non-exercisers (Anshel, 1996; van Doornen & de Geus, 1989). A meta-analysis included mainly of cross-sectional studies concluded that fit individuals have reduced physiological responses to stress compared to sedentary individuals (Crews & Landers, 1987). Findings from a few

controlled intervention trials are less conclusive. Some studies have shown that exercise training can lower HR and BP responsivity to stress (Blumenthal et al., 1988; Blumenthal et al., 1990; Georgiades et al., 2000; Sherwood, Light, & Blumenthal, 1989; Spalding, Lyon, Steel, & Hatfield, 2004), while others have failed to support such an effect on responsivity (Ray & Carter, 2010; Roskies et al., 1986; Schaeffer et al., 1988; Seraganian, Roskies, Hanley, Oseasohn, & Collu, 1987; Sinyor, Golden, Steinert, & Seraganian, 1986). A meta-analysis by Jackson and Dishman (2006) indicated a slightly greater cardiovascular reactivity in fit individuals compared to their non fit counterparts. A blunted BRS response to mental challenge has been shown in sedentary groups suggesting a lack of adaptive response in the autonomic adjustment to the stressor (Martín-Vázquez & Reyes del Paso, 2010). In this study baroreflex effectiveness index (BEI) decreased during mental task in the sedentary group but not in the physically active group showing the ability of baroreflex effectiveness in regulating cardiac activity in response to BP increase in trained individuals.

Several longitudinal studies have reported a significant reduction in cardiovascular reactivity (Blumenthal et al., 1991; Georgiades et al., 2000), however, these results have been obtained from populations with initially elevated cardiovascular reactivity to mental challenge such as hypertensive and Type A individuals. With regard to studies using normotensive participants, changes in HR and BP have been recorded. For example, Forcier et al. (2006) conducted a meta-analysis and found that aerobically fit individuals showed significantly attenuated HR (1.84 bpm) and systolic BP reactivity (3.69 mmHg) and a trend toward attenuated diastolic BP reactivity (1.2 mmHg).

Most of the exercise based studies looking at cardiovascular reactivity to mental stress have used steady state aerobic exercise (e.g., cycling, walking, jogging, and swimming). Thus, the effects of other types of exercise such as regular resistance and anaerobic training on cardiovascular reactivity are undetermined. It has been shown that high-intensity training is more effective on vagal HR control than low intensity exercise program (Martinmäki et al., 2008). This supports the notion that intensive exercise training is necessary to induce central cardiac adaptations (Leicht, et al., 2003; Melanson & Freedson, 2001). For example, Albright et al. (1992) have found no difference between exercise and control groups after 6 months aerobic training in BP responsivity to mental arithmetic stress in healthy middle-aged men and women. Blumenthal et al. (1991) also could not find any cardiovascular change in response to mental challenge determined by speech task in pre and postmenopausal women after 3 months of aerobic training. These studies have used moderate intensity training mostly walking and jogging which may not induce cardiovascular physiological changes in response to mental stressors.

High-intensity intermittent exercise (HIIE), a form of anaerobic training (Boutcher, 2011), produces a significantly greater impact on the autonomic nervous system (ANS) assessed by HR and plasma catecholamine levels compared to steady state exercise (Trapp et al., 2007). Given that HIIE induces a significant acute cardiovascular response it is feasible that HIIE training will produce greater adaptations in ANS control of the cardiovascular system. To date, however, no study has examined the effect of HIIE training on ANS response during and after mental challenge.

Although the effects of exercise training on HR and BP response to mental challenge have been extensively studied, relatively less attention has been devoted to

other aspects of cardiovascular response such as skeletal muscle blood flow and baroreceptor sensitivity. In addition, the effect of HIIE training on arterial stiffness during mental stress has yet to be examined. Consequently, it is not clear whether cardiac, vascular and autonomic measures under challenging laboratory conditions are influenced by long-term HIIE training.

Therefore, the purpose of Study II was to examine the effects of HIIE on multiple measures of cardiovascular and autonomic reactivity. It was hypothesized that a 12-week program of HIIE would result in significant reductions in reactivity and recovery from mental challenge of young, inactive men.

Summary of the Literature Review

This literature review has examined a number of health concerns related to having an inactive lifestyle. Physical inactivity can lead to overweight and obesity and its associated health complications such as metabolic syndrome and type 2 diabetes. Abnormal cardiovascular and autonomic function at rest and during laboratory stressors such as physical and mental (Stroop colour-word task) challenge is also considered as a result of sedentary lifestyle. High-intensity intermittent exercise (HIIE), an effective and time efficient type of exercise, could be used as a lifestyle modification program with various populations and has the potential to alter body composition as well as cardiovascular and autonomic function at rest and during physical and mental challenges. Furthermore, it is feasible that HIIE training could generate greater physiological adaptations in the cardiovascular system and ANS because of its ability to enhance plasma catecholamins and HR reduction.

References

ABS. (2005). Overweight and Obesity in Adults, Australia, 2004-05. *Australian Bureau of Statistics*.

ABS. (2008). Overweight and Obesity in Adults, Australia, 2004-05. *Australian Bureau of Statistics*.

ABS. (2009). Australian Social Trends, Sep 2009 *Australian Bureau of Statistics*.

Acree, L., Comp, P., Whitsett, T., Montgomery, P., Nickel, K., Fjeldstad, A., et al. (2007). The influence of obesity on calf blood flow and vascular reactivity in older adults. *Dynamic Medicine, 6*(1), 4.

Agapitov, A. V., Correia, M. L. G., Sinkey, C. A., Dopp, J. M., & Haynes, W. G. (2002). Impaired skeletal muscle and skin microcirculatory function in human obesity. *Journal of Hypertension, 20*(7), 1401-1405.

Agewall, S. (2003). Is impaired flow-mediated dilatation of the brachial artery a cardiovascular risk factor? *Current Vascular Pharmacology, 1*(2), 107-109.

Ahlborg, G., Felig, P., Hagenfeldt, L., Hendler, R., & Wahren, J. (1974). Substrate turnover during prolonged exercise in man. Splanchnic and leg metabolism of glucose, free fatty acids, and amino acids. *The Journal of Clinical Investigation, 53*(4), 1080-1090.

Albright, C. L., King, A. C., Barr Taylor, C., & Haskell, W. L. (1992). Effect of a six-month aerobic exercise training program on cardiovascular responsivity in healthy middle-aged adults. *Journal of Psychosomatic Research, 36*(1), 25-36.

Alvarez, G. E., Beske, S. D., Ballard, T. P., & Davy, K. P. (2002). Sympathetic neural activation in visceral obesity. *Circulation, 106*(20), 2533-2536.

Alvarez, G. E., Davy, B. M., Ballard, T. P., Beske, S. D., & Davy, K. P. (2005). Weight loss increases cardiovagal baroreflex function in obese young and older men. *American Journal of Physiology - Endocrinology And Metabolism, 289*(4), E665-E669.

Amano, M., Kanda, T., Ue, H., & Moritani, T. (2001). Exercise training and autonomic nervous system activity in obese individuals. *Medicine and Science in Sports and Exercise, 33*(8), 1287-1291.

Andreozzi, G. M., Leone, A., Laudani, R., Deinite, G., & Martini, R. (2007). Acute impairment of the endothelial function by maximal treadmill exercise in patients with intermittent claudication, and its improvement after supervised physical training. *International Angiology, 26*(1), 12-17.

Anshel, M. H. (1996). Effect of chronic aerobic exercise and progressive relaxation on motor performance and affect following acute stress. *Behavioral Medicine, 21*(4), 186-196.

Arciero, P. J., Goran, M. I., & Poehlman, E. T. (1993). Resting metabolic rate is lower in women than in men. *Journal of Applied Physiology, 75*(6), 2514-2520.

Arrebola-Moreno, A. L., Laclaustra, M., & Kaski, J. C. (2012). Noninvasive assessment of endothelial function in clinical practice. *Revista Española de Cardiología, 65*(1), 80-90.

Australian Institute of Health and Welfare. AIHW. (2012). The thirteenth biennial health report of the Australian Institute of Health and Welfare. *Australia's health 2012. Australia's health series no.13. Cat. no. AUS 156. Canberra: AIHW., Retrived from: www.aihw.gov.au/WorkArea/DownloadAsset.aspx?id=10737422169*.

Balkestein, E. J., van Aggel-Leijssen, D. P., van Baak, M. A., Struijker-Boudier, H. A., & Van Bortel, L. M. (1999). The effect of weight loss with or without exercise training on large artery compliance in healthy obese men. *Journal of Hypertension, 17*(12), 1831-1835.

Bartlett, J. D., Close, G. L., MacLaren, D. P. M., Gregson, W., Drust, B., & Morton, J. P. (2011). High-intensity interval running is perceived to be more enjoyable than moderate-intensity continuous exercise: Implications for exercise adherence. *Journal of Sports Sciences, 29*(6), 547-553.

Barwell, N. D., Malkova, D., Leggate, M., & Gill, J. M. (2009). Individual responsiveness to exercise-induced fat loss is associated with change in resting substrate utilization. *Metabolism: Clinical and Experimental, 58*(9), 1320-1328.

Beinder, E., & Schlembach, D. (2001). Skin flux during reactive hyperemia and local hyperthermia in patients with preeclampsia. *Obstetrics and Gynecology, 98*(2), 313-318.

Belardinelli, R., Capestro, F., Misiani, A., Scipione, P., & Georgiou, D. (2006). Moderate exercise training improves functional capacity, quality of life, and endothelium-dependent vasodilation in chronic heart failure patients with implantable cardioverter defibrillators and cardiac resynchronization therapy. *European Journal of Cardiovascular Prevention and Rehabilitation, 13*(5), 818-825.

Bergholm, R., Mäkimattila, S., Valkonen, M., Liu, M.-l., Lahdenperä, S., Taskinen, M.-R., et al. (1999). Intense physical training decreases circulating antioxidants and endothelium-dependent vasodilatation in vivo. *Atherosclerosis, 145*(2), 341-349.

Bergman, B. C., & Brooks, G. A. (1999). Respiratory gas-exchange ratios during graded exercise in fed and fasted trained and untrained men. *Journal of Applied Physiology, 86*(2), 479-487.

Bertovic, D. A., Waddell, T. K., Gatzka, C. D., Cameron, J. D., Dart, A. M., & Kingwell, B. A. (1999). Muscular strength training is associated with low arterial compliance and high pulse pressure. *Hypertension, 33*(6), 1385-1391.

Beske, S. D., Alvarez, G. E., Ballard, T. P., & Davy, K. P. (2002). Reduced cardiovagal baroreflex gain in visceral obesity: implications for the metabolic

syndrome. *American Journal of Physiology - Heart and Circulatory Physiology, 282*(2), H630-635.

Björntorp, P. (1991). Visceral fat accumulation: the missing link between psychosocial factors and cardiovascular disease? *Journal of Internal Medicine, 230*(3), 195-201.

Björntorp, P., & Rosmond, R. (2000). The metabolic syndrome--a neuroendocrine disorder? *The British Journal of Nutrition, 83 Suppl 1*, S49-57.

Blaak, E. E., Hul, G., Verdich, C., Stich, V., Martinez, A., Petersen, M., et al. (2006). Fat oxidation before and after a high fat load in the obese insulin-resistant state. *The Journal of Clinical Endocrinology and Metabolism, 91*(4), 1462-1469.

Blumenthal, J. A., Emery, C. F., Walsh, M. A., Cox, D. R., Kuhn, C. M., Williams, R. B., et al. (1988). Exercise training in healthy type A middle-aged men: Effects on behavioral and cardiovascular responses. *Psychosomatic Medicine, 50*(4), 418-433.

Blumenthal, J. A., Fredrikson, M., Kuhn, C. M., Ulmer, R. L., Walsh-Riddle, M., & Appelbaum, M. (1990). Aerobic exercise reduces levels of cardiovascular and sympathoadrenal responses to mental stress in subjects without prior evidence of myocardial ischemia. *The American Journal of Cardiology, 65*(1), 93-98.

Blumenthal, J. A., Fredrikson, M., Matthews, K. A., Kuhn, C. M., Schniebolk, S., German, D., et al. (1991). Stress reactivity and exercise training in premenopausal and postmenopausal women. *Health Psychology, 10*(6), 384-391.

Boegli, Y., Gremion, G., Golay, S., Kubli, S., Liaudet, L., Leyvraz, P.-F., et al. (2003). Endurance training enhances vasodilation induced by Nitric Oxide in human skin. *Journal of Investigative Dermatology, 121*(5), 1197-1204.

Bonetti, P. O., Pumper, G. M., Higano, S. T., Holmes, D. R., Jr, Kuvin, J. T., & Lerman, A. (2004). Noninvasive identification of patients with early coronary atherosclerosis by assessment of digital reactive hyperemia. *Journal of the American College of Cardiology, 44*(11), 2137-2141.

Bordenave, S., Metz, L., Flavier, S., Lambert, K., Ghanassia, E., Dupuy, A. M., et al. (2008). Training-induced improvement in lipid oxidation in type 2 diabetes mellitus is related to alterations in muscle mitochondrial activity. Effect of endurance training in type 2 diabetes. *Diabetes and Metabolism, 34*(2), 162-168.

Boudou, P., Sobngwi, E., Mauvais-Jarvis, F., Vexiau, P., & Gautier, J. (2003). Absence of exercise-induced variations in adiponectin levels despite decreased abdominal adiposity and improved insulin sensitivity in type 2 diabetic men. *European Journal of Endocrinology, 149*(5), 421-424.

Boutcher, S. H. (2011). High-intensity intermittent exercise and fat loss. *Journal of Obesity, doi: 10.1155/2011/868305*.

Boutcher, S. H., & Dunn, S. L. (2009). Factors that may impede the weight loss response to exercise-based interventions. *Obesity Reviews, 10*(6), 671-680.

Boutcher, S. H., & Hamer, M. (2006). *Psychobiological reactivity, physical activity and cardiovascular health. In E.O. Acevedo & P. Ekkekakis (Eds.), Psychobiology of Physical Activity.* Champaign,. IL: Human Kinetics.

Boutcher, Y. N., & Boutcher, S. H. (2005). Limb vasodilatory capacity and venous capacitance of trained runners and untrained males. *European Journal of Applied Physiology, 95*(1), 83-87.

Boyko, E. J., Fujimoto, W. Y., Leonetti, D. L., & Newell-Morris, L. (2000). Visceral adiposity and risk of type 2 diabetes: a prospective study among Japanese Americans. *Diabetes Care, 23*(4), 465-471.

Bracken, R. M., Linnane, D. M., & Brooks, S. (2009). Plasma catecholamine and nephrine responses to brief intermittent maximal intensity exercise. *Amino Acids, 36*(2), 209-217.

Braith, R. W., Pollock, M. L., Lowenthal, D. T., Graves, J. E., & Limacher, M. C. (1994). Moderate- and high-intensity exercise lowers blood pressure in normotensive subjects 60 to 79 years of age. *The American Journal of Cardiology, 73*(15), 1124-1128.

Bray, G. A., Jablonski, K. A., Fujimoto, W. Y., Barrett-Connor, E., Haffner, S., Hanson, R. L., et al. (2008). Relation of central adiposity and body mass index to the development of diabetes in the Diabetes Prevention Program. *The American Journal of Clinical Nutrition, 87*(5), 1212-1218.

Brochu, M., Starling, R. D., Tchernof, A., Matthews, D. E., Garcia-Rubi, E., & Poehlman, E. T. (2000). Visceral adipose tissue is an independent correlate of glucose disposal in older obese postmenopausal women. *The Journal of Clinical Endocrinology and Metabolism, 85*(7), 2378-2384.

Brook, R. D., Bard, R. L., Rubenfire, M., Ridker, P. M., & Rajagopalan, S. (2001). Usefulness of visceral obesity (waist/hip ratio) in predicting vascular endothelial function in healthy overweight adults. *The American Journal of Cardiology, 88*(11), 1264-1269.

Brun, J. F., Romain, A. J., & Mercier, J. (2011). Maximal lipid oxidation during exercise (Lipoxmax): From physiological measurements to clinical applications. Facts and uncertainties. *Science & Sports, 26*(2), 57-71.

Bucksch, J., & Schlicht, W. (2006). Health-enhancing physical activity and the prevention of chronic diseases — An epidemiological review. *Social and Preventive Medicine, 51*(5), 281-301.

Bunt, J. C., Boileau, R. A., Bahr, J. M., & Nelson, R. A. (1986). Sex and training differences in human growth hormone levels during prolonged exercise. *Journal of Applied Physiology, 61*(5), 1796-1801.

Burgomaster, K. A., Howarth, K. R., Phillips, S. M., Rakobowchuk, M., MacDonald, M. J., McGee, S. L., et al. (2008). Similar metabolic adaptations during exercise after low volume sprint interval and traditional endurance training in humans. *The Journal of Physiology, 586*(1), 151-160.

Burgomaster, K. A., Hughes, S. C., Heigenhauser, G. J. F., Bradwell, S. N., & Gibala, M. J. (2005). Six sessions of sprint interval training increases muscle oxidative potential and cycle endurance capacity in humans. *Journal of Applied Physiology, 98*(6), 1985-1990.

Byrne, H. K., & Wilmore, J. H. (2001). The effects of a 20-week exercise training program on resting metabolic rate in previously sedentary, moderately obese women. *International Journal of Sport Nutrition and Exercise Metabolism, 11*(1), 15-31.

Cameron, J. D., & Dart, A. M. (1994). Exercise training increases total systemic arterial compliance in humans. *American Journal of Physiology - Heart and Circulatory Physiology, 266*(2 Pt 2), H693-701.

Carroll, D., Ring, C., Hunt, K., Ford, G., & Macintyre, S. (2003). Blood pressure reactions to stress and the prediction of future blood pressure: Effects of sex, age, and socioeconomic position. *Psychosomatic Medicine, 65*(6), 1058-1064.

Carroll, D., Smith, G. D., Shipley, M. J., Steptoe, A., Brunner, E. J., & Marmot, M. G. (2001). Blood pressure reactions to acute psychological stress and future blood pressure status: A 10-year follow-up of men in the Whitehall II study. *Psychosomatic Medicine, 63*(5), 737-743.

Carter, J. B., Banister, E. W., & Blaber, A. P. (2003). The effect of age and gender on heart rate variability after endurance training. *Medicine and Science in Sports and Exercise, 35*(8), 1333-1340.

Catai, A. M., Chacon-Mikahil, M. P. T., Martinelli, F. S., Forti, V. A. M., Silva, E., Golfetti, R., et al. (2002). Effects of aerobic exercise training on heart rate variability during wakefulness and sleep and cardiorespiratory responses of young and middle-aged healthy men. *Brazilian Journal of Medical and Biological Research, 35*, 741-752.

Ceci, R., & Hassmen, P. (1991). Self-monitored exercise at 3 different RPE intensities in treadmill vs field running. *Medicine and Science in Sports and Exercise, 23*(6), 732-738.

Centers for Disease Control and Prevention, CDC (2010). *Healthy People 2010, Nutrition and Overweight*. Retrieved from Nutrition and Overweight

Chida, Y., & Steptoe, A. (2010). Greater cardiovascular responses to laboratory mental stress are associated with poor subsequent cardiovascular risk status. *Hypertension, 55*(4), 1026-1032.

Christmass, M. A., Dawson, B., & Arthur, P. G. (1999). Effect of work and recovery duration on skeletal muscle oxygenation and fuel use during sustained intermittent exercise. *European Journal of Applied Physiology and Occupational Physiology, 80*(5), 436-447.

Chrousos, G. P., & Gold, P. W. (1992). The Concepts of Stress and Stress System Disorders. *JAMA: The Journal of the American Medical Association, 267*(9), 1244-1252.

Church, T. S. (2011). Exercise in obesity, metabolic syndrome, and diabetes. *Progress in Cardiovascular Diseases, 53*(6), 412-418.

Church, T. S., LaMonte, M. J., Barlow, C. E., & Blair, S. N. (2005). Cardiorespiratory fitness and body mass index as predictors of cardiovascular disease mortality among men with diabetes. *Archives of Internal Medicine, 165*(18), 2114-2120.

Clarkson, P., Montgomery, H. E., Mullen, M. J., Donald, A. E., Powe, A. J., Bull, T., et al. (1999). Exercise training enhances endothelial function in young men. *Journal of the American College of Cardiology, 33*(5), 1379-1385.

Coker, R. H., Williams, R. H., Kortebein, P. M., Sullivan, D. H., & Evans, W. J. (2009). Influence of exercise intensity on abdominal fat and adiponectin in elderly adults. *Metabolic Syndrome and Related Disorders, 7*(4), 363-368.

Colberg, S. R., Stansberry, K. B., McNitt, P. M., & Vinik, A. I. (2002). Chronic exercise is associated with enhanced cutaneous blood flow in Type 2 diabetes. *Journal of Diabetes and Its Complications, 16*(2), 139-145.

Collier, S. R., Kanaley, J. A., Carhart, R., Jr., Frechette, V., Tobin, M. M., Hall, A. K., et al. (2008). Effect of 4 weeks of aerobic or resistance exercise training on arterial stiffness, blood flow and blood pressure in pre- and stage-1 hypertensives. *Journal of Human Hypertension, 22*(10), 678-686.

Cooke, W. H., & Carter, J. R. (2005). Strength training does not affect vagal–cardiac control or cardiovagal baroreflex sensitivity in young healthy subjects. *European Journal of Applied Physiology, 93*(5), 719-725.

Cooke, W. H., Reynolds, B. V., Yandl, M. G., Carter, J. R., Tahvanainen, K. U. O., & Kuusela, T. A. (2002). Effects of exercise training on cardiovagal and sympathetic responses to Valsalva's maneuver. *Medicine and Science in Sports and Exercise, 34*(6), 928-935.

Cornelissen, V. A., Arnout, J., Holvoet, P., & Fagard, R. H. (2009). Influence of exercise at lower and higher intensity on blood pressure and cardiovascular risk factors at older age. *Journal of Hypertension, 27*(4), 753-762.

Cornelissen, V. A., Verheyden, B., Aubert, A. E., & Fagard, R. H. (2009). Effects of aerobic training intensity on resting, exercise and post-exercise blood pressure, heart rate and heart-rate variability. *Journal of Human Hypertension, 24*(3), 175-182.

Costes, F., Roche, F., Pichot, V., Vergnon, J. M., Garet, M., & Barthelemy, J.-C. (2004). Influence of exercise training on cardiac baroreflex sensitivity in patients with COPD. *European Respiratory Journal, 23*(3), 396-401.

Cracowski, J.-L., Minson, C. T., Salvat-Melis, M., & Halliwill, J. R. (2006). Methodological issues in the assessment of skin microvascular endothelial function in humans. *Trends in Pharmacological Sciences, 27*(9), 503-508.

Crews, D. J., & Landers, D. M. (1987). A meta-analytic review of aerobic fitness and reactivity to psychosocial stressors. *Medicine and Science in Sports and Exercise, 19*(5), S121-S129.

Currie, K. D., Thomas, S. G., & Goodman, J. M. (2009). Effects of short-term endurance exercise training on vascular function in young males. *European Journal of Applied Physiology, 107*(2), 211-218.

Davis, M. C., Twamley, E. W., Hamilton, N. A., & Swan, P. D. (1999). Body fat distribution and hemodynamic stress responses in premenopausal obese women: A preliminary study. *Health Psychology, 18*(6), 625-633.

de Vries, W. R., Bernards, N. T., de Rooij, M. H., & Koppeschaar, H. P. (2000). Dynamic exercise discloses different time-related responses in stress hormones. *Psychosomatic Medicine, 62*(6), 866-872.

Deanfield, J. E., Kensett, M., Wilson, R. A., Shea, M., Horlock, P., De Landsheere, C. M., et al. (1984). Silent myocardial ischaemia due to mental stress. *The Lancet, 324*(8410), 1001-1005.

Demopoulos, L., Bijou, R., Fergus, I., Jones, M., Strom, J., & LeJemtel, T. H. (1997). Exercise training in patients with severe congestive heart failure: enhancing peak aerobic capacity while minimizing the increase in ventricular wall stress. *Journal of the American College of Cardiology, 29*(3), 597-603.

DeSouza, C. A., Shapiro, L. F., Clevenger, C. M., Dinenno, F. A., Monahan, K. D., Tanaka, H., et al. (2000). Regular aerobic exercise prevents and restores age-related declines in endothelium-dependent vasodilation in healthy men. *Circulation, 102*(12), 1351-1357.

Després, J. P. (2006). Is visceral obesity the cause of the metabolic syndrome? *Annals of Medicine, 38*(1), 52-63.

Després, J. P., Lemieux, S., Lamarche, B., Prud'homme, D., Moorjani, S., Brun, L. D., et al. (1995). The insulin resistance-dyslipidemic syndrome: contribution of visceral obesity and therapeutic implications. *International Journal of Obesity and Related Metabolic Disorders, 19 Suppl 1*, S76-86.

Deuschle, M., Blum, W. F., Frystyk, J., Orskov, H., Schweiger, U., Weber, B., et al. (1998). Endurance training and its effect upon the activity of the GH-IGFs system in the elderly. *International Journal of Sports Medicine, 19*(4), 250-254.

DiPietro, L., Mossberg, H. O., & Stunkard, A. J. (1994). A 40-year history of overweight children in Stockholm: life-time overweight, morbidity, and mortality. *International Journal of Obesity and Related Metabolic Disorders, 18*(9), 585-590.

Donnelly, J. E., Hill, J. O., Jacobsen, D. J., Potteiger, J., Sullivan, D. K., Johnson, S. L., et al. (2003). Effects of a 16-month randomized controlled exercise trial on body weight and composition in young, overweight men and women: The midwest exercise trial. *Archives of Internal Medicine, 163*(11), 1343-1350.

Donnelly, J. E., Smith, B., Jacobsen, D. J., Kirk, E., DuBose, K., Hyder, M., et al. (2004). The role of exercise for weight loss and maintenance. *Best Practice & Research Clinical Gastroenterology, 18*(6), 1009-1029.

Dougherty, C. M., Glenny, R., & Kudenchuk, P. J. (2008). Aerobic exercise improves fitness and heart rate variability after an implantable cardioverter defibrillator. *Journal of Cardiopulmonary Rehabilitation and Prevention, 28*(5), 307-311.

Dulloo, A. G. (1993). Strategies to counteract readjustments toward lower metabolic rates during obesity management. *Nutrition, 9*(4), 366-372.

Dulloo, A. G. (2007). Suppressed thermogenesis as a cause for resistance to slimming and obesity rebound: adaptation or illusion? *International Journal of Obesity, 31*(2), 201-203.

Dulloo, A. G. (2011). The search for compounds that stimulate thermogenesis in obesity management: from pharmaceuticals to functional food ingredients. *Obesity Reviews, 12*(10), 866-883.

Duncan, G. E., & Howley, E. T. (1998). Metabolic and perceptual responses to short-term cycle training in children. *Pediatric Exercise Science, 10*(2), 110-122.

Dunn, S. L. (2009). Effects of exercise and dietary intervention on metabolic syndrome markers of inactive premenopausal women. *Doctoral dissertation, University of New South Wales*.

Dyck, D. J. (2005). Leptin sensitivity in skeletal muscle is modulated by diet and exercise. *Exercise and Sport Sciences Reviews, 33*(4), 189-194.

Dziekan, G., Myers, J., Goebbels, U., Muller, P., Reinhart, W., Ratti, R., et al. (1998). Effects of exercise training on limb blood flow in patients with reduced ventricular function. *American Heart Journal, 136*(1), 22-30.

Edwards, D. G., Schofield, R. S., Lennon, S. L., Pierce, G. L., Nichols, W. W., & Braith, R. W. (2004). Effect of exercise training on endothelial function in men with coronary artery disease. *The American Journal of Cardiology, 93*(5), 617-620.

Edwards, D. G., Schofield, R. S., Magyari, P. M., Nichols, W. W., & Braith, R. W. (2004). Effect of exercise training on central aortic pressure wave reflection in coronary artery disease. *American Journal of Hypertension, 17*(6), 540-543.

Elfhag, K., & Rössner, S. (2005). Who succeeds in maintaining weight loss? A conceptual review of factors associated with weight loss maintenance and weight regain. *Obesity Reviews, 6*(1), 67-85.

Epstein, L. H., Wing, R. R., & Valoski, A. (1985). Childhood obesity. *Pediatric Clinics of North America, 32*(2), 363-379.

Esler, M., Lambert, G., Brunner-La Rocca, H. P., Vaddadi, G., & Kaye, D. (2003). Sympathetic nerve activity and neurotransmitter release in humans: translation from pathophysiology into clinical practice. *Acta Physiologica Scandinavica, 177*(3), 275-284.

Fagard, R. H. (2001). Exercise characteristics and the blood pressure response to dynamic physical training. *Medicine and Science in Sports and Exercise, 33*(6), S484-S492.

Fahs, C. A., Heffernan, K. S., & Fernhall, B. (2009). Hemodynamic and vascular response to resistance exercise with l-Arginine. *Medicine and Science in Sports and Exercise, 41*(4), 773-779.

Faizi, A. K., Kornmo, D. W., & Agewall, S. (2009). Evaluation of endothelial function using finger plethysmography. *Clinical Physiology and Functional Imaging, 29*(5), 372-375.

Farnebo, S., Thorfinn, J., Henricson, J., & Tesselaar, E. (2010). Hyperaemic changes in forearm skin perfusion and RBC concentration after increasing occlusion times. *Microvascular Research, 80*(3), 412-416.

Ferrier, K. E., Waddell, T. K., Gatzka, C. D., Cameron, J. D., Dart, A. M., & Kingwell, B. A. (2001). Aerobic exercise training does not modify large-artery compliance in isolated systolic hypertension. *Hypertension, 38*(2), 222-226.

Forcier, K., Stroud, L. R., & Papandonatos, G. D. (2006). Links between physical fitness and cardiovascular reactivity and recovery to psychological stressors: A meta-analysis. *Health Psychology, 25*(6), 723-739.

Fox, C. S., Massaro, J. M., Hoffmann, U., Pou, K. M., Maurovich-Horvat, P., Liu, C. Y., et al. (2007). Abdominal visceral and subcutaneous adipose tissue compartments: association with metabolic risk factors in the Framingham Heart Study. *Circulation, 116*(1), 39-48.

Franco, C., Brandberg, J., Lönn, L., Andersson, B., Bengtsson, B. A., & Johannsson, G. (2005). Growth hormone treatment reduces abdominal visceral fat in postmenopausal women with abdominal obesity: a 12-month placebo-controlled trial. *The Journal of Clinical Endocrinology and Metabolism, 90*(3), 1466-1474.

Franke, W. D., Stephens, G. M., & Schmid, P. G. (1998). Effects of intense exercise training on endothelium-dependent exercise-induced vasodilatation. *Clinical Physiology, 18*(6), 521-528.

Frey-Hewitt, B., Vranizan, K. M., Dreon, D. M., & Wood, P. D. (1990). The effect of weight loss by dieting or exercise on resting metabolic rate in overweight men. *International Journal of Obesity, 14*(4), 327-334.

Fuchsjäger-Mayrl, G., Pleiner, J., Wiesinger, G. F., Sieder, A. E., Quittan, M., Nuhr, M. J., et al. (2002). Exercise training improves vascular endothelial function in patients with type 1 diabetes. *Diabetes Care, 25*(10), 1795-1801.

Fujimoto, W. Y., Bergstrom, R. W., Boyko, E. J., Chen, K. W., Leonetti, D. L., Newell-Morris, L., et al. (1999). Visceral adiposity and incident coronary heart disease in Japanese-American men. The 10-year follow-up results of the Seattle Japanese-American Community Diabetes Study. *Diabetes Care, 22*(11), 1808-1812.

Gardenghi, G., Rondon, M. U. P. B., Braga, A. M. F. W., Scanavacca, M. I., Negrão, C. E., Sosa, E., et al. (2007). The effects of exercise training on arterial baroreflex sensitivity in neurally mediated syncope patients. *European Heart Journal, 28*(22), 2749-2755.

Gearhart, R. F., Riechman, S. E., Lagally, K. M., Andrews, R. D., & Robertson, R. J. (2008). RPE at relative intensities after 12 weeks of resistance-exercise training by older adults. *Perceptual and Motor Skills, 106*(3), 893-903.

Georgiades, A., Sherwood, A., Gullette, E. C. D., Babyak, M. A., Hinderliter, A., Waugh, R., et al. (2000). Effects of exercise and weight loss on mental stress-induced cardiovascular responses in individuals with high blood pressure. *Hypertension, 36*(2), 171-176.

Gibala, M. J., Little, J. P., van Essen, M., Wilkin, G. P., Burgomaster, K. A., Safdar, A., et al. (2006). Short-term sprint interval versus traditional endurance training: similar initial adaptations in human skeletal muscle and exercise performance. *The Journal of Physiology, 575*(Pt 3), 901-911.

Gibala, M. J., & McGee, S. L. (2008). Metabolic adaptations to short-term high-intensity interval training: a little pain for a lot of gain? *Exercise and Sport Sciences Reviews, 36*(2), 58-63

Gokce, N., Keaney, J. F., Hunter, L. M., Watkins, M. T., Menzoian, J. O., & Vita, J. A. (2002). Risk stratification for postoperative cardiovascular events via noninvasive assessment of endothelial function. *Circulation, 105*(13), 1567-1572.

Gokce, N., Vita, J. A., Bader, D. S., Sherman, D. L., Hunter, L. M., Holbrook, M., et al. (2002). Effect of exercise on upper and lower extremity endothelial function in patients with coronary artery disease. *The American Journal of Cardiology, 90*(2), 124-127.

Goldberg, Y., Boaz, M., Matas, Z., Goldberg, I., & Shargorodsky, M. (2009). Weight loss induced by nutritional and exercise intervention decreases arterial stiffness in obese subjects. *Clinical Nutrition, 28*(1), 21-25.

González-Castejón, M., & Rodriguez-Casado, A. (2011). Dietary phytochemicals and their potential effects on obesity: A review. *Pharmacological Research, 64*(5), 438-455.

Gordon, N. F., Scott, C. B., & Levine, B. D. (1997). Comparison of single versus multiple lifestyle interventions: are the antihypertensive effects of exercise training and diet-induced weight loss additive? *The American Journal of Cardiology, 79*(6), 763-767.

Gormley, S. E., Swain, D. P., High, R., Spina, R. J., Dowling, E. A., Kotipalli, U. S., et al. (2008). Effect of intensity of aerobic training on VO2max. *Medicine and Science in Sports and Exercise, 40*(7), 1336-1343.

Goto, C., Higashi, Y., Kimura, M., Noma, K., Hara, K., Nakagawa, K., et al. (2003). Effect of different intensities of exercise on endothelium-dependent vasodilation in humans. *Circulation, 108*(5), 530-535.

Grassi, G., Seravalle, G., Calhoun, D. A., & Mancia, G. (1994). Physical training and baroreceptor control of sympathetic nerve activity in humans. *Hypertension, 23*(3), 294-301.

Grassi, G., Seravalle, G., Cattaneo, B. M., Bolla, G. B., Lanfranchi, A., Colombo, M., et al. (1995). Sympathetic activation in obese normotensive subjects. *Hypertension, 25*(4 Pt 1), 560-563.

Grassi, G., Seravalle, G., Dell'Oro, R., Turri, C., Bolla, G. B., & Mancia, G. (2000). Adrenergic and reflex abnormalities in obesity-related hypertension. *Hypertension, 36*(4), 538-542.

Gray, A. B., Telford, R. D., & Weidemann, M. J. (1993). Endocrine response to intense interval exercise. *European Journal of Applied Physiology and Occupational Physiology, 66*(4), 366-371.

Green, D. J. (2009). Exercise training as vascular medicine: Direct impacts on the vasculature in humans. *Exercise and Sport Sciences Reviews, 37*(4), 196-202

Green, D. J., Bilsborough, W., Naylor, L. H., Reed, C., Wright, J., O'Driscoll, G., et al. (2005). Comparison of forearm blood flow responses to incremental handgrip and cycle ergometer exercise: relative contribution of nitric oxide. *The Journal of Physiology, 562*(2), 617-628.

Green, D. J., Cable, N. T., Fox, C., Rankin, J. M., & Taylor, R. R. (1994). Modification of forearm resistance vessels by exercise training in young men. *Journal of Applied Physiology, 77*(4), 1829-1833.

Green, D. J., Maiorana, A., O'Driscoll, G., & Taylor, R. (2004). Effect of exercise training on endothelium-derived nitric oxide function in humans. *The Journal of Physiology, 561*(1), 1-25.

Green, D. J., O'Driscoll, G., Joyner, M. J., & Cable, N. T. (2008). Exercise and cardiovascular risk reduction: Time to update the rationale for exercise? *Journal of Applied Physiology, 105*(2), 766-768.

Green, D. J., Spence, A., Halliwill, J. R., Cable, N. T., & Thijssen, D. H. J. (2011). Exercise and vascular adaptation in asymptomatic humans. *Experimental Physiology, 96*(2), 57-70.

Gribbin, B., Pickering, T. G., Sleight, P., & Peto, R. (1971). Effect of age and high blood pressure on barorefiex sensitivity in man. *Circulation Research, 29*(4), 424-431.

Guimarães, G. V., Ciolac, E. G., Carvalho, V. O., D'Avila, V. M., Bortolotto, L. A., & Bocchi, E. A. (2010). Effects of continuous vs. interval exercise training on blood pressure and arterial stiffness in treated hypertension. *Hypertension Research, 33*(6), 627-632.

Gulli, G., Cevese, A., Cappelletto, P., Gasparini, G., & Schena, F. (2003). Moderate aerobic training improves autonomic cardiovascular control in older women. *Clinical Autonomic Research, 13*(3), 196-202.

Gutin, B., Barbeau, P., Owens, S., Lemmon, C. R., Bauman, M., Allison, J., et al. (2002). Effects of exercise intensity on cardiovascular fitness, total body composition, and visceral adiposity of obese adolescents. *The American Journal of Clinical Nutrition, 75*(5), 818-826.

Hafstad, A. D., Boardman, N. T., Lund, J., Hagve, M., Khalid, A. M., Wisløff, U., et al. (2011). High intensity interval training alters substrate utilization and reduces oxygen consumption in the heart. *Journal of Applied Physiology, 111*(5), 1235-1241.

Hagberg, J. M., Park, J. J., & Brown, M. D. (2000). The role of exercise training in the treatment of hypertension: An update. *Sports Medicine, 30*(3), 193-206.

Hartman, M. L., Weltman, A., Patrie, J., Pritzlaff, C., Wideman, L., Kanaley, J. A., et al. (2000). *Exercise training for one year does not increase 24-h GH secretion in older adults.* Paper presented at the 82nd Annual Meeting of the Endocrine Society, Jun 21-24, Toronto, 396.

Hashimoto, H. (1993). Impaired microvascular vasodilator reserve in chronic cigarette smokers: A study of post-occlusive reactive hyperemia in the human finger. *Japanese Circulation Journal, 58*(1), 29-33.

Hayashi, K., Sugawara, J., Komine, H., Maeda, S., & Yokoi, T. (2005). Effects of aerobic exercise training on the stiffness of central and peripheral arteries in middle-aged sedentary men. *The Japanese Journal of Physiology, 55*(4), 235-239.

Hayashi, T., Boyko, E. J., Leonetti, D. L., McNeely, M. J., Newell-Morris, L., Kahn, S. E., et al. (2004). Visceral adiposity is an independent predictor of incident hypertension in Japanese Americans. *Annals of Internal Medicine, 140*(12), 992-1000.

Helgerud, J., Hoydal, K., Wang, E., Karlsen, T., Berg, P., Bjerkaas, M., et al. (2007). Aerobic high-intensity intervals improve VO_{2max} more than moderate training. *Medicine and Science in Sports and Exercise, 39*(4), 665-671

Henriksson, J. (1977). Training induced adaptation of skeletal muscle and metabolism during submaximal exercise. *The Journal of Physiology, 270*(3), 661-675.

Heydari, M., Freund, J., & Boutcher, S. H. (2012). The effect of high-intensity intermittent exercise on body composition of overweight young males. *Journal of Obesity, doi: 10.1155/2012/480467*.

Higashi, Y., Sasaki, S., Kurisu, S., Yoshimizu, A., Sasaki, N., Matsuura, H., et al. (1999). Regular aerobic exercise augments endothelium-dependent vascular relaxation in normotensive as well as hypertensive subjects: role of endothelium-derived nitric oxide. *Circulation, 100*(11), 1194-1202.

Higashi, Y., Sasaki, S., Sasaki, N., Nakagawa, K., Ueda, T., Yoshimizu, A., et al. (1999). Daily aerobic exercise improves reactive hyperemia in patients with essential hypertension. *Hypertension, 33*(1), 591-597.

Hill, J. O., & Wyatt, H. R. (2005). Role of physical activity in preventing and treating obesity. *Journal of Applied Physiology, 99*(2), 765-770.

Hodis, S., & Zamir, M. (2009). Mechanical events within the arterial wall: The dynamic context for elastin fatigue. *Journal of Biomechanics, 42*(8), 1010-1016.

Honzíková, N., Nováková, Z., Závodná, E., Paděrová, J., Lokaj, P., Fišer, B., et al. (2006). Baroreflex sensitivity in children, adolescents, and young adults with essential and white-coat hypertension. *Klinische Padiatrie, 218*(04), 237-242.

Hood, M. S., Little, J. P., Tarnopolsky, M. A., Myslik, F., & Gibala, M. J. (2011). Low-volume interval training improves muscle oxidative capacity in sedentary adults. *Medicine and Science in Sports and Exercise, 43*(10), 1849-1856.

