MOVEMENT RELATED INCREASES IN ARTERIAL BLOOD PRESSURE DURING ARM CRANK EXERCISE

by

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ABSTRACT

Few studies have evaluated the arterial blood pressure response during arm crank-exercise. The two specific aims of this study were to investigate if a higher arm cranking cadence was associated with an increase in finger arterial blood pressure and to determine the contributions that orthostatic, base, cardiac pulse and movement-related force parameters have on the blood pressure increases during arm cranking. Finger arterial blood pressure increased at a higher arm cranking cadence that maintained the same internal work (45 rpm: 83 ± 7 mm Hg; 90 rpm: 99 ±12 mm Hg; $p=0.0028$), although the magnitude of the effect may be exercise intensity dependent. Approximately 3 mm Hg of this 16 mg Hg increase was due to changes in movement-related pressure ($p<0.0001$). The results from this study show that limb movements can contribute to the increase in finger arterial blood pressure at higher arm cranking cadence.

LIST OF ABBREVIATIONS AND SYMBOLS USED

BF- Blood Flow

MAP- Mean Arterial Pressure

SV- Stroke Volume

HR- Heart Rate

TPR- Total Peripheral Resistance

EPR- Exercise Pressor Reflex

SBP- Systolic Blood Pressure

DBP- Diastolic Blood Pressure

CC- Central Command

ACE- Arm Crank Exercise

mmHg- millimeters of mercury

ECG- Electrocardiogram

RMS- Root Mean Square

BP- Blood pressure

Q- Cardiac Output

rpm- rotations per minute

BA- Bland- Altman analysis of differences

METS- Metabolic Equivalent

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CHAPTER 1: INTRODUCTION

Blood flow (BF) is the movement of blood through multitude of blood vessels (arteries, capillaries, and veins). At rest, blood flow is proportional to the arteriovenous pressure difference across the vascular bed and its vascular conductance[1]. Other determinants of muscle blood flow include, the radius of the vessel, the length of the column the blood is travelling through and the viscosity of the blood [2,3].

Determinants of mean arterial pressure include cardiac output (Q) and total peripheral resistance (TPR). Cardiac output is the amount of blood ejected from the heart within one minute. It is determined by the amount of blood expulsed per ejection and the frequency of ejection[2,3]. Total peripheral resistance is the resistance to flow within the arterial system. It is controlled by vasoconstriction and vasodilation of the arteries [2,3].

During dynamic exercise, MAP can be altered as the result of neural or mechanical mechanisms such as the activation of central command, the exercise pressor reflex, resetting of the arterial baroreceptor reflex, the muscle pump, orthostatic pressure, and movement-related forces.

Central command (CC) is a feedforward mechanism that sends efferent signals from higher brain centers to the cardiovascular and somatomotor systems within the medulla[4,5]. CC withdraws activity from the parasympathetic nervous system allowing for heart rate (HR) to rise from its resting value[4,5]. The exercise pressor reflex (EPR) involves the transmission of afferent signals from mechano- and metabo- receptors within the active skeletal muscles to the cardiovascular centers within the medulla. It will activate the sympathetic nervous system, allowing for an additional increase in heart rate and the vasoconstriction of less active muscles and regions of the body, allowing for the redistribution of blood to active tissues [6,7].

Another neural mechanism that regulates arterial blood pressure during exercise is the arterial baroreflex. Two sets of arterial baroreceptors located within the carotid sinus and aortic arch increase afferent transmission with increases in transmural pressure[8]. Firing of the baroreceptors send signals to the cardiovascular centers that set off a chain reaction that ends with the activation the parasympathetic nervous system and deactivation of the sympathetic nervous system [8]. It acts as a negative feedback loop that lowers MAP when it gets too high. During exercise, it is believed that the operating point of the arterial baroreflex is 'reset' to higher levels in direct proportion to exercise intensity via both the CC and the EPR. As such, although MAP

rises during exercise it is still perceived as being too low until it reaches the new operating level. As such, the arterial baroreflex contributes to the rise in MAP during exercise via inhibition of the parasympathetic nervous system and sympathoexcitation [8].

The muscle pump is a mechanical mechanism that has been proposed to both increase muscle blood flow during exercise and aid in the increase of venous return to the heart[9]. The milking action of the active skeletal muscles have been shown to increase the arteriovenous pressure differential allowing for a larger flow of blood across the muscle. This mechanism has also been shown to force open the one-way valves on the venous side forcing the blood to travel back to the heart. This enhanced venous return can then increase cardiac output therefore further elevating MAP[9].

There is also an effect of gravity on mean arterial pressure. The effect, also called orthostatic pressure, is dependent on the location of the blood pressure measurement relative to the heart [10–12]. The orthostatic force increases arterial blood pressure below heart height compared to blood traveling above heart height. Orthostatic pressure can be calculated by identifying the vertical distance between the heart and the point of blood pressure measurement as well as the viscosity of blood.

Motion of a limb adds an additional force that can alter mean arterial pressure. This mechanism is also known as movement-related pressure. The movement of the limb can create a 'biomechanical centrifuge' adding to the arterial blood pressure and therefore widening the arteriovenous pressure difference.[13]. Movement-related pressure can be calculated by identifying the length of the moving limb, and its angular velocity. Previously, the movement-related changes in arterial blood pressure have been evaluated in simple upper limb movements such as horizontal arm flexion[13] and in preliminary studies during cycling[14,15] , and walking[16]. The effect of movement-related pressure has yet to be evaluated in more complex upper body movement, such as arm cranking.

This thesis had two specific aims. The first was to investigate if a higher arm cranking cadence was associated with increased finger arterial blood pressure. It was hypothesized that arm cranking at 90 rotations per minute (rpm) versus 45 rpm would be associated with a larger increase in arterial blood pressure when controlling for heart rate and internal work. The second aim of this thesis was to determine the contribution that orthostatic, base, cardiac pulse, and

movement-related force components had on the finger arterial blood pressure during arm cranking.

Understanding the mechanism, or combination of mechanisms, that can affect MAP and therefore also effect blood flow can be useful in order to create exercise protocols that maximize blood flow responses. This is especially important for individuals with conditions that reduce blood flow. For example, peripheral arterial disease (PAD) is a cardiovascular disease in which patients experience pain during daily activities [17]. The cause of the pain in the limbs is due to a buildup of atherosclerotic plaque within the larger arteries of the periphery, leading to a reduction in blood flow. Exercise is a treatment modality for PAD and has been associated with changes in walking performance (i.e., increases in walking distance until pain and increased exercise time until pain onset) [17]. The local effects of movement on the blood flow response and the changes in walking performance have yet to be evaluated. If walking performance is improved via an increase in muscle blood flow, understanding all mechanisms that can increase limb blood flow will aid in the quality of life of these individuals.

CHAPTER 2: REVIEW OF LITERATURE

2.1 Blood Flow and Blood Pressure

Arterial blood flow (BF) is the movement of blood through tissues, organs, and vessels. The flow of blood starts at the left ventricle of the heart and travels through the aorta to the periphery. The drive of blood flow is determined by a pressure gradient, where blood flows from areas of higher to lower pressure. Within the systemic circulation the aorta has a mean pressure of 100 millimeters of mercury (mm Hg) while the vena cava has a pressure ~ 0 mm Hg [3,18]. As stated above, this large pressure difference is the driving force for blood flow. This decrease in pressure between the aorta and the vena cava is due to energy that is lost because of resistance to flow. As it reaches the capillaries, the pressure amplitude has almost decreased completely [3].

There are two types of blood flow, laminar and turbulent [3]. Laminar, or streamlined flow, describes the movement of blood moving in the same direction but at different velocities. As seen in Figure 1a, the blood traveling closer to the center of the vessel will have a faster velocity compared to the blood travelling closer the outer walls. Turbulent flow describes the movement of all blood within a vessel travelling at the same speed no matter its relation to the vessel wall (Figure 1b). Turbulent flow is mainly dependent on the velocity of the blood flow and the size of the vessel. Within the periphery, blood is traveling as laminar flow, while turbulent flow has been seen within the ascending aorta[3].

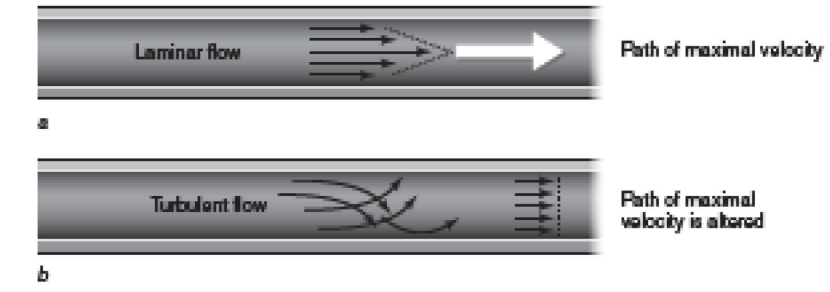

Figure 1. The difference between laminar and turbulent flow. Laminar flow has blood traveling in the same direction with the blood closer to the inside of the vessel having a higher velocity than blood travelling on the outside of the vessel. Turbulent flow has all of the blood within a vessel travelling at the same velocity but not in the same direction. Figure is reprinted from Smith & Fernhall (2011) [3].

One determinant of blood flow is the resistance to flow. This factor can be explained by Hagen-Poiseuille's Law, seen in Equation 1.

Equation 1. $\text{Resistance to Flow} = \frac{8\eta L}{\pi r^4}$

Where η is blood viscosity, L is the vessel length, and r is the radius of the vessel. Changes in any of these variables can lead to a change in the resistance to flow [2,3].

Blood flow can be difficult to measure, especially during exercise. During rest, blood pressure can instead be measured and used as an indicator for changes in blood flow[2]. Blood pressure is the measurement of the force blood exerts on the vessel walls divided by the surface area of the vessel (Equation 2) [18].

Equation 2. $\text{Pressure} = \frac{Force}{Area}$

For the purpose of this thesis, BP or more specifically the changes in mean arterial pressure (MAP) will be examined.

2.2 Determinants of Mean Arterial Pressure

Determinants of mean arterial pressure include cardiac output (Q) and total peripheral resistance (TPR), both of which are controlled by neural and mechanical mechanisms and effect MAP at the systemic level. There are two other mechanical factors that can have a local effect on MAP, orthostatic forces, and inertial forces due to movement. Both factors change the measured MAP within a limb during movement but does not affect MAP systemically. All four of these factors and their determinants can be seen in Figure 2.

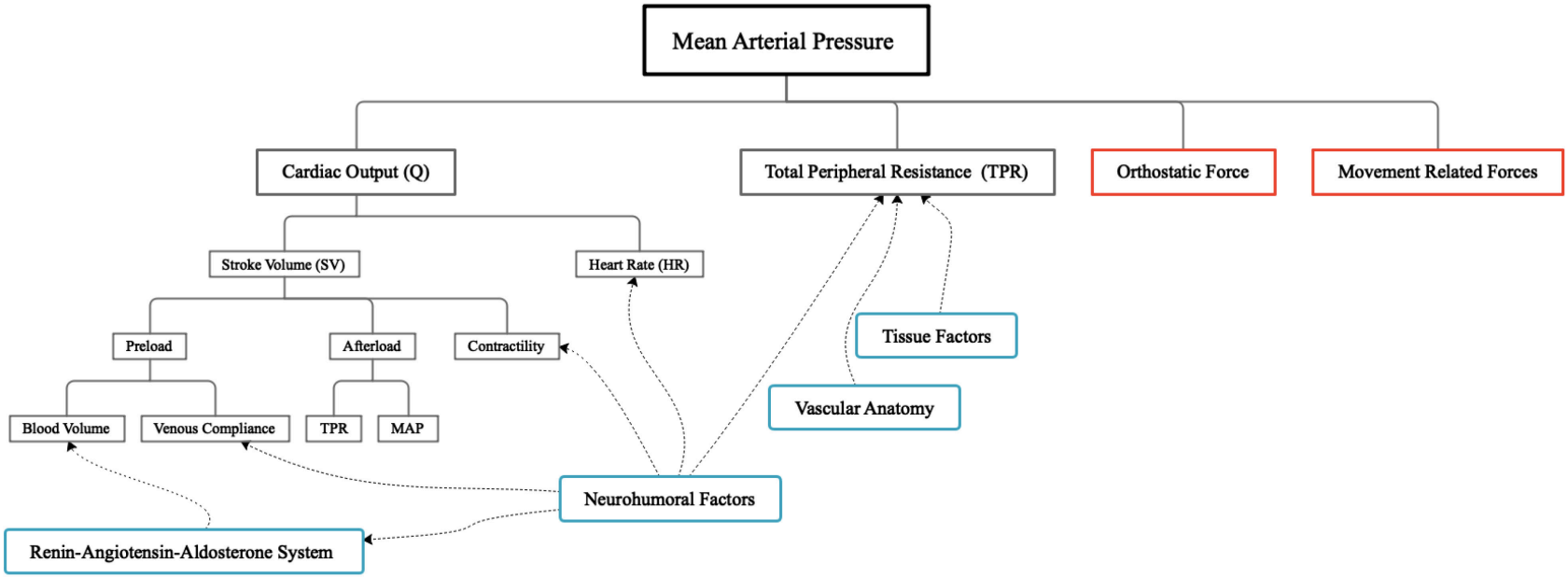

Figure 2. Flow chart of the determinants of MAP. Cardiac output (Q) and total peripheral resistance (TPR) are factors that influence MAP systemically, while orthostatic and movement related forces affect MAP locally. Cardiac output is the product of SV and HR. TPR is determined by tissue factors, vascular anatomy and neurohormonal factors all of which aid in the changing of a vessel's radius. Orthostatic force is the gravitational force applied to the blood as it travels away from the heart while, movement related forces are the inertial forces added to MAP via movement.

2.2.1 Cardiac Output

Cardiac output is the volume of blood ejected from the heart in one minute (i.e., volumetric flow rate). The elastic properties of the vessels throughout the arterial system plays an important role in the propulsion of the ejected blood volume throughout the entire arterial tree. The blood entering the aorta is pulsatile in nature due to the speed of the ejection and acts as an energy storage system. Following this systolic ejection, no blood enters the aorta until the next systolic pulse. As such, there is only a propulsion of blood into the arterial tree for the first 33% of each cardiac cycle [2,19]. To provide a continuous flow and for blood pressure to not drop to zero, the arterial system expands to stores some of the ejected blood volume during systole. This stored energy is released during diastole and creates a second pulse of blood which travels down the arterial tree. This phenomenon is called the Windkessel function and it acts as a hydraulic filter ensuring that blood travels from large to small vessels and that the pulsatile flow is gradually dampened and converted to a steady flow at the capillary level [3,19] .

Two main factors that influence Q are heart rate (HR) and stroke volume (SV). HR is determined by the activation of the sinoatrial node. Increases in HR occur via the withdrawal of the of parasympathetic and an increase in sympathetic nerve activation on the sinoatrial node, allowing for the sinoatrial node to fire more frequently [20].

Stroke volume is the volume of blood ejected from the left ventricle during each contraction. The three main determinants of stroke volume are preload, afterload and contractility. Preload, or the amount of stretch experienced by cardiac myocytes during diastole, is determined by the compliance of both the venous system and ventricles, and the changes in the amount blood volume returning to the heart [3,20]. Compliance is the vessels ability to stretch with the amount of blood volume within the vessel. A decrease in compliance within the venous system, and an increase in ventricular compliance will both lead to an increase in preload. The change in venous compliance is due to sympathetic nerve activation of the venous smooth muscle [4]. Increases in blood volume can also be aided by the muscle pump, a mechanism that will be explained in detail in the following sections.

Another determinant of stroke volume is afterload. Afterload is the mechanical load opposing ventricular ejection [21]. It changes with an increase in both aortic pressure and total

peripheral resistance. An increase in either factor will lead to a rise in afterload and corresponding decrease in stroke volume[21].

Contractility of the heart muscle is also a determining factor of stroke volume. It is independent of both preload and afterload. Contractility is the strength of the heart's contractions during systole. It is enhanced with the increase sympathetic nerve activation of the heart [20].

2.2.2 Total Peripheral Resistance

Total peripheral resistance (TPR) is used to maintain tissue perfusion. It is also an important factor in the regulation of MAP. Peripheral resistance can be explained using Hagen-Poiseuille equation (Equation 1), where TPR can be determined by the radius of the vessel, the length of the column that blood is flowing through, and the viscosity of blood. During dynamic exercise there is vasodilation within the arteries of the active limb which lead to a decrease in TPR. A corresponding increase in cardiac output allows for an increase in MAP during exercise even with the drop in TPR [22].

With an increase in the vessel radius there is an increase in muscle blood flow, also called hyperemia [22]. The increase in vessel radius is caused by relaxation of the vascular smooth muscle cells of the arteries [2,23]. Shear stress caused by blood flowing along the endothelium stimulates the release of various substances including adenosine triphosphate and substance P. The release of these substances allows for calcium channels on the endothelial cell membrane to open, allowing for the formation and release of nitric oxide (NO) and prostacyclin[22]. Shear stress also causes acetylcholine to be released from the endothelial cells, which can bind to muscarinic receptors on neighboring endothelial cells and release NO. Nitric oxide and prostacyclin both cause the vascular smooth muscle to relax, resulting in dilation of the vessel[22].

Neural factors can also influence TPR. These include the activation of the sympathetic nervous system, and activation of the exercise pressor reflex due to the activation of chemoreceptors. These neural factors will be explained in more detail in Section 2.4.

2.2.3 Orthostatic Pressure

Along with the determinants mentioned in the sections above (i.e. Q and TPR), gravitational forces will also have an effect on arterial pressure [2]. But unlike Q and TPR, this effect will only effect blood pressure at the point of measurement. Both the location of the measurement and body position will determine its effect on the recorded arterial pressure. This effect is called

orthostatic pressure. All blood must travel to and from the heart, which means that the location of the measurement relative to the heart will be the determining factor in orthostatic pressure. Gravity has a negative effect when the blood is travelling above heart height, while there is a positive effect when the blood is travelling to the feet. For example (Figure 3), a person who is 1.82 m tall with a measured MAP at heart level of 83 mm Hg would have a MAP of 39mm Hg at the top of the head and 171 mm Hg if measured at the feet [2]. The only variable that changed between the locations of measurement was the effect of gravity acting on the blood.

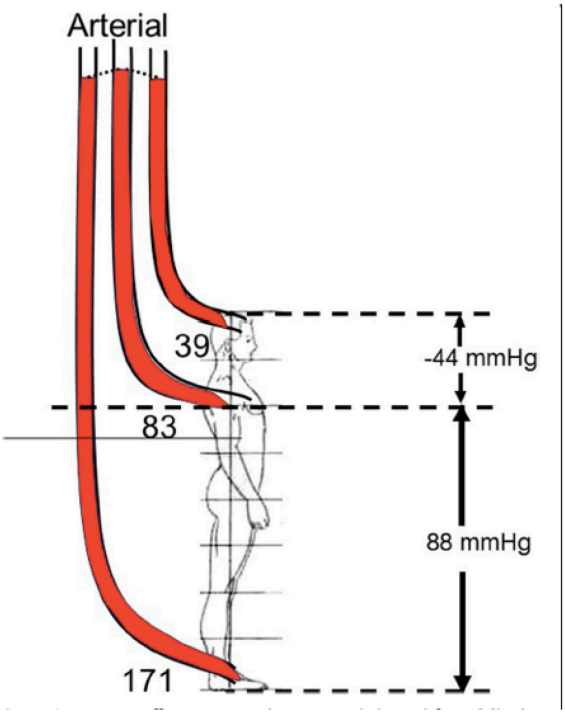

Figure 3. The orthostatic effect on blood pressure measurement. Blood pressure measured at the foot will be higher than measurement at the heart or above heart height. This is due to the change in distance from the point of measurement to the heart. Figure is reprinted from Magder (2018)[2].

Changing from a supine to upright position can also lead to a ≦20 mm Hg decrease in systolic pressure and a ≦10 mm Hg decrease in diastolic pressure when BP is measured in the brachial artery of the upper limb[10]. If blood pressure was being measured in the lower limb there would be an increase of 65 mm Hg in systolic and 62 mm Hg in diastolic blood pressure upon moving from a supine to standing position [11]. Change in the position of a single limb that is being measured can also cause a change in the recorded arterial pressure. Individuals who have their brachial blood pressure measured with their arm not in line with the location of their heart can be misdiagnosed with hypertension. This is more accurately called, orthostatic hypertension. A

change as small as 5 cm in height between the measurement location and the heart can lead to an change in mean arterial blood pressure of 3.6 mm Hg[12] .

This gravitational effect can be isolated and calculated using Equation 3. This equation is derived from a simple pressure equation (Equation 2). Any pressure can be the resultant of a force over an area. Force is the product of mass times acceleration. The only acceleration affecting the blood is the acceleration due to gravity (-9.81 m/s^2). Mass can be replaced by density times volume. Volume is the product of height and area.

Derivation for Equation 3.

$$Pressure = \frac{Force}{Area} = \frac{m * a}{Area} = \frac{m * g}{Area} = \frac{Density * Volume * g}{Area}$$

$$Pressure = \frac{Density * Height * Area * g}{Area} = Density * Height * g$$

Equation 3. $\text{Orthostatic Pressure} = \rho g h$

Where ρ is blood density (1053 kg/m^3)[26] , g is the gravitational acceleration constant (-9.81m /s^2), and h is the change in position between the heart and measurement location.

2.2.4. Movement-Related Pressure

Along with the factors of cardiac output, total peripheral resistance and orthostatic forces, reaction forces produced from the movement of a limb have been shown to alter MAP. This force, as with orthostatic forces, can only effect arterial pressure in the moving limb. Research done by Sherrif et al. (2009)[13] found that the simple movement of horizontal shoulder flexion, altered finger arterial blood pressure (FBP) compared to the static limb. Finger arterial blood pressure was measured using a finger photoplethysmography device (Finapres 2300; Ohmeda) placed on the index finger of each hand along with water-filled tubes with pressure transducers at the ends while participants performed the movement, as seen in Figure 4 [13]. The water filled tubes were used to isolate the forces acting on the blood without the effect of systolic pressure.

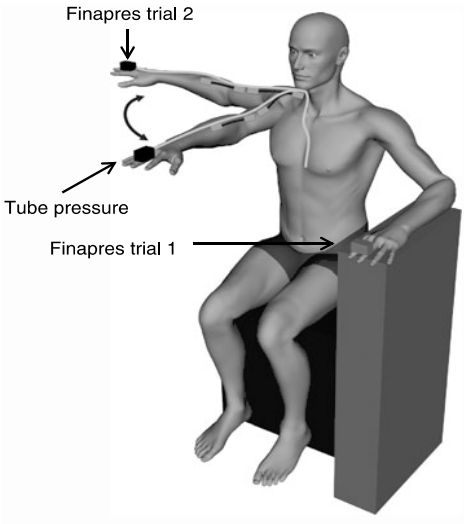

Figure 4. Experimental set up for the study evaluating movement related changes in finger arterial blood pressure during horizontal arm flexion. A finger arterial blood pressure device was measured at the index finger of both hands[13]. A water filled tube with an attached pressure transducer was also attached to the movement arm. Figure is adapted from Sheriff et al (2009)[13].

As seen in Figure 5, the moving limb (right) had a significant increase in recorded FBP (18±3 mmHg) compared to the non-active arm (8±2 mmHg, $p<0.05$)[13]. In Figure 5B, the entire measured FBP can be seen for both arms during the experiment. It should be noted that the difference in orthostatic pressure, due to the arm being placed on the chair below heart height, explains the higher non-active limb FBP before the start of the movement. The increase in arterial blood pressure related to motion was found to be approximately 10 mmHg. This value was similar to the pressure increase measured in the water tubes (11±2 mmHg). The results of the Sheriff et al. [13] study showed that angular motion can significantly increase FBP.

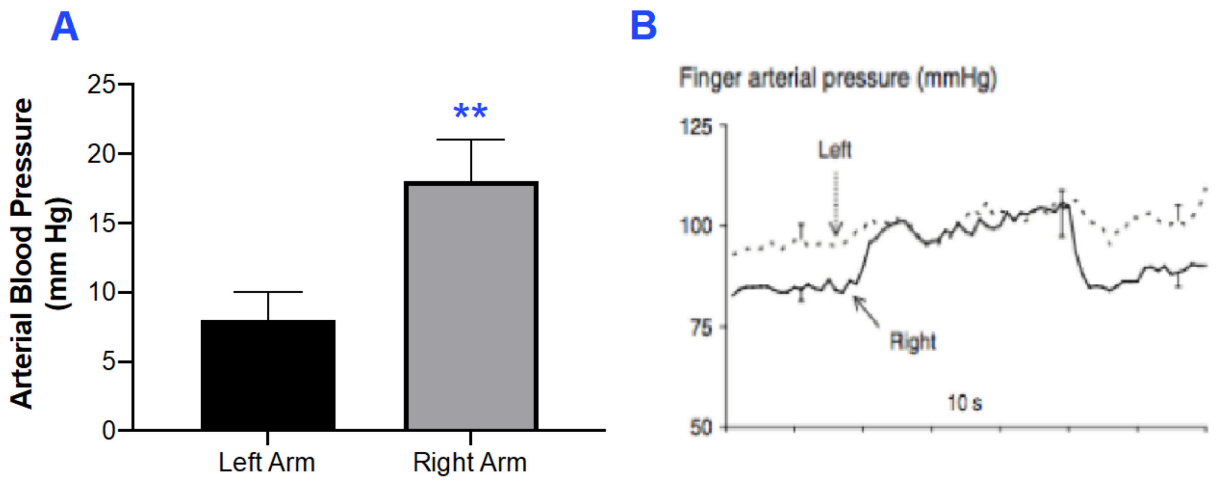

Figure 5. Finger arterial blood pressure response to horizontal shoulder flexion. A. The movement arm (right) showed a significant increase in finger arterial blood pressure (** $p<0.005$, A). The rise in FBP was ~ 10 mm Hg and was similar to the recorded change seen in the water filled tubes (11±2 mmHg). B. The complete recorded FBP during the experiment. The arrow represents the moment the movement started. Figure is adapted from Sheriff et al (2009)[13].

Movement-related forces only occur on the arterial side therefore increasing the arterio-venous pressure differential[13,27]. Studies evaluating walking discovered that venous pressure fell from 100 mm Hg to 30 mm Hg even with the added forces from gravity and limb angular motion [27]. This is due to the one-way valves on the venous side, which creates shorter columns of blood to travel through.[27] Movement-related pressure, as it will be explained in the section below, is determined by both the angular velocity of the moving limb and length of the column that contains the blood. Valves on the venous side create shorter columns, therefore allowing for less of a movement-related effect.

Movement-related pressure, like orthostatic pressure can be calculated using the simple pressure equation (Equation 2). As explained previously, a force is the product of mass times acceleration. In this instance, the acceleration is due to the movement of the limb, which can be calculated by multiplying angular velocity (ω) squared by the segment length of the limb (r) (Equation 4). Mass is the product of density (ρ) and length. The length in this equation is equal to the segment length of the moving limb, which leads the segment length to be squared. A value of 0.5 is added to the equation to find the average movement-related force occurring within a moving limb. Movement-related forces will be greater at the distal end of the segment compared

to the proximal end due to the change in the segment length. Using 0.5 allows researchers to calculate the average movement-related change in a limb.

Derivation for Equation 4.

$$Pressure = \frac{m * a}{Area} = \frac{m * r\omega^2}{Area} = \frac{Density * Volume * 0.5 * r\omega^2}{Area}$$

$$Pressure = \frac{Density * Length * Area * 0.5 * r\omega^2}{Area} = Density * Length * 0.5 * r\omega^2$$

Equation 4. $\text{Movement Related Pressure} = \rho \frac{1}{2} r^2 \omega^2$

Where ρ is blood density (1053 kg/m^3)[26] , r is the length of the rotating segment, and ω is the angular velocity of the rotating segment.

2.3 Control of MAP During Dynamic Exercise

Systemic changes in MAP are the result of the changes in cardiac output, and total peripheral resistance which causes MAP to increase during dynamic exercise. These factors are influenced by a number of stimuli. The increase in MAP can be due to an increase in both HR and SV with a corresponding decrease in TPR, which allows exercise-induced hyperemia. These changes are regulated by neural mechanisms including central command, the exercise pressor reflex and the arterial baroreflex resetting along with mechanical mechanisms such as the muscle pump. The following sections explain these mechanisms in detail.

2.3.1 Central Command

Central command is primarily the feedforward mechanism that send signals to the cardiovascular and somatomotor systems within the medulla from higher brain centers [4,5]. The area which is believed to be the origin of central command signals is the periaqueductal grey area [28]. This was identified through the recording of deep brain nuclei activation during exercise [28]. Central command initiates the cardiovascular response and determines the immediate changes of both the sympathetic and parasympathetic nervous systems [29]. At the start of exercise, CC appears to withdraw parasympathetic activity to the sinoatrial node of the heart allowing for the initial increase in HR and Q. As HR approaches 100 beats/min the sympathetic nervous system will then be activated. Sympathetic nerve activity will also increase the plasma norepinephrine concentrations, which aids in the vasoconstriction of visceral organs [30] , allowing for more blood

to flow to active muscles. Some research has also suggested that the magnitude of central command activation during exercise can be determined by an individual's perception of effort during the activity, which can be independent of the actual workload or force being produced [31].

2.3.2 Exercise Pressor Reflex

Along with central command, the exercise pressor reflex plays a key role in the regulation of MAP during exercise. The EPR is induced by both mechanical and chemical stimuli from the contracting skeletal muscle [6,7]. Signals originating from group III and IV afferents from the Pacinian corpuscles and encapsulated nerve-ending receptors are sent to the dorsal horn of the spinal cord [32]. The group III afferents primarily transmit mechanical activity that will reach the cardiovascular center in the medulla at the same time that the neural impulses arrive from central command, while the group IV muscle afferents transmitting metabolic activity are delayed as they are dependent on the increases in metabolites that arise from a contracting muscle [29]. Although the EPR acts as a feedback mechanism, its role is to help correct errors or change the cardiovascular regulation, it does not initiate the response.

2.3.3 Arterial Baroreceptor Resetting During Exercise

The third way arterial blood pressure is regulated during exercise is via the baroreflex. Baroreceptors are mechanoreceptors located within the carotid sinuses and aortic arch and they are activated with changes in transmural pressure; the difference in pressure inside a vessel relative to the pressure outside [2,3]. When baroreceptors fire, signals from the carotid sinus are sent via cranial nerve 9 to the cardiovascular centers within the medulla. These afferent signals are received at the nucleus tractus solitarius. The nucleus tractus solitarius then sends out signals to the parasympathetic nuclei and caudal ventrolateral medulla. Activation of the parasympathetic nuclei leads to an increase in parasympathetic nerve activity, which leads to a decrease in HR and a subsequent decrease in Q. Activation of the caudal ventrolateral medulla leads to an inhibition of the rostral ventrolateral medulla where activation of the sympathetic nervous system occurs [5,8]. The baroreflex is a negative feedback loop that adjusts MAP back to normal levels by activating the parasympathetic nervous system and inhibiting the sympathetic nervous system.

The baroreflex works along a sigmoidal stimulus response curve (Figure 6). Along the curve there is the operating point, centering point, threshold and saturation point. The operating point is

the point at which MAP is controlled, or the optimum MAP value. The centering point is the point of maximum sensitivity, or the point with the largest slope of the stimulus response curve. The operating range seen in Figure 6 below is the range of pressure within the carotid that will lead to changes in the outcome variable. Any pressure below the threshold point or above the saturation point will lead to no response in the outcome variable [8].

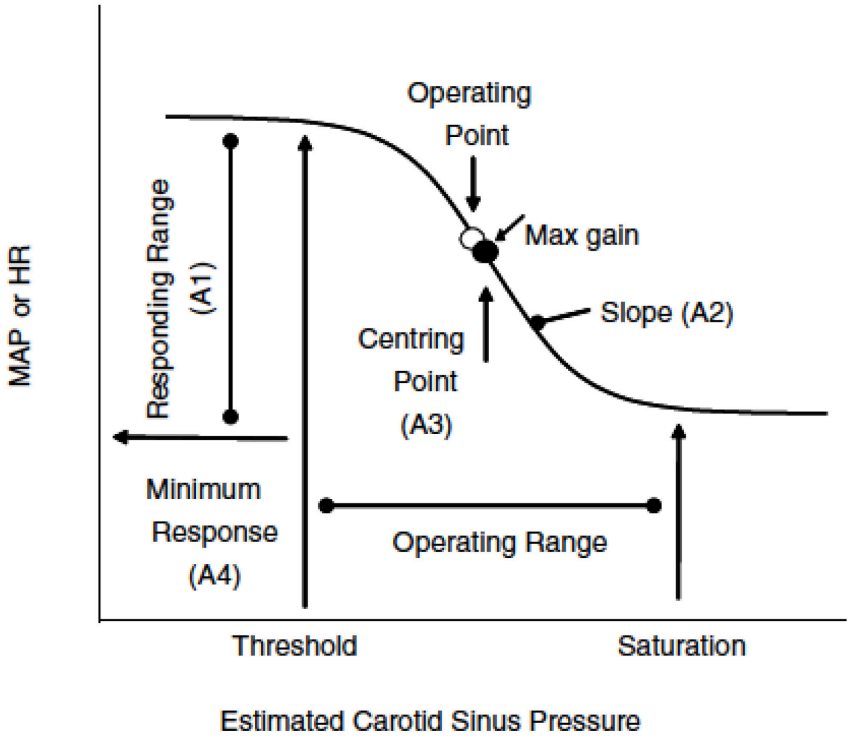

Figure 6. The stimulus response curve of the carotid baroreflex. A change in transmural pressure with the carotid sinus will lead to a change in the mechanoreceptor firing. The operating range is the range of pressure that will elicit a response to adjust either HR or MAP, correcting them to be close to their operating point. Any pressure recorded below the threshold point or above the saturation point will not elicit a response in either outcome variable. Figure is reprinted from Raven et al (2006)[8].

During exercise, the baroreceptor response-curve is 'reset'. In general, there is an overall upward and rightward shift of the response curves which occurs in a direct relationship to the intensity of the exercise being performed [8,33]. One key change in the movement of the stimulus response curve is the movement of the operating point away from the centering point and closer to the threshold of the reflex. This allows the baroreflex to be in a more optimal position to counteract hypertensive stimuli[8]. Research has shown that CC is responsible for relocating the

initial operating point for the baroreflex to a higher arterial blood pressure, as seen in Figure 7 [8,33]. This is done by the CC sending signals to the nucleus tractus solitarius inhibiting the natural response that occurs with the increase in baroreceptor firing. The muscle metaboreflex has been shown to result in vertical shifts in the baroreflex function curves which would raise the dependent variable without changing the initial operating point of the reflex [8] .

