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The Effect of Postural Perturbations on Cardiovascular and Skeletal Muscle Function in Healthy Adults

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Abstract

Maintenance of standing balance is vital to daily living. Traditionally, perspectives on maintaining balance are achieved through the study of visual, vestibular and somatosensory inputs on motor outputs. While evidence suggests cardiovascular regulation also functions to assist postural control during orthostatic stress, how the cardiovascular system responds to postural perturbations is not well established. This dissertation includes four studies that investigated the effects of postural perturbations on the cardiovascular system and skeletal muscle responses in healthy adults. All of the studies involved exposing standing participants to surface-translation perturbations at different velocities, with known or unknown timing, and occurred while spontaneously breathing and breathing at six breaths per minute in young and older adults. Beat-to-beat heart rate and systolic blood pressure were measured continuously, while cardiac baroreflex sensitivity was calculated using the sequence method analysis. The results of Study One illustrated that heart rate and systolic blood pressure response were modulated following a perturbation and the initial cardiac response scaled with perturbation intensity. Additionally, cardiac baroreflex engagement was found to be involved in heart rate recovery. The sensitivity of the cardiac baroreflex was increased post-perturbation but was not intensity dependent. In Study Two, anticipatory cardiovascular responses to perturbations were not observed when the timing of the perturbation was controlled by the participant and perceived state anxiety was correlated with the initial heart rate response post-perturbation. In Studies Three and Four, when breathing at six breaths per minute, the latency of muscle burst onset decreased in young and older adults and muscle burst amplitude decreased in the lower limb musculature in young adults. Slow breathing decreased systolic blood pressure but had no effect on heart rate or cardiac baroreflex sensitivity post-perturbation in older adults. Together, the findings provide evidence that cardiovascular modulation occurs when standing balance is perturbed and support the notion that the cardiovascular, respiratory and motor control systems interact in a complex manner during postural perturbations.

Keywords

Baroreflex, slow breathing, electromyography, postural control, aging, perturbations, hemodynamics

Summary for Lay Audience

The ability to regain control of standing balance is vital to limiting falls and injuries. It is known that standing balance requires the coordination of sensation and muscle activity. However, the importance of heart rate and blood pressure control during disruptions to standing balance is less well known. This thesis includes four studies that investigated the effects of balance disturbances on heart rate, blood pressure and skeletal muscle activity of the lower limb in healthy adults. Young and older participants stood on a treadmill which moved backwards causing them to fall forward. These balance disturbances were repeated with different treadmill movement speeds, with the timing of the treadmill movement either known or unknown, and with the participant either breathing normally (spontaneous breathing) or breathing slowly at six breaths per minute. Balance disturbances caused short-lasting effects on heart rate and blood pressure. These effects were similar regardless of whether the timing of the balance disturbance was known or not. Slow breathing can cause the muscle to respond earlier to a balance disturbance in young and older adults. Heart rate was not affected but blood pressure was elevated during balance disturbances while spontaneously breathing in older adults. This thesis provides evidence that heart rate and blood pressure responded to balance disturbances and supports the idea that the heart, lungs and muscles influence each other during postural perturbations.

Co-Authorship Statement

This dissertation includes two manuscripts that have been published in scientific journals (Chapter 2 and Chapter 4) and two manuscripts that are being prepared for publication (Chapter 3 and Chapter 5). Patrick Siedlecki is the first author of all collaborative projects included in this dissertation (Chapters 2-5). Dr. S. Jayne Garland is the principal investigator and co-author of each project included in the dissertation (Chapters 2-5). Dr. Tanya D. Ivanova co-authored Chapters 2-5 and Dr. J. Kevin Shoemaker co-authored Chapters 2 and 4.

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List of Abbreviations

cBRS, cardiac baroreflex sensitivity

COM, center of mass

COP, center of pressure

CNS, central nervous system

CB&M, community balance and mobility scale

EMG, electromyography

HR, heart rate

SEBQ-2, self-evaluation breathing questionnaire: version 2

SBP, systolic blood pressure

Chapter 1

1 Introduction

The prevalence of falls in Canada is increasing due to the increase of individuals over the age of 60 years (Public Health Agency of Canada, 2014). The effect of a fall can be devastating, especially in older adults, as it can be accompanied with an injury resulting in the loss of independence, hospitalization, or even death (Public Health Agency of Canada, 2014). Thus, understanding the basis of postural control and minimizing the potentially catastrophic effects of loss of balance is of great importance.

1.1 Postural Control

Maintenance of the upright standing posture is fundamental to the completion of various daily tasks. Postural stability is dependent on the central nervous system (CNS) tracking the body's center of mass (COM) and issuing neuromuscular adjustments to maintain the COM within the boundaries of the base of support (Guskiewicz & Perrin, 1996; Winter et al., 1998). Sensory afferents from the visual, vestibular and somatosensory systems provide information to the CNS of the COM location and its trajectories. Recent evidence has suggested the interaction of cardiovascular information with neuromuscular and sensory information which may play a role in maintaining upright posture and balance (Garg et al., 2014b; Rodrigues et al., 2018).

The COM represents the location of the overall average of mass from all segments of a body. The COM in standing humans is located approximately 10 cm below the naval and 7 cm anterior to the ankle joint (Winter et al., 1998). It shifts as each limb or segment of the body moves. The center of pressure (COP) is a vertical force projecting from the ground representing the point where all of the pressure from the body is interacting with the ground (Chen et al., 2021). Postural control during quiet standing is accomplished by regulating COM.

Maintenance of standing balance requires sensory integration from the visual, vestibular and somatosensory systems (Guskiewicz & Perrin, 1996). The visual system

relies on information from the eyes to describe the external environment. In postural control, closing both eyes and eliminating optic outflow can increase body sway (Chiba et al., 2016). Additionally, if optic outflow is large enough, such as slowly moving a wall closer to the individual, the body weight and sway shift posteriorly. The vestibular system collects information on head position and movement via the vestibular apparatus and plays an important role in the vestibular-ocular reflex which coordinates eye movement with the head (Guskiewicz & Perrin, 1996). For example, if the head rotates 15 degrees to the left, external ocular muscles will contract to move the eyes 15 degrees to the right. This reflex helps stabilize vision by allowing the eyes to focus on an object when the head is moving. If the vestibular system is impaired or disturbed with galvanic stimulation, balance can be impacted. When galvanic stimulation is applied unilaterally to the mastoid process, an individual will sway towards the direction the stimulus was applied (e.g., stimulus applied to the left ear, the body will sway to the left; Fitzpatrick et al., 1994). The somatosensory system can be subdivided into two subsystems of proprioception and tactile senses. Proprioception supplies the brain with information on the position of the limbs and body parts via muscle spindles and Golgi tendon organs (Guskiewicz & Perrin, 1996). The muscle spindles are located in the muscle belly and sense muscle length and changes in muscle length, while the Golgi tendon organs monitor muscle tension and changes in muscle tension. Tactile senses like pressure, touch and vibration can also be used to update the brain's image of the body. The somatosensory system can be manipulated using light touch, muscle vibration and changing joint angle (Guskiewicz & Perrin, 1996). Similar to disrupting the vestibular system, effects are ipsilateral.

The contribution of each multisensory input is task dependent. Less challenging postural perturbations rely more heavily on vestibular and visual feedback because the head position remains stable (Assaiante & Amblard, 1995). As perturbation intensity increases, disruption of vestibular and visual input to maintain balance would occur. One of the ways to decrease COP displacement is by keeping the eyes open. Massion (1994) indicated that anterior-posterior COP sway can be 2-3 times bigger with eyes closed than with eyes open. The role of proprioception in the maintenance of balance might be the most important. When one or more of the multisensory inputs are eliminated, the

remaining sensory inputs attempt to compensate for the others (Guskiewicz & Perrin, 1996). However, when proprioceptive input was eliminated, postural stability decreased more compared to the single elimination of the other senses. Therefore, it was noted that to negatively impact postural stability by disrupting vision or vestibular input, proprioceptive information must also be disrupted (Chiba et al., 2016). These findings signify the importance of proprioceptive input on the maintenance of balance compared to the other sensory inputs.

1.1.1 Feet-in-Place Balance Strategies

Maintenance of standing balance can be achieved through various strategies. Non-stepping strategies fall within a spectrum ranging between ankle strategy to hip strategy (Afschrift et al., 2016). Ankle and hip strategies were described by Horak and Nashner (1986). These authors noted that an ankle strategy resembled a single inverted pendulum where the body was composed of a single segment that rotated around the ankle joint. That is, during very low body sway, reactive muscle force to regulate COM is thought to be done by the intrinsic properties of muscles rather than active muscle torques (Suzuki et al., 2012; Winter et al., 1998). Thus, the COM position would be dictated by body sway.

The ankle strategy is useful in maintaining balance in the anterior-posterior plane and would utilize ankle plantarflexors and doriflexors. Muscle synergies would start at the ankle muscles (e.g., gastrocnemii, soleus and tibialis anterior) and work upwards to the hips, trunk and upper body (Horak & Nashner, 1986). Ankle strategies are used more often in lower challenging postural perturbations; as perturbation intensity increases, the strategy shifts towards more of a hip strategy (Afschrift et al., 2016). A hip strategy was compared to a double inverted pendulum which divided the body into two segments, the legs and the torso and upper body (Horak & Nashner, 1986). Joint rotation would occur at the ankle joint and the hip joint, and muscle synergies would follow a top-down pattern. The hip strategy is useful in maintaining balance in the medial-lateral plane using hip abductors and adductors. For example, if the COM needs to be moved quickly, a hip strategy is 20 times quicker at moving the COM than the ankle strategy (Huisinga et al., 2018). Therefore, the hip strategy would be beneficial in situations where COM has accelerated too quickly (Hof et al., 2005). It should also be noted that in addition to the

ankle and hip strategy, there can also be a mixed strategy that uses a combination of ankle and hip strategy depending on the situation and is often seen during quiet standing (Afschrift et al., 2016).

Situations where one strategy is selected over the other is dependent on physical, emotional and biomechanical factors. Mok and colleagues (2004) identified experience with perturbation, expectation of perturbation and environmental constraints as factors that can impact which strategy is used. In addition, Afschrift et al. (2016) identified experience as a factor, although also suggested adaptations over time and with training, as well as fear of falling and sustaining an injury as factors. In regards to fear of falling and injury, Pai et al. (2000) posited that individuals were more likely to take a step or use a hip strategy to prevent a fall backwards out of fear of hitting their heads on the ground.

Another factor that can affect determination of strategy is whether the CNS wants to focus on energy efficiency versus postural stability (Afschrift et al., 2016). Afschrift and colleagues (2016) found that individuals who prioritized postural stability were more likely to use a hip strategy over an ankle strategy. The argument was based on muscle force production from all muscles involved being overall larger during more challenging postural perturbations. During times when postural stability was more threatened, a hip strategy was used. They also found that the ankle strategy was used more often when the CNS wanted to be more energy efficient. The ankle strategy tends to focus on modulating COM through ankle joint rotation and hip muscle stiffness.

Finally, aging and disease can affect the selection of strategy used during upright standing. Older adults and populations with lower back pain have been found to use ankle strategies over hip strategies (Ciesielska et al., 2015; Guskiewicz & Perrin, 1996; Huisinga et al., 2018; Mok et al., 2004). This can occur to limit pain and to cope with fear of falling.

There have been numerous studies that have identified various ways to determine whether one non-stepping strategy was used over the other during upright standing. Huisinga et al. (2018) conducted a study that utilized accelerometers positioned on the trunk and legs in participants with and without lower back pain. They found that trunk

and leg movement were in phase when body sway was under 1 Hz. However, as sway frequency increased, especially above 1 Hz, trunk and leg movements were out of phase. The results indicated that in lower postural perturbation intensities, trunk and legs acted as a single unit, similar to a single inverted pendulum. As perturbation intensity increased, the out of phase pattern between trunk and legs resembled a hip strategy. A hip strategy creates a counter phase movement between the trunk and legs. For example, when a posterior-directed translation of a platform occurs, the hips would passively flex while the ankle joints passively plantarflex. This idea is supported by another study measuring ankle and hip joint angles. Colobert et al. (2006) found that, during a forced ankle strategy condition, the ankle joint angle fluctuations were approximately 3 degrees and hip joint angles fluctuated around 7-10 degrees. In forced hip strategy conditions, the hip rotated six times more than the ankle (5 degrees versus 30 degrees). The increased ratio between hip and ankle rotation is due to the use of a hip strategy that requires the movement of the hip joint. The concurrent increase in ankle and hip angle is due to that counter phase movement that was described by Huisinga and colleagues (2018).

Cieielska et al. (2015) conducted a study using surface electromyography (EMG) to measure the activity in the trunk and lower extremity muscles during postural perturbations in individuals who had lower back pain. They found that the clinical population group had significantly higher muscle activity at high perturbation intensities compared to a control group. This finding indicated that the lower back pain group used an ankle strategy during higher perturbation intensities than the control group. This was also found in other studies (Colobert et al., 2006; Mok et al., 2004). The increase in muscle activity in the rectus femoris and gluteus maximus would indicate that there was co-activation at the hip joint which reduced hip movement. This may have been a protective mechanism to decrease pain created by hip movement. Further, Mok et al. (2004) found that anterior leg shear forces were lower during an ankle strategy condition which would support the findings of Ciesielska et al. (2015) as movement in the hip was reduced due to joint stiffness via muscle tone.

1.1.2 Change-in-Support Balance Strategy

Traditionally, taking a step to regain control of standing balance was thought to occur when the CNS failed to maintain COM within the outer boundaries of the base of support (Horak & Nashner, 1986). In the last few decades, dynamic modelling during threats to upright posture has challenged this theory (Hof et al., 2005; Maki et al., 2003; Pai et al., 2000). Postural instability can also occur when the COM is within the base of support while the COM trajectory is accelerating horizontally outwards (Hof et al., 2005). Conversely to the feet-in-place strategy, a change in the base of support, either by taking a step or moving the trunk/arms, is required to maintain postural equilibrium when the COM travels beyond the base of support or if the instantaneous horizontal acceleration of COM is quick enough (Hof et al., 2005; Maki & McIlroy, 1997).

Discrimination between reactionary and anticipated stepping responses is possible due to distinct biomechanical and EMG patterns (McIlroy & Maki, 1993). There is initial loading and unloading of the swing leg which is only present during reactionary movement. When a step is anticipated, there is a lateral shift in body weight towards the stance leg, unloading the swing leg. The presence of a lateral shift in body weight is also present during feet-in-place perturbations. This suggests step pre-planning is initiated prior to the foot leaving the ground (Maki et al., 1993), confirming the theory that stepping does not act as a secondary response once failure to maintain COM within the base of support occurs.

A stepping response can occur 230 ms after the onset of a perturbation (Maki et al., 1993). The response time is twice as quick during a reactionary movement compared to fast voluntary stepping (Maki & McIlroy, 1997; Maki et al., 2003). Reactionary movements produce larger anterior-posterior COP displacements and more delayed muscle onset than anticipated movements (Bugnariu & Sveistrup, 2006). Thus, postural stability can be achieved earlier when perturbed standing balance is anticipated. Benefits of rapid step initiation allows for subsequent steps to regain balance and enough time to decelerate the body. Therefore, feet-in-place and change-in-support strategies are effective methods to regain control of balance, dependent on postural set.

1.1.3 Postural Perturbations

Perturbations of the COM in standing balance can be applied with internal perturbations or external perturbations (Rogers & Mille, 2018). An internal perturbation consists of internally generated actions (e.g., raising an arm) that often involves a predictive or anticipated action from the CNS to stabilize the COM (Horak, 2006). For instance, the acceleration of the COM anteriorly during a forward arm rise is counteracted by neuromuscular adjustments within the arm and/or lower limbs and trunk, occurring prior to or after the movement (Bouisset & Zattara, 1981; Bouisset & Zattara, 1987). External perturbations originate outside of the human body (e.g., slips or falls) and require reactionary postural adjustments (Rogers & Mille, 2018). A common method utilized in the application of external perturbations is through surface platform translations. The neuromuscular response to correct upright standing balance following a postural perturbation is dependent on the task.

Posteriorly directed postural perturbations accelerate the COM anteriorly as the surface platform underneath an individual translates posteriorly. Posterior muscle groups (e.g., ankle plantarflexors and hamstrings) contribute greatly to restoring postural stability during posteriorly directed perturbations. Muscle activation patterns are preprogrammed within the CNS (Ting & McKay, 2007) and occur shortly after the perturbation. Muscle activation onset in bilateral surface translations can occur within 70 to 110 ms (Horak & Nashner, 1986). When the perturbation in unexpectedly applied, the amplitude of muscle activity scales with the perturbation's magnitude and velocity (Coelho & Teixeira, 2018; Horak et al., 1989). Repeating the perturbation without modifying the perturbation's characteristics (e.g., magnitude, velocity, or direction), makes the perturbation predictable and the CNS can plan a motor response to regain equilibrium (Kaewmanee & Aruin, 2022). However, any unexpected change to the perturbation's characteristics can produce a reactionary motor response (Kaewmanee et al., 2020).

1.1.4 Cardio-Postural Interactions

Cardio-postural interactions between musculoskeletal, postural control and cardiovascular control systems exist (Garg et al., 2014b). These systems make up the posture control-mediated (musculoskeletal and postural control), baroreflex control-mediated (musculoskeletal and cardiovascular control), and the cardiopostural-mediated (postural control and cardiovascular control) interactions. Garg and colleagues found that the cardiovascular control system made up almost half of the total interactions when combined with one of the postural control (cardiopostural-mediated interaction) or musculoskeletal (baroreflex control-mediated interaction) systems. They concluded that activation of postural-related muscle groups can occur for blood pressure regulation and not directly for postural-related reasons in quiet standing.

Mild lower limb muscle contractions induced during quiet standing play a pivotal role in ensuring adequate blood supply to the heart (Masterson et al., 2006). The relationship between ankle musculature EMG and blood pressure during prolonged standing has been identified in young (Garg & Blaber, 2012; Garg et al., 2013) and older (Garg et al., 2014a) adults, and appears to remain intact with age (Verma et al., 2017). However, the effect of postural perturbations on cardiovascular regulation has not been well examined.

