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EXAMINING THE EFFECT OF EXERCISE INTENSITY ON POST-EXERCISE HYPOTENSION IN MIDDLE-AGED ADULTS

By: Seth McCarthy, B.H.K.

A thesis submitted to the Faculty of Graduate and Post- Doctoral Studies in partial fulfillment of

the requirements of the Master of Kinesiology degree

Wilfrid Laurier University

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Abstract

Acute bouts of exercise have a transient lowering effect on systolic blood pressure (SBP) and diastolic blood pressure (DBP) in the hours after termed post-exercise hypotension (PEH). While moderate-intensity continuous training (MICT) is effective in reducing BP acutely, little is known regarding the effects of higher intensity exercise. This study examined the effects of different exercise intensities on PEH. Six participants (females: 4; age: 48±9 y, Mean arterial pressure: 84 ± 8 mmHg) had their BP measured before and both immediately post- (<2 h) and for 24 h following 4 experimental sessions: 1) 30 min MICT (65% VO_{2max}); 2) 20 min high-intensity interval training (HIIT; 10 x 1 min @ 90% HR_{max} with 1 min rest) session; 3) 16 min sprint-interval training (SIT; 8x15 s "all out" sprints interspersed with 2 min rest); and 4) non-exercise control (CTRL). PEH was similar for all exercise sessions (MICT: -9/-4, HIIT: -6/-4, SIT: -7/-4 mmHg) while peak reductions were similar between protocols for SBP (MICT: -13±9, HIIT: -8±11, SIT: -12±11 mmHg; P=0.387) and DBP (MICT: -7±8, HIIT: -6±10, SIT: -10±8 mmHg; P=0.346). SBP after MICT was lower than after the CTRL (115±12 vs. 122±14 mmHg; p=0.092) and HIIT (115±12 vs. 118±11 mmHg; p=0.090) sessions, whereas DBP was lower after MICT compared to CTRL 60 min post-exercise (68±9 vs. 75±9 mmHg; P=0.079). During the night, both SBP and DBP were lower compared to day though there were no differences between sessions (P=0.242). With a limited data set, these results demonstrate there were no differences in PEH between protocols. While only MICT was able to elicit statistically significant reductions in BP over the entire post-exercise period and there were few statistical differences between the high-intensity exercise protocols and the control, it appears as if HIIT and SIT are capable of eliciting large reductions in BP similar to MICT, though more data collection is necessary to confidently determine this.

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List of Abbreviations

ACE: Angiotensin converting enzyme **BP: Blood pressure** CSEP: Canadian Society for Exercise Physiology CVD: Cardiovascular disease DBP: Diastolic blood pressure EF: Ejection fraction FMD: Flow mediated dilation HIIT: High-intensity interval training HR: Heart rate HR_{max}: Heart rate max MAP: Mean arterial pressure MICT: Moderate-intensity continuous training mmHg: Millimeter of mercury PASB-Q: Physical Activity Behaviour Questionnaire PARmed-X+: Physical Activity Readiness Medical Examination PARQ+: Physical Activity Readiness Questionnaire PEH: Post-exercise hypotension Q: Cardiac output Q_{max}: Maximum cardiac output SBP: Systolic blood pressure SIT: Sprint interval training SV: Stroke volume TPR: Total peripheral resistance VO_{2max}: Maximal oxygen uptake ^{VO2peak}: Peak oxygen uptake

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CHAPTER 1

Literature Review

Introduction

Control of blood pressure (BP) is crucial to ensure good health. Optimal BP can be maintained through regular physical activity, avoiding dietary sodium and excessive alcohol consumption, as well as the maintenance of healthy body weight (Institute of Medicine 2010). Although BP management has improved over the last 15 years in Western countries, treatment and prevention of high BP is still less than optimal (Kearney et al. 2004).

Hypertension has traditionally been defined as an elevation in arterial BP where systolic BP (SBP) is greater than 140 millimeter of mercury (mmHg) and/or diastolic BP (DBP) is greater than 90 (\geq 140/90 mmHg). However, in 2018 updated guidelines now classify hypertension as any BP \geq 130/80 mmHg, resulting in a significant increase in the prevalence of hypertension in the United States, from 31.9% to 45.6% (Whelton et al. 2018). This dramatic change means that now approximately 1 in 3 Americans and 1 in 5 Canadian adults are clinically defined as hypertensive (Padwal et al. 2016; Whelton et al. 2018).

Prevalence of Hypertension

Hypertension is the primary risk factor for cardiovascular disease (CVD) and accounts annually for 13% of all deaths world-wide (Haider et al. 2003; Lawes et al. 2008; Lloyd-Jones et al. 2002; World Health Organization 2009). Hypertension associated deaths primarily arise from CVD (myocardial infarction, stroke, peripheral vascular disease, and heart failure) and nearly half of all strokes (54%) and ischaemic heart disease (47%) worldwide is attributable to hypertension (Lawes et al. 2008; Rapsomaniki et al. 2014). Elevations in resting heart rate (HR; >80 beats per min [bpm]) is an independent risk factor for CVD and frequently accompanies hypertension (Palatini 2011). Using traditional guidelines, the prevalence of hypertension in Canadian adults is 22.6% and ~80% use medication to treat their high BP (Padwal et al. 2016). The prevalence of hypertension increases with age in Canadian adults, however the percentage of adults unaware of their high BP is significantly higher (Figure 1) in younger individuals (Wilkins et al. 2010).



Figure 1: Prevalence and knowledge of hypertension in Canadian adults (created from Wilkins et al. 2010)

Improvements of 10-12 mmHg in SBP and/or 5-6 mmHg in DBP can significantly reduce stroke risk by ~38% (Collins et al. 1990) and smaller reductions such as 2 mmHg SBP can reduce stroke mortality by 10% and ischemic heart disease mortality by 7% (Lewington et al. 2002). Importantly, moderate reductions of this magnitude are attainable using pharmaceutical and non-pharmaceutical treatments. Common pharmaceutical treatments for high BP include angiotensin-converting enzyme (ACE) inhibitors, calcium channel blockers, diuretics, and beta-blockers (Ciolac et al. 2008). Although medication is usually prescribed for high resting BP, nonadherence rates to antihypertensive medication are ~45% in most population groups (Abegaz et al. 2017). Non-pharmaceutical treatments effective in reducing high resting BP include increasing the frequency of physical activity, changes in diet (reduced sodium and alcohol consumption), and weight reduction (He et al. 2013; Leung et al. 2017; Whelton et al. 2002). These cost-effective

treatments could reduce the hypertension attributable cost (~\$14 billion per year) to the Canadian healthcare system (Weaver et al. 2015). The Canadian Physical Activity guidelines suggest that individuals who participate in 150 min of moderate-vigorous physical activity per week have a reduced risk of developing hypertension (Pescatello et al. 2004a; Tremblay et al. 2011). However only 16% of Canadian adults are meeting the suggested guidelines (Statistics Canada 2019) and 'perceived lack of time' remains an often-cited reason (Chinn et al. 1999; Trost et al. 2002). While adherence rates to starting new exercise programs are only ~50% (Dishman 1988), exercise remains an important treatment for high BP as it has numerous health benefits (physical and mental) other than its effects on BP, and does not involve the ingestion of exogenous chemicals. With the new clinical guidelines raising hypertension prevalence an additional 14%, high non-adherence to antihypertensive medication, and perceived lack of time as a key barrier to exercise participation, more research is needed to determine a more time efficient exercise prescription to reduce BP.

Types of Exercise

Moderate-intensity continuous training (MICT) is typically prescribed as a nonpharmaceutical treatment for high BP, however high-intensity interval training (HIIT) and sprint interval training (SIT) are time-efficient protocols that may be just as effective as MICT. MICT refers to aerobic exercise eliciting ~60-75% $\dot{V}O_{2max}$ and is the exercise that the Canadian Physical Activity Guidelines are based on (Gibala et al. 2014; Tremblay et al. 2011; Weston et al. 2014a). It is effective at improving health markers such as $\dot{V}O_{2max}$, waist circumference, body fat, skeletal muscle arterial-venous oxygen difference (a-vO₂ diff), flow mediated dilation (FMD), resting heart rate, maximum cardiac output (Q_{max}), skeletal muscle oxidative capacity, ejection fraction (EF), total peripheral resistance (TPR), and resting BP (Blomqvist and Saltin 1983; Fagard 2001; Hellsten and Nyberg 2015; Holloszy and Coyle 1984; Nalcakan 2014; Schrauwen-Hinderling et al. 2010; Tjonna et al. 2008). MICT is generally well tolerated both physically (low incidence of cardiovascular events and injury) and psychologically (higher affect scores compared to highintensity exercise) and is commonly recommended (Pescatello et al. 2004a) for hypertensive middle aged (40-59 y) and older adults (≥ 60 y) to improve their resting BP (Lacombe et al. 2011; Rueckert et al. 1996; Wisloff et al. 2007). Reductions in resting BP with chronic training can vary from 7-10 mmHg SBP and 5-8 mmHg DBP in pre-hypertensive and hypertensive populations (Fagard 2001; Hagberg et al. 2000; Liu et al. 2013; Tjonna et al. 2008).

HIIT can be described as periods of near maximal effort targeting 80-100% $\dot{V}O_{2max}$, interspersed with periods of recovery (Gibala et al. 2014; Weston et al. 2014a). Within HIIT, intervals can range from 1-4 min and there is variability in the intensity and duration of the recovery periods, though a popular 'low-volume' HIIT protocol has been established utilizing 10 repeats of 1 min exercise bouts at ~85-90% $\dot{V}O_{2max}$ followed by 1 min recovery periods for a total exercise time of 10 min within a 20 min session (Little et al. 2011). HIIT has shown similar improvements in health markers to MICT with reduced training volume and time commitment (Weston et al. 2014a). These include, improvements in $\dot{V}O_{2max}$, body fat, FMD, resting HR, Q_{max}, skeletal muscle oxidative capacity, EF, TPR, and resting BP (Currie et al. 2013; de Matos et al. 2018; Gillen et al. 2013; Gunjal 2013; Hood et al. 2011; Molmen-Hansen et al. 2012; Tjonna et al. 2008; Wisloff et al. 2007). HIIT is generally well tolerated both physically (low incidence of cardiovascular events and injury) and psychologically (higher affect scores compared to supramaximal exercise) in middle-aged (40-59 y) and older populations (\geq 60 y) with coronary heart disease or hypertension (Molmen-Hansen et al. 2012; Tjonna et al. 2007). In training studies reductions in resting BP range from 10-12 mmHg SBP and 6-8 mmHg DBP in hypertensive populations (Gunjal 2013; Molmen-Hansen et al. 2012; Tjonna et al. 2008).

A more intense version of HIIT known as SIT involves shorter periods of all-out supramaximal effort targeting $\geq 100\%$ VO_{2max}, interspersed with periods of recovery (Gibala et al. 2014; Weston et al. 2014a). A classic SIT protocol involves 4-6 x 30 s all-out supramaximal efforts interspersed with 4 min rest (Burgomaster et al. 2005). It has been argued that SIT may not be applicable for the general population (Hardcastle et al. 2014), though not without debate (Astorino and Thum 2016; Del Vecchio et al. 2015; Jung et al. 2015; Robertson-Wilson et al. 2017), so some have attempted modifying the traditional protocol in an effort to enhance adherence (Gillen et al. 2014; Islam et al. 2017a; McKie et al. 2018; Metcalfe et al. 2012; Townsend et al. 2017). Modified protocols developed in our lab maintain the same total work-to-rest ratio (1:8 s) as the traditional 30 s sprint bouts with 4 min rest by incorporating an increased number of shorter sprints with shorter recovery periods (8-12 x 15 s sprints interspersed with 2 min rest or 24-36 x 5 s sprints interspersed with 40 s rest). Notably, these modified SIT protocols demonstrate similar acute (energy expenditure, fat oxidation) and chronic (VO_{2max}) physiological responses while improving several acute psychological perceptions of exercise (Islam et al. 2017a; McKie et al. 2018; Townsend et al. 2017). SIT has evoked similar outcomes to MICT such as improved VO_{2max}, waist circumference, body fat, FMD, and skeletal muscle oxidative capacity (Gillen et al. 2016; Hazell et al. 2014; Macpherson et al. 2011; Nalcakan 2014; Rakobowchuk et al. 2008). There is no research investigating the effect of SIT on TPR, EF, a-vO₂ diff, and resting HR, however SIT does not improve Q_{max} (Macpherson et al. 2011). Middle-aged adults (40-60 y) have demonstrated similar improvements in \dot{VO}_{2max} following SIT (Willoughby et al. 2016), suggesting it's an effective training protocol for middle-aged adults despite some people's reservations. Chronic resting BP reductions (6 mmHg SBP) using SIT has only been investigated using a 15 week swimming protocol in sedentary premenopausal women with pre-hypertension (Mohr et al. 2014). While some may question the applicability of SIT for hypertensive populations due to misconceptions that there is a higher risk of cardiovascular events during high-intensity exercise. However, the literature indicates the risks are similar to that of moderate-intensity exercise (Rognmo et al. 2012) and that exercise-related cardiovascular events are rare (Thompson et al. 2007).