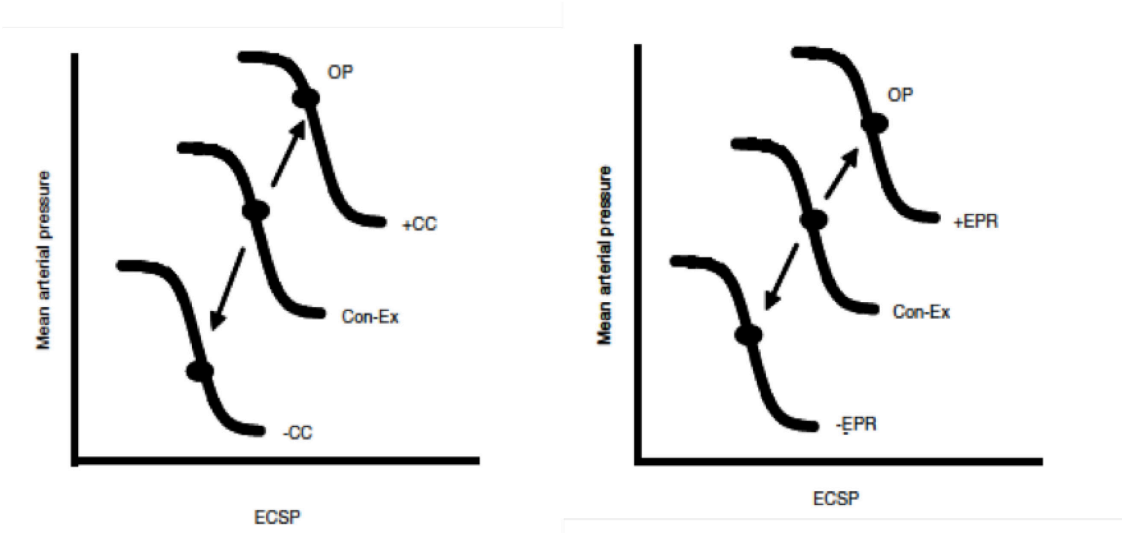

Figure 7. The lateral and vertical shift of the baroreflex stimulus response curve during exercise. Research have shown that during exercise, the rightward shift of the reflex is due to the central command, while the upward shift is due to the exercise pressor reflex. OP: operating point, ECSP: estimated carotid sinus pressure, -CC: decreased activation of the central command, +CC: increased activation of central command, +EPR: augmented exercise pressure reflex, -ERP: inhibition of the exercise pressure reflex. Figure is adapted from Raven et al. (2006)[8].

2.3.4 The Muscle Pump

The muscle pump is a mechanism that has been proposed to induce an increase in blood flow during exercise. The muscle pump functions by the compression of the veins during the contraction phase [1]. The consequent relaxation phase then creates a negative luminal pressure thereby widening the pressure gradient and allowing for an increase in flow across the active muscles[35]. This "milking action" of the muscle during the contraction and relaxation phases have been isolated in the skeletal system in pigs [9]. Bypassing the heart via an auto pumping system, allowed for a blood flow response of 100 ml/min to be observed[9]. In humans, the muscle pump has been isolated in the forearm[1]. The position of the forearm relative to the heart played a role in the muscle pump mediated blood flow response. When located above heart height the change in forearm blood flow was minimal. When placed below heart height the blood flow response was greater[1]. During dynamic exercises, the intensity of the exercise is a

determining factor in the blood flow response[1,35]. During lower leg kicking at a lower mechanical output there is an increase in blood flow promoting effects due to the relaxation of the active muscles. With loads of intermediate intensities, the muscle pump did not have a hindering or promoting effect on blood flow. At higher outputs, the muscle pump had a greater flow hindering effect[35]. The muscle pump can also increase perfusion pressure allowing for an increase in venous return and therefore an increase in cardiac output [1,36–38].

2.3.5 Effect of Cadence

The angular motion of the limb during exercise can be another mechanism that leads to the initial increase in blood flow. An unpublished master's thesis investigated the effect of linear and angular motion on pressure changes at the shank during cycling exercises[16]. Eleven participants performed eight trials of cycling exercise at 50, 80 and 110 rpm while water filled tubes with pressure transducers were attached to their lower legs. Pressure at the mid-shank significantly increased with an increase in cadence and angular motion [16]. The average pressure increases due to movement were 1.16 ± 0.75, 3.66 ± 0.87 and 6.46 ± 1.1 mmHg at 50, 80 and 110 rpm, respectively[16].

When measuring toe arterial blood pressure, an unpublished Master's thesis studied eleven participants cycling at either a cadence of 50 or 90 rpm [14,15]. Toe arterial blood pressure was measured using a Portapres®, non-invasive blood pressure measuring system, over 30 seconds of cycling at two different cadences. With an increase in cadence, there was a significant increase in measured toe MAP when controlling for the same power output (power= 79.9 ± 39.2 W, MAP at 50 rpm: 74.5 ± 30.1 mmHg; 90 rpm: 96.0 ± 30.9 mmHg, $p = 0.007$). The average increase in MAP was 18.8 ± 5.2 mmHg [14,15]. Models of toe blood pressure were then created for two participants to investigate how much of the increase of MAP was due to movement-related forces. Using lower limb kinematics collected during the cycling exercise and Equation 4, movement-related pressure was calculated to be 2.5 mm Hg while cycling at 50 rpm whereas at 90 rpm the average was 7.7 mm Hg[15]. The average increase in movement-related pressure with an increase in cadence was 5.2 mm Hg. The results from the modeling study showed that movement-related pressure accounts for approximately 27% of the increase in toe blood pressure with an increased cadence [15]. The MAP response has been investigated in lower body cycling

but has not been similarly investigated in upper arm exercise, specifically during arm crank exercise (ACE).

2.3.6 Arm Crank Ergometry

There has been lots or research on the cardiovascular response to ACE although the blood pressure response is not often investigated. The majority of research has looked at the VO_2, HR, and efficiency during ACE at a variety of workloads and cadences [39–45].

When cycling at a cadence of 90 rpm there was a higher recorded VO_2, and HR compared to cycling at 70 rpm or 50 rpm when controlling for the same external workload (Figure 8)[39,40,44]. When comparing 70 rpm versus 50 rpm, there was also a significant difference in the energy expenditure but only at higher external workloads (45 and 60 watts). A possible explanation for the increase in energy expenditure at 90 rpm compared to 50 rpm or 70 rpm could be due to the change in ventilation rate[40]. It has been shown that there are higher ventilation rates (Figure 8) at ACE of 90 rpm compared to 50 rpm when controlling for the same external workload (example at 90 W: 50 rpm: 14 ± 3 breaths/min versus 90 rpm: 16 ±3 breaths/min, $p<0.05$)[44]. This increase in ventilation rate could lead to a decrease in efficiency and be due to the increase coupling between the respiratory and locomotor systems. When evaluating gross, work (also known as net), and delta efficiencies at all three cadences, gross efficiency increased as a function of workload for all three cadences while net and delta efficiencies decreased as seen in Figure 9. Exercising at 90 rpm was always less efficient than at 50 rpm or 70 rpm [39,44]. The respiratory-locomotor coupling attempts to reduce the mechanical interactions between locomotor and ventilation systems during periods of heightened respiratory muscle conflict, which can occur during less efficient exercise (i.e., ACE at higher cadences)[40].

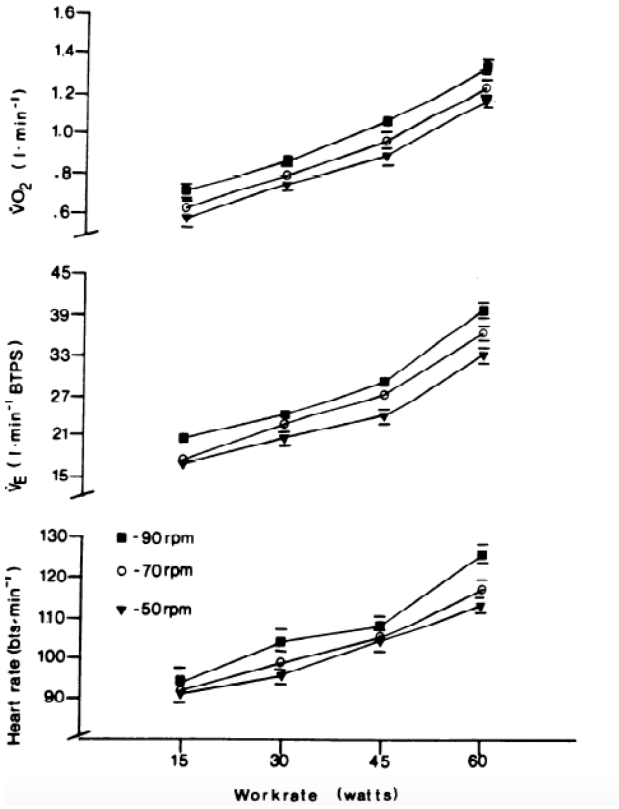

Figure 8. Oxygen consumption, ventilation rate (VE) and heart rate response to ACE at three cadences over four different external power outputs. The outcome of all three variables were always higher at 90 rpm compared to the lower two cadences. When comparing the two lower cadences, the outcome variables are not-significantly different at lower work rates (i.e., at 45 and 60 watts). Figure is reprinted from Powers et al (1984)[39].

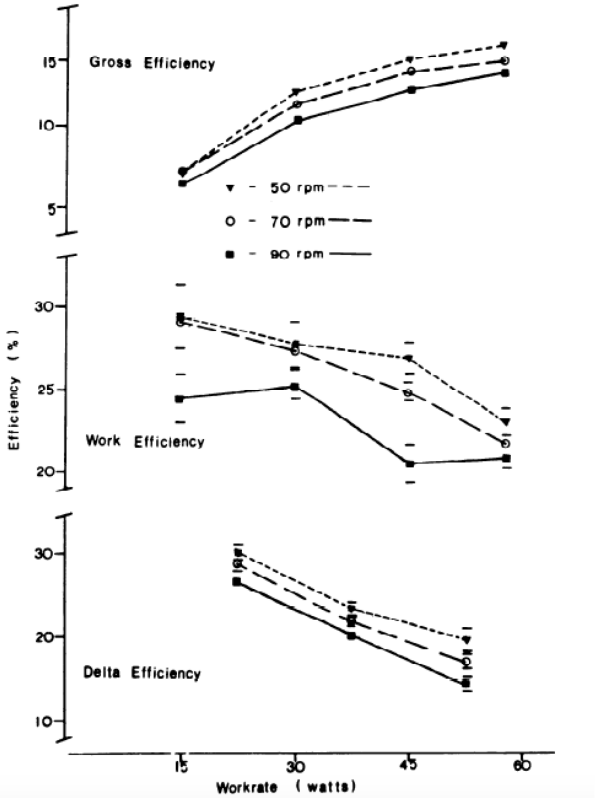

Figure 9. The gross, work and delta efficiency for ACE at three cadences over four different external power outputs. With an increase in external workload there is a decrease in work and delta efficiency at all three cadences and an increase in gross efficiency. ACE at higher cadences always produced a lower efficiency. Figure is reprinted from Powers et al (1984)[39].

Some studies have looked at the MAP responses to ACE. Comparing brachial blood pressure during ACE and elliptical exercise, both systolic (SBP, Figure 10), and diastolic blood pressure, (DBP, Figure 11) increased with an increase in exercise time [46]. When comparing SBP for the two modes of exercise at the same intensity (% of HR max) there was no significant difference

between the two measurements. There was a significant increase in the recorded DBP during ACE ($p<0.001$) [46].

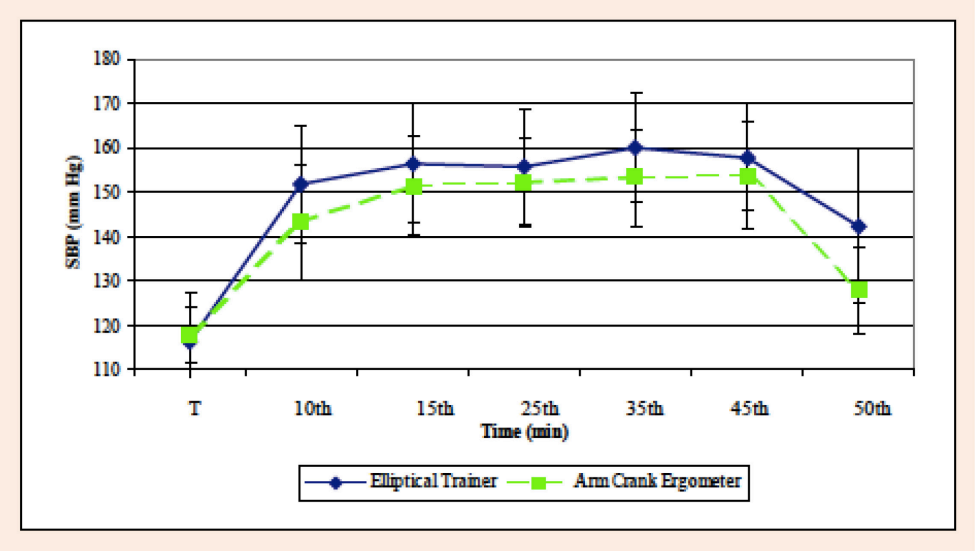

Figure 10. The systolic blood pressure response during arm crank and elliptical exercise during a 50-minute exercise bout. The SBP values for both modes of exercise were matched for internal intensity (% of HR_{MAX}) and showed no difference between the exercise modalities. Figure is reprinted from DiBlasio et al (2009)[46].

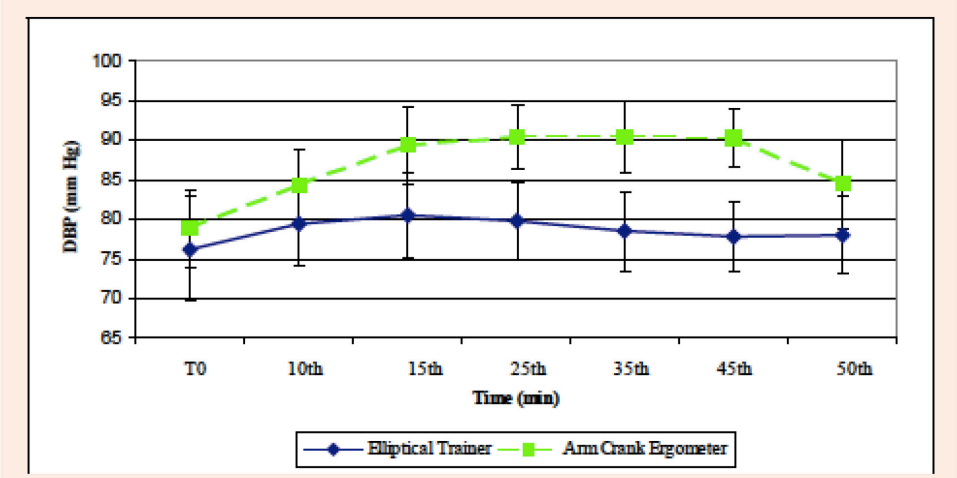

Figure 11. The diastolic blood pressure response for arm crank and elliptical exercise over a 50-minute period. When controlling for internal intensity (% of HR_{MAX}) the DBP during arm crank exercise was always recorded higher than DBP during elliptical exercise ($p<0.001$). Figure is reprinted from DiBlasio et al (2009)[46].

Other research has looked at the finger arterial blood pressure (FBP) response during ACE at two different cadences, 45 and 90 rpm, when controlling for the same internal work (60% of HR reserve) [47]. An unpublished Honours thesis found that SBP was significantly higher at a higher cadence (133±26 vs. 118±17 mmHg; $p<0.05$), as seen in Figure 12; however, there was no

significant change in the calculated MAP (80±12 mmHg at 90 rpm vs. 84±11 mmHg at 45 rpm,) due to DBP being lower at a higher cadence (54±11 vs. 66±12 mmHg; $p<0.05$) [47].

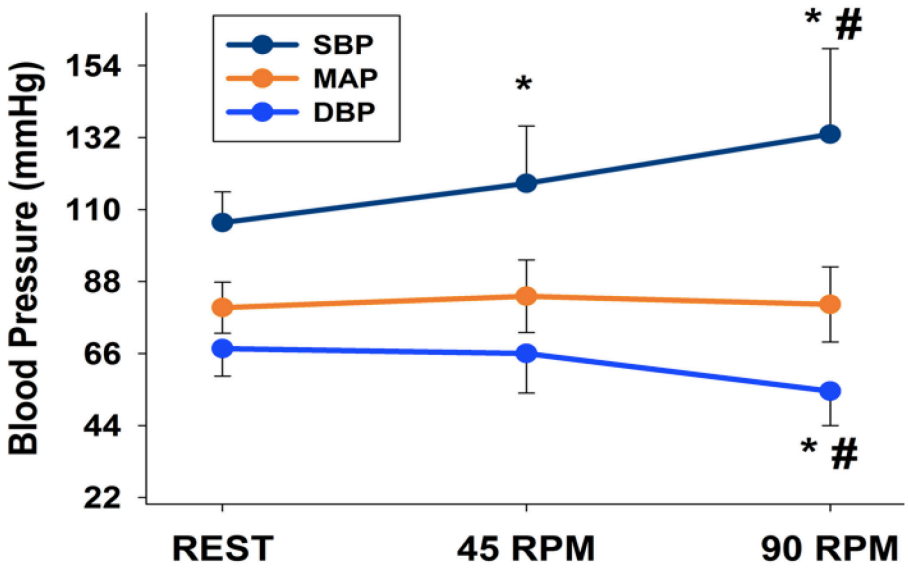

Figure 12. The systolic, diastolic and mean arterial blood pressure response to ACE at one external intensity (60% of HR reserve). * denotes a significant increase from resting levels and # denotes a significant different from 45 RPM. There was a significant increase in SBP from rest to 45 rpm and from 45 rpm to 90 rpm. There was a significant decrease in DBP only seen at 90 RPM. The calculated mean arterial pressure occurring at the finger did not change with an increase in cadence. Figure is reprinted from Billings et al (2016)[47].

Some limitations to the studies evaluating arterial blood pressure in the upper limb during ACE include, using the mercury sphygmomanometer and auscultation technique through the testing during ACE and whole-body elliptical testing [46]. This technique cannot establish the movement related effect in the periphery (aka the finger) during exercise. Furthermore, the arm could not be in motion during the measurement. Therefore, a true measurement of the BP response during ACE could not be achieved. The measurement of FBP during the study conducted by Billings[47] was done using a continuous non-invasive BP measuring device (Portapres ® Model-2, Finapres® Medical Systems, Amsterdam, The Netherlands) placed at the index finger during the exercise, but the measurements at both cadences were only evaluated at one internal workload and produced no significant difference in FBP.

Another limitation of the study was the way mean arterial pressure was identified. The SBP and DBP were identified from the recorded FBP as the peak and minimum values of the recorded

signal and then placed an equation to calculate MAP. During movement, it is harder to distinguish the difference in SBP and DBP due to orthostatic and movement-related force artifacts creating extra systolic looking peaks in the recorded BP data when the hand is at the top of a revolution[13,47] . To evaluate the true FBP response to arm crank exercise, the average of the entire FBP signal should be evaluated at each cadence.

In summary, there is a gap in the literature looking at changes in finger MAP response with an increase in cadence during incremental exercise.

2.4 Research Question

Are movement-related forces during arm cranking associated with an increase in finger arterial blood pressure?

2.5 Purpose & Hypothesis

The aim of this research project was to evaluate movement-related forces and their impact on FBP during arm crank exercise. More specifically, this thesis had two specific aims.

The first aim was to investigate if a higher arm cranking cadence was associated with an increased finger arterial blood pressure. It was hypothesized that MAP at 90 rpm would be higher in comparison to 45 rpm when controlling for heart rate and internal work.

The second aim of this thesis was to determine the contribution that orthostatic, base, cardiac pulse and movement-related force parameters had on the finger arterial BP during arm cranking. This was done by creating different models of FBP until the model that best represented the recorded FBP was discovered. The model of best fit was used to identify how much each component contributes to the rise FBP with an increase in arm cranking cadence.

CHAPTER 3: GENERAL METHODS

3.1 Study Design

This study was designed to answer one primary research question through two specific aims. First, FBP was measured during ACE at two cadences. The difference in finger MAP observed with an increase in cadence was compared while controlling for factors such as internal workload and heart rate. The second aim was designed to understand how much, if any, of the increase in MAP was explained by inertial forces created by limb movement.

3.2 Study Location

All testing was performed in the Biodynamics, Ergonomics and Neuroscience Laboratory located in room 217 of the Dalhousie University Dalplex facility.

3.3 Participants

Participants were eligible for the study if: (a) they were between the ages of 18 and 30 years old, (b) had a resting blood pressure > 100/60 mm Hg, (c) had a resting blood pressure <140/90 mm Hg, (d) did not have a history of cardiovascular, respiratory or metabolic diseases including Raynaud's disease, (e) was not taking blood pressure medication, (f) did not suffer from upper limb joint problems, (g) answered "No" to all question on the PAR-Q or (h) were not pregnant.

3.4 Sample Size

To determine the sample size for aim one of this study, previously collected data comparing the BP responses to cycling at two cadences in a young healthy population were used. Mean toe arterial BP during cycling at 50 rpm and 90 rpm were 75 ± 30 and 96 ± 31 mm Hg, respectively with an effect size of 0.688[14]. This value was entered into a power calculator (G Power v3.1.3) using a within factors repeated measures ANOVA analysis with an alpha error of 0.05 (i.e., Power=0.95). This *a priori* analysis resulted in an estimated sample size of 11.

3.5 Experimental Protocol

Testing for this study occurred over a two-day period. Each testing session was approximately one and a half hours in length with the total testing time equaling roughly three hours**.** Before each participant's first test day, an initial information letter (APPENDIX H), document of

informed consent (APPENDIX I), a Health History Questionnaire (APPENDIX J), and a Physical Activity Readiness Questionnaire (PAR-Q, APPENDIX J) were sent via email. All interested participants were encouraged to read all forms before their first session to ensure that they met all the inclusion criteria. The forms were reviewed and signed upon arrival for the first test day.

Prior to each testing session participants were asked to abstain from alcohol, caffeine and nicotine containing products, as well as engaging in vigorous physical activity for a period of 24 hours. Participants were also asked to be well rested (~8 hours of sleep) and to have consumed their last meal approximately 3 hours before the test session. Within a participant, each testing session was also scheduled for the same time of day. These instructions were given to help minimize confounding factors that can influence resting and arm exercise-mediated cardiovascular responses. Participants were also asked to bring proper attire for exercise (shorts, t-shirt and sports bra for females).

Upon arriving at the lab for the first testing day, the informed consent forms and two questionnaires were reviewed by the participant and the primary investigator. Participants were encouraged to ask questions about all aspects of the study. If all questions were answered, then the participants signed the informed consent form. Participants had their height (to nearest 0.1 cm) and body mass (to nearest 0.1 kg) measured on a physician's stadiometer and balance scale, respectively. Following the anthropometric measurements, the participants remained seated for a minimum of five minutes before an upper left arm BP measurement was recorded using an automatic patient vital signs monitor (Carescape™ v100, General Electric Healthcare). If either their SBP or DBP were above the cut-offs (see Section 3.3), they were asked to lie on their back for 5 minutes in a dark, temperature-controlled room before a second seated resting BP measurement was recorded. If the participants' BP was still greater than the cut-offs, the participant was deemed ineligible to participate in the rest of the study. Resting BP measurements were recorded a minimum of three times to ensure a reliable reading.

Participants completed a handgrip strength test using a hand grip dynamometer (GRIP-D, Takei Scientific Instruments, Japan). The test was repeated 3 times for each hand. The highest value from the dynamometer was recorded for each hand. There was a 1- minute rest period between each trial. Handgrip testing only occurred on the first testing session.

The participants were fitted with three electrocardiogram (ECG) electrodes (3M, Canada), where the negative lead was located on the right clavicle, the positive lead was on the left ribs, and the ground electrode was on the right ribcage. Participants were seated at a height adjustable chair in front of an electromagnetically-braked arm crank ergometer (Angio, Lode BV, Groningen, the Netherlands). The chair height was adjusted to have the participant's glenohumeral joint level with the crank axel, their knees at an angle of 90°, and their feet flat on the floor. The participants were fitted with a wrist and hand brace on their right forearm and hand. This brace was made up of two 0.4 cm thick pieces of perforated thermoplastic; with one piece going from the mid-forearm to the metacarpophalangeal joint on the anterior aspect of the forearm. The second piece of thermoplastic was placed on the posterior aspect of the hand with a protrusion in line with the index finger. Both pieces were secured with medical tape. A schematic of both pieces of the arm brace can be seen in Figure 13. Once secured, a finger cuff was placed on the right index finger for continuous, non-invasive blood pressure measurements (Portapres®, Finapres Medical Systems, Amsterdam, the Netherlands). A piece of Velcro was then looped around the end of the index finger and attached to the end of the protrusion on the second piece of thermoplastic. This along with the other pieces of thermoplastic allowed for the participants to keep their index finger in extension throughout the entire exercise protocol and also to protect the rest of the tubes attached to the Portapres® device by reducing bending or pinching during exercise.

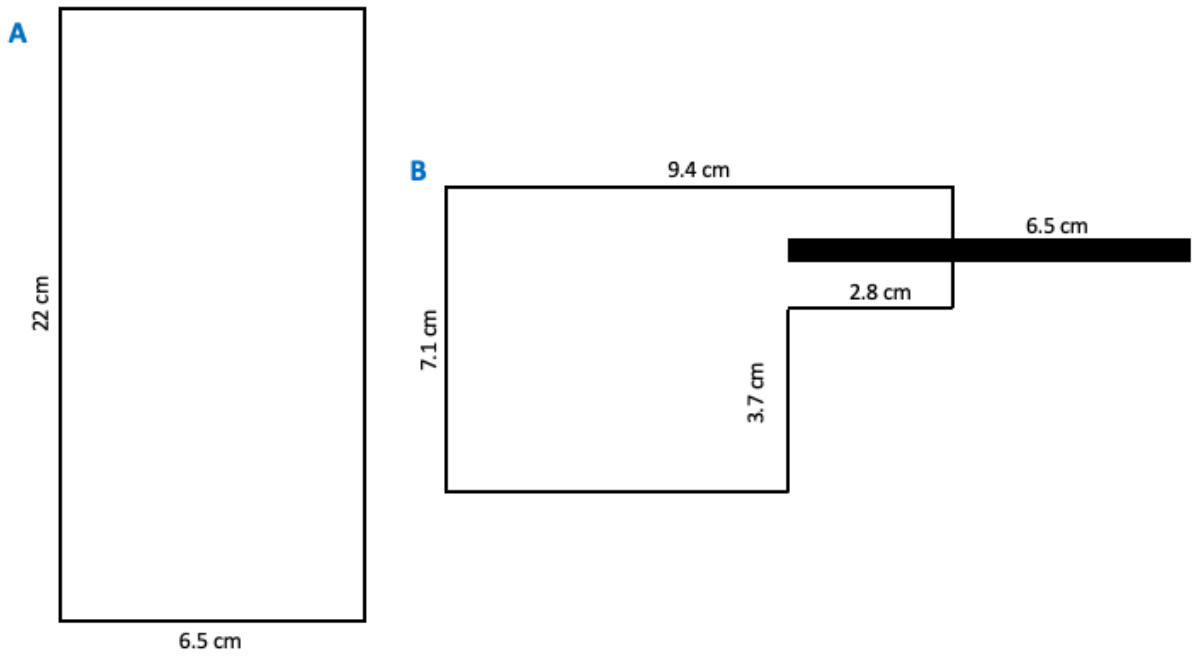

Figure 13. Schematic of arm brace for the right forearm and hand. A. Is the anterior forearm component that is molded with hot water to the participants forearm. B. Is the posterior hand component. The 6.5 cm protrusion is in-line and secured to the index finger with velcro.

The participants were fitted with a facemask that was used to measure oxygen consumption via a commercial mixing chamber-based system (TrueOne 2400®, Parvomedics Inc., Sandy, UT). Three-dimensional reflective kinematic markers (Optitrack, Natural Point, USA) were placed on the right side of the body at the acromion process, lateral epicondyle, styloid process of the ulna, the finger-tip with the Portapres ® blood pressure cuff, greater trochanter and heart height, which was identified as being at the mid-sternum .

When the participants preparation was finished, they remained seated for a 5-minute rest period. The rest period was followed by an incremental arm ergometer exercise protocol that lasted ~25 minutes. For each testing session, the same protocol was performed but at a different cadence of either 45 rpm or 90 rpm. The order of presentation of cadence for each testing session was randomized (random number generator). The external load on the ergometer increased by either 10 or 20 watts every three minutes. The incremental increases were determined for each participant based on the results from their grip strength test. If the average hand grip was above 32 kg, the external load was increased by 20 watts every three minutes. If the average was below 32 kg, the external load was increased by 10 watts. The need for a different workload-increase

protocol based on upper body strength stemmed from pilot testing for the study. Previously, research on exercise protocols for ACE suggested 10-watt increments every 2 minutes[49]. While pilot testing the protocol for this study, participants performed ACE with 10-watt increments every three minutes. The duration of the test was determined to be too long for certain participants and a novel methodology to determine the workload-increase increments for the test was determined using measurements of upper body strength (i.e. hand grip). A cut-off was set to 32 kg by looking at the most recent Statistics Canada hand grip scores [48] and arbitrarily setting a cut-off value that included 66% of the population to use a protocol with 20-watt increments.

The incremental arm ergometer exercise protocol continued until: a. the participant stopped the test, b. they were unable to maintain the target cadence (i.e.,± 5 rpm target) for at least 15 seconds, or c. they reached a score of ≥ 17 on the Borg Scale of perceived exertion [51].If participants reached a Borg rating of 17 but were still able to continue the exercise protocol they were permitted to do so until they were unable to keep up with the cadence. The participants then performed a cool down period of 5 minutes with little to no external load on the ergometer. Once they stopped exercising, three measurements of brachial blood pressure and heart rate were recorded using an automatic patient vital signs monitor (Carescape™ v100, General Electric Healthcare). Participants could leave the lab once their heart rate returned to pre-exercise levels. On the second day of testing, the participants performed the same exercise protocol with the same incremental increases but at a different cadence.

3.6 Data Collection

The experimental set-up used in this study is presented in Figure 14.

3.6.1 Finger Arterial Blood Pressure

Finger blood pressure (FBP) was collected using a Portapres®, a continuous non-invasive beat-to-beat measurement system using the volume-clamp method[52]. The volume clamp method uses infrared red light to identify the amount of blood flow within the digital artery of the index finger.The Portapres® analog output refreshes at a frequency of 200 Hz but data were sampled at 2000 Hz and recorded using a custom acquisition software (LabVIEW 2012, National Instruments, USA) during the last 45 seconds of each stage of the exercise protocol.

3.6.2 Heart Rate

A three-lead electrocardiogram (ECG) was used to calculate heart rate during each exercise stage. Electrodes were placed in a three-lead orientation on the participants' chest; where the negative lead was located on the right clavicle, the positive lead was on the left ribs, and the ground electrode was on the right ribcage. The data were sampled at 2000 Hz and collected using the same custom acquisition software as for FBP, during the last 45 seconds of each stage of the exercise protocol.

3.6.3 Oxygen Consumption

Participants had their oxygen consumption measured and averaged every 15 seconds via indirect calorimetry using a commercial mixing chamber-based system (TrueOne 2400®, Parvomedics Inc., Sandy, UT).

3.6.4 Upper-Limb Kinematics

Three-dimensional kinematics of the upper right limb and trunk were recorded using 10 Optitrack Prime 13 motion capture cameras (Natural Point, USA). The raw data were collected using Motive Computer software (Motive, 2.1.1, Optitrack Body, Natural Point, USA). The kinematic data were collected during the last 45 seconds of each stage at a frequency of 200 Hz.

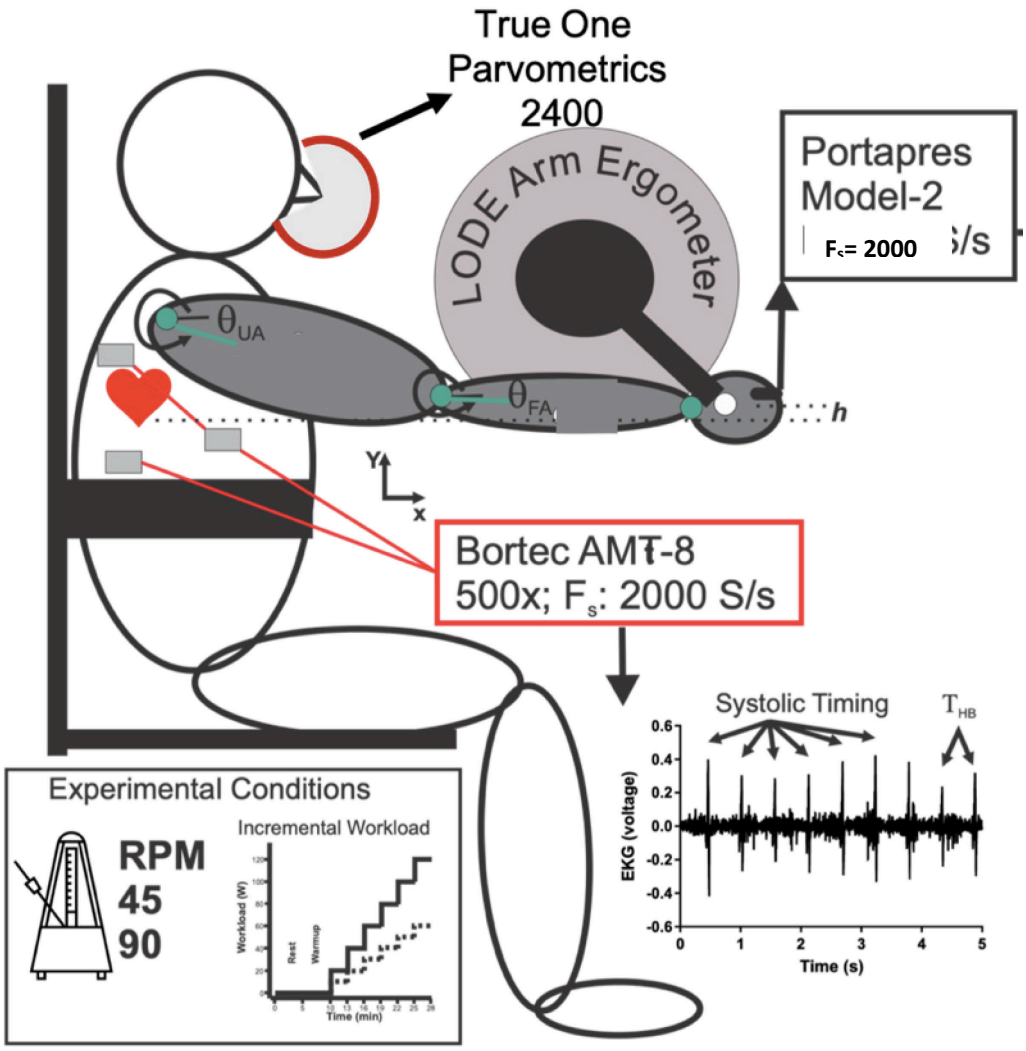

Figure 14. Schematic of experimental set up. F_s: sampling frequency, T_{HB}: timing of each heartbeat, EKG: electrocardiogram, S/s: samples per second, θ_{UA}: absolute angle of the upper limb, θ_{FA}: absolute angle of the forearm, h: finger height

CHAPTER 4: SPECIFIC AIM I METHODS AND ANALYSIS

4.1 Data Analysis

Four outcome measures were used to determine if the cardiovascular responses were different at 90 rpm compared to 45 rpm; mean arterial pressure (MAP), relative oxygen consumption, heart rate and gross efficiency.