Hubert, H. B., Feinleib, M., McNamara, P. M., & Castelli, W. P. (1983). Obesity as an independent risk factor for cardiovascular disease: a 26-year follow-up of participants in the Framingham Heart Study. *Circulation, 67*(5), 968-977.

Iellamo, F., Legramante, J. M., Massaro, M., Raimondi, G., & Galante, A. (2000). Effects of a residential exercise training on baroreflex sensitivity and heart rate variability in patients with coronary artery disease : A randomized, controlled study. *Circulation, 102*(21), 2588-2592.

Irving, B. A., Davis, C. K., Brock, D. W., Weltman, J. Y., Swift, D., Barrett, E. J., et al. (2008). Effect of exercise training intensity on abdominal visceral fat and body composition. *Medicine and Science in Sports and Exercise, 40*(11), 1863-1872.

Irving, B. A., Weltman, J. Y., Patrie, J. T., Davis, C. K., Brock, D. W., Swift, D., et al. (2009). Effects of exercise training intensity on nocturnal growth hormone secretion in obese adults with the metabolic syndrome. *Journal of Clinical Endocrinology and Metabolism, 94*(6), 1979-1986.

Ismail, I., Keating, S. E., Baker, M. K., & Johnson, N. A. (2012). A systematic review and meta-analysis of the effect of aerobic vs. resistance exercise training on visceral fat. *Obesity Reviews, 13*(1), 68-91.

Issekutz, B. (1978). Role of beta-adrenergic receptors in mobilization of energy sources in exercising dogs. *Journal of Applied Physiology, 44*(6), 869-876.

Iwasaki, K.-i., Zhang, R., Zuckerman, J. H., & Levine, B. D. (2003). Dose-response relationship of the cardiovascular adaptation to endurance training in healthy adults: how much training for what benefit? *Journal of Applied Physiology, 95*(4), 1575-1583.

Jackson, E. M., & Dishman, R. K. (2006). Cardiorespiratory fitness and laboratory stress: A meta-regression analysis. *Psychophysiology, 43*(1), 57-72.

Jakicic, J. M., & Otto, A. D. (2005). Physical activity considerations for the treatment and prevention of obesity. *The American Journal of Clinical Nutrition, 82*(1 Suppl), 226S-229S.

Jakicic, J. M., & Otto, A. D. (2006). Treatment and prevention of obesity: what is the role of exercise? *Nutrition Reviews, 64*(2 Pt 2), S57-61.

Jasperse, J. L., & Laughlin, M. H. (2006). Endothelial function and exercise training: evidence from studies using animal models. *Medicine and Science in Sports and Exercise, 38*(3), 445-454.

Joannides, R., Haefeli, W. E., Linder, L., Richard, V., Bakkali, E. H., Thuillez, C., et al. (1995). Nitric oxide is responsible for flow-dependent dilatation of human peripheral conduit arteries in vivo. *Circulation, 91*(5), 1314-1319.

Johnson, N. A., Sachinwalla, T., Walton, D. W., Smith, K., Armstrong, A., Thompson, M. W., et al. (2009). Aerobic exercise training reduces hepatic and visceral lipids in obese individuals without weight loss. *Hepatology, 50*(4), 1105-1112.

Jolliffe, J. A., Rees, K., Taylor, R. S., Thompson, D., Oldridge, N., & Ebrahim, S. (2001). Exercise-based rehabilitation for coronary heart disease. *Cochrane Database of Systematic Reviews (Online)*(1), CD001800.

Jurca, R., Church, T. S., Morss, G. M., Jordan, A. N., & Earnest, C. P. (2004). Eight weeks of moderate-intensity exercise training increases heart rate variability in sedentary postmenopausal women. *American Heart Journal, 147*(5), e21.

Kakiyama, T., Sugawara, J., Murakami, H., Maeda, S., Kuno, S., & Matsuda, M. (2005). Effects of short-term endurance training on aortic distensibility in young males. *Medicine and Science in Sports and Exercise, 37*(2), 267-271.

Kanaley, J. A., Sames, C., Swisher, L., Swick, A. G., Ploutz-Snyder, L. L., Steppan, C. M., et al. (2001). Abdominal fat distribution in pre- and postmenopausal women: The impact of physical activity, age, and menopausal status. *Metabolism: Clinical and Experimental, 50*(8), 976-982.

Karavirta, L., Tulppo, M. P., Laaksonen, D. E., Nyman, K., Laukkanen, R. T., Kinnunen, H., et al. (2009). Heart rate dynamics after combined endurance and strength training in older men. *Medicine and Science in Sports and Exercise, 41*(7), 1436-1443.

Kawano, H., Tanaka, H., & Miyachi, M. (2006). Resistance training and arterial compliance: keeping the benefits while minimizing the stiffening. *Journal of Hypertension, 24*(9), 1753-1759

Keteyian, S. J., Brawner, C. A., Savage, P. D., Ehrman, J. K., Schairer, J., Divine, G., et al. (2008). Peak aerobic capacity predicts prognosis in patients with coronary heart disease. *American Heart Journal, 156*(2), 292-300.

Kim, S. H., Lee, S. J., Kang, E. S., Kang, S., Hur, K. Y., Lee, H. J., et al. (2006). Effects of lifestyle modification on metabolic parameters and carotid intima-media thickness in patients with type 2 diabetes mellitus. *Metabolism: Clinical and Experimental, 55*(8), 1053-1059.

Kingwell, B. A., Berry, K. L., Cameron, J. D., Jennings, G. L., & Dart, A. M. (1997). Arterial compliance increases after moderate-intensity cycling. *American Journal of Physiology - Heart and Circulatory Physiology, 273*(5 Pt 2), H2186-2191.

Kingwell, B. A., Sherrard, B., Jennings, G. L., & Dart, A. M. (1997). Four weeks of cycle training increases basal production of nitric oxide from the forearm.

American Journal of Physiology - Heart and Circulatory Physiology, 272(3), H1070-H1077.

Kirwan, J. P., Costill, D. L., Mitchell, J. B., Houmard, J. A., Flynn, M. G., Fink, W. J., et al. (1988). Carbohydrate balance in competitive runners during successive days of intense training. *Journal of Applied Physiology, 65*(6), 2601-2606.

Kissebah, A. H., Vydelingum, N., Murray, R., Evans, D. J., Kalkhoff, R. K., & Adams, P. W. (1982). Relation of body fat distribution to metabolic complications of obesity. *Journal of Clinical Endocrinology and Metabolism, 54*(2), 254-260.

Kiviniemi, A., Hautala, A. J., Mäkikallio, T., Seppänen, T., Huikuri, H. V., & Tulppo, M. P. (2006). Cardiac vagal outflow after aerobic training by analysis of high-frequency oscillation of the R–R interval. *European Journal of Applied Physiology, 96*(6), 686-692.

Kobayashi, N., Tsuruya, Y., Iwasawa, T., Ikeda, N., Hashimoto, S., Yasu, T., et al. (2003). Exercise training in patients with chronic heart failure improves endothelial function predominantly in the trained extremities. *Circulation Journal, 67*(6), 505-510.

Komine, H., Sugawara, J., Hayashi, K., Yoshizawa, M., & Yokoi, T. (2009). Regular endurance exercise in young men increases arterial baroreflex sensitivity through neural alteration of baroreflex arc. *Journal of Applied Physiology, 106*(5), 1499-1505.

Koseoglu, F., Inan, L., Ozel, S., Deviren, S. D., Karabiyikoglu, G., Yorgancioglu, R., et al. (1997). The effects of a pulmonary rehabilitation program on pulmonary function tests and exercise tolerance in patients with Parkinson's disease. *Functional Neurology, 12*(6), 319-325.

Kougias, P., Chai, H., Lin, P. H., Yao, Q., Lumsden, A. B., & Chen, C. (2005). Effects of adipocyte-derived cytokines on endothelial functions: implication of vascular disease. *The Journal of Surgical Research, 126*(1), 121-129.

Kraemer, R. R., Durand, R. J., Acevedo, E. O., Johnson, L. G., Synovitz, L. B., Kraemer, G. R., et al. (2003). Effects of high-intensity exercise on leptin and testosterone concentrations in well-trained males. *Endocrine, 21*(3), 261-265.

Kramer, F. M., Jeffery, R. W., Forster, J. L., & Snell, M. K. (1989). Long-term follow-up of behavioral treatment for obesity: patterns of weight regain among men and women. *International Journal of Obesity, 13*(2), 123-136.

Krieger, E. M., Da Silva, G. J. É. J., & NegrÃO, C. E. (2001). Effects of exercise training on baroreflex control of the cardiovascular system. *Annals of the New York Academy of Sciences, 940*(1), 338-347.

Kriketos, A. D., Robertson, R. M., Sharp, T. A., Drougas, H., Reed, G. W., Storlien, L. H., et al. (2001). Role of weight loss and polyunsaturated fatty acids in improving metabolic fitness in moderately obese, moderately hypertensive subjects. *Journal of Hypertension, 19*(10), 1745-1754.

Krontorádová, K. K., Honzíková, N. N., Fiser, B. B., Nováková, Z. Z., Závodná, E. E., Hrstková, H. H., et al. (2008). Overweight and decreased baroreflex sensitivity as independent risk factors for hypertension in children, adolescents, and young adults. *Physiological Research, 57*(3), 385-391.

Kuk, J. L., Janiszewski, P. M., & Ross, R. (2007b). Body mass index and hip and thigh circumferences are negatively associated with visceral adipose tissue after control for waist circumference. *The American Journal of Clinical Nutrition, 85*(6), 1540-1544.

Kuk, J. L., Janiszewski, P. M., & Ross, R. (2007a). Exercise, visceral adipose tissue, and metabolic risk. *Current Cardiovascular Risk Reports, 1*(3), 254-264.

Kuk, J. L., Katzmarzyk, P. T., Nichaman, M. Z., Church, T. S., Blair, S. N., & Ross, R. (2006). Visceral fat is an independent predictor of all-cause mortality in men. *Obesity, 14*(2), 336-341.

La Rovere, M. T., Bersano, C., Gnemmi, M., Specchia, G., & Schwartz, P. J. (2002). Exercise-induced increase in baroreflex sensitivity predicts improved prognosis after myocardial infarction. *Circulation, 106*(8), 945-949.

Lagally, K. M., Robertson, R. J., Gallagher, K. I., Goss, F. L., Jakicic, J. M., Lephart, S. M., et al. (2002). Perceived exertion, electromyography, and blood lactate during acute bouts of resistance exercise. *Medicine and Science in Sports and Exercise, 34*(3), 552-559.

Laterza, M. C., de Matos, L. D. N. J., Trombetta, I. C., Braga, A. M. W., Roveda, F., Alves, M. J. N. N., et al. (2007). Exercise training restores baroreflex sensitivity in never-treated hypertensive patients. *Hypertension, 49*(6), 1298-1306.

Laughlin, M. H., & Roseguini, B. (2008). Mechanisms for exercise training-induced increases in skeletal muscle blood flow capacity: differences with interval sprint training versus aerobic endurance training. *Journal of Physiology and Pharmacology, 59*(Suppl 7), 71-88.

Laurent, S., Boutouyrie, P., Asmar, R., Gautier, I., Laloux, B., Guize, L., et al. (2001). Aortic stiffness is an independent predictor of all-cause and cardiovascular mortality in hypertensive patients. *Hypertension, 37*(5), 1236-1241.

Lavie, C. J., Milani, R. V., & Ventura, H. O. (2009). Obesity and cardiovascular disease: risk factor, paradox, and impact of weight loss. *Journal of the American College of Cardiology, 53*(21), 1925-1932.

Lavrencic, A., Salobir, B. G., & Keber, I. (2000). Physical training improves flow-mediated dilation in patients with the polymetabolic syndrome. *Arteriosclerosis, Thrombosis, and Vascular Biology, 20*(2), 551-555.

Lazarova, Z., Tonhajzerova, I., Trunkvalterova, Z., Brozmanova, A., Honzíková, N., Javorka, K., et al. (2009). Baroreflex sensitivity is reduced in obese normotensive children and adolescents. *Canadian Journal of Physiology and Pharmacology, 87*(7), 565-571.

Lee, C. M., Wood, R. H., & Welsch, M. A. (2003). Influence of short-term endurance exercise training on heart rate variability. *Medicine and Science in Sports and Exercise, 35*(6), 961-969.

Lee, S., Kuk, J. L., Davidson, L. E., Hudson, R., Kilpatrick, K., Graham, T. E., et al. (2005). Exercise without weight loss is an effective strategy for obesity reduction in obese individuals with and without Type 2 diabetes. *Journal of Applied Physiology, 99*(3), 1220-1225.

Leicht, A. S., Allen, G. D., & Hoey, A. J. (2003). Influence of intensive cycling training on heart rate variability during rest and exercise. *Canadian Journal of Applied Physiology, 28*(6), 898-909.

Leitch, J. W., Newling, R. P., Basta, M., Inder, K., Dear, K., & Fletcher, P. J. (1997). Randomized trial of a hospital-based exercise training program after acute myocardial infarction: Cardiac autonomic effects. *Journal of the American College of Cardiology, 29*(6), 1263-1268.

Lemmer, J. T., Ivey, F. M., Ryan, A. S., Martel, G. F., Hurlbut, D. E., Metter, J. E., et al. (2001). Effect of strength training on resting metabolic rate and physical activity: age and gender comparisons. *Medicine and Science in Sports and Exercise, 33*(4), 532-541.

Lenasi, H., & Štrucl, M. (2010). Regular physical activity alters the postocclusive reactive hyperemia of the cutaneous microcirculation. *Clinical Hemorheology and Microcirculation, 45*(2), 365-374.

Levy, W. C., Cerqueira, M. D., Harp, G. D., Johannessen, K.-A., Abrass, I. B., Schwartz, R. S., et al. (1998). Effect of endurance exercise training on heart rate variability at rest in healthy young and older men. *The American Journal of Cardiology, 82*(10), 1236-1241.

Lewington, S., Clarke, R., Qizilbash, N., Peto, R., Collins, R., & null. (2002). Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. *Lancet, 360*(9349), 1903-1913.

Lewis, T. V., Dart, A. M., Chin-Dusting, J. P., & Kingwell, B. A. (1999). Exercise training increases basal nitric oxide production from the forearm in hypercholesterolemic patients. *Arteriosclerosis, Thrombosis, and Vascular Biology, 19*(11), 2782-2787.

Lindström, J., Ilanne-Parikka, P., Peltonen, M., Aunola, S., Eriksson, J. G., Hemiö, K., et al. (2006). Sustained reduction in the incidence of type 2 diabetes by lifestyle intervention: follow-up of the Finnish Diabetes Prevention Study. *Lancet, 368*(9548), 1673-1679.

Linke, A., Schoene, N., Gielen, S., Hofer, J., Erbs, S., Schuler, G., et al. (2001). Endothelial dysfunction in patients with chronic heart failure: systemic effects of lower-limb exercise training. *Journal of the American College of Cardiology, 37*(2), 392-397.

Lira, F. S., Zanchi, N. E., Lima-Silva, A. E., Pires, F. O., Bertuzzi, R. C., Santos, R. V., et al. (2009). Acute high-intensity exercise with low energy expenditure reduced LDL-c and total cholesterol in men. *European Journal of Applied Physiology, 107*(2), 203-210.

Little, J. P., Safdar, A., Bishop, D., Tarnopolsky, M. A., & Gibala, M. J. (2011). An acute bout of high-intensity interval training increases the nuclear abundance of PGC-1α and activates mitochondrial biogenesis in human skeletal muscle. *American Journal of Physiology - Regulatory, Integrative and Comparative Physiology, 300*(6), R1303-1310.

Loimaala, A., Huikuri, H. V., Oja, P., Pasanen, M., & Vuori, I. (2000). Controlled 5-mo aerobic training improves heart rate but not heart rate variability or baroreflex sensitivity. *Journal of Applied Physiology, 89*(5), 1825-1829.

MacDougall, J. D., Ward, G. R., & Sutton, J. R. (1977). Muscle glycogen repletion after high-intensity intermittent exercise. *Journal of Applied Physiology: Respiratory, Environmental and Exercise Physiology, 42*(2), 129-132.

Madden, K. M., Levy, W. C., & Stratton, J. K. (2006). Exercise training and heart rate variability in older adult female subjects. *Clinical and Investigative Medicine, 29*(1), 20-28.

Madden, K. M., Lockhart, C., Cuff, D., Potter, T. F., & Meneilly, G. S. (2009). Short-term aerobic exercise reduces arterial stiffness in older adults with type 2 diabetes, hypertension, and hypercholesterolemia. *Diabetes Care, 32*(8), 1531-1535.

Madden, K. M., Lockhart, C., Potter, T. F., & Cuff, D. (2010). Aerobic training restores arterial baroreflex sensitivity in older adults with type 2 diabetes, hypertension, and hypercholesterolemia. *Clinical Journal of Sport Medicine, 20*(4), 312-317

Mahoney, L. T., Burns, T. L., Stanford, W., Thompson, B. H., Witt, J. D., Rost, C. A., et al. (1996). Coronary risk factors measured in childhood and young adult life are associated with coronary artery calcification in young adults: The muscatine study. *Journal of the American College of Cardiology, 27*(2), 277-284.

Maiorana, A., Driscoll, G., Taylor, R., & Green, D. (2003). Exercise and the nitric oxide vasodilator system. *Sports Medicine, 33*(14), 1013-1035.

Maiorana, A., O'Driscoll, G., Cheetham, C., Dembo, L., Stanton, K., Goodman, C., et al. (2001). The effect of combined aerobic and resistance exercise training on vascular function in type 2 diabetes. *Journal of the American College of Cardiology, 38*(3), 860-866.

Maiorana, A., O'Driscoll, G., Dembo, L., Cheetham, C., Goodman, C., Taylor, R., et al. (2000). Effect of aerobic and resistance exercise training on vascular function in heart failure. *American Journal of Physiology - Heart and Circulatory Physiology, 279*(4), H1999-H2005.

Maiorana, A., O'Driscoll, G., Dembo, L., Goodman, C., Taylor, R., & Green, D. (2001). Exercise training, vascular function, and functional capacity in middle-aged subjects. *Medicine and Science in Sports and Exercise, 33*(12), 2022-2028.

Major, G. C., Doucet, E., Trayhurn, P., Astrup, A., & Tremblay, A. (2007). Clinical significance of adaptive thermogenesis. *International Journal of Obesity, 31*(2), 204-212.

Mancia, G., Grassi, G., Giannattasio, C., & Seravalle, G. (1999). Sympathetic activation in the pathogenesis of hypertension and progression of organ damage. *Hypertension, 34*(4), 724-728.

Manson, J. E., Hu, F. B., Rich-Edwards, J. W., Colditz, G. A., Stampfer, M. J., Willett, W. C., et al. (1999). A prospective study of walking as compared with vigorous exercise in the prevention of coronary heart disease in women. *New England Journal of Medicine, 341*(9), 650-658.

Martín-Vázquez, M., & Reyes del Paso, G. A. (2010). Physical training and the dynamics of the cardiac baroreflex: A comparison when blood pressure rises and falls. *International Journal of Psychophysiology, 76*(3), 142-147.

Martin, W. H., Kohrt, W. M., Malley, M. T., Korte, E., & Stoltz, S. (1990). Exercise training enhances leg vasodilatory capacity of 65-yr-old men and women. *Journal of Applied Physiology, 69*(5), 1804-1809.

Martinmäki, K., Häkkinen, K., Mikkola, J., & Rusko, H. (2008). Effect of low-dose endurance training on heart rate variability at rest and during an incremental maximal exercise test. *European Journal of Applied Physiology, 104*(3), 541-548.

Marwick, T. H., Hordern, M. D., Miller, T., Chyun, D. A., Bertoni, A. G., Blumenthal, R. S., et al. (2009). Exercise training for type 2 diabetes mellitus: impact on cardiovascular risk: a scientific statement from the American Heart Association. *Circulation, 119*(25), 3244-3262.

Matsumoto, A., Hirata, Y., Momomura, S., Fujita, H., Yao, A., Sata, M., et al. (1994). Increased nitric oxide production during exercise. *Lancet, 343*(8901), 849-850.

Matthews, K. A. (1986). *Handbook of stress, reactivity, and cardiovascular disease*. New York: Wiley.

Mayeur, C., Campard, S., Richard, C., & Teboul, J.-L. (2011). Comparison of four different vascular occlusion tests for assessing reactive hyperemia using near-infrared spectroscopy. *Critical Care Medicine, 39*(4), 695-701.

McDonald, M. P., Sanfilippo, A. J., & Savard, G. K. (1993). Baroreflex function and cardiac structure with moderate endurance training in normotensive men. *Journal of Applied Physiology, 74*(5), 2469-2477.

McEwen, B. S. (1998). Protective and damaging effects of stress mediators. *The New England Journal of Medicine, 338*(3), 171-179.

McGavock, J., Mandic, S., Lewanczuk, R., Koller, M., Muhll, V., Quinney, A., et al. (2004). Cardiovascular adaptations to exercise training in postmenopausal women with type 2 diabetes mellitus. *Cardiovascular Diabetology, 3*(1), 1-7.

McKay, B. R., Paterson, D. H., & Kowalchuk, J. M. (2009). Effect of short-term high-intensity interval training vs. continuous training on O2 uptake kinetics, muscle deoxygenation, and exercise performance. *Journal of Applied Physiology, 107*(1), 128-138.

McMurray, R. G., & Hackney, A. C. (2005). Interactions of metabolic hormones, adipose tissue and exercise. *Sports Medicine, 35*(5), 393-412.

Meier, C. A. (1996). Leptin secretion and action: an update. *European Journal of Endocrinology, 134*(5), 543-545.

Melanson, E. L., & Freedson, P. S. (2001). The effect of endurance training on resting heart rate variability in sedentary adult males. *European Journal of Applied Physiology, 85*(5), 442-449.

Melzer, K. (2011). Carbohydrate and fat utilization during rest and physical activity. *e-SPEN, The European e-Journal of Clinical Nutrition and Metabolism, 6*(2), e45-e52.

Miller, T. D., Balady, G. J., & Fletcher, G. F. (1997). Exercise and its role in the prevention and rehabilitation of cardiovascular disease. *Annals of behavioral medicine, 19*(3), 220-229.

Miyachi, M., Kawano, H., Sugawara, J., Takahashi, K., Hayashi, K., Yamazaki, K., et al. (2004). Unfavorable effects of resistance training on central arterial compliance: a randomized intervention study. *Circulation, 110*(18), 2858-2863.

Monahan, K. D., Dinenno, F. A., Tanaka, H., Clevenger, C. M., DeSouza, C. A., & Seals, D. R. (2000). Regular aerobic exercise modulates age-associated declines in cardiovagal baroreflex sensitivity in healthy men. *The Journal of Physiology, 529*(1), 263-271.

Monahan, K. D., Tanaka, H., Dinenno, F. A., & Seals, D. R. (2001). Central arterial compliance is associated with age- and habitual exercise-related differences in cardiovagal baroreflex sensitivity. *Circulation, 104*(14), 1627-1632.

Moreau, K. L., Donato, A. J., Seals, D. R., DeSouza, C. A., & Tanaka, H. (2003). Regular exercise, hormone replacement therapy and the age-related decline in carotid arterial compliance in healthy women. *Cardiovascular Research, 57*(3), 861-868.

Moriguchi, J., Itoh, H., Harada, S., Takeda, K., Hatta, T., Nakata, T., et al. (2005). Low frequency regular exercise improves flow-mediated dilatation of subjects with mild hypertension. *Hypertension Research, 28*(4), 315-321.

Motohiro, M., Yuasa, F., Hattori, T., Sumimoto, T., Takeuchi, M., Kaida, M., et al. (2005). Cardiovascular adaptations to exercise training after uncomplicated acute myocardial infarction. *American Journal of Physical Medicine & Rehabilitation, 84*(9), 684-691.

Mourier, A., Gautier, J.-F., Kerviler, E. D., Bigard, A. X., Villette, J.-M., Garnier, J.-P., et al. (1997). Mobilization of visceral adipose tissue related to the improvement in insulin sensitivity in response to physical training in NIDDM: Effects of branched-chain amino acid supplements. *Diabetes Care, 20*(3), 385-391.

Mourot, L., Bouhaddi, M., Perrey, S., Rouillon, J. D., & Regnard, J. (2004). Quantitative Poincare plot analysis of heart rate variability: effect of endurance training. *European Journal of Applied Physiology, 91*(1), 79-87.

Moyna, N. M., & Thompson, P. D. (2004). The effect of physical activity on endothelial function in man. *Acta Physiologica Scandinavica, 180*(2), 113-123.

Munk, P. S., Butt, N., & Larsen, A. I. (2010). High-intensity interval exercise training improves heart rate variability in patients following percutaneous coronary intervention for angina pectoris. *International Journal of Cardiology, 145*(2), 312-314.

Musa, D. I., Adeniran, S. A., Dikko, A. U., & Sayers, S. P. (2009). The effect of a high-intensity interval training program on high-density lipoprotein cholesterol in young men. *The Journal of Strength & Conditioning Research, 23*(2), 587-592.

Nakamura, T., Tokunaga, K., Shimomura, I., Nishida, M., Yoshida, S., Kotani, K., et al. (1994). Contribution of visceral fat accumulation to the development of coronary artery disease in non-obese men. *Atherosclerosis, 107*(2), 239-246.

Nevill, M. E., Holmyard, D. J., Hall, G. M., Allsop, P., van Oosterhout, A., Burrin, J. M., et al. (1996). Growth hormone responses to treadmill sprinting in sprint- and endurance-trained athletes. *European Journal of Applied Physiology and Occupational Physiology, 72*(5-6), 460-467.

Nguyen-Duy, T. B., Nichaman, M. Z., Church, T. S., Blair, S. N., & Ross, R. (2003). Visceral fat and liver fat are independent predictors of metabolic risk factors in men. *American Journal of Physiology. Endocrinology and Metabolism, 284*(6), E1065-1071.

Nicholas, C. W., Williams, C., Lakomy, H. K., Phillips, G., & Nowitz, A. (1995). Influence of ingesting a carbohydrate-electrolyte solution on endurance capacity during intermittent, high-intensity shuttle running. *Journal of Sports Sciences, 13*(4), 283-290.

Nicklas, B. J., Penninx, B. W. J. H., Cesari, M., Kritchevsky, S. B., Newman, A. B., Kanaya, A. M., et al. (2004). Association of visceral adipose tissue with incident myocardial infarction in older men and women. *American Journal of Epidemiology, 160*(8), 741-749.

Niebauer, J., & Cooke, J. P. (1996). Cardiovascular effects of exercise: Role of endothelial shear stress. *Journal of the American College of Cardiology, 28*(7), 1652-1660.

Nielsen, K. E., Nielsen, D. H., Lin, S.-J., Fieseler, K. C. R., Sterling, T. M., Ver Hoef, R. L., et al. (1997). Changes in exercise response and tolerance following

an eight-week rehabilitation program. *Cardiopulmonary Physical Therapy Journal, 8*(4), 3-11.

Nieuwenhuizen, A. G., & Rutters, F. (2008). The hypothalamic-pituitary-adrenal-axis in the regulation of energy balance. *Physiology and Behavior, 94*(2), 169-177.

Noble, B. J., & Robertson, R. J. (1996). *Perceived exertion*: Human Kinetics.

Nordby, P., Saltin, B., & Helge, J. W. (2006). Whole-body fat oxidation determined by graded exercise and indirect calorimetry: a role for muscle oxidative capacity? *Scandinavian Journal of Medicine and Science in Sports, 16*(3), 209-214.

O'Donovan, G., Owen, A., Bird, S. R., Kearney, E. M., Nevill, A. M., Jones, D. W., et al. (2005). Changes in cardiorespiratory fitness and coronary heart disease risk factors following 24 wk of moderate- or high-intensity exercise of equal energy cost. *Journal of Applied Physiology, 98*(5), 1619-1625.

O'Sullivan, S. E., & Bell, C. (2000). The effects of exercise and training on human cardiovascular reflex control. *Journal of the Autonomic Nervous System, 81*(1-3), 16-24.

Obrist, P. A. (1981). *Cardiovascular psychophysiology: a perspective*. New York: Plenum Press.

Ogden, C. L., Carroll, M. D., Kit, B. K., & Flegal, K. M. (2012). Prevalence of obesity in the United States, 2009-2010. *National Center for Health Statistics. NCHS data brief, 82*, 1-8.

Ohkawara, K., Tanaka, S., Miyachi, M., Ishikawa-Takata, K., & Tabata, I. (2007). A dose-response relation between aerobic exercise and visceral fat reduction: systematic review of clinical trials. *International Journal of Obesity, 31*(12), 1786-1797.

Okamoto, T., Masuhara, M., & Ikuta, K. (2009b). Home-based resistance training improves arterial stiffness in healthy premenopausal women. *European Journal of Applied Physiology, 107*(1), 113-117.

Okamoto, T., Masuhara, M., & Ikuta, K. (2009a). Upper but not lower limb resistance training increases arterial stiffness in humans. *European Journal of Applied Physiology, 107*(2), 127-134.

Okauchi, Y., Nishizawa, H., Funahashi, T., Ogawa, T., Noguchi, M., Ryo, M., et al. (2007). Reduction of visceral fat is associated with decrease in the number of metabolic risk factors in Japanese men. *Diabetes Care, 30*(9), 2392-2394.

Østergård, T., Nyholm, B., Hansen, T. K., Rasmussen, L. M., Ingerslev, J., Sørensen, K. E., et al. (2006). Endothelial function and biochemical vascular markers in first-degree relatives of type 2 diabetic patients: the effect of exercise training. *Metabolism: Clinical and Experimental, 55*(11), 1508-1515.

Özturk M., Ö. K., & Gokce, E. (1998). Evaluation of blood lactate in young men after wingate anaerobic power test. *Eastern Journal of Medicine 3*(1), 13- 16.

Padilla, J., Simmons, G. H., Bender, S. B., Arce-Esquivel, A. A., Whyte, J. J., & Laughlin, M. H. (2011). Vascular effects of exercise: Endothelial adaptations beyond active muscle beds. *Physiology, 26*(3), 132-145.

Papaioannou, T. G., Stamatelopoulos, K. S., Gialafos, E., Vlachopoulos, C., Karatzis, E., Nanas, J., et al. (2004). Monitoring of arterial stiffness indices by applanation tonometry and pulse wave analysis: Reproducibility at low blood pressures. *Journal of Clinical Monitoring and Computing, 18*(2), 137-144.

Parati, G., Di Rienzo, M., & Mancia, G. (2000). How to measure baroreflex sensitivity: from the cardiovascular laboratory to daily life. *Journal of Hypertension, 18*(1), 7-19.

Parmer, R. J., Cervenka, J. H., & Stone, R. A. (1992). Baroreflex sensitivity and heredity in essential hypertension. *Circulation, 85*(2), 497-503.

Parnell, M. M., Holst, D. P., & Kaye, D. M. (2002). Exercise training increases arterial compliance in patients with congestive heart failure. *Clinical Science, 102*(1), 1-7.

Perry, C. G., Heigenhauser, G. J., Bonen, A., & Spriet, L. L. (2008). High-intensity aerobic interval training increases fat and carbohydrate metabolic capacities in human skeletal muscle. *Applied Physiology, Nutrition, and Metabolism, 33*(6), 1112-1123.

Persson, P. B. (2005). Baroreflexes in hypertension. *Hypertension, 46*(5), 1095-1096.

Perticone, F., Ceravolo, R., Candigliota, M., Ventura, G., Iacopino, S., Sinopoli, F., et al. (2001). Obesity and body fat distribution induce endothelial dysfunction by oxidative stress. *Diabetes, 50*(1), 159-165.

Phillips, A. C. (2011). Blunted cardiovascular reactivity relates to depression, obesity, and self-reported health. *Biological Psychology, 86*(2), 106-113.

Pichot, V., Roche, F., Denis, C., Garet, M., Duverney, D., Costes, F., et al. (2005). Interval training in elderly men increases both heart rate variability and baroreflex activity. *Clinical Autonomic Research, 15*(2), 107-115.

Plante, T. G., & Karpowitz, D. (1987). The influence of aerobic exercise on physiological stress responsivity. *Psychophysiology, 24*(6), 670-677.

Poehlman, E. T., Dvorak, R. V., DeNino, W. F., Brochu, M., & Ades, P. A. (2000). Effects of resistance training and endurance training on insulin sensitivity in nonobese, young women: a controlled randomized trial. *The Journal of Clinical Endocrinology and Metabolism, 85*(7), 2463-2468.

Pritzlaff-Roy, C. J., Widemen, L., Weltman, J. Y., Abbott, R., Gutgesell, M., Hartman, M. L., et al. (2002). Gender governs the relationship between exercise intensity and growth hormone release in young adults. *Journal of Applied Physiology, 92*(5), 2053-2060.

Pritzlaff, C. J., Wideman, L., Blumer, J., Jensen, M., Abbott, R. D., Gaesser, G. A., et al. (2000). Catecholamine release, growth hormone secretion, and

energy expenditure during exercise vs. recovery in men. *Journal of Applied Physiology, 89*(3), 937-946.

Pritzlaff, C. J., Wideman, L., Weltman, J. Y., Abbott, R. D., Gutgesell, M. E., Hartman, M. L., et al. (1999). Impact of acute exercise intensity on pulsatile growth hormone release in men. *Journal of Applied Physiology, 87*(2), 498-504.

Pullin, C. H., Bellamy, M. F., Bailey, D., Ashton, M., Davies, B., Williams, S., et al. (2004). Time course of changes in endothelial function following exercise in habitually sedentary men. *Journal of Exercise Physiology Online 7*(4), 14-22.

Racette, S. B., Evans, E. M., Weiss, E. P., Hagberg, J. M., & Holloszy, J. O. (2006). Abdominal adiposity is a stronger predictor of insulin resistance than fitness among 50–95 year olds. *Diabetes Care, 29*(3), 673-678.

Rajkumar, C., Cameron, J. D., Christophidis, N., Jennings, G. L., & Dart, A. M. (1997). Reduced systemic arterial compliance is associated with left ventricular hypertrophy and diastolic dysfunction in older people. *Journal of the American Geriatrics Society, 45*(7), 803-808.

Rakobowchuk, M., Stuckey, M. I., Millar, P. J., Gurr, L., & Macdonald, M. J. (2009). Effect of acute sprint interval exercise on central and peripheral artery distensibility in young healthy males. *European Journal of Applied Physiology, 105*(5), 787-795.

Rakobowchuk, M., Tanguay, S., Burgomaster, K. A., Howarth, K. R., Gibala, M. J., & MacDonald, M. J. (2008). Sprint interval and traditional endurance training induce similar improvements in peripheral arterial stiffness and flow-mediated dilation in healthy humans. *American Journal of Physiology - Regulatory, Integrative and Comparative Physiology, 295*(1), R236-242.

Ranadive, S. M., Yan, H., Weikert, M., Lane, A. D., Linden, M. A., Baynard, T., et al. (2012). Vascular dysfunction and physical activity in multiple sclerosis. *Medicine and Science in Sports and Exercise, 44*(2), 238-243

Ranneries, C., Bülow, J., Buemann, B., Christensen, N. J., Madsen, J., & Astrup, A. (1998). Fat metabolism in formerly obese women. *American Journal of Physiology - Endocrinology And Metabolism, 274*(1), E155-E161.

Ray, C. A., & Carter, J. R. (2010). Effects of aerobic exercise training on sympathetic and renal responses to mental stress in humans. *American Journal of Physiology - Heart and Circulatory Physiology, 298*(1), H229-H234.

Rebuffé-Scrive, M., Andersson, B., Olbe, L., & Björntorp, P. (1989). Metabolism of adipose tissue in intraabdominal depots of nonobese men and women. *Metabolism: Clinical and Experimental, 38*(5), 453-458.

Reyes Del Paso, G. A., González, I., & Hernández, J. A. (2004). Baroreceptor sensitivity and effectiveness varies differentially as a function of cognitive-attentional demands. *Biological Psychology, 67*(3), 385-395.

Reyes Del Paso, G. A., González, M. I., Hernández, J. A., Duschek, S., & Gutiérrez, N. (2009). Tonic blood pressure modulates the relationship between

baroreceptor cardiac reflex sensitivity and cognitive performance. *Psychophysiology, 46*(5), 932-938.

Rhéaume, C., Arsenault, B. J., Bélanger, S., Pérusse, L., Tremblay, A., Bouchard, C., et al. (2009). Low cardiorespiratory fitness levels and elevated blood pressure. What is the contribution of visceral adiposity? *Hypertension, 54*(1), 91-97.

Ribeiro, M. M., Silva, A. G., Santos, N. S., Guazzelle, I., Matos, L. N. J., Trombetta, I. C., et al. (2005). Diet and exercise training restore blood pressure and vasodilatory responses during physiological maneuvers in obese children. *Circulation, 111*(15), 1915-1923.

Robertson, R. J. (1982). Central signals of perceived exertion during dynamic exercise. *Medicine and Science in Sports and Exercise, 14*(5), 390-396.

Robertson, R. J. (2004). *Perceived exertion for practitioners: rating effort with the OMNI picture system*: Human Kinetics.

Robinson, T. G., Dawson, S. L., Eames, P. J., Panerai, R. B., & Potter, J. F. (2003). Cardiac baroreceptor sensitivity predicts long-term outcome after acute ischemic stroke. *Stroke, 34*(3), 705-712.

Romijn, J. A., Coyle, E. F., Sidossis, L. S., Gastaldelli, A., Horowitz, J. F., Endert, E., et al. (1993). Regulation of endogenous fat and carbohydrate metabolism in relation to exercise intensity and duration. *American Journal of Physiology - Endocrinology And Metabolism, 265*(3 Pt 1), E380-391.

Rosenwinkel, E. T., Bloomfield, D. M., Arwady, M. A., & Goldsmith, R. L. (2001). Exercise and autonomic function in health and cardiovascular disease. *Cardiology Clinics, 19*(3), 369-387.

Roskies, E., Seraganian, P., Oseasohn, R., Hanley, J. A., Collu, R., Martin, N., et al. (1986). The Montreal type A intervention project: Major findings. *Health Psychology, 5*(1), 45-69.

Ross, K. M., Milsom, V. A., Rickel, K. A., DeBraganza, N., Gibbons, L. M., Murawski, M. E., et al. (2009). The contributions of weight loss and increased physical fitness to improvements in health-related quality of life. *Eating Behaviors, 10*(2), 84-88.

Ross, R., Aru, J., Freeman, J., Hudson, R., & Janssen, I. (2002). Abdominal adiposity and insulin resistance in obese men. *American Journal of Physiology. Endocrinology and Metabolism, 282*(3), E657-663.

Ross, R., Dagnone, D., Jones, P. J. H., Smith, H., Paddags, A., Hudson, R., et al. (2000). Reduction in obesity and related comorbid conditions after diet-induced weight loss or exercise-induced weight loss in men. *Annals of Internal Medicine, 133*(2), 92-103.

Ross, R., Janssen, I., Dawson, J., Kungl, A.-M., Kuk, J. L., Wong, S. L., et al. (2004). Exercise-induced reduction in obesity and insulin resistance in women: a randomized controlled trial. *Obesity, 12*(5), 789-798.

Rossi, M., Santoro, G., Maurizio, S., & Carpi, A. (2006). Spectral analysis of skin blood flowmotion before and after exercise in healthy trained and in sedentary subjects. *International Journal of Sports Medicine, 27*(07), 540,545.

Rowell, L. B. (1986). *Human circulation: regulation during physical stress*: Oxford University Press.

Rozanski, A., Bairey, C. N., Krantz, D. S., Friedman, J., Resser, K. J., Morell, M., et al. (1988). Mental stress and the induction of silent myocardial ischemia in patients with coronary artery disease. *New England Journal of Medicine, 318*(16), 1005-1012.

Rozanski, A., Blumenthal, J. A., & Kaplan, J. (1999). Impact of psychological factors on the pathogenesis of cardiovascular disease and implications for therapy. *Circulation, 99*(16), 2192-2217.

Rubinshtein, R., Kuvin, J. T., Soffler, M., Lennon, R. J., Lavi, S., Nelson, R. E., et al. (2010). Assessment of endothelial function by non-invasive peripheral arterial tonometry predicts late cardiovascular adverse events. *European Heart Journal, 31*(9), 1142-1148.

Safar, M. E., Levy, B. I., & Struijker-Boudier, H. A. (2003). Current perspectives on arterial stiffness and pulse pressure in hypertension and cardiovascular diseases. *Circulation, 107*(22), 2864-2869.

Sallis, J. F., Patterson, T. L., Buono, M. J., & Nader, P. R. (1988). Relation of cardiovascular fitness and physical activity to cardiovascular disease risk factors in children and adults. *American Journal of Epidemiology, 127*(5), 933-941.

Salvi, P., Magnani, E., Valbusa, F., Agnoletti, D., Alecu, C., Joly, L., et al. (2008). Comparative study of methodologies for pulse wave velocity estimation. *Journal of Human Hypertension, 22*(10), 669-677.

Sandercock, G. R., Bromley, P. D., & Brodie, D. A. (2005). Effects of exercise on heart rate variability: inferences from meta-analysis. *Medicine and Science in Sports and Exercise, 37*(3), 433-439.

Saris, W. (1993). The role of exercise in the dietary-treatment of obesity. *International Journal of Obesity 17*, S17- 21.

Schachter, M. (1997). *The sympathetic nervous system and hypertension: Pocketbook*: Taylor and Francis.

Schaeffer, M. A., Krantz, D. S., Weiss, S. M., Zoltick, J. M., Yaney, S. F., Karch, R., et al. (1988). Effects of occupational based behavioral counseling and exercise interventions on type A components and cardiovascular reactivity. *Journal of Cardiopulmonary Rehabilitation and Prevention, 8*(10), 371-377.