1.2 Cardiovascular Control

The primary function of the cardiovascular system is to provide adequate oxygen and nutrient supply to tissues and organs, while removing by-products from the blood (Rowell, 1986). This is achieved through the modulation of blood volume distribution and blood circulation to and from working tissues. Most of the blood circulation is distributed to the systemic veins (70%), followed by the heart and lungs (15%), systemic arteries (10%) and capillaries (5%). During the transition to upright stance, 500-600 mL of blood is distributed to compliant veins in the lower limbs and 200-300 mL of blood to veins in the pelvic area where it pools (Rowell, 1986). Immediately after the onset of transitioning to the upright standing posture, there are reductions up to 20% in cardiac output and 40% in stroke volume, thus resulting in tachycardia and increased peripheral

vascular resistance to avoid hypotension, which, if prolonged, would lead to fainting. These cardiovascular adjustments are meant to maintain homeostasis. There are three primary mechanisms for the adjustment of hemodynamics that can be separated into central and peripheral control mechanisms (Nobrega et al., 2014).

1.2.1 Central Command

The centrally mediated influence on cardiovascular response is believed to originate in subcortical regions (Dampney, 2016). The central mechanism has a feedforward component that allows for anticipatory cardiovascular responses to stimuli. The concept of central motor impulses controlling ventilation and circulation was originally theorized in the late 1800s (Johansson, 1893; Zuntz & Geppert, 1886). It was not until Krogh and Lindhard (1913) observed cardiorespiratory changes immediately prior to the onset of physical exercise which indicated cortical structures, and not humoral factors, were responsible for the anticipatory adaptations to physical work. This was confirmed by Eldridge and colleagues (1985) who determined that the motor cortex and humoral feedback mechanisms were not required to elevate blood pressure and respiration during fictive locomotion in decerebrated cats. The central mechanism modulates sympathetic outflow to the heart and vasomotor tissue and is associated with the intensity of effort (McCloskey & Mitchell, 1972). Similarly, Gandevia and colleagues (1993) induced paralysis in participants with anesthetic and told participants to imagine contracting their skeletal muscles. They found that heart rate (HR) and blood pressure increased despite no limb movement. In a hypnosis study, cardiorespiratory responses were more exaggerated when participants were told that the intensity level of cycling was heavier, despite there being no change in physical load (Morgan et al., 1973). These studies indicate that cardiovascular responses to physical activities can adjust hemodynamics without the presence of feedback afferents. The term “central command” is now used to describe this mechanism (Goodwin et al., 1972), although the originating location of this command is poorly understood.

Carrington et al. (2001) posited that central command could work in concert with feedback mechanisms during cardiovascular control and “top up” the cardiovascular response to physical work. During the onset of lower limb static exercise, they observed

HR and blood pressure progressively increase until the contraction was terminated, at which HR and blood pressure recovered. When the muscle contraction was achieved passively through electrical stimulation, the cardiovascular response was blunted by approximately 50-75%. This study showed that centrally driven efferents have control over cardiovascular responses to physical stress.

Descending central signals, in response to anticipated or at the onset of physical work, increase sympathetic outflow to the heart and vasomotor tissue (Dampney, 2016). Regulation of both sympathetic and parasympathetic nerves is done through a combination of central (central command) and peripheral control mechanisms, such as the cardiac baroreflex and exercise pressor reflex (Dampney, 2016). Because the exercise pressor reflex is not relevant to standing perturbations, only the cardiac baroreflex will be discussed.

1.2.2 Cardiac Baroreflex

The role of the baroreceptor in blood pressure regulation was first described in the 1800s (Cooper, 1836). The baroreceptor reflex, also known as the cardiac baroreflex, is a homeostatic reflex responsible for the beat-to-beat regulation of arterial blood pressure (Eckberg & Sleight, 1992). Animal studies were used to understand this relationship. Hering (1923) was able to electrically stimulate the carotid sinus nerve in dogs inducing bradycardia and hypotension, although this hemodynamic response was absent when the carotid nerves were bilaterally transected in rabbits (Korner, 1965). Without baroreflex influence, blood pressure was unstable and blood pressure and HR increased.

In healthy humans, blood pressure can be manipulated by changes in vascular peripheral resistance (i.e., vasoconstriction and vasodilation) and/or cardiac output (i.e., HR and stroke volume). Baroreceptors are mechanosensitive afferent nerve terminals located in the adventitia of the carotid sinus, found at the base of the internal carotid artery, superior to the bifurcation of the common carotid artery and at the aortic arch (Benarroch, 2008; Tsuboki et al., 2019). Arterial baroreceptors sense acute arterial blood pressure changes and relay sensory information to the brainstem that would transmit motor commands to the myocardium and vasomotor cells, allowing arterial blood

pressure to be maintained (Figure 1; Benarroch, 2014). When blood pressure rises, baroreceptors sense stretching of the arterial walls resulting in an increased firing rate (Benarroch, 2008). The opposite occurs when blood pressure decreases. The modulation of arterial blood pressure is accomplished through direct innervation of the heart and/or blood vessels, or a hormonal response.

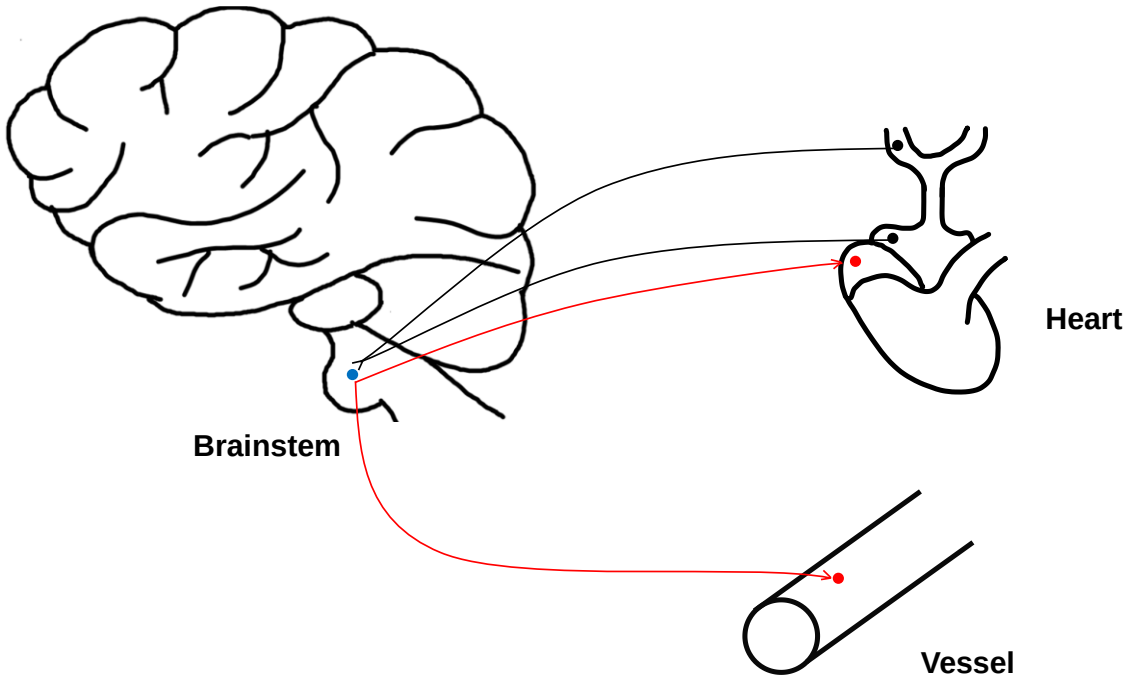

Figure 1. The cardiac baroreflex pathway. The location of baroreceptors (black dots) in the carotid sinus and aortic arch, barosensitive afferent neurons (black lines), brainstem (blue dot), efferent neurons (red lines), and target organs (red dots) are shown.

Resting HR is under cardiovagal regulation. Under no neural control, HR would be 100 bpm (Gordan et al., 2015). Sympathetic withdrawal and/or parasympathetic activity is required to lower HR, while cardiovagal withdrawal and increased sympathetic activity would produce tachycardia and thus increase cardiac output (Rowell, 1986). If sympathetic activity were to decrease, bradycardia and less cardiac contractility would occur. Baroreflex mediated changes in HR are done to regulate cardiac output. Cardiac output is influenced by HR and stroke volume. It is possible that changes in HR will have no effect on cardiac output because of inverse responses to stroke volume (Kumada et al., 1967; Sheriff et al., 1993; White et al., 1971). At rest, baroreflex mediated effects on HR only impact approximately 50% of the total cardiac beats (Ichinose et al., 2008; Sala-

Mercado et al., 2008). The time course of the cardiac response to blood pressure changes are dependent on sympathetic versus parasympathetic tone. Sympathetic cardiac responses require more time to affect HR than parasympathetic-mediated changes (Warner & Cox, 1962). The cardiac baroreflex can also directly regulate the heart. Beat-to-beat cardiac control is accomplished with cholinergic neurons decreasing the spontaneous depolarization of the sinus node. Sympathetic neurons can also project to the left side of the heart by innervating the atrioventricular node, ventricles, and increasing atrioventricular conduction.

The vascular system is under constant sympathetic and tonic control (Rowell, 1986). Elevated sympathetic activity would elicit vasoconstriction primarily with norepinephrine binding to alpha-1 type adrenergic receptors. The presence of norepinephrine inhibits potassium currents and increases intracellular calcium release in the endoplasmic reticulum (Benarroch, 2014). If norepinephrine levels were reduced, passive vasodilation would occur. At rest, the baroreflex accounts for approximately 80% of the reflex change in arterial pressure due to total peripheral resistance adjustments, while this contribution can account for almost all of the arterial pressure regulation during exercise (Raven et al., 2006). The cardiac baroreflex can also mediate hypothalamic hormone regulation (Benarroch, 2008). Inhibition of vasopressin from the pituitary gland would reduce blood pressure directly via passive vasodilation and/or indirectly through decreased osmolarity.

During physical exercise, central command modulates sympathetic outflow regulating the cardiac component of hemodynamic control, while central command does not influence vagal withdrawal (Matsukawa, 2012). Rather, cardiac vagal activity is baroreflex-mediated during physical work (Kadowaki et al., 2011). The central command exerts an inhibitory effect over cardiac control in both reflex mechanisms, although the aortic baroreflex cardiac control is attenuated more (Komine et al., 2003).

The strength and direction of the cardiac baroreflex response, called cardiac baroreflex sensitivity (cBRS), indicates the effect of autonomic control and is dependent on task and posture. Cardiac baroreflex sensitivity has been observed to decrease during

physical exercise compared to a resting physiological state (Bringard et al., 2017; Raven et al., 2019). This is caused by enhanced sympathetic outflow and reduced vagal cardiac control. Previous literature tracking cBRS during movement has been limited to passive whole-body postural changes (e.g., orthostatic stress; Akimoto et al., 2011; Javorka et al., 2018) and physical activity in fixed positions (e.g., squats, weight lifting and stationary cycling; Kazimierska et al., 2019; Kingsley et al., 2019; Vallais et al., 2009).

The upright posture produces gravitational stress to the circulatory system and blood pressure control resulting in reduced involvement from the baroreceptor afferents compared to a sitting or supine posture (Rowell, 1986). Normally, the gravitational effects on hemodynamic outcomes are mitigated with a baroreflex-mediated increase in HR and peripheral vascular resistance to support blood pressure homeostasis (Benarroch, 2014). Because of the upright posture, the baseline condition for individuals would be a state of reduced baroreflex loading and elevated HR and total peripheral resistance compared to supine. Thus, further reduction in cBRS, when standing is combined with another task that stresses the cardiovascular system, may be limited.

1.2.3 Baroreflex Resetting

The central command mechanism can interact with the baroreflex arc (McIlveen et al., 2001). Descending neural signals from the midbrain periaqueductal gray, dorsomedial and paraventricular nuclei in the hypothalamus, central nucleus of the amygdala, medial prefrontal cortex and insular cortex project to the nucleus tractus solitarius and rostral ventrolateral medulla regions (Dampney, 1994; van der Kooy et al., 1984). This can allow for interactions between respiratory neurons, vestibular receptors, skeletal receptors and barosensitive neurons (Dampney, 1994). Feedforward influence on the baroreflex can cause the phenomenon known as baroreflex resetting (Raven et al., 2019).

During physical exertion, oxygen demand in working muscles rises. This requires the need for increased blood circulation and perfusion pressure at tissues with high oxygen demand. Ventilation is the primary source to meet metabolic demand in skeletal muscles. Additionally, venous capacitance of skeletal muscles far exceeds blood supply

of the body (Rowell, 1986). To maintain arterial pressure under these circumstances, enhanced sympathetic outflow allows for vasoconstriction and tachycardia to promote venous return and cardiac preload, thus maintaining cardiac output. To prevent the cardiac baroreflex from decreasing HR during elevated arterial pressure, central command resets the baroreflex to operate at a higher HR and blood pressure range, thus allowing for continued maintenance of arterial pressure.

1.2.4 Baroreflex Methodology

There are many established methods to assess baroreflex function. Pharmacological models have focused on phenylephrine and nitroprusside injections to cause loading and unloading of arterial baroreceptors at rest (Limberg et al., 2018). Specifically, phenylephrine is used to artificially raise blood pressure, while nitroprusside can cause artificial falls in blood pressure (Lipman et al., 2003). These pressor agents are used to perturb the cardiovascular system and assess baroreflex gain as the agents do not have an effect on HR and can accentuate changes in blood pressure which mediates a slowing of HR (Robbe et al., 1987). Advantages of using pharmacological methods to measure cBRS are the short time series required and not required assumption of the stationarity of the time series (Robbe et al., 1987). Some limitations of the use of this method can include numerous injections, discomfort from artificial rises and falls in blood pressure, weak reproducibility of responses and short-term effects from the method itself (Bertinieri et al., 1985; Robbe et al., 1987). The invasive nature of this technique has led to the development of non-invasive techniques to estimate cBRS.

The sequence method is a commonly used non-invasive technique to estimate spontaneous fluctuations in baroreflex gain (Blaber et al., 1995; Pinna et al., 2015). The sequence method, also known as regression analysis, measures beat-to-beat systolic blood pressure (SBP) and R-wave interval (R-R interval that is inversely related to HR) sequences where SBP and R-R interval increase or decrease simultaneously (Bertinieri et al., 1985). A sequence is included in the analysis when there is a simultaneous increase or decrease in SBP and R-R interval for a minimum of three consecutive cardiac cycles, and there must be a change of at least 1 mmHg and 4 ms, respectively, to improve

psychometric properties of the method. Baroreflex gain is estimated by the slope of the linear regression of all sequences with an $r^2 > 0.85$, during a time series.

The sequences observed were found to not be caused by random chance (Blaber et al., 1995), and at rest, approximately 70% of the time series are a part of the baroreflex sequences (Hughson et al., 1993). Instances when R-R interval is too large (>800-900ms), a lag can be used to compensate for situations when the length of the R-R interval changes within the same cardiac cycle. A lag of 0 is used when blood pressure and R-R interval change in the same (lag of 0), following (lag of 1), and next following (lag of 2) cardiac cycle (Blaber et al., 1995). Blaber and colleagues (1995) tracked the number of sequences that occurred during lags varying from 0 to 2 cardiac cycles. They found that the number of total heart beats from the time series decreased from ~40-50% in lag 0, to 6-12% in lag 1 and 2-6% in lag 2. However, they suggested that lag should not meaningfully affect cBRS because the frequency and amplitude of R-R interval would not be different. Although cBRS has been previously calculated using sequences taken immediately after a change in posture (Gabbett et al., 2001), to our knowledge, the cBRS has not been calculated during postural perturbations to standing balance.

1.2.5 Cardiovascular Response to Postural Change

The physical demands placed on the body differ depending on the type of physical stressor. Physical exercise tends to induce a constant or rhythmic strain on the cardiovascular system, resulting in enhanced sympathetic outflow and reduced parasympathetic activity to the heart and vessels. Postural changes, however, involve brief changes to the body orientation requiring different hemodynamic responses to exercise. For example, HR and cardiac output abruptly increase in the transition from sit to stand (Pauls et al., 2018). These changes, along with elevated total peripheral resistance, decreased stroke volume, diastolic blood pressure and mean stroke ejection rate with unchanged SBP are consequences of prolonged standing (Frey et al., 1994). Similar immediate responses in HR and cardiac output are observed when actively transitioning to laying down, although the response time can be quicker to active standing (Pauls et al., 2018).

Borst and colleagues (1982) reported different cardiovascular responses between passive and active supine to standing posture. A 70-degree table tilt was used to passively place the body into a similar gravitational induced stress that occurs when in an upright standing posture. Both active and passive tasks took 2-3 seconds to complete. During passive changes to posture, the HR response was delayed by one second before it gradually increased beyond 20 seconds after transitioning to an upright posture. While actively standing, HR increases were stronger than passive movement (40% vs. 10%) and followed a bimodal pattern. Heart rate immediately increased, peaking at 3 seconds, decreased slightly between 3-5 seconds, increased once more between 5-12 seconds, before it decreased for another 6 seconds. The blood pressure response during passive movement was accompanied with a progressive increase in blood pressure, while during active movement blood pressure rapidly increased in the first second before it decreased. Blood pressure returned to resting values approximately 15 seconds after standing was initiated. The first HR response, starting around 0-5 seconds, was believed to be exercise pressor reflex mediated as sympathetic control over HR increased and vagal activity decreased during contractions of muscle groups (Borst et al., 1982). Cardiovascular responses elicited with the exercise pressor reflex can occur within 0.5 seconds of stressor onset (Kaufman et al., 1983), while a baroreflex-mediated effect can occur within 1 second of the stimulus (Pickering & Davies, 1973). The second cardiovascular response that instigated the second increase in HR was thought to have occurred due to baroreflex-mediated bradycardia. The absence of an anticipatory component raises the question as to whether muscle afferent input is required for central command to influence cardiovascular adjustments.

To further examine the role of anticipation on cardiovascular changes to transitions to upright stance, Patel and colleagues (2018) used anticipated passive head-up tilt in cats. A visual cue was presented to supine cats 30 seconds prior to a 60-degree head-up tilt. An immediate HR increase was observed at the onset of the movement, but there was no difference in mean HR 5 seconds prior to the movement compared to the time period prior to the visual cue. Additionally, the researchers found no exaggerated HR response when a surprise 20-degree head-up tilt trial was inserted. The authors

posited that feedforward responses do not occur prior to anticipated passive postural changes.