Mean arterial pressure (MAP) was calculated for each external load. To calculate MAP, the raw analog FBP from the Portapres® was collected using a custom acquisition software (LabVIEW 2012, National Instruments, USA), converted from volts to mm Hg (1V=100 mmHg), and the FBP signal was averaged for the duration of the data acquisition. This method is different from the traditional calculation of MAP (Equation 5) because during movement the distinction between systolic and diastolic blood pressure becomes less clear and the overall average is easier to define.

Equation 5. $$Mean\ Arterial\ Pressure = \frac{\boldsymbol{SBP+2(DBP)}}{\mathbf{3}}$$

MAP for each external load calculated was then adjusted for the small (i.e. <5 cm) day to day differences in chair height during data collection. On each day of testing the participant was placed in a similar chair position. The chair height was not standardized but an orthostatic difference correction was applied to the recorded data. As previously mentioned in Chapter 2, the position at which blood pressure is measured relative to the heart will influence the measurement. To account for this height difference, the average difference between the finger (point of BP measurement) and the position of the heart was calculated for each testing session when the participant was resting with their hand on the arm crank table. The difference (in meters) was entered into the orthostatic pressure equation (Equation 3) to calculate the mean orthostatic pressure difference (in mmHg) due to chair height from one day of testing to another. This difference was then added to the lower value of the recorded MAP resting measurements and all subsequent pressures calculated for that entire testing session.

Heart rate was calculated using the raw ECG signal. The raw data was imported and low-pass filtered at 120 Hz using a 4th order Butterworth filter. The filtering was done to help distinguish between a heartbeat and muscle activation. The filtered data were then graphed, and a minimum

peak height was identified. Along with the minimum peak height, the minimum time between two heart beats was also identified. For all participants, this value was set at 0.3 seconds (600 samples). This minimal delay between two heart beats represents a maximum heart rate of 200 beats per minute. The find peaks Matlab function was then used to identify the peaks in the absolute filtered ECG data that met both the minimum peak height and minimum peak distance conditions. Once all the peaks were determined, the average amount of time between each peak was calculated and any outliers identified and removed. The average period of each heartbeat was used to calculate the participants' heart rate for that stage of the exercise protocol using Equation 6.

Equation 6. $$Heart\ Rate = \frac{\frac{1}{Average\ Period}}{Sampling\ Frequency} * 60\ seconds$$

Oxygen consumption was calculated for each stage of the exercise protocol by taking the average relative VO_2 for the final minute of each stage. The relative VO_2 for each stage was then normalized to the participants resting VO_2, calculating the metabolic equivalent of each exercise stage (METS), as seen in Equation 7.

Equation 7. $$METS = \frac{Stage\ VO_2}{Rest\ VO_2}$$

Along with the METS, the gross efficiency was calculated at each stage of the exercise protocol. To calculate gross efficiency, the absolute VO_2 for each stage was used to calculate the energy expenditure experienced during each stage in watts (Derivation for Equation 8). The energy expenditure along with the stage external load was used to calculate gross efficiency, as seen in Equation 8.

Derivation for Equation 8.

$$Energy\ Expenditure\ (watts) = Absolute\ VO_2\ \frac{L}{min} * \left(\frac{5\ \frac{kcal}{L} * 4184 \frac{J}{kcal}}{60\ seconds} \right)$$

$$Energy\ Expenditure\ (watts) = Absolute\ VO_2 * 348.6$$

Equation 8.

$$Gross\ Efficiency\ (\%) = \frac{External\ Workload\ (watts)}{Energy\ Expenditure\ (watts)} * 100$$

4.2 Statistical Analysis

Statistical tests used within this thesis included two-way repeated measures ANOVAs and paired t-tests.

Before calculating the two-way repeated measures ANOVA, the following assumptions needed to be met for each data set:

a. The dependent variable needed to be continuous. All variables collected as part of this thesis were continuous in nature.
b. The data were normally distributed. Normality was identified by creating histograms, probability- probability plots (P-P plots) of all data sets used in the test. Skewness and kurtosis were also testing for using a z-table (significance set at $p<0.05$). Due to a smaller sample size used in this thesis, a Shapiro-Wilk test was also used to identify normality with each data set being identified being normally distributed with a $p>0.05$. If any data set was found to be not normally distributed all data sets within that test were transformed via the log function only for the purpose of the statistical analysis.
c. There were no outliers in either data set. Outliers were identified by creating stem and leaf plots of each data set, any value that was outside of the range of the plot was considered an outlier.
d. The within subject factors should be two categorical or matched groups
e. The variance of all difference scores among the test variables must be equal in the population (assumption of sphericity). The assumption of sphericity was testing using the Mauchly's test, with sphericity assumption being met with $p<0.05$ [53].If the assumption of sphericity was not met a Greenhouse-Geisser correction to the degrees of freedom was applied.

In the event of a statistically significant result from the ANOVA, a Tukey *post hoc* analysis was performed to establish the levels of the within subject factors that were statistically different.

Before calculating the paired t-test the following assumptions needed to be met for all sets of data;

a. The dependent variables needed to be continuous. All variables collected as part of this thesis are continuous in nature.
b. The data sets were normally distributed. Normality was identified by creating histograms, P-P plots of all data sets used in the test. Skewness and kurtosis were also testing for

using a z-table. Due to a smaller sample size used in this thesis, a Shapiro-Wilk test was also used to identify normality with each data set being identified as normally distributed with $p > 0.05$.

c. There were no outliers in either data set. Outliers were identified by creating stem and leaf plots of each data set, any value that was outside of the range of the plot was considered an outlier.
d. The two group factors should be matched.
e. The subjects were independent of one another [53].

Statistical significance was set at $p<0.05$. All statistical analyses were performed in GraphPad Software (Prims 8, La Jolla, CA).

4.2.1 Analysis of VO_2, HR, Efficiency and MAP as a Function of External Work

The effect cadence has on each of the outcome variables as a function of external work (VO_2, HR, Efficiency, MAP) was analyzed using two-way repeated measures ANOVAs (cadence × stages). Only stages that had data for both cadences and for all participants were included in the analysis. Data within each stage were collected at the same time point within the exercise protocol.

4.2.2 Analysis of the MAP as a Function of Internal Work

The relationship between MAP and METS was analyzed to answer the question whether there was a significant increase in MAP with the increase in cadence.

4.2.2.1 Comparison of the Linear Regressions between MAP and METS

For each participant, a simple linear regression was calculated between the MAP values (dependent variable) as a function of METS (independent variable). The regressions' slope and y-intercepts were extracted. The presence of an offset between the two cadences was tested by calculating a paired t-test between matched y-intercepts. The presence of a difference in the MAP response with an increase in METS was tested by calculating a paired t-test between the matched slopes of the linear regressions.

4.2.2.2 Bland-Altman Analysis of Differences

To investigate if the effect of the ACE cadence on MAP was related to the magnitude of the MAP value, a Bland-Altman (BA) method of differences was applied to difference in MAP between the two cadences for internal workloads between 1 and 7 METS. Because the experimental protocol controlled for the external workload and that internal workload was calculated post-evaluation, a linear regression was done on the MAP vs. METS data to interpolate MAP for each MET ranging between 1 and 7. This range represents the largest range of METS achieved during the ACE by at least one participant (see Figure 20; Section 4.4). The calculated MAP at each whole MET was used in the BA analysis. The differences in the measurements were analyzed to identify if there was any proportional or fixed bias in each participants data set. A Bland-Altman plot was created for each participant with the differences in the measurements on the Y-axis, while the average of the measurements at each MET for both cadences was plotted on the X-axis. Proportional bias was established by extracting the slope of the linear regression of the relationship between the difference and average measurements. A one-sample t-test was used to establish if the slope of the regression was different from "0". Fixed bias was assessed by using a one sample t-test to establish if the mean of the difference was different from "0".

4.2.2.3 Analysis of MAP at Different METS

Based on the results of the Bland-Altman analysis of difference, a subsequent two-way repeated measures ANOVA (cadence x METS) was conducted on the MAP response at each cadence for the internal work ranging from 3 to 5 METS. This range of METS encompassed the levels in which all participants were able to perform the ACE for both cadences. The MAP for each MET was extracted from the linear regression calculated in Section 4.2.2.2 (Bland-Altman Analysis of Differences).

4.2.3 The Effect of ACE Cadence on the MAP at One Moderate Level of Intensity

To get a better understanding of the difference between the recorded MAP at 45 versus 90 rpm, the difference between the two measurements were compared at one internal work value. The level of internal work , 4 METS was chosen to represent an exercise being performed at a moderate-intensity [54]. Furthermore, it also represented the median intensity reached by all participants during data collection. The MAP at 4 METS was extracted from the linear

regression calculated in Section 4.2.2.2 (Bland-Altman Analysis of Difference). The effect of ACE cadence was tested by calculating a paired t-test between the matched extracted MAP values.

4.3 Participant Characteristics

Sixteen participants were recruited for this study. As seen in Figure 15, five participants were eliminated from the study due to the inability for the Portapres® to continuously record finger arterial blood pressure during exercise. Four participants completed one or both testing sessions but did not have the necessary measurements collected during the sessions. Seven participants had full data collections and were used for the analysis of both specific aims of this study. The description of the seven participants can be seen in Table 1.

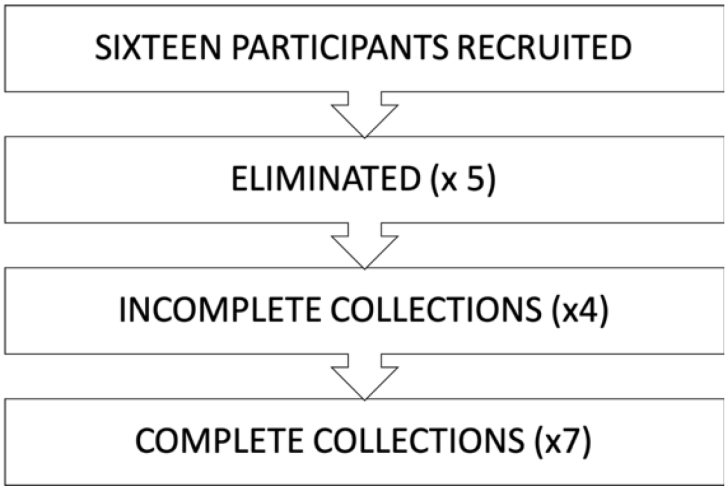

Figure 15. Schematic of total participants recruited for this study. Five participants were eliminated due to the Portapres ® unable to get a continuous reading during exercise. Four participants completed two collections sessions without VO_2 being measured and seven participants had full data collections

Table 1. Participant characteristics (n=7)

Variable	***Means ± SD***
Age (years)	27 ± 3
Height (m)	1.70 ± 0.7
Mass (kg)	79.4 ± 15.2
Sex	♀=4, ♂= 3
Resting HR (bpm)	73 ± 10
Resting SBP (mm Hg)	111 ± 11
Resting DBP (mm Hg)	69 ± 8

m, meters; kg, kilograms; mean ±standard deviation; bpm: beats per minute; SBP: systolic blood pressure, DBP: diastolic blood pressure

4.4 Results

Each testing session consisted of an average of 7 FBP measurements, one during the resting phase, one during the warm-up stage and 5 measurements occurring during the exercise protocol. Four participants performed the exercise protocol with increments of 10 watts of external load at each stage, while the other three participants performed with increments of 20 watts. Two participants ended the exercise test at one stage earlier while exercising at 90 rpm compared to 45 rpm, while another participant ended the test two stages earlier when exercising at 90 rpm. All other participants (n=4) completed the same number of stages during both exercise sessions. One FBP measurement was excluded from the analysis as the Portapres ® stopped working halfway through the 45 second collection period (Subject 007). The number of FBP measurements for each participant at 45 and 90 rpm along with the maximum external workload can be seen in Table 2 below. The range of METS each participant performed at during ACE at both cadences can be seen in Figure 16.

Table 2. The number of workload increments, FBP measurements and maximum workload achieved for each of the seven participants collected as part of this study.

Subject	Workload Increases (W)	45 RPM		90 RPM	
		# of FBP measurements	Max Workload (W)	# of FBP measurements	Max Workload (W)
003	20	7	100	7	100
007	10	7	50	4	30
008	20	8	120	8	120
010	10	8	60	7	50
013	10	6	40	6	40
014	10	7	50	6	40
015	20	6	50	6	50

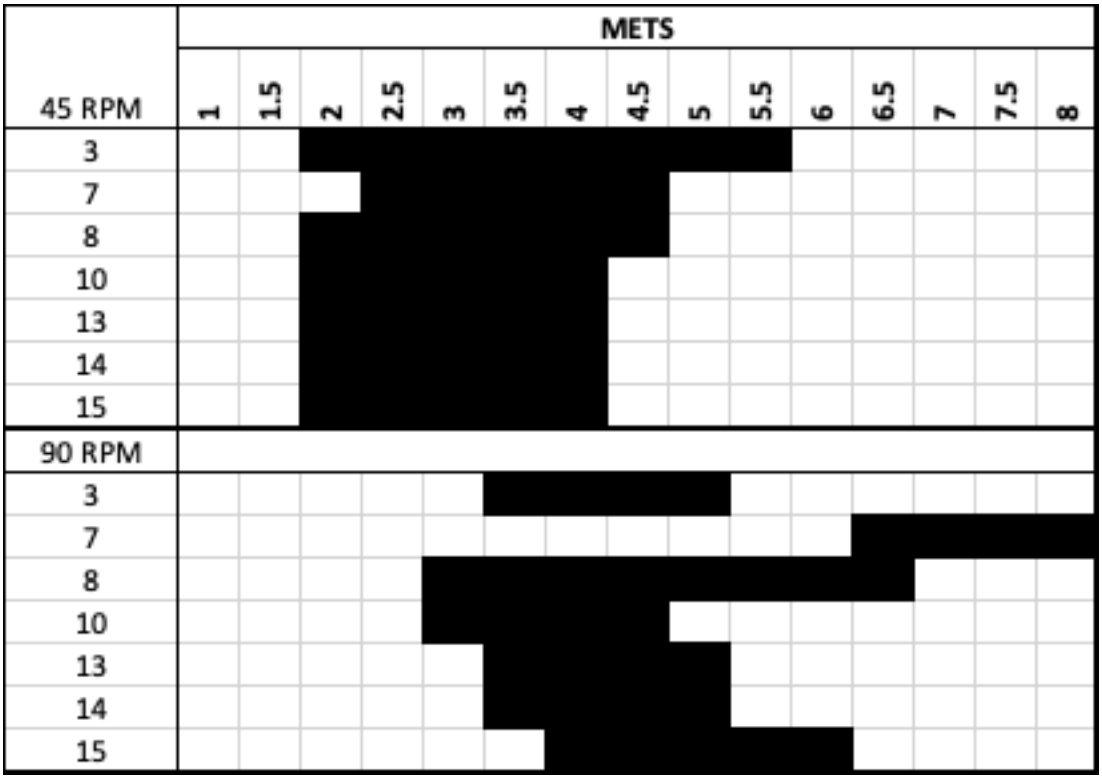

Figure 16. Range of METS performed by all participants during arm crank exercise at 45 and 90 rpm. For all participant during performed exercise between the range of 3- 5 METS during 45 rpm, while 6 out of 7 participants performed exercise in the range of 3 through 5 at 90 rpm.

4.4.1 VO_2, HR, Efficiency and MAP as a Function of External Work

The relative VO_2, heart rate, MAP and gross efficiency for each stage of exercise achieved during ACE at both cadences were graphed as a function of external workload. An example of one

participant, along with the change in gross efficiency with an increase in cadence for all participants, can be seen in Figure 17. All participants' data can be found in APPENDIX A.

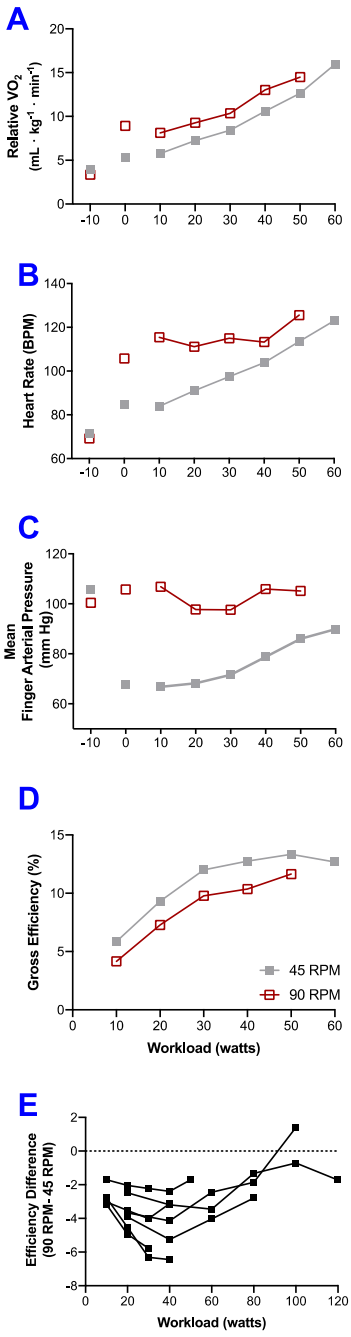

Figure 17. An example of the four-outcome measures from ACE at both cadences. A. Relative oxygen consumption, B. heart rate, C. MAP, and D. gross efficiency are shown as a function of external workload. The unlinked squares represent the measurements at rest (negative x value) and warm-up (at 0). E. shows the change in gross efficiency with an increase in cadence for all seven participants.

4.4.1.1 VO_2 and HR as a Function of External Work

The values included in the repeated measures ANOVAs performed on relative VO_2 and HR as a function of external workload included data from the warm-up stage and the first three stages of the exercise protocol.

For the effect of cadence on relative VO_2 as a function of external workload, all data sets were found to be normally distributed ($p>0.05$) and without any outliers. Mauchly's test indicated that the assumption of sphericity was met for the interaction between cadence and stage ($\chi^2(5)= 0.221$ $p=0.220$) and for the main effect of stage ($\chi^2(5)= 0.218$, $p=0.215$).

There was no significant interaction between cadence and stage of exercise being performed on the recorded relative VO_2, ($F(3,18)=0.222$, $p=0.880$, power= 0.084). There was a significant main effect of cadence on the relative VO_2 response ($F(1,6)= 30.855$, $p=0.001$) with the VO_2 response at 90 rpm (13.2± 9.79 mL/kg/min) being significantly higher than 45 rpm (8.16± 0.428 mL/kg/min, $p<0.001$, Table 3). There was also a significant main effect of stage of exercise on the relative VO_2 response ($F(3, 18)= 65.2$ $p<0.000$, Table 3). Comparisons showed no significant increase in relative VO_2 from the warm-up to stage one ($p=0.145$), but there was a significant increase in all following stages ($p<0.05$).

When comparing the changes of heart rate as a function of external workload, all data sets were found to be normally distributed ($p>0.05$) and without outliers. Mauchly's test indicated that the assumption of sphericity was met for the interaction between cadence and stage, ($\chi^2(5)= 0.105$, $p=0.064$). The assumption was violated for the main effect of stage on the recorded HR ($\chi^2(5)= 0.67$, $p=0.029$), therefore a Greenhouse-Geisser degrees of freedom correction was applied ($\varepsilon= 0.416$).

There was no significant interaction between cadence and stage of exercise being performed on the recorded HR ($F(3,18)=3.042$, $p=0.056$, power= 0.613). There was a significant main effect of cadence ($F(1,6)=12.161$, $p=0.013$, $r= 0.8183$) with arm cranking at a cadence of 90 rpm (109 ± 3.5 bpm) associated with a higher HR compared to arm cranking at a cadence of 45 rpm (92 ± 3.1 bpm, $p=0.013$, Table 3). There was also a significant main effect of stage of exercise on the HR response ($F(1,249, 7.492)=37.141$, $p<0.000$). Pairwise comparisons showed an increase in the recorded heart rate with an increase in exercise stage ($p<0.05$, Table 3).

4.4.1.2 Efficiency and MAP as a Function of External Work

The values included in the repeated measures ANOVAs of gross efficiency and MAP as a function of external workload consisted of data from the first three stages of the ACE protocol. No external work was done meaning that gross efficiency was equal to zero during the warm-up phase and MAP data were missing for one participant during the warm-up stage.

For the effect of cadence on gross efficiency as a function of external workload, all data sets were found to be normally distributed ($p>0.05$) and without outliers. Mauchly's test indicated that the assumption of sphericity was violated for the interaction between cadence and stage, ($\chi^2(2)= 0.284$, $p=0.043$), therefore a Greenhouse-Geisser correction of the degrees of freedom was applied ($\varepsilon= 0.583$). The assumption of sphericity was met for the main effect of stage ($\chi^2(2)= 0.809$, $p=0.588$).

There was not a significant interaction between cadence and stage on the calculated gross efficiency during ACE ($F(1.15,6.99)=3.48$, $p=0.102$, power= 0.383). There was a significant main effect of cadence on gross efficiency ($F(1,6)= 101.414$, $p<0.000$) , with gross efficiency at 90 rpm being lower than 45 rpm (mean 45 rpm: 10.821 % 90 rpm: 7.170 %, $p <0.0001$). There was also a significant main effect of stage of exercise on the calculated efficiency ($F(2,12)=278.0$, $p<0.000$). Pairwise comparisons showed an increase in the calculated efficiency with an increase in stage ($p<0.0001$, Table 3).

When comparing the effect of cadence and stage of exercise on the MAP response to ACE, all data sets were found to be normally distributed ($p>0.05$) and without outliers. Mauchly's test indicated that the assumption of sphericity was met for the interaction between cadence and stage ($\chi^2(2)= 0.63$, $p=0.314$), and for the main effect of stage ($\chi^2(2)= 0.770$, $p=0.520$).

The results of the repeated measures ANOVA showed that there was no significant interaction between cadence and stage ($F(2,12)= -0.29$, $p=0.75$, power= 0.087). There was a significant main effect of cadence ($F(1,6)= 31.9$, $p=0.001$), with a cadence of 90 rpm eliciting a higher MAP response (45 rpm: 76 mm Hg, 90 rpm: 97 mm Hg, $p=0.001$, Table 3). There was no significant main effect of stage on the MAP response ($F(2,12)= 0.36$, $p=0.70$, power= 0.096).

Table 3. Table of the means and standard error for the four outcomes measures grouped by cadence and stage of exercise

		Relative VO_2 (mL/kg/min)	Heart Rate (bpm)	MAP (mm Hg)	Gross Efficiency (%)
Cadence	**45 RPM**	8.16 ± 0.43	93 ± 3	76 ± 3.	10.8 ± 0.69
	90 RPM	13.2 ± 0.98*	109 ± 4*	98 ± 5*	7.17 ±0.71*
Stage	**Stage One (Warm Up)**	8.2 ± 0.45	89 ± 3	N/A	N/A
	Stage Two	9.28± 0.57	95 ± 2**	86 ± 4	5.97± 0.54
	Stage Three	11.3 ± 0.70**	106 ± 3**	87 ± 3	9.50 ±0.73**
	Stage Four	13.8 ± 0.85**	114 ± 4**	87± 3	11.5 ± 0.79 **

*denotes 90 rpm was significantly different than the 45 rpm, ** denotes stage was significantly different form stage before, $p<0.05$, means ± standard error

4.4.2 Relationship Between VO_2 and HR as a Function of External Workload

Due to the gross efficiency being different between the two cadences, it was necessary to control for the internal workload when making MAP comparisons. There were two outcome measures in the study that could have been used as a measure of internal work, heart rate and METS. Before one was chosen, an analysis between the two variables were performed. An example of one participants' METS versus MAP can been see in Figure 18A. Individual participant data can be found in APPENDIX B .

Each participants' METS and HR data for each stage were normalized to the resting values, by subtracting each stages' value from the resting value. The normalized data were then placed in two simple linear regressions, one for each cadence (Figure 18B). Data sets used in the regressions were found to violate the assumption of normality ($p=0.0068$), which led to all data sets being transformed with the log function.

At 45 rpm, the linear regression showed a significant positive relationship between HR and METS ($b= 0.8422$, 95% CI [0.6667, 1.018],$t(40)=9.7$, $p<0.0001$, $R^2=0.701$, Figure 18B). At 90 rpm, there was also a significant positive relationship was between the two variables ($b=0.8216$, 95% CI [0.61, 1.03], $t(36)=7.87$, $p<0.000$, $R^2 = 0.632$, Figure 18B). An analysis of the two slopes showed no significant difference ($F(1,76)=0.01751$, $p=0.8951$). The results of this analysis allowed for only one of HR or METS to be used as a measurement of internal work.

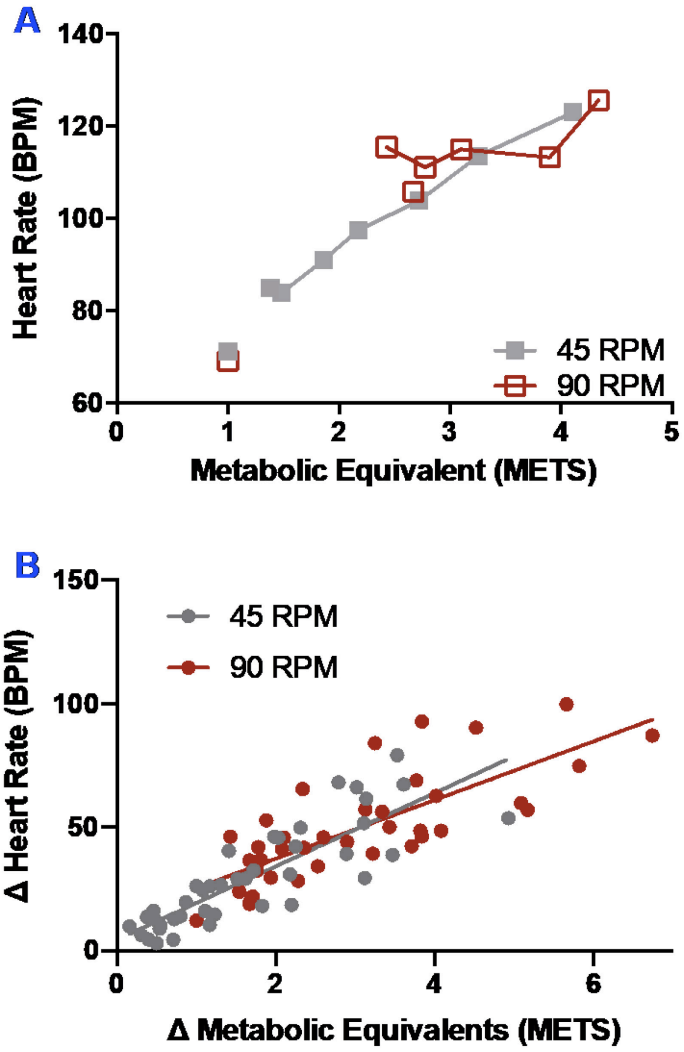

Figure 18. The relationship between METS and HR. A. An example of the relationship between the two variables at both cadences. B. The relationship, for all participants, between the change in METS and the change in HR. The relationship was shown to be positively correlated (45 rpm: r^2= 0.70; 90 rpm: r^2= 0.63). BPM: beats per minute, Δ: change in heart rate/ METS from resting levels.

4.4.3 Comparison of the Linear Regressions Between MAP and METS

Using METS as the measurement of internal work, the relationship between MAP and METS were analyzed for both cadences. An example of the relationship between MAP and METS can be found in Figure 19. All other participants' data can be found in APPENDIX C. For all participants there was an upward shift in both MAP and METS with an increase in cadence. A simple linear regression was used to extrapolate the slope and y-intercept for each cadence. The

slopes, y-intercepts and 95 % confidence intervals (CI) for each participant can be found in Table 4.

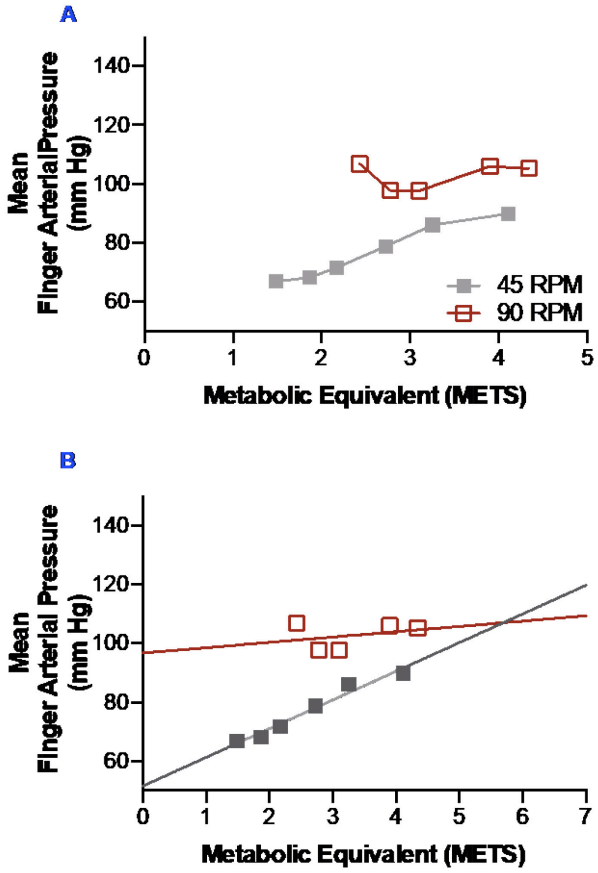

Figure 19. An example of the MAP vs METS relationship. A. The MAP as a function of METS response for one participant (Subject 010). B. The linear regression curve used to extract the slope and y-intercept There is an upward shift in both METS and MAP at 90 rpm compared to 45 rpm.

Table 4. Participant specific slopes and y-intercepts with their 95 % confidence intervals for relationship between METS and MAP.

Subject	***Slope [95 % CI]***		**Difference (90- 45)**	***Y- Intercept [95 % CI]***		**Difference (90- 45)**	***R^2***	
	45 RPM	**90 RPM**		**45 RPM**	**90 RPM**		**45 RPM**	**90 RPM**
003	**6.07** [0.11, 12.0]	**4.32** [-4.29, 12.9]	-1.75	**49.3** [26.4, 72.1]	**65.8** [32.7, 98.9]	16.5	0.78	0.46
007	**3.94** [0.12, -7.76]	**2.32** [-38.2, 42.8]	-1.58	**72.6** [59.3, 85.8]	**106.2** [-174.7, 387.2]	33.7	0.78	0.35
008	**-0.175** [-5.82, 5.47]	**-0.76** [-4.29 ,2.75]	-0.59	**87.1** [69.3, 104.8]	**102.8** [86.0, 119.5]	15.8	0.002	0.083
010	**9.726** [7.237, 12.21]	**1.80** [-8.28, 11.9]	-7.92	**51.6** [44.8, 58.4]	**96.7** [62.6, 130.8]	45.1	0.97	0.097
013	**-4.06** [-22.2, 14.0]	**-1.53** [-8.27, 5.20]	2.53	**87.7** [36.8, 138.5]	**99.7** [73.4, 126.0]	12.0	0.32	0.32
014	**3.52** [-1.59, 8.62]	**1.02** [-5.57, 7.62]	-2.50	**69.8** [55.4, 84.2]	**85.9** [59.6, 112.4]	16.2	0.62	0.18
015	**5.30** [2.74, 7.85]	**-5.89** [-20.3, 8.50]	-11.2	**65.3** [58.3, 72.3]	**121.1** [53.2, 189.0]	55.7	0.98	0.61
Average [95 % CI]	**3.47** [-0.65, 7.6]	**-0.17** [-3.55, 3.19]	**-3.29** [-7.5, 0.25]	**69.0** [54.9, 83.1]	**96.9** [80.9, 112.9]	**27.9** [11.9, 43.8]	**-**	**-**

All data sets used in the paired t-test were normally distributed ($p>0.05$) and without any outliers. The results showed that the slope at 90 rpm (-0.17 ± 3.65 mm Hg/MET) was not significantly different than the slope at 45 rpm (3±4 mm Hg/ MET, $t(6)=2.290, p=0.116$, d= -0.865 power= 0.8488). As found in Figure 20B, the slope decreased from 45 rpm to 90 rpm for two participants, increased for one participant and stayed the same for the other four participants. For the y-intercept, at 90 rpm the intercept was 96 ± 17 mm Hg, and 68 ± 15 mm Hg at 45 rpm. This difference of 28 ± 17 mm Hg was significant ($t(6)=4.294$, $p=0.0051$, ,d= 1.622, Figure 20).