Overview of Post-Exercise Hypotension

Following a single bout of exercise, there is a reduction in resting BP in the subsequent hours termed post-exercise hypotension (PEH) (Halliwill 2001; MacDonald 2002). In healthy normotensive populations, the response can reduce resting BP up to 10 mmHg with a duration of 2 h (Halliwill 2001). In hypertensive populations the response can decrease resting BP up to 20 mmHg with a duration of 16 h (Boutcher and Boutcher 2017; Halliwill 2001). PEH is characterized by a drop in total TPR that is not offset by increases in cardiac output (Q) (Halliwill 2001; MacDonald 2002). The PEH response involves both a neural and a vascular component, however the specific mechanisms are poorly understood (Halliwill 2001; MacDonald 2002). The neural component involves the reduction of sympathetic nerve activity via resetting of the aortic baroreflex (Halliwill et al. 1996), while the vascular component involves vasodilation in active and non-active limbs as a result of local vasodilators (Endo et al. 2012a; Lockwood et al. 2005). It should be noted the PEH response is more consistently seen in pre-hypertensive and hypertensive populations with less consistent results in normotensive populations (MacDonald 2002). This data, although equivocal has led some researchers to speculate that the magnitude of the PEH response is strongly correlated to pre-exercise BP (Pescatello et al. 2004a). Although

initial resting BP may not be the primary moderator of the PEH response, the BP reduction is generally higher, the higher the initial resting BP value and demonstrates the acute exercise response is important in individuals with pre-hypertension and/or hypertension.

Biological Factors

Important biological factors to consider in the PEH response are age and biological sex. The PEH response is elicited similarly in both males and females across different age groups (Cote et al. 2015; Lynn et al. 2007; MacDonald 2002; Rossow et al. 2010) though the mechanisms are different in older pre-hypertensive and hypertensive men (decrease in Q and an increase in TPR) (Hagberg et al. 1987; Lacombe et al. 2011). In females the PEH response does not appear to be affected by the menstrual phase where reductions were ~3-4.5 mmHg (MAP) at 30- and 60-min post-exercise in all three phases (Lynn et al. 2007).

Role of Exercise Intensity in Post-Exercise Hypotension

Direct comparisons of intensity on PEH show no differences, however a majority of studies have only compared submaximal exercise (MacDonald 2002). MICT generates PEH responses in both normotensive (6.9/3.5 mmHg; Table 1) and hypertensive populations (11.4/5.4 mmHg; Table 2). HIIT generates significant PEH responses ranging from 5-9 mmHg SBP and 3-5 mmHg DBP in normotensive populations and 4-20 mmHg SBP and 8 mmHg DBP in the limited data on hypertensive populations (Table 3). PEH responses following SIT are 3-5 mmHg in both SBP and DBP in normotensive populations with limited data (Table 3). The PEH response following SIT has not been investigated in hypertensive populations.

		Pre- Exercise		Mod	Duration	Change Post- Exercise
Reference	Age	Resting BP (mmHg)	Protocol	e	(h)	BP (mmHg)
Angadi et al. 2015	24.6	122/68	*30 min @ 59- 67% VO _{2max}	С	3	↓3/2
Cleroux et al. 1992a	41	106/77	30 min @ 50% VO _{2max}	С	1.5	\leftrightarrow
Costa et al. 2016	24.9	120.5/68.3	*20 min @ 70% VO _{2max}	R	1	$\downarrow 8.3/\leftrightarrow$
Hecksteden et al. 2013	49	134/88	*45 min @ 60% VO _{2max}	R	1	↓6/4
Forjaz et al. 2004	24	109/71	45 min @ 75% VO _{2peak}	С	1.5	↓9.2/4.4
Keese et al. 2011	20.7	111.5/73.9	60 min @ 65% VO _{2peak}	С	2	↓6.3/1.8
MacDonald et al. 2000a	22	126/71	45 min @ 70% VO _{2peak}	С	1	↓12/4.6
Rossow et al. 2010	25.5	116.4/62.9	*60 min @ 60% VO _{2max}	С	1	↓5.1/3.9
Senitko et al. 2002	25.4	113/86.2	60 min @ 60% VO _{2peak}	С	1	↓5.4/3.6
Mean (SD)	28.6 ± 9.1	$\frac{117.6 \pm 8.4}{72 \pm 6.8}$			1.44 ± 0.64	$\downarrow 6.9 \pm 2.6/3.5 \pm 1.0$

 Table 1. Characteristics of studies recording PEH following moderate-intensity continuous training (MICT) in normotensive populations

Note: C: cycling; HR_{max} : heart rate max; R: running; $\dot{V}O_{2max}$: maximal oxygen uptake; $\dot{V}O_{2peak}$: peak oxygen uptake; * indicates the intensity was converted to $\dot{V}O_{2max}$

Deferrer	•	Pre- Exercise		Mada	Duratio	Change Post- Exercise
Kelerence	Age	Resting BP (mmHg)	Protocol	Niode	n (h)	BP (mmHg)
Cleroux et al. 1992a	44	141/95	30 min @ 50% VO _{2max} C		1.5	↓11/4
Halliwill et al. 1996	24.5	131/71	60 min @ 60% VO _{2peak}	С	1	↓8/6
Floras et al. 1989	25	135/83	*45 min @ 52% VO _{2max}	R	1	$\downarrow 10/\leftrightarrow$
Jones et al. 2007	28	120/74	30 min @ 70% VO _{2peak}	С	0.33	\downarrow 5/ \leftrightarrow
Lacombe et al. 2011	57	130/76	21 min @ 60% VO _{2max} C		1	$\downarrow 3/\leftrightarrow$
Liu et al. 2012	53	127.5/80.5	30 min @ 65% VO _{2peak} R		0.5	↓7.2/4.2
MacDonald et al. 1999	35	132/75	30 min @ 75% VO _{2peak}	С	1	↓8/5
MacDonald et al. 2000a	23	133/79	30 min @ 70% VO _{2peak} C		1	↓14/8
MacDonald et al. 2000b	23	140/82	30 min @ 70% VO _{2peak}	С	1	↓15/8
MacDonald et al. 2001	24.5	145/72	30 min @ 70% VO _{2peak} C		1.5	$\downarrow 23/\leftrightarrow$
Mota et al. 2009	42.9	134/84.9	*20 min @ 70- 80% VO _{2max} R		7	↓11.1/4
Pescatello et al. 2004b	43.8	145/85.8	30 min @ 60% VO _{2max} C		9	↓10/4
Rueckert et al. 1996	50	150/102	*45 min @ 70% VO _{2max}	R	2	$\downarrow 11/\leftrightarrow$
Mean (SD)	39.4 ±13.6	135.7±7.9/ 81.6 ± 8.6			2.06± 2.4	11.4±5.1/ 5.4±1.6

 Table 2. Characteristics of studies recording PEH following moderate-intensity continuous training (MICT) in hypertensive populations

Note: C: cycling; HR_{max} : heart rate max; R: running; $\dot{V}O_{2max}$: maximal oxygen uptake; $\dot{V}O_{2peak}$: peak oxygen uptake; * indicates the intensity was converted to $\dot{V}O_{2max}$

(IIII) and spr	me meei	var training (D	11)			
Reference	Age	Pre- Exercise	Protocol	Mode	Duratio	Change Post- Exercise
		Resting BP (mmHg)			II (II)	BP (mmHg)
Normotensive						
Angadi et al. 2015	24.6	122/68	6 x 30 s all-out w/ 4 min active rec	С	3	↓3/3
Angadi et al. 2015	24.6	122/68	*4 x 4 min @ 82-88% VO _{2max} w/ 3 min rec	С	3	↓6/5
Costa et al. 2016	24.9	120.5/69.5	*10 x 1 min @ 78% VO _{2max} w/ 1 min rec	R	1	$\downarrow 6.8/\leftrightarrow$
Cote et al. 2014	30.3	113/62.1	*15 x 1 @ ~87.5 VO _{2max} w/ 2 min rec	С	0.5	↓9.3/3.5
Morales- Palomo et al. 2017	55	114/-	*6 x 4 min @ ~83% VO _{2max} w/ 3 min rec	С	0.75	\downarrow 7/ \leftrightarrow
Rakobowchuk et al. 2009	20.1	-	1 x 30 s all out or 4 x 30 s w/ 4 min rec	С	1	\leftrightarrow
Rossow et al. 2010	25.5	117.8/63.9	4 x 30 s all out w/ 4.5 min rec	С	1	↓5.6/5.1
Mean (SD)	29.3± 10.8	118.2±3.6/ 66.2±2.8			1.5 ± 1	$\begin{array}{c} \downarrow 6.3 \pm 1.9 / \\ 4.2 \pm 0.9 \end{array}$
Hypertensive						
Lacombe et al. 2011	57	130/76	5 x 2 min @ 85% VO _{2max} w/ 2 min rec	С	1	$\downarrow 4/\leftrightarrow$
Morales- Palomo et al. 2017	59	134/81	*5 x 4 min @ ~83% VO _{2max} w/ 3 min rec	С	0.75	↓20/8
Mean (SD)	58 ± 1	132 ± 2/78.5 ± 2.5			0.9 ± 0.1	↓12 ± 8/8

Table 3. Characteristics of studies recording PEH following high-intensity interval training(HIIT) and sprint-interval training (SIT)

Note: C: cycling; R: running; $\dot{V}O_{2max}$: maximal oxygen uptake; * indicates the intensity was converted to $\dot{V}O_{2max}$

Measurement Methods

One important limitation to consider in the PEH literature is the methods employed to measure PEH are not always consistent. Prior to exercise participants rest in a supine or seated position before measuring baseline BP (5-30 min). Following completion of exercise, participants return to the same position and BP is measured at set time intervals (10-15 min intervals) for a specified duration (1-2 h) in the laboratory setting (MacDonald 2002). Ambulatory BP monitors are often used to measure the magnitude and duration of the response once participants leave the laboratory setting. Absolute reductions while using this type of monitoring are generally lower than those recorded in the hours post-exercise in the lab setting, yet they may be more significant due to that fact that ambulatory monitoring is a more valid indicator of BP (Verdecchia 2000). Ambulatory monitoring allows for more measurements across a longer time period providing a better reflection of a participant's BP throughout the day (Pescatello et al. 2004a). Ambulatory monitoring also provides a 'pressor effect' for patients using the device for the first time for up to 6-10 h, but the effect is significantly diminished with increasing number of ambulatory monitoring on the same patient indicating the importance of a familiarization day prior to data collection (Calvo et al. 2003; Hermida et al. 2002a; Hermida et al. 2002b; Prasad et al. 1995). The 'pressor effect' is a significant increase in BP (~6/4 mmHg) due to the novelty of wearing the device for the first time (Hermida et al. 2002a; Hermida et al. 2002b). The PEH response throughout the day following exercise may be confounded as the effect of activities of daily living are rarely considered. While reductions ranging from 3-7 mmHg SBP and 2-4.5 mmHg DBP have been reported in 24-h average, daytime, and nighttime BP following exercise (Dantas et al. 2017; Sosner et al. 2016; Wallace et al. 1999) others have demonstrated no reductions (Eicher et al. 2010; Forjaz et al. 2004; Karoline de Morais et al. 2015; Pescatello et al. 2004b; Ribeiro et al. 2011).

Ambulatory measurements are important to delineate the actual PEH response, as well as benefits to overall daily BP. Exercise has been shown to attenuate the BP rise throughout the day by ~ 5-7 mmHg SBP and 2-3 mmHg DBP compared to a control day (Eicher et al. 2010; Pescatello et al. 2004b; Ribeiro et al. 2011).