It is possible that intended movement combined with an emotional event is required to initiate a cardiovascular feedforward response (Maren, 2001; Smith et al., 2000). Therefore, it would be of interest to examine cardiovascular variables during changes in posture that are induced with an emotional response. The influence of anxiety on the cardiovascular system should not be understated. There is an adrenomedullary response immediately after experiencing a stressful stimulus (Fischer et al., 2016). A rapid release of catecholamines from the adrenal medulla stimulates a concomitant increase in HR and blood pressure during rest; albeit the cardiovascular effect would lag as catecholamines circulate the blood stream. The transient effect of anxiety on hemodynamics has been reported. Salivary cortisone, a biomarker for stress, is correlated with state-trait anxiety scores and HR response following a psychological stimulus (Bae et al., 2019), while state anxiety scores scale with blood pressure during quiet standing at different platform heights (Carpenter et al., 2006).

Recent evidence suggests that the cardiovascular system (Garg et al., 2014b) and respiratory system (Rodrigues et al., 2018) can play a vital role in the maintenance of standing balance. A cardiopostural integration loop was proposed to explain the interaction between the cardiovascular (blood pressure regulation), postural (center of pressure regulation) and muscular (muscle activity) systems in upright standing (Garg et al., 2014b). During a passive sit to stand task, they found that 40% of the total interactions are amongst these three systems. Interestingly, the cardiovascular system coupled with the postural or muscular system made up almost half of the total interactions. The cardiopostural interaction was posited to function as a secondary response, in the event that adequate blood pressure regulation could not be maintained by the cardiovascular system alone. The authors suggested a linear cardiopostural subpathway between COP, EMG and SBP that worked in both directions. That is, the cardiopostural system can be mediated by either a postural stimulus or by a cardiovascular stimulus. The cardiopostural integration loop can explain the role that skeletal muscle pumps play in preventing hypotension. Increased body sway in

individuals with poor orthostatic tolerance (Claydon & Hainsworth, 2005) may act as a coping mechanism to enhance venous return to the right atrium (Inamura et al., 1996).

Research investigating the cardiopostural integration during orthostatic stress is building. However, investigating the interaction between cardiovascular and postural systems during periods of instability is absent. Mild rhythmic muscle contractions, similar to those that occur in quiet standing, are enough to mediate blood pressure regulation (Rowell, 1986). Coupled with threats to postural stability evoking a startle response (Campbell et al., 2013), unexpected threats to standing balance may evoke central- and peripheral-mediated cardiovascular mechanisms.

1.3 Respiration

Rhythmic respiratory patterns are mediated by the central respiratory drive (Eccles et al., 1962; Sears, 1964). The central respiratory drive originates from the ventral and dorsal respiratory groups within the medulla oblongata (Ezure, 1990). The diaphragm is a muscle located at the intersection between the thorax and abdomen which closely resembles a cone shape. During inspiration, the diaphragm contracts, flattening the muscle, increasing intraabdominal pressure and decreasing intrathoracic pressure in their respective cavities. The diaphragm works in association with external intercostal, parasternal, sternomastoid and scalene muscles that expand the lower ribs upwards and outwards (Russo et al., 2017). Transdiaphragmatic pressure created by the contraction of the diaphragm decrease intrathoracic and intrapleural pressure. These movements create a negative pressure inside the lungs compared to the external environment, drawing air inside the body (Mateika & Duffin, 1995). Resting expiration is a passive process that occurs due to the passive recoil of the lungs. Active or forceful expiration, however, require rectus abdominus and internal intercostal muscle involvement to quickly expel air out of the lungs.

The diaphragm assists in the maintenance of abdominal pressure and producing smooth respiratory patterns (Vostatek et al., 2013). During inhalation, blood supply to the heart is increased due to intrathoracic and intrapleural pressure decreasing, and intraabdominal pressure increasing. Compression of the hepatic veins also occurs,

limiting hepatic venous outflow. The pressure gradient between the thorax and abdomen increases venous return (Rowell, 1986). During exhalation, the opposite occurs. Intrathoracic pressure increases and intraabdominal pressure decreases, which reduces the pressure gradient between upper and lower cavities, that would normally impede venous return. However, reduced pressure in the abdomen releases blood from the hepatic veins and smoothens any blood pressure fluctuations that would hamper blood returning to the right atrium during exhalation.

Similar to how respiration affects blood circulation, respiration can also influence vagal control over the heart. Inspiration increases HR, while expiration causes a decrease (Russo et al., 2017). This is known as respiratory sinus arrhythmia. Respiratory sinus arrhythmia operates around 0.25 Hz under resting conditions, but is dependent on respiratory rate (Russo et al., 2017). Many central and peripheral factors, such as baroreceptors, chemoreceptors, metabolic and local mechanical factors can impact respiratory sinus arrhythmia (Berntson et al., 1993). Many of the neural pathways associated with respiratory sinus arrhythmia (i.e., nucleus tractus solitarius and nucleus ambiguus) are major neural networks found within mechanical and reflex cardiovascular mechanisms (Zec & Kinney, 2001). Thus, respiration can influence HR and blood pressure oscillations due to its effect on venous filling, stroke volume, cardiac output and peripheral blood flow (Elstad, 2012; Laude et al., 1993).

1.3.1 Slow Breathing

The brainstem respiratory centres involved with automatic breathing are also activated during volitional breathing. Volitional breathing also activates the motor cortex, premotor cortex and supplementary motor areas, which are regions of the brain associated with motor movement (McKay et al., 2003). Breathing at a pace of six breaths per minute can increase the magnitude of blood pressure and HR fluctuations when compared to spontaneously breathing (Chang et al., 2013). The effect of slow breathing on hemodynamics can be mechanical and neural in nature. As mentioned above, respiration affects the internal pressure gradient that alters blood flow. At six breaths per minute, blood pressure fluctuations can be three-to-four fold larger compared to

spontaneously breathing due to pressure differentials as the diaphragm contracts and relaxes (Reyes del Paso et al., 2015).

Respiration can also affect blood pressure and HR through its direct effect on the cardiovascular, cardiorespiratory and autonomic nervous systems. A review of the physiological effects associated with slow breathing identified the following cardiovascular effects of slow breathing (Russo et al., 2017). Slow breathing increases venous return, which leads to increased stroke volume, and thus, cardiac output; increased heart rate variability and blood pressure fluctuations; decreased mean blood pressure; and the synchronization of blood pressure and HR fluctuations. The cardiorespiratory effects from slow breathing include increased cBRS and increased respiratory sinus arrhythmia. The effects of slow breathing on the autonomic nervous system comprise of increased vagal activity, a shift towards parasympathetic nervous system dominance, optimization of acetylcholine release and hydrolysis at the sinoatrial node of the heart, enhanced phasic modulation of sympathetic nervous system activity and increased autonomic responsiveness to physical perturbations, such as standing (Russo et al., 2017). The physiological effects of slow breathing can then create optimal internal environments for the body when the cardiovascular system is perturbed.

In recent years, there has been an influx of literature describing the effects of volitional and/or slow breathing on skeletal muscle activity. Barbosa and colleagues have found that Pilates breathing can lead to increased EMG activation of biceps brachii, rectus abdominis, transverse abdominis and interior oblique muscles during maximal voluntary contractions (Barbosa et al., 2015; Barbosa et al., 2013), and increased EMG activation in the longissimus dorsi and transversus abdominus muscles at 50% maximum voluntary contraction (Barbosa et al., 2018) compared to spontaneously breathing. Their findings have also been applied to dynamic movements. During a squat, they found increased EMG activity in the rectus femoris, biceps femoris, and tibialis anterior throughout the flexion phase of the squat, with no change in the medial gastrocnemius while participants performed Pilates breathing compared to spontaneously breathing (Barbosa et al., 2017). During the extension phase of the squat, the medial gastrocnemius had decreased EMG activity, while the other muscles saw no change during Pilates

breathing compared to spontaneously breathing. Their findings indicated task- and muscle-specific responses to slow breathing.

After transitioning to upright standing, the effect of slow breathing can intensify cardiac autonomic reactivity (Vidigal et al., 2016). This may be due to the frequency of respiratory rate coinciding with spontaneous blood pressure fluctuations which would increase cardiac oscillations as the sympathetic and vagal systems would synchronize (Berntson et al., 1993). The next step would be to examine the effects of slow breathing on muscle activity in a population with impaired or inhibited neuromuscular responses to physical tasks.

To examine the effect of slow breathing on orthostatic stress in older adults, Rodrigues et al. (2018) compared COP displacement in older women when deep breathing at six breaths per minute, controlled breathing at 15 breaths per minute and spontaneously breathing. Controlled breathing was accomplished by voluntarily breathing at 15 breaths per minute. Volitional breathing, whether at six breaths per minute or 15 breaths per minute increased EMG root mean square activity of the tibialis anterior throughout the first six minutes of orthostatic stress compared to spontaneously breathing, while there were no differences in the soleus and lumbar iliocostalis between breathing conditions. Prolonged deep breathing was found to be associated with larger COP displacement at the sixth minute after orthostasis compared to the other breathing conditions. The increased body sway was believed to have contributed to the skeletal muscle pump promoting blood back to the heart (Claydon & Hainsworth, 2005).

1.4 Aging

Aging populations are known to have cardiovascular impairments (Karavidas et al., 2010; Monahan, 2007; Paneni et al., 2017) and balance deficits (Lord et al., 1991; McIlroy & Maki, 1996; Paillard, 2017). Cardiovascular issues occur largely due to altered blood pressure regulation (i.e., increased vascular resistance, decreased ability for the heart to respond to acute fluctuations in blood pressure and reduced cBRS). Deterioration of sensory and neuromuscular systems affects postural control (Guskiewicz & Perrin, 1996; Henry & Baudry, 2019). Claydon and Hainsworth (2005) suggested that

increased body sway when standing may be a coping strategy for poor orthostatic tolerance to avoid fainting. More frequent and larger body sway can occur to promote the use of skeletal muscle contractions (muscle pumps) to push pooled blood from the lower limbs and body up towards the right atrium (Claydon & Hainsworth, 2005).

Cardiovascular age-related changes can affect the vasculature, cardiac cells and the heart. The loss of distensibility in large vessels from increased collagen and deceased elastin and increased vasoconstrictor tone can have a profound effect on vasculature stiffness (Paneni et al., 2017). Increased stiffness leads to elevated SBP and decreased diastolic blood pressure after the sixth decade (Karavidas et al., 2010). Left ventricle wall thickness also increases with age. Wall thickness is believed to be attributed to prolonged elevated systolic pressure that can modify the shape of the left ventricle, increasing afterload and decreasing coronary perfusion (Paneni et al., 2017). Furthermore, the autonomic nervous system can be impacted due to fat build-up, less muscle mass and reduced parasympathetic response on cardiac cells (Karavidas et al., 2010). The structural and functional changes to the cardiovascular system would influence the hemodynamics to physical stress.

Cardiac baroreflex sensitivity is estimated through the relationship between SBP and HR (via R-R interval). The gain or sensitivity of the reflex is inversely related to age (Monahan et al., 2000). Stiffening of vasculature near baroreceptors (i.e., aorta and carotid artery) and inhibited sympathetic outflow affect the responsiveness of the baroreflex (Monahan, 2007). In upright standing, body sway can enhance blood circulation via mechanical muscle pumps in older adults (Verma et al., 2017; Verma et al., 2019). Conversely, baroreflex-mediated control over skeletal muscle activation is limited in older adults (Verma et al., 2017). In addition to change in the cardiovascular system, biomechanical changes to balance also take place due to aging.

Biological systems and their ability to function deteriorate with age. Components vital for balance performance, such as muscle force production, contractility, tendinous and muscle stiffness, muscle tissue elasticity, sensory integration, intermuscular coordination, number of type 2 twitch fibers, range of motion and reaction time are

negatively affected with age (Massion, 1994; McIlroy & Maki, 1996; Paillard, 2017; Roman-Liu, 2018).

Subtle balance performance deficits in the upright standing posture have been observed in adults as early as in the sixth decade, although balance deficits are more prominent at 60+ years of age (Johnson et al., 2020). Sensory input deterioration is partly to blame as visual, vestibular and proprioceptive signals from postural musculature are negatively affected by aging. Pathologies that impact vision (e.g., cataracts, glaucoma and age-related macular degeneration) are more prominent in older adults (Kahiel et al., 2021). Age-related effects can cause inhibited visual acuity, visual field, motion detection threshold, contact sensitivity and depth perception which are strongly related to poor balance performance (Althomali et al., 2019; Kahiel et al., 2021). Similarly, vestibular loss is influenced by age-related neuronal loss and reductions in sensory hair cells within vestibular structures (e.g., otolith organs and semicircular canals) that can negatively impact the transmission of vestibular evoked myogenic potentials (Allen et al., 2017). The most detrimental age-related effects may be due to changes in the proprioceptive system. The efficiency and sensitivity of the proprioceptive system to communicate changes in muscle length and joint torques are impeded by alterations to muscle spindles, Golgi tendon organs and neural pathways with age (Henry & Baudry, 2019). Alterations include increased capsular thickness of muscle spindles, decreased total number of nerve fibers and proportion of large fibers in muscle spindles, lower discharge frequency from stretch receptors, slower conduction velocity speeds and smaller axon diameters (Henry & Baudry, 2019). To compensate for these functional and neuronal changes, older adults may have larger COM and COP excursions and increased coactivation of lower limb muscles during quiet standing (Henry & Baudry, 2019; Massion, 1994). These adaptations are believed to be coping strategies to reduced sensory information. Overexaggerated body swaying allows for inhibited sensory thresholds to be surpassed, enhancing stability. Furthermore, sensory information re-weighting occurs to allow uninhibited sensory systems to compensate for dysfunctional sensory systems. For instance, in older adults, there is a greater reliance on visual feedback compared to younger adults (Parijat et al., 2015).

During perturbed standing balance that requires a stepping reaction, swing duration, swing velocity, step length and COM changes in response to step initiation were the same in young and older adults (McIlroy & Maki, 1996). However, McIlroy and Maki (1996) found that reaction time to the perturbation was delayed and, if a step was required to regain balance, older adults took more steps compared to young adults. These findings suggest that automatic postural responses to external perturbations are similar throughout age, albeit delayed in older adults.

Fear of falling is a component to balance that should not be overlooked, especially in older adults. Coping strategies for fear of falling are similar between young and older adults (Carpenter et al., 2006). However, older adults are more likely to have this emotional response to fear of sustaining an injury due to a fall. Therefore, the CNS in older adults must compensate for greater sway frequency and decreased sway magnitude during quiet standing (Adkin & Carpenter, 2018).

1.5 Purpose

The overall objective of this dissertation is to examine the effect of surface support postural perturbations on the cardiovascular system and skeletal muscle activation in healthy adults. This dissertation describes the cardiovascular and neuromuscular responses to postural perturbations through four projects that repeated surface-translation perturbations at different velocities, with known or unknown timing, and while spontaneously breathing and breathing at six breaths per minute in young and older adults.

Study One

Cardiovascular response to postural perturbations of difference intensities in healthy young adults

The primary purpose of this study was to examine the cardiovascular response following a standing balance perturbation of varying intensities. Secondary aims were to quantify cBRS during standing perturbations and to establish the stability of the baroreflex during quiet standing before and after balance disturbances.

Study Two

Cardiovascular Response to Anticipatory and Reactionary Postural Perturbations in Young Adults

The primary purpose of this study was to determine the effect of anticipated and reactionary perturbations on HR and SBP responses in healthy young adults. A secondary aim was to determine whether perceived state anxiety scores were correlated with the change in HR response to postural perturbations.

Study Three

The effects of slow breathing on postural muscles during standing perturbations in young adults

The purpose of this study was to examine the effect of slow breathing on the onset latency and amplitude of postural muscle responses to perturbations of the base of support in healthy, young adults.

Study Four

The effects of slow breathing on cardiovascular response and electromyography response during unexpected standing perturbations in older adults

The purpose of this study was to determine: 1) the effect of slow breathing on HR and SBP response following surface support postural perturbations in older adults; and 2) the effect of slow breathing on lower limb muscle onset latency and burst amplitude during surface support postural perturbations in older adults.

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Chapter 2

2 Cardiovascular Response to Postural Perturbations of Different Intensities in Healthy Young Adults

A version of this manuscript has been published: Siedlecki, P., Shoemaker, J. K., Ivanova, T. D., & Garland, S. J. (2022). Cardiovascular response to postural perturbations of difference intensities in healthy young adults. *Physiological Reports, 10*(9), e15299. doi:10.14814/phy2.15299

2.1 Introduction

It is reported that 37.3 million falls occur each year that require medical attention and that the risk of sustaining a fall in adults increases with age (World Health Organization, 2018). Standing balance relies on the central nervous system' control of skeletal muscle torques to regulate the COM following an external perturbation (Ogaya et al., 2016; Silva et al., 2018; Winter et al., 1998). Additionally, the autonomic nervous system modulates cardiovascular function during postural adjustments (Carpenter et al., 2006; Olufsen et al., 2005). Recent findings illustrated temporal associations between SBP, muscle activity and postural control during quiet standing (Garg et al., 2014), supporting the concept of a coupling between cardiovascular and skeletal muscle control to support balance. To date, the role of the baroreflex in supporting postural blood pressure adjustments are limited to quiet standing conditions. The cardiovascular adjustments to more severe postural perturbations, and how they relate to baroreflex function, are not known.

Automatic adjustments to physical stress can be centrally- and/or reflex-mediated (Dombrowski et al., 2018). The role of baroreflex regulation of blood pressure is complex, representing contributions from central neural systems (McCloskey & Mitchell, 1972), as well as ascending feedback from baroreceptors, chemoreceptor and mechanosensors located in skeletal muscle (see Raven, Young, & Fadel (2019) for review). The gain or sensitivity of the reflex is highly modifiable and can change rapidly due to its relationship to cardiovagal dominance of HR (La Rovere et al., 2001). This

process of baroreflex engagement represents a critical element of achieving rapid cardiovascular adjustments to exercise (Raven et al., 2019; Zamir et al., 2017) and postural shifts (Schwartz & Stewart, 2012). Whether changes in cBRS accompany adjustments to acute postural perturbations is not known. Therefore, HR and blood pressure responses could be explained by baroreflex involvement to hemodynamic regulation following postural perturbations.