Schmitt, M., Qasem, A., McEniery, C., Wilkinson, I. B., Tatarinoff, V., Noble, K., et al. (2004). Role of natriuretic peptides in regulation of conduit artery distensibility. *American Journal of Physiology - Heart and Circulatory Physiology, 287*(3), H1167-H1171.

Schuit, A. J., van Amelsvoort, L. G., Verheij, T. C., Rijneke, R. D., Maan, A. C., Swenne, C. A., et al. (1999). Exercise training and heart rate variability in older people. *Medicine and Science in Sports and Exercise, 31*(6), 816-821.

Sciacqua, A., Candigliota, M., Ceravolo, R., Scozzafava, A., Sinopoli, F., Corsonello, A., et al. (2003). Weight loss in combination with physical activity improves endothelial dysfunction in human obesity. *Diabetes Care, 26*(6), 1673-1678.

Seals, D. R., Tanaka, H., Clevenger, C. M., Monahan, K. D., Reiling, M. J., Hiatt, W. R., et al. (2001). Blood pressure reductions with exercise and sodium restriction in postmenopausal women with elevated systolic pressure: role of arterial stiffness. *Journal of the American College of Cardiology, 38*(2), 506-513.

Seematter, G., Guenat, E., Schneiter, P., Cayeux, C., Jéquier, E., & Tappy, L. (2000). Effects of mental stress on insulin-mediated glucose metabolism and energy expenditure in lean and obese women. *American Journal of Physiology - Endocrinology and Metabolism, 279*(4), E799-E805.

Seraganian, P., Roskies, E., Hanley, J. A., Oseasohn, R., & Collu, R. (1987). Failure to alter psychophysiological reactivity in type a men with physical exercise or stress management programs. *Psychology and Health, 1*(3), 195-213.

Sharman, J. E., Davies, J. E., Jenkins, C., & Marwick, T. H. (2009). Augmentation index, left ventricular contractility, and wave reflection. *Hypertension, 54*(5), 1099-1105.

Sherwood, A., Light, K. C., & Blumenthal, J. A. (1989). Effects of aerobic exercise training on hemodynamic responses during psychosocial stress in normotensive and borderline hypertensive type A men: a preliminary report. *Psychosomatic Medicine, 51*(2), 123-136.

Shi, X., Wray, D. W., Formes, K. J., Wang, H.-W., Hayes, P. M., O-Yurvati, A. H., et al. (2000). Orthostatic hypotension in aging humans. *American Journal of Physiology - Heart and Circulatory Physiology, 279*(4), H1548-H1554.

Shin, K., Minamitani, H., Onishi, S., Yamazaki, H., & Lee, M. (1995). Assessment of training-induced autonomic adaptations in athletes with spectral analysis of cardiovascular varialbility signals. *The Japanese Journal of Physiology, 45*(6), 1053-1069.

Silber, D., McLaughlin, D., & Sinoway, L. (1991). Leg exercise conditioning increases peak forearm blood flow. *Journal of Applied Physiology, 71*(4), 1568-1573.

Silva, C. A. d., Ribeiro, J. P., Canto, J. C. A. U., Silva, R. E. d., Silva Junior, G. B., Botura, E., et al. (2012). High-intensity aerobic training improves endothelium-dependent vasodilation in patients with metabolic syndrome and type 2 diabetes mellitus. *Diabetes Research and Clinical Practice, 95*(2), 237-245.

Silveira, L. C. R., Tezini, G. C. S. V., Schujmann, D. S., Porto, J. M., Rossi, B. R. O., & Souza, H. C. D. (2011). Comparison of the effects of aerobic and

resistance training on cardiac autonomic adaptations in ovariectomized rats. *Autonomic Neuroscience, 162*(1-2), 35- 41.

Sinyor, D., Golden, M., Steinert, Y., & Seraganian, P. (1986). Experimental manipulation of aerobic fitness and the response to psychosocial stress: heart rate and self-report measures. *Psychosomatic Medicine, 48*(5), 324-337.

Skender, M. L., Goodrick, G. K., Del Junco, D. J., Reeves, R. S., Darnell, L., Gotto Jr, A. M., et al. (1996). Comparison of 2-year weight loss trends in behavioral treatments of obesity: Diet, exercise, and combination interventions. *Journal of the American Dietetic Association, 96*(4), 342-346.

Slentz, C. A., Aiken, L. B., Houmard, J. A., Bales, C. W., Johnson, J. L., Tanner, C. J., et al. (2005). Inactivity, exercise, and visceral fat. STRRIDE: a randomized, controlled study of exercise intensity and amount. *Journal of Applied Physiology, 99*(4), 1613-1618.

Slentz, C. A., Duscha, B. D., Johnson, J. L., Ketchum, K., Aiken, L. B., Samsa, G. P., et al. (2004). Effects of the amount of exercise on body weight, body composition, and measures of central obesity: STRRIDE--a randomized controlled study. *Archives of Internal Medicine, 164*(1), 31-39.

Sloan, R. P., Shapiro, P. A., DeMeersman, R. E., Bagiella, E., Brondolo, E. N., McKinley, P. S., et al. (2009). The effect of aerobic training and cardiac autonomie regulation in young adults. *American Journal of Public Health, 99*(5), 921-928.

Smith, L. L., Kukielka, M., & Billman, G. E. (2005). Heart rate recovery after exercise: a predictor of ventricular fibrillation susceptibility after myocardial infarction. *American Journal of Physiology - Heart and Circulatory Physiology, 288*(4), H1763-H1769.

Somers, V. K., Conway, J., Johnston, J., & Sleight, P. (1991). Effects of endurance training on baroreflex sensitivity and blood pressure in borderline hypertension. *The Lancet, 337*(8754), 1365-1368.

Sørensen, T. I., Rissanen, A., Korkeila, M., & Kaprio, J. (2005). Intention to lose weight, weight changes, and 18-y mortality in overweight individuals without co-morbidities. *PLoS Medicine, 2*(6), e171.

Spalding, T. W., Lyon, L. A., Steel, D. H., & Hatfield, B. D. (2004). Aerobic exercise training and cardiovascular reactivity to psychological stress in sedentary young normotensive men and women. *Psychophysiology, 41*(4), 552-562.

Speiser, P. W., Rudolf, M. C. J., Anhalt, H., Camacho-Hubner, C., Chiarelli, F., Eliakim, A., et al. (2005). Childhood obesity. *Journal of Clinical Endocrinology and Metabolism, 90*(3), 1871-1887.

Stiegler, P., & Cunliffe, A. (2006). The role of diet and exercise for the maintenance of fat-free mass and resting metabolic rate during weight loss. *Sports Medicine, 36*(3), 239-262.

Stoudemire, N. M., Wideman, L., Pass, K. A., McGinnes, C. L., Gaesser, G. A., & Weltman, A. (1996). The validity of regulating blood lactate concentration during running by ratings of perceived exertion. *Medicine and Science in Sports and Exercise, 28*(4), 490-495.

Stunkard, A. J. (1996). Current views on obesity. *The American Journal of Medicine, 100*(2), 230-236.

Sugawara, J., Akazawa, N., Miyaki, A., Choi, Y., Tanabe, Y., Imai, T., et al. (2012). Effect of endurance exercise training and curcumin intake on central arterial hemodynamics in postmenopausal women: Pilot study. *American Journal of Hypertension, 25*(6), 651-656.

Sugawara, J., Inoue, H., Hayashi, K., Yokoi, T., & Kono, I. (2004). Effect of low-intensity aerobic exercise training on arterial compliance in postmenopausal women. *Hypertension Research, 27*(12), 897-901.

Talanian, J. L., Galloway, S. D. R., Heigenhauser, G. J. F., Bonen, A., & Spriet, L. L. (2007). Two weeks of high-intensity aerobic interval training increases the capacity for fat oxidation during exercise in women. *Journal of Applied Physiology, 102*(4), 1439-1447.

Tanaka, H., DeSouza, C. A., & Seals, D. R. (1998). Absence of age-related increase in central arterial stiffness in physically active women. *Arteriosclerosis, Thrombosis, and Vascular Biology, 18*(1), 127-132.

Tanaka, H., Dinenno, F. A., Monahan, K. D., Clevenger, C. M., DeSouza, C. A., & Seals, D. R. (2000). Aging, habitual exercise, and dynamic arterial compliance. *Circulation, 102*(11), 1270-1275.

Tanasescu, M., Leitzmann, M. F., Rimm, E. B., Willett, W. C., Stampfer, M. J., & Hu, F. B. (2002). Exercise type and intensity in relation to coronary heart disease in men. *JAMA: The Journal of the American Medical Association, 288*(16), 1994-2000.

Tanisho, K., & Hirakawa, K. (2009). Training effects on endurance capacity in maximal intermittent exercise: comparison between continuous and interval training. *Journal of Strength and Conditioning Research 23*(8), 2405-2410.

Tentolouris, N., Liatis, S., & Katsilambros, N. (2006). Sympathetic system activity in obesity and metabolic syndrome. *Annals of the New York Academy of Sciences, 1083*(1), 129-152.

Thijssen, D. H. J., De Groot, P. C. E., Smits, P., & Hopman, M. T. E. (2007). Vascular adaptations to 8-week cycling training in older men. *Acta Physiologica, 190*(3), 221-228.

Thijssen, D. H. J., Maiorana, A., O'Driscoll, G., Cable, N. T., Hopman, M. T. E., & Green, D. (2010). Impact of inactivity and exercise on the vasculature in humans. *European Journal of Applied Physiology, 108*(5), 845-875.

Thompson, P. D., Buchner, D., Piña, I. L., Balady, G. J., Williams, M. A., Marcus, B. H., et al. (2003). Exercise and physical activity in the prevention and

treatment of atherosclerotic cardiovascular disease. *Arteriosclerosis, Thrombosis, and Vascular Biology, 23*(8), e42-e49.

Thomson, J. A., Green, H. J., & Houston, M. E. (1979). Muscle glycogen depletion patterns in fast twitch fibre subgroups of man during submaximal and supramaximal exercise. *Pflugers Archiv : European Journal of Physiology, 379*(1), 105-108.

Tinken, T. M., Thijssen, D. H. J., Black, M. A., Cable, N. T., & Green, D. J. (2008). Time course of change in vasodilator function and capacity in response to exercise training in humans. *The Journal of Physiology, 586*(20), 5003-5012.

Tjønna, A. E., Lee, S. J., Rognmo, Ø., Stølen, T. O., Bye, A., Haram, P. M., et al. (2008). Aerobic interval training versus continuous moderate exercise as a treatment for the metabolic syndrome. *Circulation, 118*(4), 346-354.

Tjønna, A. E., Stølen, T. O., Bye, A., Volden, M., Slørdahl, S. A., Ødegård, R., et al. (2009). Aerobic interval training reduces cardiovascular risk factors more than a multitreatment approach in overweight adolescents. *Clinical Science, 116*(4), 317-326.

Tordi, N., Mourot, L., Colin, E., & Regnard, J. (2010). Intermittent versus constant aerobic exercise: effects on arterial stiffness. *European Journal of Applied Physiology, 108*(4), 801-809.

Tousoulis, D., Antoniades, C., & Stefanadis, C. (2005). Evaluating endothelial function in humans: a guide to invasive and non-invasive techniques. *Heart, 91*(4), 553-558.

Trapp, E. G., Chisholm, D. J., & Boutcher, S. H. (2007). Metabolic response of trained and untrained women during high-intensity intermittent cycle exercise. *American Journal of Physiology - Regulatory, Integrative and Comparative Physiology, 293*(6), R2370-R2375.

Trapp, E. G., Chisholm, D. J., Freund, J., & Boutcher, S. H. (2008). The effects of high-intensity intermittent exercise training on fat loss and fasting insulin levels of young women. *International Journal of Obesity, 32*(4), 684-691.

Trayhurn, P., & Beattie, J. H. (2001). Physiological role of adipose tissue: white adipose tissue as an endocrine and secretory organ. *The Proceedings of the Nutrition Society, 60*(3), 329-339.

Trayhurn, P., & Wood, I. S. (2004). Adipokines: inflammation and the pleiotropic role of white adipose tissue. *The British Journal of Nutrition, 92*(3), 347-355.

Trayhurn, P., & Wood, I. S. (2005). Signalling role of adipose tissue: adipokines and inflammation in obesity. *Biochemical Society Transactions, 33*(Pt 5), 1078-1081.

Tremblay, A., Simoneau, J.-A., & Bouchard, C. (1994). Impact of exercise intensity on body fatness and skeletal muscle metabolism. *Metabolism: Clinical and Experimental, 43*(7), 814-818.

Treuth, M. S., Hunter, G. R., Weinsier, R. L., & Kell, S. H. (1995). Energy expenditure and substrate utilization in older women after strength training: 24-h calorimeter results. *Journal of Applied Physiology, 78*(6), 2140-2146.

Tsekouras, Y. E., Magkos, F., Kellas, Y., Basioukas, K. N., Kavouras, S. A., & Sidossis, L. S. (2008). High-intensity interval aerobic training reduces hepatic very low-density lipoprotein-triglyceride secretion rate in men. *American Journal of Physiology - Endocrinology And Metabolism, 295*(4), E851-E858.

Tulppo, M. P., Hautala, A. J., Mäkikallio, T. H., Laukkanen, R. T., Nissilä, S., Hughson, R. L., et al. (2003). Effects of aerobic training on heart rate dynamics in sedentary subjects. *Journal of Applied Physiology, 95*(1), 364-372.

U.S. Department of Health and Human Services [USDHHS]. (2008). *Physical Activity Guidelines for American.* Retrieved from http://www.health.gov/paguidelines/.

Ueno, L. M., & Moritani, T. (2003). Effects of long-term exercise training on cardiac autonomic nervous activities and baroreflex sensitivity. *European Journal of Applied Physiology, 89*(2), 109-114.

Uusitalo, A. L. T., Laitinen, T., Väisänen, S. B., Länsimies, E., & Rauramaa, R. (2004). Physical training and heart rate and blood pressure variability: a 5-yr randomized trial. *American Journal of Physiology - Heart and Circulatory Physiology, 286*(5), H1821-H1826.

Vahl, N., Jørgensen, J. O., Skjaerbaek, C., Veldhuis, J. D., Orskov, H., & Christiansen, J. S. (1997). Abdominal adiposity rather than age and sex predicts mass and regularity of GH secretion in healthy adults. *American Journal of Physiology - Endocrinology And Metabolism, 272*(6 Pt 1), E1108-1116.

Vaitkevicius, P. V., Fleg, J. L., Engel, J. H., O'Connor, F. C., Wright, J. G., Lakatta, L. E., et al. (1993). Effects of age and aerobic capacity on arterial stiffness in healthy adults. *Circulation, 88*(4), 1456-1462.

van Aggel-Leijssen, D. P., Saris, W. H., Wagenmakers, A. J., Hul, G. B., & van Baak, M. A. (2001). The effect of low-intensity exercise training on fat metabolism of obese women. *Obesity Research, 9*(2), 86-96.

van Doornen, L. J. P., & de Geus, E. J. C. (1989). Aerobic fitness and the cardiovascular response to stress. *Psychophysiology, 26*(1), 17-28.

van Langen, H., van Driel, V. J. H. M., Skotnicki, S. H., & Verheugt, F. W. A. (2001). Alterations in the peripheral circulation in patients with mild heart failure. *European Journal of Ultrasound, 13*(1), 7-15.

van Popele, N. M., Grobbee, D. E., Bots, M. L., Asmar, R., Topouchian, J., Reneman, R. S., et al. (2001). Association between arterial stiffness and atherosclerosis : The rotterdam study. *Stroke, 32*(2), 454-460.

Venner, A. A., Lyon, M. E., & Doyle-Baker, P. K. (2006). Leptin: a potential biomarker for childhood obesity? *Clinical Biochemistry, 39*(11), 1047-1056.

Verheyden, B., Eijnde, B. O., Beckers, F., Vanhees, L., & Aubert, A. E. (2006). Low-dose exercise training does not influence cardiac autonomic control in healthy sedentary men aged 55 – 75 years. *Journal of Sports Sciences, 24*(11), 1137-1147.

Wadden, T. A. (1993). Treatment of obesity by moderate and severe caloric restriction. Results of clinical research trials. *Annals of Internal Medicine, 119*(7 Pt 2), 688-693.

Wahl, P., Zinner, C., Achtzehn, S., Bloch, W., & Mester, J. (2010). Effect of high- and low-intensity exercise and metabolic acidosis on levels of GH, IGF-I, IGFBP-3 and cortisol. *Growth Hormone and IGF Research, 20*(5), 380-385.

Waldstein, S. R., Burns, H. O., Toth, M. J., & Poehlman, E. T. (1999). Cardiovascular reactivity and central adiposity in older African Americans. *Health Psychology, 18*(3), 221-228.

Walsh, J. H., Bilsborough, W., Maiorana, A., Best, M., O'Driscoll, G. J., Taylor, R. R., et al. (2003). Exercise training improves conduit vessel function in patients with coronary artery disease. *Journal of Applied Physiology, 95*(1), 20-25.

Walsh, J. H., Yong, G., Cheetham, C., Watts, G. F., O'Driscoll, G. J., Taylor, R. R., et al. (2003). Effects of exercise training on conduit and resistance vessel function in treated and untreated hypercholesterolaemic subjects. *European Heart Journal, 24*(18), 1681-1689.

Warburton, D. E., McKenzie, D. C., Haykowsky, M. J., Taylor, A., Shoemaker, P., Ignaszewski, A. P., et al. (2005). Effectiveness of high-intensity interval training for the rehabilitation of patients with coronary artery disease. *The American Journal of Cardiology, 95*(9), 1080-1084.

Watts, K., Jones, T. W., Davis, E. A., & Green, D. (2005). Exercise training in obese children and adolescents: current concepts. *Sports Medicine, 35*(5), 375-392.

Weil, B. R., Stauffer, B. L., Mestek, M. L., & DeSouza, C. A. (2011). Influence of abdominal obesity on vascular endothelial function in overweight/obese adult men. *Obesity, 19*(9), 1742-1746.

Weinstein, Y., Bediz, C., Dotan, R., & Falk, B. (1998). Reliability of peak-lactate, heart rate, and plasma volume following the Wingate test. *Medicine and Science in Sports and Exercise, 30*(9), 1456-1460.

Weltman, A., Pritzlaff, C. J., Wideman, L., Considine, R. V., Fryburg, D. A., Gutgesell, M. E., et al. (2000). Intensity of acute exercise does not affect serum leptin concentrations in young men. *Medicine and Science in Sports and Exercise, 32*(9), 1556-1561.

Weltman, A., Weltman, J. Y., Schurrer, R., Evans, W. S., Veldhuis, J. D., & Rogol, A. D. (1992). Endurance training amplifies the pulsatile release of growth hormone: effects of training intensity. *Journal of Applied Physiology, 72*(6), 2188-2196.

Westhoff, T. H., Franke, N., Schmidt, S., Vallbracht-Israng, K., Meissner, R., Yildirim, H., et al. (2007). Too old to benefit from sports? The cardiovascular

effects of exercise training in elderly subjects treated for isolated systolic hypertension. *Kidney and Blood Pressure Research, 30*(4), 240-247.

Weston, A. R., Myburgh, K. H., Lindsay, F. H., Dennis, S. C., Noakes, T. D., & Hawley, J. A. (1997). Skeletal muscle buffering capacity and endurance performance after high-intensity interval training by well-trained cyclists. *European Journal of Applied Physiology and Occupational Physiology, 75*(1), 7-13.

WHO. (2004). Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *Lancet, 363*(9403), 157-163.

WHO. (2011). Cardiovascular diseases (CVDs). Retrieved 11 January 2012, from http://www.who.int/mediacentre/factsheets/fs317/en/index.html

Whyte, L. J., Gill, J. M. R., & Cathcart, A. J. (2010). Effect of 2 weeks of sprint interval training on health-related outcomes in sedentary overweight/obese men. *Metabolism: Clinical and Experimental, 59*(10), 1421-1428.

Wideman, L., Weltman, J. Y., Patrie, J. T., Bowers, C. Y., Shah, N., Story, S., et al. (2000). Synergy of L-arginine and GHRP-2 stimulation of growth hormone in men and women: modulation by exercise. *American Journal of Physiology. Regulatory, Integrative and Comparative Physiology, 279*(4), R1467-1477.

Wideman, L., Weltman, J. Y., Shah, N., Story, S., Veldhuis, J. D., & Weltman, A. (1999). Effects of gender on exercise-induced growth hormone release. *Journal of Applied Physiology, 87*(3), 1154-1162.

Wijnen, J. A., Kool, M. J., Kooman, J. P., van Baak, M. A., Hoeks, A. P., Struijker Boudier, H. A., et al. (1993). Vessel wall properties of large arteries and endurance training. *Journal of Hypertension, 11*, S88-S89.

Wilding, J. P. H. (2001). Leptin and the control of obesity. *Current Opinion in Pharmacology, 1*(6), 656-661.

Wildman, R. P., Mackey, R. H., Bostom, A., Thompson, T., & Sutton-Tyrrell, K. (2003). Measures of obesity are associated with vascular stiffness in young and older adults. *Hypertension, 42*(4), 468-473.

Wilkinson, I. B., Fuchs, S. A., Jansen, I. M., Spratt, J. C., Murray, G. D., Cockcroft, J. R., et al. (1998). Reproducibility of pulse wave velocity and augmentation index measured by pulse wave analysis. *Journal of Hypertension, 16*(12), 2079-2084.

Wilmore, J. H., Després, J. P., Stanforth, P. R., Mandel, S., Rice, T., Gagnon, J., et al. (1999). Alterations in body weight and composition consequent to 20 wk of endurance training: the HERITAGE Family Study. *The American Journal of Clinical Nutrition, 70*(3), 346-352.

Wilmore, J. H., Stanforth, P. R., Gagnon, J., Rice, T., Mandel, S., Leon, A. S., et al. (2001). Heart rate and blood pressure changes with endurance training: The HERITAGE Family Study. *Medicine and Science in Sports and Exercise, 33*(1), 107-116.

Wisløff, U., Ellingsen, Ø., & Kemi, O. J. (2009). High-intensity interval training to maximize cardiac benefits of exercise training? *Exercise and Sport Sciences Reviews, 37*(3), 139-146

Wisloff, U., Stoylen, A., Loennechen, J. P., Bruvold, M., Rognmo, O., Haram, P. M., et al. (2007). Superior cardiovascular effect of aerobic interval training versus moderate continuous training in heart failure patients: a randomized study. *Circulation, 115*(24), 3086-3094.

Wong, B. J., Wilkins, B. W., Holowatz, L. A., & Minson, C. T. (2003). Nitric oxide synthase inhibition does not alter the reactive hyperemic response in the cutaneous circulation. *Journal of Applied Physiology, 95*(2), 504-510.

Wong, S. L., Katzmarzyk, P., Nichaman, M. Z., Church, T. S., Blair, S. N., & Ross, R. (2004). Cardiorespiratory fitness is associated with lower abdominal fat independent of body mass index. *Medicine and Science in Sports and Exercise, 36*(2), 286-291.

Wu, T., Gao, X., Chen, M., & Van Dam, R. M. (2009). Long-term effectiveness of diet-plus-exercise interventions vs. diet-only interventions for weight loss: a meta-analysis. *Obesity Reviews, 10*(3), 313-323.

Xiang, G. D., & Wang, Y. L. (2004). Regular aerobic exercise training improves endothelium-dependent arterial dilation in patients with impaired fasting glucose. *Diabetes Care, 27*(3), 801-802.

Xuefeng, C., Jian-min, M., Xiaorong, X., Mohamed, E., Robin, B., Linda, C., et al. (2004). Post-occlusive reactive hyperemia in patients with peripheral vascular disease. *Clinical Hemorheology and Microcirculation, 31*(1), 11-21.

Yamamoto-Suganuma, R., & Aso, Y. (2009). Relationship between post-occlusive forearm skin reactive hyperaemia and vascular disease in patients with Type 2 diabetes—a novel index for detecting micro- and macrovascular dysfunction using laser Doppler flowmetry. *Diabetic Medicine, 26*(1), 83-88.

Yamamoto, K., Miyachi, M., Saitoh, T., Yoshioka, A., & Onodera, S. (2001). Effects of endurance training on resting and post-exercise cardiac autonomic control. *Medicine and Science in Sports and Exercise, 33*(9), 1496-1502.

Yasumasu, T., Reyes Del Paso, G. A., Takahara, K., & Nakashima, Y. (2006). Reduced baroreflex cardiac sensitivity predicts increased cognitive performance. *Psychophysiology, 43*(1), 41-45.

Yeung, A. C., Vekshtein, V. I., Krantz, D. S., Vita, J. A., Ryan, T. J., Ganz, P., et al. (1991). The effect of atherosclerosis on the vasomotor response of coronary arteries to mental stress. *New England Journal of Medicine, 325*(22), 1551-1556.

Yokoyama, H., Emoto, M., Fujiwara, S., Motoyama, K., Morioka, T., Koyama, H., et al. (2004). Short-term aerobic exercise improves arterial stiffness in type 2 diabetes. *Diabetes Research and Clinical Practice, 65*(2), 85-93.

Yoon, E. S., Jung, S. J., Cheun, S. K., Oh, Y. S., Kim, S. H., & Jae, S. Y. (2010). Effects of acute resistance exercise on arterial stiffness in young men. *Korean Circulation Journal, 40*(1), 16-22.

Yoshimura, E., Kumahara, H., Tobina, T., Ayabe, M., Matono, S., Anzai, K., et al. (2011). A 12-week aerobic exercise program without energy restriction improves intrahepatic fat, liver function and atherosclerosis-related factors. *Obesity Research & Clinical Practice, 5*(3), e249-e257.

Yoshizawa, M., Maeda, S., Miyaki, A., Misono, M., Saito, Y., Tanabe, K., et al. (2009). Effect of 12 weeks of moderate–intensity resistance training on arterial stiffness: a randomised controlled trial in women aged 32–59 years. *British Journal of Sports Medicine, 43*(8), 615-618.

Zalesin, K. C., Franklin, B. A., Miller, W. M., Peterson, E. D., & McCullough, P. A. (2011). Impact of obesity on cardiovascular disease. *Medical Clinics of North America, 95*(5), 919-937.

Zhao, J. L., Pergola, P. E., Roman, L. J., & Kellogg, D. L. (2004). Bioactive nitric oxide concentration does not increase during reactive hyperemia in human skin. *Journal of Applied Physiology, 96*(2), 628-632.

Zieman, S. J., Melenovsky, V., & Kass, D. A. (2005). Mechanisms, pathophysiology, and therapy of arterial stiffness. *Arteriosclerosis, Thrombosis, and Vascular Biology, 25*(5), 932-943.

Zouhal, H., Jacob, C., Delamarche, P., & Gratas-Delamarche, A. (2008). Catecholamines and the effects of exercise, training and gender. *Sports Medicine, 38*(5), 401-423.

Chapter 2: Metabolic Response of Trained and Untrained Males during and After Acute High-Intensity Intermittent Exercise

Mehrdad Heydari, Daniel Ghareman, Stephen H. Boutcher

Submitted to a peer-reviewed journal

Author Contributions

DG and MH collected data, and contributed to writing the manuscript. MH also produced results and figures and was responsible for statistical analysis. SHB conceived of the study and contributed to writing the manuscript.

Abstract

Objective: The metabolic response of males during and after acute high-intensity intermittent exercise (HIIE) was examined.

Methods: Trained (n= 10) and untrained (n= 10) healthy young males, aged 24.9 ± 1.3 years, completed 20 min of HIIE (8-sec sprint, 12-sec recovery) on a cycle ergometer followed by 1 h of post-exercise recovery. Lactate, plasma glycerol, and catecholamine concentration were assessed at rest, during, and after HIIE.

Results: For both groups glycerol levels were significantly elevated during exercise ($P < 0.05$). Lactate concentration was also increased during HIIE but was higher for untrained males ($P < 0.05$). Both groups had a similar and significant increase ($P < 0.05$) in epinephrine during HIIE, in contrast, untrained compared to trained males recorded significantly ($P < 0.05$) greater levels of norepinephrine. During the post-exercise recovery period from minutes 45 to 75 fat oxidation was significantly increased. Plasma glycerol levels at rest and 15 min after HIIE were significantly higher ($P < 0.05$) for both groups. Plasma norepinephrine concentrations were significantly higher 15 min post exercise ($P < 0.05$) for both groups, whereas plasma epinephrine levels showed a significant increase after 20 min of HIIE for both groups, $P < 0.05$.

Conclusions: For both groups HIIE resulted in significant elevations in glycerol and epinephrine during and after HIIE. The untrained compared to the trained showed a significantly greater rise in blood lactate levels and increase in norepinephrine during HIIE, however, both groups showed elevated fat oxidation after exercise.

Introduction

Studies examining high-intensity intermittent exercise (HIIE) have mainly utilized the Wingate test which consists of 30 s of all-out sprint with a high resistance. Participants typically perform the Wingate test 4 to 6 times with 4 min of recovery between sprints. Insight into the skeletal muscle adaptation to HIIE has mainly been achieved using this type of exercise (Gibala & McGee, 2008). As this protocol is extremely demanding, however, participants have to be willing to tolerate significant discomfiture, thus the Wingate protocol is unlikely to be suitable for long-term interventions with overweight individuals wanting to lose body fat.

Consequently, HIIE protocols more suitable for fat loss have been developed. For example, Trapp et al. (2008) conducted a HIIE program in young women for 15 weeks with three 20-min HIIE sessions per week. HIIE consisted of an 8-s sprint followed by 12 s of low intensity cycling, continuously for 20 min. Another group of women carried out an aerobic cycling protocol for 40 min each session. Results showed that women in the HIIE group lost 2.5 kg of subcutaneous fat, whereas no change occurred with steady state aerobic exercise. Fat loss accruing through 15 weeks of HIIE was attained with 50% less exercise time and a similar energy expenditure to that of steady state exercise. Similar results were found by Heydari et al. (2012) who showed that 12 weeks of HIIE significantly reduced both total body (2.0 kg) and visceral fat (17%) of overweight males. How these longer, less intense HIIE protocols cause significant reductions in total and visceral fat, however, is undetermined.

The hormonal response during HIIE may contribute to enhanced fat oxidation during and after this form of exercise. For example, using the 8-sec/12-sec protocol

Trapp et al. (2007) found that in both trained and untrained females HIIE was accompanied by a significant elevation of catecholamines. Bracken et al. (2009) examined the catecholamine response of 12 males who completed ten 6-sec cycle ergometer sprints with a 30-sec recovery between each sprint. From baseline, plasma epinephrine increased 6.3 fold, whereas norepinephrine increased 14.5 fold at the end of sprinting. The significant catecholamine response to HIIE is in contrast to moderate, steady state aerobic exercise that results in small increases in epinephrine and norepinephrine (Zouhal et al., 2008). The HIIE catecholamine response is an important feature of this type of exercise as catecholamines have been shown to drive lipolysis and are largely responsible for fat release from both subcutaneous and intramuscular fat stores (Issekutz, 1978).

The catecholamine, lactate, and glycerol response of trained and untrained males during and after the lower intensity form of HIIE, however, is undetermined. Therefore, the purpose of this study was to compare the metabolic response of physically trained and untrained males during and after a 20-min bout of HIIE.

Methods

Participants

Twenty healthy young, non-smoking males aged 24.9 ± 1.3 years were recruited via emails, fliers, and magazine advertisements on campus or in parks and recreation centres. Any participant with a known or suspected cardiovascular or musculoskeletal disorder was eliminated. The study was approved by a university human ethics committee. All males were healthy and none were obese (Table 2.1). The trained group consisted of cyclists who had performed a minimum of three

sessions of cycling a week for at least 45 min each session, for at least one year. Untrained participants had to participate in no regular physical activity during the past six months.

Table 2.1. Participant characteristics (mean and standard error)

Variables	**Untrained (n=10)**	**Trained (n=10)**
Age (yrs)	26.8 ± 1.9	23.0 ± 1.6
Height (cm)	176 ± 2.8	178 ± 1.1
Weight (kg)	81.2 ± 4.7	71.5 ± 1.6
BMI	26.3 ± 1.3*	22.6 ± 0.3
% Body fat	20.0 ± 1.7*	13.3 ± 0.8
$\dot{V}O_{2max}$ ($ml.kg^{-1}.min^{-1}$)	36.6 ± 1.9*	62.3 ± 1.8
Total cholesterol	4.0 ± 0.3	3.8 ± 0.2
HDL ($mmol.L^{-1}$)	1.2 ± 0.1	1.3 ± 0.1
TG ($mmol.L^{-1}$)	1.1 ± 0.2	0.7 ± 0.1
LDL ($mmol.L^{-1}$)	2.3 ± 0.2	1.9 ± 0.1
TC/HDL	3.7 ± 0.5	2.9 ± 0.1
Glucose ($mmol.L^{-1}$)	5.1 ± 0.1	5.0 ± 0.1
Resting HR	60.2 ± 1.5	56.1 ± 3.5

BMI: body mass index; $\dot{V}O_{2max}$: maximal oxygen uptake.
*$P < 0.05$, significantly different between groups.

Study Design

All participants were assigned into trained or untrained groups based on their weekly physical activity. Blood collection and a $\dot{V}O_{2max}$ test were carried out during the first session. The acute response to HIIE was examined in session two. Participants, who were advised to avoid strenuous activity and caffeine for 24 hours prior to testing, came into the laboratory after an 8-10 h overnight fast and were tested between 8:00

and 10:00 am. Personal medical history was collected to record the potential use of tobacco products, medication, birth weight, and exercise history. Participants were asked to fill in a Physical Activity Readiness Questionnaire (Thomas, Reading, & Shephard, 1992) that screened for contraindications to exercise. Body weight was measured with minimum clothing and percentage body fat was assessed by bioeletrical impedance (Tanita, Illinois, USA). Body-mass index (BMI) was calculated by dividing mass by height squared ($kg \cdot m^{-2}$). Baseline blood samples were taken from an antecubital vein (either the cephalic or brachial) after overnight fasting and were stored in EDTA vacutainers.

Aerobic Power Assessment

Aerobic power was assessed using a TrueMax 2400 Metabolic Cart (ParvoMedics Inc, USA). All participants started with a 3-min warm-up at 30 watts (W) and then power output was increased by 1 W every 2 seconds. Participants were asked to maintain 60-70 rpm throughout the test. Power output continued to increase until participants failed to maintain pedal frequency despite verbal encouragement. All $\dot{V}O_{2max}$ sessions were performed on an electronically braked Monark cycle ergometer (Ergomedic 839E, Sweden). Temperature in the laboratory was maintained between 20-23°C and participants were asked to give a rating of perceived exertion (RPE) every minute throughout the test (Borg, 1982). Heart rate was recorded during this session using a Polar S810I telemetry system (Polar, Finland).

Resting Metabolic Rate

Resting metabolic rate (RMR) was measured by using a ventilated canopy for 30 min after an 8-10 h overnight fast. $\dot{V}O_2$, $\dot{V}CO_2$, and respiratory quotient (RQ) were

obtained using a TrueOne 2400 Canopy System linked to a metabolic cart (ParvoMedics, Utah, USA). Heart rate was monitored continuously using telemetry with the Polar Watch S810i. RQ was also obtained during exercise and the post exercise recovery.

Fat Oxidation Rate

Fat oxidation rate was calculated during rest and minutes 45 to 75 post exercise recovery using the following formula:

Fat oxidation = $1.695\dot{V}O_2 - 1.701\dot{V}CO_2$ (Murase, Nagasawa, Suzuki, Hase, & Tokimitsu, 2002).

High-intensity intermittent exercise protocol

After the first blood sample, participants performed a 5-min warm-up on the cycle ergometer at 30 W. The HIIE consisted of 60 bouts of fast pedalling for 8 sec at 65% of maximum workload (assessed from the prior $\dot{V}O_{2max}$ test) followed by 12-sec of slow pedalling at 25% of maximum power output. Power output was adjusted by a computerized program (ParvoMedics, Utah, USA) and participants‘ pedal rate was directed by pre recorded audio. Exercise consisted of twenty minutes of HIIE followed by a 5-min cool down at 30 W. Heart rate was recorded constantly during the test. Due to frequent blood sampling during the HIIE session, a 22-guage cannula was used to collect blood samples (Becton Dickinson, Plymouth, UK). The cannula was inserted into an antecubital vein and a 3-way stopcock (Becton Dickinson, Plymouth, UK) was attached for blood sampling to allow for repeated collection. The catheter was kept patent by flushing with 0.9% isotonic saline (Pfizer,

New York, USA) after each blood sample. During the second session four blood samples were collected. RPE was collected at minute 7, 14, and 20 during HIIE.

Biochemical Assays

Blood lipid profiles and fasting glucose were quantified by automated enzymatic methods (Cholestech LDX, USA) from whole blood. The remaining blood was spun immediately in a chilled centrifuge (Model Megafuge 1.0R, Heraeus, Germany) at 4^{o} C and plasma was stored immediately at -86 ^{o} C for later analysis. Blood lactate was measured after 30 min of rest and immediately before the start of exercise, in minutes 7 and 20 of HIIE using a lactate analyser (Accutrend Plus, Cobas, Germany). Catecholamine analysis was carried out using a 5973N Mass Selective Detector, coupled to a 6890N gas chromatograph, and a SGE Forte BPX5 x 0.25 IDx 0.25 micron column. The catecholamines were derivatised in a number of steps and single ion monitoring was used to determine the concentrations of the substrate. Internal standards were used to create a standard curve for the assay. Glycerol was measured using a commercially available ELISA immunoassay kit. The degree of enzymatic turnover of the substrate was determined by dual wavelength absorbance measurement at 450 and 540 nm (Sigma FG0100).

Statistical analysis

Data analysis was completed using SPSS 20.0 software to perform two-way repeated measures analyses of variance (ANOVA) examining differences between the trained and untrained. The Bonferroni adjustment was used to further examine main effects between groups. Effect sizes were calculated using partial eta squared (η^2) with values of 0.1, 0.3, and above 0.5 considered to be a small, medium, and large effect.

All values are mean ± SE and a significance level of $P < 0.05$ was adopted.

Results

Power output and heart rate

The trained group (337 ± 8.4 W) produced a significantly higher power output $t(18) = 7.26$, $P < 0.001$, than the untrained group (246 ± 9.1 W). There was a significant main effect for time, $F(8, 11) = 92.33$, $P < 0.001$, $\eta^2 = 0.99$, with both groups showing an increase in heart rate with a significant difference between groups, $F(1, 18) = 7.89$, $P = 0.012$, $\eta^2 = 0.31$. There was a significant time by group interaction, $F(8, 11) = 5.16$, $P = 0.007$, $\eta^2 = 0.79$, Figure. 2.1.

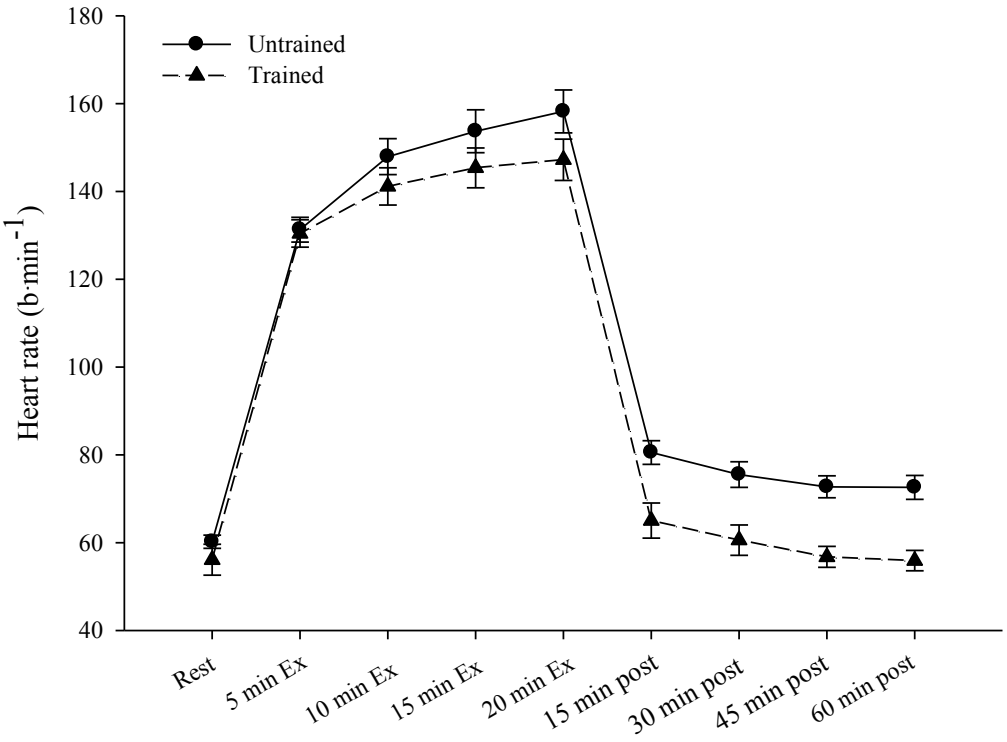

Figure 2.1. Heart rate at rest and during high-intensity intermittent exercise of trained and untrained males

Lactate

There was a significant main effect for time, $F(4, 15) = 17.79$, $P < 0.001$, $\eta^2 = 0.83$, with both groups showing an increase in lactate level across the five time points (Figure. 2.2) with no significant difference between groups, $F(1, 18) = 2.62$, $P = 0.12$, $\eta^2 = 0.13$, however, a significant time by group interaction existed, $F(4, 15) = 3.21$, $P = 0.043$, $\eta^2 = 0.46$, indicating that the blood lactate of the trained was significantly lower than the untrained group at the end of exercise.