Although rarely reported in studies there are different ways to calculate PEH (Table 4). The reproducibility and reliability of these calculations was tested and there was no systematic bias observed (Fecchio et al. 2017). Type 2 showed the highest reliability of the three methods when considering both SBP and DBP. The sample contained a mix of both sexes, a wide age range, individuals of different BP status, and individuals taking (or not) anti-hypertensive medication however this is the only study investigating the reproducibility of the post-exercise response. Even though it is not often reported time of day plays an important role in the PEH response. Circadian variation exhibits strong influence over resting BP characterized by a 'morning surge' in the hours after waking (Jones et al. 2008b). The mechanisms responsible for the 'morning surge' may be caused by endogenous circadian rhythm, the effects of wakening or the activation of the sympathetic nervous system and other hemodynamic adjustments due to waking up (Khoury et al. 1992). The physical activity associated with beginning activities of daily living does cause an increase in resting BP and HR, however this response has shown the highest reactivity in the morning period (0800-1000 h) compared to other times of day attributing to the 'morning surge' (Jones et al. 2006). The PEH response is greater following evening exercise (-6/-1 mmHg SBP/DBP) compared with morning exercise (-4 mmHg SBP) (de Brito et al. 2015), and in some cases BP increases following morning exercise (3 mmHg MAP) compared to decreases following evening exercise (-7 mmHg MAP) (Jones et al. 2008b). Even when controlling for sleep, BP was still 8-14 mmHg higher following morning exercise compared to evening exercise

(Jones et al. 2008a). While they are important to consider, issues regarding measuring BP using ambulatory BP monitors, the calculation of PEH, and the time of day when measuring PEH will not be addressed in this thesis.

Table 4. Different Calculations for PEH

Mean values and reproducibility parameters of PEH calculated using different methods (adapted from Fecchio et al. 2017).

post-exercise BP – pre-exercise BP						
post-exercise BP – post-control BP						
(post-exercise BP – pre-exercise BP) – (post-control BP – pre-control BP)						
Test	Retest	P Value	ICC	TE (mmHg)	MDD (mmHg)	
-4.7 ± 3.8	-4.2 ± 4.4	0.50	0.76	2.6	7.2	
-9.6 ± 8.8	-8.3 ± 8.8	0.26	0.90	3.8	10.5	
-10.2 ± 7.9	-10.1 ± 6.3	0.90	0.74	4.6	12.8	
0.7 ± 3.3	0.5 ± 3.7	0.83	-0.03	3.5	9.8	
-5.7 ± 4.6	-4.9 ± 5.2	0.51	0.48	4.1	11.3	
-5.3 ± 5.3	-6.1 ± 6.1	0.60	0.10	5.6	15.4	
	post-exercise post-exercise Test -4.7 ± 3.8 -9.6 ± 8.8 -10.2 ± 7.9 0.7 ± 3.3 -5.7 ± 4.6 -5.3 ± 5.3	post-exercise BP – pre-exercisepost-exercise BP – post-col(post-exercise BP – pre-exerciseTestRetest -4.7 ± 3.8 -4.2 ± 4.4 -9.6 ± 8.8 -8.3 ± 8.8 -10.2 ± 7.9 -10.1 ± 6.3 0.7 ± 3.3 0.5 ± 3.7 -5.7 ± 4.6 -4.9 ± 5.2 -5.3 ± 5.3 -6.1 ± 6.1	post-exercise BP – pre-exercise BPpost-exercise BP – post-control BP(post-exercise BP – pre-exercise BP) –TestRetestP Value -4.7 ± 3.8 -4.2 ± 4.4 0.50 -9.6 ± 8.8 -8.3 ± 8.8 0.26 -10.2 ± 7.9 -10.1 ± 6.3 0.90 0.7 ± 3.3 0.5 ± 3.7 0.83 -5.7 ± 4.6 -4.9 ± 5.2 0.51 -5.3 ± 5.3 -6.1 ± 6.1 0.60	post-exercise BP – pre-exercise BPpost-exercise BP – pre-exercise BP) – (post-construction BP)(post-exercise BP – pre-exercise BP) – (post-construction BP)TestRetestP ValueICC-4.7 ± 3.8 -4.2 ± 4.4 0.500.76-9.6 ± 8.8 -8.3 ± 8.8 0.260.90-10.2 ± 7.9 -10.1 ± 6.3 0.900.740.7 ± 3.3 0.5 ± 3.7 0.83-0.03-5.7 ± 4.6 -4.9 ± 5.2 0.510.48-5.3 ± 5.3 -6.1 ± 6.1 0.600.10	post-exercise BP – pre-exercise BPpost-exercise BP – post-control BP(post-exercise BP – pre-exercise BP) – (post-control BP – pre-coTestRetestP ValueICCTE (mmHg)-4.7 \pm 3.8-4.2 \pm 4.40.500.762.6-9.6 \pm 8.8-8.3 \pm 8.80.260.903.8-10.2 \pm 7.9-10.1 \pm 6.30.900.744.60.7 \pm 3.30.5 \pm 3.70.83-0.033.5-5.7 \pm 4.6-4.9 \pm 5.20.510.484.1-5.3 \pm 5.3-6.1 \pm 6.10.600.105.6	

Values are mean \pm SD; ICC = intraclass coefficient correlation; TE = typical error; MDD = minimal detectable difference

Clinical Importance

Acute exercise is effective in eliciting PEH and with training can reduce resting BP in populations with hypertension (Fagard 2001; MacDonald 2002), among improvements in other important cardiovascular (FMD, resting HR, EF) and health markers (waist circumference, body fat) (Fagard 2001; Nalcakan 2014; Schrauwen-Hinderling et al. 2010; Tjonna et al. 2008). It has been suggested that the continual occurrence of PEH with chronic exercise may be related to chronic adaptations that improve resting BP (Halliwill 2001; Pescatello et al. 2004a; Thompson et al. 2001). In normotensive and hypertensive groups, the acute response has been demonstrated to be predictive of the chronic training response using MICT protocols (Hecksteden et al. 2013; Liu et al. 2012; Wegmann et al. 2018). The reported correlations range from 0.66-0.89 for SBP and from 0.66-0.77 for DBP (p = < 0.05) suggesting greater acute responses are associated with greater chronic adaptations (Hecksteden et al. 2013; Liu et al. 2012; Wegmann et al. 2013; Liu et al. 2012; Wegmann et al. 2018). These results emphasize the importance of determining what intensities of exercise will generate the greatest acute changes.

Summary

MICT is effective in eliciting PEH and reductions in resting BP with chronic training, however, 'perceived lack of time' is a commonly cited reason for not participating in physical activity. Considering the acute hypotensive effects of the more time efficient HIIT and SIT protocols in normotensive populations, the lack of research in hypertensive populations is troubling as they would have the most to benefit from the potential effects. No studies to date have compared the PEH response following SIT in hypertensive populations, however, examining the effect of SIT may offer new insights into potential differences as a result of exercise intensity, and may lead to improved strategies for lowering high resting BP.

Purpose

The original purpose was to examine the effect of exercise intensity (MICT, HIIT, SIT) on PEH in hypertensive middle-aged adults. Specifically, PEH was to be measured in the immediate hours post exercise (<2 h) in a lab setting and then for the rest of the day (~24 h) throughout activities of daily living. Difficulties recruiting hypertensive participants lead us to recruit normotensive participants as well, leading us to adjust our purpose. The adjusted purpose was to examine the effect of exercise intensity (MICT, HIIT, SIT) on PEH in middle-aged adults. Specifically, PEH was measured in the immediate hours post-exercise (< 2 h) in the lab setting and then for the rest of the day (~24 h) throughout activities of daily living.

Hypotheses

Based on the literature reviewed demonstrating a greater reduction in TPR following HIIT compared to MICT (Rossow et al. 2010), PEH of a longer duration following HIIT compared to MICT and SIT (Angadi et al. 2015), and greater reductions in BP following HIIT in the limited studies in hypertensive samples (Lacombe et al. 2011; Morales-Palomo et al. 2017), the following hypotheses were put forth.

1a. PEH will be a larger magnitude following HIIT and SIT, compared to MICT in hypertensive participants.

1b. PEH will be longer in duration following HIIT and SIT, compared to MICT in hypertensive participants.

2a. PEH will be larger in magnitude in hypertensive participants compared to normotensive participants.

2b PEH will be a longer duration in hypertensive participants compared to normotensive participants.

Hypotheses 1a and 1b were also adjusted based on changes in recruitment efforts.

1a. PEH will be a larger magnitude following HIIT and SIT, compared to MICT.

1b. PEH will be longer in duration following HIIT and SIT, compared to MICT.

CHAPTER 2

EXAMINING THE EFFECT OF EXERCISE INTENSITY ON POST-EXERCISE HYPOTENSION IN MIDDLE-AGED ADULTS

McCarthy SF, Ferguson EJ, Hazell TJ. Examining the effect of exercise intensity on postexercise hypotension in middle-aged adults. To be submitted to the Journal of Medicine & Science in Sports & Exercise.

Introduction

Exercise has beneficial effects on blood pressure (BP) as a single bout of exercise can induce post-exercise hypotension (PEH) which is a reduction in resting BP in the subsequent hours following the exercise session (Halliwill 2001; MacDonald 2002). PEH is characterized by a reduction in total peripheral resistance that is not completely offset by an increase in cardiac output (Cleroux et al. 1992a, 1992b; Halliwill 2001; Halliwill et al. 1996; MacDonald 2002) and involves both a vascular and neural component (Halliwill 2001). The PEH response is elicited inconsistently in normotensive populations and is of a greater magnitude and longer duration in hypertensive populations (MacDonald 2002). PEH occurs independent of biological sex (Cote et al. 2015; Lynn et al. 2007; MacDonald 2002; McCord et al. 2006; Pescatello et al. 2003; Rossow et al. 2010; Senitko et al. 2002) and while some suggest age as well (MacDonald 2002), some research suggests the magnitude of the response may be different in older compared to younger populations due to resting BP or other factors (Liu et al. 2013; Pescatello et al. 2004b).

PEH has most commonly been elicited following moderate-intensity continuous training (MICT; 30-60 min at 60-70% $\dot{V}O_{2max}$) in normotensive (-7/-4 mmHg) (Angadi et al. 2015; Cleroux et al. 1992b; Costa et al. 2016; Forjaz et al. 2004; Hecksteden et al. 2013; Keese et al. 2011; MacDonald et al. 2000b; Rossow et al. 2010; Senitko et al. 2002) and hypertensive populations (-11/-5 mmHg) (Cleroux et al. 1992b; Halliwill et al. 1996; Liu et al. 2012; MacDonald et al. 1999; MacDonald et al. 2000a, 2000b; Mota et al. 2009; Pescatello et al. 2004b). However, high-intensity interval training (HIIT) has become an increasingly popular exercise modality characterized by periods of near maximal effort interspersed with periods of recovery (Gibala et al. 2014) and has demonstrated similar improvements in physiological outcomes such as $\dot{V}O_{2max}$, body fat, and resting BP (Gillen et al. 2013; Molmen-Hansen et al. 2012) as MICT with reduced

training volume and time commitment (Weston et al. 2014b; Wisloff et al. 2007). Similarly, HIIT has elicited PEH in normotensive (-7/-4 mmHg) (Angadi et al. 2015; Costa et al. 2016; Cote et al. 2015; Morales-Palomo et al. 2017; Rossow et al. 2010) and hypertensive populations (-12/-8 mmHg) (Lacombe et al. 2011; Morales-Palomo et al. 2017) in limited studies. Sprint-interval training (SIT), a more intense version of HIIT is characterized by short periods of all-out effort interspersed with periods of rest (Gibala et al. 2014) has also elicited PEH in normotensive populations (-4/-4 mmHg), although it has only been documented in two studies (Angadi et al. 2015; Rossow et al. 2010).