The primary purpose of this study was to examine the cardiovascular response following a standing balance perturbation of varying intensities. Secondary aims were to quantify cardiac baroreflex sensitivity during standing perturbations and to establish the stability of the baroreflex during quiet standing before and after balance disturbances. The study tested the hypothesis that postural perturbations would induce intensity-dependent increases in HR and blood pressure that would coincide with an elevated cBRS.

2.2 Methods

2.2.1 Ethical Approval

Twenty young adults, who reported no neurological disorders, respiratory diseases, or musculoskeletal disorders, and considered themselves to be healthy, completed the study. Although medication use and the presence of cardiovascular disease were not used as exclusion criteria, all participants were normotensive, had normal resting HR while standing and had a body mass index < 30 kg/m^2. Participants were asked to fast for a minimum of 4 hours, to refrain from consuming caffeinated and alcoholic beverages, and to avoid any strenuous physical activity for 24 hours prior to their scheduled appointment. Participants provided written consent to the study procedures that had been approved by the University of Western Ontario Health Sciences' Research Ethics Board (#110471). The study conformed to the standards set by the Declaration of Helsinki, except for registration in a database.

2.2.2 Experimental Protocol

Participants began by filling out the Self-Evaluation Breathing Questionnaire (SEBQ-2) to identify respiratory-related symptoms that could be associated with impaired breathing (Courtney & van Dixhoorn, 2014). The 25-item self-report questionnaire ranks statements regarding symptoms on a 0-3 Likert scale, 0 indicating the statement is not true and 3 indicating the statement is true and that the symptoms occur very frequently. Overall scores greater than 11 out of 75 indicate the possibility of respiratory-related problems (Courtney & van Dixhoorn, 2014). The Community Balance and Mobility Scale (CB&M) was performed to assess ambulatory balance (e.g., unilateral stance, tandem walking, hopping, walking forwards and backwards, etc.). Each of the 19 items (including one bonus point) were rated by the same researcher (P.S.) on a scale of 0 to 5, with 96 as the best overall score (Howe et al., 2006).

Participants completed the perturbation testing using the Gait in Real-time Analysis Interactive Lab (GRAIL; Motekforce Link, Amsterdam, The Netherlands) system. The GRAIL consists of a split-belt treadmill and a 180-degree virtual reality screen in a quiet, dimly lit room. The virtual reality screen, positioned in front of the participant, displayed a cobble stone path through an open grass field. The movement of the image was linked to the treadmill belts (e.g., if the belts moved posteriorly, the path on the screen would appear to be moving towards the participant). The virtual reality screen was used to create a more realistic experimental environment compared to traditional laboratory settings (Teel et al., 2016; Teel & Slobounov, 2015). Participants wore an upper body safety harness that did not provide any body weight support but would prevent a fall. Participants stood on the treadmill and were fitted with a 3-Lead Bio Amp ECG (ADInstruments, Bella Vista, Australia) and a finger cuff with brachial Finometer sphygmomanometer (Finapres Medical System, Amsterdam, The Netherlands) placed on the right arm to collect cardiovascular measures throughout the experiment. An arm sling was worn by participants to restrict movement of the right arm as the sphygmomanometer was sensitive to movement.

Postural perturbations were introduced using simultaneous posteriorly directed movements of both treadmill belts with a 300 ms duration, which caused a forward

movement of the participant's COM. Participants were instructed to regain balance without taking a step or grasping the treadmill handles. If participants had to take a step, they were told to do so with their left leg. Participants were instructed to limit head movement by focusing on a fixation point (horizon) located on a virtual reality screen approximately 2.5 m in front of them. During a familiarization period, the perturbation velocity was increased in a stepwise fashion. Three perturbation intensity levels, low (LOW), medium (MED) and high (HIGH) were determined for each participant. The maximum velocity at which a participant was able to maintain balance without taking a step was selected as the MED condition. The LOW and HIGH conditions were determined to be 50% below and 50% above the MED velocity, respectively. Therefore, only the HIGH condition required a step to regain balance. There were no trials in which participants took a step in the LOW or MED conditions. The average treadmill belt velocities for the perturbation intensities were; 0.19 m/s for LOW, 0.35 m/s for MED and 0.62 m/s for HIGH conditions with peak velocities being 0.31 m/s, 0.61 m/s and 0.92 m/s for LOW, MED and HIGH, respectively. The condition order was randomized, and each condition consisted of 25 perturbations of the same intensity level, delivered 8-10 s apart with a 1-min rest between conditions. Each condition lasted 4-4.5 min. Participants began each condition standing in the middle of the treadmill track. Participants re-positioned themselves only in the MED condition to avoid falling off the treadmill track every 5-10 perturbations. These corrections were made after the ~8 s period of cardiovascular reaction following the perturbation. The subsequent perturbation was delayed if re-positioning occurred too close to the next planned perturbation.

The treadmill perturbations were triggered using an application created in the GRAIL software D-flow (Motekforce Link, Amsterdam, The Netherlands). The speed of each treadmill belt was recorded through a Phidget Analog 4-output #1002_0B (Phidgets, Inc., Calgary, AB, Canada).

2.2.3 Blood Pressure and Heart Rate Response Calculations

The blood pressure and electrocardiogram tracings, sampled at 1000 Hz (Powerlab 8/35; ADInstruments, Bella Vista, Australia) were used to derive the beat-to-beat SBP and HR, respectively and exported for further analysis. Belt velocity signals

together with SBP and HR for each perturbation condition were imported into Spike2 v.8.13 (Cambridge Electronic Design Limited, Milton, England). The onset of each perturbation was determined by threshold-crossing on the filtered left treadmill belt speed signals. The threshold was calculated as the point where the signal reached two standard deviations (SD) above the mean in a 500 ms epoch prior to the perturbation. The beat-to-beat data were down-sampled to 50 Hz and a 12 s window starting 4 s prior to the onset of the perturbation was selected for each trial. The SBP and HR data were normalized to each participant's SBP and HR at Baseline during quiet stance, respectively. Trials with artifacts in the SBP or HR tracings were excluded. Individual trials were averaged for each participant within each perturbation condition. Data from five minutes of quiet standing before and following the test trials were used for Baseline and Recovery periods, respectively.

2.2.4 Baroreflex Sensitivity Calculations

One of our aims was to determine changes in cBRS during the period immediately following the balance perturbation until re-stabilization. All calculations were performed with MATLAB R2019b (MathWorks Inc., Natick, MA, USA). For baseline conditions, the sequence method (Parati, Di Rienzo, & Mancia, 2000) was applied to the beat-to-beat R-R interval and SBP data from Baseline (5 min) and Recovery (5 min) periods. Following observations of the rapid but transient HR and SBP changes after the perturbations (see Figure 2A), the sequence method was applied to a time period (1 to 8 s) following the onset of each perturbation (+ 0.4 s if the onset occurred between two heart beats). This method was adapted from Gabbett and colleagues (2001) to view the immediate cardiovascular response. Artifacts in R-R interval and SBP, identified by visual inspection, occurred rarely, and only affected a single data point when present. These data points were replaced with interpolated data one cardiac cycle before and after the missing data point.

The sequence method calculated cBRS with a lag set at 0 beats using non-normalized R-R interval and SBP data. This lag was determined post-hoc based on the average R-R interval in each condition being less than 775 ms (Blaber et al., 1995). A sequence was determined as three or more consecutive cardiac cycles where R-R interval

and SBP increased or decreased together. A minimum change in R-R interval (4 ms) and SBP (1 mmHg) between beats must have occurred to have been considered part of a sequence. The slopes of the regression line between R-R interval and SBP was calculated for each sequence, and only sequences that had regression lines with $r^2 > 0.85$ were used. Cardiac baroreflex sensitivity was determined to be the average of the slopes of all sequences within the selected time periods (Bertinieri et al., 1985).

2.2.5 Statistical Analysis

All statistical analyses were performed with SPSS v.25 (IBM SPSS, Armonk, NY, USA). To compare beat-to-beat SBP and HR response between perturbation conditions, the change between the SBP and HR values at each second after the perturbation and the perturbation onset was calculated. Separate two-way repeated measures ANOVAs with condition (LOW, MED, HIGH) and time (0, 1…8 s) were performed to compare the change in SBP and HR for 8 s after a perturbation. One-way repeated measures ANOVAs were used to determine the effect of perturbation intensity on cBRS. As no statistically significant differences in cBRS between perturbation intensities were found, the data were averaged across perturbation intensity. This also increased the number of sequences in the perturbation tasks (~53 sequences) so that they were closer to the total number of sequences found during Baseline (75 sequences). Paired sampled t-tests were used to determine the effect of perturbations (combined across intensity conditions vs. Baseline) on cBRS characteristics. Post-hoc pairwise comparisons with Bonferroni corrections were performed following all ANOVAs. Paired samples t-tests were used to examine the differences in cBRS between Baseline and Recovery periods. A mixed model, intraclass correlation coefficient (ICC) was used to determine the stability of the cardiac baroreflex between Baseline and Recovery quiet stance periods. The level of statistical significance was set to $p = 0.05$ for all analyses.

Table 1. Participant characteristics

Age *years*	**Sex**[+] *m/f*	**Height** *cm*	**Weight** *kg*	**SEBQ Scores** */ 75*	**CB&M Score** */ 96*
24.2 (3.3)	10/10	170.1 (8.9)	70.1 (12.6)	7.6 (6.1)	95.4 (1.0)

Data presented as mean (SD); [+] number of participants; SEBQ: Self-Evaluation Breathing Questionnaire; CB&M: Community Balance & Mobility Scale

2.3 Results

The participant characteristics are summarized in Table 1 and raw SBP and HR values for 4 s (~ five cardiac beats) pre-perturbation and the maximum SBP and HR value in the 8 s after the onset of the perturbation can be found in Table 2.

Table 2. Raw cardiovascular measures during perturbation tasks

	LOW	**MED**	**HIGH**
HR (bpm)			
Pre perturbation	82 (13)	81 (12)	82 (12)
Post perturbation peak	89 (13)	89 (13)	92 (12)
SBP (mmHg)			
Pre perturbation	122 (12)	124 (11)	129 (10)
Post perturbation peak	129 (12)	132 (13)	140 (12)

Heart rate (HR; n=18) and systolic blood pressure (SBP; n=19) data presented as mean (SD) in LOW, MED, and HIGH conditions.

2.3.1 Perturbation Intensity Effect on Cardiovascular Response

Figure 2 presents the average SBP (n=18) and HR (n=19) responses to the three perturbation intensities (Figure 2A) together with the average change from perturbation onset (time 0) for each second post-perturbation (Figure 2B). The SBP and HR data from one participant were excluded due to missing treadmill data and the SBP data were excluded from another participant in a single intensity condition due to movement artifacts caused by finger contractions occurring throughout the entire condition. There

was a significant effect of *time* for SBP changes ($p = 0.002$). No interaction effect between *condition* and *time* ($p = 0.156$) or main effect of *condition* ($p = 0.128$) were found for SBP. Pairwise comparisons across conditions showed that SBP was elevated at the 4th and 5th s after the perturbation ($p = 0.037$ and $p = 0.027$, respectively), returning to baseline at 6 s. There were significant main effects of *time* ($p = 0.001$) and *condition* ($p = 0.004$) for HR with no interaction effect between *condition* and *time* ($p = 0.287$). The HR was significantly elevated compared to baseline across intensity conditions at the 1st and 2nd s post-perturbation ($p = 0.006$ and $p = 0.002$, respectively). Also, the HR response was intensity dependent as HR was less elevated in the LOW intensity condition after the perturbation as compared to MED or HIGH ($p = 0.035$ and $p = 0.012$, respectively). There was no difference in how HR changed after the perturbation between MED and HIGH intensity conditions ($p = 1.00$).

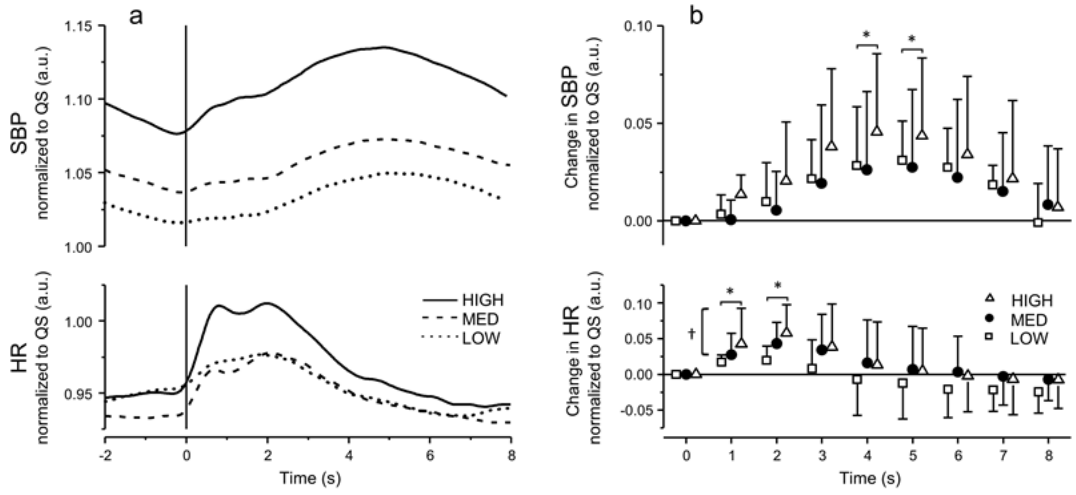

Figure 2. Systolic Blood Pressure (SBP) and Heart Rate (HR) during perturbations with different intensities. (a) Average beat-to-beat SBP (top) and HR (bottom) response 2 s prior to the perturbation and 8 s post-perturbation in the LOW (dotted line), MED (dashed line), and HIGH (solid line) intensity conditions. The vertical line represents the onset of the perturbation. (b) Average change in beat-to-beat SBP (top) and HR (bottom) for each second post-perturbation in LOW (open square), MED (filled circle), and HIGH (open triangle) intensity conditions. All data are normalized to quiet stance. *Significant differences from time 0 ($p < 0.05$).

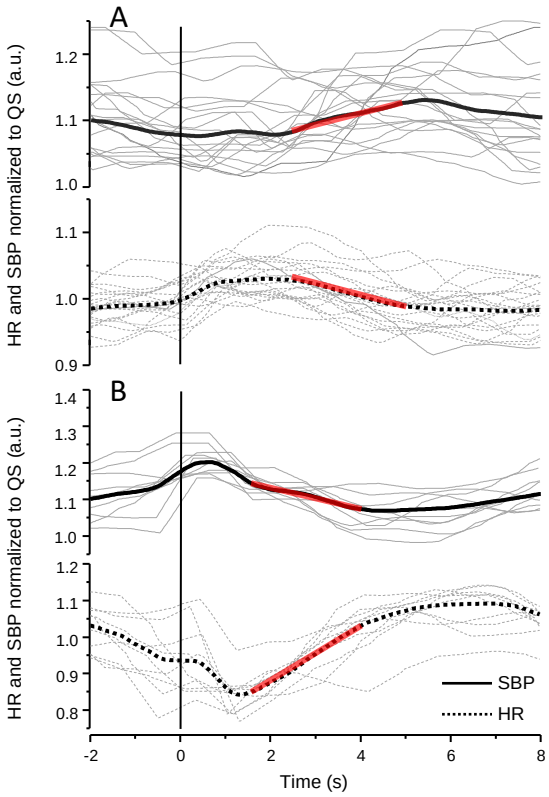

Figure 3. Beat-to-beat Systolic Blood Pressure (SBP) and Heart Rate (HR) for two participants during medium intensity perturbations. Examples of beat-to-beat SBP (solid line) and HR (dotted line) during MED perturbation demonstrating a commonly observed (a) and uncommonly observed (b) response. Data are presented as individual trials (grey lines) and the average (bolded lines). The vertical line represents the onset of the perturbation. The red lines over the SBP and HR data show the sequences used to calculate cardiac baroreflex sensitivity (cBRS).

The inter-individual variability in timing and direction of the cardiovascular response is illustrated in Figure 3. Two types of responses in SBP and HR to the perturbations were observed. A rapid tachycardia and delayed blood pressure response to postural perturbations occurred in most participants (Figure 3A), and a bradycardia response that aligned with a high SBP at the onset of the perturbation occurred in two participants (Figure 3B).

2.3.2 Perturbation Effect on Cardiac Baroreflex Response

The characteristics of the cardiac baroreflex sequence analysis are presented in Table 3. No effect of perturbation intensity was observed in cBRS gain (p = 0.570), the

length of sequences ($p = 0.723$), the ratio between the number of sequences and the number of perturbation trials ($p = 0.673$), the percentage of up sequences (R-R interval and SBP increased; $p = 0.636$), or the percentage of down sequences (R-R interval and SBP decreased; $p = 0.782$). When the data were averaged across perturbation intensities, cBRS was elevated during perturbations compared to Baseline ($p = 0.046$) whereby, of the sequences identified in the post-perturbation segment, the proportional number of up-sequences was higher compared to Baseline ($p < 0.0001$). There was no difference in the length of sequences between perturbations and Baseline ($p = 0.099$; Table 4).

Table 3. The characteristics of cardiac baroreflex sensitivity measures from the sequence analysis during perturbation tests

	Perturbation Intensity		
	LOW	MED	HIGH
Gain (ms/mmHg)	11.2 (6.1)	11.1 (6.5)	10.4 (4.9)
Length (# of RRIs)	3.6 (0.3)	3.6 (0.4)	3.6 (0.3)
Seq / Pert (%)	70 (27)	67 (23)	71 (20)
R^2	0.94	0.95	0.95
Up Seq (%)	75 (15)	76 (20)	79 (19)
Down Seq (%)	27 (15)	27 (20)	24 (19)

Data presented as mean (SD) for the LOW, MED, and HIGH intensity perturbations. For all sequence characteristics n=18, except for the Down Seq where n=15; RRI: R-R interval; Seq / Pert: ratio between the number of sequences to the number of perturbation trials; R^2: goodness-of-fit measure for the linear regression models (range: 0-1); Up Seq: sequences where both RRI and systolic blood pressure are increasing; Down Seq: sequences where both RRI and systolic blood pressure are decreasing expressed as the percentage of the total number of sequences.