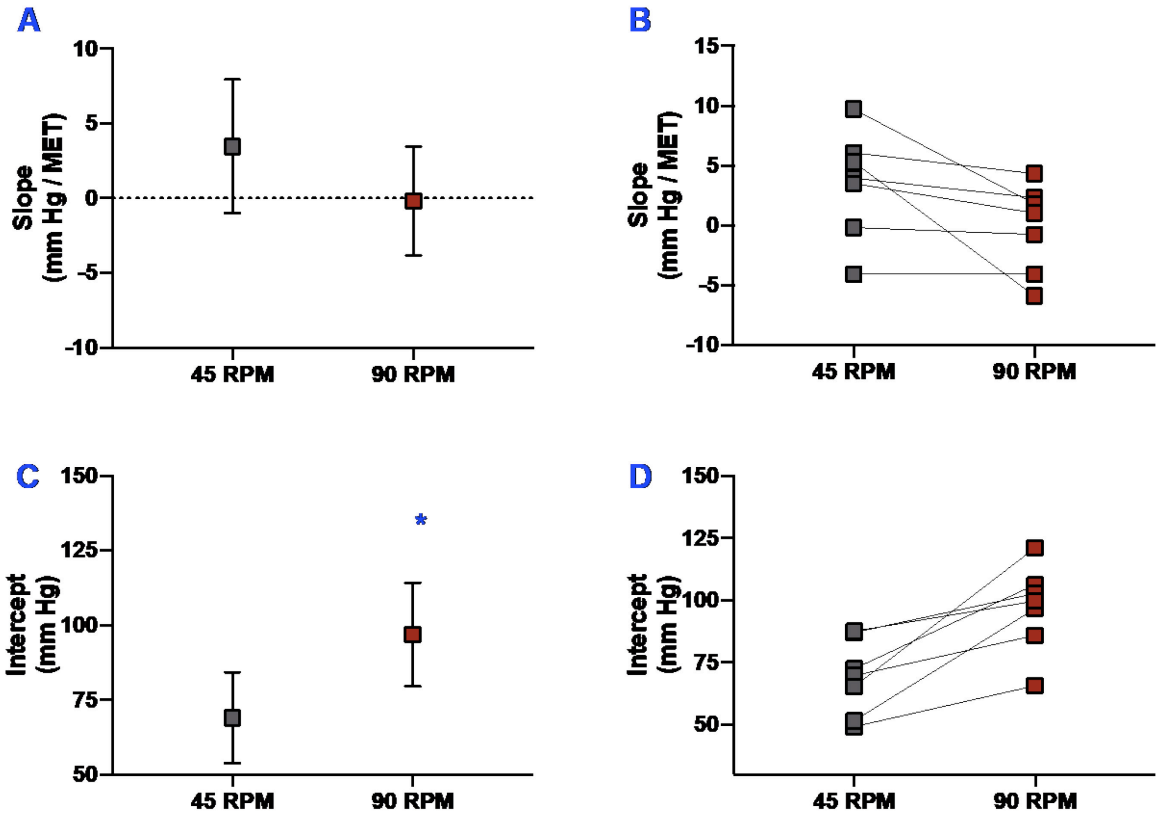

Figure 20. The slope and y-intercepts from the linear regression during both ACE cadences. A. The results from the paired t-test showed no significant difference in the slope at 45 rpm and 90 rpm ($p=0.116$). B. The slope decreased from 45 to 90 rpm for two participants, increased for one participant and stayed the same for the other four participants. C. For the y-intercept the paired t-test showed a significant increase from 45 rpm to 90 rpm with D. all seven participants showed an increase from 45 rpm to 90 rpm (* denotes $p=0.005$).

4.4.4 The Effect of Cadence on the MAP Response in Relation to the Magnitude of the MAP Values

The results of the BA analysis of differences showed proportional bias for all participants and fixed bias for five out of seven participants. The overall Bland-Altman plot for all participants' data can be found in Figure 21. From the pooled data, the BA analysis found a fixed bias of 15.7 ± 14.4 mm Hg ($p<0.0001$) between the MAP measurements at 90 rpm compared to 45 rpm with no proportional bias (slope= 0.014 ± 0.192, $p=0.9422$). Each participants' Bland-Altman plot can be found in APPENDIX D, and the results from the Bland-Altman analysis can be found in Table 5.

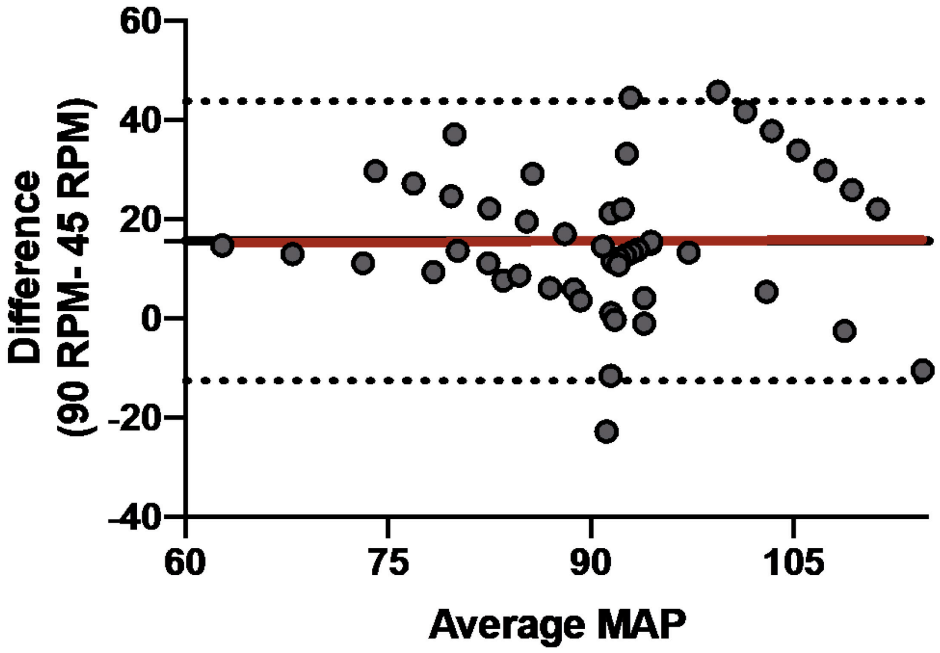

Figure 21. Bland- Altman analysis of differences of the measurements of MAP at two cadences while matched for the same internal intensity (METS). Red line: regression line; dashed lines: limits of agreement (i.e. 95% confidence intervals).

Table 5. Results of Bland-Altman analysis of differences in finger arterial blood pressure between the two ACE cadence.

Subject	Slope [95 % CI]	p-value	P Bias	Mean Diff ± S.E.M [95% CI]	p-value	Fixed Bias
003	-0.34 [-0.34, -0.34]	<0.0001	Yes	9.49 ± 1.43 [5.98, 13.0]	0.0006	Yes
007	-2 [-2, -2]	n/a	Yes	33.9±3.22 [26.0, 41.8]	<0.0001	Yes
008	1.34 [1.20, 1,45]	<0.0001	Yes	13.5 ± 0.56 [12.1, 14.8]	<0.0001	Yes
010	-1.37 [-1.37, -1.37]	<0.0001	Yes	13.4 ± 6.47 [-2.45, 29.1]	0.0841	No
013	-0.91 [-0.91, -0.91]	<0.0001	Yes	22.2 ± 2.07 [17.1, 27.3]	<0.0001	Yes
014	-1.07 [-1.11, -1.04]	<0.0001	Yes	6.25 ± 2.01 [1.32, 11.2]	0.021	Yes
015	37.9 [37.8, 38.0]	<0.0001	Yes	11.0± 9.14 [-11.5, 33.3]	0.277	No

Diff: difference between the measurements at 45 and 90 rpm, P Bias: proportional bias proportional bias, if 95% CI for slope does not include 0; fixed bias, if 95% CI for average difference does not include 0.

4.4.5 The Effect of Cadence on the MAP in Relation to the Intensity of the Internal Workload

Since the BA analysis showed proportional bias for all participants, the effect of cadence on the MAP was evaluated at multiple discrete levels of internal work (METS). The values of MAP at 3 through 5 METS were included in a two-way repeated measures ANOVA (cadence × METS). The range of METS values included in the analysis (3 to 5 METS) was chosen in order to include the range of internal work (METS) recorded for all participants at both cadences. As found in Figure 16, participants performed ACE at intensities close to the selected range except for one at 90 rpm.

For the effect of cadence on MAP as a function of internal work (METS), all data sets were found to be normally distributed and without any outliers. Mauchly's test indicated that the assumption of sphericity had been violated for the main effect of METS and the interaction between METS and cadence, ($\chi^2(2)<0.00$, $p<0.0001$), therefore Greenhouse-Geisser degrees of freedom correction was applied ($\varepsilon=0.5$ for both).

There was no significant interaction between cadence and internal work ($F(1,6)=4.336$, $p=0.082$, power=0.417, Table 6) . There was a significant main effect of cadence on the MAP response ($F(1,6)=19.153$, $p=0.005$) with 90 rpm eliciting a higher MAP response (45 rpm: 83 ± 3 mm Hg, 90 rpm: 99 ± 5 mm Hg, $p<0.05$, Table 6). There was no significant main effect of internal work on the MAP response ($F(1,6)=2.006$, $p=0.206$, power=0.224). The results showed that with an increase in cadence there was a significant increase in MAP of approximately 16 mm Hg.

Table 6. Means, standard error and 95 % CI of the MAP as a function of cadence and internal workload

	3 METS	**4 METS**	**5 METS**
	Mean ± S.E.M (mm Hg) [95 % CI]	**Mean ± S.E.M (mm Hg) [95 % CI]**	**Mean ± S.E.M (mm Hg) [95 % CI]**
45 RPM	79 ± 2 [73.6, 85.3]	83 ± 3 [76.6, 85.3]	86 ± 4 [76.7, 96.2]
90 RPM	99 ± 5 [86.2, 111.2]	99 ± 5 [87.1, 110. 1]	98 ± 5 [87.2, 109.7]

4.4.6 Effect of ACE Cadence on the MAP at a Moderate Level of Exercise Intensity

Since the results of the repeated measures ANOVA showed no significant effect of internal work on the MAP response during ACE, MAP was evaluated at one value of internal work. The internal work value of 4 METS was chosen because all participants (except for one at 90 rpm, Figure 16) performed ACE at a comparable intensity. The data sets used in the paired t-test were normally distributed ($p>0.05$) and without outliers. The results showed an increase in MAP at 4 METS when cycling at a cadence of 90 rpm (99 ± 13 mm Hg) compared to 45 rpm (83 ±8 mm Hg, $t(6)=4.365$, $p= 0.0028$, $d=1.65$, Figure 22). The average increase in finger MAP observed between the two cadences was 16 ± 10 mm Hg.

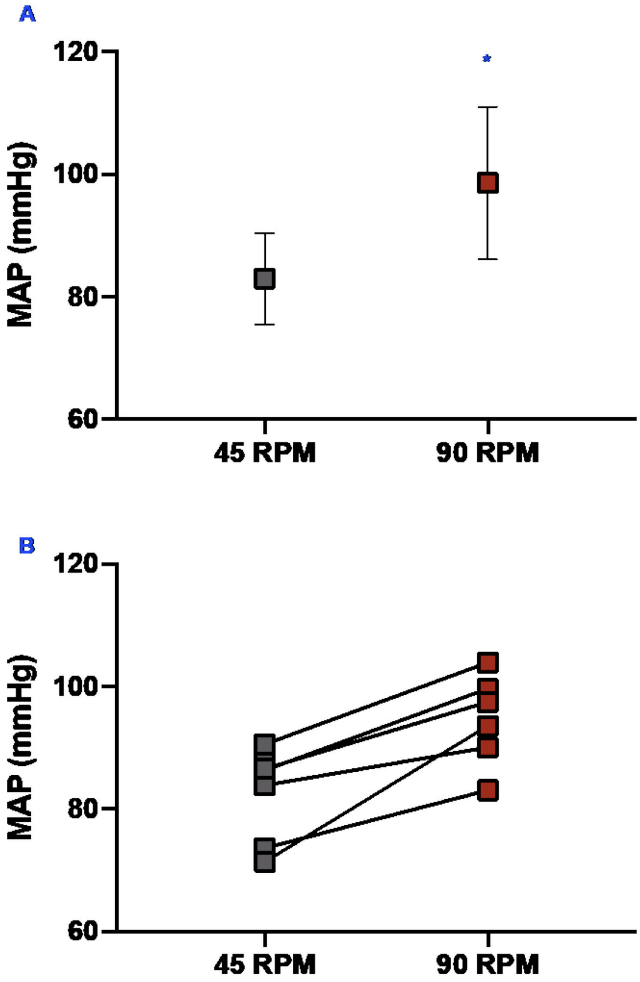

Figure 22. Increase in MAP with an increase in ACE cadence. A. Results of the paired t-test of MAP at 45 and 90 rpm at an exercise intensity of 4 METS. There was a significant increase of ~ 16 mm Hg in the MAP response to exercise at 90 rpm when controlling for the same internal work (* denotes p= 0.0028). B. All participants showed an increase in finger MAP with an increase in cadence.

CHAPTER 5: SPECIFIC AIM II METHODS AND RESULTS

5.1 Establishing the Goodness of Fit of the Different Models

The goodness of fit of each proposed model was established by calculating a percent explained variable. The percent explained variable was calculated by: a. summing the root mean square (RMS) of the recorded FBP signal ($RMS_{RECORDED}$, Components of Equation 9, Where n is equivalent to the number of samples and i is the sample index); b. calculating the root mean square of the error signal of the model by summing the difference between the calculated signal and recorded FBP signal ($RMSE_{MODEL}$, Components of Equation 9); c. using both the $RMS_{RECORDED}$ and $RMSE_{MODEL}$ values to calculate how much the calculated model explains the overall recorded FBP (Percent Explained, Equation 9).

Components of Equation 9.

$$RMS_{RECORDED} = \sqrt{\sum_{i=1}^{n} \frac{Recorded_i^2}{n}}$$

$$RMSE_{MODEL} = \sqrt{\sum_{\boldsymbol{i=1}}^{\boldsymbol{n}} \frac{(\boldsymbol{Predicted_i - Recorded_i})^{\boldsymbol{2}}}{\boldsymbol{n}}}$$

Equation 9.

$$Percent\ Explained\ (\%) = 100 - (\frac{RMSE_{MODEL}}{RMS_{Recorded}} * 100)$$

5.2 Model I: Orthostatic Pressure

5.2.1 Model Equations

All kinematic data were splined, and then filtered with a 4th order low pass filter with a 120 Hz cut-off. The column that represented the finger position in the vertical axis was then located within each data set and subtracted by the column that represented the vertical height of the

heart. This difference was then inputted into the equation to calculate orthostatic pressure (Equation 3). The calculated pressure was then converted from Pascals to mm Hg. This orthostatic pressure model was then compared to the Portapres ® FBP signal.

5.2.2 Results

Within model I, orthostatic pressure explained -19 ± 17 % of recorded FBP when exercising at 45 rpm and -14 ± 5 % when exercising at 90 rpm. An example of the orthostatic model and the comparison of the orthostatic component at both cadences can be found in Figure 23. An example of the calculated model I for all participants can be found in APPENDIX G. Each participants' average orthostatic pressure at both cadences can be found in Table 7. The percent explained and overall orthostatic pressure values are negative due to the negative orthostatic pressure calculated (Figure 23A). The heart is positioned below the finger height which means that gravitational forces have less of an effect on the arterial blood within the finger. On average the orthostatic pressure makes up -13 ± 3 mm Hg of arterial pressure when exercising at 45 rpm while accounting for -12 ± 4 mm Hg during exercise at 90 rpm. A paired t-test completed on the average orthostatic pressure at each cadenced showed no significant change in the orthostatic component with an increase in cadence ($t(6) = 0.5795$, $p = 0.59$, Figure 23D).

Table 7. Each participants' average orthostatic pressure (mm Hg) component during arm crank cycling at 45 and 90 rpm.

Subject	Cadence (rpm)	
	45	90
3	-7.9	-5.8
7	-11.2	-11.6
8	-10.7	-10.5
10	-13.1	-18.0
13	-14.8	-12.7
14	-16.9	-14.4
15	-16.5	-13.9

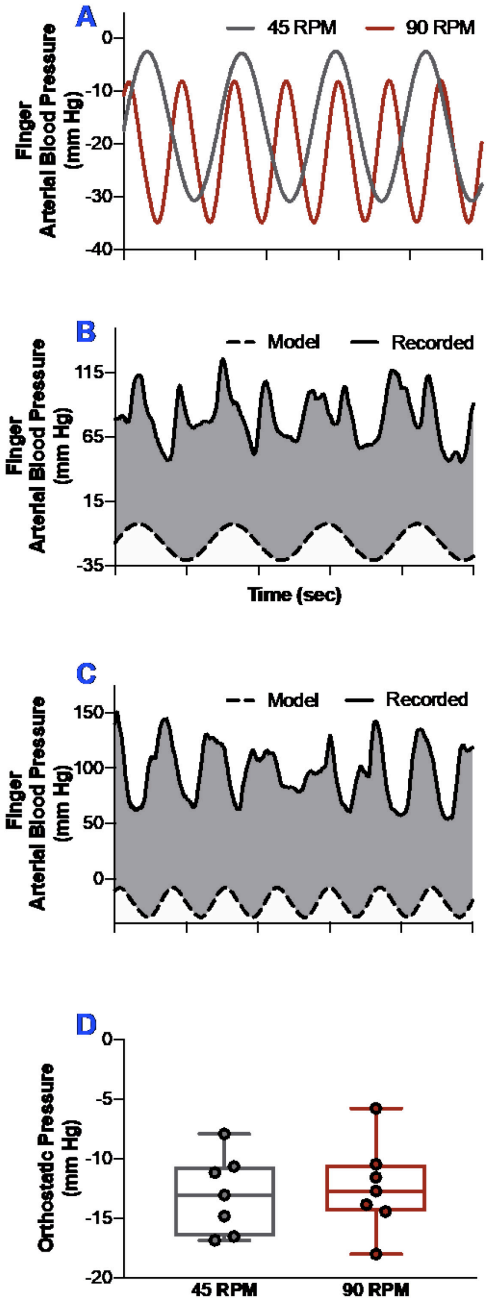

Figure 23. Model including orthostatic pressure during ACE at both cadences. A. Orthostatic pressure was negative due to the finger being above heart height. The models of FBP were then compared to the recorded FBP at B. 45 and C. 90 rpm. D. On average, orthostatic pressure did not change with an increase in cadence (p= 0.58). The individual circles represent each participant's average orthostatic component. grey line, 45 RPM model, red line, 90 rpm model, dashed line, modelled FBP, solid black line, recorded FBP, shaded area: difference between the two signals.

5.3 Model II: Orthostatic and Movement Related Pressures

5.3.1 Model Equations

Model II adds a new component, movement-related pressure, to model I. Like orthostatic pressure, movement-related pressure at the distal end of the segment was calculated using Equation 4. The movement-related pressure was calculated for each segment of the upper limb before finding the overall movement-related pressure occurring at the finger, as seen in Equation 10.

Components of Equation 10:

$$Movement\ Related\ Pressure_{Hand} = \rho \frac{1}{2} (r_{Hand} \omega_{Hand})^2$$

$$Movemet\ Related\ Pressure_{Forearm} = \rho \frac{1}{2} (r_{Forearm} \omega_{Forearm})^2$$

$$Movement\ Related\ Pressure_{UpperArm} = \rho \frac{1}{2} (r_{UpperArm} \omega_{UpperArm})^2$$

To calculate movement-related pressure, a series of equations were used to calculate the segment length, absolute angle and joint angle velocity for each segment. Segment length was calculated by subtracting the distal endpoint of the segment from the proximal end. The absolute angle of each segment was calculated by taking the inverse tangent of the segment length. Finally, the angular velocity was calculated using the 7-point central difference method (CDM), which takes the change in angle over the change in time.

Components of Equation 10: Segment Length

$$r_{UpperArm} = Lateral\ Epicondyle - Acromion\ Process$$

$$r_{Forearm} = Styloid\ Process - Lateral\ Epicondyle$$

$$r_{Hand} = Right\ Index\ Finger - \ Styloid\ Process$$

Components of Equation 11: Absolute Angle

$$\theta_{Forearm} = \arctan\ (r_{UpperArm})$$

$$\theta_{UpperArm} = \arctan\ (r_{Forearm})$$

$$\theta_{Hand} = \arctan\ (r_{Hand})$$

Components of Equation 12: Joint Angular Velocity

$$\omega_{UpperArm_i} = \frac{\theta_{UpperArm_{i+3}} - \theta_{UpperArm_{i-3}}}{t_{UpperArm_{i+3}} - t_{UpperArm_{i-3}}}$$

$$\omega_{Forearm} = \frac{\theta_{Forearm_{i+3}} - \theta_{Forearm_{i-3}}}{t_{Forearm_{i+3}} - t_{Forearm_{i-3}}}$$

$$\omega_{Hand} = \frac{\theta_{Hand_{i+3}} - \theta_{Hand_{i-3}}}{t_{Hand_{i+3}} - t_{Hand_{i-3}}}$$

Equation 13.

$$Movement\ Related\ Pressure_{Finger} = Pressure_{UpperArm} + Pressure_{Forearm} + Pressure_{Hand}$$

Once movement related pressure was calculated, it was added to the orthostatic pressure component to create model II (Equation 11). This second model was then compared to the recorded FBP signal by calculating the percent explained for the new model. The amount that movement-related pressure contributed to the overall FBP signal was also calculated by taking the average movement-related pressure for all stages of the exercise protocol at both cadences.

Equation 14.

$$Model\ II = Orthostatic\ Pressure + Movement\ Related\ Pressure$$

5.3.2 Results

An example of one participant's model II can be found in Figure 24 (all participants' model II can be found in APPENDIX G). Each participant's average movement-related component at each cadence can be found in Table 8. With adding the movement related pressure to model I, the percent explained changed to -18±6 % at 45 rpm and -9±5 % of the recorded signal when cycling at 90 rpm (Figure 24C, Figure 24D). The percent explained were still negative due to the newly calculated movement related pressure not completely counteracting the calculated orthostatic pressure. During ACE at 45 rpm, the average movement-related pressure accounted for 1±0.25 mm Hg of FBP, while at 90 rpm it accounted for 5±1 mm Hg.In the example within the figure below Model II at 45 rpm still looks sinusoidal due to the small amount of pressure that was calculated as the movement-related pressure component (Figure 24B).

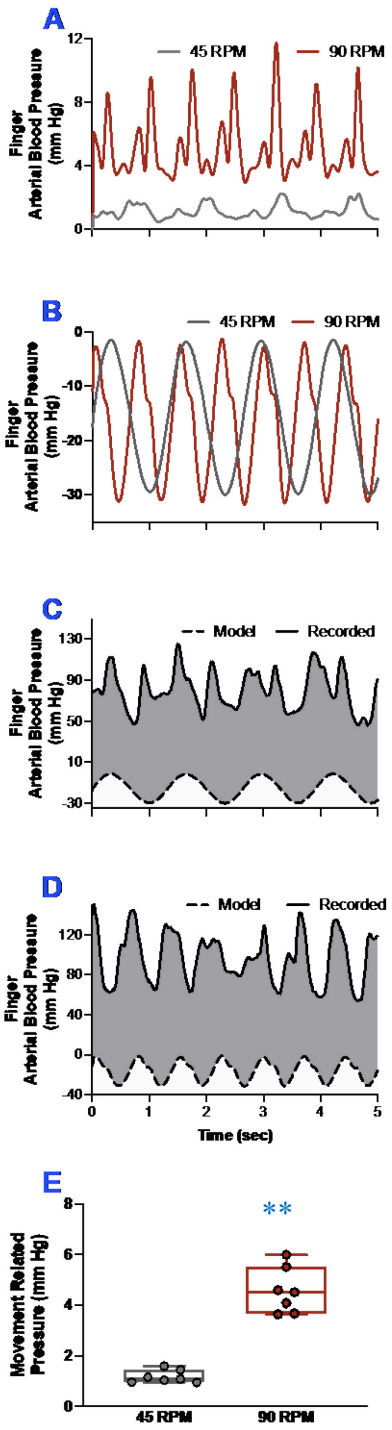

Figure 24. Model of FBP including orthostatic and movement related pressure. A. The new component was added to B. model I and then C and D. compared to the recorded FBP for both cadences. E. There was a significant increase in movement related pressure with an increase in cadence (** denotes p <0.0001). Dark grey line, 45 rpm model, red line, 90 rpm model, dashed line, modelled FBP, solid black line, recorded FBP, shaded grey area: difference between two signals.

Table 8. Average movement related pressure (mm Hg) component for each participant during arm crank exercise at 45 and 90 rpm.

Subject	Cadence (rpm)	
	45	90
3	1.0	6.0
7	1.2	4.1
8	1.5	3.6
10	1.0	4.6
13	1.0	3.7
14	1.6	5.5
15	1.1	4.5

Models I and II had a large amount of unexplained finger arterial blood pressure to arm crank exercise. This was due to the missing baseline pressure within the arterial system that would offset the calculated models to be positive.

5.4 Model III: Orthostatic, Movement Related, External Work Specific Base and Cardiac Pulse Pressures

5.4.1 Model Equations

Model III adds two new components, the external work specific base pressure and the cardiac pulse. External work specific base means that the base pressure was calculated for each stage of the exercise protocol. In order to find both components the error calculated between model two and the recorded FBP was used, an example of which can be found in Figure 25A. The continuous error signal was cut 0.2 seconds after the timing of each heartbeat to 0.7 seconds after (Figure 25B). The timing of each heartbeat was previously found when analyzing the raw ECG data to calculate heart rate. These values were chosen based off of the average pulse length found in one participant during exercise at 45 rpm (Subject 010). This delay from 0.2 seconds to 0.7 seconds was set as a constant for all participants at all intensities of exercise. The cut error signals were then superimposed on top of each other to calculate the mean signal after each heartbeat, an

example of which can be found in Figure 25C. The minimum value of the average pulse, as found in Figure 25D, becomes the base pressure value and was added to model two.

The cardiac pulse was then calculated by taking the mean pulse signal (example in Figure 25E) and subtracting the base value from the curve. This new pulse was added to the model 0.2 seconds after each heartbeat (Equation 12). Model III was then compared to the recorded FBP signal by calculating the percent explained. This process was done for each stage of the exercise protocol for each participant performed with a new base and cardiac pulse pressure being calculated at each stage.

Equation 15.

$$Model\ III = Orthostatic\ Pressure + Movement\ Related\ Pressure + External\ Work\ Specific\ Base\ Pressure + Cardiac\ Pulse_{HB+0.2s:HB+0.7s}$$

5.4.2. Results

Each participant's calculated base and cardiac pulse pressures for each stage of the exercise protocol can be found in APPENDIX E and APPENDIX F. With the two new components, model III accounted for 74 ± 4 % of the recorded finger arterial blood pressure signal during exercise at 45 rpm and 68 ± 8% of the signal during exercise at 90 rpm. An example of the Model III can be found in Figure 26 and all participant graphs can be found in APPENDIX G . The addition of the base pressure in this model adjusted the large offset that was found in both models I and II.

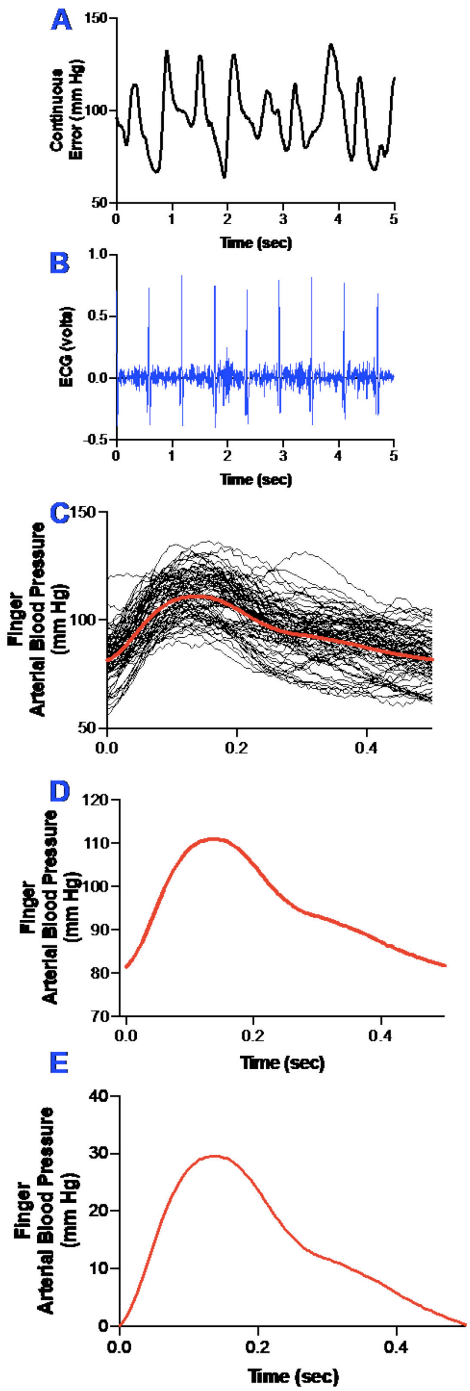

Figure 25. Example of how the base pressure and cardiac pulse pressure were calculated for model III. A. The difference between model II and the recorded FBP gets cut based off the B. timing of each heartbeat. C. The average arterial blood pressure change after each heartbeat is then found. D. The minimum value on the curve gets set as the base pressure value and E. the rest of the curve was added to model II every time there is a heartbeat.

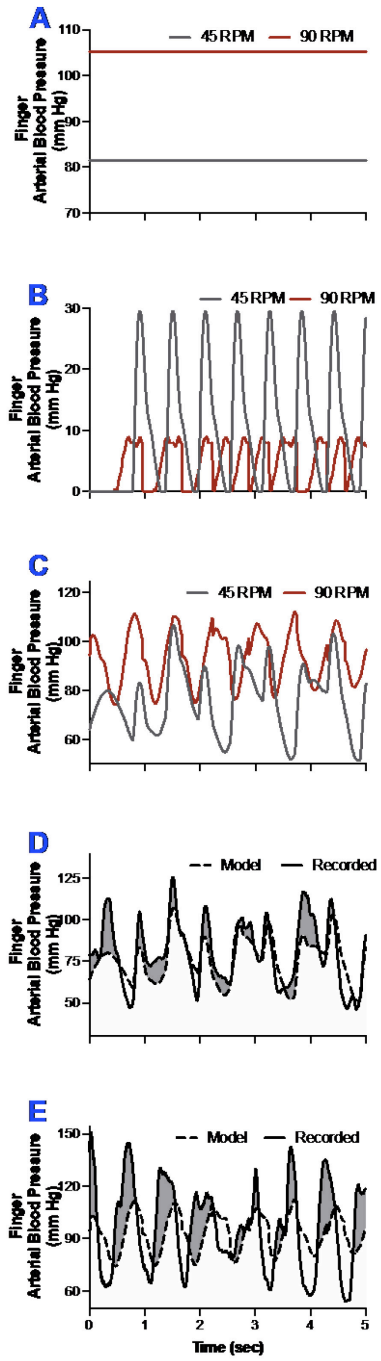

Figure 26. Model III including orthostatic, movement related pressure, external work specific base and cardiac pulse of a constant delay and length. The two new components, A. base and B. cardiac pulse, were C. added to model II and compared to the recorded FBP at both cadences (D and E). Dark grey line:45 rpm model, red line: 90 rpm model, dashed line: modelled FBP, solid black line: recorded FBP, shaded area between dotted line and black line: difference between the two signals.

5.5 Model IV: Orthostatic, Movement Related, Constant Base and Cardiac Pulse Pressures

5.5.1 Model Equations

With Model IV, no new components were added to the model, rather changes were made to the way the base pressure was calculated. The base pressure was adjusted in this model so that it stays as a constant value for all external workloads within a data collection session. The constant pressure was identified as the average base pressure calculated in the rest trials. The constant base was then subtracted from the average pulse calculated in model III to find the new cardiac pulse. These two new components where then added to model II to create model IV (Equation 13). The percent explained was then calculated for the new model.

Equation 16.

$$Model\ IV = Orthostatic\ Pressure + Movement\ Related\ Pressure + Constant\ Base\ Pressure + Cardiac\ Pulse_{HB+0.2s:HB+0.7s}$$

5.5.2 Results

Each participant's individual calculated base and cardiac pulse pressures for this model can be found in APPENDIX E. The new model explained 70 ± 8 % of the recorded FBP at 45 rpm while the model accounts for 56± 10 % of the recorded FBP at 90 rpm. An example of the new model for one participant at both cadences can be found in Figure 27 and all participant graphs can be found in APPENDIX G. The percent explained calculated for Model IV was lower than Model III due to the new base pressure that was calculated for all participants. As found in APPENDIX F, for most participants with an increase in external workload there was an increase in the calculated base pressure. The new model was created with the assumption that the base pressure did not increase as a function of external work, therefore the calculated base during the resting phase of the exercise protocol was selected as the constant base pressure. The decrease in the percent explained was due to the lower base pressure and lower calculated cardiac pulse pressure as seen in APPENDIX E.

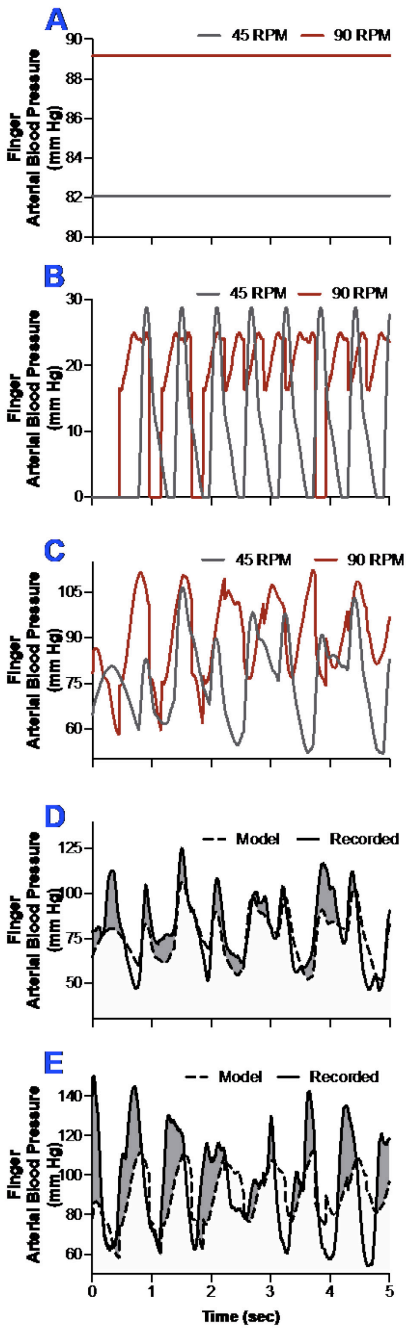

Figure 27. Model IV including orthostatic pressure, movement related pressure, constant base, and cardiac pulse pressure. A constant base pressure was set for all stages of the exercise protocol (Panel A). From the new base pressure a new cardiac pulse pressure was also calculated (Panel B). The two new components were added to model II (Panel C) and then compared to the recorded FBP at both 45 (Panel D) and 90 rpm (Panel E). Dark grey line: 45 RPM model, red line: 90 RPM model, dashed line: modelled FBP, solid black line: recorded FBP, shaded area between dotted line and black line: difference between the two signals.