Most studies show no effect of exercise intensity on PEH following MICT (Eicher et al. 2010; Forjaz et al. 2004; Guidry et al. 2006; Jones et al. 2007; MacDonald 2002; Pescatello et al. 2004b). Direct comparisons of high-intensity-interval training and MICT show similar PEH responses (Angadi et al. 2015; Ciolac et al. 2009; Costa et al. 2016; Lacombe et al. 2011; Rossow et al. 2010), however only three of these studies measured BP post-exercise for greater than 1 h, and one measured 24 h BP not reporting acute BP. In studies measuring PEH for >1 h, the response lasts at least 2 h, enhancing the importance of longer measurement periods to document the entire response (de Brito et al. 2019). In normotensive participants, HIIT has been shown to elicit a longer PEH response compared to MICT and SIT when measured for 3 h post-exercise (Angadi et al. 2015). To date, no studies have examined the effect of SIT on PEH in hypertensive populations where it may have a more beneficial effect on post-exercise BP. The identification of the PEH response has clinical importance as it has a strong correlation with chronic BP reductions (Hecksteden et al. 2013; Liu et al. 2012; Moreira et al. 2016; Wegmann et al. 2018), while also assisting in the detection of responders and non-responders to different exercise protocols (Costa et al. 2016). Acute reductions of -7/-4 mmHg (Liu et al. 2012) and -9/-4 mmHg (Hecksteden et al. 2013) were strongly correlated (r=0.65) chronic with reductions (-9/-7 and -7/-5 mmHg) following 4 (Hecksteden et al. 2013) and 8 weeks of training (Liu et al. 2012).

To our knowledge, no study has compared the effect of exercise intensity on PEH in hypertensive middle-aged adults both in the immediate hours following exercise, as well as the 24 h period afterwards. Considering the recent changes to hypertension guidelines to increase awareness of blood pressure management (Whelton et al. 2018), and the numerous health benefits of HIIT and SIT (Gibala et al. 2014; Weston et al. 2014b), more research to examine the effect on PEH is justified. Therefore, the purpose was to examine the effect of exercise intensity (MICT, HIIT, SIT) on PEH in hypertensive middle-aged adults. Specifically, PEH was measured in the immediate hours post exercise (<2 h) in a lab setting and AMBP will be measured for the rest of the day (~24 h) throughout activities of daily living.

Methods

Participants

A sample size calculation was completed a priori using GPower 3.1 with an α level set to 0.05, desired power set to 0.80, and an effect size (*f*=0.95) based on previous work examining changes in BP following HIIT in a normotensive population (Morales-Palomo et al. 2017) demonstrating eight participants were necessary. Originally, hypertensive participants were the target population during early recruitment and while we were able to recruit one hypertensive and one pre-hypertensive participant respectively, recruiting more participants was difficult resulting in us eventually beginning to recruit normotensive participants as well. Thirteen recreationally active participants initially volunteered to participate in this study, however, due to the unfortunate circumstances related to the COVID-19 pandemic only six (Table 5) were able to complete all 4

experimental sessions (despite the remaining 7 all being scheduled through March, April, and early May). Using previous hypertension guidelines (that all the existing literature use) the six participants included one hypertensive participant (143/77 mmHg), one pre-hypertensive participant (123/69 mmHg, a controlled hypertensive), and 4 normotensive participants (109/65 mmHg). A BP reading of \geq 140 mmHg SBP and/or \geq 90 mmHg DBP was considered hypertensive, 120-139 mmHg SBP and/or 80-89 mmHg was considered pre-hypertensive, <120 mmHg SBP and <80 mmHg DBP was considered normotensive (Pescatello et al. 2004a). Using the new hypertension guidelines that classify a BP reading of \geq 130 mmHg SBP and/or \geq 80 mmHg DBP as hypertensive, ≥120-129 mmHg SBP as pre-hypertensive, and <120 mmHg SBP and <80 mmHg DBP as normotensive (Whelton et al. 2018) the number of participants in each blood pressure category remains the same. Participants were non-smokers and screened using the Physical Activity Readiness Questionnaire. Participant's physical activity level was assessed using the Canadian Society for Exercise Physiology Physical Activity and Sedentary Behaviour Questionnaire. Exclusion criteria include any past medical history of cardiovascular disease as well as the use of beta blockers to treat hypertension. The experimental procedures were explained in full detail to all participants and all provided written informed consent before any data collection. The Research Ethics Board at Wilfrid Laurier University approved this study in accordance with the ethical standards of the 1964 Declaration of Helsinki.

2/4
2/4
48±9
1.72±0.10
72.8±15.6
24.4 ± 3.8
34.41±6.17
117±15
67±6

Table 5. Participant characteristics (N=6)

NOTE: SBP: systolic blood pressure, DBP: diastolic blood pressure

Study Design

Participants completed 4 experimental sessions (~3.5 h each) during which heart rate (HR) and BP were measured. Experimental sessions consisted of 1 control session (CTRL) and 3 exercise sessions of differing intensity: (i) MICT; (ii) HIIT; (iii) SIT. The order of experimental sessions was systematically rotated to avoid any learning effects. Participants were instructed to refrain from physical activity, alcohol, and caffeine for at-least 12 h before each experimental session.

Pre-experimental Procedures

All participants completed a laboratory familiarization session before data collection to introduce testing procedures and reduce any learning effects during subsequent experimental sessions. Participants had their BP measured 4 times using an automated oscillometric device (Dinamap Carescape V100, Critikon, Tampa, FL., USA) with 2 min between each measurement. The first measurement was discarded and the final 3 were averaged to determine participant's resting BP. Participants had their $\dot{V}O_{2max}$ determined during a graded exercise test to exhaustion performed on a motorized treadmill (4Front, Woodway, Wis., USA). $\dot{V}O_2$ and $\dot{V}CO_2$ were measured continuously using an online breath-by-breath gas collection system (MAX-II; AEI Technologies, Pa., USA), which was calibrated with gases of known concentrations and a 3-L syringe for flow and silicon facemask (Vmask, Hans Rudolph Inc., Kans., USA). Following a 5min treadmill warm-up, each participant ran at a self-selected pace (4-7 mph) with incremental increases in grade (2%) applied every 2 min until volitional fatigue. Heart rate was recorded beatto-beat throughout the test using an integrated HR monitor (FT1; Polar Electro, Que., Canada). $\dot{V}O_{2max}$ was taken as the greatest 30-s average in presence of a plateau in $\dot{V}O_2$ values (<1.35) ml/kg/min increase) despite increasing workload, or 2 of the following criteria: (i) a respiratory exchange ratio (RER) value >1.15; (ii) within 10 bpm of age-predicted HR_{max} (220-age); and/or (iii) voluntary exhaustion. After a 5-min cooldown followed by sufficient rest (>5 min), participants were allowed to practice each of the three different exercise protocols using the motorized treadmill in which all the exercise sessions would be performed. Each participant completed 3 min of continuous running (at ~65% VO_{2max}; MICT), 2 x 1 min running efforts (at ~90% HR_{max}) with 1 min recovery (HIIT), and 2 x 15 sec "all-out" sprints with 2 min rest (SIT) to familiarize them to the respective protocols. Participants were given sufficient rest (5 min) in between each. Following this, participants were fitted with an ambulatory blood pressure monitor (AMBP; ABP320, ScottCare, Cleveland, OH., USA) attached to their left arm that they would wear for the next 24-h. Participants recorded their breakfast the day of their first experimental session and replicated it for the remaining sessions.

Experimental Session

Participants arrived at the laboratory at 0800 h after having consumed breakfast 1 h prior to arrival (0700 h) and limited their activity on their way to the laboratory (i.e. drove or used public transport). The breakfast participants ate before their first session was recorded and replicated for the final 3 sessions. They remained in the laboratory for the next ~3.5 h. After arriving participants rested quietly (seated rest for: 30 min MICT and CTRL, 40 min HIIT, 44 min SIT) prior to BP

measurements to ensure resting state was achieved. Participants had their resting BP measured using an automated oscillometric device (Carescape V100) with 2 min between measurements. The first measurement was discarded and the final 3 measurements were averaged. Participants were fitted with a HR monitor prior to warm-up for exercise. Participants then completed the exercise protocol followed by 2 h of seated rest for post-exercise BP measurements. BP was measured every 15 min post-exercise during the first h (0940, 0955, 1010, 1025 h), and every 30 min during the second h (1055 and 1125 h) post-exercise. At each time point BP was measured 3 times, one after another (~30 s between measurements), the first measurement was discarded and the remaining 2 were averaged. After the last BP measurements participants had the opportunity to shower, then had an AMBP (ABP320) attached to their left arm. The device was worn for 24 h and automatically measured BP and HR every 30 min during the daytime and once per h during the nighttime. The daytime and nighttime periods were based on each participant's typical sleep schedule. Participants were asked to perform their regular daily activities, not to engage in physical activity, and to relax and straighten the arm during the recording interval during the day. Participants were also asked to document their activities and food/fluid intake during the day. All participants returned their activity and food journals and did not self-report any physical activity when the monitor was worn. Common activities noted in the activity journals included: working, preparing food, completing housework, and watching television. Identical experimental procedures were followed for the control session except participants were seated quietly during the exercise period (0845-0925 h).

Exercise Protocols

All exercise protocols began with a 5 min warm-up (at 3 mph) followed by the MICT (30 min), HIIT (20 min), or SIT (16 min) session and a 5 min cooldown at a self-selected pace. Warm-

up and cool-down along with the exercise protocols were performed on a motorized treadmill (Woodway 4Front) for consistency. For the SIT session the motorized treadmill (Woodway 4Front) was switched into dynamic mode so the belt was self-propelled by the participant. Exercise sessions involved 3 protocols of differing intensity: (i) MICT (30 min of continuous running at 65% $\dot{V}O_{2max}$), (ii) HIIT (10 x 1 min at 90% HR_{max} with 1 min recovery), (iii) SIT (8 x 15 sec "all-out" sprint efforts interspersed with 2 min rest). The start of the CTRL, HIIT, and SIT session were staggered by ~5, ~10, and ~14 min respectively so all protocols finished by 0925 h. Verbal encouragement was provided to participants during all 3 exercise sessions. The desired intensity for the MICT (65% $\dot{V}O_{2max}$) and HIIT (90% HR_{max}) sessions respectively was calculated using the ACSM Running Equation (Glass et al. 2007), using the speed from the graded exercise test and $\dot{V}O_2$ data. Specifically, for the 90% HR_{max}, the $\dot{V}O_2$ value used in the ACSM Running Equation aligned with 90% HR_{max}. When participants were familiarized with the different exercise protocols the treadmill speed and grade was adjusted if needed to elicit the desired intensity.

Post-exercise Hypotension Calculation

To calculate PEH, at each time point BP from the exercise sessions was subtracted from the BP at the same time point during the control session. When considering both systolic blood pressure (SBP) and diastolic blood pressure (DBP) this method had the highest intraclass correlation as previously reported (Fecchio et al. 2017).

PEH = control *BP* – exercise *BP*

Statistical Analysis

All statistical analyses were performed using SPSS version 26 (IBM, Chicago, IL) and post hoc analyses were used when necessary. Statistical significance was accepted as P < 0.05 and P < 0.1 was reported as "approaching significance" or "trending" for transparency, and all data are
presented as mean±standard deviation (SD). Partial eta-squared (η_p^2) values were calculated to estimate the effect sizes (small 0.04, medium 0.25, large 0.64) for main effects and interactions where necessary. Cohen's d was calculated to estimate effect size (small 0.2, medium 0.5, large 0.8, very large 1.3) for individual post hoc comparisons where necessary. Due to limited sample size, time points were condensed as follows: pre (unchanged), 30 min post- (average of 15 and 30 min post-), 60 min post- (average of 45 and 60 min post-), and 120 min post- (average of 90 and 120 min post-). Time points were condensed instead of using stand alone values to utilize all the data collected. A series of two-way repeated measures of analyses of variance (RM ANVOA) were conducted to compare changes in SBP and DBP PEH at each new time point (session x time), changes in SBP and DBP at each new time point (session x time) and to compare changes in 24 h SBP and DBP during different measurement periods (session x period of measurement). Measurement periods consisted of the daytime and nighttime periods which were based on each participant's typical sleep schedule. A series of one-way RM ANOVAs were conducted to compare 24 h AMBP, day AMBP, night AMBP, total area under the curve (AUC), and peak reductions in SBP and DBP. Bonferroni corrections were used for post hoc analysis where necessary. For the exercise responses a series of one-way RM ANOVAs were conducted to compare average % VO2max, average % HRmax, average peak HR % HRmax, and RER between sessions. All AUC calculations were performed using the trapezoid method using changes in each BP relative to baseline and all the original BP measurements (pre, 15 min, 30 min, 45 min, 60 min, 90 min, and 120 min post-exercise). Peak reductions were considered the largest absolute reduction in average SBP and DBP compared to the same time-point during the CTRL session.