2.3.3 Stability of the Baroreflex

Out of the 19 participants, 17 provided a complete data set for quiet standing (Table 4). All sequences during the 5-min quiet standing conditions were analyzed. The time between Baseline and Recovery period recordings was a minimum of 15 mins. There were no significant differences in cBRS ($p = 0.216$), sequence length ($p = 0.810$),

and total number of sequences (p = 0.243). However, during Recovery, the proportional number of up-sequences were elevated (p = 0.008) compared to Baseline. The ICC for quiet stance cBRS between quiet standing conditions was excellent (ICC = 0.896; 95% CI = 0.715 to 0.962).

Table 4. The characteristics of cardiac baroreflex sensitivity measures from the sequence analysis during quiet standing and averaged across perturbation conditions

	Task (n=19)		Quiet Standing (n=17)	
	Perturbation	Baseline	Baseline	Recovery
Gain (ms/mmHg)	10.6 (5.4)*	8.3 (2.4)	8.5 (3)	9.1 (3)
Length (# of RRIs)	3.6 (0.3)	3.8 (0.4)	3.7 (0.4)	3.6 (0.4)
Seq / Pert (%)	70 (20)	-	-	-
Total Sequences (#)	53 (7)	75 (10)	75 (9)	71 (12)
R^2	0.94	0.94	0.94	0.94
Up Seq (%)	77 (13)*	42 (5)	41 (4)	48 (4)*

Data presented as mean (SD) for the averaged LOW, MED, and HIGH intensity perturbations, Baseline, and Recovery conditions; RRI: R-R interval; Seq / Pert: ratio between the number of sequences to the number of perturbation trials; R^2: goodness-of-fit measure for the linear regression models (range: 0-1); Up Seq: sequences where both RRI and systolic blood pressure are increasing; * indicates a significant difference from Baseline ($p < 0.05$).

2.4 Discussion

The primary results from the study indicated that, overall, postural perturbations induced transient but rapid HR acceleration, accompanied with a delayed SBP increase. Heart rate response was affected by perturbation intensity. Subsequently, HR was decreasing towards baseline when SBP was increasing. The resulting cBRS was unaffected by perturbation intensity but was elevated during perturbations compared to Baseline.

2.4.1 Perturbation Intensity Effect on Cardiovascular Response

To our knowledge, this is the first study to measure the cardiovascular response during periods of postural instability. The data indicate that postural perturbations exhibit a form of physical stress that is reactionary in nature, comparable to voluntary exercise (Morgan et al., 1973; Wong et al., 2007). Therefore, the mechanisms mediating these responses might be comparable.

The HR response to postural perturbations was intensity dependent, a pattern that was not observed in the SBP response. The initial cardiovascular response to postural perturbations encompassed rapid and immediate tachycardia post-perturbation with the SBP elevation delayed by 2-4 s but both had recovered before the subsequent perturbation (Figure 2). A notable observation is the early and large rate of increase in HR, particularly the HIGH condition, that was recovering prior to, or consequent with, the rise in SBP. A second and unexpected observation was that of a “continuous” bradycardia during the immediate post-perturbation stage if the perturbation was initiated concurrently with a spontaneous rise in SBP. These results will have affected the variability in SBP and HR responses to perturbations although they also indicate that the baroreflex was operating well in this phase.

The mechanisms mediating the early and the late phases of cardiovascular response to the postural perturbations appear to be complex. First, the overall increase in cBRS suggests that the baroreflex was featured in the response. It might be argued that an expected outcome would be a reduction in cBRS in this period that scales with intensity, which is typical of exercise-induced changes (Bringard et al., 2017). The resolution of this unexpected outcome might be found in the pattern of HR and SBP changes in this post-perturbation period which suggest the potential for two mechanisms. First, the rapid HR response may be driven by the rapid vagal withdrawal common in volitional exercise, with slower adrenergic response in both cardiac and vascular smooth muscle (Borst & Karemaker, 1983; Fagius & Wallin, 1980; Qing et al., 2018; Stauss et al., 1997). Consequently, a rapid rise in HR (or reductions in R-R interval) while SBP is relatively stable during the first 2-3 s of recovery would be quantified as a marked resetting of the baroreflex set point. The return of HR to baseline when SBP was rising would be

predicted by a classic baroreflex mechanism that, likely, is returning to its baseline cBRS at this time.

Importantly, these studies were performed in the upright posture where considerable reduction in vagal dominance over HR had already occurred (Zamir et al., 2017), but the speculation that the rapid HR response was related to vagal withdrawal is consistent with recent evidence that vagal input still exists during exercise stress such that baroreflex manipulations can be made across a range of elevations in HR (Raven et al., 2019). Second, the relatively concurrent reduction in R-R interval and rise in SBP suggest baroreflex resetting is occurring (Raven et al., 2019). While the exact cause of baroreflex resetting is not fully understood, the invocation of a baroreflex resetting outcome immediately following the perturbation is consistent with the concept of a feed forward mechanism emanating from central neural sites (Krogh & Lindhard, 1913; Matsukawa, 2012; Migdal & Robinson, 2018). Whereas the muscle metaboreflex associated with fatiguing muscle contractions are also suspected in the baroreflex resetting process (Raven et al., 2019), it is unlikely that this mechanism participated in the current study because of the very brief and submaximal levels of the leg muscles during the approximately 8 s period of work. In contrast, the second phase of the post-perturbation period is what would be expected from a baroreflex inhibitory effect whereby increasing SBP would result in bradycardia.

2.4.2 Perturbation Effect on Baroreflex Response

The re-establishment of HR and SBP after the initial response to the perturbation suggests involvement of the cardiac baroreflex. As blood pressure increased, loading of the arterial baroreceptors would lead to deceleration of the heart. However, inter-individual variability in the time course of HR and SBP indicated that the cardiac baroreflex can operate in response to elevated or depressed SBP post-perturbation. The presence of baroreflex influence following a brief postural shift has been observed (Borst et al., 1982). The authors posited baroreflex-mediated bradycardia occurred secondary to the initial pressor response in a sit-to-stand task. The elevated cBRS found in the current study indicates that the cardiac baroreflex can modulate greater changes in HR with

similar changes to SBP. The benefit of elevated cBRS during postural perturbations might involve improved stabilization of arterial blood pressure.

The reasons for variability in cardiovascular response and timing of cardiac baroreflex involvement post-perturbation remains speculative. The upright posture and nature of the study provides additional influences on cardiovascular control that must be considered. Ventilation is a known determinant of HR. Also, the sequence method is influenced by respiration (Silva et al., 2019), although, the similar length of sequences during the conditions makes it unlikely that there was a large respiration effect on the cardiac baroreflex. Contributions from the vestibular system and emotional arousal may have impacted the results, both of which provide neural inputs into the brainstem nuclei that form the neural pathway of baroreflex function (Benarroch, 2018; McCall et al., 2017; Yates, 1996). Although acute psychological stress decreases cBRS in healthy adults (Truijen et al., 2011; Virtanen et al., 2003), in balance studies, anxiety created by fear of falling was correlated with blood pressure rises that influenced the selection of balance strategy (Carpenter et al., 2006).

2.4.3 Stability of the Baroreflex

Stability of the cardiac baroreflex measured during quiet standing before and after the perturbation conditions was strong, with an ICC value of 0.896. These data support the ability of the current protocol to evoke rapid and brief changes in cBRS. Also, the pre and post perturbation values of cBRS were similar to other studies that measured cBRS in upright standing (Bringard et al., 2017; Xu et al., 2017), although our values were on the lower end of the spectrum.

2.4.4 Limitations

The specific impact of respiration on the current data was not studied and breathing patterns were spontaneous. The perturbations were applied without reference to respiration, probably affecting the variability in R-R interval and SBP data. While the specific effects of breathing on the current outcomes are not known, they are expected to be diminished through the averaging of multiple trials in each condition. Also, the cardiovascular responses appear to have been affected by the timing of the perturbations

relative to spontaneous fluctuations in SBP. Lastly, it is not known if the cardiovascular response observed was due to postural shifts or a defense/alerting response. Additional studies are required to address these issues. The study results are delimited by the choice of perturbations and the state of health across the participants.

2.4.5 Perspectives

A novel approach to study cardiovascular response during active postural perturbations was conducted in healthy young adults. Results indicated central and reflex mediated hemodynamic response and recovery to postural perturbations. The importance of this regulatory mechanism in balance control may relate to the prevalence of falls in older adults who have been shown to demonstrate impaired cardiac baroreflex function in standing balance studies (Verma et al., 2017; Verma et al., 2019). Populations with balance deficits, such as older adults (Lord et al., 1991), are known to express an attenuated HR response (Muller et al., 2012) and altered blood pressure regulation (i.e., increased vascular resistance, and decreased ability for the heart to respond to acute fluctuations in blood pressure; Monahan, 2007; Rodrigues et al., 2018).

2.5 Conclusion

The results of this study provide evidence that HR response is intensity dependent, and that the cBRS is elevated compared to quiet standing but remains relatively consistent across the three levels of perturbation used in the current study. Maintaining balance during unexpected postural perturbations increased HR, followed by an increase in SBP. The mechanism is unknown, but it is speculated that the initial cardiovascular response to perturbations was followed by a robust secondary cardiac baroreflex response that drove HR and SBP recovery. In addition, stability of the cardiac baroreflex during quiet standing on a treadmill was strong. Therefore, monitoring cardiovascular response and cBRS during balance may be of interest and future studies can utilize this protocol’s design.

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Chapter 3

3 Cardiovascular Response to Anticipatory and Reactionary Postural Perturbations in Young Adults

3.1 Introduction

The autonomic nervous system controls the blood circulation and blood volume distribution to meet the metabolic demands of working skeletal muscles (Roatta & Farina, 2010; Xu et al., 2017). Autonomic adjustments to physical stress can be centrally mediated using a feedforward anticipatory mechanism, and/or through feedback reflex-mediated mechanisms (Dombrowski et al., 2018). Descending efferent commands result in motor and cardiovascular responses in anticipation of an increased workload (Williamson, 2010). The feedforward component of cardiovascular regulation works in conjunction with a feedback component to make minor adjustments throughout the task.

Skeletal muscles receive descending neural input from motor and sympathetic neurons (Barker & Saito, 1981), highlighting autonomic influence on skeletal muscle function (Blackwood & Katz, 2019; Cairns & Borrani, 2015). Interactions between cardiovascular and postural control systems during standing balance have been suggested (Garg et al., 2014). We have shown previously that postural perturbations resulted in immediate and transient tachycardia followed by increased SBP (Siedlecki et al., 2022b). The immediate cardiovascular response post-perturbation was suspected to be centrally mediated, accompanied by a secondary baroreflex response when SBP was increased concurrently with the decreased HR. It was also reported that the HR response, but not cBRS, scaled with intensity during reactionary postural perturbations (Siedlecki et al., 2022b).

Cardiovascular adjustments can occur prior to the onset of cycling when the timing of physical work is known and the workload is predetermined (Krogh & Lindhard, 1913). A concurrent rise in blood pressure and HR is often associated with the central command for physical exercise and is affected by the type of exercise, intensity of exercise, time after onset, and the effectiveness of blood flow in supplying metabolites to

working muscles (Mitchell, 2012). State anxiety also has a transient effect over the cardiovascular system at rest (i.e., HR, SBP; Virtanen et al., 2003), and has been observed to be positively correlated with blood pressure during postural control (Carpenter et al., 2006). The anticipatory and reactionary neuromuscular responses to postural perturbations have been well delineated (Bugnariu & Sveistrup, 2006; McIlroy & Maki, 1993; Piscitelli et al., 2017; Walchli et al., 2017). Thus, a possible rationale for the cardiac response scaling with perturbation intensity in Siedlecki et al. (2022b) could be as a result from the anxiety induced by postural perturbations.

The primary purpose of this study was to determine the effect of anticipated and reactionary perturbations on HR and SBP responses in healthy young adults. A secondary aim was to determine whether perceived state anxiety scores were correlated with the change in HR response during postural perturbation. It was hypothesized that if a centrally mediated response, with an anticipatory component, were driving any cardiovascular changes, anticipated challenges to standing balance would elevate HR and SBP response prior to postural perturbations, with larger responses occurring in more difficult perturbation tasks. It was also hypothesized that perceived state anxiety scores would be highest in the unpredictable and highest intensity conditions and would be correlated with the change in HR post-perturbation.

3.2 Methods

3.2.1 Participants

Twenty adults aged between 18-35 years, who met the inclusion criteria of having no history of cardiovascular, neurological, or respiratory health issues, completed the study. The study was approved by the Western University's Health Sciences' Research Ethics Board (#110471) and adhered to the principles and practices set out in the Declaration of Helsinki (World Medical Association, 2013). Prior to the experimental session, participants refrained from performing strenuous physical activity for 12 hours. Additionally, participants avoided consumption of alcoholic and caffeinated beverages, and fasted for a minimum of 4 hours before visiting the lab. Once written consent was

obtained, participants completed a health history and medication screening form to ensure the study inclusion criteria were met.

3.2.2 Experimental Protocol

The experimental procedures consisted of administering the CB&M scale and the SEBQ-2 followed by a standing balance protocol. The CB&M is a collection of 19 balance tests (e.g., unilateral stance, descending a set of stairs, walking forwards and backwards, etc.) that assess ambulatory balance in adults (Howe et al., 2006). Tests are scored by the researcher on a 0-5-point interval scale. The highest total score available is 96, which includes one bonus point. Higher scores reflect better balance performance. Participants in a similar age range have been reported to score approximately 95 on the CB&M (Siedlecki et al., 2022a; Siedlecki et al., 2022b). The SEBQ-2 is a 25-item self-report questionnaire that was used to assess respiratory-related health issues (Courtney & van Dixhoorn, 2014). Items are ranked on a 4-point Likert scale, ranging from 0 (never/not true at all) to 3 (very frequently/very true). An overall score greater than 24 out of 75 indicate the possibility of respiratory-related health problems (Kiesel et al., 2017).

The standing balance protocol consisted of three conditions: a 5-min quiet standing period and two perturbation types (self-triggered and computer-triggered), each comprising two perturbation intensities. The self-triggered perturbation (perturbation timing controlled by participant) was used to enable an anticipatory response, while a computer-triggered perturbation (exact timing of perturbation unknown) was used to stimulate a reactionary response to loss of balance. There was a total of four perturbation conditions: self-triggered/anticipatory perturbation causing a Step (STS) and No Step (STN), and computer-triggered/reactionary perturbation causing a Step (CTS) and No Step (CTN), described in more detail below. All perturbation conditions contained 25 trials occurring every 8-12 seconds. We have used a similar protocol to measure cardiovascular responses at different perturbation intensities (Siedlecki et al., 2022b).

The Gait in Real-time Analysis Interactive Lab (GRAIL; Motekforce Link, Amsterdam, The Netherlands) system was used to perform perturbation tests. The

GRAIL, consisting of an instrumented split-belt treadmill in front of a 180-degree virtual-reality screen, delivered bilateral, posteriorly directed translations of the treadmill belts (300 ms duration) while participants were standing. Participants wore an upper body safety harness which was attached to the ceiling; the safety harness did not provide any body weight support. Participants were fitted with a 3-Lead Colin Pilot-9200 Bedside Monitor ECG (Colin Medical, San Antonio, TX, USA), and a finger cuff with brachial Finometer sphygmomanometer (Finapres Medical System, Amsterdam, The Netherlands) placed on the right arm to collect continuous cardiovascular measures. An arm sling worn around the right arm limited the movement of the sphygmomanometer.

Participants were familiarized with the postural perturbations prior to data collection, as the velocity of the belt movements (perturbation intensity) increased with subsequent perturbations until participants were consistently taking a step to regain balance. The No Step intensity was determined as the highest intensity at which a participant was able to regain balance without taking a step or grabbing the handrails. The Step intensity was set to 50% above the intensity selected for the No Step intensity. The perturbation type order was randomized, as was the order of the intensities within the self-triggered and computer-triggered conditions. This meant that the Step and No Step intensities of the same perturbation type would always occur consecutively but in a different order across participants.

An application created in the GRAIL software D-flow (Motekforce Link, Amsterdam, The Netherlands) was used to trigger treadmill perturbations. A Phidget Analog 4-output #1002_0B (Phidget, Inc., Calgary, AB, Canada) recorded the speed of the treadmill belts. During the self-triggered perturbation type, a series of 25 perturbations was triggered by a touch sensor that was fixed to the participant's left thigh at a height that did not require a change in posture when touched to trigger the perturbation. The participant was told to wait for verbal instruction ("Whenever you are ready, touch the button") and then touch the button 2-3 s (or longer) after notification was received, and not to react immediately. After a perturbation was triggered, the button would automatically deactivate until the next trial (8-12 s). The computer-triggered perturbation type consisted of 25 trials that occurred simultaneously with an auditory cue.

To reduce the participant anticipating the computer-triggered perturbation, a perturbation was only triggered in approximately 70% of trials resulting in 17-18 perturbations over the 25 trials.

Participants were asked to rate their perceived state of anxiety during quiet stance (QS) and after each performed series of perturbations on a scale from 0 (“no anxiety”) to 10 (“the most anxious you have ever felt”). The perceived state anxiety scale was chosen over other anxiety questionnaires and scales due to quick administration and single-word responses that would limit arousal during the experimental session.