5.6 Model V: Orthostatic, Movement Related, External Work Specific Base and Participant Specific Cardiac Pulse Pressure

5.6.1 Model Equations

Since model IV did not produce a higher percent explained than model III, a fifth model was created adjusting the cardiac pulse length for each participant. Different delay periods and pulse lengths were used to cut the difference between model II and the recorded FBP for each participant. The different cutting times were compared against each other graphically until a delay and period length were found that incorporated the entire pulse for all external workloads within the exercise session. Once the participant specific delay and pulse length were identified, the external workload specific base and cardiac pulse pressures were calculated and added to model II to create model V (Equation 18). This new model then had its percent explained calculated.

Equation 17.

$$Model\ V = Orthostatic\ Pressure + Movement\ Related\ Pressure + External\ Work\ Specific\ Base\ Pressure + Participant\ Specific\ Cardiac\ Pulse$$

5.6.2 Results

Each participant's individual calculated base and cardiac pulse pressures for this model can be found in APPENDIX E. The participant specific delays and bases were similar to the constant values selected in model III. The largest difference was one participant having a 0.3 second delay rather than a 0.2 delay for model III and another participant having a 0.35 second pulse length rather than a pulse length of 0.5 seconds. Model V explained 73 ± 4 % of the recorded FBP during exercise at 45 rpm while explaining 67 ± 8 % of the recorded FBP during exercise at 90 rpm. An example of this model for one participant can be found in Figure 28 (all participant graphs can be found in APPENDIX G).

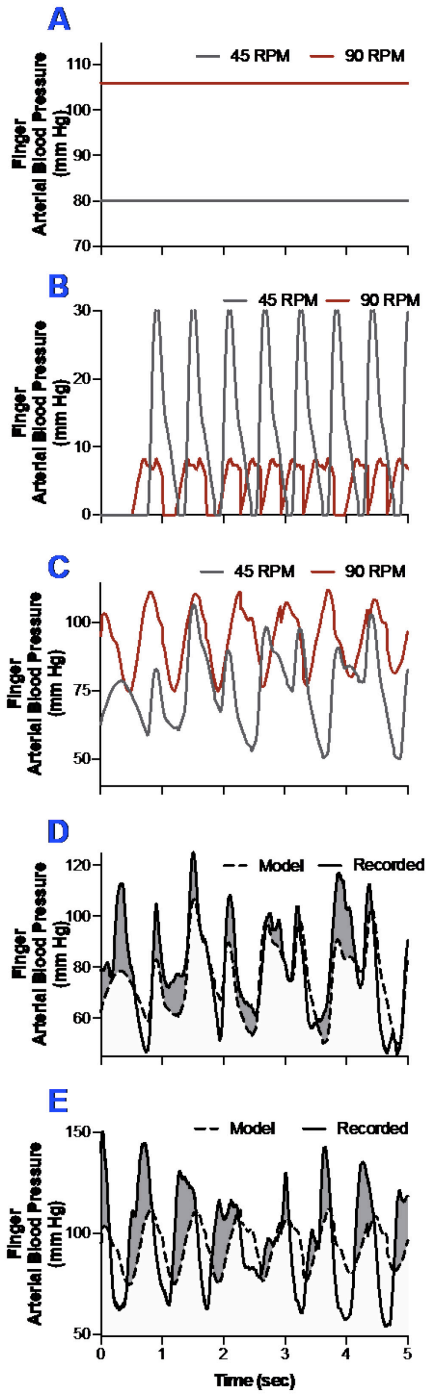

Figure 28. Model V including orthostatic, movement related pressure, external work specific base pressure and participant specific cardiac pulse pressure. A. From the new pulse lengths, a new average pulse, base pressure and B. cardiac pulse were calculated. C. The two components were then added to model II and then D. and E. compared to the recorded FBP at both cadences Dark grey line: 45 RPM model, red line: 90 RPM model, dashed line: modelled FBP, solid grey line: recorded FBP, shaded area: difference between the two signals .

5.7 Comparison of Five Different Models

The values included in the two-way repeated measure ANOVA (cadence × model) to compare the goodness of fit of the models consisted of the percent explained from Model III, IV and V. The data from Model I and II were not included because it did not contain the four components.

All data sets were normally distributed and without outliers. The assumption of sphericity was violated for both the model and interaction between cadence and model (model: $\chi^2(2)= 98.863$, $p=0.000$; interaction: $\chi^2(2)= 97.046$, $p=0.000$), therefore Greenhouse-Geisser corrections of the degrees of freedom were applied (model: $\varepsilon= 0.514$; interaction $\varepsilon= 0.515$). There was a significant interaction between cadence and model on the FBP percent explained ($F(1.030,36.038) =32.265$, $p=0.000$). There was also a significant effect of both cadence ($F(1,35)=40.171$, $p=0.000$) and model ($F(1.028,35.982)=103.071$, $p=0.000$). The models had a greater FBP percent explained value for the lower ACE cadence (45 rpm: 72.9% ± 0.6; 90 rpm: 64.4% ± 1.3). Model IV (63.1% ± 1.1) had a statistically lower FBP percent explained compared to Model III (71.4% ± 0.8) and Model V (71.5% ± 0.8). The averages by cadence and by model of the FBP percent explained are presented in Figure 29, Table 10 and Table 11. It was discovered that the reduced percent explained for the 90-rpm condition by Model IV had a statistically significant effect on the interaction between cadence and model.

There were no differences in the percent explained between model III and V. However, because of its lower complexity model III was identified as the model of best fit.

Table 9. FBP percent explained (± SE) for each of the models of FBP created for each ACE cadence.

Model	45 rpm	**90 rpm**	**Average**
Model III	74.4±0.5	68.4±1.3	71.4±0.8
Model IV	70.3±1.3	55.9±1.5	63.1±1.1
Model V	74.1±0.4	68.9±1.4	71.5±0.8
Average	72.9±0.6	64.4±1.3	

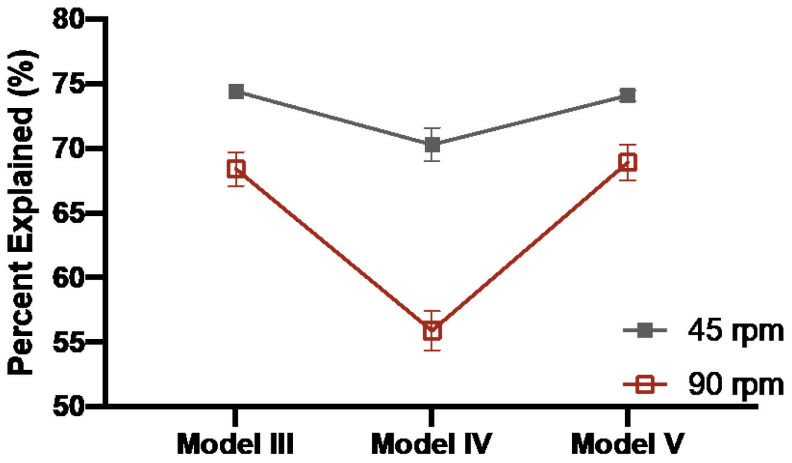

Figure 29. Percent explained for models including four components of finger arterial blood pressure during two ACE cadences.

Table 10. Post hoc analysis of the repeated measures ANOVA on the FBP percent explained for the models of FBP created for each ACE cadence.

Pairing	45 RPM			90 RPM		
	Mean±SE	q	p-value	Mean±SE	q	p-value
Models III vs. IV	3.8±1.1	4.935	0.01	12.6±1.1	16.87	<0.00
Models III vs. V	0.3±0.1	4.499	0.02	-0.5±0.2	3.335	0.15
Models IV vs. V	-3.5±1.1	4.535	0.02	-13.0±1.0	17.62	<0.00

5.8 Each FBP Components' Contribution to the Increases in Finger Arterial Blood Pressure at One Moderate-Intensity of ACE

A more thorough analysis of the four-component model was done to establish the contribution from each of those components to the increase in FBP associated with an increase in ACE cadence. The analysis consisted of comparing the changes in calculated MAP values for each component with the increase in ACE cadence at a moderate intensity of exercise (4 METS).

The value for each component was extracted by applying the equations of Model III for an ACE intensity of 4 METS (for the calculation methodology see section 5.3). In this model, both orthostatic and movement-related pressures remained constant with an increase in ACE intensity and did not need to be adjusted. However, the base and cardiac pulse pressures component values were dependent on exercise intensity. The MAP values for the two components were

adjusted for an ACE intensity of 4 METS. As presented above (Section 4.4.5) this intensity represented the median value of ACE intensity for all participants for both ACE cadences. To find the base and cardiac pulse pressure for each participant at four METS, a simple linear regression was calculated, for both components, as a function of METS and the value at four METS was extracted.

The comparison consisted of calculating a paired t-test on the MAP values for each of the components

5.8.1 Results

For the four paired t-tests, all data sets were found to be normally disturbed ($p>0.05$) and without outliers. The average finger arterial blood pressure for each component for each ACE cadence can be found in Figure 30 and in Table 10.

Orthostatic pressure ($t(6)= 0.5795$, $p=0.5834$, $d= 0.219$, power= 0.118), base pressure ($t(6)= 1.184$, $p=0.2813$, $d= 0.4473$, power=0.3414) and cardiac pulse pressure ($t(6)= 1.551$, $p=0.1719$, $d= 0.586$, power= 0.528) did not show a significant change with an increase in cadence. Movement-related pressure did significantly increase by 3 mm Hg with an increase in cadence ($t(6)=9.555$, $p<0.0001$, $d= 3.6112$).

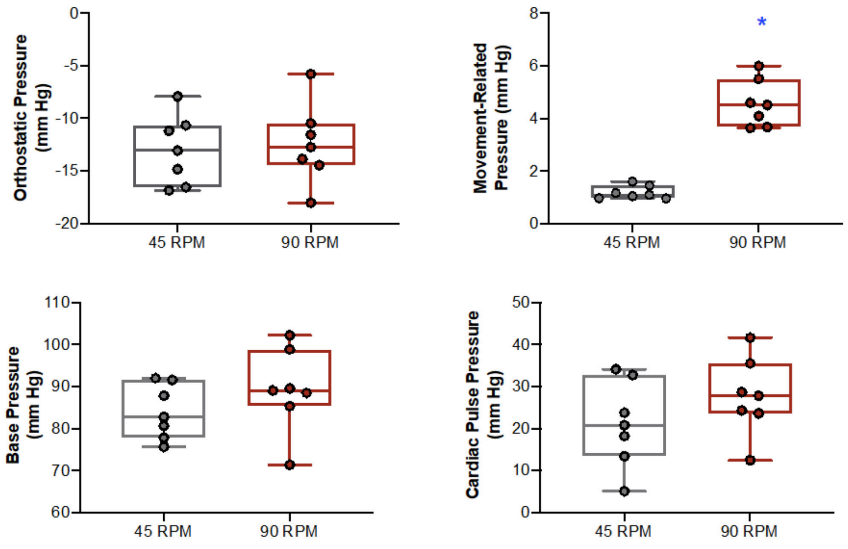

Figure 30. Contribution to the increase in MAP by each of the four components calculated within model III including orthostatic, movement-related, external work specific base and cardiac pulse pressures.*, denotes a significant difference in component at 90 rpm compared to 45 rpm, $p<0.05$

Table 11. Table of the mean and standard deviation of each component calculated at part of Model III including orthostatic, movement related, external work specific base and cardiac pulse pressures during arm crank exercise at 45 and 90 rpm

Component	**45 rpm (Mean ± SD)**	**90 rpm (Mean ± SD)**	**Difference (Mean ± SD)**
Orthostatic	-13 ± 3 mm Hg	-12 ± 4 mm Hg	0.59 ± 3 mm Hg
Movement-Related	1 ± 0.25 mm Hg	5 ± 0.89 mm Hg	3 ± 0.93 mmHg
Base	84 ± 7 mm Hg	89 ± 10 mm Hg	5 ± 12 mm Hg
Cardiac Pulse	21 ± 10 mm Hg	28 ± 9 mm Hg	7 ± 11 mm Hg

CHAPTER 6: DISCUSSION

This thesis had two specific aims. The first aim was to determine if an increase in ACE was associated with an increased finger MAP. The second aim of this thesis was to determine the contribution of orthostatic, base, cardiac pulse, and movement-related force parameters on the increase in finger arterial blood pressure during ACE. These specific aims were answered by performing arm cranking incremental workload protocols at either 45 rpm or 90 rpm while measuring finger arterial blood pressure (Portapres), HR, VO_2, and upper limb kinematics.

The first aim was answered by comparing the recorded finger MAP during ACE at 45 and 90 rpm for similar internal work values (i.e. METS). An increase in finger MAP with the increase in ACE cadence was demonstrated by: 1) a greater y-intercepts of the linear regression between MAP and METS (28 ± 17 mm Hg); 2) an effect of cadence on the values of MAP at discrete METS (16 mm Hg); and 3) an increase of MAP for the 90 rpm condition at one moderate intensity of ACE (16 ± 10 mm Hg).

The second aim of the study was answered by creating different models of FBP and identifying the model of best fit (i.e. highest percent explained). The model that included orthostatic pressure, movement-related pressure, external workload specific base pressure and cardiac pulse pressure of a constant delay and pulse length (Model III) had the highest percent explained value of the recorded finger arterial blood pressure during ACE (45 rpm: 74 ± 4 % ; 90 rpm: 68 ± 8%). The contributions of the four calculated components of the model to the 16 mm Hg increase in MAP at an ACE intensity of 4 METS was identified. Movement-related pressure was the only significant difference between the two ACE cadences (3 ± 0.93 mm Hg, $p<0.0001$) and accounted for only 19 % of the rise in MAP associated with the increase in ACE cadence. There were no significant increases found in the orthostatic pressure component (0.59 ± 3 mm Hg, $p=0.218$), base pressure component (5 ± 12 mm Hg, $p=0.2813$), or cardiac pulse pressure component (7 ± 11 mm Hg, $p=0.1719$) with an increase in ACE cadence.

This thesis was unique as it recorded finger arterial blood pressure while the limb was performing a cyclical, more complex, movement (i.e. arm cranking) to determine the effect of movement-related forces on arterial blood pressure. Previous literature has looked at the MAP response in the upper limb during upper body cycling, but took measurements at the brachial artery[46], and did not look at the overall change in the magnitude of the blood pressure response[47].

6.1 Higher ACE Cadence Increased Relative $VO_{2,}$ HR and MAP for the Same External Workload

When controlling for external power output, both higher cadence and greater ACE intensity increased the relative VO_2 and HR response. Previously, Price et al (2007)[40] found similar results in the VO_2 response to arm crank exercise at different cadences. Participants performed 3 incremental arm crank exercise protocols at cadences of 50, 70 and 90 rpm. At power outputs of 50, 70 and 90 watts, VO_2 was higher at a cadence of 90 rpm that at 70 and 50 rpm ($p<0.05$)[40]. Heart rate was also higher at a cadence of 90 rpm compared to both 70 and 50 rpm during arm crank exercise at increasing power outputs, but no significant difference between exercising at a cadence of 50 rpm or 70 rpm ($p>0.05$) [40].

There have been several mechanisms proposed to explain the increase in both VO_2 and HR for the same external power output when doing ACE at different cadences[40,55], as seen previously in research in by Price et al[40] and within the results of this thesis (Table 3). The first one proposes an increase in the recruitment of fast-twitch (type II either oxidative or glycolytic) fibers at lower cadences, which could reduce the O_2 response [55]. The second one suggests an increase in isometric muscle activity needed to isolate the torso during exercise at a higher cadence [40] . Since isometric contractions elicit the same VO_2 per unit of muscle mass as dynamic muscle contractions, faster cadence arm ergometry may also result in postural muscle contractions that elevates VO_2 without directly contributing to the force output or propulsion of the crank shaft [55]. A third proposed mechanism is that with a decrease in gross efficiency associated with an increase in ACE cadence there is a greater prevalence of the locomotor-respiratory coupling (LRC) [40,55] . LRC, also known as entrainment, is the natural synchronization between respiration and locomotion during various forms of locomotion[55,56] . It is expressed as the ratio of breathing cycles over locomotion cycles and is generally understood as originating from mechanical and neurological interactions [55,56]. Research has investigated the entrainment effect during arm cranking at cadences of 50, 70 and 90 rpm [55]. Eight active men were recruited for the study with each performing moderate- and severe-intensity ACE for 4 minutes[55]. The results showed that participants synchronised their locomotor and respirator rhythms more frequently when arm cranking at higher cadences (i.e., 70 rpm and 90 rpm). Other research has suggested that a greater LRC at higher cadences may result in a greater respiratory frequency [40], although not all studies show an increase in respiration with an increase in ACE cadence [55].

An analysis of the gross efficiency of ACE at 45 rpm (10.82 ± 0.699 %) and 90 rpm (7.17 ± 0.713 %) showed a decrease in efficiency with an increase in cadence (difference: 3.65 ± 3.63 %, $p<0.0001$, Table 3, Section 4.4). There was also a significant effect of stage of exercise on the efficiency at both cadences, with efficiency increasing with an increase in external power output ($p<0.0001$, Table 3). Similarly, Powers (1984)[39] had 10 male subjects perform incremental ACE at cadences of 50, 70 and 90 rpm. For each external workload (ranging from 0- 60W), gross, net and delta efficiencies were calculated. As shown in Figure 9 in Section 2.3.6, with an increase in cadence there was a decrease in the calculated gross efficiency, and also with an increase in workload there was an increase in economy. The increase observed with changes in workload can be explained by the decreasing effect that resting metabolic rate had on the denominator in the calculation for gross efficiency [39]. Gross efficiency considers all the energy expended at a given workload without the subtraction of any energy expenditure not directly involved with the exercise intensity. However, Powers[39] noted that the increase across work rates becomes smaller at higher work rates due to the decrease in the percentage that resting metabolic rate contributes to the total energy expenditure. The changes found with different ACE cadences was due to the change in absolute energy expenditure as noted in both this thesis (Section 4.4.1.2) and in Powers[39] (Figure 8). The difference in energy expenditure with a change in ACE cadence led to an offset in the calculated efficiency but the change across power outputs remained the same.

Mean finger arterial pressure was shown to be higher for the increased ACE cadence (21 ± 4 mm Hg). Similarly, Goreham (2014)[14], found that the recorded toe MAP was higher when cycling at a cadence of 90 rpm (87 ± 34 mm Hg) compared to 50 rpm (71 ± 36 mm Hg, $p<0.027$) when controlling for the same external power output. There was no effect of stage on the MAP response when controlling for workload. This could be due to the small sample size and number of stages used in the analysis. These changes could be due to both systemic and local changes on MAP. As previously explained (Section 4.4.1.2), there is an increase in heart rate with an increase in ACE cadence. This could lead to an increase in Q leading to an increase in SBP and overall increase in MAP[9].

A systemic change in finger MAP has been reported by Sheriff et at (2009)[13], with the non-moving arm showing an increase of 8 ± 2 mm Hg compared to the moving arm, which had an increase of 18 ± 3 mm Hg. The overall 8 mm Hg increase found in both limbs was due to an increase in heart rate from base line ($p<0.05$)[13].

6.2 Higher ACE Cadence Increases MAP at Matched Internal Workloads

To control for the difference in gross efficiency related to ACE cadence, the MAP response was analyzed as a function of internal work (i.e. METS). The effect of ACE cadence increased the MAP recorded at the finger at matched internal workloads. The magnitude of the effect depended on the analysis method used but the increase in MAP can be estimated to be 16 mm Hg when comparing the MAP recorded at a cadence of 90 rpm compared to 45 rpm.

The second aim of this study was to establish the contribution of orthostatic, movement-related, base, and cardiac pulse forces to the increase in MAP with the increase in ACE cadence. Three models were created that included all four components (Models III through Model V). Both Model III and Model V showed no difference in the percent of FBP explained in the model. But due to its lower complexity model III was identified as the model of best fit.

This model was able to explain between 60- 80 % of the recorded finger arterial blood pressure during ACE. Of those components calculated, movement-related pressure was found to increase by ~3 mm Hg with an increase in cadence, accounting for approximately 20% of the increase recorded. Orthostatic, base and cardiac pulse pressures were shown not to have a significant change with an increase in cadence ($p>0.05$), although these results are inconclusive due to a low calculated power.

The results of this thesis are the opposite of those found in Goreham (2014)[14], when comparing the mean arterial toe blood pressure response to cycling at 50 and 90 rpm when controlling for the same internal work. During cycling at the same heart rate, approximately ~120 beats per minute, Goreham[14] found that the average toe blood pressure during cycling at 50 rpm (89.9 ± 36.6 mm Hg) was significantly higher than the measured toe blood pressure at 90 rpm (80.2 ±37.4 mm Hg, $p<0.05$). In the study completed by Goreham[14], internal work was not controlled for, as was done in this thesis. Although if Goreham[14] did control for METS it may not change the findings as it was shown in this study that heart rate and METS were positively correlated to one another.

Other research has looked at the response in finger arterial blood pressure during exercise, but did not evaluate the overall average of the blood pressure signal[47]. As previously mentioned in Section 2.3.5, Billings (2016)[47] compared the changes in SBP, DBP and MAP in the finger during ACE. The results showed no change in MAP with an increase in cadence when exercising

at 60 % of heart rate reserve (Figure 12) [47]. This could be due to the way the MAP was calculated as part of the study. From the raw FBP signal peaks were identified as either a systolic or diastolic peak and then both values were inputted into Equation 5. When measuring the changes in arterial blood pressure in a moving limb it is difficult to differentiate the values that represent the true SBP and DBP because of the contamination of the signal generated by the added arterial pressures added by the ongoing change in orthostatic pressure and movement-related changes in arterial pressure. If the finger rose during diastole then an extra systole could be produced. This phenomenon could also augment the systolic blood pressure being recorded[13].

6.3 Estimating the Contribution of Movement Related Forces to the Increase in Finger Arterial Blood Pressure

As presented in Section 5.8.1 , it was estimated that movement-related forces increase finger arterial blood pressure between 45 rpm and 90 rpm by 3 mm Hg (45 rpm:1± 0.3 mm Hg; 90 rpm:5 ± 0.9 mm Hg). Previously Sheriff et al (2009)[13], had participants perform horizontal flexion of the upper limb at a frequency of 0.75 Hz. The increase in MAP compared to the non-active limb was 11±2 mmHg (Figure 5) [13]. This study did not look at the changes in the MAP with a change in frequency of the motion, rather it was the first of its kind to quantify the movement-related component on changes in MAP during upper body exercise. By comparing the changes in MAP in the active limb to the non-active limb, the systemic change in MAP due to an increase in HR was able to be removed from the overall increase found in finger mean arterial blood pressure during movement allowing for the movement-related component to be isolated[13]. The reason why there is a difference in the Sherrif[13] study and this thesis is due to the type of movement and its effect on the values used in the movement-related pressure equation. As explained in Equation 5 in Chapter 2 of this thesis, movement-related pressure can be calculated by taking the density of blood, segment length squared, and the angular velocity of the limb squared. In Sheriff[13], the entire upper limb was considered one segment from the glenohumeral joint all the way to the finger as both the humeroradial and radiocarpal joints were kept in extension throughout the entire data collection. This longer column would lead to a larger calculated movement-related pressure. The average arm length of participants used in the study was 0.75m, and the angular velocity was 2.35 rad/seconds, which leads to a calculated movement-related pressure of 12 mm Hg (Equation 5), similar to the change in the recorded finger arterial blood pressure[13]. In this thesis, there was movement at the humeroulnar and

radiocarpal joints, which led to movement-related pressure calculations for three separate segments of the upper limb. Each segment has a smaller segment length, which would result in a different movement-related pressure compared to Sheriff et al[13] as the segments do not move at the same angular velocity.

Changes in movement-related pressure with a change in cadence have also been investigated in lower body cycling[15,16]. In an unpublished Master's thesis, Ewig[16] used two plastic water-filled tubes and pressure transducers at the mid-shank levels to measure pressure at seven different pedaling cadences. Eleven subjects pedaled at 50, 80 and 110 rpm for 30 seconds at each bout. The net shank movement-related pressure at each cadence was 1.16 ± 0.75 mm Hg, 3.66 ± 0.87 mm Hg, and 6.46 ± 1.1 mm Hg. There was a significant effect of cadence on the net movement-related pressure ($p<0.01$, with $p<0.05$ at 80 and 110 rpm). These results show that with an increase in cadence from 50 to 80 rpm there is an increase of ~2.5 mm Hg, and between 50 and 110 rpm an increase of ~ 5.3 mm Hg. This net increase in movement-related pressure was similar to the results of this study that found a 3 mm Hg increase in movement-related pressure with an increase in cadence from 45 rpm to 90 rpm. Although, movement-related pressure was not calculated by Ewig[16] using Equation 4, movement-related pressure was isolated by subtracting the orthostatic pressure effect from the recorded tube pressure[16]. Movement-related pressure was also measured at the mid-shank level and not at the most distal end of the leg during cycling so the true movement-related component occurring at the most distal end of the leg was not evaluated.

The movement-related pressure changes occurring at the toe were evaluated in an unpublished Honours thesis by Grant (2016) [15]. Comparing cycling in two participants at 50 and 90 rpm, the calculated average movement-related pressure occurring at the toe was calculated to be ~3 ± 0 mm Hg at 50 rpm and ~ 8 ± 0.28 mm Hg at 90 rpm. These results showed that with an increase in cadence there was a corresponding increase in the movement-related forces on MAP of 5 mm Hg. These results show that the increases found in Ewig[16] were due to the movement- related pressure changes with an increase in cadence. These unpublished findings also prove similar to this thesis that changes in arterial blood pressure can be due to movement-related pressure and its effect can be modeled using Equation 4.

6.4 Modulation of the Effect of Movement-Related Forces as a Function of Exercise Intensity

As reported in the results in Section 4.4 internal work did not have a significant effect on the recorded MAP and there was no significant interaction between cadence and internal work ($p>0.05$). However, our study was underpowered as the post-hoc calculated power for the effect of internal work and the interaction effect (Cadence × internal work) was low. To achieve a higher power (power =0.8), a sample size of 14 (i.e., 7 more participants) would need to be reached. A graph of the MAP as a function of internal work for the two arm-cranking cadences (Figure 31) showed some interaction between cadence and internal work. The MAP at 90 rpm seems to be stable whereas there seem to be an increase with of the MAP as a function of internal work at 45 rpm. With a larger sample size, there could be significant main effect of internal work on MAP and interaction between cadence and METS, as it was found in the Bland-Altman analysis of differences that all participants had proportional bias when evaluating the measurements of finger MAP at 45 and 90 rpm (Table 5, Appendix D). The interaction between intensity and cadence could be explained by the limitations of the muscle pumps ability to increase blood flow.

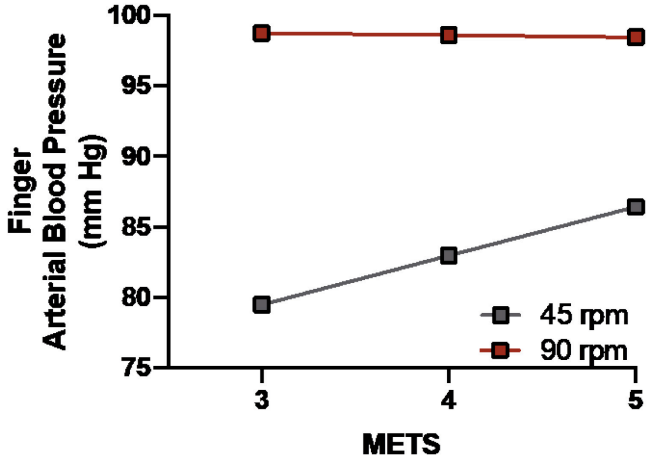

Figure 31. MAP response as a function of internal work and ACE cadence. From the results of the repeated measures ANOVA, there is was no significant interaction (cadence × internal work, $p=0.082$) or main effect of internal work ($p=0.206$). There was a significant main effect of cadence on the MAP response ($p=0.005$).

Previous research has looked at the changes in the muscle pumps ability to increase muscle blood flow and mean arterial pressure[57]. Participants performing knee-kicking exercise at a rate of 40 kicks per minute at seven different stages of power outputs ranging from 60-75% of peak

aerobic work rate (actual range 0.07-9.80 W). The results showed that at the lightest work rate rhythmic muscle contraction enhanced muscle blood flow during exercise, compared with blood flow early in the exercise recovery stage [57]. At higher work rates, there was no systematic enhancement of mean muscle blood flow during steady-state exercise and at the highest recorded work rates muscle contraction-relaxation was an impedance to flow[57]. Mean arterial pressure within the femoral artery was also analyzed and was not significantly different between exercise and the early recovery stage (i.e. within the first 5 cardiac cycles after cessation of exercise) during lighter work rates. This suggests that the muscle pump did not augment blood flow above that achievable by blood pressure and vascular conductance alone[57]. At higher work rates, MAP was progressively higher during exercise than during recovery, suggesting that the net effect of the muscle contraction-relaxation cycle was progressively impeding flow, which necessitated a higher MAP to achieve the mean exercise flow under these conditions[57].

6.5 Estimating the Contribution of Cardiac Pulse and Base Pressure Forces to the Increase in Finger Arterial Blood Pressure

Although not statistically significant, there was an average increase of 7 mm Hg and 5 mm Hg with the cardiac pulse and base pressure components, respectively when assessing Model III at 4 METS of exercise intensity. As shown in Figure 28 and Table 9 , the average amount of cardiac pulse pressure during exercise at 45 rpm was 21 ± 10 mm Hg and at 90 rpm 28 ± 10 mm Hg ($p= 0.1719$), as five participants showed an increase while two showed a decrease with a faster cadence. For the base pressure, during exercise at 45 rpm it was calculated to be 84 ± 7 mm Hg and at 90 rpm 89 ± 10 mm Hg ($p=0.2814$). Since both paired t-tests produced results with low power (power= 0.528 and 0.3414 for cardiac pulse and base pressure, respectively), it is not conclusive that the distribution between the components at both cadences were the same. In order to achieve a higher power (power =0.8), 19 participants (i.e., 12 more participants) would need to be tested. With a larger sample size, it is likely that there will be a significant increase found in the cardiac pulse component of finger arterial blood pressure. This increase could be due to an increase in cardiac output related to an increase in the venous return to the heart with the aid of the muscle pump[37]. The pumping action created by muscle contraction and relaxation allows for opening of the one-way valves propelling blood back towards the heart[35,36]. With the increase in venous return there would be a corresponding increase in stroke volume due to an increase in preload [20,20]. Along with an increase in cardiac output, which would lead to an

increase in cardiac pulse pressure, there could also be an increase in the calculated base pressure due to the Windkessel function. The Windkessel function is the elastic property of the vascular walls of the aorta, which can distend during systole storing some of the ejected blood volume only for it to be released during diastole [19]. Its role is to aid in blood pressure staying above 0 mm Hg in the periphery between heart contractions. With the increase in stroke volume and cardiac output, the aorta would be distended further holding more blood during systole for it then to be released during diastole leading to an increase in the measured base pressure.

6.6 Estimating the Contribution of Orthostatic Forces to the Increase in Finger Arterial Blood Pressure

Although not statistically significant, the calculated power of the paired t-test performed on the average orthostatic pressure at 45 rpm and 90 rpm was low (power= 0.118), which would lead to inconclusive results. The low calculated power was due to the small sample size. In order to achieve a higher power (i.e., power =0.8), data from 27 more participants would be needed, although it would not create a significant difference between the calculated orthostatic component at 45 rpm and 90 rpm. Orthostatic pressure is determined by the position of the point of blood pressure measurement relative to the heart position and a change in cadence cannot have an effect of the calculated pressure.

6.7 Negative Percent Explained Results in the Models that Did not Include the Base pressure (Model I and II)

The purpose of specific aim II was to determine the contribution of orthostatic, base, cardiac pulse, and movement-related forces parameters on the finger arterial blood pressure during ACE.

Model I was created with only one component, orthostatic pressure, while Model II added movement related pressure. The percent explained calculated for both models were negative. This can only occur when the RMS value recorded is less than the error calculated as the RMS of the model making the quotient of the calculated ratio of RMS model/RMS record greater than 1 as shown in Equation 9. This is due to a large offset missing from the calculated model that would later be calculated as the base pressure calculated in models III-V. The reason why the base pressure was not calculated first to prevent models from having a negative percent explained was due to the way base pressure was calculated. In model III base pressure was calculated by taking the missing blood pressure signal calculated by taking the difference

between model II and the recorded FBP, finding the average change in FBP after each heartbeat and the lowest pressure found was the base pressure.

6.8 Assumptions and Limitations of the Study

There are several limitations and assumptions related to this research project. One limitation was the small sample size, which led to low calculated powers within the analysis. As seen in Sections 4.4, results of the repeated measures ANOVA on the MAP response as a function of METS, and Section 5.8.1 with the paired t-test for cardiac pulse, base and orthostatic pressure, all had low calculated powers, making the results unclear about the effect intensity of exercise had on the MAP response during arm crank exercise and the possible contributions base and cardiac pulse pressure has on the 16 mm Hg increase in arterial blood pressure seen with an increase in cadence.

Another limitation within this study was the number of time points used in each session data collection. Smaller testing session lengths led to less data points being used in the analysis of MAP. With the use of interpolation and extrapolation smaller sample number per testing session led to large amounts of variations for each of the interpolated and extrapolated values.

This thesis assumed that the recordings of arterial blood pressure from the Portapres® are representative measurements of the arterial blood pressure within the digital artery of the index finger. The Portapres® was not initially designed to measure FBP of a limb that is performing exercise. As such, movement artifact and changes in the finger cuff position could influence the recordings. Movement could have led to the blood pressure cuff to be misalign on the finger. Alignment of the photocell is essential for the measurement of finger arterial blood pressure. If only a portion of light travelled through the digital arteries the then recorded blood pressure would be overestimated. On the other hand, movement artifact that could have occurred from compression of any of the tubes attached to the Portapres® device or blood pressure cuff could lead to overestimations of the recorded arterial blood pressure within the finger. Researchers attempted to minimize these possible confounding factors by bracing the hand to limit the amount of finger flexion and cord movement during exercise, although these factors cannot be eliminated from having affected the recordings. Another assumption made in this study is within specific aim II. One main assumption was made in model III and IV. These models assumed that all participants had the same cardiac pulse delay and length. An example of the modeling

limitations can be seen in Figure 27 in Chapter 5 of this thesis. In the calculated cardiac pulse pressure at 90 rpm the calculated pressure does not go down to zero in between each heartbeat. This is due to the heartbeats occurring closer together than the model can account for. With a constant 0.5 second pulse length, any heart rate above 120 beats per minute would have some cardiac pulse curves overlapping.