Results

Exercise Responses

The exercise sessions were performed correctly as reflected by the % $\dot{V}O_{2max}$, % HR_{max}, peak HR % HR_{max}, and RER during each session, thus the changes in BP post-exercise can be attributed to the different protocols. Average % $\dot{V}O_{2max}$ was not different (P=0.130, η_p^2 =0.493) between MICT (64±3% of $\dot{V}O_{2max}$), HIIT (51±10% of $\dot{V}O_{2max}$), and SIT (54±6% of $\dot{V}O_{2max}$). There were no differences (P=0.351, η_p^2 =0.408) between average % HR_{max} between MICT (80±5% of HR_{max}), HIIT (74±5% of HR_{max}), and SIT (78±3% of HR_{max}). Average peak HR % HR_{max} was not different (P=0.059, η_p^2 =0.757) between MICT (88±7% of HR_{max}), HIIT (93±5% of HR_{max}), and SIT (88±3% of HR_{max}). RER was significantly different between sessions (P=0.001, η_p^2 =0.907) such that it was higher during SIT (1.25±0.15) compared to both MICT (0.97±0.05; P=0.035) and HIIT (1.01±0.07; P=0.027). There were no differences between MICT and HIIT (P=0.471).

Acute 2 h PEH

Two-way (session x time) RM ANOVA revealed no significant interaction (P=0.767, η_p^2 =0.084) for changes in SBP PEH over time (Figure 2A). There was no main effect of session (P=0.254, η_p^2 =0.240) or time (P=0.202, η_p^2 =0.274). The peak reduction in SBP post-exercise were similar between protocols (P=0.387, η_p^2 =0.173; Table 6).

Two-way (session x time) RM ANOVA revealed no significant interaction (P=0.430, η_p^2 =0.167) for changes in DBP PEH over time (Figure 2B). There was no main effect of session (P=0.919, η_p^2 =0.017) or time (P=0.224, η_p^2 =0.258). Peak reductions in DBP post-exercise were similar between protocols (P=0.346, η_p^2 =0.191; Table 6).



Figure 2. Changes in PEH for SBP (A) and DBP (B) following MICT, HIIT, and SIT. NOTE: Values are mean±SD, n=6.

Table 6. Peak reductions in SBP and DBP following exercise protocols.					
	MICT	HIIT	SIT		
SBP (mmHg)	-13±9	-8±11	-12±11		
DBP (mmHg)	-7±8	-6±10	-10±8		

NOTE: SBP: systolic blood pressure, DBP: diastolic blood pressure, mmHg: millimetres of mercury, MICT: moderate-intensity continuous training, HIIT: high-intensity interval training, SIT: sprint interval training. Values are mean±SD, n=6.

Acute 2 h BP

Resting SBP for each session was: CTRL: 118±17, MICT: 116±14, HIIT: 119±15, SIT: 117±13 mmHg. Two-way (session x time) RM ANOVA revealed no significant interaction (P=0.138, η_p^2 =0.245) for changes in SBP over time (Figure 3A). There was a main effect of session (P<0.05, η_p^2 =0.488), whereby SBP for MICT was lower than after the CTRL (115±12 vs. 122±14 mmHg; P=0.092, d=-1.46) and HIIT sessions (115±12 vs. 118±11 mmHg; P=0.090, d=-1.43). SBP was similar for HIIT (118 \pm 11 vs. 122 \pm 14 mmHg; P=0.820, d=-0.67) and SIT (117 \pm 11 vs. 122±14 mmHg; P=0.783, d=-0.71) compared to CTRL. There was no main effect of time (P=0.619, η_p^2 =0.109). For SBP AUC, potential differences were approaching significance (P=0.095, η_p^2 =0.337), however post-hoc analysis revealed no differences between exercise and CTRL sessions (Figure 3B; MICT: P=0.235, *d*=-1.13; HIIT: P=0.521, *d*=-0.87; SIT: P>0.999, *d*=-0.63).

Resting DBP for each session was: CTRL: 67±8, MICT: 67±5, HIIT: 68±8, SIT: 68±5 mmHg. Two-way (session x time) RM ANOVA revealed an interaction (P=0.055, η_p^2 =0.291) for changes in DBP over time (Figure 3C), where MICT was lower than CTRL (P=0.079) at 60 min post-exercise. As the interaction was approaching significance (P=0.055), the main effects were still interpreted. There was no main effect of session (P=0.219, η_p^2 =0.270) and though a main effect of time (p=0.056, η_p^2 =0.387) was approaching significance, post-hoc analysis revealed no differences between time points (P>0.342). For DBP, AUC was different between sessions (P=0.037, η_p^2 =0.421), such that HIIT was lower than CTRL (P=0.070, *d*=-1.58; Figure 3D) though there were no differences for MICT (P=0.940, *d*=-0.68) or SIT (P=0.226, *d*=-1.15).

24 h Ambulatory BP

One participant refused to wear the ambulatory BP monitor at night, therefore the following analyses were run using data from the remaining 5 participants. One-way RM ANOVAs revealed no differences in 24 h (P=0.803, η_p^2 =0.076), day (P=0.930, η_p^2 =0.035), or night (P=0.757, η_p^2 =0.090) SBP following all 4 experimental sessions (Table 7). For DBP, one-way ANOVAs revealed no differences in 24 h (P=0.741, η_p^2 =0.095), day (P=0.943, η_p^2 =0.001), or night (P=0.242, η_p^2 =0.285) DBP following all 4 experimental sessions (Table 7).



Figure 3. Changes in SBP and DBP over the acute 2 h period following CTRL, MICT, HIIT, and SIT. A) SBP over time; B) SBP AUC; (C) DBP over time; (D) SBP AUC. NOTE: Values are mean±SD, n=6. \$ - denotes MICT trending to be lower than CTRL P=0.079; # - denotes HIIT trending to be lower than CTRL P=0.070.

	CTRL	MICT	HIIT	SIT
SBP (mmHg)				
24 h DBP (mmHg)	121±15	121±8	124±9	122±13
24 h	76±12	75±7	77±8	76±8
SBP (mmHg) Day Night	128±17 109±10	126±11 112±4	123±18 112±7	128±14 111±8
DBP (mmHg) Day	81±13	78±9	84±8	80±8
Night	67±8	68±3	65±6	69±6

Table 7. 24 h AMBP SBP and DBP following CTRL, MICT, HIIT, and SIT

NOTE: SBP: systolic blood pressure, DBP: diastolic blood pressure, mmHg: millimetres of mercury, CTRL: control, MICT: moderate-intensity continuous training, HIIT: high-intensity interval training, SIT: sprint interval training. Values are mean±SD, n=5.

Discussion

To our knowledge this is the first study to investigate the effects of three different exercise intensities on PEH immediately (2 h) and 24 h post-exercise. With a limited data set (n=6), there were no differences in PEH between protocols in the immediate post-exercise period. While only MICT was able to elicit statistically significant reductions in BP over the entire post-exercise period, when considering the AUC, effect sizes, and large absolute reductions in BP following HIIT and SIT, it is likely they will both be effective when an adequate sample is collected. It is important to note, while our middle-aged population was normotensive, absolute reductions observed after all exercise protocols were similar to those seen in hypertensive populations (Angadi et al. 2015; Cleroux et al. 1992b; Costa et al. 2016; Cote et al. 2015; Floras et al. 1989; Forjaz et al. 2004; Halliwill et al. 1996; Hecksteden et al. 2013; Jones et al. 2007; Keese et al. 2011; Lacombe et al. 2011; Liu et al. 2012; MacDonald et al. 1999; MacDonald et al. 2000a, 2000b; MacDonald et al. 2001; Morales-Palomo et al. 2017; Mota et al. 2009; Pescatello et al. 2004b; Rakobowchuk et al. 2009; Rossow et al. 2010; Rueckert et al. 1996; Senitko et al. 2002). The effects on 24 h BP are unclear as none of the exercise protocols reduced BP compared to control. Though previous work has examined the effect of different sub-maximal exercise intensities (40-60% $\dot{V}O_{2max}$) in middle-aged adults, our study is the first to compare the effects of submaximal and supramaximal exercise intensities in middle-aged adults in the immediate and 24 h post-exercise period and more data collection (as planned) is imperative.

The exercise data accurately reflected the exercise protocols such that changes in BP are indicative of their respective intensities. The MICT session was completed at $65\pm3\%$ of $\dot{V}O_{2max}$ matching the desired exercise intensity. Although average %HR_{max} during the HIIT session was similar to MICT and SIT sessions, the average values during the work bouts ($87\pm4\%$ of HR_{max}) matched the intended stimulus (90% HR_{max}) and that of previous work ($88\pm3\%$ of HR_{max}) (Little et al. 2011). The % $\dot{V}O_{2max}$ and %HR_{max} for the SIT session was similar to, or lower compared to the MICT and HIIT sessions. This is due to the short work bouts (15 s) and longer rest periods (2 min) which has also been demonstrated in previous work comparing SIT to other protocols (Hazell et al. 2012; Islam et al. 2017b). The greater intensity of the SIT session was reflected in average RER during the exercise period which has higher during SIT (1.25 ± 0.14) compared to HIIT (1.01 ± 0.07) and MICT (0.97 ± 0.05), also seen in previous work (Hazell et al. 2012; Islam et al. 2017b).

PEH was similar following MICT (-9/-4 mmHg), HIIT (-6/-4 mmHg), and SIT (-7/-4 mmHg) for both SBP and DBP. For SBP, the PEH response appeared to be greatest at 60 min post-exercise (-10 mmHg), and was still large (-7 mmHg) at 120 min post-exercise. Although

there was no main effect of time (P=0.202), these findings are supported by a medium effect size $(\eta_p^2=0.274)$ and would suggest that the PEH response lasted the entire duration of the acute 2 h period. Similarly, there was no main effect of time for DBP (P=0.224) although there was also a medium effect size ($\eta_p^2=0.258$). It appears the PEH response may be greatest at 60 min postexercise (-7 mmHg) compared to 120 min post-exercise (-3 mmHg), suggesting the PEH response for DBP may have only lasted up to 60 min after exercise cessation. These interpretations are speculative as the data set presented is only preliminary, however based on this data, when a full data set is collected we anticipate important benefits of all exercise protocols on BP. Peak reductions in BP compared to CTRL following MICT (-13/-7 mmHg; d=1.44/0.88 for SBP and DBP respectively) were similar to those recorded in previous work (-9/-5 mmHg) across a wide age range and resting BP status (Angadi et al. 2015; Cleroux et al. 1992a, 1992b; Costa et al. 2016; Forjaz et al. 2004; Halliwill et al. 1996; Hecksteden et al. 2013; Jones et al. 2007; Keese et al. 2011; Lacombe et al. 2011; Liu et al. 2012; MacDonald et al. 1999; MacDonald et al. 2000a, 2000b; Mota et al. 2009; Pescatello et al. 2004b; Rossow et al. 2010; Rueckert et al. 1996; Senitko et al. 2002). Peak reductions in BP following HIIT (-8/-6 mmHg) and SIT (-12/-10 mmHg) were similar to MICT in the current study supported by medium-large effect sizes (HIIT: d=0.67/0.60; SIT: d=0.58/1.25 for SBP and DBP respectively), despite both high-intensity protocols not being statistically different from CTRL (Table 6). These peak reductions following HIIT (-8/-6 mmHg) and SIT (-12/-10 mmHg) were comparable to previous studies using high-intensity exercise (-8/-5 mmHg) across a wide age range and BP status (Angadi et al. 2015; Costa et al. 2016; Cote et al. 2015; Lacombe et al. 2011; Morales-Palomo et al. 2017; Rossow et al. 2010). It is important to note the reductions in BP are clinically significant as reductions as small as 2 mmHg SBP can reduce stroke mortality by 10% and ischemic heart disease mortality by 7% (Lewington et al.

2002). While these are acute changes and BP does return to normal levels in the hours following exercise, the regular occurrence of these reductions could contribute to reduced risk of mortality. Although currently underpowered, these data demonstrate that high-intensity exercise is likely capable of eliciting large reductions in BP in middle-aged adults, providing additional support for the efficacy of these exercise protocols.