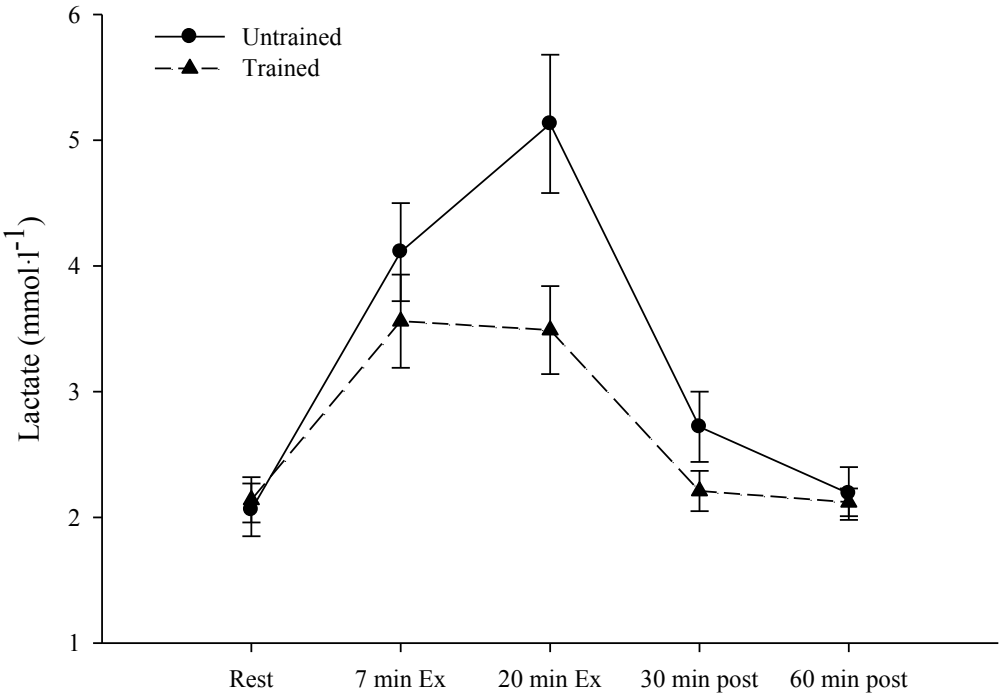

Figure 2.2. Lactate levels at rest and during high-intensity intermittent exercise of trained and untrained males

$\dot{V}O_2$ Response

There was a significant main effect for time, $F(8, 11) = 188.14$, $P < 0.001$, $\eta^2 = 0.99$, with both groups showing an increase in $\dot{V}O_2$ but the trained recorded greater $\dot{V}O_2$

compared to the untrained, $F(1, 18) = 23.27$, $P < 0.001$, $\eta^2 = 0.56$. There was also a significant time by group interaction, $F(8, 11) = 9.94$, $P < 0.001$, $\eta^2 = 0.88$, Figure. 2.3.

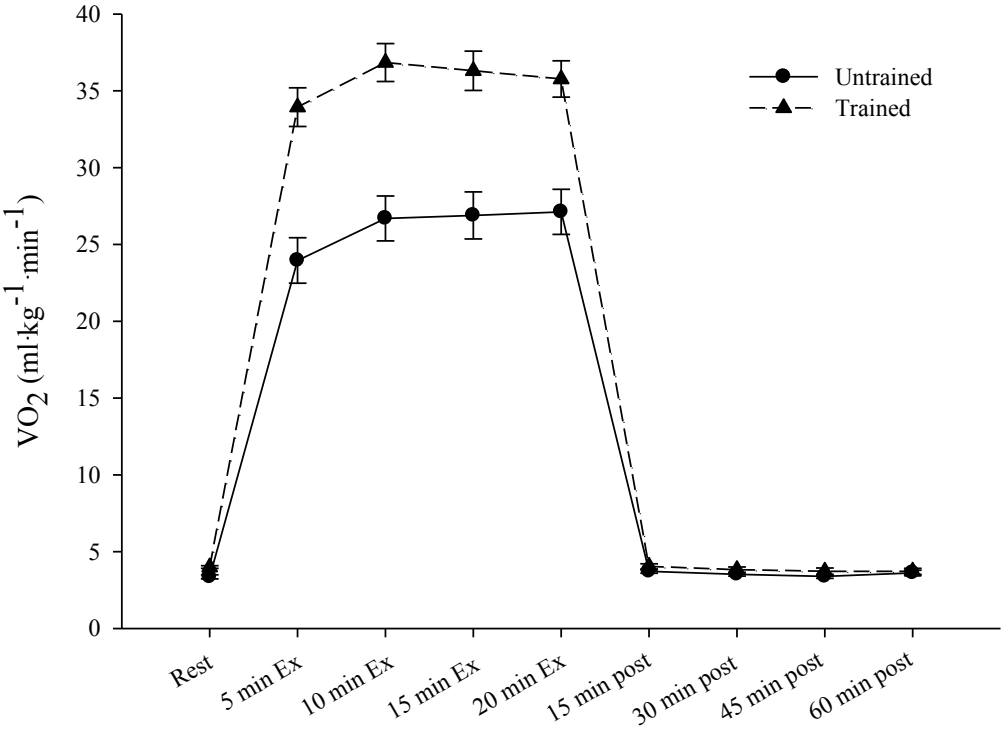

Figure 2.3. $\dot{V}O_2$ levels at rest and during high-intensity intermittent exercise of trained and untrained males

Respiratory Quotient (RQ)

There was a significant main effect for time, $F(5, 14) = 13.16$, $P < 0.001$, $\eta^2 = 0.83$, with both groups showing an increase in RQ level across the six time points with no significant difference between groups, $F(1, 18) = 0.52$, $P = 0.48$, $\eta^2 = 0.03$. There was no significant time by group interaction, $F(5, 14) = 2.05$, $P = 0.13$, $\eta^2 = 0.42$, Figure. 2.4.

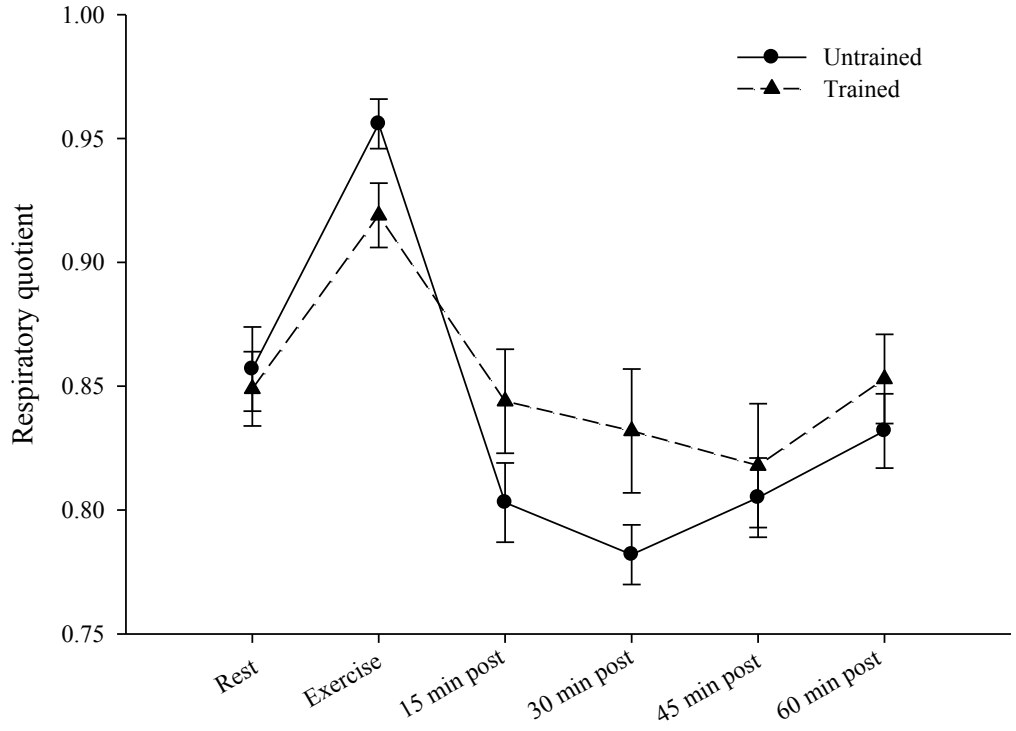

Figure 2.4. Respiratory quotient at rest and during high-intensity intermittent exercise of trained and untrained males

Fat Oxidation Rate

There was a significant main effect for time, $F(5, 14) = 5.82$, $P = 0.004$, $\eta^2 = 0.68$, with both groups showing an increase in fat oxidation across the six time points with no significant difference between groups, $F(1, 18) = 2.24$, $P = 0.11$, $\eta^2 = 0.44$. There was no significant time by group interaction, $F(5, 14) = 2.79$, $P = 0.089$, $\eta^2 = 0.25$, Figure. 2.5.

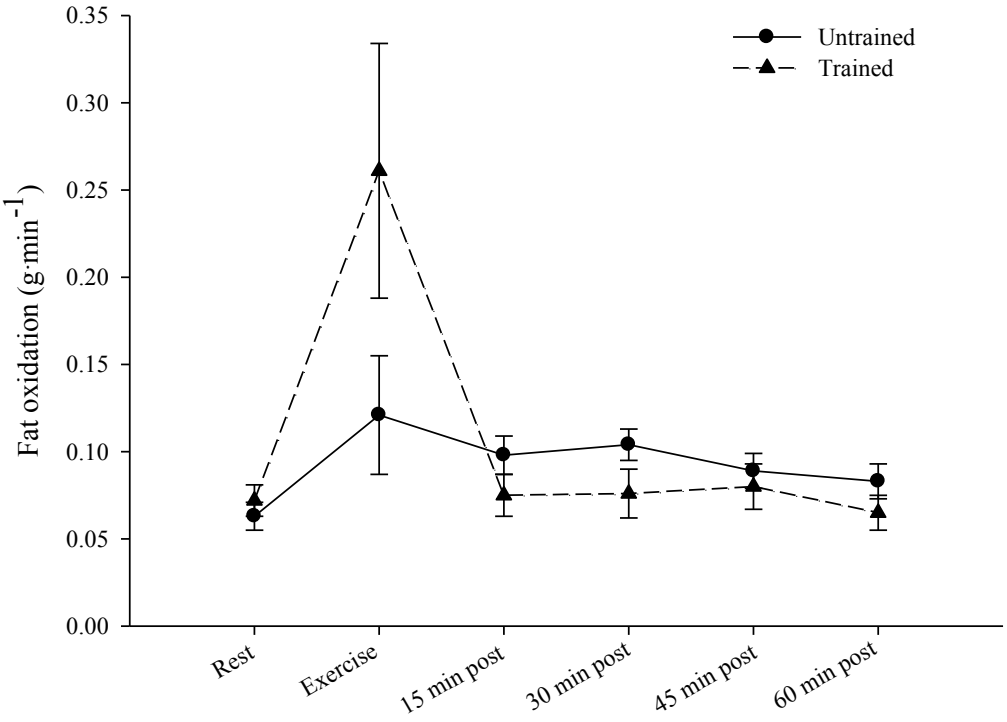

Figure 2.5. Fat oxidation rate at rest and during high-intensity intermittent exercise of trained and untrained males

Relative Fat Oxidation Rate

There was a significant main effect for time, $F(5, 14) = 6.03$, $P = 0.004$, $\eta^2 = 0.68$, with both groups showing an increase in fat oxidation across the six time points with no significant difference between groups, $F(1, 18) = 1.55$, $P = 0.23$, $\eta^2 = 0.08$. There was no significant time by group interaction, $F(5, 14) = 2.30$, $P = 0.10$, $\eta^2 = 0.45$, Figure. 2.6.

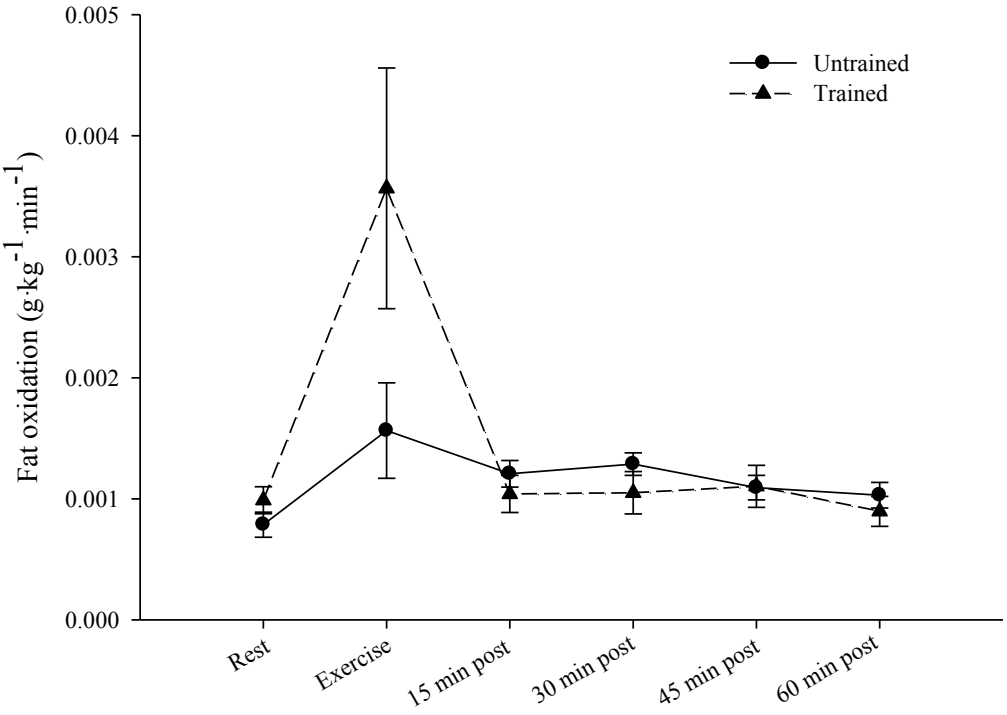

Figure 2.6. Relative fat oxidation rate at rest and during high-intensity intermittent exercise of trained and untrained males

Glycerol and catecholamines

There was a significant main effect for time, $F(8, 11) = 8.94$, $P = 0.001$, $\eta^2 = 0.87$, with both groups showing an increase in glycerol level but the trained recorded greater glycerol response compared to the untrained, $F(1, 18) = 4.75$, $P = 0.043$, $\eta^2 = 0.21$. There was no significant time by group interaction, $F(8, 11) = 0.81$, $P = 0.61$, $\eta^2 = 0.37$, Figure 2.7.

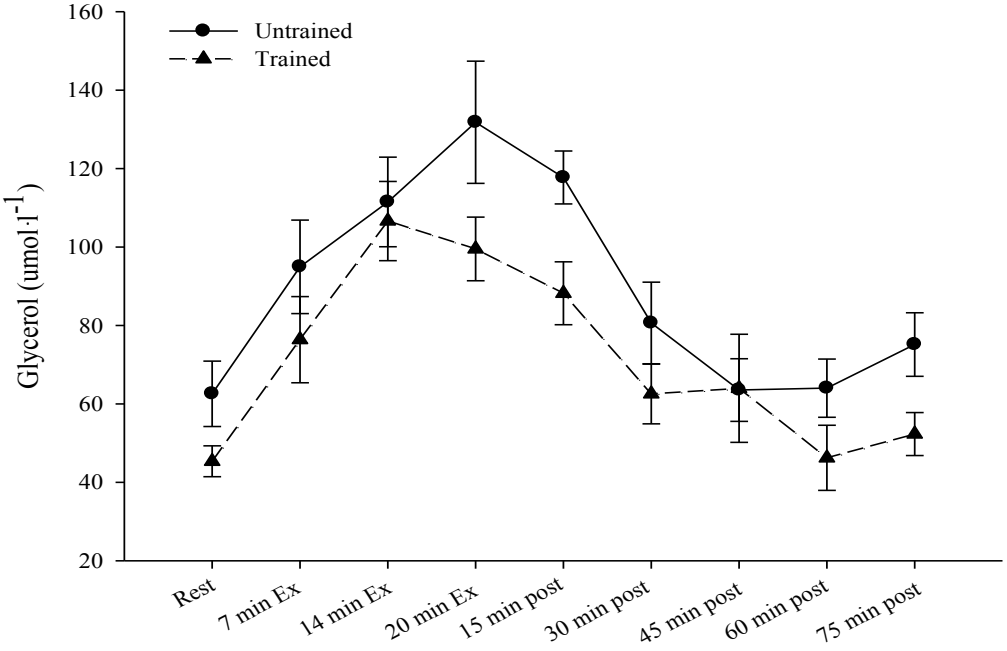

Figure 2.7. Glycerol levels at rest and during high-intensity intermittent exercise of trained and untrained males

There was a significant main effect for time, $F(2, 17) = 27.91$, $P < 0.001$, $\eta 2 = 0.77$, with both groups showing an increase in epinephrine level across the three time points with no significant difference between groups, $F(1, 18) = 0.14$, $P = 0.91$, $\eta 2 = 0.001$. There was no significant time by group interaction, $F(2, 17) = 0.30$, $P = 0.75$, $\eta 2 = 0.03$, Figure. 2.8. There was a significant main effect for time, $F(2, 17) = 20.83$, $P < 0.001$, $\eta 2 = 0.71$, with both groups showing an increase in norepinephrine level across the three time points with no significant difference between groups, $F(1, 18) = 2.66$, $P = 0.12$, $\eta 2 = 0.13$. There was no significant time by group interaction, $F(2, 17) = 0.70$, $P = 0.51$, $\eta 2 = 0.08$, Figure 2.9.

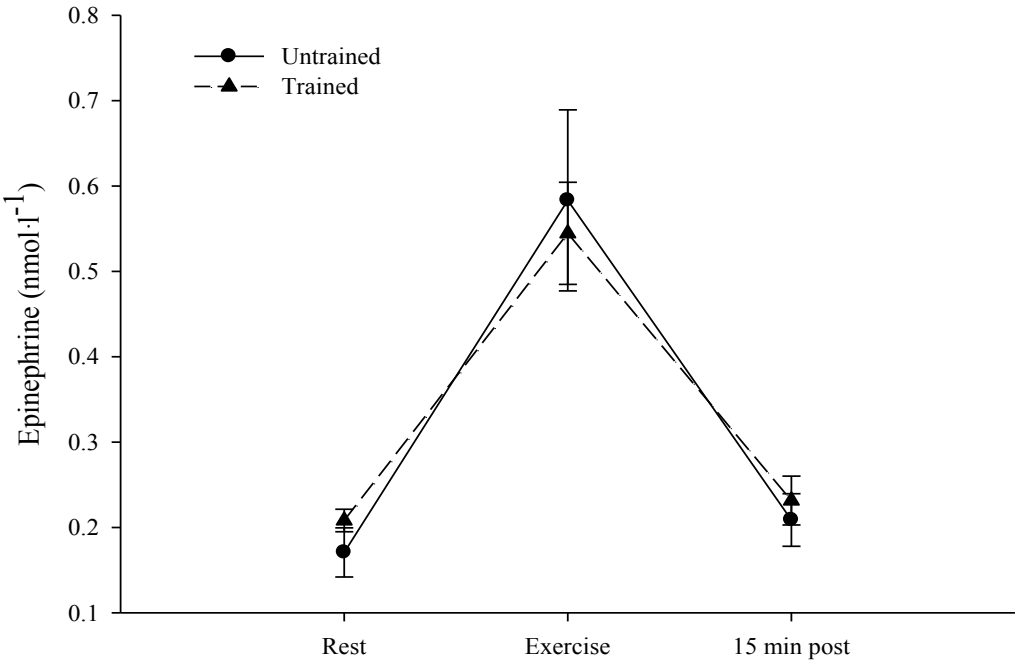

Figure 2.8. Epinephrine levels at rest and during high-intensity intermittent exercise of trained and untrained males

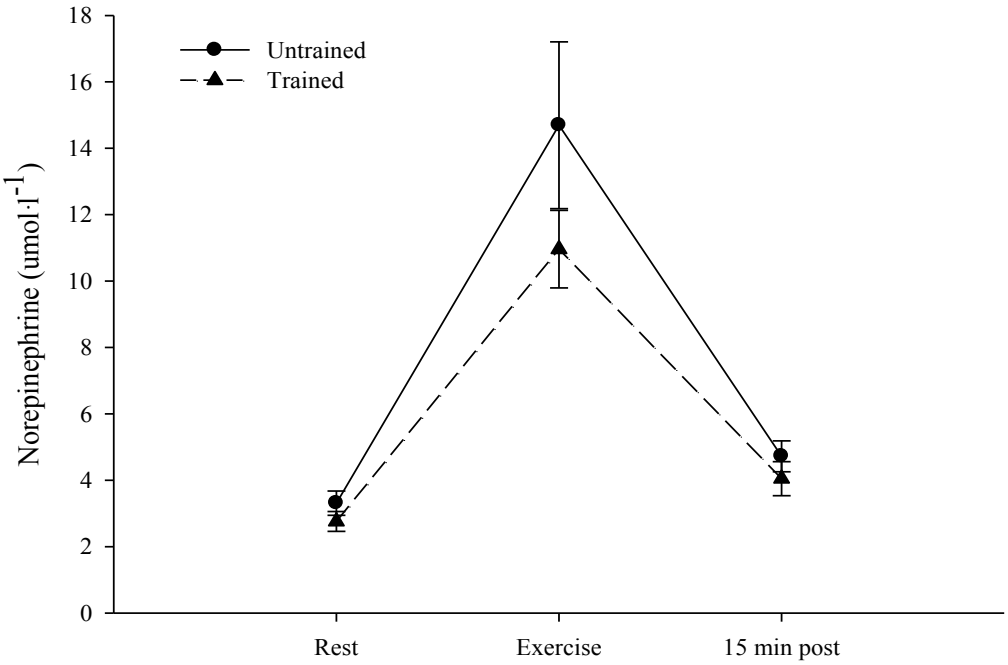

Figure 2.9. Norepinephrine levels at rest and during high-intensity intermittent exercise of trained and untrained males

Rating of perceived exertion (RPE)

The average RPE across the 20 min of HIIE for both trained (M = 13.2 ± 1.5) and untrained (M = 13.2 ± 1.7) groups was similar. There was a significant main effect for time, $F(2, 17) = 27.50$, $P < 0.001$, $\eta^2 = 0.76$, with both groups showing an increase in RPE level across the three time points with no significant difference between groups, $F(1, 18) = 0.00$, $P = 1.00$, $\eta^2 = 0.00$. There was no significant time by group interaction, $F(2, 17) = 2.68$, $P = 0.10$, $\eta^2 = 0.24$.

Discussion

The major finding of this study was that plasma glycerol, lactate, and catecholamine concentration were significantly increased during 20 min of HIIE for both trained and untrained males. The untrained compared with the trained, however, showed a significantly greater rise in blood lactate levels and increase in norepinephrine during HIIE. After HIIE, compared to rest, fat oxidation rate was significantly increased without an increase in oxygen consumption ($\dot{V}O_2$) or energy expenditure for both groups.

The acute heart rate and lactate response during HIIE found in the males in the present study was similar to that found in females using exactly the same HIIE protocol (Trapp et al., 2007). Thus, in both trained and untrained females and males acute HIIE resulted in elevated heart rate and blood lactate levels. The lactate response after 20 min of HIIE (60 sprints) for both trained and untrained males (4.5 $mmol \cdot l^{-1}$) was markedly lower than the 8-14 $mmol \cdot l^{-1}$ increase that is typically found after one 30-sec Wingate test (Gratas-Delamarche, Le Cam, Delamarche, Monnier, & Koubi, 1994; Vincent et al., 2004). The significant increase in plasma catecholamine concentration during HIIE parallels that found previously in trained and untrained females (Trapp et al., 2007) and untrained males (Bracken, Linnane, & Brooks, 2009). The similar increase in glycerol levels during HIIE for both trained and untrained males in the current study, however, is in contrast to the findings of Trapp et al. (2007) who showed that trained female cyclists had a greater glycerol response than untrained females. In the current study the absolute levels of glycerol during HIIE was appreciably greater for the males compared to that of females in the Trapp et al. study. As the $\dot{V}O_{2max}$ of trained and untrained males and females was

similar in these studies it appears that gender effects may account for these differing glycerol responses to HIIE.

The increase in glycerol concentration during HIIE suggests increased usage of free fatty acids (FFA) as an energy source despite elevated lactate levels. Elevated blood lactate concentrations have been shown to inhibit carnitine-acyl CoA transferase which results in a slowing down of β-oxidation (Starritt, Howlett, Heigenhauser, & Spriet, 2000). Thus, despite lactate concentrations being elevated during HIIE fat use increased throughout exercise. The ability of exercising muscle to utilize FFAs despite high lactate levels may be due to the intermittent nature of HIIE (Tremblay et al., 1990). For example, during the sprint component of HIIE, ATP and creatine phosphate are catabolised for energy and then are resynthesised during the non-intensive aerobic period (Essen, Hagenfeldt, & Kaijser, 1977). Because the 12-sec, non-intensive, aerobic period used in the current study was brief it is likely that this resynthesis was incomplete and anaerobic glycolysis had to provide the required energy for the next sprint. Glycogen, the substrate for anaerobic glycolysis, has been shown to be depleted during HIIE (Essén, 1978). This depletion of muscle glycogen may result in a greater reliance on fatty acid utilization as Essén et al. (1977) have shown that progressive depletion of PCr and glycogen inhibit glycolysis and lead to reduced lactate accumulation and increased fatty acid oxidation. The source of these FFAs utilized during HIIE is unclear but may include intramuscular triacylglycerol stores (Tremblay et al., 1994) and/or plasma FFAs, blood triglycerides, low density lipoproteins, and chylomicrons (Gaitanos, Williams, Boobis, & Brooks, 1993; McCartney et al., 1986; Spriet, Lindinger, McKelvie, Heigenhauser, & Jones, 1989; van Loon, 2004). Intramuscular triacylglycerol stores

are probably the source of fat oxidation during HIIE as the glycogen depletion occurring through interval sprinting is likely to impede glycolysis resulting in increased oxidation of intramuscular triacylglycerol (Essén, 1978).

The enhanced catecholamine response to HIIE appears to be a feature of this kind of exercise (Boutcher, 2011) and is in contrast to moderately hard aerobic exercise which results in a small increase in blood catecholamines (Zouhal et al., 2008). Catecholamines have been shown to be the major hormones initiating lipolysis and fat release from subcutaneous and intramuscular fat stores (Issekutz, 1978). Consequently, the HIIE-induced increase in catecholamines may have implications for long term fat loss (Boutcher, 2011).

After steady state exercise a significant increase in fat oxidation levels compared to the pre-exercise fasting state has been found (Kuo, Fattor, Henderson, & Brooks, 2005). During intense sprinting exercise glycogen stores suffer greater depletion than steady state exercise (Malatesta et al., 2009). Thus, the post-exercise period after HIIE should demonstrate enhanced lipid oxidation so that remaining carbohydrates can be utilized for glycogen resynthesis (Malatesta, Vismara, et al., 2009). Results of the present study support this notion as lower RER and greater fat oxidation rates occurred during the last 30 min of the post exercise period for both trained and untrained males. McGarvey et al (2005) have also shown that when total work was similar, intermittent compared to steady state exercise resulted in significantly lower RQ during a 2-h post-exercise recovery period. Results of the present study also show that after HIIE fat oxidation rate is enhanced throughout the post exercise period (minutes 45 to 75 post exercise) for both trained and untrained males. Only the values for fat oxidation rate at rest and during minutes 45 to 75 post

exercise were used because RER does not represent substrate utilization when blood and tissue lactate concentrations are changing (Malatesta, Werlen, Bulfaro, Cheneviere, & Borrani, 2009). Metabolic response monitoring over an hour recovery time is a limitation of this study as excess post-exercise oxygen consumption (EPOC) may continue to occur many hours after exercise (Tomlin & Wenger, 2001).

The active participants in this study were cyclists or tri-athletes performing at least three exercise sessions per week for the last year at a moderate to hard exercise intensity. That they possessed low resting heart rate and above average $\dot{V}O_{2max}$ supports the notion that they were trained. Their lower lactate levels during HIIE indicate a trained status and that they were better adapted to this form of intermittent sprint exercise even though none had carried out this kind of training previously. Despite their lack of cycle training, however, the inactive males also showed significant elevations in glycerol and catecholamines during HIIE and enhanced fat oxidation after HIIE.

In conclusion, one bout of HIIE resulted in enhanced catecholamine levels during and after exercise in trained and untrained males. This increase was accompanied by an elevation in lipolysis indicated by the increase in blood glycerol levels during HIIE. After HIIE enhanced fat oxidation occurred for both trained and untrained males.

Acknowledgments

We would like to thank Sonia Bustamante from the Bioanalytical Mass Spectrometry Facility (BMSF), University of New South Wales, for help with catecholamine analysis.

References

Borg, G. A. (1982). Psychophysical bases of perceived exertion. *Medicine and Science in Sports and Exercise, 14*(5), 377-381.

Boutcher, S. H. (2011). High-intensity intermittent exercise and fat loss. *Journal of Obesity, doi: 10.1155/2011/868305*.

Bracken, R., Linnane, D., & Brooks, S. (2009). Plasma catecholamine and nephrine responses to brief intermittent maximal intensity exercise. *Amino Acids, 36*(2), 209-217.

Essén, B. (1978). Glycogen depletion of different fibre types in human skeletal muscle during intermittent and continuous exercise. *Acta Physiologica Scandinavica, 103*(4), 446-455.

Essén, B., Hagenfeldt, L., & Kaijser, L. (1977). Utilization of blood-borne and intramuscular substrates during continuous and intermittent exercise in man. *The Journal of Physiology, 265*(2), 489-506.

Gaitanos, G. C., Williams, C., Boobis, L. H., & Brooks, S. (1993). Human muscle metabolism during intermittent maximal exercise. *Journal of Applied Physiology, 75*(2), 712-719.

Gibala, M. J., & McGee, S. L. (2008). Metabolic adaptations to short-term high-intensity interval training: a little pain for a lot of gain? *Exercise and Sport Sciences Reviews, 36*(2), 58-63

Gratas-Delamarche, A., Le Cam, R., Delamarche, P., Monnier, M., & Koubi, H. (1994). Lactate and catecholamine responses in male and female sprinters during a Wingate test. *European Journal of Applied Physiology and Occupational Physiology, 68*(4), 362-366.

Heydari, M., Freund, J., & Boutcher, S. H. (2012). The effect of high-intensity intermittent exercise on body composition of overweight young males. *Journal of Obesity, doi:10.1155/2012/480467*.

Issekutz, B. (1978). Role of beta-adrenergic receptors in mobilization of energy sources in exercising dogs. *Journal of Applied Physiology, 44*(6), 869-876.

Kuo, C. C., Fattor, J. A., Henderson, G. C., & Brooks, G. A. (2005). Lipid oxidation in fit young adults during postexercise recovery. *Journal of Applied Physiology, 99*(1), 349-356.

Malatesta, D., Vismara, L., Menegoni, F., Galli, M., Romei, M., & Capodaglio, P. (2009). Mechanical external work and recovery at preferred walking speed in obese subjects. *Medicine and Science in Sports and Exercise, 41*(2), 426-434.

Malatesta, D., Werlen, C., Bulfaro, S., Cheneviere, X., & Borrani, F. (2009). Effect of high-intensity interval exercise on lipid oxidation during postexercise recovery. *Medicine and Science in Sports and Exercise, 41*(2), 364-374.

McCartney, N., Spriet, L. L., Heigenhauser, G. J., Kowalchuk, J. M., Sutton, J. R., & Jones, N. L. (1986). Muscle power and metabolism in maximal intermittent exercise. *Journal of Applied Physiology, 60*(4), 1164-1169.

McGarvey, W., Jones, R., & Petersen, S. (2005). Excess post-exercise oxygen consumption following continuous and interval cycling exercise. *International Journal of Sport Nutrition and Exercise Metabolism, 15*(1), 28-37.

Murase, T., Nagasawa, A., Suzuki, J., Hase, T., & Tokimitsu, I. (2002). Beneficial effects of tea catechins on diet-induced obesity: stimulation of lipid catabolism in the liver. *International Journal of Obesity and Related Metabolic Disorders, 26*(11), 1459-1464.

Spriet, L. L., Lindinger, M. I., McKelvie, R. S., Heigenhauser, G. J., & Jones, N. L. (1989). Muscle glycogenolysis and H+ concentration during maximal intermittent cycling. *Journal of Applied Physiology, 66*(1), 8-13.

Starritt, E. C., Howlett, R. A., Heigenhauser, G. J. F., & Spriet, L. L. (2000). Sensitivity of CPT I to malonyl-CoA in trained and untrained human skeletal muscle. *American Journal of Physiology - Endocrinology and Metabolism, 278*(3), E462-E468.

Thomas, S., Reading, J., & Shephard, R. J. (1992). Revision of the physical activity readiness questionnaire (PAR-Q). *Canadian Journal of Sport Sciences, 17*(4), 338-345.

Tomlin, D. L., & Wenger, H. A. (2001). The relationship between aerobic fitness and recovery from high intensity intermittent exercise. *Sports Medicine 31*(1), 1-11.

Trapp, E. G., Chisholm, D. J., & Boutcher, S. H. (2007). Metabolic response of trained and untrained women during high-intensity intermittent cycle exercise. *American Journal of Physiology - Regulatory, Integrative and Comparative Physiology, 293*(6), R2370-R2375.

Trapp, E. G., Chisholm, D. J., Freund, J., & Boutcher, S. H. (2008). The effects of high-intensity intermittent exercise training on fat loss and fasting insulin levels of young women. *International Journal of Obesity, 32*(4), 684-691.

Tremblay, A., Després, J. P., Leblanc, C., Craig, C. L., Ferris, B., Stephens, T., et al. (1990). Effect of intensity of physical activity on body fatness and fat distribution. *The American Journal of Clinical Nutrition, 51*(2), 153-157.

Tremblay, A., Simoneau, J.-A., & Bouchard, C. (1994). Impact of exercise intensity on body fatness and skeletal muscle metabolism. *Metabolism: Clinical and Experimental, 43*(7), 814-818.

van Loon, L. J. C. (2004). Use of intramuscular triacylglycerol as a substrate source during exercise in humans. *Journal of Applied Physiology, 97*(4), 1170-1187.

Vincent, S., Berthon, P., Zouhal, H., Moussa, E., Catheline, M., Bentué-Ferrer, D., et al. (2004). Plasma glucose, insulin and catecholamine responses to a Wingate test in physically active women and men. *European Journal of Applied Physiology, 91*(1), 15-21.

Zouhal, H., Jacob, C., Delamarche, P., & Gratas-Delamarche, A. (2008). Catecholamines and the effects of exercise, training and gender. *Sports Medicine, 38*(5), 401-423.

Chapter 3: The Effect of High-Intensity Intermittent Exercise on Body Composition of Overweight Young Males

Mehrdad Heydari, Judith Freund, Stephen H. Boutcher

Published Citation: Heydari, M., et al., The effect of high-intensity intermittent exercise on body composition of overweight young males. Journal of Obesity. doi: 10.1155/2012/480467.

Author Contributions

MH collected data, contributed to writing the manuscript, produced results and figures and was responsible for carrying out the statistical analysis. JF organized body composition analysis. SHB conceived of the study and contributed to writing the manuscript.

Abstract

Objective: To determine the effect of a 12-week high intensity intermittent exercise (HIIE) intervention on total body, abdominal, trunk, visceral fat mass, and fat free mass of young overweight males.

Methods: Participants were randomly assigned to either an exercise or control group. The intervention group received HIIE three times per week, 20 min per session, for 12 weeks.

Results: Aerobic power improved significantly ($P < 0.001$) by 15% for the exercising group. Exercisers compared to controls experienced significant weight loss of 1.5 kg ($P < 0.005$) and a significant reduction in total fat mass of 2 kg ($P < 0.001$). Abdominal and trunk adiposity was also significantly reduced in the exercising group by 0.1 kg ($P < 0.05$) and 1.5 kg ($P < 0.001$). Also the exercise group had a significant ($P < 0.01$) 17% reduction in visceral fat after 12 weeks of HIIE, whereas waist circumference was significantly decreased by week six ($P < 0.001$). Fat free mass was significantly increased ($P < 0.05$) in the exercising group by 0.4 kg for the leg and 0.7 kg for the trunk. No significant change ($P > 0.05$) occurred in levels of insulin, HOMA-IR, and blood lipids.

Conclusions: Twelve weeks of HIIE resulted in significant reductions in total, abdominal, trunk, and visceral fat and significant increases in fat free mass and aerobic power.

Introduction

Obesity levels continue to increase in both developed and developing countries (Speiser et al., 2005). As being overweight is associated with numerous health problems effective fat loss strategies are required (Jakicic et al., 2001). Although dieting has been the major fat loss method aerobic exercise programs have been shown to increase cardiorespiratory fitness (Ross, et al., 2000) and preserve fat free mass (Evans et al., 1999). Most aerobic exercise interventions have consisted of moderate intensity steady state exercise, for about 30 to 40 min for 3 to 4 days per week, over a four to six month period. Disappointingly, these kinds of exercise programs have resulted in minimal fat loss (Boutcher & Dunn, 2009; Wu et al., 2009).

In contrast, high intensity intermittent exercise (HIIE) has been shown to result in greater fat loss (Boutcher, 2011). For example, Trapp et al. (2008) conducted a HIIE program in young women for 15 weeks with three 20-min sessions per week. HIIE consisted of an 8-s sprint followed by 12 s of low intensity cycling, repeated for 20 min. Another group of women carried out an aerobic cycling protocol for 40 min each session. Results showed that women in the HIIE group lost 2.5 kg of subcutaneous fat, whereas no change occurred with steady state aerobic exercise. Fat loss accruing through 15 weeks of HIIE was attained with 50% less exercise time commitment and a similar energy expenditure to that of steady state exercise. Importantly, the women in this study also showed a significant 0.6 kg increase in fat free mass (FFM) after HIIE, whereas FFM of the steady state exercise group was unchanged. The lack of increase in FFM accompanying steady state exercise is in agreement with prior research in this area (Stiegler & Cunliffe, 2006).

With regard to abdominal fat 15 weeks of HIIE led to a 0.15 kg reduction of fat in previously untrained young women (Trapp et al., 2008). As women in this study possessed moderate levels of abdominal fat it is feasible that the greater abdominal, trunk, and visceral fat of men may show greater reductions after exposure to HIIE. For example, Boudou et al. (2003) studied older type 2 diabetic males and found that after 8 weeks of HIIE abdominal adiposity was decreased by 44%. Whether regular HIIE will also reduce the abdominal and visceral fat of young non-diabetic but overweight males is undetermined.

Therefore, the purpose of this study was to examine the effects of 20 min bouts of HIIE, repeated three times weekly for 12 weeks, on body composition of overweight males. It was hypothesized that HIIE would result in significant reductions in total abdominal, trunk, and visceral fat and a significant increase in fat free mass and aerobic power.

Methods

Subjects

Forty six inactive, overweight men were recruited from a university population and randomly allocated into either exercise (n=25) or control groups (n=21). The exercisers and controls were similar in terms of age (24.7 ± 4.8 and 25.1 ± 3.9 years) and body mass index (BMI: 28.4 ± 0.5 and 29 ± 0.9 $kg \cdot m^{-2}$). The study received approval from a University Research Ethics Committee. Forty six subjects underwent initial testing, however, for various reasons five withdrew from the exercise group and three from the control group. There was no significant difference for any variable between the non-adherents and those males who completed the study.

Procedures

Subjects were advised to avoid strenuous activity and caffeine consumption for 24 hours prior to testing and attended the laboratory after a 10-hour overnight fast. Tests for all subjects in control and exercise groups were completed at the same time of day. The Physical Activity Readiness Questionnaire (Thomas et al., 1992) was filled out and information on subjects‘ personal and familial medical history obtained. Fasting blood (300 ml) was drawn at baseline, and at weeks 3, 6, and 12 from an antecubital vein in EDTA vacutainers. An automated enzymatic method (Cholestech LDX, USA) was applied to quantify blood lipid profiles and glucose concentrations from whole blood. The remaining whole blood in EDTA tubes was spun immediately in a chilled centrifuge (Model Megafuge 1.0R, Heraeus, Germany) at 4^{o}C and frozen at -86^{o} C for later analysis. Aerobic power was assessed using a TrueMax 2400 Metabolic Cart (ParvoMedics Inc, USA) and an electronically braked cycle ergometer, Monark 869 (Monark, Sweden). For subjects who could not achieve the criteria for $\dot{V}O_{2max}$, due to the strenuous nature of the exercise session $\dot{V}O_{2peak}$ was used as an indicant of aerobic power.

Resting Metabolic Rate (RMR)

Fasted subjects relaxed in a reclined position for 30 minutes. Resting heart rate, resting energy expenditure (REE), and $\dot{V}O_2$ and $\dot{V}CO_2$ were assessed using a metabolic cart (TrueMax 2400 Metabolic Cart, ParvoMedics Inc, USA). $\dot{V}O_2$ represents the rate of oxygen utilised by subjects during exercise whereas $\dot{V}CO_2$ represents the rate of carbon dioxide exhaled. Subjects were advised not to sleep and

breathe naturally during testing. The first 10 minutes of data collection were excluded from analysis to allow for subject stabilization.

Diet

Subjects in both exercise and control groups were advised to maintain their normal eating habits during the study. On their first and last visit to the laboratory subjects provided a 3-day diet inventory which was analyzed using diet analysis software (SERVE Nutrition Management Systems, Professional Edition, version 5, Australia).