6.9 Future Direction of Research

This thesis explored the effect of movement-related forces on the finger arterial blood pressure response during ACE. The study showed that an increase in arm cranking cadence was associated with an increase in finger arterial blood pressure and that some of that increase was related to movement-related forces. However, the lack of statistical power did not allow for conclusions regarding the exercise intensity specificity of the effect of movement-related forces on the MAP, as well as changes in base and cardiac pulse pressure related to the increase in arm cranking cadence. More research is needed to understand the role of the muscle pump on increases in MAP during arm crank exercise, including its effect on changes in cardiac output and the efficiency of the muscle pump at different intensities of exercise. More research can also be done to understand why when evaluating rhythmical movement like ACE the increase found with an increase cadence is not completely accounted for by the increase in movement-related pressure, as it was seen with evaluating more simple movement such as shoulder flexion. In this thesis, movement-related pressure only accounted for ~ 20 % of the increase between ACE cadences, while Sheriff et al. [13] were able to account for all of the increases observed in FBP.

Understanding factors that can change MAP, and in associated blood flow during exercise can aid in creating optimal exercise treatment plans. For example, the knowledge of the factors that can influence MAP, and blood flow during exercise could be applied to the treatment modalities of individuals suffering from peripheral arterial disease (PAD). PAD is a serious cardiovascular condition, which is primarily characterized as the build-up of atherosclerotic plaque in the arteries of the lower legs[58]. PAD affects approximately 12% of the general adult population and upwards of 20% of people over the age of 75 [59] . When symptomatic, PAD most commonly presents as pain in the legs known as intermittent claudication [60] . Intermittent claudication is thought to be caused by a reduction in blood perfusion to muscles due to plaque build-up [59]. Currently, exercise, mainly walking, is one form of treatment for the management of PAD [59–61]. The main goal of the walking program is to increase walking distance and time without

experiencing pain. Research has shown that walking, cycling and arm cranking have all been able to improve an individual's walking performance [62–64,64–66]. In one study by Walker et al[64], both upper body and lower body cycling training programs significantly improved the length of pain-free and maximum walking distances ($p<0.001$) [64]. The underlying mechanism that aids in the improvement in walking performance has yet to be identified. Exercise training can lead to increases in cardiac stroke volume, which has been known to account for the rapid improvement in cardiorespiratory capacity [63]. Exercise training can also lead to changes in nitric oxide metabolism and endothelial vasoreactivity, and could also enhance microcirculatory blood flow to exercising skeletal muscles[63]. A study performed by Gardner et al (2004)[62] showed that individuals who performed both high and low intensity walking exercise programs showed a significant increase in perfusion of the calf muscles post exercise ($p<0.05$)[62]. Increased limb blood flow may result in increased oxygen supply and perfusion, reduced submaximal VO_2, improved walking economy and reduced claudication pain [65]. Research in this field has yet to explore the local effects of movement on the blood flow response and the changes in walking performance. If walking performance is improved via an increase in muscle blood flow, understanding all mechanisms that can increase limb blood flow will aid in the quality of life of these individuals.

6.10 Conclusion

It can be concluded from this study that finger arterial blood pressure increased with a higher arm cranking cadence (16 mm Hg between 45 and 90 rpm). The movement-related forces have been shown to account for 3 mm Hg or 19 % of the increase in recorded MAP between 45 rpm and 90 rpm. These findings provide evidence that frequency of movement during exercise can be a factor in the increased finger arterial MAP during arm cranking.

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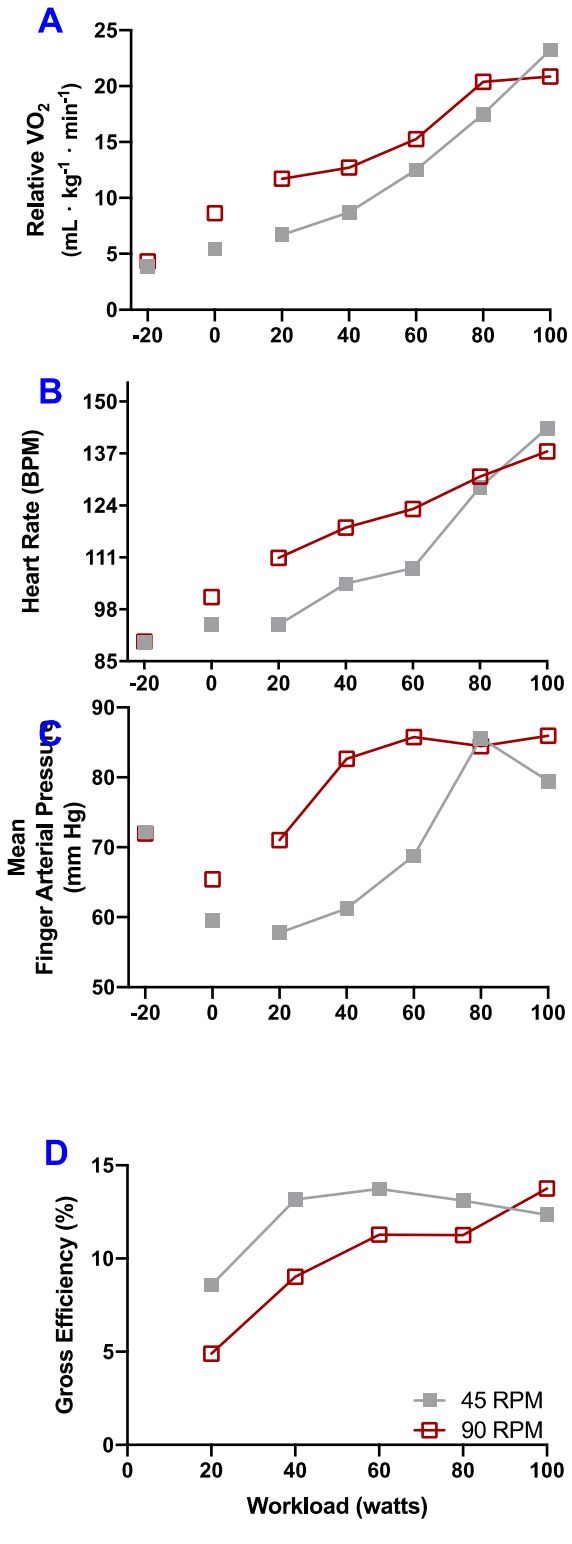
APPENDIX A: INDIVIDUAL PARTICIPANT RESULTS

SUBJECT 003



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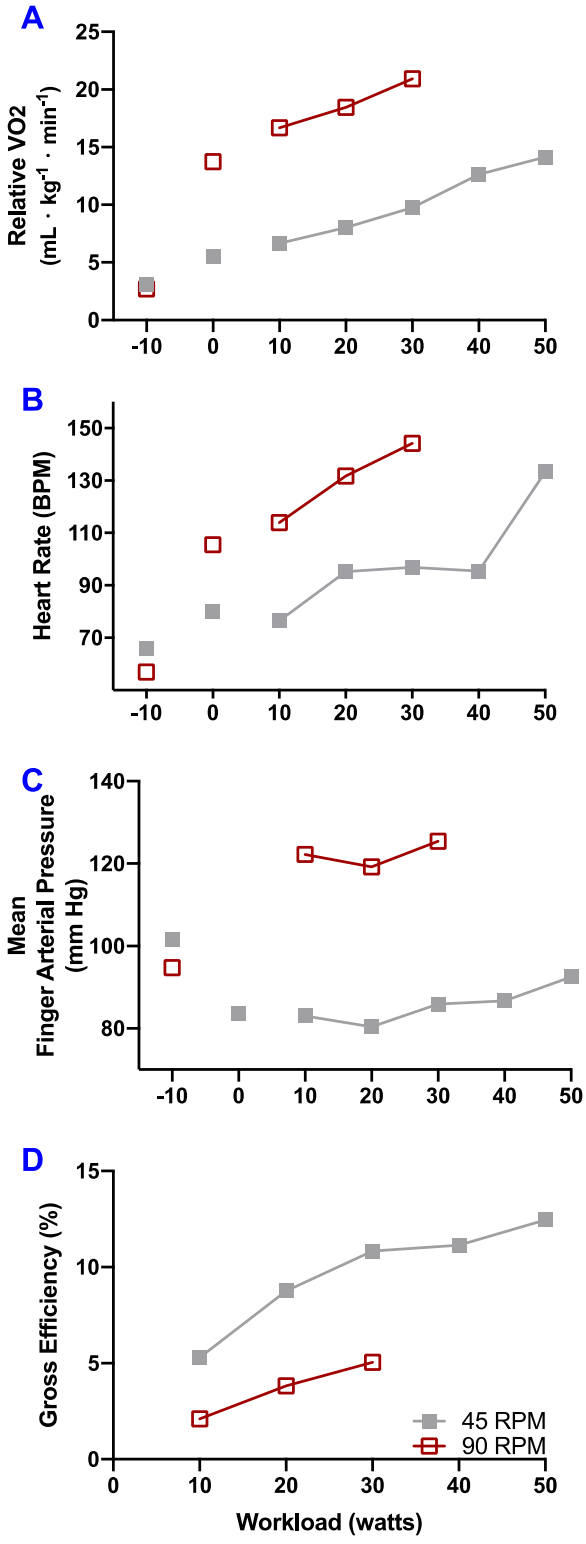
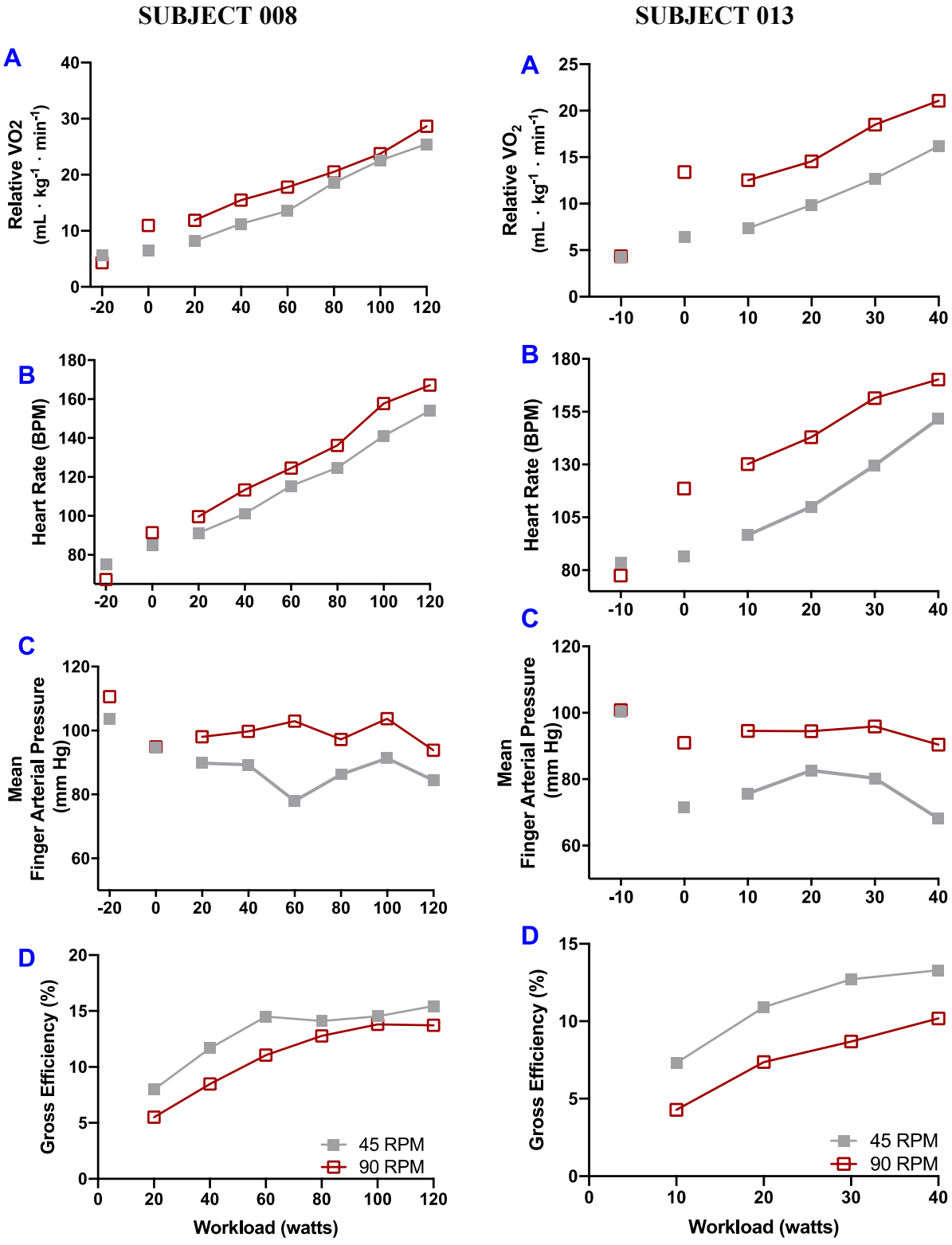
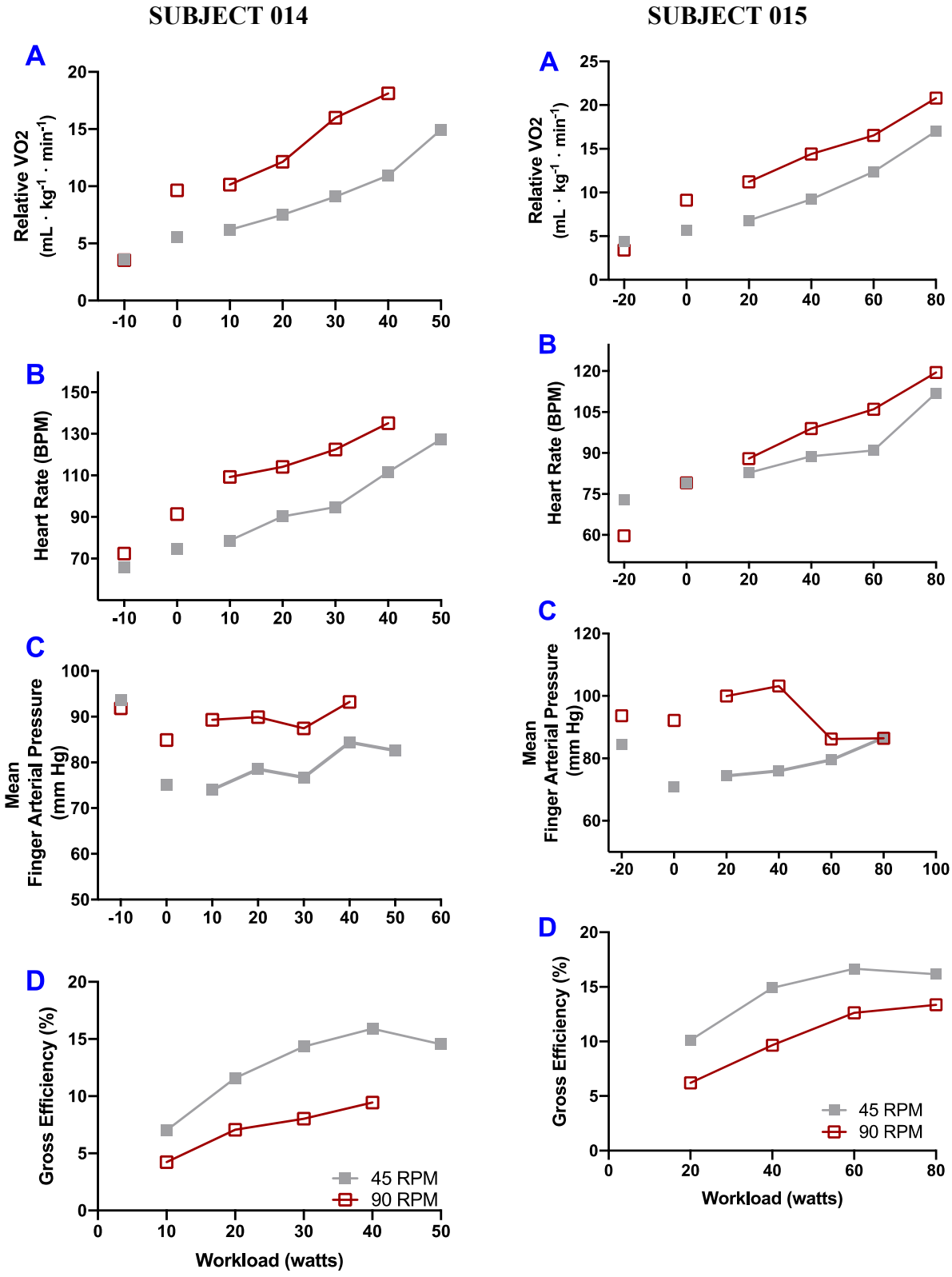
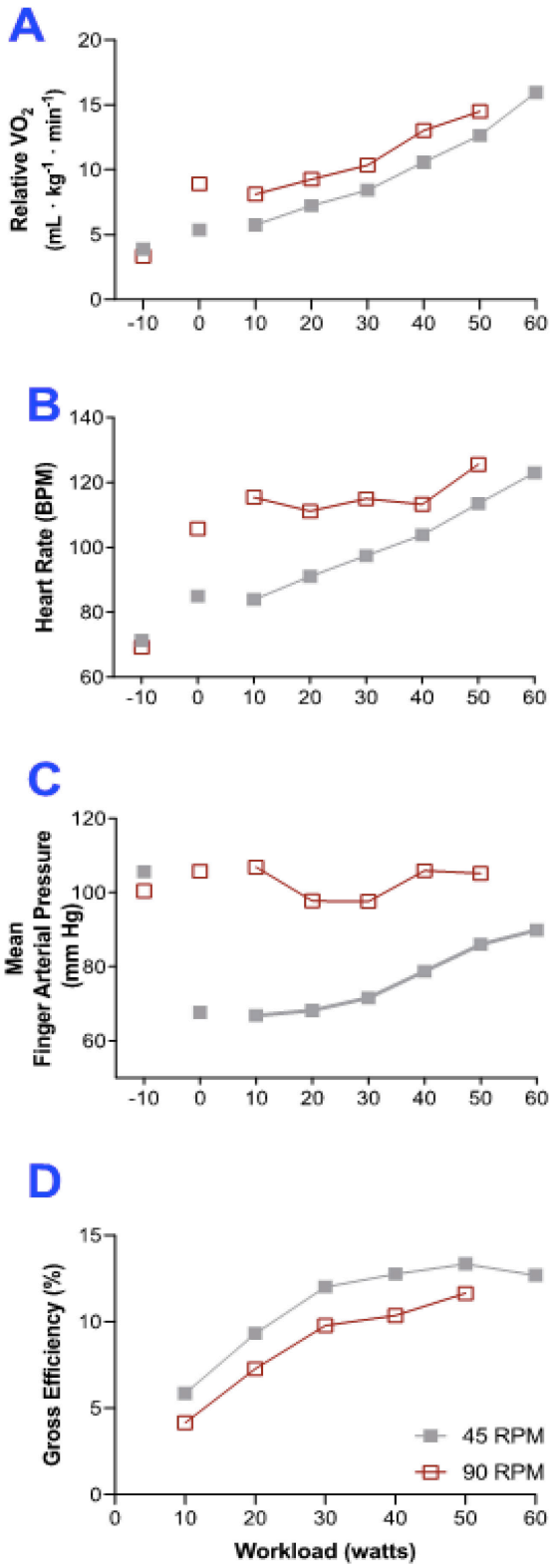


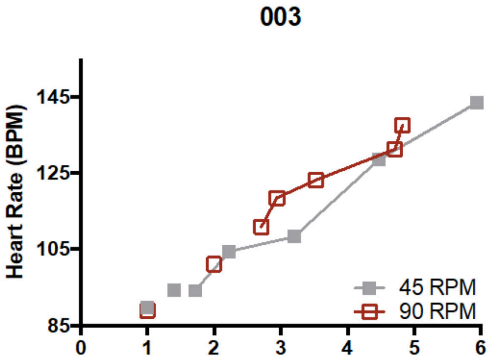

SUBJECT 008
SUBJECT 013
A
B
C
D
Relative VO2 (mL · kg-1 · min-1)
Relative VO2 (mL · kg-1 · min-1)
Heart Rate (BPM)
Mean Finger Arterial Pressure (mm Hg)
Gross Efficiency (%)
45 RPM
90 RPM
Workload (watts)

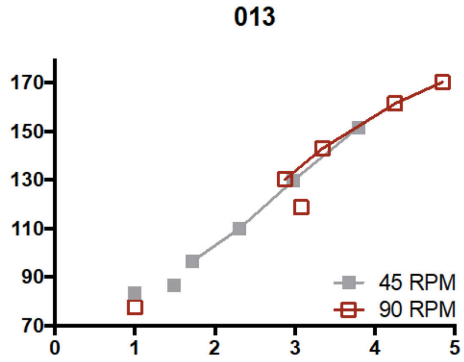

SUBJECT 014
SUBJECT 015
A
B
C
D
Relative VO2
(mL · kg-1 · min-1)
Heart Rate (BPM)
Mean
Finger Arterial Pressure
(mm Hg)
Gross Efficiency (%)
45 RPM
90 RPM
Workload (watts)

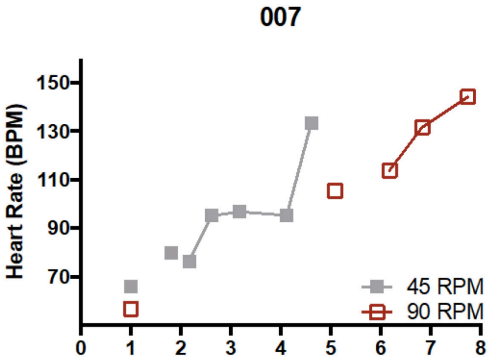
SUBJECT 010

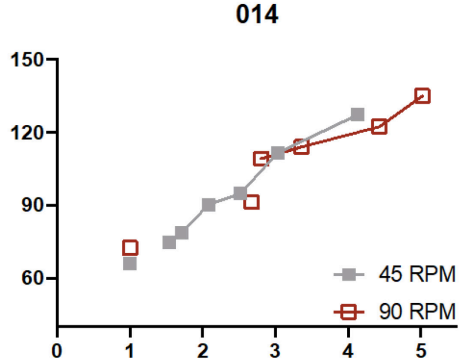

A
Relative VO_2 ($mL \cdot kg^{-1} \cdot min^{-1}$)
20
15
10
5
0
-10
0
10
20
30
40
50
60
B
Heart Rate (BPM)
140
120
100
80
60
C
Mean Finger Arterial Pressure (mm Hg)
120
100
80
60
D
Gross Efficiency (%)
15
10
5
0
45 RPM
90 RPM
Workload (watts)

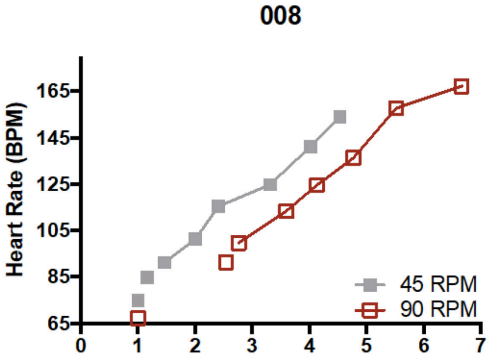
APPENDIX B: HEART RATE VERSUS METS

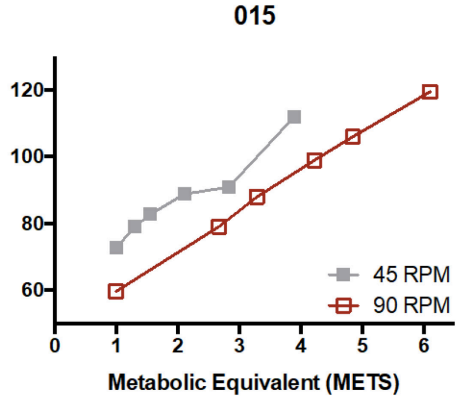


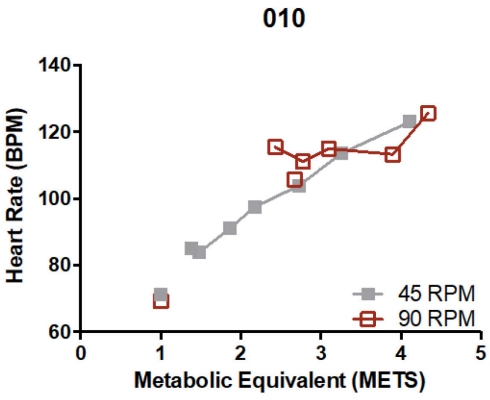




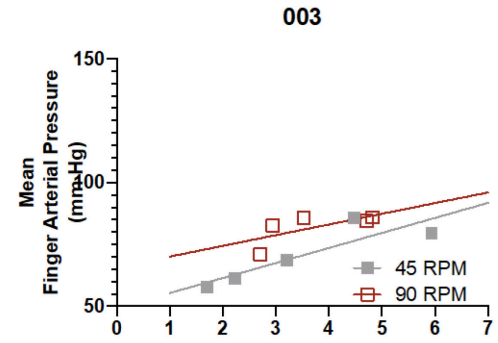


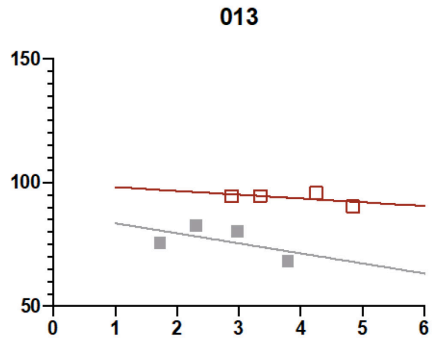


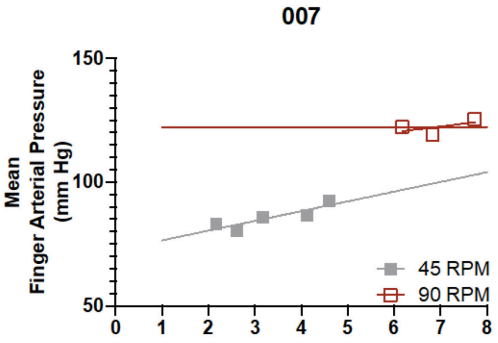


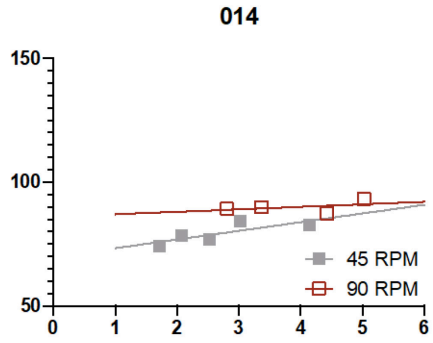


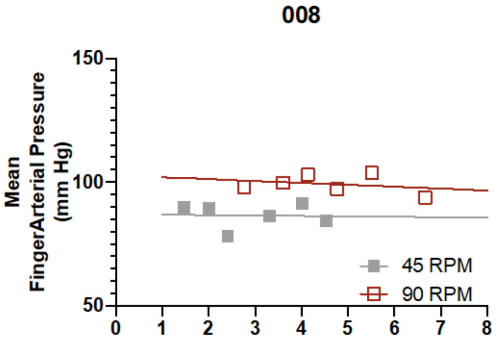
APPENDIX C: MAP VERSUS METS

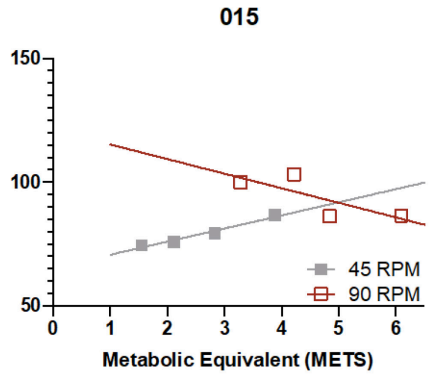


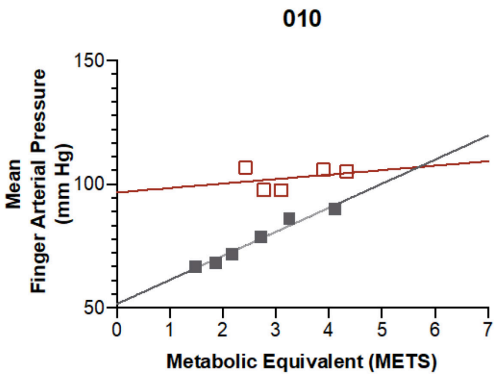




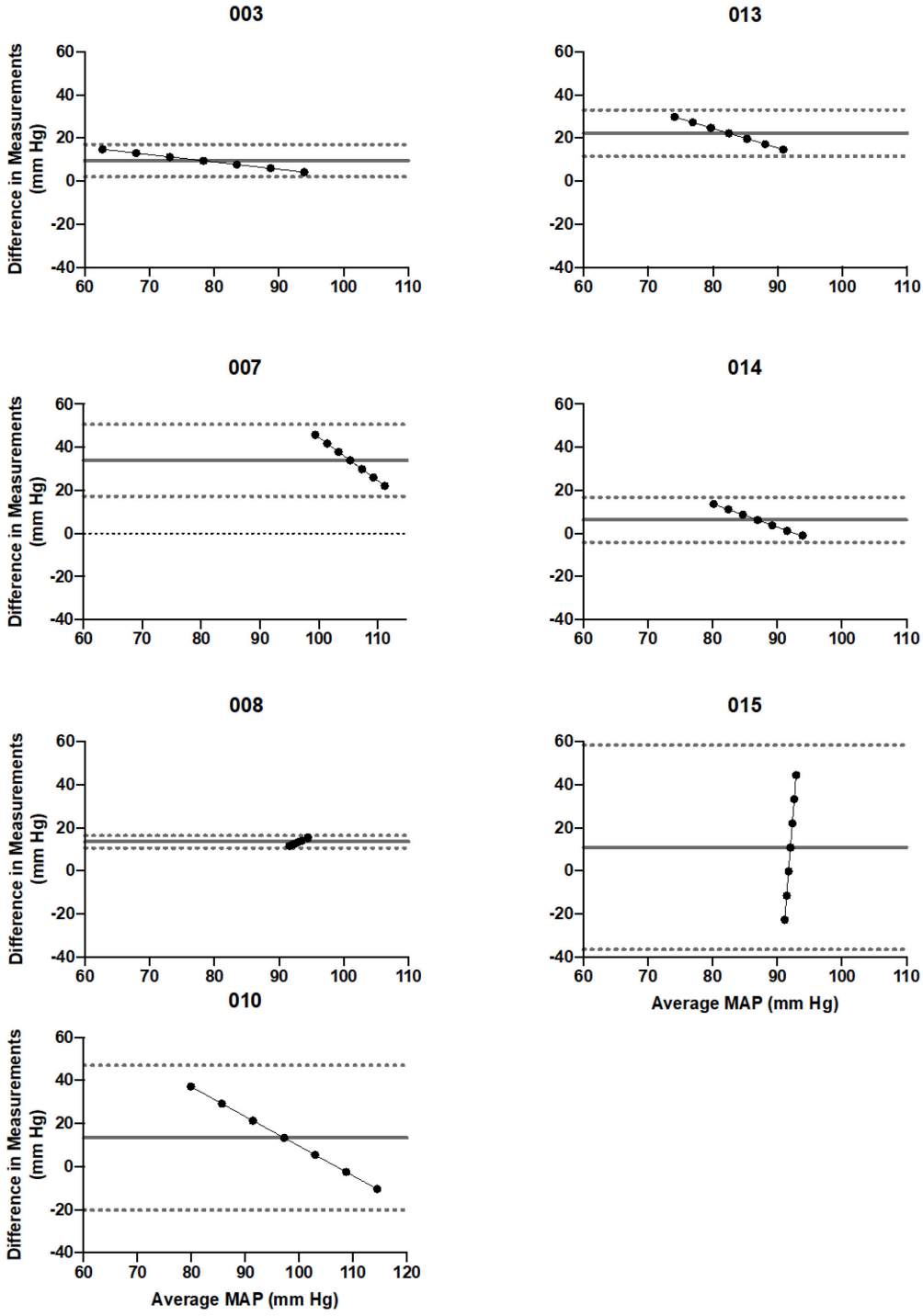








APPENDIX D: BLAND-ALTMAN ANALYSIS OF DIFFERENCES



APPENDIX E: PARTICIPANT MODEL COMPONENTS

Model III: Orthostatic + Movement Related, External Work Specific Base and Cardiac Pulse Pressures

45 rpm:

Stage		Specifics		Rest		Warm-Up		Stage One		Stage Two		Stage Three		Stage Four		Stage Five		Stage Six	
Component		Delay (s)	P.L (s)	Base	C.P	Base	C.P	Base	C.P	Base	C.P	Base	C.P	Base	C.P	Base	C.P	Base	C.P
Subject	3	0.2	0.5	67	46	56	29	56	21	62	17	68	20	87	10	85	4		
	7	0.2	0.5	76	50	78	41	78	33	85	30	87	26	94	19				
	8	0.2	0.5	91	72	92	45	87	42	88	40	78	29	88	23	92	23	48	22
	10	0.2	0.5	86	57	71	32	71	30	72	30	72	26	80	30	86	30	84	28
	13	0.2	0.5	78	48	77	22	79	25	86	23	87	16	78	10				
	14	0.2	0.5	69	55	75	39	76	29	80	31	79	30	86	29	86	26		
	15	0.2	0.5	70	44	73	38	75	38	78	33	79	33	93	24				

Delay: delay before cardiac pulse, P.L: pulse length, s: seconds, Base: calculated base pressure (mm Hg), C.P: calculated cardiac pulse amplitude (mm Hg),

90 rpm:

Stage		Specifics		Rest		Warm-Up		Stage One		Stage Two		Stage Three		Stage Four		Stage Five		Stage Six	
Component		Delay (s)	P.L (s)	Base	C.P	Base	C.P	Base	C.P	Base	C.P	Base	C.P	Base	C.P	Base	C.P	Base	C.P
Subject	3	0.2	0.5	44	54	52	31	56	26	76	6	72	18	74	17	75	18		
	7	0.2	0.5	65	53			68	7	107	39	114	43						
	8	0.2	0.5	67	66	80	66	88	52	90	47	96	38	91	36	101	26	96	13
	10	0.2	0.5	89	24	114	12	106	5	104	9	112	7	115	61	75	47		
	13	0.2	0.5	80	45	95	14	94	16	100	13	100	17	99	9				
	14	0.2	0.5	72	42	89	12	87	25	87	30	85	28	92	29				
	15	0.2	0.5	73	44	92	29	101	22	100	26	84	26	88	26				

Delay: delay before cardiac pulse, P.L: pulse length, s: seconds, Base: calculated base pressure (mm Hg), C.P: calculated cardiac pulse amplitude (mm Hg),

Model IV: Orthostatic, Movement Related, Constant Base and Cardiac Pulse Pressures

45 rpm:

		Specifics		Rest		Warm-Up		Stage One		Stage Two		Stage Three		Stage Four		Stage Five		Stage Six	
		Delay (s)	P.L (s)	Base	C.P	Base	C.P	Base	C.P	Base	C.P	Base	C.P	Base	C.P	Base	C.P	Base	C.P
Subject	3	0.2	0.5	67	46	67	17	67	10	67	12	67	20	67	29	67	21		
	7	0.2	0.5	73	53	73	47	73	38	73	42	73	40	73	40				
	8	0.2	0.5	91	72	91	47	91	38	91	37	91	15	91	20	91	24	91	21
	10	0.2	0.5	82	62	82	21	82	20	82	19	82	16	82	29	82	34	82	31
	13	0.2	0.5	78	48	78	21	78	27	78	32	78	26	78	10				
	14	0.2	0.5	69	55	69	45	69	36	69	42	69	40	69	46	69	43		
	15	0.2	0.5	70	44	70	42	70	43	70	42	70	42	70	47				

Delay: delay before cardiac pulse, P.L: pulse length, s: seconds, Base: calculated base pressure (mm Hg), C.P: calculated cardiac pulse amplitude (mm Hg),

90 rpm:

		Specifics		Rest		Warm-Up		Stage One		Stage Two		Stage Three		Stage Four		Stage Five		Stage Six	
		Delay (s)	P.L (s)	Base	C.P	Base	C.P	Base	C.P	Base	C.P	Base	C.P	Base	C.P	Base	C.P	Base	C.P
Subject	3	0.2	0.5	44	54	44	40	44	38	44	39	44	46	44	47	44	49		
	7	0.2	0.5	65	53			65	10	65	81	65	92						
	8	0.2	0.5	67	66	67	79	67	73	67	70	67	68	60	60	67	60	67	42
	10	0.2	0.5	89	24	89	31	89	27	89	25	89	25	89	52	89	50		
	13	0.2	0.5	80	45	80	29	80	30	80	34	80	37	80	28				
	14	0.2	0.5	72	42	72	29	72	41	72	45	72	41	72	50				
	15	0.2	0.5	73	44	73	47	73	50	73	52	73	37	73	40				

Delay: delay before cardiac pulse, P.L: pulse length, s: seconds, Base: calculated base pressure (mm Hg), C.P: calculated cardiac pulse amplitude (mm Hg),

Model V: Orthostatic, Movement Related, External Work Specific Base and Participant Specific Cardiac Pulse Pressures

45 rpm:

		Specifics		Rest		Warm-Up		Stage One		Stage Two		Stage Three		Stage Four		Stage Five		Stage Six	
		Delay (s)	P.L (s)	Base	C.P	Base	C.P	Base	C.P	Base	C.P	Base	C.P	Base	C.P	Base	C.P	Base	C.P
Subject	3	0.2	0.5	67	46	56	29	56	21	62	17	68	20	87	10	85	4		
	7	0.125	0.55	75	51	76	50	78	41	78	34	83	32	94	27				
	8	0.15	0.4	91	72	92	45	87	42	88	40	78	29	88	23	92	23	48	22
	10	0.3	0.5	86	57	87	32	71	30	71	30	72	26	72	31	80	30	85	28
	13	0.2	0.45	78	48	77	50	79	22	86	25	87	23	78	16				
	14	0.15	0.5	69	55	75	39	76	29	80	31	78	31	86	30	86	26		
	15	0.15	0.55	70	44	67	38	73	38	75	33	78	33	92	25				

Delay: delay before cardiac pulse, P.L: pulse length, s: seconds, Base: calculated base pressure (mm Hg), C.P: calculated cardiac pulse amplitude (mm Hg),

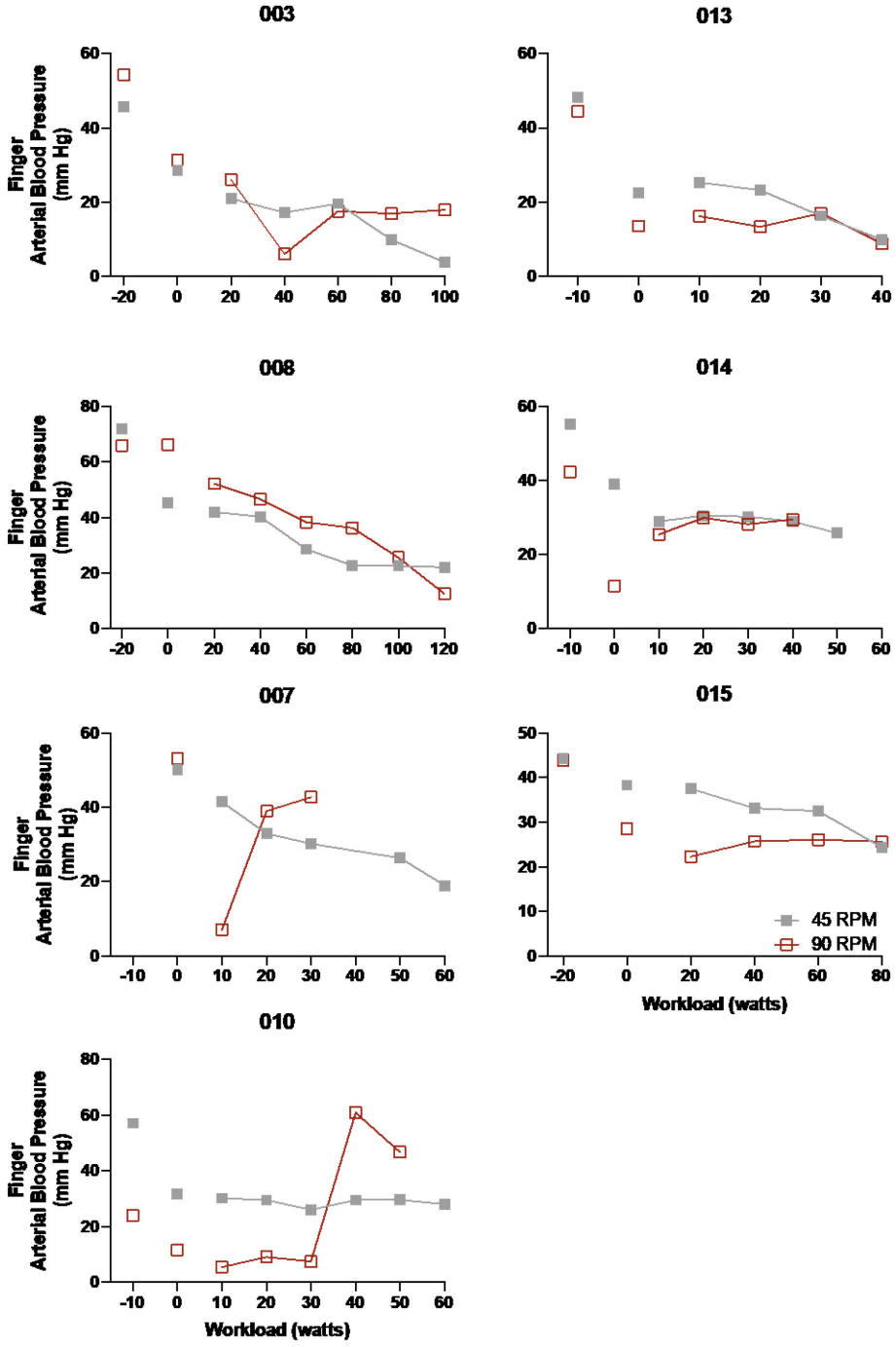
90 rpm:

		Specifics		Rest		Warm-Up		Stage One		Stage Two		Stage Three		Stage Four		Stage Five		Stage Six	
		Delay (s)	P.L (s)	Base	C.P	Base	C.P	Base	C.P	Base	C.P	Base	C.P	Base	C.P	Base	C.P	Base	C.P
Subject	3	0.15	0.45	44	54	52	31	56	26	76	6	70	19	74	16	74	19		
	7	0.15	0.45	65	53			67	8	107	39	114	43						
	8	0.15	0.35	67	66	83	63	88	52	90	47	97	37	91	37	101	26	96	13
	10	0.25	0.5	91	22	103	19	116	7	111	4	106	8	107	7	81	61		
	13	0.15	0.35	90	8	104	1	98	4	106	2	109	3	103	3				
	14	0.15	0.45	83	5	89	6	97	4	95	6	96	4	101	4				
	15	0.15	0.6	73	44	92	29	101	22	96	26	83	27	88	26				

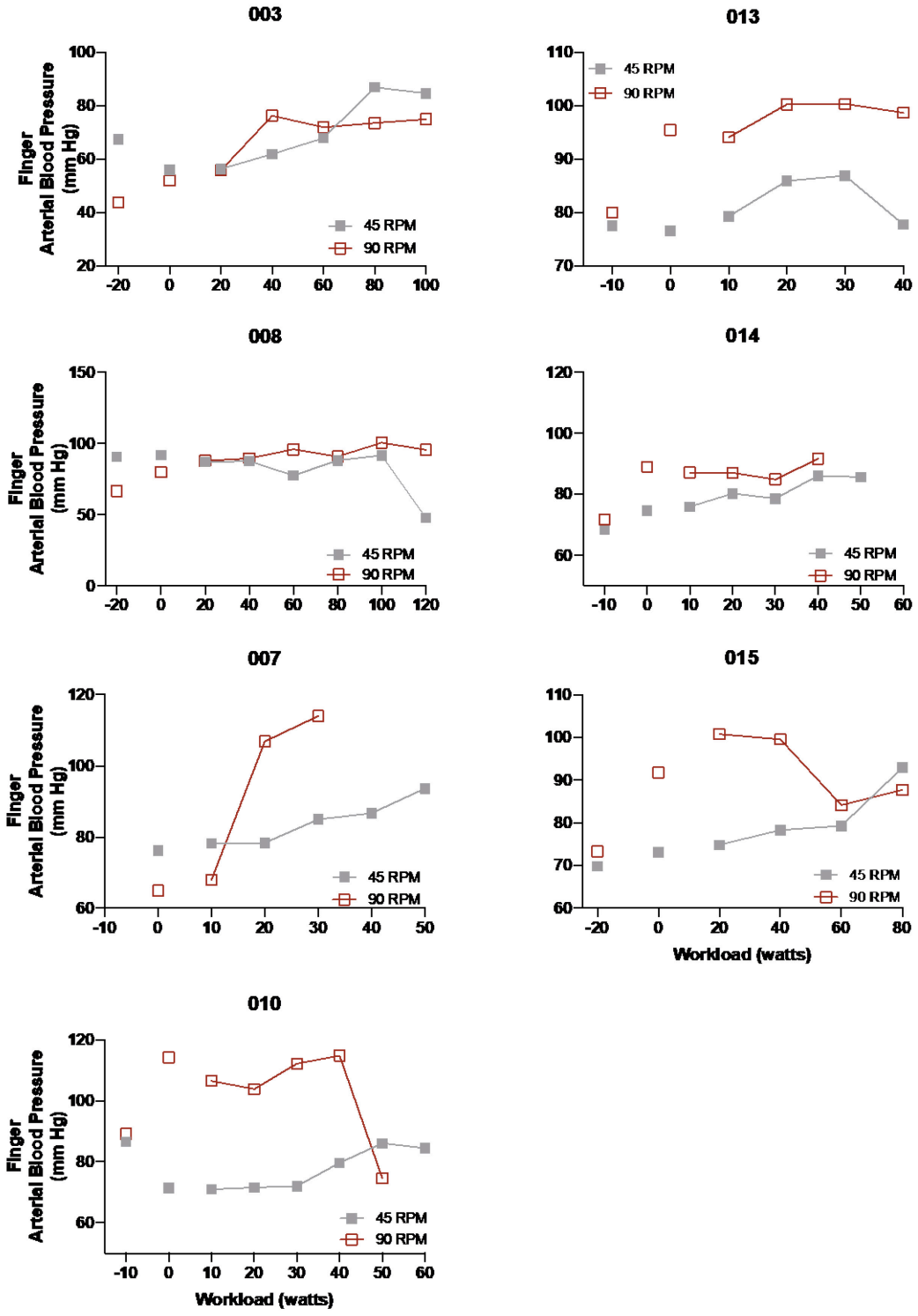
Delay: delay before cardiac pulse, P.L: pulse length, s: seconds, Base: calculated base pressure (mm Hg), C.P: calculated cardiac pulse amplitude (mm Hg),

APPENDIX F: BASE AND CARDIAC PULSE PRESSURE

Calculated cardiac pulse pressures from Model III for each external load for each participant at each cadence .

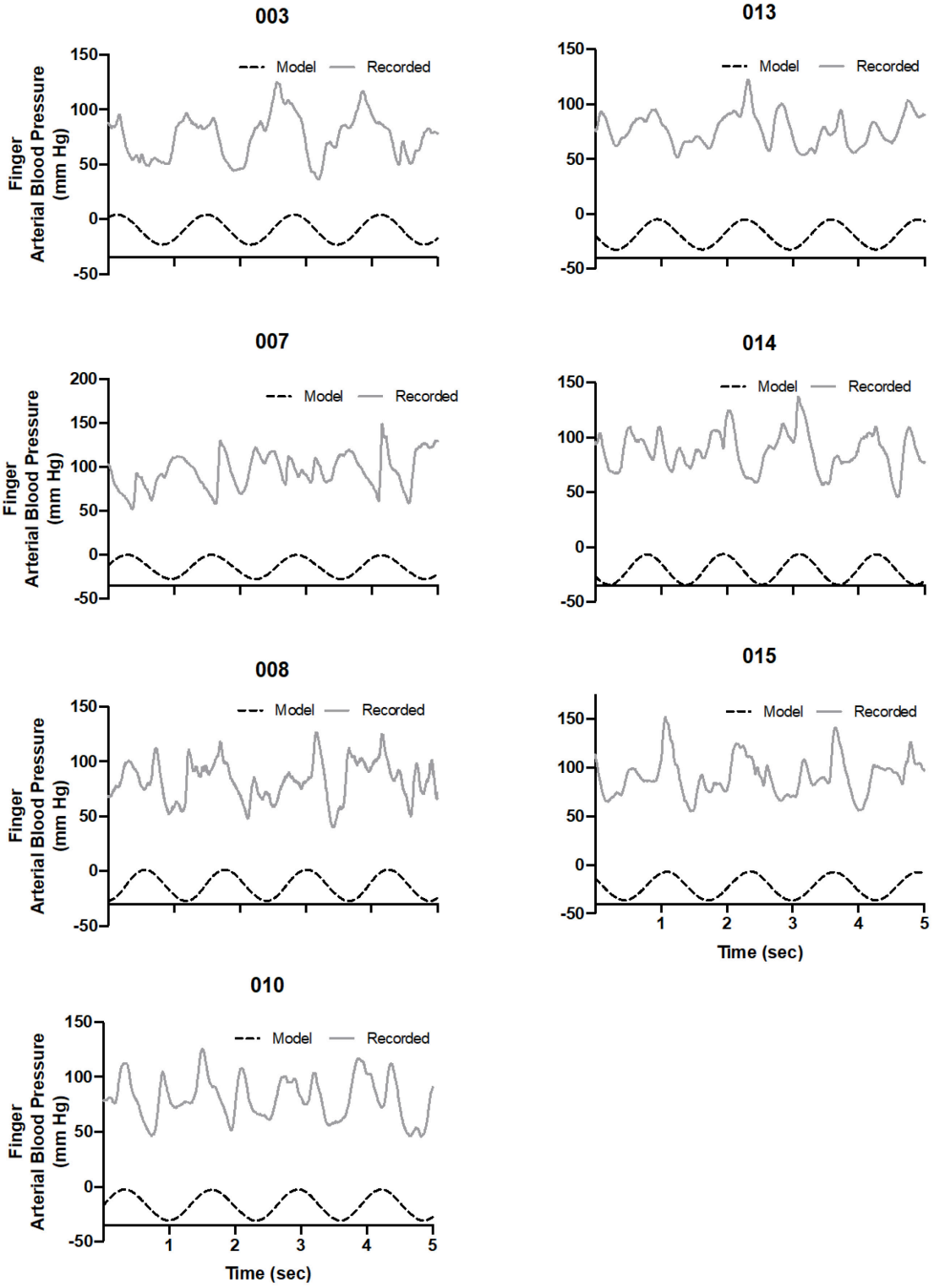


Calculated base pressure from Model III for each external load for each participant at both cadences.

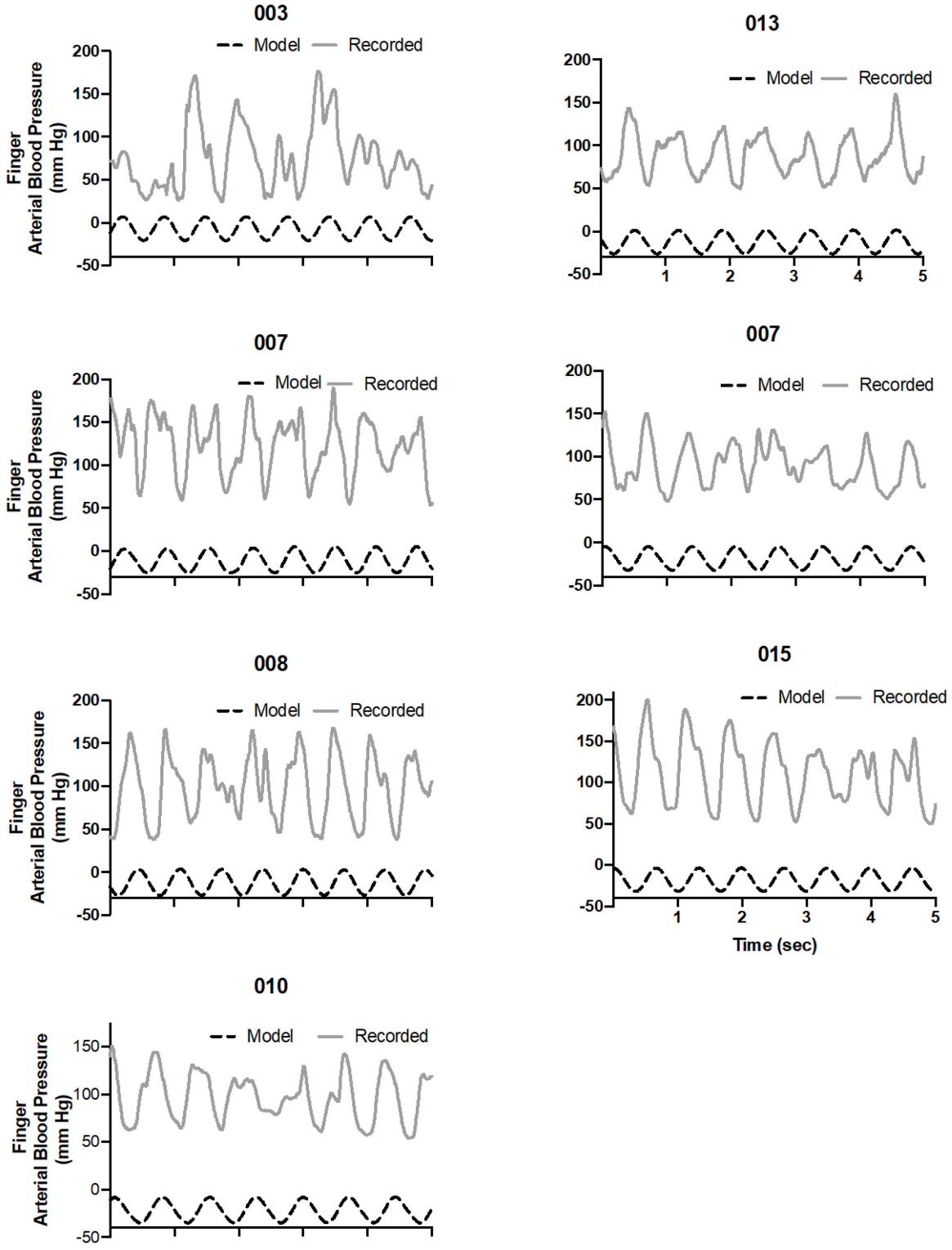


APPENDIX G: CALCULATED MODELS OF FBP

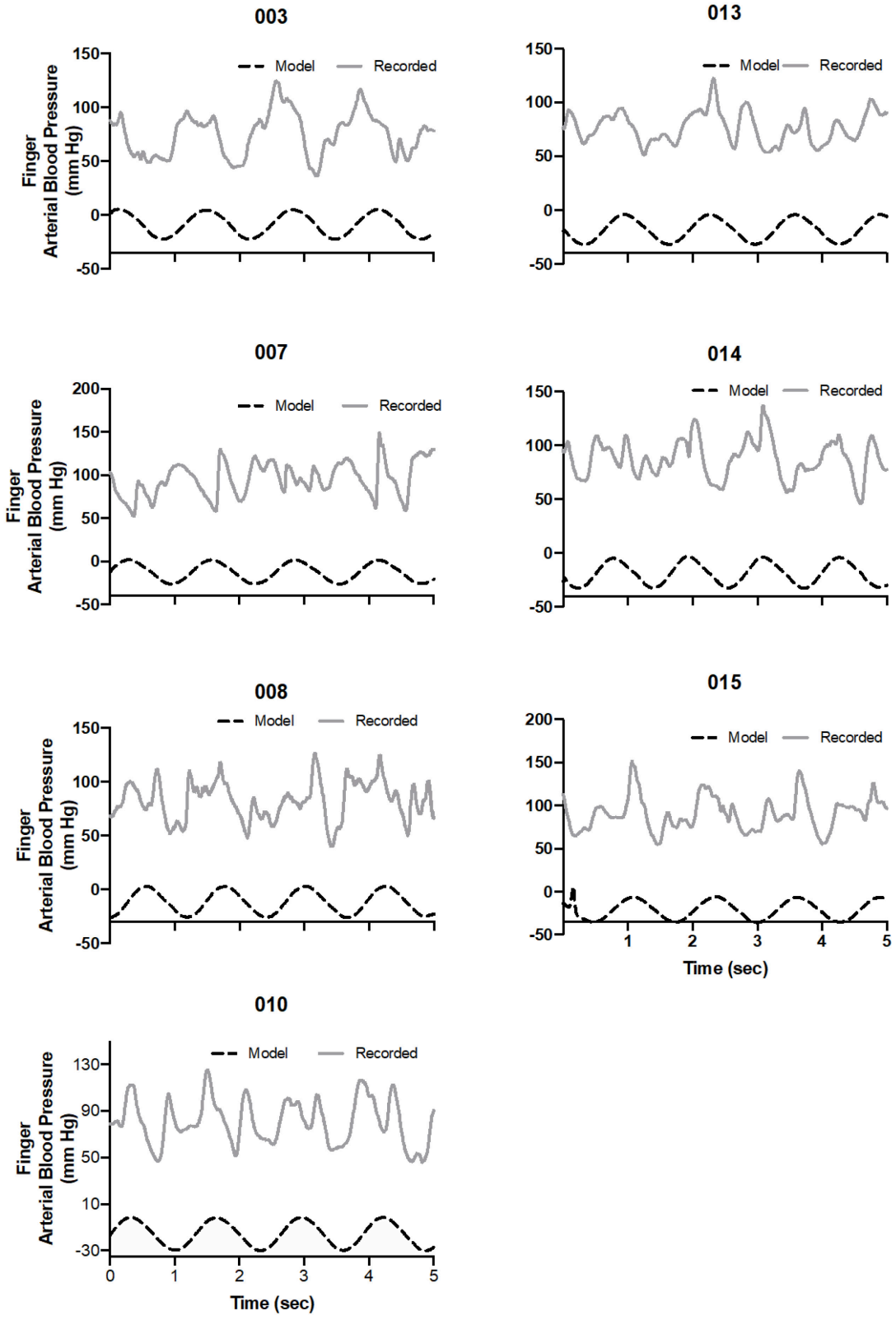
Model I: Orthostatic Pressure (45 rpm)



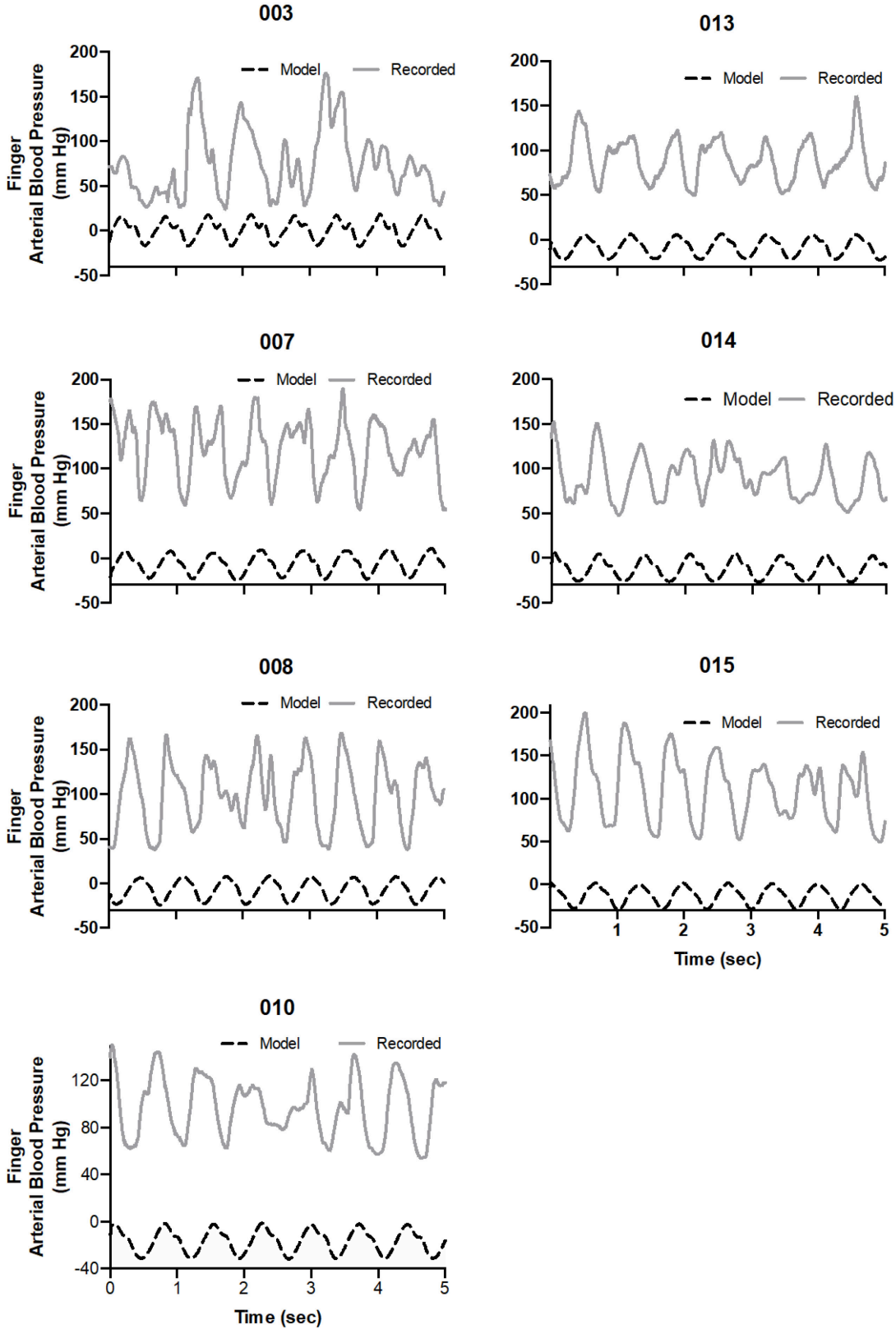
Model I: Orthostatic Pressure (90 rpm)



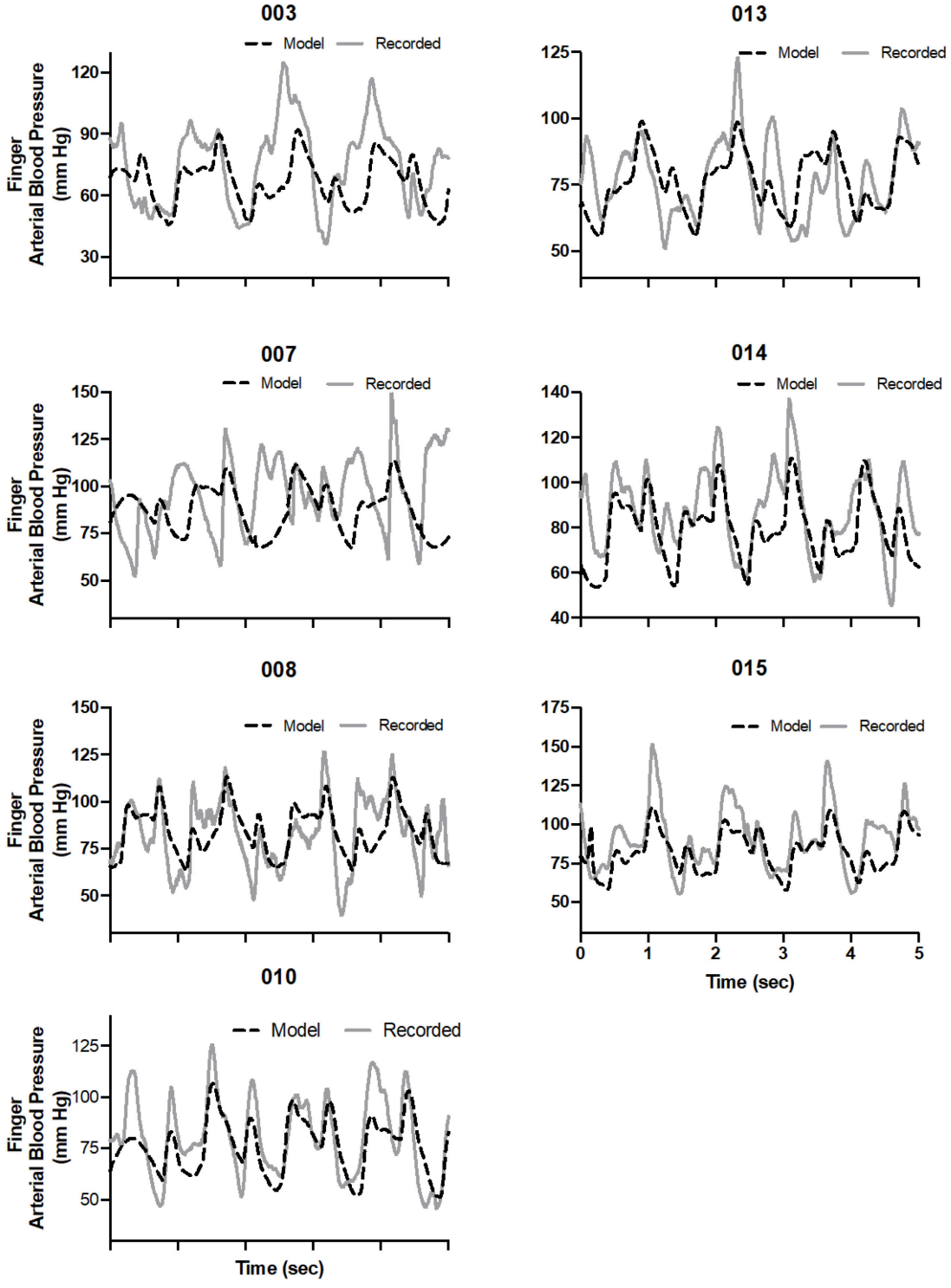
Model II: Orthostatic + Movement Related Pressure (45 rpm)



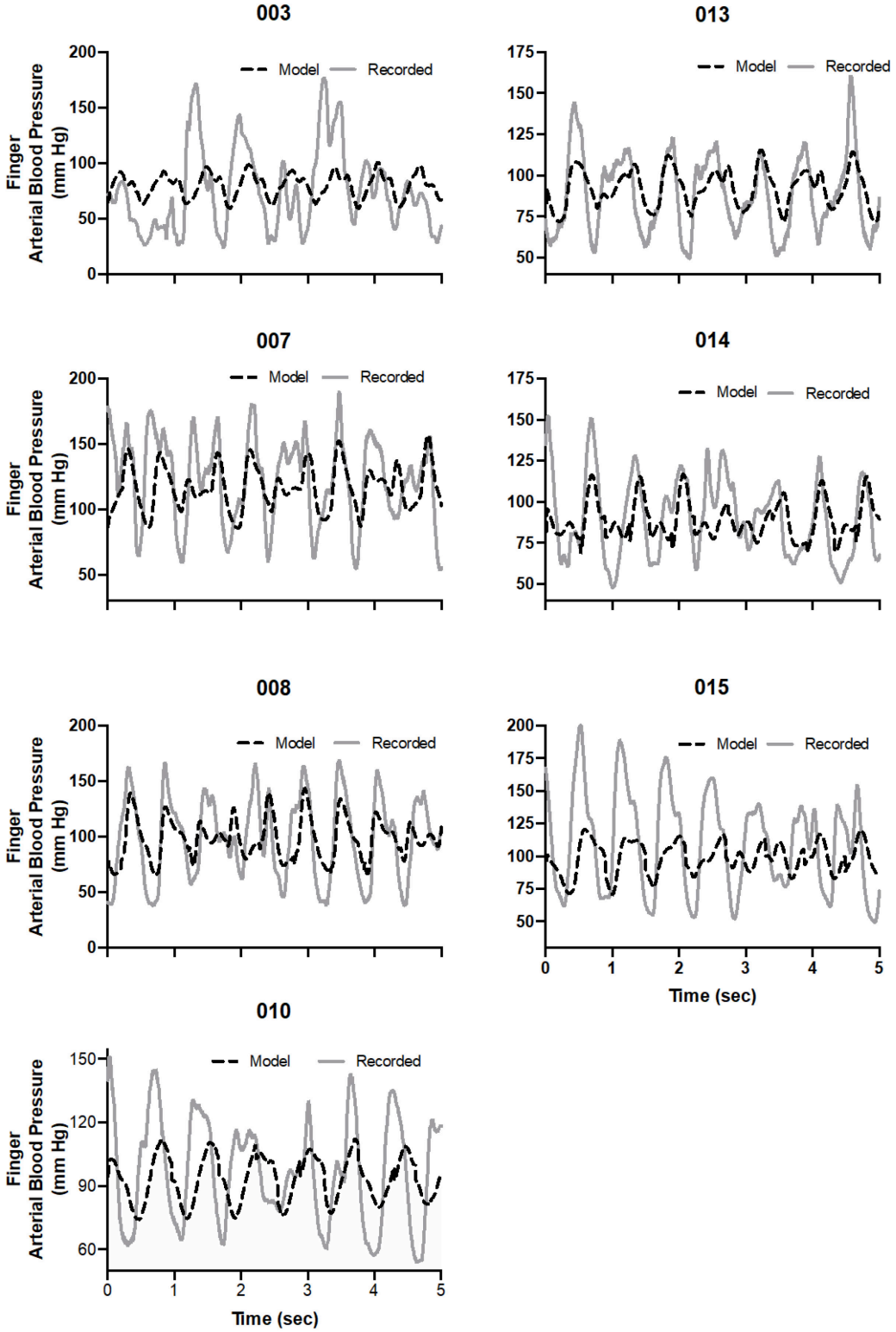
Model II: Orthostatic + Movement Related Pressure (90 rpm)