With the current data set, only MICT induced statistically significant reductions in BP (-7/-3 mmHg for SBP and DBP respectively) in the acute hours following exercise. Despite HIIT and SIT not eliciting statistical differences compared to CTRL, both were capable of reducing BP (-4/-3 and -5/-3 mmHg respectively) with medium effect sizes (d=-0.67 and d=-0.71 respectively) in the 2 h period post-exercise. Only one other study has compared the PEH response to MICT, HIIT, and SIT, though in a young (25 y) and normotensive (122/68 mmHg) sample (n=11), demonstrating significant reductions in BP following all 3 protocols (Angadi et al. 2015). The absolute reductions following MICT (-3/-2 mmHg), HIIT (-6/-5 mmHg), and SIT (-3/-3 mmHg) were similar to the current study. Specifically, there were larger reductions following HIIT compared to MICT and SIT in the second h post-exercise and the reductions lasted for 3 h postexercise. Although neither study assessed mechanisms involved in the response, it could be speculated that similar mechanistic changes occurred (reduction in TPR due to release of local vasodilators and withdrawal of sympathetic nervous system) as absolute BP reductions were similar between studies. It should be noted that Angadi and colleagues (2015) used a cycle ergometer for their exercise modality whereas we are the first study to utilize the low-volume HIIT protocol (10 x 1 min at 90% HR_{max} with 1 min recovery) on a treadmill. Whether there is are differences based on mode of exercise on PEH is currently unknown.

The ability of all exercise protocols to induce PEH is further supported by the BP AUC. For SBP, AUC was reduced compared to CTRL by 130% (d=-1.13), 123% (d=-0.87), and 93% (d=-0.63) following MICT, HIIT, and SIT respectively demonstrating a clear effect of exercise on SBP in the acute hours following exercise. For DBP, AUC was reduced by 47% (d=-0.68), 76% (d=-1.58), and 78% (d=-1.15) following MICT, HIIT, and SIT respectively compared to CTRL. Though AUC has not been calculated in previous research studies, a rough calculation of the AUC from Angadi and colleagues (2015) demonstrates larger effects on both SBP AUC (reductions of 194%, 245%, and 110% following MICT, HIIT, and SIT respectively compared to CTRL) and DBP AUC (reductions of 82%, 137%, and 143% following MICT, HIIT, and SIT respectively compared to CTRL). These differences may be due to the exercise as protocols as the exercise intensity/volume was greater compared to the protocols used in the current study. While speculative, greater exercise intensity/volume may have resulted in greater concentrations of local vasodilators (histamine and bradykinin) released in response to physical stimuli and muscular contraction (McCord et al. 2006; Moraes et al. 2007) leading to a greater overall response. Collectively, the absolute changes in BP over the acute 2 h period, the peak reductions in BP, and the reduced AUC compared to CTRL all demonstrate that the exercise protocols were similarly effective in reducing BP. Additional data collection will be required to provide greater support to these preliminary findings.

While most PEH studies examine an acute post-exercise period (~2 h), longer duration reductions (>2 h) in BP following exercise may be indicative of a protective effect of exercise on BP. With that in mind we designed this study to measured AMBP over 24 h post-exercise. Our data demonstrate no differences in 24 h AMBP following MICT (0/-1 mmHg), HIIT (+3/+1 mmHg), or SIT (+1/0 mmHg) compared to CTRL. Previous work has demonstrated reductions

(MICT: -5/-3 mmHg; HIIT: -3/-2 mmHg) in 24 h AMBP following MICT and HIIT (Ciolac et al. 2008; Ciolac et al. 2009; Dantas et al. 2017; Sosner et al. 2016; Wallace et al. 1999). While the mechanisms involved in the acute PEH response are well understood, the mechanisms responsible for longer lasting reductions in BP have not been established. Interestingly, Sosner and colleagues (2016) did note reductions in arterial stiffness following a single HIIT session that coincided with reduced AMBP during the day. These lack of changes between sessions may be due to other factors that were not controlled for during the period the monitor was worn. For example, participants were instructed not to engage in physical activity during the time they wore the monitor and although all participants followed the instructions, sedentary behaviour was not assessed which could play a role in the differences. Additionally, participants were asked to maintain their regular sleep schedule on days the monitor was worn, however there was no assessment of sleep length or quality. Future studies assessing the effect of exercise on AMBP should consider these other factors. Therefore, while the present data set appears to suggest no benefit on 24 AMBP, more data collection is required.

Despite no differences in 24 AMBP, both SBP and DBP were lower (-15/-14 mmHg) during the night compared to during the day which is in line with previous research (Bevan et al. 1969) and is in part due to changes in posture and physical activity between night and day (Morris et al. 2013). Previous work assessing changes in AMBP following exercise have also observed greater BP during the day (Ciolac et al. 2008; Ciolac et al. 2009; Dantas et al. 2017; Ferrari et al. 2017; Karoline de Morais et al. 2015; Sosner et al. 2016; Wallace et al. 1999). Interestingly, during the day DBP was lower following MICT (-6 mmHg) and SIT (-4 mmHg) compared to HIIT, whereas during the night DBP was lower following HIIT (-4 mmHg) compared to SIT. These divergent changes may be the reason why there were no differences in 24 AMBP as lower BP

during the day would be negated by higher BP at night. While the effect sizes associated with these changes are very large (>1.3), no previous work has found divergent findings like this and we are unsure what may have attributed to these changes. It is possible that reductions in day BP are masked by activities of daily living and reductions are only evident once physical activity has ceased during the night. MacDonald and colleagues (2001) demonstrated the PEH response was sustained throughout simulated activities of daily living (e.g., seated rest, standing, slow walking/cycling, walking with briefcase) performed after exercise, however the simulated activities of daily living were only performed for 70 minutes and measurement did not extend throughout the entire day. More data collection is required to establish if these differences do exist or are due to low sample size with the current data set.

Studies examining the possible predictive nature of the PEH response have found strong, significant correlations (r >0.65) between acute reductions (1 h post-exercise) and chronic reductions (4 and 8 weeks) in BP (Hecksteden et al. 2013; Liu et al. 2012). Our peak changes in BP (MICT: -13/-7 mmHg; HIIT: -8/-6 mmHg; and SIT: -12/-10 mmHg) post-exercise are in line with previous work (MICT: -9/-4 and -7/-4 mmHg) suggesting that HIIT and SIT may also have long term effects on BP (Hecksteden et al. 2013; Liu et al. 2012). Using a similar design, future research should examine if the acute response following HIIT and SIT is predictive of chronic changes similar to MICT. Moreover, as much of the work examining PEH in middle-aged and older adults focuses on MICT, our results suggest a potential similar benefit to HIIT and SIT. Though some might fear the use of high-intensity exercise in these populations, the risk of cardiovascular events is similar between MICT and HIIT in at-risk populations such as individuals recovering from coronary heart disease (Rognmo et al. 2012). While no study has assessed the risk of SIT, there is work using SIT in overweight/obese (Allen et al. 2017; Heiskanen et al. 2017;

Keating et al. 2014; Sjoros et al. 2018) and Type 2 Diabetic (Banitalebi et al. 2019; Heiskanen et al. 2017; Sjoros et al. 2018) middle-aged adults suggesting it can be completed with beneficial outcomes. In the present data set there were no adverse events during data collection, though our sample was normotensive and had good-excellent age-specific cardiorespiratory fitness ($\dot{V}O_{2max}$: 34.41±6.17 mL·kg⁻¹·min⁻¹) using $\dot{V}O_{2max}$ norms (American College of Sports Medicine 2017). Overall, our preliminary data adds to the various health benefits (e.g., improved $\dot{V}O_{2max}$ and body composition) and associated with HIIT and SIT (Gibala et al. 2014).

Limitations

While the study provides valuable information regarding the effect of exercise intensity on PEH, it is important to highlight several limitations. Most importantly, our interpretations and conclusions are limited to an under powered sample of 6. A larger sample (as originally planned) would have allowed us to draw more accurate conclusions regarding the effect of exercise intensity on PEH in middle-aged adults (in fact 7 additional participants were scheduled to complete the study by May prior to the COVID-19 pandemic). Further, hypertensive participants were the target population during early recruitment and while we were only able to recruit one hypertensive and one pre-hypertensive participant respectively. When we continue data collection we will aim to recruit more pre-hypertensive and hypertensive participants. It is important to note that our sample was also recreationally active with good-excellent VO2max scores. This should be considered when interpreting the PEH response as a less active sample may not respond similarly. While a potential limitation is that we did not assess hydration status before and after exercise as the effects of hydration may be involved in the PEH response (Endo et al. 2012b), the majority of studies used in designing the current project allow ad libitum water consumption post-exercise. While replacing the exact amount of water lost during exercise with a saline infusion has been shown to

diminish the PEH response (Charkoudian et al. 2003), this would likely not occur with oral consumption during a real-life scenario. While the activity journals did provide important information regarding participant's activities while wearing the monitor, other important information the should be considered in future studies using AMBP includes: length and quality of sleep, occupation, and sedentary activity.

Conclusion

Overall, MICT, HIIT, and SIT exercise sessions produced similar PEH during a 2 h postexercise measurement period, with peak reductions occurring ~45 min after exercise, and the effects on 24 h BP are inconclusive due to limited sample size. Despite our current samples size, it appears that HIIT and SIT elicit similar PEH responses 2 h post-exercise as MICT, providing individuals with a greater 'menu of options' to control their BP though a greater sample is required to confidently determine this. Further work is needed to determine their effects on 24 h BP. While the physical activity guidelines and the majority of research focus on the benefits of MICT, many people are not doing this for a variety of reasons. This research adds to a growing body of literature demonstrating the potential health benefits associated with HIIT/SIT and provide individuals with a greater 'menu of options' for exercise. Future work should focus on chronic training studies using these protocols to further investigate the possible predictive nature of the PEH response, while also examining the efficacy of these protocols as long-term options to reduce BP.

CHAPTER 3

Infographic, Case Study, and Exercise Prescription

Not So Under Pressure

Effects of Exercise Intensity on Blood Pressure



No dose response of exercise intensity on reducing acute blood pressure, all exercise appears beneficial - <u>so take your pick</u>



While hypertensive individuals were the target population for the research study, recruitment was difficult and only one hypertensive participant volunteered. Below is a case study for this participant to speculate as to potential differences had more hypertensive participants been recruited.

Hypertensive Case Study Resting BP: 143/77 mmHg

While SBP on the CTRL day did not change drastically, all exercise reduced BP as evident by the changes post-exercise (Figure 4A) and the AUC (Figure 4B). All exercise protocols were able to reduce SBP compared to CTRL with the largest reductions at 60 min post-exercise (MICT: -15, HIIT: -17, SIT: -22 mmHg). For DBP, there was a steady increase following CTRL and MICT, whereas HIIT and SIT were able to reduce BP (Figure 4C & D). Although DBP did increase following MICT, HIIT reduced DBP by ~10 mmHg, and by larger magnitudes following SIT (18-20 mmHg). Taken together, for this hypertensive participant the reductions following MICT (-15/-7 mmHg) were similar to the normotensive participants (-12/-6 mmHg), whereas the reductions following HIIT (-17/-11 mmHg) and SIT (-22/-20 mmHg) were greater compared to the normotensive participants (HIIT: -5/-4; SIT: -10/-8 mmHg). Additionally, for the current sample there were no differences between protocols (MICT: -13/-7 mmHg; HIIT: -8/-5; SIT: -12/-10 mmHg), whereas the changes for this participant show HIIT and SIT may be able to elicit larger reductions specifically for DBP in hypertensive populations. Although this is only one participant, this data shows the potential larger acute reductions in BP following HIIT and SIT for hypertensive participants.



Figure 4. Changes in SBP and DBP over acute 2 h period following CTRL, MICT, HIIT, and SIT for hypertensive case study. A) SBP over time; B) SBP AUC; C) DBP over time; D) DBP AUC.

Prescription of MICT, HIIT, and SIT

Prescription and adherence of these exercise protocols is important considering their effect on post-exercise BP. Participants should be screened prior to participation. For MICT participants could begin with 20 min of walking/running per session. The participant should be exercising at a pace at which they could still carry a conversation with another person. The program could increase by 5 min every 2 weeks such that by the end of 6 weeks participants would be completing 30 min of running. For HIIT participants could begin with 5 x 1 min bouts with 1 min rest. The participant should be exercising at a faster pace such that they would not be able to actively carry a conversation, however not so fast that they are going all out. The participant will increase to 7 bouts for weeks 3 and 4 and 10 bouts for weeks 5 and 6. Finally for SIT, the participants could begin with 4 x 15 s sprints with 2 min rest. The participant should be exercising at an all-out pace. To do this the participant can set up 2 cones ~35-50 metres apart and sprint from one cone to the other. The participant will increase to 6 bouts for weeks 3 and 4 and 8 bouts for weeks 5 and 6.