Body Composition

A Dual Energy X-Ray Absorptiometry (DEXA) scan with a Lunar Prodigy scanner (software version 7.51, GE Corporation, USA) was used to measure body mass and percentage body fat. Fat mass (FM) along with FFM in kg were measured for the whole body. DEXA also provided information on abdominal and trunk fat, as indicators of central adiposity. Computerised tomography (CT) scans (Philips Gemini GXL 16, the Netherlands) was also used to measure abdominal and visceral fat distribution. Axial slices (3 x 10 mm) were performed through the abdomen at L2/L3 and L4/L5. Fat density of 0.9 mg/L was assumed (Lohman, Slaughter, Boileau, Bunt, & Lussier, 1984) and it was automatically selected at any tissue between -150 to -50 Hounsfield Units (HU). Gemini software (GXL Host system) was used to analyse the CT images. Abdominal, visceral, subcutaneous fat were determined at the levels of L2/L3 and L4/L5. BMI was calculated by dividing weight by height squared ($kg \cdot m^{-2}$).

High Intensity Intermittent Exercise Training

Subjects in the exercise group completed supervised exercise (8 s sprint, 12 s recovery) continuously throughout each 20-min session. The HIIE workload was set at 80-90% of each subject's heart rate (HR) peak at a cadence between 120 and 130 r.p.m and recovery was set at the same amount of resistance but at a cadence of 40 r.p.m. Subjects were instructed to keep their exercise intensity at a level necessary to produce a HR between 80-90% of HR peak. As subjects adapted to HIIE training workload was increased so HR stayed at the appropriate 80-90% HR peak level. HIIE was coordinated with a pre-recorded compact disc counting down each sprint in a 3-2-1 manner. Subjects performed a 5-min warm-up and cool-down on the bike prior to and after each exercise session. All training cycling data included continuous recording of HR and r.p.m, whereas rating of perceived exertion (Borg, 1982) (RPE) was assessed at 5-min intervals.

Assays

Insulin was measured using commercially available ELISA immunoassay kits. The degree of enzymatic turnover of the substrate was determined by dual wavelength absorbance measurement at 450 and 620 nm (Dako K6219, Denmark). HOMA-IR, an insulin resistance index (Stern et al., 2005), was calculated as follows:

HOMA-IR = [fasting insulin (μIU/ml) x fasting blood glucose ($mmol \cdot l^{-1}$)] / 22.5.

Statistical Analysis

Data were analysed with the Statistical Package for Social Science for Windows software (SPSS 18, USA). To examine changes after the intervention an analysis of

covariance (ANCOVA) was used to evaluate differences between the two groups for variables that did not violate ANCOVA assumptions. Pre intervention values were used as covariates. Where assumptions were violated an independent *t*-test was conducted on the difference scores. The statistical analysis was considered significant when the probability level was less than 0.05.

Results

There was no significant difference between the two groups for body mass, BMI (Table 3.1), and age prior to the training program.

Exercise Heart Rates, RPE, and Work Load

The average HR during the HIIE training sessions for the exercise group was 160 ± 9 beats min^{-1} which corresponded to 88% of HR peak and the average RPE was 13.6 ± 0.5. Maximal work load significantly increased in the exercise group ($P < 0.001$) by 43.5 watts (Table 3.1).

Response in Aerobic Power Following the Intervention

HIIE resulted in a significant increase in both absolute and relative $\dot{V}O_{2peak}$ ($P < 0.005$) with absolute $\dot{V}O_{2peak}$ being increased by 13% and relative $\dot{V}O_{2peak}$ by 15% (Table 3.1).

Table 3.1. Change in body composition, aerobic power, resting heart rate, RQ, resting energy expenditure, carbohydrate and fat oxidation for the high-intensity intermittent exercise and no exercise control group (N=38; mean and standard error)

	Exercise		**Control**	
	Pre*	**Post**	**Pre***	**Post**
Weight (kg)	87.8 ± 2.7	86.3 ± 2.7 **	89 ± 2.9	89.4 ± 3.1
BMI ($kg \cdot m^{-2}$)	28.4 ± 0.5	27.9 ± 0.5 **	29 ± 0.9	29.1 ± 0.9
Waist circumference (cm)	93.3 ± 1.4	89.8 ± 1.4 **	93.7 ± 1.9	95.1 ± 1.9
Fat mass (kg)	29.8 ± 1.6	27.8 ± 1.5 **	31.7 ± 2.2	31.8 ± 2.3
% Fat mass	34.8 ± 1.1	32.8 ± 1.1 **	36.3 ± 1.4	36.0 ± 1.5
Fat free mass (kg)	54.3 ± 1.5	55.5 ± 1.4 **	53.8 ± 1.3	54.2 ± 1.3
$\dot{V}O_{2peak}$ ($l\ min^{-1}$)	3.0 ± 0.1	3.4 ± 0.1 **	2.6 ± 0.1	2.7 ± 0.1
$\dot{V}O_{2peak}$ ($ml\ kg^{-1} min^{-1}$)	34.2 ± 1.0	39.4 ± 0.8 **	29.1 ± 1.3	30.6 ± 1.4
Work output (watts)	246.3 ± 8.1	289.8 ± 8.0 **	224.4 ± 7.3	225.9 ± 6.3
HR (bpm)	62.2 ± 2.5	57.9 ± 1.8 **	62.7 ± 2.0	63.7 ± 1.7
RQ	0.85 ± 0.01	0.83 ± 0.01 **	0.82 ± 0.02	0.86 ± 0.01
REE (Kcal/day)	1793 ± 54	1841 ± 56	1788 ± 58	1794 ± 53
Carbohydrate oxidation (g/day)	232.6 ± 14.3	201.5 ± 13.1 **	186.7 ± 22.3	252.1 ± 21.2
Fat oxidation (g/day)	93.8 ± 6.6	106.1 ± 6.5 **	110.2 ± 10.0	82.0 ± 10.9

*Pre vales were used as covariates for ANCOVA.

**$P < 0.05$, change in exercise group significantly greater compared to that of control group. BMI: body mass index; REE: resting energy expenditure; HR: heart rate; RQ: respiratory quotient; REE: resting energy expenditure.

Total Body Mass and Body fat Assessed by DEXA

Total body mass significantly decreased ($P < 0.005$) in the exercise group (Table 3.1) by 1.5 kg (2%), whereas total FM significantly decreased ($P < 0.005$) by 2.0 kg (6.7%; Figure 3.1). The FM of controls was unchanged after 12 weeks (Table 3.1). Percent body fat in exercisers at pre test was not correlated to changes in percent body fat after the intervention ($r = 0.17$, $P > 0.05$).

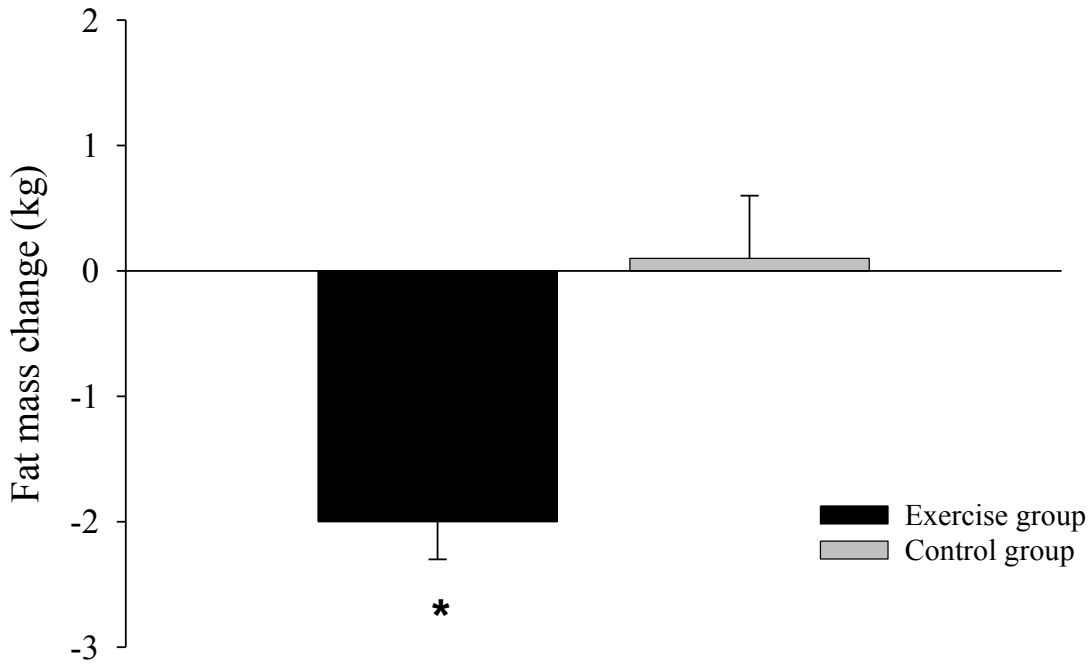

Figure 3.1. Total fat change for the high-intensity intermittent exercise and no exercise control groups (N=38, mean and standard error)

Abdominal and trunk fat assessed by DEXA

There was a significant decrease in abdominal fat by 0.14 kg (6.6%) for the exercise group ($P < 0.05$) with no change for the control group (Table 3.2). The exercise group also significantly decreased ($P < 0.001$) trunk fat by 1.4 kg (8.4%), whereas trunk fat was slightly increased in controls (Table 3.2).

Table 3.2. Regional changes in body composition for the high-intensity intermittent exercise and no exercise control groups (N=38; mean and standard error)

	Exercise		**Control**	
Region of fat mass	**Pre***	**Post**	**Pre***	**Post**
Leg fat (kg)	9.6 ± 0.8	9.0 ± 0.7	9.9 ± 0.7	9.8 ± 0.7
Leg lean (kg)	18.6 ± 0.6	19.0 ± 0.6 **	18.5 ± 0.6	18.5 ± 0.5
Arm fat (kg)	2.7 ± 0.2	2.5 ± 0.2 **	2.6 ± 0.1	2.7 ± 0.2
Arm lean (kg)	6.7 ±0.2	6.7 ± 0.2	6.4 ± 0.4	6.6 ± 0.3
Abdominal fat (kg)	2.3 ± 0.1	2.2 ± 0.1 **	2.4 ± 0.2	2.4 ± 0.2
Abdominal lean (kg)	3.7 ± 0.1	3.7 ± 0.1	3.5 ± 0.1	3.5 ± 0.1
Trunk fat (kg)	17.0 ± 0.9	15.5 ± 0.9 **	17.2 ± 1.2	17.3 ± 1.3
Trunk lean (kg)	24.9 ± 0.7	25.6 ± 0.7 **	24.0 ± 0.8	23.9 ± 0.7

*Pre vales were used as covariates for ANCOVA.
**$P < 0.05$, change significantly greater compared to that of control group.

Regional Body Composition Assessed by DEXA

There was no significant difference between groups in absolute FM loss in the leg ($P < 0.05$), whereas arm FM loss was greater for exercisers ($P < 0.01$; Table 3.2). Total, leg, and trunk FFM ($P < 0.05$) were significantly increased after 12 weeks of HIIE in the exercise group compared to the control group, whereas arm FFM ($P > 0.05$) showed no significant change after the intervention (Figure 3.2).

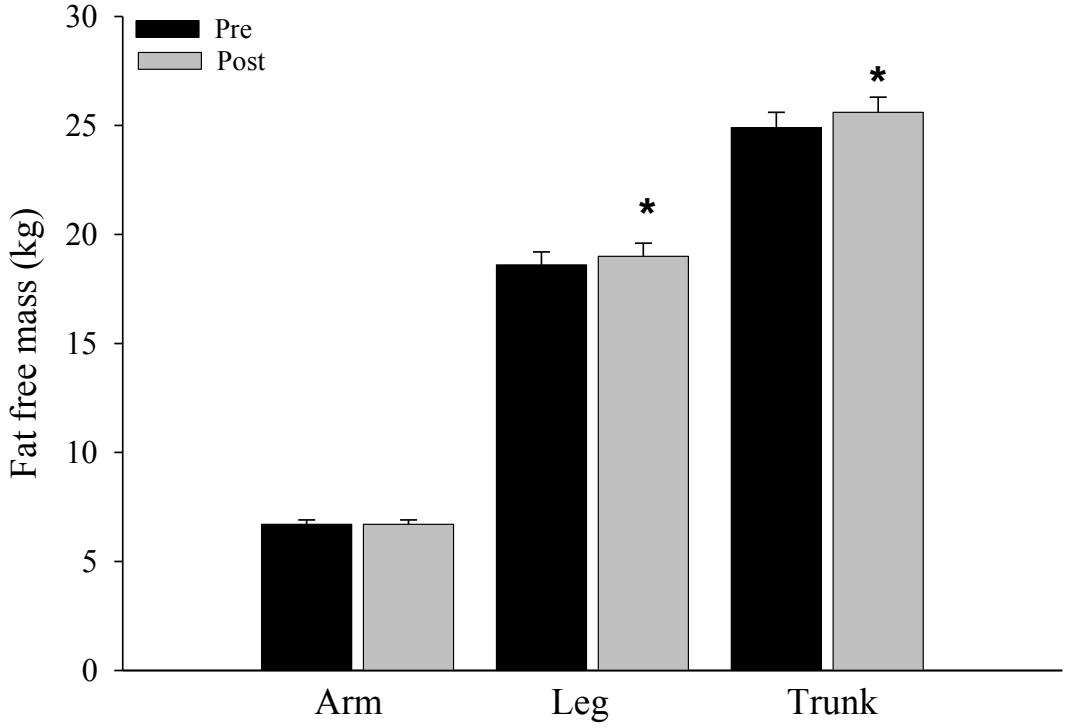

Figure 3.2. Fat free mass change for the high-intensity intermittent exercise groups (N=38; mean and standard error).
*Significant difference between pre and post testing ($P < 0.05$).

Abdominal, Visceral, and Subcutaneous Fat Mass Assessed by CT

Total, abdominal, visceral and subcutaneous FM at levels of L2/L3 and L4/L5 were significantly reduced ($P < 0.05$) after 12 weeks of HIIE compared to the control

group (Table 3.3). Abdominal fat decreased by 8.5% at L2/L3 and 6.6% at L4/L5. Visceral fat was significantly decreased ($P < 0.05$) by 17% at level L2/L3 and 10% at level L4/L5 (Table 3.3; Figure 3.3).

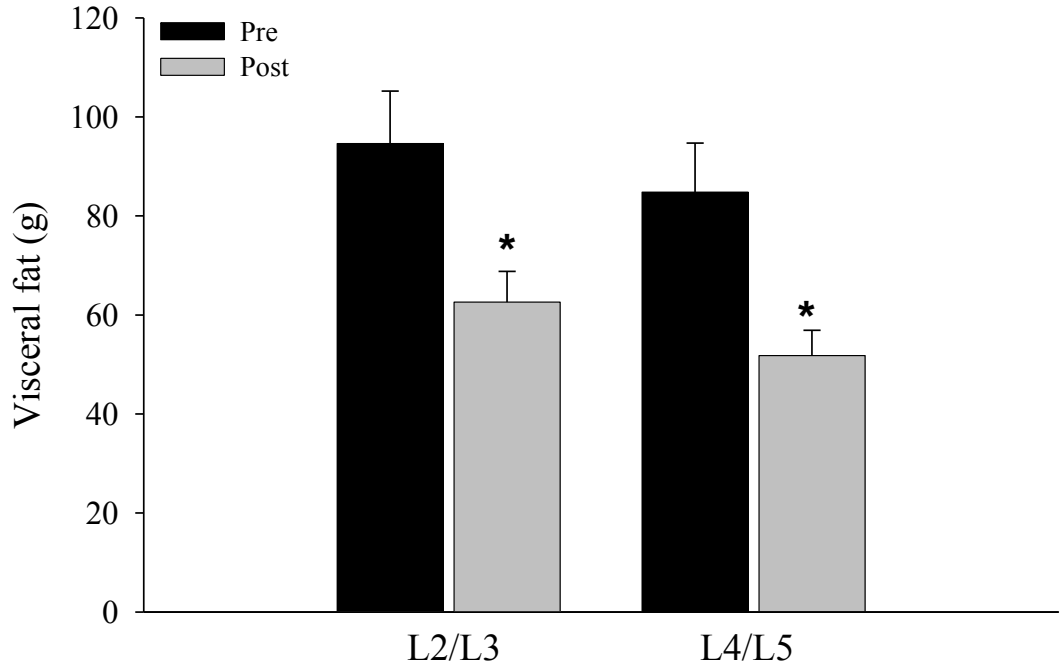

Figure 3.3. Visceral fat change for the high-intensity intermittent exercise and no exercise control groups (N=38; mean and standard error)

*Significantly different from control group ($P < 0.05$).

Table 3.3. Changes in computed tomography scan variables for the high-intensity intermittent exercise and no exercise control groups (N=38; mean and standard error)

	Exercise		**Control**	
	Pre*	**Post**	**Pre***	**Post**
L2/L3 total fat mass (g)	564.0 ± 22.3	538.0 ± 21.4 **	587.1 ± 26.3	591.0 ± 30.6
L2/L3 abdominal fat (g)	280.0 ± 21.4	256.1 ± 19.6 **	304.8 ± 26.5	311.9 ± 30.6
L2/L3 visceral fat (g)	94.6 ± 10.6	84.8 ± 9.9 **	102.1 ± 11.5	101.5 ± 11.4
L2/L3 subcutaneous (g)	177.3 ± 16.3	161.7 ± 14.7 **	194.2 ± 20.2	200.4 ± 23.4
L4/L5 total fat mass (g)	576.9 ± 24.3	555.7 ± 21.7 **	595.7 ± 28.4	602.2 ± 32.7
L4/L5 abdominal fat (g)	327.8 ± 23.0	306.3 ± 20.9 **	346.5 ± 27.3	355.5 ± 31.0
L4/L5 visceral fat (g)	62.6 ± 6.2	51.8 ± 5.1 **	69.7 ± 9.7	67.3 ± 8.4
L4/L5 subcutaneous (g)	259.7 ± 22.1	247.8 ± 20.0 **	271.7 ± 26.1	281.7 ± 27.7

*Pre vales were used as covariates for ANCOVA.
**$P < 0.05$, change significantly greater compared to that of control.

Change in Body Composition after 3, 6, and 9 Weeks

At weeks 3 and 6 there were no change in body mass and BMI, however, after 9 weeks body mass ($P < 0.005$) and BMI ($P < 0.005$) were significantly decreased. At the end of the trial body mass and BMI were significantly decreased ($P < 0.001$; Table 3.1), yet at week 6, WC was significantly lower than that at baseline, from 93.3 to 90.7 cm ($P < 0.001$). There was a further WC reduction from week 6 (90.7 cm) to week 12, (89.8 cm), which was not significant ($P > 0.05$). Also the major reduction in visceral fat brought about by HIIE appears to have occurred within the first six weeks as reduction in waist circumference was significantly correlated ($r = 0.57$, $P < 0.05$) with reduction in visceral fat (L4/L5) at week six.

Response in Resting Metabolic Rate Following the Intervention

After the intervention exercise subjects had significantly lower resting HR ($P < 0.01$) and respiratory quotient (RQ; $P < 0.01$) compared to subjects in the control group. There was no significant change in resting metabolic rate after the intervention ($P > 0.05$), however, subjects in the exercise group had significantly higher (13%) fat oxidation ($P < 0.001$) and lower carbohydrate oxidation ($P < 0.001$) after the intervention compared to the control group (Table 3.1).

Response in Blood Variables Following the Intervention

Fasting glucose, plasma insulin, glucose, HOMA-IR, and lipid levels were unchanged in the exercise compared to the control group ($P > 0.05$). For exercisers and controls pre-intervention levels of insulin, glucose, HOMA-IR, total cholesterol, triglyceride, low density lipoprotein, high density lipoprotein (Table 3.4) were within

the normal range for males of this age (Expert panel on detection, evaluation, and treatment of high blood cholesterol in adults, 2001).

Table 3.4. Glucose, insulin, HOMA-IR, and lipid change for the high-intensity intermittent exercise and no exercise control groups (N=38; mean and standard error)

	Exercise		**Control**	
	Pre	**Post**	**Pre**	**Post**
Glucose ($mmol \cdot l^{-1}$)	4.86 ± 0.14	4.97 ± 0.10	4.91 ± 0.14	4.91 ± 0.14
Insulin ($\mu U \cdot ml^{-1}$)	6.98 ± 0.66	6.72 ± 0.63	8.67 ± 0.90	8.29 ± 0.67
HOMA-IR	1.51 ± 0.15	1.47 ± 0.14	1.90 ± 0.24	1.82 ± 0.17
Total cholesterol ($mmol \cdot l^{-1}$)	4.18 ± 0.25	3.97 ± 0.24	4.59 ± 0.21	4.36 ± 0.18
Triglycerides ($mmol \cdot l^{-1}$)	1.20 ± 0.27	1.18 ± 0.36	1.52 ± 0.21	1.31 ± 0.18
High density lipoprotein ($mmol \cdot l^{-1}$)	1.31 ± 0.09	1.35 ± 0.09	1.08 ± 0.09	1.03 ± 0.08
Low density lipoprotein ($mmol \cdot l^{-1}$)	2.51 ± 0.16	2.35 ± 0.18	2.82 ± 0.18	2.81 ± 0.16
Very low density lipoprotein ($mmol \cdot l^{-1}$)	0.48 ± 0.07	0.43 ± 0.10	0.66 ± 0.09	0.56 ± 0.09
TC: HDL ratio	3.51 ± 0.32	2.99 ± 0.20	4.62 ± 0.31	4.52 ± 0.27

Table 3.5. Marco-nutrient levels before and after the 12-week intervention (N=38; mean and standard error)

	Exercise		**Control**	
	Pre	**Post**	**Pre**	**Post**
Kilojoules	8102 ± 428	8142 ± 414	8569 ± 343	8642 ± 343
% carbohydrate	43.6 ± 1.8	42.9 ± 1.5	46.2 ± 1.8	46.8 ± 1.9
% protein	19.8 ± 1.1	19.5 ± 1.1	18.2 ± 1.1	18.3 ± 1.5
% fat	36.4 ± 1.7	37.5 ± 1.4	35.7 ± 1.7	34.9 ± 1.4
% saturated fat	13.2 ± 0.8	13.0 ± 0.7	12.4 ± 0.7	11.3 ± 0.6
% monounsaturated fat	13.6 ± 0.7	14.2 ± 0.7	13.6 ± 0.7	13.8 ± 0.7
% polyunsaturated fat	6.3 ± 0.6	7.0 ± 0.7	6.3 ± 0.6	6.5 ± 0.7
Cholesterol (mg)	397.3 ± 37.5	394.7 ± 41.9	304.8 ± 41.6	381.8 ± 57.0
Fibre (g)	19.5 ± 2.5	19.5 ± 2.4	20.3 ± 2.4	21.4 ± 2.8
Sodium (mg)	2564 ± 320	2709 ± 335	2390 ± 345	2547 ± 335

Diet

There was no significant change in macro- or micronutrient content before or after the intervention for the 3-day diet diary of the exercise or control group. Macro-nutrient levels before and after the 12-week intervention are shown in Table 3.5.

Discussion

The major findings of this study were that HIIE significantly increased $\dot{V}O_{2peak}$ and significantly reduced total, abdominal, trunk, and visceral fat of young, overweight males. Also trunk and leg fat free mass was significantly increased after HIIE.

The 15% increase in $\dot{V}O_{2max}$ is similar to results of a previous study that used a 8 s/12 s HIIE protocol (Trapp et al., 2008). Talanian et al. (2007) also found that a HIIE program significantly elevated aerobic power. In this study the oxidative enzyme β-hydroxy-acyl-CoA dehydrogenase was used as a marker of mitochondrial volume and showed that intermittent sprinting enhances mitochondrial capacity. Different forms of HIIE have also been shown to significantly increase aerobic power (Gorostiaga, Walter, Foster, & Hickson, 1991; Weston, Helsen, MacMahon, & Kirkendall, 2004). Thus, collectively these data show that HIIE results in significant improvements in aerobic fitness. The improvement in cardiorespiratory fitness after HIIE is an attractive feature of this mode of exercise as aerobic fitness has been shown to be an important predictor of positive health (Blair, 2009).

That HIIE resulted in significant subcutaneous fat reduction supports prior research in women using a similar protocol (Trapp et al., 2008). Results of the present study with males extend these findings showing that HIIE is an effective and efficient way of controlling body composition in both genders. With regard to

abdominal fat, it has been found that 15 weeks of HIIE led to significantly reduced abdominal fat (0.15 kg) in untrained young women (Trapp et al., 2008). The 0.13 kg decrease in abdominal fat and 1.5 kg decrease in trunk fat found in the current study demonstrates that this effect is also present in young males and supports findings by Boudou et al. (2003) who showed that 8 weeks of HIIE significantly reduced abdominal adiposity in older diabetic males.

The significant 17% decrease in visceral fat found in the present study extends the findings of Mourier et al. (1997) who showed a significant reduction in visceral fat, measured by MRI, following an exercise regimen consisting of steady state exercise and HIIE for 8 weeks. These findings also add to the results of studies that have shown that aerobic training interventions decrease visceral adipose tissue (Ohkawara et al., 2007). The present study, however, appears to be the first to examine the effects of 20-min bouts of HIIE on visceral fat of young males. As visceral compared to overall obesity is more strongly associated with cardiovascular disease risk (Kuk et al., 2006) the ability of HIIE to reduce visceral fat may have positive health implications. For example, it was shown that reduction in visceral fat was associated with improvement in glucose and lipid metabolism, (Ross et al., 2000) whereas Okauchi et al. (2007) found that a reduction in visceral fat lowered risk of atherosclerotic cardiovascular disease. Interestingly, Ohkawara et al. (2007) estimated the optimal dose of aerobic exercise necessary to significantly reduce visceral fat and concluded that 3,780 kcal expended per week was needed. As an exercise session (e.g., cycling on a stationary cycle ergometer) lasting around an hour at a moderate exercise intensity expends about 520-550 kcal then to reach an optimal exercise caloric expenditure of 3,780 kcal per week an individual would have to

perform approximately seven one-hour exercise sessions per week. In contrast, subjects in the present study exercised for only one hour per week. Also Donnelly et al. (2003) conducted a 16-month, 5 hours of aerobic exercise per week program with overweight young males and recorded a 23% decrease in visceral fat. Thus, it appears HIIE can bring about significant decreases in visceral fat with programs that are both significantly shorter in length (e.g., 16 months versus 3 months) and have less exercise commitment per week (5 hours versus 1 hour). Also the major decrease in visceral fat brought about by HIIE may have occurred within the first six weeks as reduction in visceral fat was correlated with reduction in waist circumference (r = 0.57, $P < 0.05$) at week six after which waist circumference did not further decrease.

Although the effect of HIIE on FFM has not been extensively examined one study using DEXA found that trunk muscle mass was significantly increased in young females by 0.6 kg after 15 weeks of HIIE, (Trapp et al., 2008) whereas another study using MRI showed a significant increase in thigh muscle cross sectional area of older males and females after HIIE (Boudou et al., 2003). The 1.2 kg increase in total FFM found after HIIE in the present study confirms the ability of this type of exercise to increase FFM. However, the length of this 12-week intervention was 3 weeks less than that conducted by Trapp et al. (2008) that used females as subjects. As exercise HRs and relative exercise intensity of the two trials were similar it appears that males responded with a similar decrease in total fat but a greater increase in FFM after HIIE. FFM increase in the trunk after HIIE was 0.7 kg for males and 0.4 kg for females, whereas in the legs was 0.4 kg for males and 0.1 kg for females. Thus, males compared to females recorded greater increases in FFM in the trunk and legs. This characteristic may be important for fat loss programs as it

has been shown that muscle mass is typically decreased after dietary restriction (Saris, 1993) and is typically unchanged after aerobic exercise training (Stiegler & Cunliffe, 2006). The significant increase in leg FFM may also reflect important metabolic adaptations resulting in enhanced insulin sensitivity (Burgomaster et al., 2005).

Possible mechanisms underlying the HIIE-induced fat loss effect are undetermined but may include enhanced exercise and post exercise fat oxidation and suppressed post exercise appetite (Boutcher, 2011). For example, Burgomaster et al. (2005) and Talanian et al. (2007) have shown that 6 to 7 sessions of HIIE had significant increases in whole body and skeletal muscle capacity for fatty acid oxidation. The excess post exercise oxygen consumption response to HIIE does not appear to have been examined; however, it is feasible that the significant levels of catecholamines generated during acute HIIE (Trapp et al., 2007) could elevate post exercise fat oxidation. The significant catecholamine response to HIIE is in contrast to moderate, steady state aerobic exercise that results in small increases in epinephrine and norepinephrine (Zouhal et al., 2008). Also the high levels of catecholamines produced by HIIE may underlie its ability to reduce visceral fat as catecholamines have been shown to drive lipolysis and are mainly responsible for fat release from both visceral fat stores (Issekutz, 1978). Also significantly more β-adrenergic receptors have been found in visceral compared to subcutaneous fat (Rebuffé-Scrive et al., 1989) suggesting that HIIE may have greater potential than steady-state exercise (e.g., jogging, cycling) to reduce visceral fat. Furthermore, increased fat oxidation after HIIE may occur as a result of the need to remove lactate and H^+ and to re-synthesize glycogen. Uncoupled respiration, protein turnover, and

sympathetic nervous system activity may also contribute to increased energy expenditure and fat oxidation after exercise (Stiegler & Cunliffe, 2006). Finally, HIIE may also have a suppressive effect on appetite as exposing rats to hard exercise has been repeatedly reported to reduce food intake (Bilski, Teleglów, Zahradnik-Bilska, Dembiński, & Warzecha, 2009).

As this HIIE program required minimal time commitment it has implications regarding subject compliance with exercise interventions. Thus, physical activity prescriptions, which require the least effort, while still producing adequate reductions in subcutaneous and visceral fat are likely to be optimal (Stiegler & Cunliffe, 2006) and HIIE would seem to fall under this category as subject‘s total exercise commitment was 60 min per week. In conclusion, 20 min of HIIE, performed three times per week for 12 weeks, resulted in significant reductions in total body, abdominal, trunk, and visceral fat and a significant increase in fat free mass of overweight young males.

Acknowledgements

The authors wish to thank Diabetes Australia for supporting this project (Grant no. RM06599) and also would like to thank Chau Tran, Joshua Lane, Roger Burrell, and Lucas Webb for help with data collection.

References

Bilski, J., Teległów, A., Zahradnik-Bilska, J., Dembiński, A., & Warzecha, Z. (2009). Effects of exercise on appetite and food intake regulation. *Medicina Sportiva, 13*(2), 82-94.

Blair, S. N. (2009). Physical inactivity: the biggest public health problem of the 21st century. *British Journal of Sports Medicine, 43*(1), 1-2.

Borg, G. A. (1982). Psychophysical bases of perceived exertion. *Medicine and Science in Sports and Exercise, 14*(5), 377-381.

Boudou, P., Sobngwi, E., Mauvais-Jarvis, F., Vexiau, P., & Gautier, J. (2003). Absence of exercise-induced variations in adiponectin levels despite decreased abdominal adiposity and improved insulin sensitivity in type 2 diabetic men. *European Journal of Endocrinology, 149*(5), 421-424.

Boutcher, S. H. (2011). High-intensity intermittent exercise and fat loss. *Journal of Obesity, doi: 10.1155/2011/868305.*

Boutcher, S. H., & Dunn, S. L. (2009). Factors that may impede the weight loss response to exercise-based interventions. *Obesity Reviews, 10*(6), 671-680.

Burgomaster, K. A., Hughes, S. C., Heigenhauser, G. J. F., Bradwell, S. N., & Gibala, M. J. (2005). Six sessions of sprint interval training increases muscle oxidative potential and cycle endurance capacity in humans. *Journal of Applied Physiology, 98*(6), 1985-1990.

Donnelly, J. E., Hill, J. O., Jacobsen, D. J., Potteiger, J., Sullivan, D. K., Johnson, S. L., et al. (2003). Effects of a 16-month randomized controlled exercise trial on body weight and composition in young, overweight men and women: The midwest exercise trial. *Archives of Internal Medicine, 163*(11), 1343-1350.

Expert panel on detection, evaluation, and treatment of high blood cholestrol in adults. (2001). Executive summary of the third report of the national cholesterol education program (NCEP) Expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III). *The Journal of the American Medical Association, 285*(19), 2486-2497.

Evans, E. M., Saunders, M. J., Spano, M. A., Arngrimsson, S. A., Lewis, R. D., & Cureton, K. J. (1999). Effects of diet and exercise on the density and composition of the fat-free mass in obese women. *Medicine and Science in Sports and Exercise, 31*(12), 1778- 1787.

Gorostiaga, E., Walter, C., Foster, C., & Hickson, R. (1991). Uniqueness of interval and continuous training at the same maintained exercise intensity. *European Journal of Applied Physiology and Occupational Physiology, 63*(2), 101-107.

Issekutz, B. (1978). Role of beta-adrenergic receptors in mobilization of energy sources in exercising dogs. *Journal of Applied Physiology, 44*(6), 869-876.

Jakicic, J. M., Clark, K., Coleman, E., Donnelly, J. E., Foreyt, J., Melanson, E., et al. (2001). American college of sports medicine position stand. Appropriate

intervention strategies for weight loss and prevention of weight regain for adults. *Medicine and Science in Sports and Exercise, 33*(12), 2145-2156.

Kuk, J. L., Katzmarzyk, P. T., Nichaman, M. Z., Church, T. S., Blair, S. N., & Ross, R. (2006). Visceral fat is an independent predictor of all-cause mortality in men. *Obesity, 14*(2), 336-341.

Lohman, T., Slaughter, M., Boileau, R., Bunt, J., & Lussier, L. (1984). Bone mineral measurements and their relation to body density in children, youth and adults. *Human Biology 56*(4), 667 -679

Mourier, A., Gautier, J.-F., Kerviler, E. D., Bigard, A. X., Villette, J.-M., Garnier, J.-P., et al. (1997). Mobilization of visceral adipose tissue related to the improvement in insulin sensitivity in response to physical training in NIDDM: Effects of branched-chain amino acid supplements. *Diabetes Care, 20*(3), 385-391.

Ohkawara, K., Tanaka, S., Miyachi, M., Ishikawa-Takata, K., & Tabata, I. (2007). A dose-response relation between aerobic exercise and visceral fat reduction: systematic review of clinical trials. *International Journal of Obesity, 31*(12), 1786-1797.

Okauchi, Y., Nishizawa, H., Funahashi, T., Ogawa, T., Noguchi, M., Ryo, M., et al. (2007). Reduction of visceral fat is associated with decrease in the number of metabolic risk factors in Japanese men. *Diabetes Care, 30*(9), 2392-2394.

Rebuffé-Scrive, M., Andersson, B., Olbe, L., & Björntorp, P. (1989). Metabolism of adipose tissue in intraabdominal depots of nonobese men and women. *Metabolism: Clinical and Experimental, 38*(5), 453-458.

Ross, R., Dagnone, D., Jones, P. J. H., Smith, H., Paddags, A., Hudson, R., et al. (2000). Reduction in obesity and related comorbid conditions after diet-induced weight loss or exercise-induced weight loss in men. *Annals of Internal Medicine, 133*(2), 92-103.

Saris, W. (1993). The role of exercise in the dietary-treatment of obesity. *International Journal of Obesity 17*, S17- 21.

Speiser, P. W., Rudolf, M. C. J., Anhalt, H., Camacho-Hubner, C., Chiarelli, F., Eliakim, A., et al. (2005). Childhood obesity. *Journal of Clinical Endocrinology and Metabolism, 90*(3), 1871-1887.

Stern, S. E., Williams, K., Ferrannini, E., DeFronzo, R. A., Bogardus, C., & Stern, M. P. (2005). Identification of individuals with insulin resistance using routine clinical measurements. *Diabetes, 54*(2), 333-339.

Stiegler, P., & Cunliffe, A. (2006). The role of diet and exercise for the maintenance of fat-free mass and resting metabolic rate during weight loss. *Sports Medicine, 36*(3), 239-262.

Talanian, J. L., Galloway, S. D. R., Heigenhauser, G. J. F., Bonen, A., & Spriet, L. L. (2007). Two weeks of high-intensity aerobic interval training increases the capacity for fat oxidation during exercise in women. *Journal of Applied Physiology, 102*(4), 1439-1447.

Thomas, S., Reading, J., & Shephard, R. J. (1992). Revision of the physical activity readiness questionnaire (PAR-Q). *Canadian Journal of Sport Sciences, 17*(4), 338-345.

Trapp, E. G., Chisholm, D. J., & Boutcher, S. H. (2007). Metabolic response of trained and untrained women during high-intensity intermittent cycle exercise. *American Journal of Physiology - Regulatory, Integrative and Comparative Physiology, 293*(6), R2370-R2375.

Trapp, E. G., Chisholm, D. J., Freund, J., & Boutcher, S. H. (2008). The effects of high-intensity intermittent exercise training on fat loss and fasting insulin levels of young women. *International Journal of Obesity, 32*(4), 684-691.

Weston, M., Helsen, W., MacMahon, C., & Kirkendall, D. (2004). The impact of specific high-intensity training sessions on football referees‘ Fitness Levels. *The American Journal of Sports Medicine, 32*(1 suppl), 54S-61S.

Wu, T., Gao, X., Chen, M., & Van Dam, R. M. (2009). Long-term effectiveness of diet-plus-exercise interventions vs. diet-only interventions for weight loss: a meta-analysis. *Obesity Reviews, 10*(3), 313-323.

Zouhal, H., Jacob, C., Delamarche, P., & Gratas-Delamarche, A. (2008). Catecholamines and the effects of exercise, training and gender. *Sports Medicine, 38*(5), 401-423.

Chapter 4: High-Intensity Intermittent Exercise and Cardiovascular and Autonomic Function

Mehrdad Heydari, Yati N. Boutcher, Stephen H. Boutcher

Published Citation: Heydari, M., et al., High-intensity intermittent exercise and cardiovascular and autonomic function. Clinical Autonomic Research. doi: 10.1007/s 10286-012-0179-1

Author Contributions

MH collected data, wrote the manuscript, produced results and figures and was responsible for carrying out the statistical analysis. SHB conceived of the study and edited the manuscript. YNB contributed to editing the manuscript.

Abstract

Objective: The effect of 12 weeks of high-intensity intermittent exercise (HIIE) on cardiac, vascular, and autonomic function of young males was examined.

Methods: Thirty-eight young men with a BMI of 28.7±3.1 $kg \cdot m^{-2}$ and age 24.9±4.3 years were randomly assigned to either an HIIE or control group. The exercise group underwent HIIE three times per week, 20 min per session, for 12 weeks. Aerobic power and a range of cardiac, vascular, and autonomic measures were recorded before and after the exercise intervention.

Results: The exercise, compared to the control group, recorded a significant reduction in heart rate accompanied by an increase in stroke volume. For the exercise group forearm vasodilatory capacity was significantly enhanced, $P < 0.05$. Arterial stiffness, determined by pulse wave velocity and augmentation index, was also significantly improved, after the 12-week intervention. For the exercise group heart period variability (low and high frequency power) and baroreceptor sensitivity were significantly increased.

Conclusions: HIIE induced significant cardiac, vascular, and autonomic improvements after 12 weeks of training.

Introduction

The majority of studies examining resting cardiac, vascular, and autonomic change to chronic exercise have focused on steady state aerobic training such as regular running and cycling. The major cardiac adaptations to these forms of aerobic exercise have included a lowering of resting heart rate and an increase in stroke volume (Wilmore et al., 2001). Vascular adaptations to aerobic exercise have been examined by assessing variables such as limb blood flow, limb vasodilatory capacity, and arterial stiffness. Limb blood flow and vasodilatory capacity, indicants of the ability of the arterioles to dilate, has been enhanced by aerobic training in the exercising (Martin et al., 1990) and non exercising muscle (Silber et al., 1991). Boutcher and Boutcher (2005) also found higher vasodilatory capacities in forearm and leg muscles in runners compared with the untrained. Regular aerobic training has also been shown to reduce arterial stiffness in healthy young, older, congestive heart failure, and diabetic adults.

Autonomic adaptations occurring with aerobic exercise include changes in vagal influence on the heart and arterial baroreceptor sensitivity (BRS). Heart period variability (HPV) has typically been used to assess cardiac vagal influence. Vagal influence on the heart, as measured by HPV, has been shown to increase after steady state endurance exercise training (Tulppo et al., 2003). A significant effect of exercise training on resting high frequency power was found in a meta-analysis with the greatest effect shown in younger participants and longer interventions (Sandercock et al., 2005). With regard to aerobic exercise training and BRS some researchers have found an increase in arterial BRS following endurance training

(Monahan et al., 2000), whereas others have reported either no change or a decrease (Bowman et al., 1997).

In contrast to aerobic exercise examination of the resting cardiac, vascular, and autonomic function response to other forms of exercise has been scant. For example, little is known about the potential resting cardiovascular changes that may occur after exposure to regular high-intensity intermittent exercise (HIIE). HIIE typically consists of repeated short sprints on a cycle ergometer (6 s to 30 s) followed by a brief period of low intensity cycling (Boutcher, 2011a). HIIE has been shown to result in significant increases in both anaerobic and aerobic fitness (Boutcher, 2011a). In a series of studies Gibala and colleagues (2012) have examined skeletal muscle adaptations to HIIE and have demonstrated that HIIE consistently elevates maximal activity and protein content of a number of mitochondrial enzymes. Participation in HIIE also results in significant decreases in total and abdominal fat (Boutcher, 2011a). Also, compared to steady state aerobic exercise, HIIE has been shown to have a significantly greater acute impact on the autonomic nervous system, determined by heart rate and plasma catecholamine response to a single bout of exercise (Trapp et al., 2007). Although the effect of long term HIIE training on autonomic function has not been examined it has been shown that high-intensity endurance training was more effective for enhancing cardiac vagal control than a low intensity exercise program (Martinmäki et al., 2008). Thus, carrying out more intensive exercise training may induce greater autonomic and cardiovascular adaptations. Therefore, the aim of this study was to examine the effect of 12 weeks of HIIE on resting heart rate, stroke volume, limb blood flow, limb vasodilatory capacity, arterial stiffness, HPV, and BRS in young males.