3.2.3 Blood Pressure and Heart Rate Response Calculations

The electrocardiogram, blood pressure, and belt velocity signal tracings were sampled at 1000 Hz in Powerlab 8/35 (ADInstruments, Bella Vista, Australia) to collect beat-to-beat HR and SBP data and to identify perturbation onset, respectively. The data for each series of perturbations were imported into Spike2 v.8.13 (Cambridge Electronic Design Limited, Milton, England). The beat-to-beat data were down-sampled to 50 Hz and an 11 s window starting 3 s prior to the onset of a perturbation was selected for each trial. The rationale for analyzing data 3 s prior to the perturbation was based on the time given to participants to trigger a perturbation in the self-triggered condition. Trials with artifacts in the HR and SBP tracings were excluded. An artifact was defined as a change in HR that was caused by the Powerlab software’s algorithm incorrectly labelling an ECG waveform or a change in SBP that was caused by pressure from an adjacent finger applying force against the finger cuff. These artifacts produced unrealistic HR (> 200 bpm) and SBP (> 300 mmHg) recordings. Individual trials were averaged for each participant within each perturbation type and intensity. Data averaged from the entire five-minute quiet standing period were used for QS.

Heart rate and SBP responses were compared across the perturbation types and intensities with 1-dimensional statistical parametric mapping (1-D SPM) analyses using an open source spm1d-package (spm1d.org, T. Pataky). The SPM method was selected over traditional scalar extractions because SPM provides a comprehensive analysis of dependent variables as a function of time, without concerns over data reduction, and

accounting for multiple comparisons (Pataky et al., 2013). Recently, 1-D SPM has been employed in human movement sciences comparing independent variables throughout a time series (Robinson et al., 2015; Serrien et al., 2019; Tretriluxana et al., 2021).

Continuous data, for dependent variables HR and SBP, were plotted in the first dimension (-3 s to +8 s). The data were converted into residuals and an F-statistic was calculated for each individual point (550 time points), creating an F-curve. Random field theory randomly sampled data and calculated the maximum F-value for each permutation across all data points and created a maximum F-statistic distribution for each permutation. The critical F-value (threshold) is determined based on the alpha level ($p = 0.05$) of the maximum F-statistic distribution and signifies the maximum F-statistic where the null hypothesis is true. The critical F-value is compared to the F-curve and any clusters above the critical F-value have a p-value less than 0.05, indicating that the null hypothesis must be rejected. Random field theory is used to calculate each cluster's specific p-value (Adler & Taylor, 2007).

The change in HR was also calculated by subtracting the HR at the time of the perturbation onset from the peak HR post-perturbation in all perturbation types and intensities.

3.2.4 Statistical Analysis

Statistical analyses were performed with SPSS v.25 (IBM SPSS, Armonk, NY, USA), R v.4.2.1 (R Core Team, 2022), and MATLAB 2019b (MathWorks Inc., Natick, MA, USA). The HR and SBP data were analyzed using 1D-SPM. A non-parametric two-way repeated measures ANOVA 1-D SPM (SnPM) test, for both HR and SBP, was used as the cardiovascular data were not normally distributed. The 1-D SnPM compared the response of the cardiovascular data over the function of time (-3 s to +8 s) between perturbation type (self-triggered and computer-triggered) and intensity (Step and No-Step).

A one-way repeated measures ANOVA was performed to evaluate the difference in perceived state anxiety scores across conditions (QS and perturbations). If a significant

difference was found, a Bonferroni post-hoc analysis was used to identify where the statistical difference occurred. A second analysis to determine the relationship between state anxiety scores and the change in HR post-perturbation was performed with a repeated measures correlation using the "rmcorr R package". The repeated measures correlation satisfies the assumption of independent observations and has greater statistical power than other simple correlation tests (Bakdash & Marusich, 2017).

The level of significance was set to $p < 0.05$ for all statistical tests mentioned above. Data are presented as mean (standard deviation; SD) unless otherwise stated.

3.3 Results

The participant characteristics can be found in Table 5. Data from two participants were excluded from the analysis due to incomplete HR data as a result of technical issues during data collection. During QS, the mean HR across participants was 84 (12) bpm, while SBP was 118 (13) mmHg.

Table 5. Participant characteristics

Age	**Sex**[+]	**Height**	**Weight**	**SEBQ Scores**	**CM&M Score**
years	*m/f*	*cm*	*kg*	*/ 75*	*/ 96*
24 (3.7)	10/10	172.5 (8.8)	70.9 (14.8)	4.8 (5.4)	95.6 (0.6)

Data are presented as mean (SD); [+] number of participants, m: male, f: female; SEBQ: Self-Evaluation Breathing Questionnaire; CB&M: Community Balance & Mobility Scale

3.3.1 Cardiovascular Response to Postural Perturbations

The mean HR and SBP during the four postural perturbation tasks for each individual can be found in Figure 4. It is apparent from Figure 4 that cardiovascular responses to the perturbation were occurring after the perturbation and were not starting prior to the perturbation in anticipation of the self-triggered perturbation type.

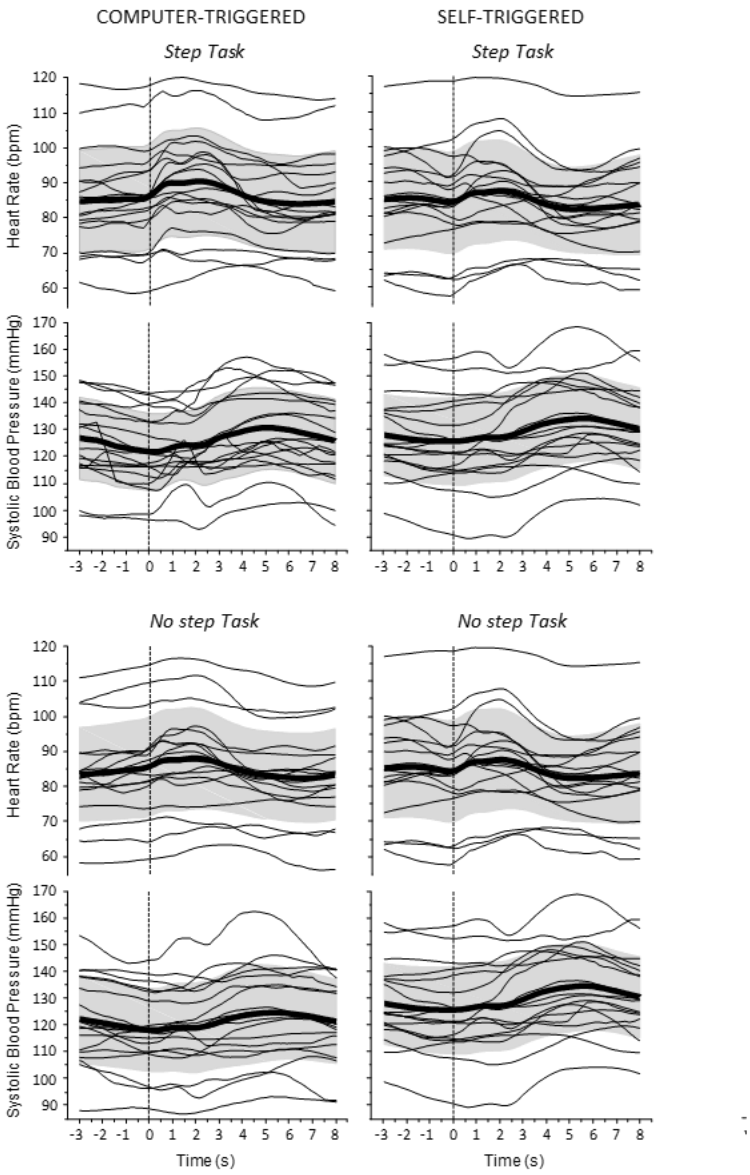

Figure 4. Heart rate (HR) and systolic blood pressure (SBP) response for computer-triggered (left column) and self-triggered (right column) perturbation conditions with Step (top row) and No Step (bottom row) perturbation intensities. The group means and standard deviations are presented with bolded black lines and grey shaded areas, respectively. The individual participants' HR and SBP (average across trials) are represented with thin lines. The dashed vertical line indicates the onset of the perturbation.

The average HR response in the self-triggered and computer-triggered perturbation types at two intensities is illustrated in Figure 5. The SnPM identified two supra-threshold clusters ($F^* = 5.874$) in the effect of perturbation *intensity* on HR. Heart rate was elevated in the Step intensity compared to the No Step intensity between 0.56 s

to 1.32 s ($p < 0.001$) and 1.92 s to 3.44 s ($p < 0.001$) after the postural perturbation regardless of whether the perturbation was self-, or computer-triggered. There was no statistically significant interaction effect between *perturbation type* and *intensity* ($F^* = 5.964$) or main effect of *perturbation type* ($F^* = 5.964$) for HR.

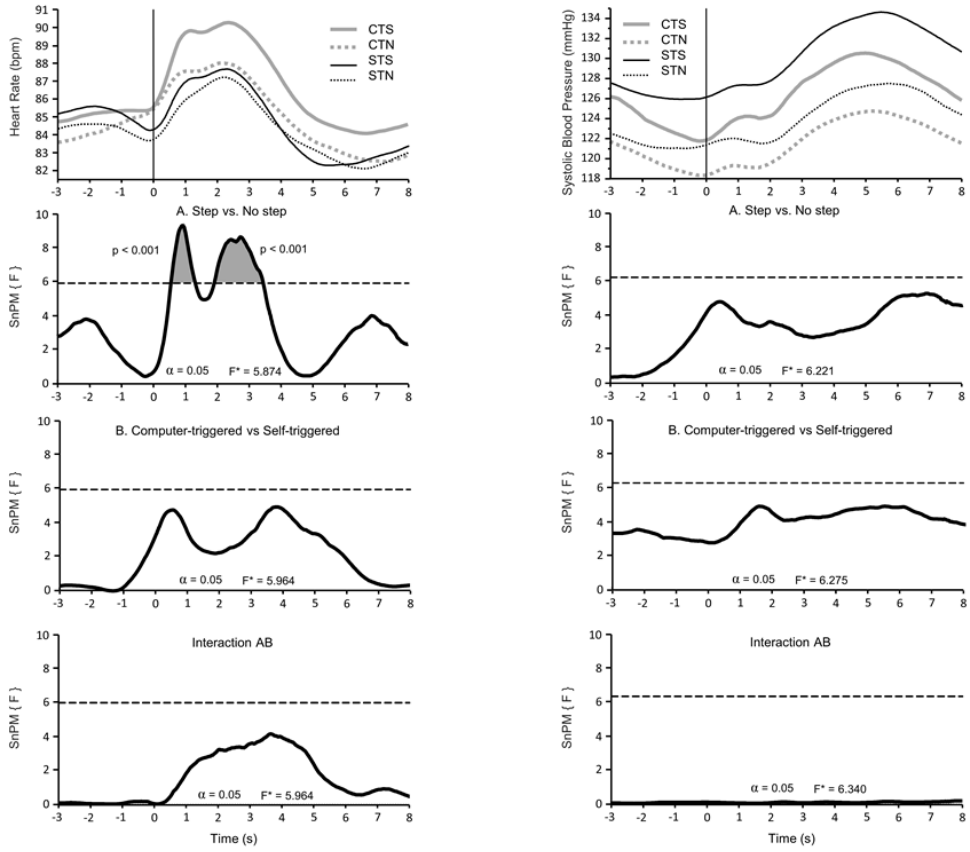

Figure 5. Statistical non-parametric mapping (SnPM) analysis for heart rate (HR; left column) and systolic blood pressure (SBP; right column). In the top row are presented the average HR and SBP in computer-triggered Step (CTS; grey solid line), computer-triggered No Step (CTN; grey dotted line), self-triggered Step (STS; black solid line), and self-triggered No Step (STN; black dotted line) tasks with the onset of the perturbation indicated with vertical line at time 0. The three rows below contain the plots of the SnPM F statistic (solid black lines) for the effect of perturbation intensity (A. Step vs. No step), effect of perturbation type (B. computer-triggered vs. self-triggered) and for the interaction between perturbation type and intensity (Interaction AB). Dashed horizontal lines in each panel represent the critical threshold for the non-parametric SPM tests.

No statistically significant interaction effect between *perturbation type* and *intensity* ($F^* = 6.34$), or main effect of *perturbation type* ($F^* = 6.221$), or main effect of

intensity (F^* = 6.275), was found for SBP. The average SBP responses during the perturbations can also be found in Figure 5.

3.3.2 Perturbation Effect on Perceived State Anxiety

There was a difference in perceived state anxiety scores between QS (1.2 (1.2)), STS (1.8 (1.3)), STN (1.5 (1.0)), CTS (2.9 (1.9)), and CTN (2.0 (1.6)) perturbations (F (4, 68) = 8.119, $p < 0.001$, $1\text{-}\beta = 0.965$). Perceived anxiety was rated higher in CTS compared to QS ($p = 0.001$), but there was no difference between QS and STN (p = 1.00), STS ($p = 0.668$), and CTN ($p = 0.274$). There were also no statistical differences in anxiety scores between STS and STN ($p = 1.00$), CTS and CTN ($p = 0.090$), STS and CTS ($p = 0.068$), and STN and CTN ($p = 1.00$) perturbations. The correlation analysis found that state anxiety scores were correlated with the change in HR post-perturbation ($r_{rm} = 0.331$, $p = 0.013$; Figure 6), indicating that higher state anxiety scores were moderately correlated with greater changes in HR following a perturbation.

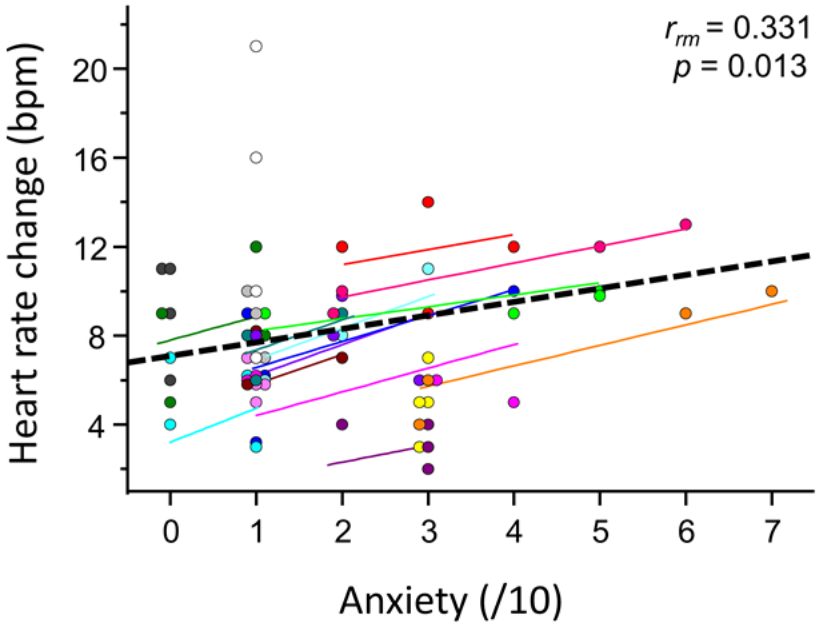

Figure 6. The repeated measures correlation between the change in heart rate (HR) and state anxiety scores following postural perturbations (bolded black line). The data for each participant comprising of individual's peak change in HR (averaged across trials) vs. anxiety score after a perturbation task (filled circle) and the line of best fit (thin solid line) are plotted in the same color. The overall line of best fit and correlation coefficient were calculated from the above mentioned lines of best fit of all participants.

3.4 Discussion

The main outcomes of the study are as follows: 1) The HR response scaled with the intensity of the perturbation; 2) Knowing the timing of the perturbation had no effect on HR and SBP prior to and after the postural perturbation; and 3) The perceived state-anxiety scores did not differ by perturbation condition but were correlated with the change in HR post-perturbation. These findings partially support the null hypotheses.

3.4.1 Cardiovascular Response to Postural Perturbations

No anticipatory response prior to the perturbation was found for HR and SBP when the timing of the perturbation was known. The similarities between pre-perturbation and QS HR and SBP also suggests a lack of an anticipatory response to perturbations. Additionally, a similar HR and SBP response occurred post-perturbation

regardless of whether the timing of the perturbation was known. Postural perturbations, regardless of intensity and knowing the timing of the perturbation or not, elicited immediate tachycardia followed by elevated SBP with HR recovering prior to the SBP recovery. The SBP response was not intensity-dependent, while HR was elevated in the Step compared to No Step task during the initial rise in HR (0.56 - 1.32 s) and during the recovery (1.92 - 3.44 s). The HR and SBP responses post-perturbation were in agreement with previous findings where the exact timing of the perturbation was unknown (Siedlecki et al., 2022b).

The similar findings between self- and computer-triggered perturbations could be partly due to the emotional response to the perturbations. Anticipatory HR and blood pressure changes can be affected by the effortful nature of a task (Gandevia et al., 1993; Morgan et al., 1973). Volitional limb movements alone are not enough to evoke an anticipatory cardiovascular response as movement must also be accompanied with emotional content (Smith et al., 2000). The self-triggered postural perturbations were not accompanied by lower state anxiety scores than computer-triggered perturbations. It should be noted that perceived anxiety scores only increased during computer-triggered Step perturbations despite HR response scaling with intensity in both perturbation conditions.

Whereas elevated state anxiety enhances the physiological arousal of the sympathetic nervous system, consequently triggering tachycardia during stressful events (Dimitriev et al., 2016), it would appear that the participants did not consider any of these perturbations to be particularly anxiety provoking as most participants rated anxiety below 4 out of 10 during perturbation tasks. The difference in anxiety scores between the intervention and placebo conditions can vary by approximately 10 units when using the state-trait anxiety inventory (Bae et al., 2019), further suggesting that postural perturbations in the current study may not have been perceived as being challenging. Although the timing of the perturbation was unknown in the computer-triggered condition, participants still knew that they would be perturbed. However, the CTS perturbations may have been perceived as more challenging than the other perturbation tasks as the timing of the perturbation was unknown and required a step to regain

balance. A commonly utilized inventory to rate state anxiety is the state-trait anxiety inventory where state anxiety scores range between 40 and 80 units (Spielberger et al., 1983). Following psychological stress, salivary cortisone, a biomarker for stress, is moderately correlated with state-trait anxiety inventory scores and strongly correlated with HR response (Bae et al., 2019). Our findings support this notion as state anxiety scores in the current study were moderately correlated to the change in HR post-perturbation. This may suggest that anxiety influenced the amplitude of the initial cardiac response, as more anxiety provoking perturbations induced greater increases in HR.