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Appendix A

June 14, 2019

Dear Seth McCarthy

REB # 6158 Project, "Examining the effect of exercise intensity on post-exercise hypotension, energy balance, and psychological perceptions towards exercise in sedentary middle-aged adults." REB Clearance Issued: June 14, 2019 **REB Expiry / End Date: May 31, 2021**

The Research Ethics Board of Wilfrid Laurier University has reviewed the above proposal and determined that the proposal is ethically sound. If the research plan and methods should change in a way that may bring into question the project's adherence to acceptable ethical norms, please submit a "Request for Ethics Clearance of a Revision or Modification" form for approval before the changes are put into place. This form can also be used to extend protocols past their expiry date, except in cases where the project is more than four years old. Those projects require a new REB application.

Please note that you are responsible for obtaining any further approvals that might be required to complete your project.

Laurier REB approval will automatically expire when one's employment ends at Laurier.

If any participants in your research project have a negative experience (either physical, psychological or emotional) you are required to submit an "Adverse Events Form" within 24 hours of the event.

You must complete the online "Annual/Final Progress Report on Human Research Projects" form annually and upon completion of the project. ROMEO will automatically keeps track of these annual reports for you. When you have a report due within 30 days (and/or an overdue report) it will be listed under the 'My Reminders' quick link on your ROMEO home screen; the number in brackets next to 'My Reminders' will tell you how many reports need to be submitted. Protocols with overdue annual reports will be marked as expired. Further the REB has been requested to notify Research Finance when an REB protocol, tied to a funding account has been marked as expired. In such cases Research Finance will immediately freeze funding tied to this account.

All the best for the successful completion of your project.

(Useful links: ROMEO Login Screen ; REB Students Webpage; REB Connect Webpage)

Yours sincerely,

All -

Jayne Kalmar, PhD Chair, University Research Ethics Board Wilfrid Laurier University

Please do not reply directly to this e-mail. Please direct all replies to reb@wlu.ca

Appendix B



CONSENT TO PARTICIPATE IN RESEARCH

LETTER OF INFORMATION

Date: _____

Title of Study: **Examining the effect of exercise intensity on post-exercise hypotension**, energy balance, and psychological perceptions towards exercise in sedentary middle-aged adults (REB #6158)

Dear _____:

You are being invited to participate in a research study conducted by Dr. Tom J. Hazell and Seth McCarthy (BHK), Abigail Broad (BA Kin), Derek Bornath (BHK, MHK), and Emily Ferguson (BKin student) from the Energy Metabolism Research Laboratory and Dr. Jennifer Robertson-Wilson in the Department of Kinesiology and Physical Education at Wilfrid Laurier University.

PURPOSE OF THE STUDY

The purpose of the study is to examine the effect of exercise intensity on post-exercise hypotension, energy balance, and the psychological perceptions towards exercise in sedentary middle-aged adults.

PROCEDURES

This study requires you to visit the Energy Metabolism Research Laboratory 5 times, once for a familiarization session (~1 h) and then for four testing sessions (~3.5 h each) for a total time commitment of ~15 hours. Parking passes will be provided to participants for each session. The familiarization session will include a test of cardiorespiratory fitness ($\dot{V}O_{2max}$ test), consisting of a graded running test performed until exhaustion. Following a 5 min warm up, you will begin the test running at a speed between 5-7 mph at 0% incline. Every 2 minutes thereafter, incline on the treadmill will increase by 2%. The test will continue until volitional fatigue. After this an ambulatory blood pressure monitor will be attached to your left arm for you to wear for the next 24-h. It will automatically measure your blood pressure twice an hour during the day and once an hour during the night. This is to familiarize you to the monitor for subsequent sessions. You will

return it directly to the Exercise Metabolism Research Laboratory or one of its researchers the next day, whichever is convenient for you.

All experimental sessions (separated by 7 days) will include an exercise session followed by a 2 h post-exercise period where participants rest comfortably and quietly in the laboratory (e.g., reading). The four exercise treatments will be: 1) a moderate-intensity continuous training (MICT) session characterized by 30 min of continuous running at 65% VO_{2max}; 2) a high-intensity interval training (HIIT) session characterized by 10 bouts of 60 sec efforts at 90% HR_{max} followed by 60 sec rest; 3) a sprint interval training (SIT) session characterized by 8 bouts of 15 sec "all-out" efforts followed by 120 sec of rest; and 4) a non-exercise control session where participants do not exercise. The time of the sessions will vary depending on the exercise protocol (MICT: 40 min; HIIT: 30 min; SIT: 26 min). While in the laboratory, a measurement of resting gas exchange will occur for 15 minutes before the exercise session, 30 minutes post-exercise, and for the final 15 minutes of each of the remaining 2 hours post-exercise. This measurement involves wearing a respiratory mask connected to a metabolic cart measuring how much oxygen you are consuming. Blood pressure will be measured once prior to exercise, and 6 times following exercise (every 15 min for the first hour, and every 30 min for the second hour). Blood samples will also be drawn from the forearm pre- and post-exercise (two 3 mL samples per draw, 5 total blood draws). Blood draws will be taken from the inner elbow while lying supine by a trained researcher. You will also be asked several questions before and after exercise to determine your feelings of hunger and satiety as well as receive instructions on how to record dietary intake the day before the trial, on trial day, and the day after. You will also be asked several questions before and 30 min after exercise as well as one question during and immediately after the exercise sessions to determine your degree of pleasure, confidence, enjoyment, and intentions regarding the different exercise bouts. At the 2 h post-exercise period you will have the opportunity to shower followed by being fitted with an ambulatory blood pressure monitor to your left arm for you to wear for the next 24h. It will automatically measure your blood pressure twice an hour during the day and once an hour during the night. You will return it directly to the Exercise Metabolism Research Laboratory or one of it's researchers the next day, whichever is convenient for you.

POTENTIAL RISKS AND DISCOMFORTS

There is a possibility of mild muscle soreness and/or fatigue typical of an exercise session. You may feel some discomfort (light headedness, nausea, sore muscles) due to the intensity of the training or $\dot{V}O_{2max}$ test typical of strenuous physical exertion. You will be closely monitored throughout the duration of the $\dot{V}O_{2max}$ test will limit this risk to ensure the test proceeds in a safe manner and will be immediately terminated should you display any signs of distress or upon your request. Although phlebotomy is safe when done by certified and trained individuals there is a small risk of bruising at the puncture site which can be reduced by keeping pressure on the site for several minutes after the needle is withdrawn. In some rare cases the vein may become inflamed after the sample is withdrawn however using a warm compress can alleviate this. There is a small risk of infection any time the skin is broken however this rarely occurs when equipment is properly sterilized and disposed of. Some people may also experience light-headedness if they are

uncomfortable with needles and if this occurs the experiment will be terminated immediately. The risk of falling or fainting is minimum as you will be lying supine.

POTENTIAL BENEFITS TO SUBJECTS AND/OR SOCIETY

The potential benefits of your participation include a better understanding of your cardiorespiratory fitness based on the results of a $\dot{V}O_{2max}$ test, an assessment which typically costs ~\$120 when performed at commercial facilities. You will also have the opportunity to try different exercise modalities. If you wish to adopt one of the exercise protocols, the researchers could provide you with information regarding your response to the different protocols and which would be most beneficial for you. Additionally, as we expect to see a PEH response in the hours after each session, this would be beneficial to your health.

CONFIDENTIALITY

All information obtained in connection with this study will be de-identified. It is possible that data related to your participation (i.e. your $\dot{V}O_{2max}$ value, blood pressure, hormone levels, appetite scores, energy intake data) and basic demographic (physical activity level, height, weight, and age) will be submitted to an 'open access' database upon publication. This data will be completely anonymized and de-identified by removing names and any other information that could possibly identify any participant. All contact information is collected and stored on a master list in a password-protected file with access to only the study investigators. All participants will be assigned an arbitrary number to ensure anonymity. This study number will be used in all data collection files and mean data will be stored in a password protected file for comparison with future studies. All results will be collapsed before analysis. All blood samples will be stored in secured location until analysis and subsequently destroyed after a period of 5 years. All other data will also be retained and destroyed after 5 years.

PARTICIPATION AND WITHDRAWAL

Your participation in this research study is completely voluntary. You may withdraw at any time without any repercussions. If you are a student, please be assured that withdrawing will not have any impact on your status at Wilfrid Laurier University. You may also refuse to answer any questions you feel are inappropriate and still remain in the study. The investigators may withdraw you from this research if circumstances arise which warrant doing so (i.e. difficulty scheduling, repeatedly missing scheduled sessions, etc.).

FEEDBACK OF THE RESULTS OF THIS STUDY

If you would like a copy of a lay summary of the results please check the box below. The results from this study will be reported in general terms in the form of speech or writing that may be represented in manuscripts submitted for publication in scientific journals, or oral and/or poster presentations at scientific meetings, seminars, and/or conferences. We plan to publish this study in an academic journal. The information published in a journal or subsequent studies will not identify you in any way. Copies will be available upon request.

SUBSEQUENT USE OF DATA

This de-identified data may be used in subsequent studies (with no link to your personal information). You will receive a copy of the consent form after it has been signed and do not waive any legal rights by signing it.

This letter is yours to keep. If you have any questions about this research project feel free to call:

Dr. Tom Hazell 519-884-1970 x3048

Further, if you have any questions about the conduct of this study or your rights as a research subject you may contact Dr. Jayne Kalmar, Research Ethics Board (REB) Chair (<u>REBchair@wlu.ca</u> / 519-884-0710 x 3131). This project has been reviewed and approved by the REB – Approval #6158.

Sincerely,

Seth McCarthy (mcca1479@mylaurier.ca), MKin Student

Abigail Broad (broa6880@mylaurier.ca), MKin Student

Derek Bornath (born3950@mylaurier.ca), P.h.D. Student

Emily Ferguson (ferg8310@mylaurier.ca), BKin Student

Dr. Jennifer Robertson-Wilson (jrobertsonwilson@wlu.ca), Associate Professor

Dr. Tom Hazell (thazell@wlu.ca), Associate Professor

Energy Metabolism Research Laboratory

Department of Kinesiology and Physical Education

Wilfrid Laurier University
Title of Study: **Examining the effect of exercise intensity on post-exercise hypotension**, **energy balance**, and psychological perceptions towards exercise in sedentary middle-aged adults

(REB #6158)

Consent Statement

Principal Investigators: Dr. Tom Hazell, Seth F. McCarthy

I have read the accompanying "Letter of Information" and have had the nature of the study and procedures to be used explained to me. All of my questions have been answered to my satisfaction.

By signing below, I agree to participate in this study

NAME (please print): _____

SIGNATURE:

DATE:

NAME OF PERSON OBTAINING INFORMED CONSENT (please print):

SIGNATURE OF PERSON OBTAINING INFORMED CONSENT:

DATE: _____

Appendix C





ADULTS NEEDED FOR BLOOD PRESSURE STUDY!

Purpose: To determine which exercise intensities are most beneficial to blood pressure following exercise.

Who can participate?

- Non-smoking, middle-aged adults 30-60 years of age
- Any blood pressure status

Time commitment:

- $\,\circ\,$ One familiarization session \rightarrow ~ 1.5 h
- 4 experimental exercise sessions → ~ 3.5 h each
- 3 exercise sessions with ~30 min of exercise
- Total commitment of 15.5 h

Details:

- Involves 3 exercise protocols of differing intensities
- Blood pressure measurements during session and for 24 h after with a take home blood pressure monitor
- During the session blood samples will be drawn from by certified individuals

If interested, please contact: **Seth McCarthy (mcca1479@mylaurier.ca)** *This project has been reviewed and approved by the REB (#6158)*

Appendix D

2019 PA

The Physical Activity Readiness Questionnaire for Everyone The health benefits of regular physical activity are clear, more people should engage in physical activity every day of the week. Participating in physical activity is very take for MOST people. This questionnaire will tell you whether it is necessary for you to seek further advice from your doctor OR a qualified exercise professional before becoming more physically active.