Methods

This study was an open-label, parallel-group with allocation concealment (sealed envelopes) individually randomized trial. The allocation ratio was 1:1 for two groups. The study took place in the exercise physiology laboratories, University of New South Wales, Sydney, Australia from March 2009 to November 2010. The trial has been registered in the Australian New Zealand Clinical Trials Registry (registration number: ACTRN12612001003864).

Subjects

After obtaining approval from a University Ethics Committee, males aged 18-35 years and a BMI of 23-35 $kg \cdot m^2$ were invited to participate in the intervention through advertisements and notice boards placed in public areas and student magazines. Study inclusion criteria included being a non-smoker, being physically inactive, not being diagnosed with any type of cardiovascular and pulmonary disease, and not being on any regular medication. Out of 38 participants recruited and consented, 20 participants were randomly allocated to an intervention group to receive a 12-week supervised HIIE training and 18 participants were assigned to a control group and were asked to maintain their normal daily routine (Figure 4.1). For a variety reasons five subjects withdrew from the exercise group and three from the control group. There was no significant difference for any variable between the drop-outs and subjects who completed the study. Allocation concealment was conducted by randomly picking a piece of paper labeled ―exe" or ―eon" from the subject pool in an envelope. The trial was not blinded for participants because of the nature of the exercise intervention, but outcome assessors and data analyzers were

blinded. Subject number was based on results of prior research examining aerobic power increase to the same exercise protocol (Trapp et al., 2008). Aerobic power increase to HIIE produced a large effect size of .9. Thus, based on a moderately large effect size, sample sizes of 10-12 males per group provides a statistical power of 0.8 at an alpha of $P < 0.05$. Consequently, having greater than 16 males in each group provided a buffer for drop-out.

Pre and Post Testing

Participant recruitment, assignment, and drop-out are shown in Figure 4.1. Pre testing involved participants coming to the laboratory after an overnight fast between 7 am and 11 am. The testing room was quiet and was maintained at a constant ambient air temperature of 22-23°C. Participants were also instructed to abstain from caffeine, tobacco, and alcohol for at least 8 hrs before testing to avoid any confounding effects of stimulants or depressants on autonomic function. Participants were instructed not to exercise within 24 hrs of the test to eliminate the residual effects of exercise.

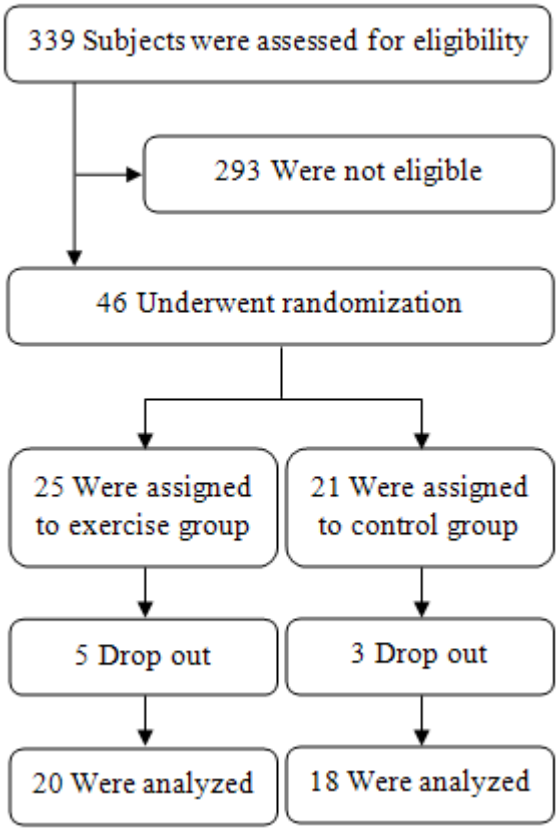

Figure 4.1. Flow chart of participant recruitment, assignment and drop-out

HIIE Training Program

The intervention group performed supervised HIIE training on a cycle ergometer (Monark 828E) at a frequency of 3 times a week for 12 weeks. Participants were instructed to cycle at a workload of 80-90% of their maximum heart rate with a cadence between 120 and 130 rpm. During recovery, the cadence was reduced to 40 rpm with no change in resistance. Each exercise session consisted of a 5-min warm-up, 20-min of 8 s sprint and a12-s recovery, and a 5-min cool-down. Workload was gradually increased during the trial depending on the participant‘s heart rate which was monitored by a Polar Heart Rate monitor (Polar Electro Oy, Kempele, Finland).

Heart Period Variability (HPV)

Resting supine R-R intervals were recorded for 30 min, at a sampling rate of 1000 Hz, using the Polar RS800CX Heart Rate Monitor (Polar Electro Oy, Kempele, Finland) and data were analyzed with the Polar ProTrainer 5^{TM} software. Total power (TP), parasympathetic (HF, RMSSD, and pNN50) and measures of cardiac sympathetic influence (VLF, LF, and TP) of HPV were evaluated.

Arterial Baroreflex Sensitivity

Arterial BRS was determined under spontaneous behaviour using the sequence method (BaroCor™ AFx, AtCor Medical, Australia). This technique has been shown to be a valid and reproducible method for determining arterial BRS in humans (Parlow, Viale, Annat, Hughson, & Quintin, 1995).

Augmentation Index (AIx)

Blood pressure was recorded (BP Monitor; UNSW) with a wrist sensor placed on the left wrist radial pulse (Model 7000, Colin Medical, Japan). Central aortic waveforms were derived from the recorded radial arterial pressure waveform by using SphygmoCor software (SphygmoCor, SCOR-2000, AtCor Medical, Australia). The use of a transfer function (SphygmoCor) has been validated against directly measured central aortic pressure (Söderström, Nyberg, O'Rourke, Sellgren, & Pontén, 2002). An index of arterial stiffness (AIx) was defined as the ratio of the difference between the first (early systolic shoulder) and second peaks (late systolic shoulder) to pulse pressure and was expressed as a percentage. Because AIx is influenced by heart rate it was normalized to a rate of 75 b·min^{-1}.

Pulse Wave Velocity (PWV)

Central PWV was measured between the carotid and femoral arteries using a SphygmoCor® pulse wave velocity system model SCOR-Vx and was analyzed with SphygmoCor Cardiovascular Management Suite (CvMS) software version 8. An ECG lead II was recorded during the test as well as pre systolic and diastolic blood pressure.

Impedance Cardiography (ICG)

ICG was measured using a Minnesota impedance cardiograph (Model 304B; Surcom, Minneapolis MN) and included the recoding of heart rate, stroke volume, cardiac output, pre-ejection period (PEP), and left ventricle ejection time (LVET). Data were analyzed using cardiac output program software (COP, Microtronics Inc, Chapel Hill, NC).

Forearm Blood Flow and Peak Forearm Blood Flow

FBF was assessed by using a plethysmograph (Model EC4, D.E. Hokansen, Inc, Bellvue, WA, USA) as has been previously described (Boutcher, Hopp, & Boutcher, 2011b). Peak FBF was used as a measure of vasodilatory capacity and was determined by a reactive hyperaemia condition using the venous occlusion technique. It has been shown that 5 min of blood flow occlusion induces a maximal vascular response. More details of peak FBF measurement can be found in a previously published article (Boutcher, et al., 2011b). Forearm vascular resistance was also calculated by dividing mean arterial pressure (MAP) by FBF.

Arterial Blood Pressure and R-R Interval

Participants‘ pulse rates were obtained using the standard lead II of a surface electrocardiogram (LifePulse model LP10, HME), and beat-to-beat blood pressure was measured continuously using the Colin Jentow (Model 7000, Colin Medical, Japan).

Aerobic Power

Maximal or peak oxygen consumption was measured using an electrically braked cycle ergometer (Ergomedic 839E, Monark) and open-circuit spirometry (True Max 2400, ParvoMedics). Participants cycled at a cadence of 70 rpm until volitional exhaustion. A ramp protocol was used, after a 3-min warm-up period at 30 W, the workload increased by 1 W every 2 s. Heart rate was monitored by the Polar SC800 heart rate monitor. The end point was achieved when the participant was unable to continue.

Statistical Analysis

Data were analyzed using Statistical Package for Social Science for Windows software (SPSS 18, USA). To examine changes after the intervention an analysis of covariance (ANCOVA) was used to evaluate differences between the two groups for variables that did not violate ANCOVA assumptions. Pre-intervention values were used as covariates. Where assumptions were violated an independent *t*-test was conducted on the difference scores. No primary or secondary outcomes were defined. The statistical analysis was considered significant when the probability level was less than 0.05. Effect sizes were calculated using partial eta squared (η^2) with values of

0.1, 0.3, and above 0.5 considered to be a small, medium, and large effect. Results are reported as mean and standard deviation of the mean.

Results

Exercise Heart Rates and Power Output

The average heart rate during the HIIE training sessions for the exercise group was 160 ± 9 b·m^{-1} which corresponded to 88% of HR peak. The average power output during the HIIE training sessions for the exercise group was 200 ± 10 W which corresponded to 81% of maximal power output.

Body Mass and Aerobic Power

Compared to controls the exercise group‘s body mass was significantly decreased (P = 0.001, η^2 = 0.20) and aerobic power was significantly increased (P = 0.001, η2 = 0.39) by 15% for the exercise group (Table 4.1).

Table 4.1. Changes in body composition and aerobic power after the 12-week intervention (mean and standard deviation)

	Exercise		**Control**	
Variables	**Pre**	**Post**	**Pre**	**Post**
Weight (kg)	87.8 ± 11.7	86.3 ± 11.6 *	89 ± 12.4	89.4 ±12.9
BMI (kg.m^{-2})	28.4 ± 2.4	27.9 ± 2.4 *	29 ± 3.9	29.1 ± 3.8
Waist circumference (cm)	93.3 ± 6.1	89.8 ± 6.4 *	93.7 ± 8.0	95.1 ± 8.2
$\dot{V}O_{2max}$ (l.min^{-1})	3.0 ± 0.6	3.4 ± 0.6 *	2.6 ± 0.5	2.7 ± 0.5
$\dot{V}O_{2max}$ (ml.kg^{-1}.min^{-1})	34.2 ± 4.4	39.4 ± 3.5 *	29.0 ± 5.0	30.4 ± 5.5

BMI: body mass index; $\dot{V}O_{2max}$: maximal oxygen uptake.
*P < 0.01, change greater compared to that of control.

Cardiac Response

Resting heart rate was significantly reduced in the exercise compared to the control group after 12 weeks of HIIE ($P = 0.001$, $\eta^2 = 0.37$), whereas stroke volume increased significantly ($P = 0.000$, $\eta^2 = 0.45$) after the intervention. Pre-ejection period (PEP) did not show a significant change ($P = 0.142$, $\eta^2 = 0.07$) but left ventricular ejection time (LVET) significantly increased ($P = 0.003$, $\eta^2 = 0.26$) and PEP/LVET ratio was significantly decreased ($P = 0.014$, $\eta^2 = 0.19$; Table 4.2).

Table 4.2. Changes in cardiac measures after the 12-week intervention (mean and standard deviation)

	Exercise		**Control**	
Variables	**Pre**	**Post**	**Pre**	**Post**
HR ($b.m^{-1}$)	67.4 ± 9.7	61.2 ± 8.9 *	68.9 ± 7.7	70.4 ± 6.7
SV (ml)	77.2 ± 24.9	90.4 ± 26.3 *	75.6 ± 18.9	70.2 ± 20.9
PEP (ms)	133.0 ± 12.6	129.2 ± 16.2	126.0 ± 16.3	130.1 ± 9.9
LVET (ms)	271.5 ± 26.5	286.8 ± 26.0 *	281.1 ± 18.5	273.4 ± 16.6
PEP/LVET	0.49 ± 0.06	0.45 ± 0.07 *	0.45 ± 0.07	0.48 ± 0.05

HR: heart rate; SV: stroke volume; PEP: pre-ejection period; LVET: left ventricular ejection time. *$P < 0.05$, change greater compared to that of control.

Blood pressure

Systolic blood pressure (SBP), $P = 0.005$ ($\eta^2 = 0.21$) diastolic blood pressure (DBP), $P = 0.003$ ($\eta2 = 0.23$) and mean arterial pressure (MAP), $P = 0.001$ ($\eta^2 = 0.27$) were all significantly lower in the exercise compared to control group after the intervention (Table 4.3).

Table 4.3. Changes in vascular measures after the 12-week intervention (mean and standard deviation)

Variables	**Exercise**		**Control**	
	Pre	**Post**	**Pre**	**Post**
AIx (%)	9.8 ± 12.4	6.2 ± 11.0 *	7.1 ± 7.2	10.4 ± 6.8
FBF (ml.100ml tissue^{-1}.min^{-1})	1.9 ± 0.8	2.4 ± 0.7	2.1 ± 0.5	2.1 ± 0.7
FVR (mmHg.ml^{-1}.100 ml tissue^{-1}.min^{-1})	47.6 ± 15.3	36.7 ± 13.2 *	39.8 ± 8.8	44.1 ± 13.8
FVR (mmHg.ml^{-1}.100 ml tissue^{-1}.min^{-1}) [a]	4.2 ± 2.0	3.0 ± 0.8 *	3.5 ± 1.1	3.6 ± 0.9
SBP (mmHg)	119.6 ± 9.9	115.5 ± 9.7 *	117.4 ± 13.4	121.7 ± 12.8
DBP (mmHg)	63.7 ± 7.3	59.2 ± 7.5 *	62.2 ± 7.0	65.8 ± 6.6
MAP (mmHg)	83.1 ± 8.2	78.7 ± 8.0 *	80.7 ± 8.6	84.3 ± 7.0

AIx: augmentation index; FBF: forearm blood flow; FVR: forearm vascular resistance; SBP: systolic blood pressure; DBP: diastolic blood pressure; MAP: mean arterial pressure.

[a] FVR during vasodilatory capacity measurement. *$P < 0.05$, change greater compared to that of control.

FBF and Vasodilatory Capacity

Resting forearm blood flow did not show a significant change after the exercise intervention ($P = 0.092$, $\eta^2 = 0.08$) although it increased in the exercise group. Forearm vascular resistance (FVR) was significantly lower in the exercise compared to control group ($P = 0.008$, $\eta^2 = 0.18$; Table 3). Vasodilatory capacity (peak FBF), $P = 0.003$ ($\eta^2 = 0.31$) and FVR were significantly changed in the exercise group ($P = 0.001$, $\eta^2 = 0.34$; Figure. 4.2; Table 4.3).

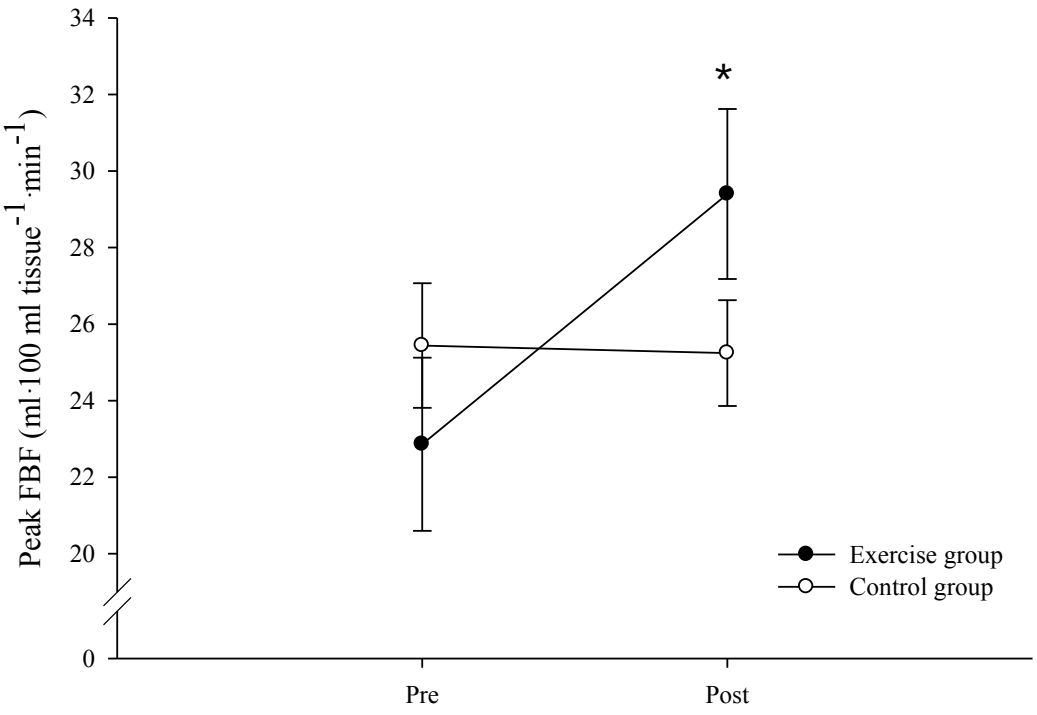

Figure 4.2. Peak forearm blood flow change after 12 weeks of high intensity intermittent exercise

*Post relative to pre values in exercise group are significantly different from control group ($P < 0.05$).

PWV and Augmentation Index

Pulse wave velocity (PWV) and augmentation index (AIx) were used as indicators of arterial stiffness. PWV was significantly reduced in the exercise compared to control group after 12 weeks of HIIE ($P = 0.013$, $\eta^2 = 0.21$; Figure. 3). AIx at a heart rate of 75 b.m^{-1} was also significantly reduced in the exercise compared to control group ($P = 0.024$, $\eta^2 = 0.13$; Table 4.3).

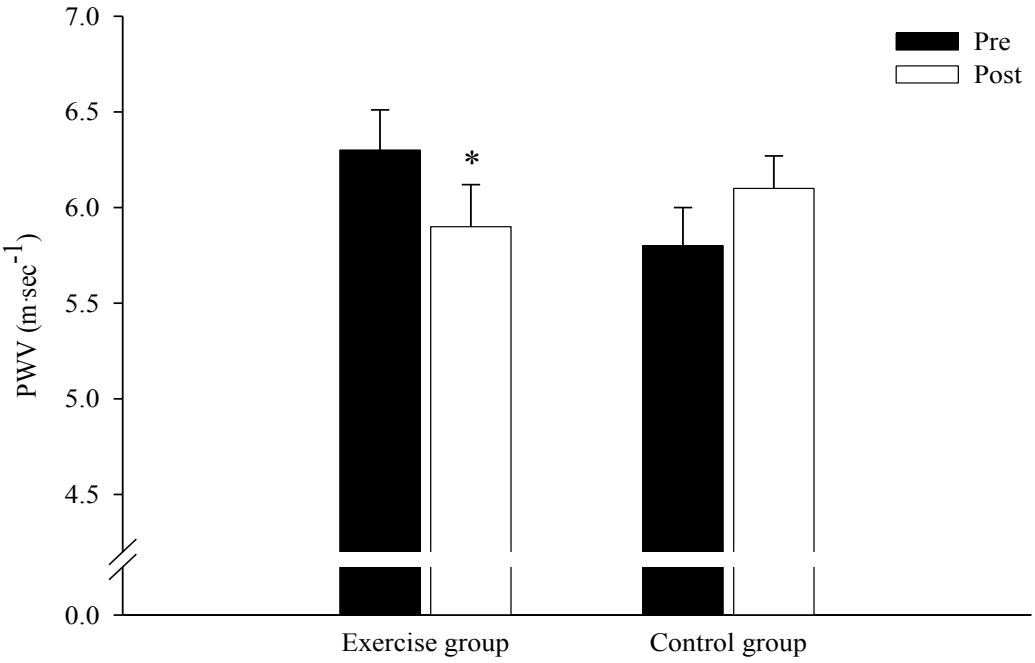

Figure 4.3. Pulse wave velocity change after 12 weeks of high intensity intermittent exercise

*Post relative to pre values in exercise group are significantly different from control group ($P < 0.05$).

HPV

Participants in the exercise group showed a significant increase in low (P = 0.032, η^2 = 0.32) and high frequency power (ln) compared to the control group (P = 0.014, η^2 = 0.32). R-R interval, RMSSD, and pNN50% were also significantly increased (P = 0.001, η^2 = 0.35; P = 0.033, η^2 = 0.14; P = 0.019, η^2 = 0.17 respectively; Table 4.4).

Table 4.4. Changes in resting heart period variability after the 12-week intervention (mean and standard deviation)

Variables	Exercise		Control	
	Pre	**Post**	**Pre**	**Post**
TP (au)	34181 ± 45536	63035 ± 108894	48208 ± 60290	47226 ± 66536
TP (ln)	9.8 ± 1.2	10.0 ± 1.5	10.4 ± 0.8	10.0 ± 1.4
VLF (au)	29650 ± 39944	57958 ± 104643	44786 ± 59352	44238 ± 65330
VLF (ln)	9.6 ± 1.4	9.7 ± 1.8	10.2 ± 1.0	9.7 ± 1.6
LF (au)	1956 ± 1728	2812 ± 2424	1542 ± 941	1598 ± 1372
LF (ln)	7.3 ± 0.8	7.7 ± 0.8 *	7.1 ± 0.7	7.0 ± 0.9
HF (au)	2575 ± 5175	2265 ± 2648	1880 ± 1887	1391 ± 1426
HF (ln)	6.9 ± 1.4	7.2 ± 1.1 *	7.1 ± 1.0	6.8 ± 1.1
RMSSD (ms)	67.3 ± 62.0	74.4 ± 42.9 *	65.9 ± 35.7	56.6 ± 29.7
pNN50 (%)	15.1 ± 12.4	19.3 ± 10.5 *	17.7 ± 9.3	14.8 ± 9.0

TP: total power (0.0-0.4 Hz); VLF: very low frequency power (0.0-0.04 Hz); LF: low frequency power (0.04-0.15 Hz); HF: high frequency power (0.15-0.40 Hz); ln: natural logarithm; RMSSD: root mean square of successive differences; pNN50: percentage of interval differences of successive N–N intervals greater than 50 ms.
*P < 0.05, change greater compared to that of control.

BRS

Baroreflex sensitivity was significantly increased for the exercise group after the 12-week intervention compared to the control group ($P = 0.011$, $\eta^2 = 0.17$; Figure. 4.4).

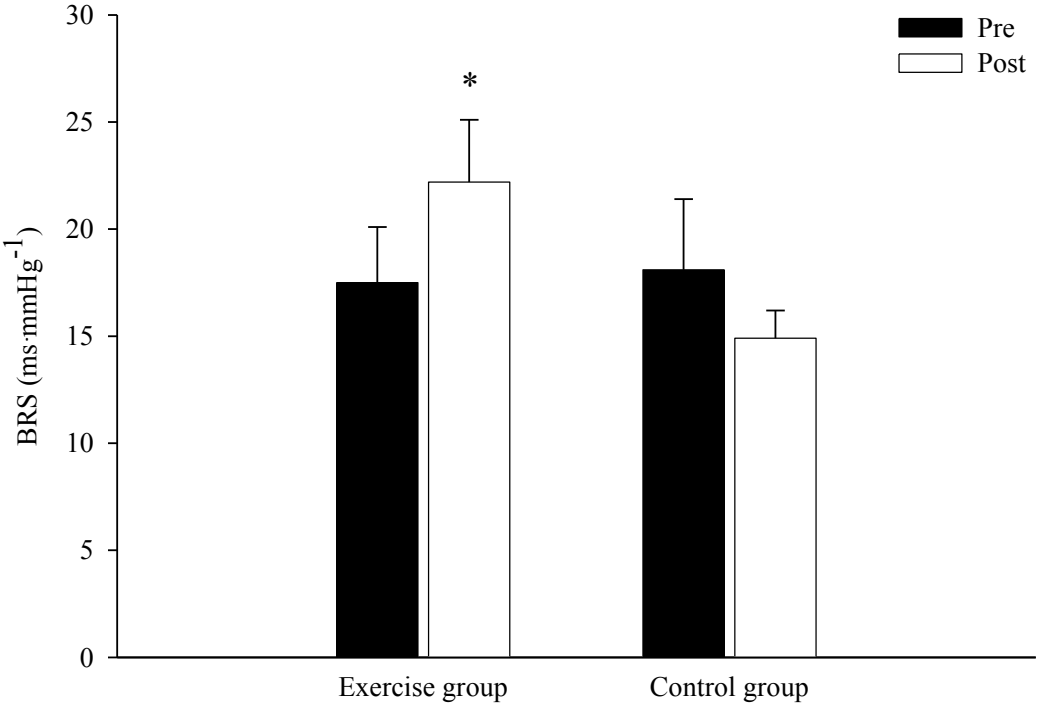

Figure 4.4. Baroreflex sensitivity change after 12 weeks of high intensity intermittent exercise

*Post relative to pre values in exercise group are significantly different from control group ($P < 0.05$).

Discussion

Exercisers compared to controls experienced a significant reduction in heart rate and arterial stiffness, whereas stroke volume, limb vasodilatory capacity, heart period variability, and baroreflex sensitivity were significantly increased. Aerobic power

also improved significantly by 15% for the exercise group. Thus, HIIE induced significant cardiac, vascular, and autonomic improvements after 12 weeks of training.

HIIE training resulted in a significant decrease in resting heart rate. These results are similar to the results of numerous longitudinal aerobic exercise studies that have also documented exercise-induced bradycardia (Wilmore et al., 2001). Unfortunately, the mechanism that causes bradycardia has not been identified. It is considered to reflect a combination of reduced intrinsic heart rate, decreased sympathetic tone, and enhanced parasympathetic or vagal tone. Endurance training-induced decrease in intrinsic heart rate has been consistently found by several studies (Katona, McLean, Dighton, & Guz, 1982) although the increase in vagal influence on the heart found in the present study (discussed later) may have contributed to the decrease in resting heart rate found after HIIE training.

Schairer et al. (1992) have demonstrated that the large exercise stroke volume of elite cyclists and runners was primarily influenced by increased preload and to a lesser extent by myocardial contractility. This indicates that, in younger subjects, endurance training may increase cardiac performance by inducing cardiac dilatation during exercise. Such dilatation is also present during rest, as young endurance trained athletes typically possess significantly larger resting stroke volumes and lower resting heart rates compared to sedentary individuals (Schairer et al., 1992). These greater stroke volumes at rest could be achieved by increased myocardial contractility although increased end-diastolic volume appears to be the more likely mechanism (Schairer et al., 1992). Enhanced end-diastolic volume has been shown to

be increased as a result of aerobic exercise-induced blood volume expansion (Convertino, 1991).

With regard to the 15% increase in resting stroke volume found in the present study the underlying mechanism is undetermined as blood volume change to HIIE was not assessed. However, the significant increase in resting cardiac contractility reflected by the systolic time intervals of left ventricular ejection time and pre ejection period/ left ventricular ejection time (Table 4.2) suggests that increased myocardial contractility may play a role in stroke volume enhancement after HIIE. For example, aerobic exercise training alters the contractile properties of cardiac muscle fibers of exercising rats. Changes include increased sensitivity of cardiac muscle fibers to Ca^{2+} activation and an enhanced cardiac fiber force-length relationship (Diffee, Seversen, & Titus, 2001). Also it has been shown that increased myocardial Ca^{2+} sensitivity of steady-state tension accompanies aerobic interval training in mice (Kemi et al., 2007). As these studies used aerobic training to examine myocardial contractility change future research using interval sprinting as the exercise modality are needed.

The significant increases in vasodilatory capacity found after HIIE training supports the results of long-term aerobic exercise training that has shown enhanced vasodilatory capacity (arteriolar dilation) in exercising muscles. Cross-sectional studies have revealed that aerobically trained individuals possessed greater vasodilatory capacity compared to untrained individuals, whereas longitudinal research (Martin et al., 1990) found enhanced vasodilatory capacity in calf muscles after 6 months of cycling and jogging in older men and women. In terms of non-exercising muscles, Silber et al. (1991) have reported augmentation of vasodilatory

capacity in the forearm after 4-weeks of leg cycling exercise, whereas a number of studies have shown vascular function improvement of upper limb following lower limb exercise in healthy subjects in both conduit arteries such as brachial and radial (Clarkson et al., 1999; Pullin et al., 2004; Tinken et al., 2008) and resistance arteries (DeSouza et al., 2000; Goto et al., 2003; Kingwell, Sherrard et al., 1997). Thus, the increase in forearm vasodilatory capacity found in the present study also shows that HIIE can increase limb capacity in non-exercising muscles. The mechanisms underlying this phenomenon have not been fully elucidated. The endothelial adaptation in conduit arteries may be attributed to increased shear rate, whereas its effect on resistance arteries is undetermined (Green et al., 2011). Other possible mechanisms influencing forearm vasodilatory adaptation include an increase in endothelial NO synthase (eNOS) and prostaglandin release and a decline in free radical-mediated NO degradation and sympathetic vasoconstrictor tone (Niebauer & Cooke, 1996).

Although longitudinal data examining arterial stiffness and exercise are limited Tanaka et al. (2000) assessed arterial stiffness in middle-aged men before and after 3 months of aerobic exercise training and found a reduction in resting arterial stiffness. In addition, other studies have also found lowered arterial stiffness after training in patients with congestive heart failure and in type 2 diabetes. Sugawara and colleagues (2004) assessed central arterial stiffness in postmenopausal women before and after 15 weeks of aerobic exercise training at a low and moderate intensity and found the same amount of reduction in arterial stiffness regardless of training intensity. The 37% decrease in arterial stiffness found in the present study (Figure. 4.3) extends these results to HIIE.

The increase in HPV, reflecting increased vagal influence on the heart, found after 12-weeks of HIIE training supports the results of prior research with aerobic exercise (Sandercock et al., 2005). In contrast, Sloan et al. (2009) showed that autonomic control of the heart did not improve after resistance training. Madden et al. (2006) also found similar results in comparing aerobic endurance and resistance training after 6 months in older women. Two studies have examined HPV using aerobic interval training in older physically active males and coronary artery disease patients. It was found that HPV increased after interval training (Munk et al., 2010; Pichot et al., 2005). In contrast, to the aerobic interval training of the prior two studies the interval exercise of the present study was anaerobic in nature. Thus, these results appear to be the first to show that high-intensity intermittent sprinting accompanied by brief low intensity exercise can significantly increase vagal influence on the heart. HRV was only assessed during spontaneous breathing at rest. That HPV was not also measured during paced breathing at rest is a limitation of this study.

The 12% increase in arterial BRS (Figure. 4.4) found after HIIE training supports research examining aerobic exercise that found an increase in arterial BRS following training. Monahan et al. (2000) determined arterial BRS before and after a 3-month walking program in sedentary middle aged and older men. They reported an average 25% increase in arterial BRS. Other studies utilizing aerobic exercise, however, have not reported change.

An inverse relationship between arterial stiffness and baroreflex sensitivity has been previously reported (Lipman, Grossman, Bridges, Hamner, & Taylor, 2002). According to Lipman et al. (2002) baroreflex sensitivity can be, in part, defined by

vascular stiffness. Although the mechanism underlying this relationship is not fully understood, one possible explanation might be that the increased stiffness of the arteries, in which the arterial baroreceptors are located, decreases the engagement of the stretch-sensitive baroreceptors. This may be the reason why a reduction in arterial stiffness after HIIE training was accompanied with an increase in BRS. Future studies are required to test this hypothesis. Arterial baroreflex activity during HIIE, as opposed to rest, should also be examined as it is reset during aerobic exercise in an intensity-dependent manner which enables it to continuously control blood pressure (Fadel & Raven, 2012).

The improvements in cardiovascular and autonomic indicators following HIIE training are likely to have health implications as low $\dot{V}O_{2max}$ has been shown to predict cardiac disease and high levels of arterial stiffness are associated with increased cardiovascular morbidity and mortality (Laurent et al., 2001). Furthermore, low vasodilatory capacity and baroreceptor sensitivity (Ookuwa et al., 1987) have been linked to hypertension development and reduced HPV is a predictor of a number of cardiac complications (Olshansky, Sabbah, Hauptman, & Colucci, 2008).

In conclusion, HIIE brought about a significant reduction in heart rate and arterial stiffness, whereas aerobic fitness, stroke volume, limb vasodilatory capacity, heart period variability, and baroreflex sensitivity were significantly increased. Thus, regular HIIE induced significant cardiac, vascular, and autonomic improvements after 12 weeks.

Acknowledgements

We would like to thank Chau Tran, Joshua Lane, Roger Burrell, and Lucas Webb for help with data collection. This study was supported by the Diabetes Australia Research Trust [Grant #RM06599].

Conflict of Interest

None of the authors had a personal or financial conflict of interest.

References

Boutcher, S. H. (2011a). High-intensity intermittent exercise and fat loss. *Journal of Obesity, doi: 10.1155/2011/868305*.

Boutcher, Y., & Boutcher, S. (2005). Limb vasodilatory capacity and venous capacitance of trained runners and untrained males. *European Journal of Applied Physiology, 95*(1), 83-87.

Boutcher, Y. N., Hopp, J. P., & Boutcher, S. H. (2011b). Acute effect of a single bout of aerobic exercise on vascular and baroreflex function of young males with a family history of hypertension. *Journal of Human Hypertension, 25*(5), 311-319.

Bowman, A. J., Clayton, R. H., Murray, A., Reed, J. W., Subhan, M. F., & Ford, G. A. (1997). Baroreflex function in sedentary and endurance-trained elderly people. *Age and Ageing, 26*(4), 289-294.

Clarkson, P., Montgomery, H. E., Mullen, M. J., Donald, A. E., Powe, A. J., Bull, T., et al. (1999). Exercise training enhances endothelial function in young men. *Journal of the American College of Cardiology, 33*(5), 1379-1385.

Convertino, V. A. (1991). Blood volume: its adaptation to endurance training. *Medicine and Science in Sports and Exercise, 23*(12), 1338-1348.

DeSouza, C. A., Shapiro, L. F., Clevenger, C. M., Dinenno, F. A., Monahan, K. D., Tanaka, H., et al. (2000). Regular aerobic exercise prevents and restores age-related declines in endothelium-dependent vasodilation in healthy men. *Circulation, 102*(12), 1351-1357.

Diffee, G. M., Seversen, E. A., & Titus, M. M. (2001). Exercise training increases the Ca2+sensitivity of tension in rat cardiac myocytes. *Journal of Applied Physiology, 91*(1), 309-315.

Fadel, P. J., & Raven, P. B. (2012). Human investigations into the arterial and cardiopulmonary baroreflexes during exercise. *Experimental Physiology, 97*(1), 39-50.

Gibala, M. J., Little, J. P., MacDonald, M. J., & Hawley, J. A. (2012). Physiological adaptations to low-volume, high-intensity interval training in health and disease. *The Journal of Physiology, 590*(5), 1077-1084.

Goto, C., Higashi, Y., Kimura, M., Noma, K., Hara, K., Nakagawa, K., et al. (2003). Effect of different intensities of exercise on endothelium-dependent vasodilation in humans. *Circulation, 108*(5), 530-535.

Green, D. J., Spence, A., Halliwill, J. R., Cable, N. T., & Thijssen, D. H. J. (2011). Exercise and vascular adaptation in asymptomatic humans. *Experimental Physiology, 96*(2), 57-70.

Katona, P. G., McLean, M., Dighton, D. H., & Guz, A. (1982). Sympathetic and parasympathetic cardiac control in athletes and nonathletes at rest. *Journal of Applied Physiology, 52*(6), 1652-1657.

Kemi, O. J., Ellingsen, Ø., Ceci, M., Grimaldi, S., Smith, G. L., Condorelli, G., et al. (2007). Aerobic interval training enhances cardiomyocyte contractility and Ca2+ cycling by phosphorylation of CaMKII and Thr-17 of phospholamban. *Journal of Molecular and Cellular Cardiology, 43*(3), 354-361.

Kingwell, B. A., Sherrard, B., Jennings, G. L., & Dart, A. M. (1997). Four weeks of cycle training increases basal production of nitric oxide from the forearm. *American Journal of Physiology - Heart and Circulatory Physiology, 272*(3), H1070-H1077.

Laurent, S., Boutouyrie, P., Asmar, R., Gautier, I., Laloux, B., Guize, L., et al. (2001). Aortic stiffness is an independent predictor of all-cause and cardiovascular mortality in hypertensive patients. *Hypertension, 37*(5), 1236-1241.

Lipman, R. D., Grossman, P., Bridges, S. E., Hamner, J. W., & Taylor, J. A. (2002). Mental stress response, arterial stiffness, and baroreflex sensitivity in healthy aging. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences, 57*(7), B279-B284.

Madden, K. M., Levy, W. C., & Stratton, J. K. (2006). Exercise training and heart rate variability in older adult female subjects. *Clinical and Investigative Medicine, 29*(1), 20-28.

Martin, W. H., Kohrt, W. M., Malley, M. T., Korte, E., & Stoltz, S. (1990). Exercise training enhances leg vasodilatory capacity of 65-yr-old men and women. *Journal of Applied Physiology, 69*(5), 1804-1809.

Martinmäki, K., Häkkinen, K., Mikkola, J., & Rusko, H. (2008). Effect of low-dose endurance training on heart rate variability at rest and during an incremental maximal exercise test. *European Journal of Applied Physiology, 104*(3), 541-548.

Monahan, K. D., Dinenno, F. A., Tanaka, H., Clevenger, C. M., DeSouza, C. A., & Seals, D. R. (2000). Regular aerobic exercise modulates age-associated declines in cardiovagal baroreflex sensitivity in healthy men. *The Journal of Physiology, 529*(1), 263-271.

Munk, P. S., Butt, N., & Larsen, A. I. (2010). High-intensity interval exercise training improves heart rate variability in patients following percutaneous coronary intervention for angina pectoris. *International Journal of Cardiology, 145*(2), 312-314.

Niebauer, J., & Cooke, J. P. (1996). Cardiovascular Effects of Exercise: Role of Endothelial Shear Stress. *Journal of the American College of Cardiology, 28*(7), 1652-1660.

Olshansky, B., Sabbah, H. N., Hauptman, P. J., & Colucci, W. S. (2008). Parasympathetic nervous system and heart failure. *Circulation, 118*(8), 863-871.

Ookuwa, H., Takata, S., Ogawa, J., Iwase, N., Ikeda, T., & Hattori, N. (1987). Abnormal cardiopulmonary baroreflexes in normotensive young subjects with a family history of essential hypertension. *Journal of Clinical Hypertension 3*(4), 596-604.

Parlow, J., Viale, J.-P., Annat, G., Hughson, R., & Quintin, L. (1995). Spontaneous cardiac baroreflex in humans : Comparison with drug-induced responses. *Hypertension, 25*(5), 1058-1068.

Pichot, V., Roche, F., Denis, C., Garet, M., Duverney, D., Costes, F., et al. (2005). Interval training in elderly men increases both heart rate variability and baroreflex activity. *Clinical Autonomic Research, 15*(2), 107-115.

Pullin, C. H., Bellamy, M. F., Bailey, D., Ashton, M., Davies, B., Williams, S., et al. (2004). Time course of changes in endothelial function following exercise in habitually sedentary men. *Journal of Exercise Physiology Online 7*(4), 14-22.

Sandercock, G. R., Bromley, P. D., & Brodie, D. A. (2005). Effects of exercise on heart rate variability: inferences from meta-analysis. *Medicine and Science in Sports and Exercise, 37*(3), 433-439.

Schairer, J. R., Stein, P. D., Keteyian, S., Fedel, F., Ehrman, J., Alam, M., et al. (1992). Left ventricular response to submaximal exercise in endurance-trained athletes and sedentary adults. *The American Journal of Cardiology, 70*(9), 930-933.

Silber, D., McLaughlin, D., & Sinoway, L. (1991). Leg exercise conditioning increases peak forearm blood flow. *Journal of Applied Physiology, 71*(4), 1568-1573.

Sloan, R. P., Shapiro, P. A., DeMeersman, R. E., Bagiella, E., Brondolo, E. N., McKinley, P. S., et al. (2009). The effect of aerobic training and cardiac autonomie regulation in young adults. *American Journal of Public Health, 99*(5), 921-928.

Söderström, S., Nyberg, G., O'Rourke, M. F., Sellgren, J., & Pontén, J. (2002). Can a clinically useful aortic pressure wave be derived from a radial pressure wave? *British Journal of Anaesthesia, 88*(4), 481-488.

Sugawara, J., Inoue, H., Hayashi, K., Yokoi, T., & Kono, I. (2004). Effect of low-intensity aerobic exercise training on arterial compliance in postmenopausal women. *Hypertension Research, 27*(12), 897-901.

Tanaka, H., Dinenno, F. A., Monahan, K. D., Clevenger, C. M., DeSouza, C. A., & Seals, D. R. (2000). Aging, habitual exercise, and dynamic arterial compliance. *Circulation, 102*(11), 1270-1275.

Tinken, T. M., Thijssen, D. H. J., Black, M. A., Cable, N. T., & Green, D. J. (2008). Time course of change in vasodilator function and capacity in response to exercise training in humans. *The Journal of Physiology, 586*(20), 5003-5012.

Trapp, E. G., Chisholm, D. J., & Boutcher, S. H. (2007). Metabolic response of trained and untrained women during high-intensity intermittent cycle exercise.

American Journal of Physiology - Regulatory, Integrative and Comparative Physiology, 293(6), R2370-R2375.