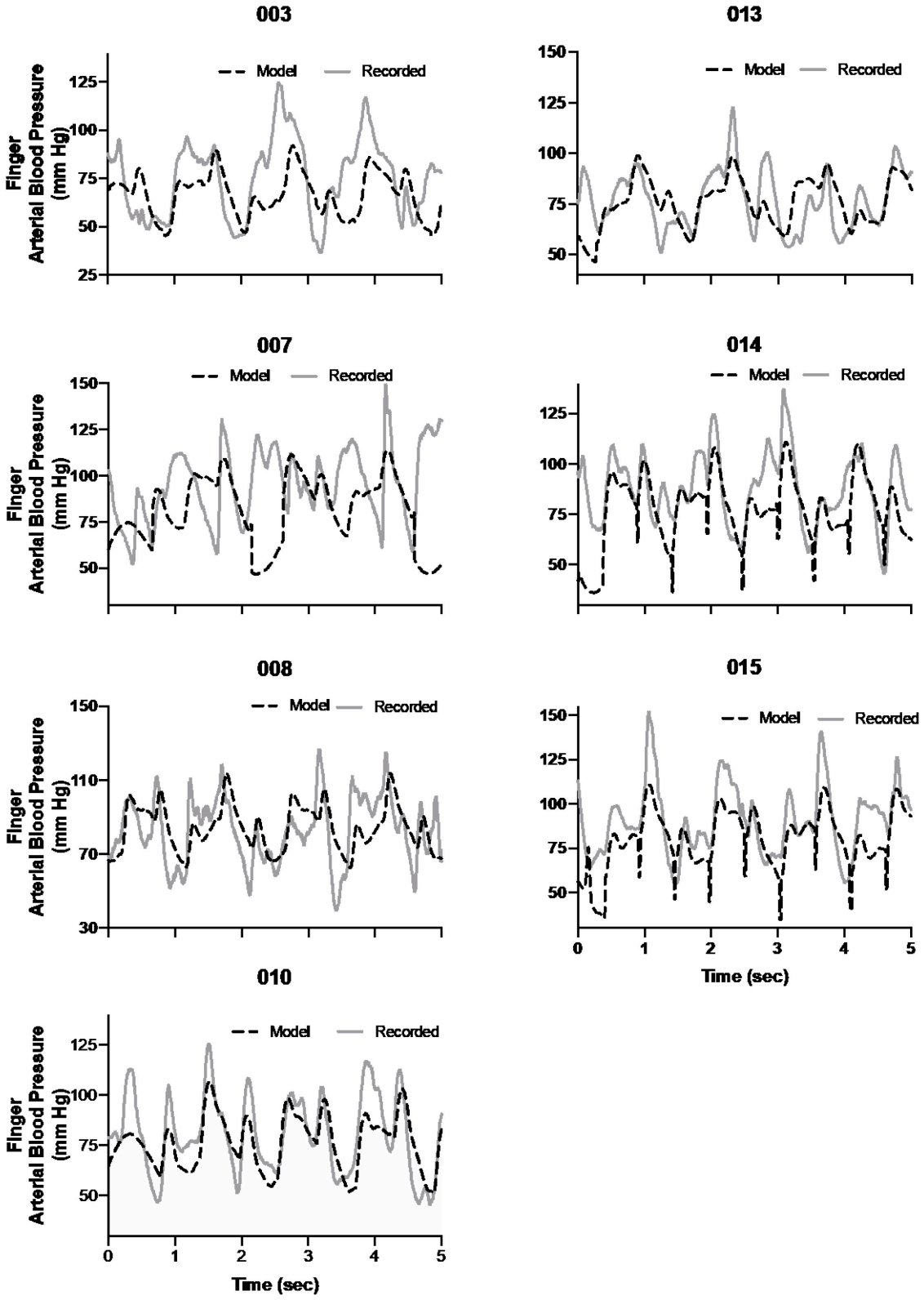
Model III: Orthostatic+ Movement-Related, External Work Specific Base + Cardiac Pulse Pressures (45 rpm)



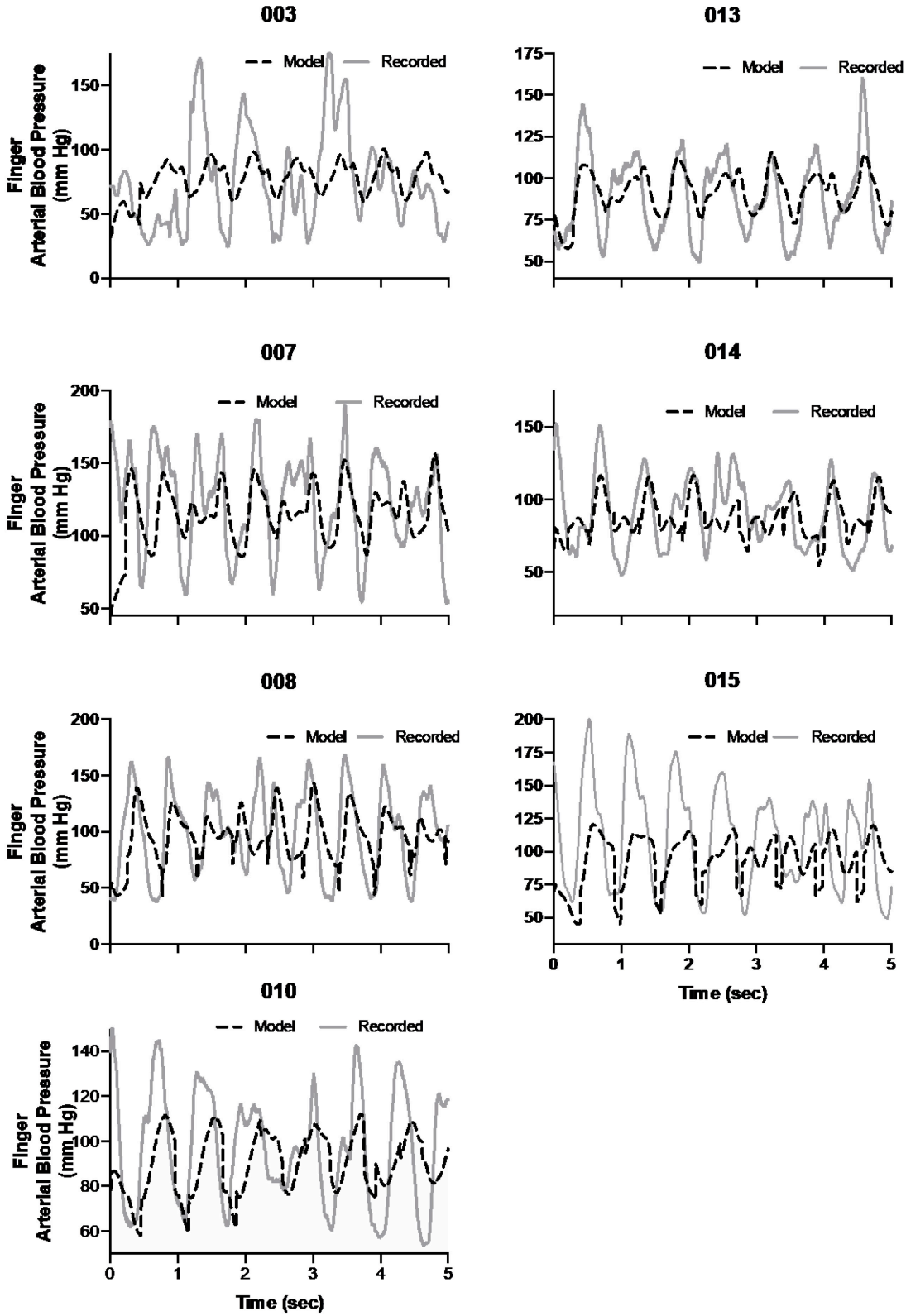
Model III: Orthostatic+ Movement-Related, External Work Specific Base + Cardiac Pulse Pressures (90 rpm)



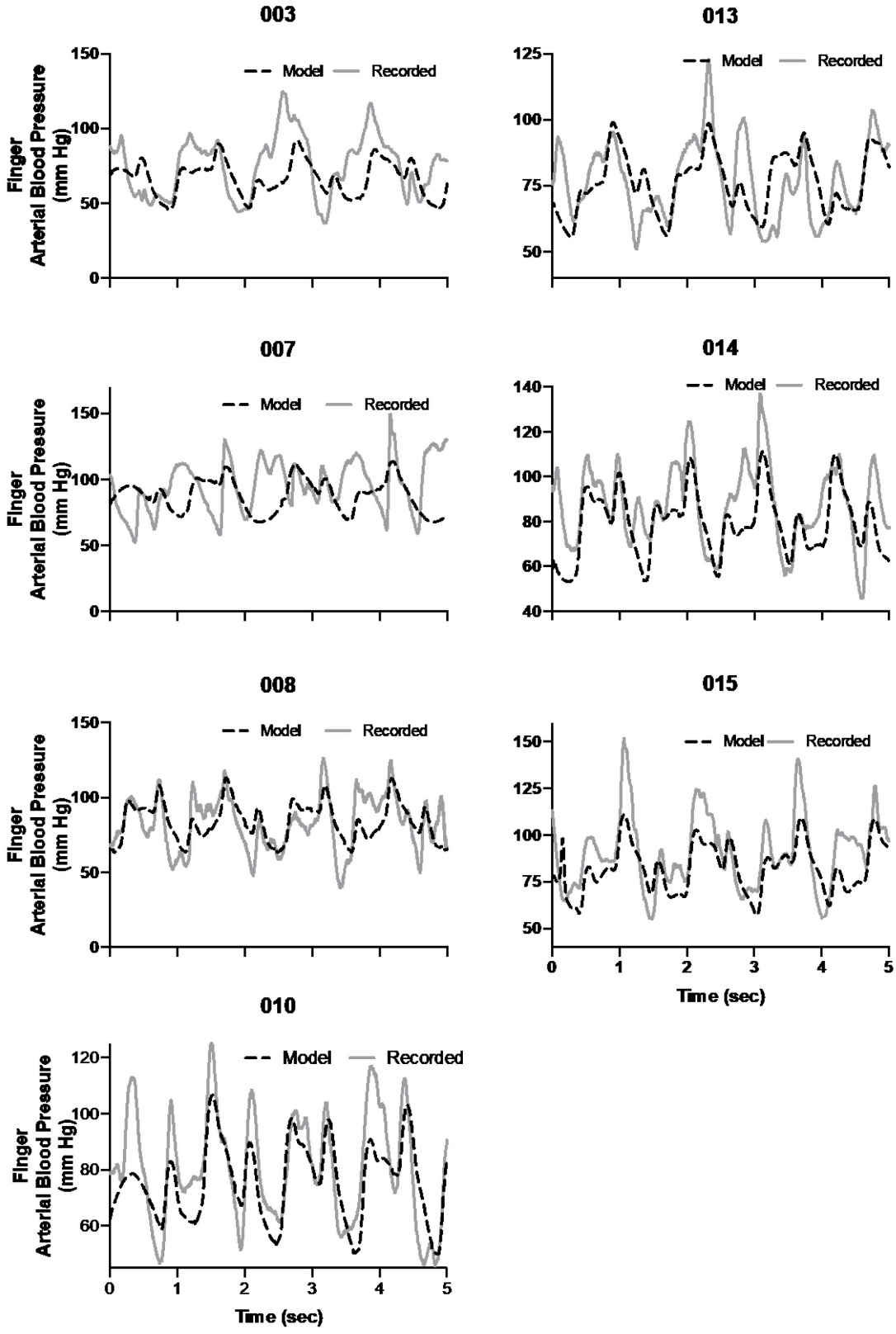
Model IV: Orthostatic + Movement-Related+ Constant Base + Cardiac Pulse Pressure (45 rpm)



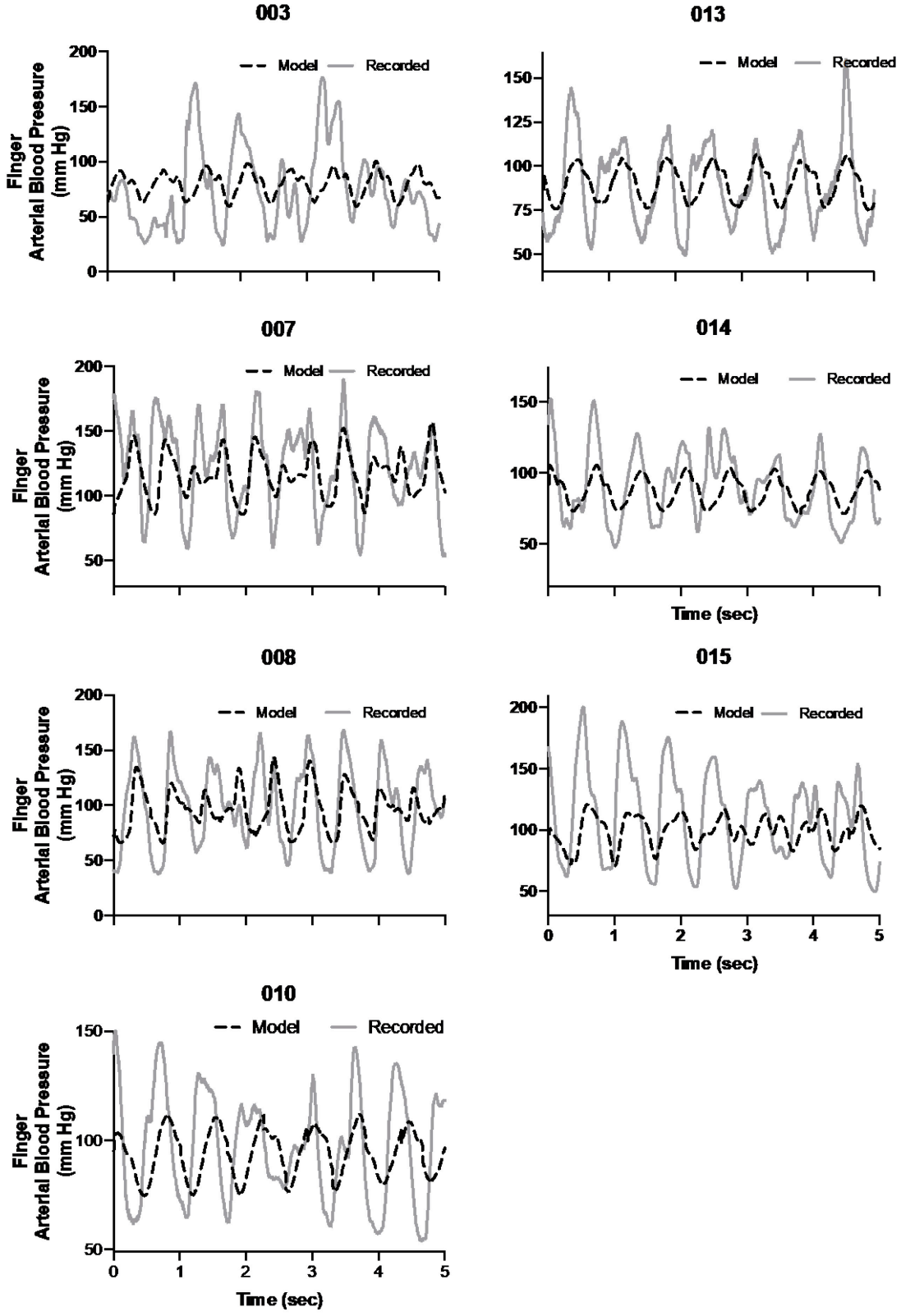
Model IV: Orthostatic + Movement-Related+ Constant Base+ Cardiac Pulse Pressures (90 rpm)



Model V: Orthostatic+ Movement-Related+ External Work Specific Base+ Participant Specific Cardiac Pulse (45 rpm)



Model V: Orthostatic+ Movement-Related+ External Work Specific Base+ Participant Specific Cardiac Pulse (90 rpm)



APPENDIX H: STUDY RECRUITMENT POSTER

VOLUNTEERS WANTED FOR RESEARCH STUDYING THE CARDIOVASCUALR RESPONSE TO ARM CYCLING EXERCISE

We are looking for volunteers for a research study conducted by the Division of Kinesiology at Dalhousie University looking at the cardiovascular response to arm crank cycling exercise.

You would be asked to report to the Biomechanics, Ergonomics and Musculoskeletal Laboratory located in Room 217 of the Dalplex (2360 South Street). You will perform an incremental arm cycling exercise test to fatigue while wearing a facemask used to measure oxygen consumption.

Participation involves 2 study visits, each lasting approximately one hour in duration.

You may be eligible to participate if you:

- ✓ Are between 18-30 years of age

You will not be eligible to participate if you:

- ✓ Suffer from any cardiovascular, metabolic or respiratory medical conditions

For more information about this study, or to volunteer, please contact the BEN Laboratory (biodynamics.dalhousie@gmail.com)

APPENDIX I: STUDY INFORMED CONSENT FORM

Project Title: Cardiorespiratory and Biomechanical Responses to Arm-Crank Exercise at Different Frequencies

You are invited to take part in a research study being conducted by Dr. Michel Ladouceur, Assistant Professor of Kinesiology at Dalhousie University, School of Health and Human Performance. Your participation in this study is voluntary and you may withdraw from the study at any time. There will be no impact on your studies, employment, performance evaluation or the services you receive if you decide not to participate in the research. The information below tells you about what you will be asked to do and about any benefit, risk, or discomfort that you might experience.

Who will be conducting the research?

The Principal Investigator will be Dr. Michel Ladouceur from the School of Health and Human Performance at Dalhousie University. Dr. Ladouceur can be contacted via email (michel.ladouceur@dal.ca) or telephone at (902) 494-2754 should have any questions or concerns about the study.

Purpose and Outline of the Research Study

The rapid rise in heart rate (HR) during exercise is accomplished by nerve signals from the brain that are directed to the heart and muscles. Previous research has shown that the primary motor cortex is an important brain area involved with this response. The intensity of exercise has a direct effect on how much your HR increases and how much oxygen your muscles use. For cycling exercise, the intensity of exercise is determined by both the pedalling rate and the resistance on the flywheel. It has long been thought that the overall intensity was the only variable that determined the HR response and amount of oxygen used during exercise. However, it has also been shown that the magnitude of the HR response and oxygen use to cycling is also directly related to how fast you're pedalling, even if the overall intensity is the same.

Reasons for having a higher HR and greater oxygen use with faster pedalling speed could be due to differences in the information coming from the primary motor cortex or due to other factors that influence how efficient your muscle movements are. However, we do not know for sure how important either of these possible reasons are. As such, the purpose of this study is to determine if arm pedalling rate changes the HR response and oxygen use during maximal arm cycling exercise.

Who Can Participate in the Research Study?

You may participate in this study if you are between 18 and 30 years old and do not have a chronic condition or disease that affects the heart or blood vessels.

You may not participate for this study if you:

- Have a resting blood pressure >140 mmHg (systolic) or >90 mmHg (diastolic).
- Have been diagnosed with a medical condition that effects your cardiovascular system.
- Have been told not to engage in strenuous physical activity by a physician.
- Have answered 'Yes' to any questions on the Physical Activity Readiness-Questionnaire or Health History Questionnaire.
- Suffer from joint problems or other physical limitations that will not permit you to perform upper arm exercise.
- Are pregnant

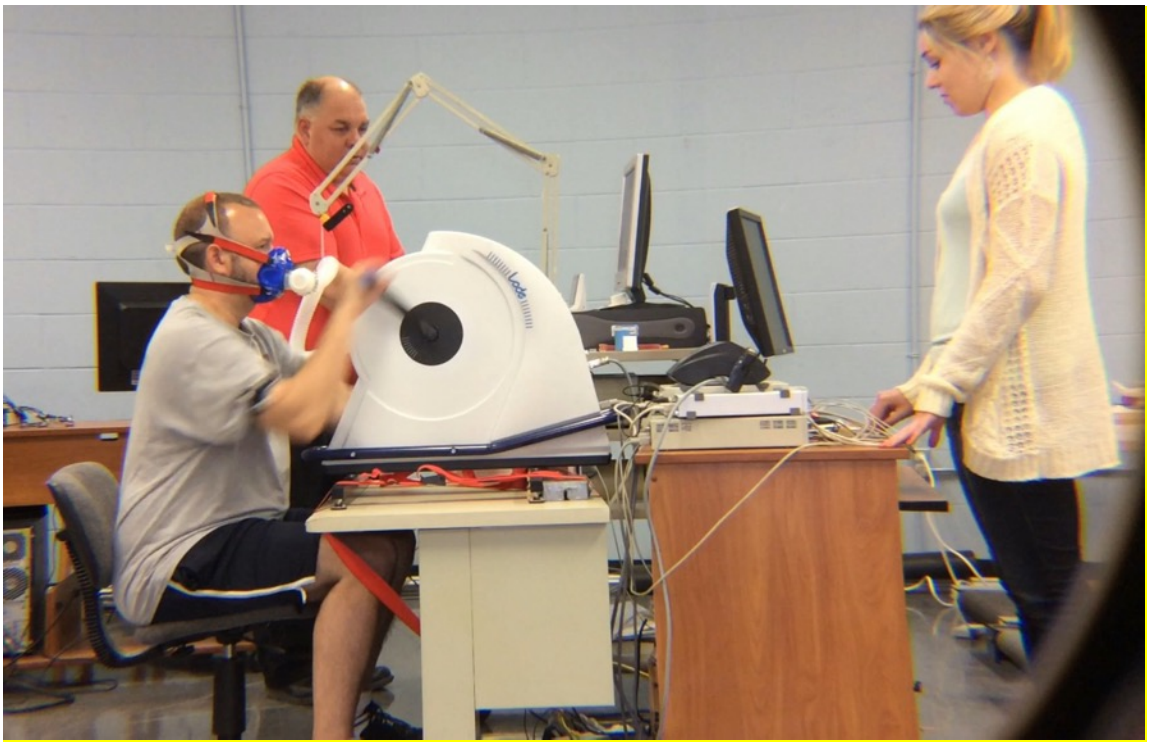
What You Will Be Asked to Do?

The study will involve a total of two visits each lasting approximately 1 hour of your time (~2 hours total).

If you have not done so already, we will ask you to fill in some questionnaires on the first day of testing. We will also measure your height, and weight, record your resting seated blood pressure from the upper left arm using an automated patient monitor, and explain all the equipment and procedures used for the study.

On the two days, you will secure a wireless strap heart rate monitor around your chest and we will have you place some sticky patches on your chest, shoulders, stomach, and arms to help us record the activity and movement of your heart and muscles. We will place a small pressure cuff around an index or middle finger of your right hand to help use measure your blood pressure. Finally, you will wear a facemask (or mouthpiece and nose clip) to measure the amount of oxygen you use. You will then perform an incremental arm cranking exercise test to fatigue. The arm cranking test will involve having you rest for a couple of minutes while you grip the handles but keeping them still. You will then perform 2 minutes of load less cycling followed by 3 minutes of 'light' cycling (~30-50 Watts) for a 'warm-up'. The intensity will then increase gradually (10 Watts) every minute until you want to stop or can no longer maintain the desired pedaling rate (see below for details). You will then cycle at the 'warm-up' intensity again for a minimum of 5 minutes for a 'cool down' period. We will continue to record our measurements during this time.

There will be some differences regarding the arm cycling pedaling speed used over the two days. Specifically, you will be asked to arm cycle at a speed of either 45 revolutions per minute and at 90 revolutions per minute on different days. The order of these possible combinations will be determined randomly (like a coin-flip).



The picture above illustrates the measuring equipment and activity you will be doing.

Possible Benefits, Risks and Discomforts?

You will not receive any direct benefits for participating in this study. However, information regarding your general cardiovascular health including upper body aerobic fitness, resting blood pressure, and heart rate, will be provided to you upon request.

Maximum-Intensity Arm Crank Exercise: Performing maximum-intensity exercise is safe but can induce unpleasant side effects such as sweating, an elevated heart rate, shortness of breath dizziness, and light-headedness. These feelings will start to decrease once exercise stops. First aid qualified personnel will ensure your safety by helping you manage these symptoms if they arise. We will call for medical assistance if necessary.

Heart Rate Measurements: A chest strap wireless monitor will be placed around your upper chest that will record the electrical activity of your heart. Redness may develop on the skin after you remove the strap but should disappear within a few hours. In addition, an electrocardiogram (ECG) will be used to measure heart rate, which involves having two sticky patches positioned on your right shoulder and left rib cage. You or a trained investigator will attach these sticky patches.

Finger Blood Pressure Measurements: You may experience slight discomfort as a result of these measurements, including sensations of "pins and needles" in your fingers. When in use, the finger cuffs will inflate with air and you should feel it gently squeeze your fingers. Your fingers

may turn slightly blue and feel numb or tingly when this cuff is inflated. The symptoms go away once the cuff pressure is reduced. Some people may feel slight pain in this procedure. Pain is not expected to be any worse than what you would feel when a physician takes your blood pressure. If you have felt pain due to blood pressure cuffs in the past you may not want to take part in this study.

Automated Upper Arm Blood Pressure Measurements: Slight discomfort may be experienced as the arm blood pressure cuff is inflated, which may or may not include feelings of "pins and needles" in your hand. This sensation should be relieved as soon as the cuff has been deflated.

Motion Analysis: Movement data will be measured using a camera system. Four sets of markers attached to the shoulder, arm and hands will capture movement. The camera system only shows positions of bony landmarks. This movement data is used to measure velocity and acceleration of your arms. By signing this document you consent to having your exercise movement measured by a camera system.

Steps have been taken to ensure that all procedures will be performed in clean, sterile conditions with minimal risks of any adverse health effects. Throughout the study we will be recording numerous measures of your health. If for any reason we find information that may show a possible health risk (e.g. high resting blood pressure), we will explain the issue to you and strongly recommend that you visit your family doctor. If this occurs, you may no longer be eligible to participate in the study.

Compensation / Reimbursement

There is no compensation for being part of this research study. We will reimburse you for out-of-pocket transportation-related expenses you incur as a result of participating in this study (e.g. city transportation or on-campus parking). These expenses will be reimbursed following completion of each study day. The maximum amount of reimbursement for transportation costs will be $20. Furthermore, after the two experimental sessions you will receive a T-shirt with the laboratory logo.

Privacy and Confidentiality

Information that you provide to us will be kept private. Only the research team at Dalhousie University will have access to this information. We will describe and share our findings in a class presentation and written thesis. We may also submit our findings for publication to an academic journal. We will be very careful to only talk about group results so that no one will be identified. This means that ***you will not be identified in any way in our reports***. The people who work with your information have special training and have an obligation to keep all research information private. Also, we will use a participant number (not your name) in our written and computerized records so that the information we have about you contains no names. All your identifying information will be kept in a separate file, in a locked cabinet, in a locked room in the Dalplex. All electronic records will be kept secure in a password-protected, encrypted file on the researcher's personal computer (or on a Dalhousie University secure server) and all written

documents will be stored in a locked cabinet where only the supervising professor will have access.

If You Decide to Stop Participating

You are free to leave the study at any time. If you decide to stop participating at any point in the study, you can also decide whether or not you want any of the information that you have contributed up to that point to be removed. You may decide to have your information removed up to one month after your final testing day. After that time, it will become impossible for us to remove it because it will already be analyzed.

How to Obtain Results?

You can obtain either group results or your individual results by including your contact information at the end of the signature page and we will send them to you via your preferred method.

Questions

We are happy to talk with you about any questions or concerns you may have about your participation in this research study. Please contact Dr. Michel Ladouceur at michel.ladouceur@dal.ca or (902) 494-2754, at any time. We will also tell you if any new information comes up that could affect your decision to participate.

If you have any ethical concerns about your participation in this research, you may also contact Catherine Connors, Director, Research Ethics, Dalhousie University at (902) 494-1462, or email: ethics@dal.ca

CONSENT FOR STUDY PARTICIPATION

Project Title: Cardiorespiratory and Biomechanical Responses to Arm-Crank Exercise at different frequencies

I, _____ have read the explanation about this study. I have been given the opportunity to discuss it and my questions have been answered to my satisfaction. I agree to take part in this study. However I realize that my participation is voluntary and that I am free to withdraw from the study at any time.

_____
Participant's Signature

_____ _____
Print Name of Participant DATE

I confirm that I have explained the nature and purpose of the study to the participant named above and have answered all questions. In my judgment the participant is voluntarily and knowingly giving informed consent to participate in this research study.

_____ _____
Name of Person Signature
Obtaining Consent

Please send me (please circle):

GROUP RESULTS INDIVIDUAL RESULTS BOTH NEITHER

Please contact me at (please list a phone number, e-mail address, or mailing address):

_____

_____

E-mail address:

APPENDIX J: QUESTIONNAIRES

Participant I.D. #:

Height (cm):

Weight (kg):

Date of Birth (Month/Year):

These questions are designed to determine your eligibility for the study. If you answer 'Yes" to any question you will not be able to participate in the study.

1.	Have you been diagnosed with diabetes?	Yes	No
2.	Have you ever had chest pain, heart disease or a heart murmur?	Yes	No
3.	Do you have any bleeding or clotting problems?	Yes	No
4.	Have you ever had kidney disease?	Yes	No
5.	Have you ever had liver disease such as hepatitis?	Yes	No
6.	Have you ever had any thyroid disease?	Yes	No
7.	Have you ever had asthma or lung disease?	Yes	No
8.	In the past 6 months, have you taken any medication that might stimulate or depress your nervous system (e.g. anti-depressants, amphetamines, Ritalin, Valium)?	Yes	No
9.	Will it be a problem wearing a face mask or mouthpiece with nose clip during arm cycling exercise.	Yes	No

Physical Activity Readiness Questionnaire - PAR-Q (revised 2002)

PAR-Q & YOU

(A Questionnaire for People Aged 15 to 69)

Regular physical activity is fun and healthy, and increasingly more people are starting to become more active every day. Being more active is very safe for most people. However, some people should check with their doctor before they start becoming much more physically active.

If you are planning to become much more physically active than you are now, start by answering the seven questions in the box below. If you are between the ages of 15 and 69, the PAR-Q will tell you if you should check with your doctor before you start. If you are over 69 years of age, and you are not used to being very active, check with your doctor.

Common sense is your best guide when you answer these questions. Please read the questions carefully and answer each one honestly: check YES or NO.

YES	NO		
☐	☐	1.	**Has your doctor ever said that you have a heart condition and that you should only do physical activity recommended by a doctor?**
☐	☐	2.	**Do you feel pain in your chest when you do physical activity?**
☐	☐	3.	**In the past month, have you had chest pain when you were not doing physical activity?**
☐	☐	4.	**Do you lose your balance because of dizziness or do you ever lose consciousness?**
☐	☐	5.	**Do you have a bone or joint problem (for example, back, knee or hip) that could be made worse by a change in your physical activity?**
☐	☐	6.	**Is your doctor currently prescribing drugs (for example, water pills) for your blood pressure or heart condition?**
☐	☐	7.	**Do you know of any other reason why you should not do physical activity?**

If you answered

YES to one or more questions

Talk with your doctor by phone or in person BEFORE you start becoming much more physically active or BEFORE you have a fitness appraisal. Tell your doctor about the PAR-Q and which questions you answered YES.

- You may be able to do any activity you want — as long as you start slowly and build up gradually. Or, you may need to restrict your activities to those which are safe for you. Talk with your doctor about the kinds of activities you wish to participate in and follow his/her advice.
- Find out which community programs are safe and helpful for you.

NO to all questions

If you answered NO honestly to all PAR-Q questions, you can be reasonably sure that you can:

- start becoming much more physically active – begin slowly and build up gradually. This is the safest and easiest way to go.
- take part in a fitness appraisal – this is an excellent way to determine your basic fitness so that you can plan the best way for you to live actively. It is also highly recommended that you have your blood pressure evaluated. If your reading is over 144/94, talk with your doctor before you start becoming much more physically active.

DELAY BECOMING MUCH MORE ACTIVE:

- if you are not feeling well because of a temporary illness such as a cold or a fever – wait until you feel better; or
- if you are or may be pregnant – talk to your doctor before you start becoming more active.

PLEASE NOTE: If your health changes so that you then answer YES to any of the above questions, tell your fitness or health professional. Ask whether you should change your physical activity plan.

Informed Use of the PAR-Q: The Canadian Society for Exercise Physiology, Health Canada, and their agents assume no liability for persons who undertake physical activity, and if in doubt after completing this questionnaire, consult your doctor prior to physical activity.

No changes permitted. You are encouraged to photocopy the PAR-Q but only if you use the entire form.

NOTE: If the PAR-Q is being given to a person before he or she participates in a physical activity program or a fitness appraisal, this section may be used for legal or administrative purposes.

"I have read, understood and completed this questionnaire. Any questions I had were answered to my full satisfaction."

Participant ID#:

Note: This physical activity clearance is valid for a maximum of 12 months from the date it is completed and becomes invalid if your condition changes so that you would answer YES to any of the seven questions.

Supported by: Health Canada Santé Canada

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