Please read the 7 questions below carefully and answer each one honestly: check YES or NO.	YES	NO	
) Has your doctor ever said that you have a heart condition OR high blood pressure ??			
2) Do you feel pain in your chest at rest, during your daily activities of living, OR when you do physical activity?			
I) Do you lose balance because of dizziness OR have you lost consciousness in the last 12 months? Please answer NO if your dizziness was associated with over-breathing (including during vigorous exercise).			
I) Have you ever been diagnosed with another chronic medical condition (other than heart disease or high blood pressure)? PLEASE UST CONDITION(S) HERE:			
i) Are you currently taking prescribed medications for a chronic medical condition? PLEASE LIST CONDITION(S) AND MEDICATIONS HERE:			
5) Do you currently have (or have had within the past 12 months) a bone, joint, or soft tissue (muscle, ligament, or tendon) problem that could be made worse by becoming more physically active? Please answer NO if you had a problem in the past, but it does not limit your current ability to be physically active. PLEASE UST CONDITION(S) HERE:			
7) Has your doctor ever said that you should only do medically supervised physical activity?		C	
If you are over the age of 45 yr and NOT accustomed to regular vigorous to maximal effort exercise, consult a qualified exposes sional before engaging in this intensity of exercise.	ercise		
 If you are over the age of 45 yr and NOT accustomed to regular vigorous to maximal effort exercise, consult a qualified exposes sional before engaging in this intensity of exercise. If you have any further questions, contact a qualified exercise professional. PARTCENANT DECLARATION If you are less than the legal age required for consent or require the assent of a care provider, your parent, guardian or care provider may also sign this form. I, the undersigned, have read, understood to my full satisfaction and completed this questionnaire. Lacknowledge that this physic clearance is valid for a maximum of 12 months from the date it is completed and becomes invalid if my condition changes, I also acknowledge that the same, complying with applicable law. 	encise ust ical acti- the	nty	
If you are over the age of 45 yr and NOT accustomed to regular vigorous to maximal effort exercise, consult a qualified expressional before engaging in this intensity of exercise. If you have any further questions, contact a qualified exercise professional. PARTICIPANT DECLARATION If you are less than the legal age required for consent or require the assent of a care provider, your parent, guardian or care provider m also sign this form. L the undersigned, have read, understood to my full satisfaction and completed this questionnaire. Lacknowledge that this physic clearance is valid for a maximum of 12 months from the date it is completed and becomes invalid if my condition changes, I also acknowledge that the community/fitness center may relain a copy of this form for its records. In these instances, it will maintain to confidentiality of the same, complying with applicable law. NAMEDATE	encise ust ical activ	nty	
If you are over the age of 45 yr and NOT accustomed to regular vigorous to maximal effort exercise, consult a qualified expressional before engaging in this intensity of exercise. If you have any further questions, contact a qualified exercise professional. PARTICIPANT DECLARATION If you are less than the legal age required for consent or require the assent of a care provider, your parent, guardian or care provider m also sign this form. I, the undersigned, have read, understood to my full satisfaction and completed this questionnaire. Facknowledge that this physic clearance is valid for a maximum of 12 months from the date it is completed and becomes invalid if my condition changes. Falso acknowledge that the community/fitness center may retain a copy of this form for its records. In these instances, it will maintain to confidentiality of the same, complying with applicable law. NAME DATE SIGNATURE WITNESS	ercise ust ical activ	nty -	
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	$2019 PAR_{-}O_{+}$				
	ZUIJIANQT				
	FOLLOW-UP QUESTIONS ABOUT YOUR MEDICAL CONDITION(S)				
1.	Do you have Arthritis, Osteoporosis, or Back Problems? If the above condition(s) is/are present answer questions 1a-1c If NO go to question 2				
1a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer NO if you are not currently taking medications or other treatments)	YES NO			
1b.	Do you have joint problems causing pain, a recent fracture or fracture caused by osteoporosis or cancer, displaced vertebra (e.g., spondylolisthesis), and/or spondylolysis/pars defect (a crack in the bony ring on the back of the spinal column)?	YES NO			
1c.	Have you had steroid injections or taken steroid tablets regularly for more than 3 months?				
2.	Do you currently have Cancer of any kind?	11.			
	If the above condition(s) is/are present, answer questions 2a-2b If NO go to question 3				
2a.	Does your cancer diagnosis include any of the following types: lung/bronchogenic, multiple myeloma (cancer of plasma cells), head, and/or neck?				
2b.	Are you currently receiving cancer therapy (such as chemotheraphy or radiotherapy)?	YES NO			
3.	Do you have a Heart or Cardiovascular Condition? This includes Coronary Artery Disease, Heart Failur Diagnosed Abnormality of Heart Rhythm	e,			
	If the above condition(s) is/are present, answer questions 3a-3d If NO go to question 4				
3a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer NO if you are not currently taking medications or other treatments)	YES NO			
3b.	Do you have an irregular heart beat that requires medical management? (e.g., atrial fibrillation, premature ventricular contraction)				
Зс.	Do you have chronic heart failure?	YES NO			
3d.	Do you have diagnosed coronary artery (cardiovascular) disease and have not participated in regular physical activity in the last 2 months?				
4.	Do you have High Blood Pressure?				
	If the above condition(s) is/are present, answer questions 4a-4b If NO go to question 5				
4a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer NO if you are not currently taking medications or other treatments)	YES NO			
4b.	Do you have a resting blood pressure equal to or greater than 160/90 mmHg with or without medication? (Answer YES if you do not know your resting blood pressure)	YES NO			
5.	Do you have any Metabolic Conditions? This includes Type 1 Diabetes, Type 2 Diabetes, Pre-Diabetes				
	If the above condition(s) is/are present, answer questions 5a-5e If NO go to question 6				
5a.	Do you often have difficulty controlling your blood sugar levels with foods, medications, or other physician- prescribed therapies?	YES NO			
5b.	Do you often suffer from signs and symptoms of low blood sugar (hypoglycemia) following exercise and/or during activities of daily living? Signs of hypoglycemia may include shakiness, nervousness, unusual irritability, abnormal sweating, dizziness or light-headedness, mental confusion, difficulty speaking, weakness, or sleepiness.	YES NO			
5c.	Do you have any signs or symptoms of diabetes complications such as heart or vascular disease and/or complications affecting your eyes, kidneys, OR the sensation in your toes and feet?	YES NO			
5d.	Do you have other metabolic conditions (such as current pregnancy-related diabetes, chronic kidney disease, or liver problems)?	YES NO			
5e.	Are you planning to engage in what for you is unusually high (or vigorous) intensity exercise in the near future?	YES NO			

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6.	Do you have any Mental Health Problems or Learning Difficulties? This includes Alzheimer's, Dement: Depression, Anxiety Disorder, Eating Disorder, Psychotic Disorder, Intellectual Disability, Down Syndr.	ia, ome
	If the above condition(s) is/are present, answer questions 6a-6b If NO 🗌 go to question 7	
ба.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer NO if you are not currently taking medications or other treatments)	YES NO
6b.	Do you have Down Syndrome AND back problems affecting nerves or muscles?	YES NO
7.	Do you have a Respiratory Disease? This includes Chronic Obstructive Pulmonary Disease, Asthma, Pu Blood Pressure	ulmonary High
	If the above condition(s) is/are present, answer questions 7a-7d If NO go to question 8	
7a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer NO if you are not currently taking medications or other treatments)	
7b.	as your doctor ever said your blood oxygen level is low at rest or during exercise and/or that you require VES NO	
7c.	If asthmatic, do you currently have symptoms of chest tightness, wheezing, laboured breathing, consistent cough YES NO (more than 2 days/week), or have you used your rescue medication more than twice in the last week?	
7d.	Has your doctor ever said you have high blood pressure in the blood vessels of your lungs?	YES NO
8.	Do you have a Spinal Cord Injury? This includes Tetraplegia and Paraplegia If the above condition(s) is/are present, answer questions 8a-8c If NO go to question 9	
8a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer NO if you are not currently taking medications or other treatments)	YES NO
8b.	Do you commonly exhibit low resting blood pressure significant enough to cause dizziness, light-headedness, and/or fainting?	YES NO
8c.	Has your physician indicated that you exhibit sudden bouts of high blood pressure (known as Autonomic Dysreflexia)?	YES NO
9.	Have you had a Stroke? This includes Transient Ischemic Attack (TIA) or Cerebrovascular Event If the above condition(s) is/are present, answer questions 9a-9c If NO go to question 10	
9a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer NO if you are not currently taking medications or other treatments)	YES 🗌 NO 💭
9b.	Do you have any impairment in walking or mobility?	YES NO
9c.	Have you experienced a stroke or impairment in nerves or muscles in the past 6 months?	YES NO
10.	Do you have any other medical condition not listed above or do you have two or more medical cond	itions?
	If you have other medical conditions, answer questions 10a-10c If NO 🗌 read the Page 4 re	commendation
10a.	Have you experienced a blackout, fainted, or lost consciousness as a result of a head injury within the last 12 months OR have you had a diagnosed concussion within the last 12 months?	YES NO
10b.	Do you have a medical condition that is not listed (such as epilepsy, neurological conditions, kidney problems)?	YES NO
10c.	Do you currently live with two or more medical conditions?	YES NO
	PLEASE LIST YOUR MEDICAL CONDITION(S) AND ANY RELATED MEDICATIONS HERE:	

GO to Page 4 for recommendations about your current medical condition(s) and sign the PARTICIPANT DECLARATION.

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2019 PAR-Q+

 If you answered NO to all of the FOLLOW-I you are ready to become more physically a lit is advised that you consult a qualified exercis activity plan to meet your health needs. 	UP questions (pgs. 2-3) about your medical condition, active - sign the PARTICIPANT DECLARATION below: se professional to help you develop a safe and effective physical		
You are encouraged to start slowly and build u. 3-5 days per week including aerobic and muscl	p gradually - 20 to 60 minutes of low to moderate intensity exercise, e strengthening exercises.		
As you progress, you should aim to accumulate	e 150 minutes or more of moderate intensity physical activity per week.		
If you are over the age of 45 yr and NOT accust qualified exercise professional before engaging	omed to regular vigorous to maximal effort exercise, consult a g in this intensity of exercise.		
If you answered YES to one or more of	the follow-up questions about your medical condition:		
the specially designed online screening and exercise visit a qualified exercise professional to work through	recommendations program - the ePARmed-X+ at www.eparmedx.com and/or h the ePARmed-X+ and for further information.		
Delay becoming more active if:			
You have a temporary illness such as a cold or fever; it is best to wait until you feel better.			
You are pregnant - talk to your health care practitioner, your physician, a qualified exercise professional, and/or complete the ePARmed-X+ at www.eparmedx.com before becoming more physically active.			
Your health changes - talk to your doctor or qu activity program.	alified exercise professional before continuing with any physical		
consult your doctor prior to physical activity. PARTICIPANT DECLARATION			
All persons who have completed the PAR-Q+ please	e read and sign the declaration below.		
 If you are less than the legal age required for conser provider must also sign this form. 	nt or require the assent of a care provider, your parent, guardian or care		
l, the undersigned, have read, understood to my fu that this physical activity clearance is valid for a ma invalid if my condition changes. I also acknowledge form for records. In these instances, it will maintain	Ill satisfaction and completed this questionnaire. I acknowledge aximum of 12 months from the date it is completed and becomes e that the community/fitness center may retain a copy of this the confidentiality of the same, complying with applicable law.		
AME	DATE		
IGNATURE	WITNESS		
IGNATURE OF PARENT/GUARDIAN/CARE PROVIDER			
For more information please contact			
www.eparmedx.com	The PAR-Q+ was created using the evidence-based AGREE process (1) by the PAR-Q+ Collaboration chaired by Dr. Darren E. R. Warburton with Dr. Norman Gledhill, Dr. Veronica		
Email: eparmedx@gmail.com Citation for PAR-Q+	Jamnik, and Dr. Donald C. McKenzie (2). Production of this document has been made possible		
warouron bars, zamini xwi, ared ni sobjand Glednilli No ni dinari di the PAR-Q+ Colaboration. The Physical Activity Readiness Questionnaire for Everyone (PAR-Q+) and Electronic Physical Activity Readiness Medical Examination (ePARmed X+). Health & Ritness Journal of Canada 4(2):3-23, 2011.	through manical contributions from the Public Health Agency of Lanada and the BC Ministry of Health Services. The views expressed herein do not necessarily represent the views of the Public Health Agency of Compdo as the RC Ministry of Health Services.		
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