Trapp, E. G., Chisholm, D. J., Freund, J., & Boutcher, S. H. (2008). The effects of high-intensity intermittent exercise training on fat loss and fasting insulin levels of young women. *Internatonal Journal of Obesity, 32*(4), 684-691.

Tulppo, M. P., Hautala, A. J., Makikallio, T. H., Laukkanen, R. T., Nissila, S., Hughson, R. L., et al. (2003). Effects of aerobic training on heart rate dynamics in sedentary subjects. *Journal of Applied Physiology, 95*(1), 364-372.

Wilmore, J. H., Stanforth, P. R., Gagnon, J., Rice, T., Mandel, S., Leon, A. S., et al. (2001). Heart rate and blood pressure changes with endurance training: The HERITAGE Family Study. *Medicine and Science in Sports and Exercise, 33*(1), 107-116.

Chapter 5: The Effects of High-Intensity Intermittent Exercise Training on Cardiovascular Response to Mental and Physical Challenge

Mehrdad Heydari, Yati N. Boutcher, Stephen H. Boutcher

Published Citation: Heydari, M., et al., The effects of high-intensity intermittent exercise training on cardiovascular response to mental and physical challenge. International Journal of Psychophysiology. doi: 10.1016/j.ijpsycho.2012.11.013.

Author Contributions

MH collected data, wrote the manuscript, produced results and figures and was responsible for carrying out the statistical analysis. SHB conceived of the study and edited the manuscript. YNB contributed to editing the manuscript.

Abstract

Objective: The purpose was to examine the effect of a 12-week exercise intervention on the cardiovascular and autonomic response of males to mental and physical challenge.

Methods: Thirty-four young overweight males were randomly assigned to either an exercise or control group. The exercise group completed a high-intensity intermittent exercise (HIIE) program three times per week for 12 weeks. Cardiovascular response to the Stroop task was determined before and after the intervention by assessing heart rate (HR), stroke volume (SV), arterial stiffness, baroreflex sensitivity (BRS), and skeletal muscle blood flow.

Results: The exercise group improved their aerobic fitness levels by 17% and reduced their body weight by 1.6 kg. Exercisers compared to controls experienced a significant reduction in HR ($p < 0.001$) and a significant increase in SV ($p < 0.001$) at rest and during Stroop and exercise. For exercisers, arterial stiffness significantly decreased at rest and during Stroop ($p < 0.01$), whereas BRS was increased at rest and during Stroop ($p < 0.01$). Forearm blood flow was significantly increased during the first two minutes of Stroop ($p < 0.05$).

Conclusions: HIIE induced significant cardiovascular and autonomic changes at rest and during mental and physical challenge after 12 weeks of training.

Introduction

The traditional cardiovascular risk factors of smoking, obesity, diabetes, physical inactivity, and family history predict about 50% of the variance of new cardiovascular disease cases (WHO, 2011), therefore, a number of other risk factors must contribute to cardiovascular disease development. One such factor is psychological stress which has been identified as playing a role in the development of cardiovascular disease (Chida & Steptoe, 2010). An exaggerated cardiovascular response to laboratory stressors such as mental arithmetic and the Stroop color-word task has been shown to have a small but significant contribution of about 2% to the future development of hypertension (Carroll et al., 2003; Carroll et al., 2001).

As regular aerobic exercise has been shown to reduce cardiovascular reactivity to acute exercise it has been proposed that exercise participation can also decrease cardiovascular reactivity to mental challenge (Boutcher & Hamer, 2006). Several longitudinal studies have reported a significant reduction in cardiovascular reactivity (Blumenthal et al., 1991; Georgiades et al., 2000), however, these results have been obtained from populations with initially elevated cardiovascular reactivity to mental challenge such as hypertensive and Type A individuals. With regard to studies using normotensive participants, changes in heart rate (HR) and blood pressure (BP) have been recorded. For example, Forcier et al. (2006) conducted a meta-analysis and found that aerobically fit individuals showed significantly attenuated HR (1.84 bpm) and systolic BP reactivity (3.69 mmHg) and a trend toward attenuated diastolic BP reactivity (1.2 mmHg).

These results have been derived mainly from studies using steady state aerobic exercise (e.g., cycling, jogging, and swimming). Thus, the effects of other types of

exercise such as regular resistance and anaerobic training on cardiovascular reactivity are undetermined. High-intensity intermittent exercise (HIIE), a form of anaerobic training (Boutcher, 2011), involves repeated short bouts of high-intensity exercise interspersed with recovery periods (light exercise). It has been shown that HIIE, compared to steady state exercise, produces a significantly greater impact on the autonomic nervous system (ANS) assessed by HR and plasma catecholamine levels (Trapp et al., 2007). Given that HIIE induces a significant acute cardiovascular response it is feasible that HIIE training will also produce greater adaptations in ANS control of the cardiovascular system. HIIE sessions are also typically much shorter than aerobic exercise sessions and this reduced time commitment is likely to be appealing to individuals interested in improving cardiovascular health. To date, however, no study has examined the effect of HIIE training on cardiovascular response during mental and physical challenge.

Although the effects of aerobic exercise training on HR and BP response to mental challenge have been extensively studied, relatively less attention has been devoted to other aspects of cardiovascular response such as skeletal muscle blood flow and baroreceptor sensitivity (BRS). In addition, the effect of HIIE training on arterial stiffness during mental challenge has yet to be studied. Consequently, it is not clear whether autonomic control of the heart determined by BRS and arterial stiffness under mental and physical challenge is influenced by HIIE training. Therefore, the purpose of this study was to examine the effects of HIIE, repeated three times per week for 12 weeks, on multiple measures of cardiovascular and autonomic reactivity. It was hypothesized that a program of HIIE would result in

significant reductions in the reactivity response during both mental and physical challenge of young, inactive men.

Methods

Participants

Males aged 18-35 years and BMI 25-35 kg/m^2 were invited to participate through advertisements placed on the notice boards of public areas and student magazines (Table 5.1). Participants were non-smokers, physically inactive, free of any type of cardiovascular and pulmonary disease, and were not taking any medication. The initial participant pool was 41 with 21 participants being randomly allocated to an exercise intervention group and 20 to a control group. For various reasons such as job commitment, moving overseas, and a car accident four participants withdrew from the exercise and three from the control group. There was no significant difference for any variable between the drop-outs and those males who completed the study. Of the 17 participants in the intervention group (age 24.4 ± 4.7 yrs) 12 were overweight and 5 were obese, whereas of the 17 participants in the control group (age 25.2 ± 4.0 yrs) 13 were overweight and 4 were obese. Participants completed the Physical Assessment Readiness Questionnaire, PAR-Q, (Thomas et al., 1992) which provided information on health status and determined whether participants were suitable to undergo $\dot{V}O_{2peak}$ testing. PAR-Q assessment indicated that none of the participants had a heart condition or chest pain during physical activity or rest. None of the participants were involved in regular physical activity during the last 6 months. Participants in both exercise and control groups were advised to maintain their normal eating habits during the study. The control group

was also asked to keep to their normal lifestyle during the trial period. The study protocol was approved by a university Ethics Committee and conformed to the declaration of Helsinki. Informed written consent was obtained before testing.

Table 5.1. Changes in body composition and aerobic power after the 12-week intervention for the exercise and control groups (mean and standard error)

Variable	**Pre Ex**	**Post Ex**	**Pre Cont**	**Post Cont**
Weight (kg)	89.2 ± 2.9	87.6 ± 2.9*	89.9 ± 2.9	90.4 ± 3.1
BMI ($kg \cdot m^2$)	28.4 ± 0.6	27.9 ± 0.6*	29.2 ± 0.9	29.3 ± 0.9
Waist circumference (cm)	93.5 ± 1.6	89.8 ± 1.7*	93.9 ± 2.0	95.2 ± 2.0
$\dot{V}O_{2peak}$ ($l \cdot min^{-1}$)	3.0 ± 0.2	3.5 ± 0.1*	2.6 ± 0.1	2.7 ± 0.1
$\dot{V}O_{2peak}$ ($ml \cdot kg^{-1} \cdot min^{-1}$)	33.9 ± 1.1	39.8 ± 0.9*	29.1 ± 1.3	30.6 ± 1.4

BMI: Body mass index. *$P < 0.05$, Post relative to pre values in exercise group are significantly different from control group.

Measurements

Heart Rate and Blood Pressure

Participants‘ HR was obtained using the standard lead II of a surface electrocardiogram (LifePulse model LP10, HME), and beat-to-beat BPs were measured continuously using the Colin Jentow (Model 7000, Colin Medical, Japan), which has been validated using simultaneous intra-arterial monitoring (Sato, Nishinaga, Kawamoto, Ozawa, & Takatsuji, 1993). A sensor was placed around the wrist where the radial artery was maximally pulsatile and indirect continuous 5-min

beat-to-beat BPs were recorded. Rate pressure product (RPP) was calculated during baseline and the Stroop task by multiplying HR by systolic BP and dividing by 100.

Stroke Volume

Cardiac function was measured using the Minnesota impedance cardiograph (Model 304B; Surcom, Minneapolis, MN) and included the recording of HR, stroke volume (SV), cardiac output (CO), pre-ejection period (PEP), left ventricle ejection time (LVET), Heather index (HI), and $dZ/dt_{(max)}$. PEP is an index of cardiac contractility and is inversely related to left ventricular contractility and sympathetic (beta-adrenergic) influences on the myocardium. The HI is another index of myocardial contractility and is defined as the ratio of $dZ/dt_{(max)}$ to the electromechanical time interval (Q-Z interval). This index reflects changes in cardiac contractility. $dZ/dt_{(max)}$ correlates well with aortic blood flow and represents the magnitude of the largest impedance change during systole and maximal speed of blood ejection (Sherwood et al., 1990). Data were analyzed with the cardiac output program software (COP, Microtronics Inc, Chapel Hill, NC).

Arterial Stiffness Determined By Augmentation Index

Radial artery pressure waveform was collected with a wrist sensor placed on the left arm radial pulse (Model 7000, Colin Medical, Japan) and was stored by BP Monitor software (BP Monitor, UNSW). The central aortic waveform was derived from the recorded radial arterial pressure waveform by using SphygmoCor software (SphygmoCor, SCOR-2000, AtCor Medical, Australia). An index of arterial stiffness (AIx) was defined as the ratio of the difference between the first (early systolic shoulder) and second peaks (late systolic shoulder) to pulse pressure and expressed

as a percentage. Because Alx has an inverse correlation with HR, it was normalised to a HR of 75 $b \cdot min^{-1}$. This technique has been reported to be reliable and reproducible (Wilkinson et al., 1998). The use of a transfer function (SphygmoCor) to synthesize a central aortic pressure from radial arterial pressure has been validated against directly measured central aortic pressure (Söderström et al., 2002).

Arterial Baroreflex Sensitivity

Arterial baroreflex sensitivity (BRS) was determined under a condition of spontaneous behavior using the sequence method (BaroCor™ AFx, AtCor Medical, Australia). The software identified the sequences in which RR interval and SBP concurrently increase (up sequence) or decrease (down sequence) over three or more beats. The minimum change had to be 1 mmHg for systolic BP and 5 ms for the R-R interval. The linear regression between R-R interval and systolic BP was computed for each sequence. Only sequences with a correlation coefficient greater than 0.85 were used. The average regression slope for these sequences was considered as the BRS for the entire data sampling period. BRS was calculated over 4 min (equal to 80% of total recording time) for each baseline and during the Stroop and exercise tasks. The sequence method has been shown to be a valid and reproducible method for determining arterial BRS in humans (Parlow et al., 1995).

Forearm Blood Flow

Forearm blood flow (FBF) was measured using the venous occlusion technique. A mercury strain gauge was fitted at the widest part of the forearm, 5 cm distal from the antecubital vein, and was attached to a plethysmograph (Model EC4, D.E. Hokanson, Inc, Bellevue, WA, USA) which was interfaced with a computer for data storage. A

cuff inflator air source (Hokanson, Model AG101) and a rapid cuff inflator (Hokanson, Model E20) were used to inflate the upper arm cuff to 50 mmHg every 10 s for 5 s duration. Arterial wrist cuff was inflated to 180 mmHg for at least 1 min before measurement to avoid disturbance of limb arterial inflow. The change in circumference of the forearm, due to arterial inflow, was recorded as a change in electrical resistance of the mercury-in-silastic strain gauge. Forearm vascular resistance also was calculated by dividing mean arterial BP by forearm blood flow. All above variables were assessed during baseline and Stroop, however, due to movement artifact generated by the cycling task only HR, CO, and SV were measured during exercise.

Aerobic Fitness

Peak oxygen consumption was measured using an electrically braked cycle ergometer (Ergomedic 839E, Monark). Open-circuit spirometry (True Max 2400, ParvoMedics) attached to a Hans Rudolph two way-rebreathing valve was used to measure peak oxygen uptake ($\dot{V}O_{2peak}$). Participants cycled at a cadence of 70 rpm until volitional exhaustion. After a 3-min warm-up period at 30 W, the workload was increased by 1 W every 2 s. HR was monitored by a Polar SC800 HR monitor (Polar Electro Oy, Kempele, Finland). The end-point was achieved when one or more of the following indices was attained: HR within ± 10 $b \cdot min^{-1}$ of age-predicted maximal HR, a plateau in oxygen consumption, an inability to maintain the required cadence equal to at least 50 revolutions per min (rpm) and an RER of >1.15 (Cooke, 2009). Because participants in the present study were untrained and unused to cycling

exercise, some stopped cycling before achieving a true maximal oxygen uptake and thus $\dot{V}O_{2peak}$ was accepted as an indicant of aerobic power.

Procedure

All participants were requested to come to the laboratory after an 8-hour overnight fast between 7 am and 11 am and were instructed to abstain from caffeine and alcohol for at least 8 hrs before testing. Two participants consumed more than 3 alcohol drinks per week and three participants consumed more than 3 cups of tea and/or coffee per day. The Stroop color-word task, which was used to induce cognitive challenge (Stroop, 1935), consisted of a series of slides that were presented on a PowerPoint presentation on a laptop computer. Each slide contained a word denoting a color, such as RED, but the ink color of each word was printed in a different color, such as BLUE. Participants were instructed to state the ink color of each word. Slides appeared at a rate of one per second. The Stroop and cycling tasks were separated by 10 min rest. HR and BP were recorded during the 5-min Stroop task and the last 5 min of exercise. The cycling task involved participants cycling in a semi-recumbent position on a stationary cycle ergometer (Monark 828E) for 8 min at 20% of maximal workload assessed from each participant‘s $\dot{V}O_{2peak}$ test. Participants in the exercise intervention group received supervised HIIE training on a cycle ergometer (Monark 828E) at a frequency of 3 times a week for 12 weeks. Participants were instructed to cycle at a workload of 80-90% of their age-predicted maximum HR with a pedal cadence between 120 and 130 rpm. Each exercise session consisted of a 5-min warm-up, 20-min of 8 s sprint and 12 s recovery, and a 5-min cool-down. During recovery, the cadence was reduced to 40 rpm with no change in

resistance. Participants kept their exercise intensity at a level which ensured their average HR was within 80-90% of their maximum HR. Intensity was increased when exercise HR dropped below their HR peak range. HR was recorded continuously during each training session using Polar Heart Rate monitor (Polar Electro Oy, Kempele, Finland). Rating of perceived exertion (RPE) was obtained in 5 min interval during the 20 min HIIE cycling using the 6-20 point Borg's RPE scale (Borg, 1962).

Data Analysis

All signals from ECG, BP, and plethysmography were connected to a computer via a National Instruments PCI-MIO-16E-4 Interface and were converted to digital data using Software (BP Monitor, UNSW) with a sampling rate of 1000 Hz to define the R peaks of the QRS complexes, systolic, and diastolic pressures.

Statistical Analysis

Results are expressed as mean and standard error of the mean. Data were analyzed with the Statistical Package for Social Science for Windows software (SPSS 20, USA). To examine changes after the intervention an analysis of covariance (ANCOVA) was used to evaluate differences between the two groups for variables that did not violate ANCOVA assumptions. Pre-intervention values were used as covariates. In the Stroop color-word task, all variables collected over time (baseline and task) were assessed with repeated measures ANOVA. The Mauchly sphericity test was performed to test for homogeneity of covariance for the within subjects factor. Non-homogeneity was corrected by employing the Greenhouse-Geisser adjustment. The statistical analysis was considered significant when the probability

level was less than 0.05. Effect sizes were calculated using partial eta squared (η^2) with values of 0.1, 0.3, and above 0.5 considered to be a small, medium, and large effect.

Results

Participant Characteristics

There were no significant differences between the two groups on any measured variable prior to the training program (Table 5.1). There was, however, a significant decrease in body weight and waist circumference for the HIIE compared to the control group ($p < 0.01$) after the exercise intervention and a significant 17% increase ($p < 0.001$) in $\dot{V}O_{2peak}$ (Table 5.1). All participants completed all 36 sessions of HIIE training. The average HR and rating of perceived exertion (RPE) during HIIE training for the intervention group were 160 ± 9 b·min^{-1} and 13.6 ± 0.5.

Cardiovascular Changes at Baseline

There were no significant differences between the two groups on the majority of cardiovascular variables prior to the training program, however, HR was significantly decreased in the exercise compared to the control group, whereas SV was significantly increased (Table 5.2). CO and PEP, and forearm blood flow were unchanged (Table 5.2). The HI was significantly increased, however, $dZ/dt_{(max)}$ did not change (Table 5.2). Systolic and diastolic BP and RPP were also significantly decreased in the exercise compared to the control group (Table 5.2). AIx was significantly decreased and BRS was significantly increased in the exercise compared to control group (Table 5.2).

Absolute Cardiovascular Response to Mental and Physical Challenge

Absolute heart rate (HR), stroke volume (SV), and cardiac contractility

Absolute HR was significantly reduced and absolute SV was significantly increased during Stroop and exercise for the exercise compared to control group (Tables 5.3 and 5.4). CO and PEP did not change during Stroop or exercise (Tables 5.3 and 5.4). The absolute HI was unchanged during Stroop (Table 5.3) but was significantly increased during exercise (Table 5.4). $dZ/dt_{(max)}$ did not change during Stroop or exercise (Tables 5.3 and 5.4). Absolute RPP was also significantly decreased in the exercise compared to the control group during the Stroop task (Table 5.3).

Table 5.2. Changes in resting cardiovascular measures after the 12-week intervention for the exercise and control groups (mean and standard error)

Variable	**Pre Ex**	**Post Ex**	**Pre Cont**	**Post Cont**	**Δ Ex**	**Δ Cont**	**Statistic and effect size**
HR ($b \cdot min^{-1}$)	67 ± 2.5	61 ± 2.3*	69 ± 1.9	70 ± 1.6	-6.1 ± 1.6	1.5 ± 2.0	$F = 13.91$, $p = 0.001$, $\eta^2 = .32$
SV (ml)	72 ± 4.2	86 ± 5.1*	76 ± 4.9	70 ± 5.4	13.2 ± 2.3	-5.3 ± 2.8	$F = 21.84$, $p = 0.000$, $\eta^2 = .45$
CO ($L \cdot min^{-1}$)	4.9 ± 0.2	5.1 ± 0.2	5.2 ± 0.2	4.9 ± 0.3	0.3 ± 0.2	-0.2 ± 0.2	$F = 3.96$, $p = 0.06$, $\eta^2 = .13$
PEP (ms)	134 ± 3.2	129 ± 4.5	126 ± 4.2	129 ± 2.4	-3.8 ± 2.6	4.1 ± 2.8	$F = 2.45$, $p = 0.13$, $\eta^2 = .08$
HI (Ω/sec^2)	10.1 ± 0.6	11.2 ± 0.8*	9.7 ± 0.6	9.4 ± 0.7	0.9 ± 0.5	-0.3 ± 0.4	$F = 4.99$, $p = 0.034$, $\eta^2 = .16$
$dZ/dt_{(max)}$ (Ω/sec)	1.9 ± 0.1	2.1 ± 0.1	1.7 ± 0.1	1.7 ± 0.1	0.2 ± 0.1	0.0 ± 0.1	$F = 3.11$, $p = 0.09$, $\eta^2 = .10$
Systolic BP (mmHg)	120 ± 2.4	115 ± 2.5*	117 ± 3.3	122 ± 3.2	-4.8 ± 4.7	1.6 ± 2.5	$F = 9.78$, $p = 0.004$, $\eta^2 = .24$
Diastolic BP (mmHg)	64 ± 1.8	58 ± 1.8*	62 ± 1.7	66 ± 1.6	-5.9 ± 3.3	1.6 ± 2.3	$F = 11.49$, $p = 0.002$, $\eta^2 = .27$
RPP (bpm·mmHg)	80.4 ± 4.5	71.0 ± 3.8*	81.4 ± 3.8	86.5 ± 3.9	-9.4 ± 2.6	5.1 ± 3.2	$F = 14.27$, $p = 0.001$, $\eta^2 = .35$
FBF ($ml \cdot 100ml\ tissue^{-1} \cdot min^{-1}$)	2.1 ± 0.2	2.5 ± 0.2	2.1 ± 0.1	2.2 ± 0.2	0.48 ± 0.03	0.18 ± 0.17	$F = 3.84$, $p = 0.059$, $\eta^2 = .11$
AIx (%)	8.2 ± 2.9	5.1 ± 2.7*	7.5 ± 1.8	9.5 ± 1.4	-3.1 ± 1.9	2.0 ± 1.9	$F = 4.23$, $p = 0.048$, $\eta^2 = .12$
BRS ($ms \cdot mmHg^{-1}$)	18.3 ± 2.9	23.8 ± 3.8*	18.4 ± 3.0	15.0 ± 1.4	5.5 ± 2.0	-3.4 ± 2.8	$F = 7.98$, $p = 0.008$, $\eta^2 = .21$

HR: Heart rate; SV: Stroke volume; CO: Cardiac output; PEP: pre-ejection period; HI: Heather index; $dZ/dt_{(max)}$: Peak ejection velocity; BP: Blood pressure; RPP: Rate pressure product divided by 100; FBF: Forearm blood flow; AIx: Augmentation index; BRS: Baroreflex sensitivity. *$P < 0.05$, Post relative to pre values in exercise group are significantly different from control group.

Table 5.3. Change in cardiovascular measures after the 12-week intervention for the exercise and control groups during the Stroop task (mean and standard error)

Variable	**Pre Ex**	**Post Ex**	**Pre Cont**	**Post Cont**	**Δ Ex**	**Δ Cont**	**Statistic and effect size**
HR ($b \cdot min^{-1}$)	78 ± 2.7	71 ± 2.5*	81 ± 2.1	81 ± 1.5	-6.7 ± 1.6	0.2 ± 1.5	$F = 17.75$, $p = 0.000$, $\eta^2 = .39$
SV (ml)	60 ± 3.9	77 ± 4.9*	69 ± 3.9	65 ± 4.2	7.9 ± 2.4	-4.6 ± 1.9	$F = 14.57$, $p = 0.001$, $\eta^2 = .35$
CO ($L \cdot min^{-1}$)	5.3 ± 0.2	5.4 ± 0.3	5.6 ± 0.3	5.2 ± 0.3	0.1 ± 0.2	-0.3 ± 0.2	$F = 2.49$, $p = 0.13$, $\eta^2 = .08$
PEP (ms)	129 ± 3.6	128 ± 3.7	121 ± 4.2	128 ± 1.8	-1.4 ± 1.7	7.2 ± 3.1	$F = 2.19$, $p = 0.15$, $\eta^2 = .08$
HI (Ω/sec^2)	10.2 ± 0.5	10.7 ± 0.9	9.7 ± 0.6	9.2 ± 0.6	0.5 ± 0.6	-0.5 ± 0.4	$F = 1.79$, $p = 0.19$, $\eta^2 = .06$
$dZ/dt_{(max)}$ (Ω/sec)	1.8 ± 0.1	1.9 ± 0.2	1.6 ± 0.1	1.6 ± 0.1	0.1 ± 0.1	0.0 ± 0.1	$F = 0.62$, $p = 0.44$, $\eta^2 = .02$
Systolic BP (mmHg)	129 ± 2.1	118 ± 2.5	128 ± 2.2	120 ± 2.7	-10.8 ± 1.8	-7.4 ± 1.2	$F = 0.73$, $p = 0.40$, $\eta^2 = .02$
Diastolic BP (mmHg)	70 ± 2.4	60 ± 2.1	71 ± 2.5	64 ± 1.6	-9.7 ± 1.2	-7.0 ± 1.4	$F = 1.65$, $p = 0.21$, $\eta^2 = .05$
RPP (bpm·mmHg)	96.7 ± 4.8	81.9 ± 3.7*	101.9 ± 4.5	96.9 ± 3.7	-14.7 ± 2.4	-5.0 ± 2.3	$F = 16.58$, $p = 0.000$, $\eta^2 = .38$
FBF ($ml \cdot 100ml\ tissue^{-1} \cdot min^{-1}$) Stroop min 1	3.9 ± 0.2	4.6 ± 0.4*	4.2 ± 0.3	3.9 ± 0.3	0.7 ± 0.3	-0.4 ± 0.2	$F = 5.81$, $p = 0.022$, $\eta^2 = .16$
FBF ($ml \cdot 100ml\ tissue^{-1} \cdot min^{-1}$) Stroop min 2	2.4 ± 0.2	3.1 ± 0.3*	3.1 ± 0.3	2.9 ± 0.3	0.6 ± 0.2	-0.2 ± 0.2	$F = 4.42$, p = 0.044, $\eta^2 = .13$
AIx (%)	12.5 ± 1.5	8.8 ± 1.6*	11.4 ± 1.4	13.0 ± 1.3	-3.8 ± 0.9	1.6 ± 1.6	$F = 8.49$, p = 0.007, $\eta^2 = .22$
BRS ($ms \cdot mmHg^{-1}$)	12.6 ± 1.8	14.5 ± 1.6*	11.8 ± 1.9	9.1 ± 0.9	1.9 ± 1.4	-2.6 ± 1.8	$F = 10.65$, $p = 0.003$, $\eta^2 = .26$

HR: Heart rate; SV: Stroke volume; CO: Cardiac output; PEP: pre-ejection period; HI: Heather index; $dZ/dt_{(max)}$: Peak ejection velocity; BP: Blood pressure; RPP: Rate pressure product divided by 100; FBF: Forearm blood flow; AIx: Augmentation index; BRS: Baroreflex sensitivity.
*$P < 0.05$, Post relative to pre values in exercise group are significantly different from control group.

Table 5.4. Change in cardiovascular measures after the 12-week intervention for the exercise and control groups during the exercise task (mean and standard error)

Variable	**Pre Ex**	**Post Ex**	**Pre Cont**	**Post Cont**	**Δ Ex**	**Δ Cont**	**Statistic and effect size**
HR ($b \cdot min^{-1}$)	100 ± 2.5	93 ± 2.6*	101 ± 1.4	101 ± 1.2	-6.6 ± 1.4	0.2 ± 1.4	$F = 14.37$, $p = 0.001$, $\eta^2 = .34$
SV (ml)	90 ± 5.2	106 ± 5.4*	91 ± 4.0	88 ± 5.3	16.1 ± 2.8	-2.7 ± 2.7	$F = 23.13$, $p = 0.000$, $\eta^2 = .46$
CO ($L \cdot min^{-1}$)	8.8 ± 0.4	9.2 ± 0.4	9.2 ± 0.4	8.9 ± 0.5	0.4 ± 0.2	-0.3 ± 0.3	$F = 3.53$, $p = 0.07$, $\eta^2 = .12$
PEP (ms)	97 ± 4.0	91 ± 4.7	83 ± 4.1	87 ± 4.0	-5.3 ± 3.7	4.3 ± 3.7	$F = 0.60$, $p = 0.45$, $\eta^2 = .02$
HI (Ω/sec^2)	16.4 ± 0.9	18.9 ± 1.4*	14.9 ± 0.9	14.9 ± 0.9	2.5 ± 0.9	-0.2 ± 0.6	$F = 4.98$, $p = 0.034$, $\eta^2 = .16$
$dZ/dt_{(max)}$ (Ω/sec)	2.3 ± 0.1	2.6 ± 0.2	2.0 ± 0.1	2.1 ± 0.1	0.3 ± 0.1	0.0 ± 0.1	$F = 3.05$, $p = 0.09$, $\eta^2 = .10$

HR: Heart rate; SV: Stroke volume; CO: Cardiac output; PEP: pre-ejection period; HI: Heather index; $dZ/dt_{(max)}$: Peak ejection velocity.
*$P < 0.05$, Post relative to pre values in exercise group are significantly different from control group.

Absolute Arterial Stiffness and Baroreceptor Sensitivity Response (BRS)

During the Stroop task, absolute augmentation index (AIx) was significantly decreased in the exercise compared to control group (Table 5.3). After 12 weeks of HIIE, absolute BRS determined during the Stroop task, was significantly increased in the exercise compared to control group (Table 5.3). No significant difference in BRS existed between the exercise and control group during exercise (Table 5.4). The average number of sequences during baseline was 40 ± 2, during Stroop was 29 ± 2, and during exercise was 18 ± 2.

Forearm Blood Flow and Blood Pressure (BP)

Forearm blood flow, relative to baseline, was significantly increased for the exercise compared to the control group during minutes one and two of Stroop (Table 5.3) but was unchanged during minutes three, four, and five ($p > 0.05$). Absolute and relative systolic, diastolic, and mean arterial BP did not change during Stroop ($p > 0.05$; Table 5.3).

Correlations between Variables

Arterial stiffness and BRS were not significantly correlated at baseline for either group ($r = 0.06$, $p > 0.05$). Decrease in arterial stiffness and increase in BRS for the exercising group was not significantly correlated ($r = 0.03$, $p > 0.05$). The reduction in waist circumference and the increase in BRS of the exercising group also was not significantly correlated at baseline ($r = 0.20$, $p > 0.05$) or during Stroop ($r = 0.15$, $p > 0.05$). Similarly, the reduction in waist circumference and the increase in forearm

blood flow of the exercising group was not significantly correlated at baseline (r = 0.35, p > 0.05) or during min1 (r = 0.18, p > 0.05) and min2 (r = 0.22, p > 0.05) of Stroop.

Discussion

Twelve weeks of HIIE significantly increased $\dot{V}O_{2peak}$ and significantly reduced body weight and waist circumference. Significant differences in cardiovascular and autonomic levels during mental and physical challenge were also found. Specifically, exercisers compared to controls experienced a significant reduction in absolute HR and RPP and a significant increase in absolute SV during both Stroop and a bout of acute cycling exercise. Exercisers compared to controls also showed decreased absolute arterial stiffness and increased BRS during Stroop. For exercisers, forearm blood flow was significantly increased during the first two min of Stroop after training. Thus, HIIE training significantly changed baseline levels of HR, RPP, SV, arterial stiffness, and BRS which resulted in lower absolute levels of these variables during mental challenge and lower levels of HR, SV, and the HI during physical challenge.

The increase in aerobic fitness levels (17%) and decrease in body weight (1.6 kg) of the males in the exercise group are similar to results of a HIIE protocol conducted over 15 weeks with women (Trapp et al., 2008) and 12 weeks with men (Heydari et al., 2012). Collectively results indicate that HIIE protocols result in a significant increase in aerobic power and a significant decrease in body weight in both young males and females.

The above training effects were also accompanied by a significant decrease in absolute HR at rest and during Stroop and mild cycle exercise challenge. These

results support findings from previous longitudinal studies that have indicated that autonomic modulation on the cardiovascular system is altered after aerobic exercise training at rest (Carter et al., 2003). The decrease in absolute HR during mental challenge has been found consistently in cross sectional studies that have compared the absolute HR response to mental challenge of aerobically trained and untrained individuals (Boutcher, Nugent, McLaren, & Weltman, 1998). Thus, although HR reactivity (baseline HR minus task HR) was not changed absolute value decreases in HR after training were found at rest and during both mental and physical challenge. The decrease in HR brought about by HIIE was also accompanied by an increase in SV at rest and during both mental and physical challenge. The mechanism underlying the HIIE-induced increase in SV is unclear but may include plasma volume expansion and/or enhanced myocardial contractility. Plasma volume expansion contributes to increased cardiac filling pressure (central venous pressure) at rest and typically results in an elevation of resting and exercise SV (Convertino, 1991). Plasma volume expansion typically occurs after moderately hard aerobic exercise (Convertino, 1991) but the plasma volume response to HIIE is undetermined. Thus, a limitation of the present study is that the plasma volume response to HIIE was not assessed. HIIE-induced increase in SV may also have occurred as a result of enhanced cardiac contractility (Helgerud et al., 2007). The change in HI (Tables 5.3 and 5.4), indicating increased myocardial contractility, supports this notion. The lowered HR and increased SV may have health benefits as it has been shown that lowering HR during submaximal exercise resulted in reduced vascular resistance and increased ventricular filling (Georgiades et al., 2000).

That RPP was significantly reduced during rest and mental challenge mirrors the HR and SV response described above. RPP reflects the stress experienced by the heart caused by an increase in HR an elevated systolic BP. RPP directly indicates the energy demand of the heart and is strongly related to myocardial blood flow (Ansari et al., 2012). Mental stress causes an increase in myocardial blood flow and RPP of about 30% (Strike & Steptoe, 2003). Increases in RPP have been shown to trigger myocardial ischemia (Deanfield et al., 1984), consequently, the 15% reduction in RPP found during mental challenge in the current study appears to be beneficial from a myocardial ischemia perspective. That RPP was reduced at rest after HIIE training by about 12% underlines the effect of HIIE which appears to lower absolute cardiovascular response during mental and physical challenge by changing resting values.

Absolute arterial stiffness was significantly increased for both groups during Stroop which confirms previous research that has shown that mental challenge elevates stiffness in the large conduit arteries (Vlachopoulos et al., 2006). Although arterial stiffness response to Stroop was significantly increased in both groups the exercisers displayed reduced absolute stiffness after 12 weeks of HIIE. The exerciser‘s 38% arterial stiffness reduction during Stroop was accompanied by a 30% reduction at rest, reinforcing the pattern described above, whereby changes in resting cardiovascular levels appear to influence absolute levels during mental challenge. The reduction in absolute arterial stiffness levels during Stroop suggests that in response to mental challenge the large arteries of exercisers experienced less vasoconstriction after the exercise intervention. Long term reduction in arterial stiffness response to mental challenge may have health implications as elevated

arterial stiffness has been shown to be a risk factor for cardiovascular morbidity and mortality (Laurent et al., 2001) and independently correlates with left ventricular hypertrophy (Marchais et al., 1993), coronary artery disease and cardiovascular events (Weber et al., 2004), and all cause mortality (London et al., 2001).

Absolute BRS response to Stroop was significantly increased in the exercise compared to the control group. BRS is an important physiological mechanism which controls the homeostasis of both short and long term BP (Persson, 2005). The homeostatic influence of BRS is of crucial importance to cardiovascular flexibility and its inhibition during challenging situations has been shown to be an integral part of the autonomic response to stressful conditions (Reyes Del Paso et al., 2004). The exerciser‘s 13% increase in BRS during Stroop was accompanied by a 38% increase at rest, reinforcing the pattern described above, whereby changes in resting cardiovascular levels resulted in a concomitant decrease in absolute levels during mental challenge. These results suggest that during mental challenge, after HIIE training, the baroreflex improves its effectiveness when regulating cardiac activity in response to BP increase.

Lipman et al. (2002) found an inverse relationship between BRS and arterial stiffness and has suggested that BRS is influenced by vascular stiffness. Thus, the increased stiffness of arteries, in which the arterial baroreceptors are located, decreases the engagement of the stretch-sensitive baroreceptors during Stroop. However, in the current study no significant correlation between BRS and arterial stiffness was found suggesting that the decrease in arterial stiffness was not influenced by the increase in BRS after 12 weeks of HIIE.

Systolic BP reactivity during Stroop was also reduced by 10% in the exercise group although this effect was not significant. Encouragingly, Ribeiro et al. (2005) demonstrated that a 4-month exercise/diet intervention conducted on obese children improved limb blood flow response to the Stroop task and decreased BP reactivity.

Overweight and obese individuals possessing elevated waist circumference have reduced BRS response to mental challenge (Honzíková et al., 2006; Lazarova et al., 2009). Thus, the reduction in waist circumference brought about by HIIE in the current study could have contributed to the increase in BRS response to mental challenge experienced by the exercising group. However, the lack of relationship between decrease in waist circumference and increase in BRS probably suggests that the amount of abdominal fat lost by exercising participants was not enough to influence BRS sensitivity. Similar to BRS the enhanced forearm blood flow response of lean subjects to mental challenge is typically reduced in the overweight and obese (Agapitov et al., 2002). The inability to vasodilate skeletal muscle during mental challenge results in increased systemic vascular resistance which is typically accompanied by an increase in BP (Seematter et al., 2000). Also a number of studies have shown that central adiposity, independent of total adiposity, is more strongly associated with increased systemic vascular resistance and BP reactivity to mental challenge. Similar to the BRS results, however, the increase in forearm blood flow during Stroop was not significantly related to the reduction in waist circumference brought about by HIIE training. Although waist circumference is strongly correlated with abdominal and visceral fat a limitation of this study is that these measures were not directly assessed.

The cardiac, vascular, and autonomic changes to mental challenge found after participation in HIIE appear to be notable and are likely to have health implications as cardiac disease is predicted by low $\dot{V}O_{2max}$ (Keteyian et al., 2008), whereas enhanced arterial stiffness is associated with increased cardiovascular mortality (Laurent et al., 2001). Blunted limb blood flow (Takeshita et al., 1982) and reduced baroreceptor sensitivity during mental challenge (Ookuwa et al., 1987) also predict hypertension development. Given that the major reason given for not exercising is time (Inelmen et al., 2004) it is likely that the brevity of HIIE protocols (one hour of exercise per week) should be appealing to most individuals interested in improving cardiovascular health. In summary, a HIIE program conducted for 12 weeks resulted in significant changes in aerobic fitness and body weight and also enhanced cardiovascular efficiency during mental and physical challenge.

Acknowledgements

We would like to thank Lucas Webb for help with data collection. We wish to thank Diabetes Australia for supporting this project (Grant #RM06599). None of the authors had a personal or financial conflict of interest.

References

Agapitov, A. V., Correia, M. L. G., Sinkey, C. A., Dopp, J. M., & Haynes, W. G. (2002). Impaired skeletal muscle and skin microcirculatory function in human obesity. *Journal of Hypertension, 20*(7), 1401-1405.

Ansari, M., Javadi, H., Pourbehi, M., Mogharrabi, M., Rayzan, M., Semnani, S., et al. (2012). The association of rate pressure product (RPP) and myocardial perfusion imaging (MPI) findings: a preliminary study. *Perfusion, 27*(3), 207-213.

Blumenthal, J. A., Fredrikson, M., Matthews, K. A., Kuhn, C. M., Schniebolk, S., German, D., et al. (1991). Stress reactivity and exercise training in premenopausal and postmenopausal women. *Health Psychology, 10*(6), 384-391.

Borg, G. (1962). *Physical performance and perceived exertion*: C. W. K. Gleerup.

Boutcher, S. H. (2011). High-intensity intermittent exercise and fat loss. *Journal of Obesity, doi: 10.1155/2011/868305*.

Boutcher, S. H., & Hamer, M. (2006). *Psychobiological reactivity, physical activity and cardiovascular health. In E.O. Acevedo & P. Ekkekakis (Eds.), Psychobiology of Physical Activity.* Champaign,. IL: Human Kinetics.

Boutcher, S. H., Nugent, F. W., McLaren, P. F., & Weltman, A. L. (1998). Heart period variability of trained and untrained men at rest and during mental challenge. *Psychophysiology, 35*(1), 16-22.

Carroll, D., Ring, C., Hunt, K., Ford, G., & Macintyre, S. (2003). Blood pressure reactions to stress and the prediction of future blood pressure: Effects of sex, age, and socioeconomic position. *Psychosomatic Medicine, 65*(6), 1058-1064.

Carroll, D., Smith, G. D., Shipley, M. J., Steptoe, A., Brunner, E. J., & Marmot, M. G. (2001). Blood pressure reactions to acute psychological stress and future blood pressure status: A 10-year follow-up of men in the Whitehall II study. *Psychosomatic Medicine, 63*(5), 737-743.

Carter, J. B., Banister, E. W., & Blaber, A. P. (2003). The effect of age and gender on heart rate variability after endurance training. *Medicine and Science in Sports and Exercise, 35*(8), 1333-1340.

Chida, Y., & Steptoe, A. (2010). Greater cardiovascular responses to laboratory mental stress are associated with poor subsequent cardiovascular risk status. *Hypertension, 55*(4), 1026-1032.

Convertino, V. A. (1991). Blood volume: Its adaptation to endurance training. *Medicine and Science in Sports and Exercise, 23*(12), 1338-1348.

Cooke, C. B. (2009). *Maximal oxygen uptake, economy and efficiency. In: Eston RG, Reilly T, editors.* (Third ed.). London (UK): Routledge, 174-212.

Deanfield, J., Kensett, M., Wilson, R., Shea, M., Horlock, P., De Landsheere, C., et al. (1984). Silent myocardial ischaemia due to mental stress. *The Lancet, 324*(8410), 1001-1005.

Forcier, K., Stroud, L. R., & Papandonatos, G. D. (2006). Links between physical fitness and cardiovascular reactivity and recovery to psychological stressors: A meta-analysis. *Health Psychology, 25*(6), 723-739.

Georgiades, A., Sherwood, A., Gullette, E. C. D., Babyak, M. A., Hinderliter, A., Waugh, R., et al. (2000). Effects of exercise and weight loss on mental stress-induced cardiovascular responses in individuals with high blood pressure. *Hypertension, 36*(2), 171-176.