In our previous study, the immediate HR and blood pressure responses to postural perturbations were thought to be centrally-mediated with a secondary baroreflex response to aid recovery (Siedlecki et al., 2022b). It is possible that postural perturbations do not illicit an anticipatory response because centrally mediated hemodynamics only occur after a change in posture. Patel and colleagues (2018) examined HR responses during anticipated passive head-up tilts in a feline model. Their protocol consisted of a light flash 30 s prior to a passive 60-degree head-up tilt with randomly inserted 20-degree head-up tilts. They found no anticipatory HR response 5 s prior to the onset of movement, while immediately after the onset of the movement HR increased. We found a similar HR response in the post-perturbation timeframe in the current study.

The lack of a difference between anticipatory and reactionary perturbations on the initial cardiovascular response may suggest a non cardiovascular-mediated mechanism was partially responsible for the rapid HR increase post-perturbation. Although participants were instructed to limit head movement, the horizontal acceleration of the body immediately following the perturbation would have activated the vestibular system because the otolith organs sense linear acceleration. The cardiovascular system and vestibular apparatus share neural pathways within the rostral ventrolateral medulla in cats (Gagliuso et al., 2019; Yates et al., 1993; Yates et al., 1991), while the effect of vestibular inputs on hemodynamics has been reported in humans (Bent et al., 2006; Yates et al., 1999). When horizontally accelerated, a rapid and immediate increase in HR and blood pressure occurs (Goldberg & Fernandez, 1984) that is independent of psychological arousal elicited by the task (Yates et al., 1999). Thus, activation of the vestibular system

may partially explain why HR rapidly increased post-perturbation while there being no difference between perceived state anxiety scores between perturbation tasks.

A similar experimental protocol examining the postural response to anticipatory perturbations showed that the neuromuscular responses were anticipatory in a self-triggered perturbation (Pollock et al., 2017). Since the self-triggered perturbations in the current study were similar to the perturbations in Pollock and colleagues (2017) study, it is likely that the sensory-motor system anticipated the postural perturbations, but the cardiovascular system did not.

3.4.2 Limitations

The inability to distinguish between whether 1) young adults did not perceive the perturbations as being anxiety-provoking or 2) the perceived state anxiety scale was not sensitive enough to discriminate between the perturbation types and intensities was a limitation of the current study.

3.4.3 Perspectives and Significance

Our results indicated that anticipatory cardiovascular responses to postural perturbations were absent when the timing of the perturbation was known. Furthermore, the knowledge of the exact timing of the perturbation did not affect the HR and SBP response, suggesting the importance of reflex-mediated hemodynamics following a perturbation. In addition, the Computer Triggered Step-evoking perturbation may have been perceived as the most challenging task, as noted by higher perceived state anxiety scores. Higher anxiety scores were related to greater changes in HR during the initial cardiac response. Future focus should be placed on the effects of postural perturbations on the cardiovascular response in older adults as this population is known to have age-associated cardiovascular (Karavidas et al., 2010; Paneni et al., 2017) and balance impairments (Paillard, 2017; Roman-Liu, 2018). Thus, the generalization of our findings is limited to young adults.

3.5 Conclusion

Comparable hemodynamics between self- and computer-triggered postural perturbation types suggest similar mechanisms are responsible for cardiovascular regulation immediately after a postural perturbation. Any effects of anticipation on cardiovascular responses prior to the perturbation are believed to be minimal. It is also likely that anxiety influenced HR during the initial cardiac response.

3.6 References

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Chapter 4

4 The Effects of Slow Breathing on Postural Muscles during Standing Perturbations in Young Adults

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4.1 Introduction

Maintaining standing balance is vital to completing activities of daily living. Upright standing balance requires the COM to be kept within the base of support by regulating body sway through adjustments in postural muscle activity (Winter et al., 1998). Perturbations to the base of support result in rapid adjustments in postural muscle activity and body position (Pai et al., 2000; Paillard, 2017) to minimize the movement of the COM and prevent a fall or injury.

Feet-in-place strategies for maintaining balance after perturbation fall within a spectrum ranging between the “ankle strategy” and the “hip strategy” (Afschrift et al., 2016). The ankle strategy resembles a single inverted pendulum whereby the body rotates around the ankle joint and muscle activation follows a distal to proximal pattern. The hip strategy is compared to a double inverted-pendulum dividing the body into two segments: the legs and the torso and the upper body, and follows a proximal to distal muscle activation pattern (Horak & Nashner, 1986). Selection of strategy is dependent on 1) the features of the perturbation (timing, direction, magnitude, predictability); 2) the central set of the individual (affect, arousal, attention, expectations, prior experience); 3) ongoing activity (cognitive or motor); and 4) environment constraints on reaction force generation and limb movement (Adkin & Carpenter, 2018). Ankle strategies are used more often in low intensity postural perturbation conditions. As perturbation intensity increases, the strategy shifts towards a preference for a hip strategy as the COM can move 20 times more quickly when a hip strategy is used over an ankle strategy (Afschrift et al., 2016;

Huisinga et al., 2018). Similarly, the muscle force generated in the lower limbs in response to perturbations of the support surface scales with perturbation intensity, although the effect on muscle onset latency is minimal if the velocity of the platform remains consistent (Diener et al., 1988; Jacobs & Horak, 2007). The CNS modulates muscle onset latency and burst amplitude appropriate for the perturbation to provide equilibrium when the base of support is perturbed (Horak & Nashner, 1986).

Evidence suggests the interaction of cardiovascular and postural muscle responses plays a role in maintaining upright posture and balance (Garg et al., 2014). A bi-directional interaction between the cardiovascular system and postural system has been proposed during orthostatic stress (Garg et al., 2014). That is, blood pressure regulation can have a direct effect on skeletal muscle activation, and conversely blood pressure regulation can be driven by postural sway in quiet standing. Similarly, cardiovascular modulation occurs immediately following a postural perturbation (Siedlecki et al., 2022). The interactions between the cardiovascular and postural systems are enhanced during slow, deep breathing (Rodrigues et al., 2018). Specifically, slow, deep breathing (six breaths per minute) can cause blood pressure fluctuations to synchronize with HR (Russo et al., 2017; Vidigal et al., 2016). Deep breathing can also increase blood pressure fluctuations three-to-four-fold compared to spontaneous breathing due to activation of skeletal muscle pumps and changes to intrapleural, intrathoracic, and intraabdominal pressure (Reyes del Paso et al., 2015). Although an emerging field, most research examining the physiological effects of slow breathing has occurred outside postural control research and performed while in supine or seated.

In addition to cardiovascular adjustments to changes in respiration, studies using microneurography have delineated sympathetic outflow alterations dependent on respiratory patterns. Seals and colleagues (1993) identified fluctuations in muscle sympathetic nerve burst frequency that were attenuated during inspiration and began rising after initiation of expiration. Furthermore, slow breathing decreases muscle sympathetic nerve activity in the common peroneal nerve (Oneda et al., 2010), which directly innervates the short head of the biceps femoris and, through its branches, innervates muscles in the anterior and lateral compartments of the lower leg (Netter,

2018). In addition, the sympathetic nervous system modulates blood flow to the heart, redistributes blood circulation to working muscles, and affects skeletal muscle cell and membrane metabolism, which can have a direct impact on skeletal muscle performance (force amplitude and contraction velocity; Roatta & Farina, 2010). Thus, deep breathing techniques may impact muscle performance.

Respiration is controlled by brainstem respiratory centers, whereas regions of the motor cortex, premotor cortex, and supplementary motor areas responsible for controlling respiratory muscles are activated during volitional breathing (McKay et al., 2003; Mitchell & Berger, 1975). Takai, Brown, and Liotti (2010) identified overlap between somatotopic regions associated with respiration and lip/tongue movements, while respiratory and motor control systems have also been found to share common cortical and subcortical pathways, such as the corticospinal and reticulospinal tracts (Glover & Baker, 2022; Urfy & Suarez, 2014). Studies have found that voluntary breathing and deep breathing increase corticospinal excitability and shorten the latency of motor-evoked potentials in the arms and legs (Ozaki & Kurata, 2015; Shirakawa et al., 2015). Researchers have found changes in lower limb (Barbosa et al., 2017; Shirakawa et al., 2015), upper limb (Barbosa et al., 2013; Ozaki & Kurata, 2015), and trunk (Barbosa et al., 2018; Barbosa et al., 2015; Hamilton et al., 2015) muscle activity depending on respiratory pattern. Similarly, voluntary breathing can improve visual reaction time (Manandhar & Pramanik, 2019) and improve passive hip range of motion (Hamilton et al., 2015). Nevertheless, the effects of slow breathing on muscular responses to postural perturbation have yet to be examined.

The purpose of this study was to examine the effect of slow breathing on the onset latency and amplitude of postural muscle responses to perturbations of the base of support in healthy, young adults. It was hypothesized that, in response to the perturbation, the latency of muscle activation would be lower, and the muscle burst amplitude would be larger in the slow breathing condition compared to the spontaneous breathing condition.

4.2 Methods

Experimental data used in this study were part of a larger study examining the cardiovascular response to varying postural perturbation intensities in healthy adults (Siedlecki et al., 2022). This single session experimental design was performed with 27 young adults (15 males and 12 females; age 23.9 (3.2) yrs; height 172 (9.2) cm; weight 71.0 (12.3) kg) who gave informed consent to participate in the study. All participants were free of neurological disorders, respiratory diseases, and musculoskeletal disorders, as well as considered themselves to be healthy at the time of participation. Participants had not consumed any caffeinated or alcoholic beverages, had fasted for a minimum of 4 hours, and had not engaged in any strenuous physical activity for 24 hours prior to their arrival. The study was approved by the University of Western Ontario Health Sciences' Research Ethics Board (#110471) in compliance with the latest revision of the Declaration of Helsinki (World Medical Association, 2013).

4.2.1 Experimental Protocol

First, respiratory-related health problems were assessed using a 25-item self-report questionnaire (SEBQ-2). Participants ranked items on a 4-point Likert scale, ranging from 0 (never/not true at all) to 3 (very frequency/very true). An overall score of 75 indicates maximum perceived respiratory discomfort, while overall scores greater than 24 suggest the possibility of respiratory-related problems (Courtney & van Dixhoorn, 2014; Kiesel et al., 2017).

Next, ambulatory balance was assessed using the CB&M scale. Participants were rated by the same researcher (P.S.), while performing 19 balance tasks (e.g., unilateral stance, tandem walking, unilateral hopping, walking forwards and backwards, etc.), on a 0-to-5-point interval scale with one bonus point for a total score of 96 (Howe et al., 2006).

The perturbation protocol consisted of a 5-min quiet standing period (QS), and two perturbation tasks that were performed a minimum of 5 mins apart. The two perturbation tasks were: 1) spontaneous breathing (SPON); and 2) slow breathing (SLOW). The perturbation tasks were completed using the Gait in Real-time Analysis

Interactive Lab (GRAIL; Motekforce Link, Amsterdam, The Netherlands) system which consisted of a 1 m x 2 m split-belt treadmill and 180-degree virtual reality screen. Participants wore an upper body safety harness connected to the ceiling that did not provide any body weight support but would prevent a fall. Postural perturbations were posteriorly directed bilateral translations of the treadmill belts (duration: 300 ms), which caused an anterior displacement of the COM. A familiarization period allowed participants to experience postural perturbations that increased in intensity in a stepwise fashion until a step was required to maintain upright balance. The SPON and SLOW task intensity was set to the individual's highest intensity level of perturbation that did not induce a stepping reaction (mean and peak velocity being 0.38 (0.08) m/s and 0.63 (0.09) m/s, respectively) and was the same intensity in both breathing conditions. Participants were instructed to focus their gaze on a projected horizon, located 2.5 m in front of them, and to regain balance without grasping the treadmill handles or taking a step.

Perturbation tasks consisted of 25 perturbations, with pseudorandomized timing (8-12 s apart). A visual guided-breathing metronome, set to six breaths per minute, was projected at eye-level on the virtual reality screen. The metronome consisted of 4-s inhale and 6-s exhale periods, repeated for the duration of the condition. It guided participants on when to start transitioning between respiratory phases. Participants were allowed time to practice following the metronome and the experiment continued once they felt comfortable slow breathing.

4.2.2 Data Collection

A Pneumotrace II respiratory belt transducer was fitted around the participant's chest, over the xiphoid process, to measure continuous respiratory rate throughout the experiment via Powerlab 8/35 with Labchart 8.0 (AdInstruments, Bella Vista, Australia).

Muscle activity was recorded with a wireless surface EMG system (Trigno^{TM} with Avanti bipolar sensors, Delsys, Inc., Natick, MA, USA) from five lower body muscle groups (quadriceps, QUADS; medial hamstring, MH; gastrocnemii, GASTROC; soleus, SOL; and tibialis anterior, TA) on the participant's right side. For QUADS, individual sensors were placed on vastus medialis, vastus lateralis, and rectus femoris. For

GASTROC, individual sensors were placed on medial gastrocnemius and lateral gastrocnemius. The skin was cleaned using NuPrep skin gel and the surface electrodes were placed according to SENIAM guidelines (Hermens et al., 1999). The EMG signals were collected at 2000 Hz using DelsysTalker, an interface to the Trigno telemetry system and Spike2 v.8.13 (Cambridge Electronic Design Limited, Milton, England).

Treadmill belt speeds were outputted as analog signals using a Phidget Analog 4-output #10020B (Phidgets, Inc., Calgary, Canada), and collected by Power 1401, 16-bit data acquisition interface, with Spike2 v8.13 (Cambridge Electronic Design Limited, Milton, England) at 2000 Hz, and Powerlab 8/35 at 1000 Hz. The treadmill belt velocity signal was recorded on all systems for signal synchronization.

4.2.3 Data Analysis

Respiratory rate was calculated in Labchart 8.0 by identifying the maximum inspiration peaks during each condition. A peak was determined by threshold crossing set at two standard deviations above the mean signal over the entire condition. The total number of peaks was divided by the total time within each condition to obtain the number of breaths per minute.

All EMG analyses were performed using Spike2 v8.13 (Cambridge Electronic Design Limited, Milton, England). The onset of each perturbation was determined by threshold crossing on the filtered treadmill belt velocity signal. The threshold was calculated as the point the signal reached two standard deviations above the mean of a 500 ms epoch prior to the perturbation. The perturbation onsets were visually inspected for accuracy. In some participants, muscles were excluded due to missing EMG signals (n=1), and the absence of an EMG burst post-perturbation (QUADS, n=2).

The EMG signals were band-pass filtered (10-450 Hz) and full-wave rectified. To assess the muscle activity during perturbations, the EMG was averaged for a duration of 1.5 s starting 0.5 s prior to the perturbation onset. The first perturbation trial was excluded from the average because the response to the first trial routinely differed from subsequent trials for the same stimulus intensity (Allum et al., 2011). The EMG burst was

identified when the peak amplitude exceeded 1.5 times the mean amplitude of the baseline activity taken 500 ms prior to the perturbation. The onset of the EMG burst for each muscle was determined by threshold crossing set at two standard deviations above the mean of a 500 ms epoch prior to the perturbation. The average rectified value (ARV) of EMG amplitude was calculated for 500 ms prior to the perturbation onset (baseline) and for 200ms after the onset of muscle activity. Electromyography amplitude during the burst was normalized by dividing with the baseline EMG amplitude. Muscle activation latency was calculated as the difference between onsets of the muscle burst and the perturbation. The muscle pre-activation prior to perturbation was assessed by comparing ARV EMG during a 60-s sample within the 5-min QS period and the average of 500 ms epochs prior to each perturbation. Based on the initial analyses showing that RF, VL, and VM exhibited similar activation behaviour, the measured parameters from these muscles were grouped and averaged as QUADS. Similarly, MG and LG were grouped and averaged to represent GASTROC for further analysis. A schematic of data analysis process for EMG data from a representative sample is depicted in Figure 7.

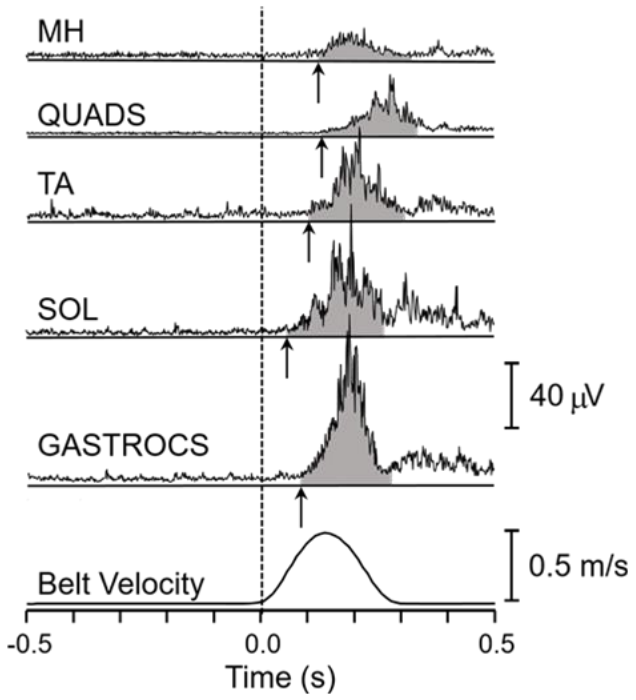

Figure 7. Electromyography (EMG) recordings in the spontaneous (SPON) breathing condition from a representative participant. The perturbation onset (dashed line), EMG burst onset (arrow), and where the average rectified value (ARV) amplitude is calculated (shaded area under curve) are shown. EMG data are averages of 24 perturbations. MH, Medial hamstring; QUADS, Quadriceps; TA, Tibialis anterior; SOL, Soleus; GASTROCS, Gastrocnemii.

4.2.4 Statistical Analysis

Data from one participant were excluded because of poor EMG signals. Therefore, statistical analyses included data from 26 participants. All statistical analyses were performed with SPSS v.25 (IBM Corp, Armonk, New York). An alpha level of $p < 0.05$ was considered statistically significant and data were reported as mean and standard deviation. A one-way, repeated measures ANOVA was performed to compare respiratory rate among QS, SPON and SLOW conditions. A two-way repeated measures MANOVA was performed to compare EMG latency and EMG amplitude between condition (SPON and SLOW), and muscle group (QUADS, MH, GASTROC, SOL, TA). Univariate analyses (two-way repeated measures ANOVAs) with Bonferroni corrections (corrected $p = 0.025$) were used as a post-hoc analysis of the EMG latency and EMG amplitude differences between conditions and muscle groups. Friedman tests were performed to evaluate the differences in muscle activity pre-perturbation among QS, SPON, and

SLOW conditions in each muscle group, as the data were not normally distributed. A Bonferroni correction ($p = 0.01$) was applied to account for performing five Friedman tests using muscle groups within the same persons.