Helgerud, J., Hoydal, K., Wang, E., Karlsen, T., Berg, P., Bjerkaas, M., et al. (2007). Aerobic high-intensity intervals improve VO_{2max} more than moderate training. *Medicine & Science in Sports & Exercise, 39*(4), 665-671

Heydari, M., Freund, J., & Boutcher, S. H. (2012). The effect of high-intensity intermittent exercise on body composition of overweight young males. *Journal of Obesity, doi:10.1155/2012/480467*.

Honzíková, N., Nováková, Z., Závodná, E., Paděrová, J., Lokaj, P., Fišer, B., et al. (2006). Baroreflex sensitivity in children, adolescents, and young adults with essential and white-coat hypertension. *Klinische Padiatrie, 218*(04), 237-242.

Inelmen, E. M., Toffanello, E. D., Enzi, G., Gasparini, G., Miotto, F., Sergi, G., et al. (2004). Predictors of drop-out in overweight and obese outpatients. *International Journal of Obesity 29*(1), 122-128.

Keteyian, S. J., Brawner, C. A., Savage, P. D., Ehrman, J. K., Schairer, J., Divine, G., et al. (2008). Peak aerobic capacity predicts prognosis in patients with coronary heart disease. *American Heart Journal, 156*(2), 292-300.

Laurent, S., Boutouyrie, P., Asmar, R., Gautier, I., Laloux, B., Guize, L., et al. (2001). Aortic stiffness is an independent predictor of all-cause and cardiovascular mortality in hypertensive patients. *Hypertension, 37*(5), 1236-1241.

Lazarova, Z., Tonhajzerova, I., Trunkvalterova, Z., Brozmanova, A., Honzíková, N., Javorka, K., et al. (2009). Baroreflex sensitivity is reduced in obese normotensive children and adolescents. *Canadian Journal of Physiology and Pharmacology, 87*(7), 565-571.

Lipman, R. D., Grossman, P., Bridges, S. E., Hamner, J. W., & Taylor, J. A. (2002). Mental stress response, arterial stiffness, and baroreflex sensitivity in healthy aging. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences, 57*(7), B279-B284.

London, G. M., Blacher, J., Pannier, B., Guérin, A. P., Marchais, S. J., & Safar, M. E. (2001). Arterial wave reflections and survival in end-stage renal failure. *Hypertension, 38*(3), 434-438.

Marchais, S., Guerin, A., Pannier, B., Levy, B., Safar, M., & London, G. (1993). Wave reflections and cardiac hypertrophy in chronic uremia. Influence of body size. *Hypertension, 22*(6), 876-883.

Ookuwa, H., Takata, S., Ogawa, J., Iwase, N., Ikeda, T., & Hattori, N. (1987). Abnormal cardiopulmonary baroreflexes in normotensive young subjects with a family history of essential hypertension. *Journal of Clinical Hypertension 3*(4), 596-604.

Parlow, J., Viale, J.-P., Annat, G., Hughson, R., & Quintin, L. (1995). Spontaneous cardiac baroreflex in humans : Comparison with drug-induced responses. *Hypertension, 25*(5), 1058-1068.

Persson, P. B. (2005). Baroreflexes in hypertension. *Hypertension, 46*(5), 1095-1096.

Reyes Del Paso, G. A., González, I., & Hernández, J. A. (2004). Baroreceptor sensitivity and effectiveness varies differentially as a function of cognitive-attentional demands. *Biological Psychology, 67*(3), 385-395.

Ribeiro, M. M., Silva, A. G., Santos, N. S., Guazzelle, I., Matos, L. N. J., Trombetta, I. C., et al. (2005). Diet and exercise training restore blood pressure and vasodilatory responses during physiological maneuvers in obese children. *Circulation, 111*(15), 1915-1923.

Sato, T., Nishinaga, M., Kawamoto, A., Ozawa, T., & Takatsuji, H. (1993). Accuracy of a continuous blood pressure monitor based on arterial tonometry. *Hypertension, 21*(6), 866-874.

Seematter, G., Guenat, E., Schneiter, P., Cayeux, C., Jéquier, E., & Tappy, L. (2000). Effects of mental stress on insulin-mediated glucose metabolism and energy expenditure in lean and obese women. *American Journal of Physiology - Endocrinology and Metabolism, 279*(4), E799-E805.

Sherwood, A., Allen, M. T., Fahrenberg, J., Kelsey, R. M., Lovallo, W. R., & van Doornen, L. J. P. (1990). Methodological guidelines for impedance cardiography. *Psychophysiology, 27*(1), 1-23.

Söderström, S., Nyberg, G., O'Rourke, M. F., Sellgren, J., & Pontén, J. (2002). Can a clinically useful aortic pressure wave be derived from a radial pressure wave? *British Journal of Anaesthesia, 88*(4), 481-488.

Strike, P. C., & Steptoe, A. (2003). Systematic review of mental stress-induced myocardial ischaemia. *European Heart Journal, 24*(8), 690-703.

Stroop, J. P. (1935). Studies in interference in serial verbal reactions. *Journal of Experimental Psychology, 18*, 643-662.

Takeshita, A., Imaizumi, T., Ashihara, T., Yamamoto, K., Hoka, S., & Nakamura, M. (1982). Limited maximal vasodilator capacity of forearm resistance vessels in normotensive young men with a familial predisposition to hypertension. *Circulation Research, 50*(5), 671-677.

Thomas, S., Reading, J., & Shephard, R. J. (1992). Revision of the physical activity readiness questionnaire (PAR-Q). *Canadian Journal of Sport Sciences, 17*(4), 338-345.

Trapp, E. G., Chisholm, D. J., & Boutcher, S. H. (2007). Metabolic response of trained and untrained women during high-intensity intermittent cycle exercise. *American Journal of Physiology - Regulatory, Integrative and Comparative Physiology, 293*(6), R2370-R2375.

Trapp, E. G., Chisholm, D. J., Freund, J., & Boutcher, S. H. (2008). The effects of high-intensity intermittent exercise training on fat loss and fasting insulin levels of young women. *Internatonal Journal of Obesity, 32*(4), 684-691.

Vlachopoulos, C., Kosmopoulou, F., Alexopoulos, N., Ioakeimidis, N., Siasos, G., & Stefanadis, C. (2006). Acute mental stress has a prolonged unfavorable effect on arterial stiffness and wave reflections. *Psychosomatic Medicine, 68*(2), 231-237.

Weber, T., Auer, J., O'Rourke, M. F., Kvas, E., Lassnig, E., Berent, R., et al. (2004). Arterial stiffness, wave reflections, and the risk of coronary artery disease. *Circulation, 109*(2), 184-189.

Wilkinson, I. B., Fuchs, S. A., Jansen, I. M., Spratt, J. C., Murray, G. D., Cockcroft, J. R., et al. (1998). Reproducibility of pulse wave velocity and augmentation index measured by pulse wave analysis. *Journal of Hypertension, 16*(12), 2079-2084.

World Health Organization. (2011). Cardiovascular diseases (CVDs). Retrieved 11 January 2012, from http://www.who.int/mediacentre/factsheets/fs317/en/index.html

Conclusion

Study 1 reported in Chapter 2 investigated and compared the metabolic response of acute HIIE in both trained and untrained males. Participants in the trained group had significantly higher $\dot{V}O_{2max}$ than those in the untrained group. The trained group also showed higher $\dot{V}O_2$ and $\dot{V}CO_2$ during exercise and lower lactate and heart rate during exercise. For both groups glycerol levels were significantly elevated during exercise. Both groups had a similar and significant increase in epinephrine during HIIE, in contrast, untrained compared to trained males recorded significantly greater levels of norepinephrine. During the post-exercise recovery period from minutes 45 to 75 fat oxidation was significantly increased. Plasma glycerol levels at rest and 15 min after HIIE were significantly higher for both groups. Plasma norepinephrine concentrations were significantly higher 15 min post exercise for both groups, whereas plasma epinephrine levels showed a significant increase after 20 min of HIIE for both groups. In conclusion, one bout of HIIE resulted in enhanced catecholamine levels during and after exercise in trained and untrained males. This increase was accompanied by an elevation in lipolysis indicated by the increase in blood glycerol levels during HIIE. The enhanced fat oxidation occurred for both trained and untrained males following HIIE. These findings may have clinical implications for the management of overweight and obesity. Furthermore, the increased catecholamine concentrations during HIIE have the potential for improvement in cognitive performance. More research is necessary to elucidate the physiological mechanisms underlying mental improvement induced by an acute exercise bout. This study, however, has a number of limitations. The measurement of fat oxidation during post exercise recovery period was limited to only one hour. An

extended monitoring of fat oxidation following this type of exercise might provide additional information to help understand possible fat burning benefits. Furthermore, this study investigated the effects of HIIE on metabolic and hormonal changes but did not attempt to identify possible underlying mechanisms. More invasive methods such as muscle biopsies could be utilized to identify these mechanisms.

Study 2 reported in Chapter 3 presented an investigation into the effect of HIIE on body composition of overweight young males. Aerobic power improved significantly by 15% for the exercising group. Exercisers compared to controls experienced significant weight loss of 1.5 kg and a significant reduction in total fat mass of 2 kg. Abdominal and trunk adiposity was also significantly reduced in the exercising group by 0.1 kg and 1.5 kg. Also the exercise group had a significant 17% reduction in visceral fat after 12 weeks of HIIE, whereas waist circumference was significantly decreased by week six. Fat free mass was significantly increased in the exercising group by 0.4 kg for the leg and 0.7 kg for the trunk. No significant change occurred in levels of insulin, HOMA-IR, and blood lipids. A limitation of this study is that we did not include a continuous exercise group or an HIIE group that differed in exercise/recovery duration. As this HIIE program required minimal time commitment it has implications regarding subject compliance to exercise interventions. Thus, physical activity prescriptions, which require the least effort, while still producing adequate reductions in subcutaneous and visceral fat need to be considered and HIIE would seem to fall under this category as subject‘s total exercise commitment was 60 min per week. More research is needed to evaluate and confirm the outcomes from our results by conducting long term studies. In conclusion, 20 min of HIIE, performed three times per week for 12 weeks, resulted in significant reductions in total body, abdominal, trunk, and visceral fat and a

significant increase in fat free mass of overweight young males. These findings have important implications for public health and may have potential to be used as part of a weight management program to reduce visceral obesity which contributes to diseases such as cardiovascular, hypertension, diabetes, and metabolic syndrome. The effectiveness of HIIE on fat loss in other parts of the body such as the heart and pericardium needs further research. Also, it might be of an interest for future research to investigate the body composition change following this type of exercise training modality in other population groups such as patients with cardiovascular disease, hypertension, or diabetes. It is also recommended that the response of individuals from different ethnic groups to HIIE be studied.

Study 3 reported in Chapter 4 investigated the effects of HIIE on cardiovascular and autonomic function. This study concluded that the exercise, compared to the control group, recorded a significant reduction in heart rate accompanied by an increase in stroke volume. Forearm vasodilatory capacity was also significantly enhanced for the exercise group. Arterial stiffness, determined by pulse wave velocity and augmentation index, was significantly improved, after the 12-week intervention. Besides, heart period variability (low and high frequency power) and baroreceptor sensitivity were significantly increased for the exercise group. The improvements in cardiovascular and autonomic indicators following HIIE training are likely to have health implications for preventive cardiovascular programs. Low $\dot{V}O_{2max}$ has been shown to predict cardiac disease and high levels of arterial stiffness are associated with increased risk of morbidity and mortality related to cardiovascular diseases. In addition, low vasodilatory capacity and baroreceptor sensitivity have been linked to hypertension development and reduced HPV is a predictor of a number of cardiac complications. These findings are particularly

important and may have implications for people under constant daily stress who by exercising may get benefit from a range of improved cardiovascular and autonomic functions with a minimal time commitment. HIIE training program might also show beneficiary results in patients with cardiac disease, hypertension, and diabetes and benefits of this type of exercise to other population groups needs further investigation. Also it is recommended that the cardiovascular and autonomic responses of female participants or males from different age groups to HIIE be studied by future research.

In Study 4 reported in Chapter 5 the effects of HIIE training on cardiovascular response to mental and physical challenge was investigated. Exercisers compared to controls experienced a significant reduction in HR and a significant increase in SV at rest and during Stroop and exercise. For exercisers, arterial stiffness significantly decreased at rest and during Stroop whereas BRS was increased at rest and during Stroop. Forearm blood flow was significantly increased during the first two minutes of Stroop. In summary, a HIIE program conducted for 12 weeks resulted in significant enhanced cardiovascular efficiency during mental and physical challenge.

The implications of these results are that HIIE may be used as an efficient method to reduce psychological stress experienced by many people in daily life. The improved cardiovascular and autonomic response of the body to mental challenge, found after participation in HIIE training, are likely to have implications for cardiovascular health. As exaggerated cardiovascular responses to psychological stressors contribute to cardiovascular diseases, possible clinical benefits of this study might be the protective effects of HIIE against the development of stress-related disorders such as cardiovascular disease.

An improved level of physical fitness plays an important role in an attenuated response of physiological and cardiovascular reactivity to acute psychological stressors. Therefore, the increased level of aerobic fitness in this study has implications to promote cardiovascular health and results indicate that fitness might be an important confound in the stress reactivity response. Furthermore, it may offer extra ammunition for health care providers to encourage sedentary individuals to start exercising.

Although in this study the Stroop task was used as a mental laboratory stressor, other types of mental stressors such as mental arithmetic, public speaking, light tracking, cold pressor, reaction time, video games, and intelligence tests should be examined. Also, more powerful stressors experienced in real life may cause greater impairments to cardiovascular and autonomic measures and may provoke different responses to HIIE. Further work is also necessary to investigate stress reactivity and the underlying mechanisms during recovery from mental and physical challenge. In this study, stress hormones such as cortisol were not measured during the Stroop task, which is another limitation of this study. Finally, the findings of this study are limited to young overweight males and, therefore, cannot be generalised to female populations or males from different age groups. The possible beneficiary effects of HIIE in mediating the cardiovascular response of the body to mental and physical stress in diverse population groups also needs further research attention.

Appendixes

THE UNIVERSITY
OF
NEW SOUTH WALES

Approval No (HREC 0365)

THE UNIVERSITY OF NEW SOUTH WALES

Appendix A: Participant Information Statement and Consent Form

Effect of High Intensity Intermittent Exercise on Fat Oxidation in Overweight Males

You, _____ are invited to participate in a study examining the effects of high intensity intermittent exercise on fat oxidation. We, Associate Professor Stephen Boutcher and Yati Boutcher hope to show that high intensity cycle exercise significantly induce fat oxidation. Fat oxidation involves the body burning up its fat stores. You were selected as a possible participant in this study because you are a male under the age of 35 years.

If you decide to participate, you will be involved in three testing sessions at UNSW. During Session 1 you will undergo a 30-minute resting metabolic rate evaluation. This will involve lying on a bed while your breathing is monitored through a metabolic cart. The cart will assess how much oxygen you are consuming and how much carbon dioxide you are producing. Then you will get on to a stationary bicycle and cycle at ever increasing workloads until you reach your maximum exercise capacity. A heart rate monitor will be strapped around your chest to measure heart rate and your blood pressure will be taken regularly. Body composition measures will also be assessed (bioimpedance, mass, and height).

There may be some discomfort associated with the exercise if you are unaccustomed to regular exercise but this is likely to be minimal and you will recover rapidly. If you are not used to bicycling you may find you have delayed onset muscle soreness for a day or two after the exercise bout, but this resolves quickly. Most individuals rapidly adjust to breathing through a mouthpiece.

During Session 2 you will again have your resting metabolic rate assessed after which you will perform 20 minutes of high intensity intermittent exercise. This exercise will consist of sprinting on a stationary bike for 8 seconds and then cycling for 12 seconds at a slow pedal rate. This will be performed continuously for 20 minutes. A small needle (venous catheter) will be placed in a vein in the back of your hand or forearm so that we can take a small amount of blood for testing at regular intervals. After the exercise session you will lie on a comfortable bed for an hour while your body's response to the exercise is monitored. The two exercise sessions will occur at least a week apart.

The total time involvement for you for the three testing sessions will be about one hour for the first session and two hours for the second session. In total this will involve two separate sessions at the University over a two week period.

You will also be asked to complete a food intake diary in which you record the quantity and type of food you eat each day. Random days will be selected for this purpose. We ask that you do not change your normal food intake over the period of this study.

Any information that is obtained in connection with this study and that can be identified with you will remain confidential and will be disclosed only with your permission or except as required by law. If you give us your permission by signing this document, we plan to publish the results in scientific journals. In any publication, information will be provided in such a way that you cannot be identified.

Complaints may be directed to the Ethics Secretariat, The University of New South Wales, SYDNEY 2052 AUSTRALIA (phone 9385 4234, fax 9385 6648, email ethics.sec@unsw.edu.au).

Your decision whether or not to participate will not prejudice your future relations with The University of New South Wales. If you decide to participate, you are free to withdraw your consent and to discontinue participation at any time without prejudice.

If you have any questions, please feel free to ask us. If you have any additional questions later, Steve Boutcher on 9385 2877 or email (s.boutcher@unsw.edu.au), will be happy to answer them.

You will be given a copy of this form to keep.

There should be little discomfort associated with the insertion and/or withdrawal of the needle and we have found little discomfort to be associated with exercising with a needle inserted in the hand or forearm.

THE UNIVERSITY OF NEW SOUTH WALES

Participant Information Statement and Consent Form (continued)

Effect of High Intensity Intermittent Exercise on Fat Oxidation in Overweight Males

You are making a decision whether or not to participate. Your signature indicates that, having read the information provided above, you have decided to participate.

.....	.....
Signature of Research Participant	Signature of Witness
.....	.....
(Please PRINT name)	(Please PRINT name)
.....	.....
Date	Signature of Witness

.....
Signature(s) of Investigator(s)

.....
Please PRINT Name

Revocation of Consent

Effect of High Intensity Intermittent Exercise on Fat Oxidation in Overweight Males

I hereby wish to **WITHDRAW** my consent to participate in the research proposal described above and understand that such withdrawal **WILL NOT** jeopardise any treatment or my relationship with The University of New South Wales.

....
Signature Date

.....
Please PRINT Name

The section for Revocation of Consent should be forwarded to:
Associate Professor Steve Boutcher
School of Medical Sciences
Faculty of Medicine
UNSW
Kensington NSW 2052

THE UNIVERSITY
OF
NEW SOUTH WALES

Approval No (HREC 0365)

THE UNIVERSITY OF NEW SOUTH WALES

Appendix B: Participant Information Statement and Consent Form

High Intensity Exercise Training Study

You, _____ are invited to participate in a training study examining the effects of high intensity intermittent exercise on fat loss. We, Associate Professor Steve Boutcher and Yati Boutcher hope to show that high intensity cycle exercise significantly reduces fat loss in men. You were selected as a possible participant in this study because you are a male under the age of 36 years and not currently exercising.
If you decide to participate, we will get you to do an exercise fitness test on a stationary bicycle before you commence and after 12 weeks of cycle training. On each of these occasions, you will be breathing through a mouthpiece so that we can measure the amount of oxygen you breathe in and the amount of carbon dioxide you breathe out. A small needle (venous catheter) will be placed in a vein in the back of your hand or forearm so that we can take a small amount of blood for testing at regular intervals. A heart rate monitor will be strapped around your chest to measure heart rate and your blood pressure will be taken regularly.

During the initial and final tests you will be asked to cycle at ever increasing workloads until you reach your maximum exercise capacity. The total time involvement for you for the testing procedures before and after the training program is about three to four hours. This will involve two separate sessions of approximately one to two hours at the University. During these sessions you will perform three tasks designed to assess the status of your vasculature. These tasks will include 8 minutes of light cycle exercise, 5 minutes responding to slides on a computer (the Stroop task).
The training will involve three sessions per week of high intensity intermittent cycle training. There will be one training group and one control group, one of which you will be assigned to on the toss of a coin (random selection). The training regime will involve high intensity, intermittent work periods separated by low intensity rest periods with a work to rest ratio of 8s:12s. The total

exercise time per session will start at 10 min. and progress over the training period to a total of 20 min. These time allocations include a 5 minute warm-up. It is suggested that after you have completed the session you do five minutes of cool down followed by stretching to reduce the likelihood of post exercise soreness. Please do not do any additional physical activity (other than your normal daily activities) for the period of the study. Subjects allocated to the control group will be asked to maintain their normal daily activity patterns until after the study is complete, at which time they will be given an exercise program if they so desire.

You will also be asked to complete a food intake diary in which you record the quantity and type of food you eat each day. Random days will be selected for this purpose. We ask that you do not change your normal food intake over the period of this study to ensure that any changes are a result of the exercise program and not because you have changed your eating habits.

Before the first test and at the end of the training period, body composition measures will be taken. Body composition measures include DEXA (see below), CT (see below), bioimpedance, skinfold, girth, mass and height measures.

Dual Energy X-ray Absorptiometry Scan (DEXA scan). This procedure is routinely undertaken in many people for the diagnosis of osteoporosis, but it gives a very accurate estimation of fat tissue as well as bone. The study will be performed in the Department of Nuclear Medicine, St Vincent‘s Clinic, and involves lying flat on a table for about 10 minutes while an X-ray beam measures body composition (particularly fat and bone). The radiation dose (0.0005 mSv) involved is very small and is the equivalent of $1/10^{th}$ the radiation dose involved in a single chest x-ray.

Abdominal CT scan: This will be performed in the Medical Imaging (X-ray) Department of St Vincent‘s Hospital and involves lying on a table in a ―tunnel" in the CT machine for about 5 minutes, while an X-ray beam measures the tissue composition at four levels in the abdomen. The radiation dose involved is small and is equivalent to about five times that of a plain x-ray of the abdomen but the radiation dose is less than a standard CT of the abdomen done for diagnostic purposes.

This research study involves exposure to a very small amount of radiation. As part of everyday living, everyone is exposed to naturally occurring background radiation and receives a dose of about 2 millisieverts (mSv) each year. The effective dose from this study is about 2 mSv. At this dose level, no harmful effects of radiation have been demonstrated, and the risk is very low.

Have you participated in other research studies involving extra x-rays or nuclear medicine tests that were not part of your normal treatment in the last five years? If YES please inform the study coordinator of the details of these involvements as there is a radiation dose limit for volunteers of 10 mSv per five year period.

There may be some discomfort associated with the exercise if you are unaccustomed to regular exercise but this is likely to be minimal and you will recover rapidly. If you are not used to bicycling you may find you have delayed onset muscle soreness for a day or two after the exercise bout, but this resolves quickly. There should be little discomfort associated with the insertion

and/or withdrawal of the needle and we have found little discomfort to be associated with exercising with a needle inserted in the hand or forearm. Most individuals rapidly adjust to breathing through a mouthpiece. DEXA and CT measures involve lying on a bed while the machine scans your body. There is no discomfort associated with these procedures.

There are few risks associated with exercise for adult males below the age of 36 years. The most likely outcome is post exercise soreness but this may not occur. There is a small risk of bruising associated with the withdrawal of blood but all care will be taken to ensure this does not happen. Radiation exposure associated with DEXA and CT is limited.

Participants who reveal serious medical condition during the testing will be excluded from the study and referred to a General Practitioner. Participants having a family history of youthful cardiac events will also be excluded from the study. In the case of an adverse event, testing will be immediately ceased. If necessary emergency resuscitation will be applied and emergency services contacted.

Any information that is obtained in connection with this study and that can be identified with you will remain confidential and will be disclosed only with your permission or except as required by law. If you give us your permission by signing this document, we plan to publish the results in scientific journals. In any publication, information will be provided in such a way that you cannot be identified.

Complaints may be directed to the Ethics Secretariat, The University of New South Wales, SYDNEY 2052 AUSTRALIA (phone 9385 4234, fax 9385 6648, email ethics.sec@unsw.edu.au).

Your decision whether or not to participate will not prejudice your future relations with The University of New South Wales. If you decide to participate, you are free to withdraw your consent and to discontinue participation at any time without prejudice.

If you have any questions, please feel free to ask us. If you have any additional questions later, Steve Boutcher on 9385 2877 or email (s.boutcher@unsw.edu.au), will be happy to answer them.

You will be given a copy of this form to keep.

THE UNIVERSITY OF NEW SOUTH WALES

Participant Information Statement and Consent Form (continued)

High Intensity Exercise Training Study

You are making a decision whether or not to participate. Your signature indicates that, having read the information provided above, you have decided to participate.

.....	.....
Signature of Research Participant	Signature of Witness
.....	.....
(Please PRINT name)	(Please PRINT name)
.....	.....
Date	Nature of Witness

.....
Signature(s) of Investigator(s)

.....
Please PRINT Name

Revocation of Consent

High Intensity Exercise Training Study

I hereby wish to **WITHDRAW** my consent to participate in the research proposal described above and understand that such withdrawal **WILL NOT** jeopardise any treatment or my relationship with The University of New South Wales.

....
Signature Date

.....
Please PRINT Name

The section for Revocation of Consent should be forwarded to:
Associate Professor Steve Boutcher
School of Medical Sciences
Faculty of Medicine
UNSW
Kensington NSW 2052

Appendix C: Personal and Familial Medical History Questionnaire

Research Questionnaire -- Subject ID_____

1. How often do you exercise?
2. What do you do for exercise?
3. What time of day do you exercise?
4. Have you ever exercised on a stationary bike or tried a spinning class before?
5. Have you tried to lose weight or been on a diet in the last year?
6. Has your weight fluctuated by more than 2kg throughout your life?
7. What was your birth weight?
8. Does anyone in your family have diabetes, if so who?
9. Have you ever checked your insulin/blood sugar levels?
10. Would you be willing to be contacted about the results from this study?
11. Would you be interested in Sarah contacting you if you are eligible for other research studies in our department in the next year?
12. Can we take photos of you while we are performing the research, to be used for presentations?
13. Is it ok for students to help out with the research while we are testing you?
14. Are you currently on any medication, if so what and how much?
15. Are you currently taking any supplements or vitamins?
16. Have you ever smoked cigarettes? If so, for how long and are you a current smoker?
17. What is your ethnicity?
18. Contact info & Date of birth
    a. Phone
    b. Email
    c. DOB

Appendix D: Physical Activity Readiness Questionnaire

Name:

Par-Q
Pre Exercise Screening Test

1. Has your doctor ever said you have heart trouble?	**Yes**	**No**
2. Do you frequently have pains in your heart and chest?	**Yes**	**No**
3. Do you often feel faint or have spells of severe dizziness?	**Yes**	**No**
4. Has a doctor ever said your blood pressure was high?	**Yes**	**No**
5. Has your doctor ever told you that you have a bone or joint problem such as arthritis that has been aggravated by exercise or might be made worse with exercise?	**Yes**	**No**
6. Is there a good physical reason not mentioned here why you should not follow an activity program even if you wanted to?	**Yes**	**No**
7. Are you over the age of 65 and not accustomed to vigorous exercise?	**Yes**	**No**

If you answered ***yes*** to one or more questions:

If you have not recently done so consult with your personal physician by telephone or in person **BEFORE** increasing your physical activity and/or taking a fitness appraisal. Tell your physician what questions you answered YES to PAR-Q or present your PAR-Q copy.

After medical evaluation seek advice from your physician as to your suitability for:

√ Unrestricted physical activity starting off easily and progressing gradually.

√ Restricted or supervised activity to meet your specific needs at least on an initial basis. Check in your community for special programs or services.

If you answered ***no*** to all questions:

√ If you answered the PAR-Q accurately, you have reasonable assurance of your present suitability for exercise testing.

√ Postpone the testing if you have a temporary minor illness such as a common cold.

Signed_____ Name_____

Date_____

Appendix E: Pre- Participant Questionnaire

DATE:	
Subject Code (Office use): VEIN:	
First Name:	Surname:
DOB:	Age:
Address:	
Tel (H):	Mobile number:
Email:	
Subject Information	
Your country of birth:	
Mother‘s country of birth:	Father‘s country of birth:
If you were born overseas, Date of Arrival:	
Your Ethnicity:	
Birth weight:_____ kg (please find out beforehand)	
Were you breast or formula fed as a baby?	
Are you a student or in the working world?	
Do you live on campus (UNSW) or off?	
What is your dominant arm? right left	
Do you have any <u>existing</u> and <u>past</u> medical conditions? Y N	
Please specify:	
Have you had any sort of infection recently? Y N	
Please specify:	
Are you currently taking any medication? Y N	
Please specify: e.g. oral contraceptives, beta-blockers	
Are you currently taking any supplements or vitamins? Y N	
Please specify: e.g. multi-vitamin, phytonutrients	
Have you ever smoked before? Y N	
If yes, currently or in the past and when in the past?	
How many years and/or months were you smoking?	

How many cups of tea and/or coffee do you consume per day? ❑ none at all ❑ 1 cup ❑ 2-3 ❑ 4-5 ❑ > 5	
Do you have any allergies?	
Do you exercise regularly? Y N	
What type of exercise do you do?	
What time of day do you exercise? morning noon evening/night	
How many times a week do you exercise?	
How many hours do you typically sleep at night?	
When you wake up are your refreshed or tired? refreshed tired	
What time do you go to sleep?	
What is the quality of your sleep? good Ok bad	
Have you ever suffered from sleep deprivation or lack of sleep?	
Have you recently been on a diet or tried to lose weight?	
Has your weight fluctuated more than 2 (kg) in the last 6 months?	
Have you ever checked the following before and if so what was your reading? Insulin Y N Last Reading: Blood Pressure Y N Last Reading: Glucose Y N Last Reading:	
Do/did any members of your family suffer from a medical condition? (especially Type II diabetes, hypertension, high cholesterol)	
Condition(s):	Relation to you:
This Study	
How did you hear about this study? ❑Blitz ❑friends ❑email ❑lecture ❑media/TV/newspaper ❑posted sign	
Can we take photos of you during testing? The photos may be used in a poster presentation of this study. Y N	
Is it ok with you that students help out during your testing session? Y N	
Would you like to participate in other studies in the future for our department? Y N	

Appendix F: POST Participant Questionnaire (Exercise Group)

DATE: Subject Code (Office use):
Have you had any sort of infection while in the study? Y N
Please specify (what & when):
Did you smoke during the study? Y N If yes, how much?
How many cups of tea and/or coffee did you consume per day? ❑ none at all ❑ 1 cup ❑ 2-3 ❑ 4-5 ❑ > 5
How many hours did you typically sleep at night during the study?
When you woke up were you refreshed or tired? refreshed tired
What time did you typically go to sleep?
What was the quality of your sleep? good ok bad
Did you suffer from sleep deprivation or lack of sleep?
Will you continue to exercise after the study?
Did you enjoy the exercise component of the study? Y N
Rate the intensity of all the exercise sessions? ❑ Very Hard ❑ Hard ❑ Somewhat Hard ❑ Fairly Light ❑ Very Light
What foods will you go back to or start eating now that the study is over?
Please specify:
Is there anything we can change to make the study better or more enjoyable?
Please specify:
Would you like to participate in other studies for our department? Y N
Has any of your contact details changed since the start of the study? Y N If yes, please write the new details on the back of this form.

Appendix G: POST Participant Questionnaire (Control Group)

DATE: Subject Code (Office use):
Have you had any sort of infection while in the study? Y N
Please specify (what & when):
Did you smoke during the study? Y N If yes, how much?
How many cups of tea and/or coffee did you consume per day? ❑ none at all ❑ 1 cup ❑ 2-3 ❑ 4-5 ❑ > 5
How many hours did you typically sleep at night during the study?
When you woke up were you refreshed or tired? refreshed tired
What time did you typically go to sleep?
What was the quality of your sleep? good ok bad
Did you suffer from sleep deprivation or lack of sleep?
Will you continue to exercise after the study?
Did you enjoy the exercise component of the study? Y N
Rate the intensity of all the exercise sessions? ❑ Very Hard ❑ Hard ❑ Somewhat Hard ❑ Fairly Light ❑ Very Light
What foods will you go back to or start eating now that the study is over?
Please specify:
Is there anything we can change to make the study better or more enjoyable?
Please specify:
Would you like to participate in other studies for our department? Y N
Has any of your contact details changed since the start of the study? Y N If yes, please write the new details on the back of this form.

Appendix H: Diet Diary and Food Information

Instructions for Food Diary

Try to be as specific as possible!!!!!!!

- Please read through the EXAMPLE entry
- If you have dishes that you don‘t know the name of, try to describe the contents, take note of the quantity and the way it is cooked. For example, a stir-fry with hokkien noodles (approximately 2 cups), beef (less than ½ cup), capsicum, onion, cabbage and shallots, cooked in vegetable oil and seasoned with hoi-sin sauce.
- Try to record your food intake on days that are closest to what your normal diet is like.
- Try to estimate the size of the servings as best as you can. Think: teaspoons, tablespoons, cups, grams, mL etc.
- When eating fruit or veggies, try to figure out if it is small, medium or large and what type
- If you are eating a muesli bar or something coated in chocolate or yogurt make sure to put that down, briefly describe contents
- Do you know if the food you are eating was cooked in oil or fat?
- If you are eating cheese, what type and how much?
- For meats try to say white meat, dark meat, thigh, breast, cutlet, etc…
    - also think about how it was cooked, fried, grilled, baked
    - with or without skin
- Write down flavours of yogurt, ice cream, etc. . .
- Think of things in amounts, grams, teaspoons, cups, etc. . .
- Don‘t forget liquids, alcohol, soda, **water**, etc. . .
- Don‘t forget lollies, chocolates, cookies, traditional sweets, etc…
- Did you put sugar or sweet-n-low in your coffee or tea
    - What size is your coffee or tea?

The main message is

be specific

and

write down anything and everything!!!!!

Example

NAME Faith

DATE 21/05/06

DAY OF THE WEEK Saturday

Time	Meal	Food Item	Serving
8:30 am/~~pm~~	Breakfast	Wonton, filled with pork (10g each) x 12	120g
am/pm		Water	300 mL
am/pm		Vitamin C	1 tablet
11:30 am/~~pm~~	Morning Tea	Bagel (wheat) small, toasted	1
am/pm		Strawberry jam	2 teaspoons
1:00 ~~am~~/pm	Lunch	Chicken skewers (breast and thigh)	10 pieces
am/pm		Satay sauce	1/3 cup
am/pm		Rice, white (cooked)	½ cup
am/pm		Water	300 mL
am/pm		Violet crumble bar 50g	1
3:45 ~~am~~/pm	Snack	Pretzels (small bag)	20 g
7:30 ~~am~~/pm	Dinner	Beef stir fry with black bean sauce	200 g
am/pm		Chinese broccoli (gai lum) cooked with olive oil	1 cup (160mL)
am/pm		Oyster sauce	2 tablespoons
am/pm		Green salad	1 cup
am/pm		Salad dressing (French low fat)	2 tablespoons
am/pm		Rice, white (cooked)	1 cup
am/pm		Strongbow cider x 2	375 mL x2
am/pm		Chocolate ice cream	½ cup

Day 1

Food Diary

NAME _____

DATE _____

DAY OF THE WEEK _____

Time	Meal	Food Item	Serving
am/pm			
am/pm			
am/pm			
am/pm			
am/pm			
am/pm			
am/pm			
am/pm			
am/pm			
am/pm			
am/pm			
am/pm			
am/pm			
am/pm			
am/pm			
am/pm			
am/pm			
am/pm			
am/pm			
am/pm			
am/pm			

Day 2

Food Diary

NAME

DATE

DAY OF THE WEEK

Time	Meal	Food Item	Serving
am/pm			
am/pm			
am/pm			
am/pm			
am/pm			
am/pm			
am/pm			
am/pm			
am/pm			
am/pm			
am/pm			
am/pm			
am/pm			
am/pm			
am/pm			
am/pm			
am/pm			
am/pm			
am/pm			
am/pm			
am/pm			

Day 3

Food Diary

NAME

DATE

DAY OF THE WEEK

Time	Meal	Food Item	Serving
am/pm			
am/pm			
am/pm			
am/pm			
am/pm			
am/pm			
am/pm			
am/pm			
am/pm			
am/pm			
am/pm			
am/pm			
am/pm			
am/pm			
am/pm			
am/pm			
am/pm			
am/pm			
am/pm			
am/pm			
am/pm			

Appendix I: Cardiovascular and Autonomic Testing Protocol

Stroop first (evens) Date **Study ID**

Mins		Event	COP	Comments
1	Prep	Impedance (Heart sound)		Front: Back:
2	Prep	Hokanson & Jentow & ECG apparatus on subject		Forearm size:
3	Prep	Get BP Monitor (settings 5/15/5) & COP ready		time of day:
	Jentow Calib			BP: / HR:
4-13	PWV			Distal: Proximal:
14	Base		( )	
15	Base			
16	Base			
17	Base			
18	Base		( )	
	Jentow Calib			BP: / HR:
19	FBF-base ready	Sensor on & inflate wrist cuff for Hokhanson to 60 mmHg above SBP		
20		Press Continue on computer 55s after inflation of wrist cuff		
	FBF-base		( )	
21	FBF-base		( )	
22	Rest	Release wrist cuff & press **PAUSE** (2 min Rest)		
23	Rest	Psych questions		SAI ( )
	Jentow Calib			BP: / HR:
24	Stroop-ready	Inflate wrist cuff for Hokhanson to 60 mmHg above SBP		
25		Press Continue on computer 55s after inflation of wrist cuff		
26	Stroop		( )	Have subject say color **NOT** text
27	Stroop			
28	Stroop			
29	Stroop			
30	Stroop		( )	Stroop mistakes ( )

31	FBF-recovery	Stop Stroop but still take FBF measures	(-)	
32	Rest	Release wrist cuff & press **PAUSE**		
33	Rest	Wall questions and SAI		SAI ( )
34	Rest	5 min Rest		Enjoyment ( )
35	Rest			Concentration ( )
36	Rest			Difficulty ( )
	Jentow Calib			BP: / HR:
37	Exercise	Have person cycle at 20% Max for **8 min**	( )	20% Max:
38	Exercise			
39	Exercise			
40	Exercise			
41	Exercise			
42	Exercise			
43	Exercise			
44	Exercise	Inflate wrist cuff for Hokhanson to 60 mmHg above SBP. Press Continue on computer 55s after inflation of wrist cuff	( )	
45	FBF-recovery	stop exercise but still take BF measures	(-)	
46	Rest	Ask subject RPE		RPE ( )
47	Rest	5 min Rest		
48	Hyper	Inflate (manually) arm cuff for Hokhanson to 60 mmHg above SBP for **5 min**		BP + 60mmHg
49	Hyper	Change setting on BP Monitor (settings 5/10/5)		
50	Hyper	Wait 4 mins		
	Jentow Calib			BP: / HR:
51	Hyper	Inflate wrist cuff for Hokhanson to 60 mmHg above SBP		
52	Hyper	Press Continue on computer 55s after inflation of wrist cuff		
53		Deflate arm cuff (manually) to 50 mmHg& HIT CUFF/PRESET button		
54		Measure 3 FBFs		
55	Done	Push stop on computer & deflate both cuffs& take equipment off subject		

Exercise first (odds) Date **Study ID**

Mins		Event	COP	Comments
1	Prep	Impedance (Heart sound)		Front: Back:
2	Prep	Hokanson & Jentow & ECG apparatus on subject		Forearm size:
3	Prep	Get BP Monitor (settings 5/15/5) & COP ready		time of day:
	Jentow Calib			BP: / HR:
4-13	PWV			Distal: Proximal:
14	Base		( )	
15	Base			
16	Base			
17	Base			
18	Base		( )	
	Jentow Calib			BP: / HR:
19	FBF-base ready	Sensor on & Inflate wrist cuff for Hokhanson to 60 mmHg above SBP		
20		Press Continue on computer 55s after inflation of wrist cuff		
	FBF-base		( )	
21	FBF-base		( )	
22	Rest	Release wrist cuff & press **PAUSE** (2 min Rest)		
23	Rest			
	Jentow Calib			BP: / HR:
24	Exercise	Have person cycle at 20% Max for **8 min**	( )	20% Max:
25	Exercise			
26	Exercise			
27	Exercise			
28	Exercise			
29	Exercise			
30	Exercise		( )	
31	Exercise	Inflate wrist cuff for Hokhanson to 60 mmHg above SBP. Press Continue on computer 55s after inflation of wrist cuff	( )	

32	FBF-recovery	Stop exercise but still take BF measures	(-)	
33	Rest	Ask subject RPE		RPE ( )
34	Rest	5 min Rest		
	Jentow Calib			BP: / HR:
35	Stroop-ready	Inflate wrist cuff for Hokhanson to 60 mmHg above SBP		
36		Press Continue on computer 55s after inflation of wrist cuff		
37	Stroop		( )	Have subject say color **NOT** text
38	Stroop			
39	Stroop			
40	Stroop			
41	Stroop		( )	Stroop mistakes ( )
42	FBF-recovery	Stop Stroop but still take FBF measures	(-)	
43	Rest	Release wrist cuff & press **PAUSE**		
44	Rest	Wall questions and SAI		SAI ( )
45	Rest	5 min Rest		Enjoyment ( )
46	Rest			Concentration ( )
47	Rest			Difficulty ( )
48	Hyper	Inflate (manually) arm cuff for Hokhanson to 60 mmHg above SBP **5 min**		BP + 60mmHg
49	Hyper	Change setting on BP Monitor (settings 5/10/5)		
50	Hyper	Wait 4 mins		
	Jentow Calib			BP: / HR:
51	Hyper	Inflate wrist cuff for Hokhanson to 60 mmHg above SBP		
52	Hyper	Press Continue on computer 55s after inflation of wrist cuff		
53		Deflate arm cuff (manually) to 50 mmHg& HIT CUFF/PRESET button		
54		Measure 3 FBFs		
55	Done	Push stop on computer & deflate both cuffs& take equipment off subject		