4.3 Results

All participants achieved SEBQ-2 scores below the cut-off threshold of 24 (6.4 (4.9)), while all CB&M scores (95.5 (0.9)) were above the average scores reported in healthy young adults (Zbarsky et al., 2010). There was an effect of condition on respiratory rate (F (2,50) = 194.975, $p < 0.001$). Respiratory rate was higher in the SPON (17.5 (2.8); $p < 0.001$) condition and was lower in the SLOW (6.1 (0.3); $p < 0.001$) condition when compared to QS (14.1 (3.0)). Similarly, respiratory rate was significantly reduced in SLOW when compared to SPON ($p < 0.001$).

4.3.1 Neuromuscular Response

The MANOVA indicated that there was a statistically significant difference in neuromuscular response based on *condition* (F (2, 21) = 6.221, $p = 0.008$; Wilks' Λ = 0.628) and *muscle group* (F (8, 174) = 26.984, $p < 0.001$; Wilks' $\Lambda = 0.199$). There was no statistically significant interaction effect between *condition* and *muscle group* difference on neuromuscular response on the combined dependent variables, F (8, 174) = 1.443, $p = 0.182$; Wilks' $\Lambda = 0.879$.

4.3.2 Muscle Latency

The univariate analysis yielded a significant effect of *condition* (F (1,22) = 6.051, $p = 0.022$), and a significant effect of *muscle group* (F (4,88) = 43.765, $p < 0.001$) in the onset of muscle activation (Figure 8). Reducing respiratory rate to six breaths per minute significantly shortened the onset latency compared to spontaneous breathing within the muscles of the lower limb. The onset latency was significantly longer in the QUADS and the MH compared to the GASTROC ($p < 0.001$; $p < 0.001$), SOL ($p < 0.001$; $p < 0.001$), and TA ($p = 0.007$; $p = 0.001$), but there was no difference in onset latency between thigh muscle groups ($p = 1.00$). The onset latency of the SOL was significantly shorter than the

GASTROC ($p < 0.001$) and TA ($p < 0.001$), while the GASTROCs onset latency was significantly shorter than the TA ($p = 0.005$).

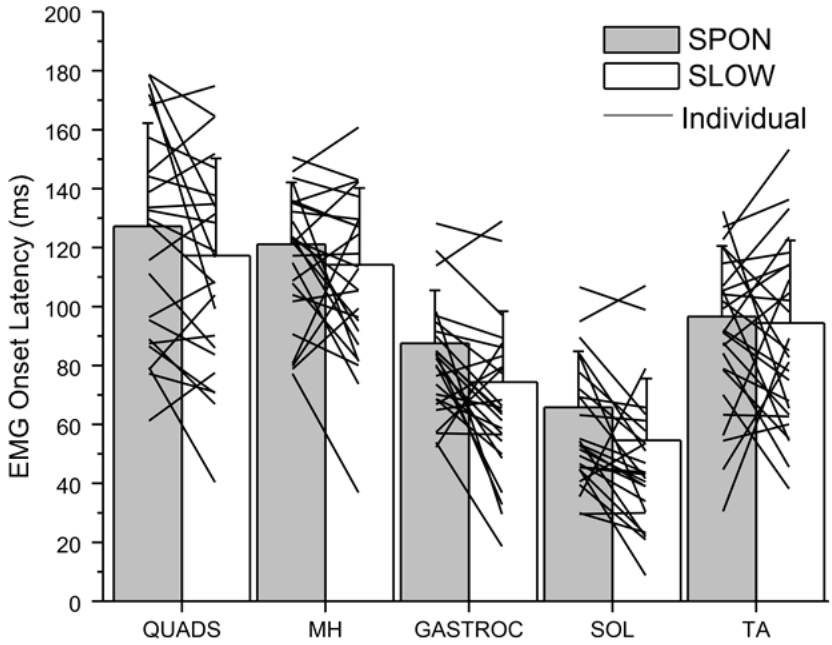

Figure 8. Muscle onset latency post-perturbation in spontaneous (SPON; gray) and SLOW (white) breathing conditions. Data represents group mean and standard deviation bars with lines connecting individual participant's values between conditions in each muscle group. EMG, Electromyography; QUADS, Quadriceps; MH, Medial hamstring; GASTROC, Gastrocnemii; SOL, Soleus; TA, Tibialis anterior.

4.3.3 Burst Amplitude

Muscle burst amplitude comparisons between SPON and SLOW tasks for each muscle can be found in Figure 9. There was a significant effect of *condition* (F (1,22) = 7.654, $p = 0.011$) and significant effect of *muscle group* (F (4,88) = 19.573, $p < 0.001$) on muscle burst amplitude. There was a significant decrease in muscle activity during the SLOW condition when compared to spontaneous breathing. The burst amplitude was significantly smaller in the QUADS compared to the MH ($p < 0.001$), GASTROC ($p < 0.001$), SOL ($p = 0.001$), and TA ($p = 0.005$). The muscle activity in the GASTROC was significantly greater than the MH ($p = 0.004$), SOL ($p = 0.003$), and TA ($p = 0.003$). There was no significant difference in burst amplitude between the MH, SOL, or TA ($p = 1.00$ for all comparisons).

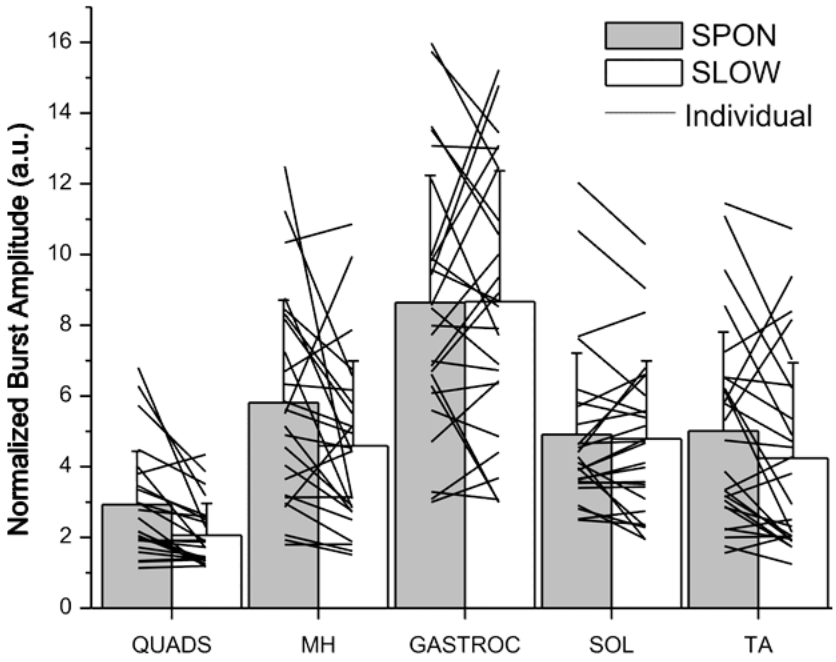

Figure 9. Normalized electromyography amplitude for 200 ms from the onset of muscle activation following a postural perturbation in spontaneous (SPON; gray) and SLOW (white) breathing conditions. Data shown are group mean and standard deviation bars with lines connecting individual participant's values between conditions in each muscle group. QUADS, Quadriceps, MH, Medial hamstring; GASTROC, Gastrocnemii; SOL, Soleus; TA, Tibialis anterior.

4.3.4 Electromyography Pre-activation

The EMG pre-perturbation activation was not significantly different in any muscle group between QS and both perturbation tasks (QUADS (χ^2 (2) = 3.583, p = 0.167), MH (χ^2 (2) = 2.96, p = 0.228), GASTROC (χ^2 (2) = 2.385, p = 0.304), SOL (χ^2 (2) = 2.385, p = 0.304), and TA (χ^2 (2) = 2.154, p = 0.341); Table 6). Thus, it would appear the participants were not preactivating their muscles in anticipation of the perturbations.

Table 6. Pre-perturbation EMG activity of the Right Leg

	Pre-perturbation EMG activity (μV)				
	QUADS	MH	GASTROC	SOL	TA
QS	2.2 (1.2)	1.8 (1.5)	3.4 (2.0)	6.5 (3.6)	2.2 (1.3)
SPON	2.7 (1.7)	2.4 (2.3)	3.9 (2.1)	6.3 (2.8)	2.5 (1.3)
SLOW	2.1 (1.1)	2.0 (2.0)	3.3 (1.9)	6.1 (2.9)	2.3 (1.1)

Data presented as mean (SD) for pre-perturbation EMG activity in QUADS, Quadriceps; MH, Medial hamstring; GASTROC, Gastrocnemii; SOL, Soleus; TA, Tibialis anterior (n=23).

4.4 Discussion

The present study compared neuromuscular responses from five lower body muscle groups in response to postural perturbations during spontaneous and slow breathing. The key findings from this study indicated that breathing at six breaths per minute shortened EMG latency in lower limb musculature during perturbations when compared to spontaneous breathing, as hypothesized. It was also observed that EMG burst amplitude was reduced following a postural perturbation while slow breathing – this result was unexpected.

The resting respiratory rate in our current study is congruent with other studies that have measured respiration during quiet standing on a treadmill (Siedlecki et al., 2017; Siedlecki et al., 2018). The respiratory rate was significantly lower when following a breathing-guided metronome compared to spontaneous breathing conditions. Thus, participants were successful in following the visual metronome and were able to lower their respiratory rate to the intended six breaths per minute target.

The postural perturbations instilled a forward sway in participants immediately after the perturbation which was accompanied by a distal to proximal activation of muscles about the ankle first (54-96 ms), followed by the thigh muscles (114-127 ms). This pattern of muscle activation occurred during both tasks, congruent with the ankle

strategy (Horak & Nashner, 1986). Activation onset of ankle, and thigh muscles displayed similar onset latencies reported in previous studies that have documented this strategy (Fontanari et al., 1996; Horak & Nashner, 1986). Although all tasks incorporated the ankle strategy, there were neuromuscular response differences between conditions and muscles.

The onset activation and the burst amplitude of the lower limb muscles were sensitive to the effects of respiration. A faster onset of muscle activation may have reduced the need for a larger burst amplitude in the postural response. The modulation of motor response observed during the SLOW task in this study provides further proof of a respiratory-motor interaction (Ikeda et al., 2009; Li & Rymer, 2011), and expands the concept to include activities such as non-stepping postural perturbations.

The respiratory-motor interaction is respiratory phase-dependent, task- and muscle-specific (Balzamo et al., 1999; Barbosa et al., 2017; Filippi et al., 2000; Fontanari et al., 1996; Ikeda et al., 2009). Barbosa and colleagues (2017) compared normalized EMG RMS in four lower limb muscles during a full squat while spontaneously or slow breathing. They found the EMG RMS, for the first 2 s into the flexion phase of a 60-degree squat, to be higher in the rectus femoris, biceps femoris, and TA, while there was no change in the medial gastrocnemius when using slow, deep breathing techniques. However, in the extension phase of the squat, medial gastrocnemius muscle activity significantly decreased during slow breathing, while there were no changes in the other muscles. In conjunction with previous literature, our findings suggest task-specific motor responses with both EMG amplitude and EMG onset latency changes during postural perturbations.

One possible explanation for the respiratory-driven response is that the CNS favoured energy efficiency over postural instability at lower perturbation intensities (Afschrift et al., 2016). Postural strategies in this study were consistent with an ankle strategy. Utilizing a predictive model, Afschrift and colleagues (2016) demonstrated that when the CNS prioritized minimizing mechanical work, an ankle strategy to regain stability would be favoured. Our data support the notion of favouring energy efficiency

because participants in our study maintained balance while utilizing lower muscle burst amplitude to regain balance following the onset of a perturbation. It is possible that during the SLOW task, the perturbation was perceived as less challenging by the CNS. Slow, deep breathing can have psychophysiological benefits, such as increased alertness (Zaccaro et al., 2018) and shortened visual reaction time (Manandhar & Pramanik, 2019) compared to spontaneous breathing, which may positively impact postural stability.

Another possible explanation for the postural responses observed during the SLOW task is that voluntary breathing modulated corticospinal excitability. Voluntary, deep breathing has been shown to have a global effect on corticospinal excitability. Regions of the M1 associated with lower limb musculature are also activated with regions associated with voluntary breathing (Fink et al., 1995). Motor-evoked potential amplitudes can increase, and latency decrease with voluntary, deep breathing in hand muscles during seated rest compared to spontaneous breathing (Ozaki & Kurata, 2015). Similarly, increased corticospinal excitability has also been observed during lower limb muscle contractions, i.e., the vastus lateralis, during 10% isometric maximal voluntary contractions during controlled breathing compared to spontaneous, uncontrolled breathing (Shirakawa et al., 2015). In the previous two studies, motor-evoked potentials were evoked with transcranial magnetic stimulation. Thus, it is not possible to separate cortical and spinal changes that were responsible for the increases in corticospinal excitability.

It is possible that both corticospinal and reticulospinal descending outputs are modulated by slow breathing. The importance of the reticulospinal tract in postural adjustments has been reported in a feline model (Schepens & Drew, 2006). Descending signals originating in the reticulospinal tract are more favourable for tasks requiring gross movements, and quicker response times (Davis & Gendelman, 1977; Zaaimi et al., 2018), while tasks requiring finer movements likely involve signals utilizing the corticospinal tract (Zaaimi et al., 2018). However, the coordination of both tracts is required (Drew et al., 2004). An imbalance between corticospinal and reticulospinal tracts has been suggested in animal (Glover & Baker, 2022) and human models (Sangari & Perez, 2019, 2020). More specifically, an imbalance can be found in humans, where reticulospinal

output is enhanced over the corticospinal output when experiencing an unexpected stimulus (Sangari & Perez, 2020). It is possible that the neuromuscular response during postural perturbations was driven by enhanced reticulospinal activity due to the slow breathing task.

The involvement of the autonomic and central nervous system at the spinal level should not be overlooked. An anatomical connection between thoracic preganglionic neurons and lumbar spinal interneurons has also been observed (Chopek, 2022; Deuchars & Lall, 2015), although the effect on postural control is unknown. Reduced sympathetic nerve activity (Oneda et al., 2010) and increased parasympathetic dominance (Russo et al., 2017) via slow breathing may indirectly lead to reduced burst amplitude following a postural perturbation. Taken together, the findings illustrated the potential impact of voluntary breathing on the descending motor drive to non-respiratory skeletal muscles. However, without directly measuring cortical, subcortical, and spinal excitability, the neural substrate for the impact of slow breathing on muscle onset latency and burst amplitude remains speculative in this study.

4.4.1 Limitations and Future Directions

A limitation in this study is the absence of reliable kinetic and kinematic data. Another possible limitation is that treadmill perturbations were not triggered in-phase with respiration. The results observed in the present study indicate different neuromuscular responses depending on respiratory rate. Future studies would benefit from measuring motor-evoked potentials as it would allow for a better understanding of the mechanism involved in neuromuscular changes with slow breathing. Additionally, similar studies with older adults or clinical populations are needed to explore if individuals who are trained to reduce their respiration rate would exhibit similar neuromuscular changes. The results of the current study, in concert with recent findings suggesting cardiovascular changes are driven by postural perturbations during spontaneous breathing (Siedlecki et al., 2022), suggest that an interaction between cardiovascular, respiratory, and postural control systems may exist during postural perturbations. Future focus on the interaction between these three systems is thus necessary.

4.5 Conclusion

This study showed that breathing at six breaths per minute can have immediate effects on neuromuscular responses to postural perturbations. The mechanism remains speculative, however, a shift in the CNS to favour energy efficiency was theorized.

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Chapter 5

5 The effect of slow breathing on cardiovascular and electromyography response during standing perturbations in older adults

5.1 Introduction

A bi-directional interaction between the cardiovascular system and postural control system (cardio-postural interaction) exists during orthostatic stress (Garg et al., 2014b). When standing balance is perturbed in young adults, we found an immediate increase in HR, followed by a secondary baroreflex response, where SBP increased and HR decreased (Siedlecki et al., 2022b). As the effects of aging on the cardiovascular system are well known (e.g., loss of distensibility in large vessels, increased vasoconstrictor tone, thickened left ventricle walls, and inhibited cBRS; Karavidas et al., 2010; Monahan et al., 2000; Paneni et al., 2017), older adults can experience challenges in the regulation of arterial pressure in the standing posture (Hofsten et al., 1999). It has been posited that larger postural sway in older adults could be a coping strategy to mitigate poor cardiovascular and autonomic response to prolonged orthostatic stress (Claydon & Hainsworth, 2005). Yet, the effects of postural perturbations on the cardiovascular response in older adults are poorly understood.

Standing balance performance diminishes in individuals 60+ years of age (Johnson et al., 2020), in conjunction with the deterioration of sensory organs and neural pathways associated with neuromuscular signaling (Paillard, 2017; Roman-Liu, 2018). In older adults, slower reaction time and greater muscle activation are common responses to surface translation perturbations (Arsenault et al., 2022; Martelli et al., 2017; Wang et al., 2017).

The cardiovascular and respiratory systems are closely linked, sharing similar neural pathways (Eckberg & Sleight, 1992). Lowering the breathing rate to six breaths per minute can affect autonomic outflow by enhancing vagal control of the heart (Vidigal et al., 2016), lowering blood pressure and HR (Russo et al., 2017), and increasing cBRS

(Bernardi et al., 2001). Thus, slow breathing can be used to manipulate cardiovascular mechanisms. The skeletal muscle response during postural perturbations is modulated while slow breathing in young adults; slow breathing, when compared to spontaneous breathing, shortened muscle onset latency, and reduced muscle burst amplitude in lower limb musculature (Siedlecki et al., 2022a).

Although the effects of slow breathing have not been examined during postural perturbations in older adults, breathing at six breaths per minute can affect muscle activity during orthostatic stress in an older population (Rodrigues et al., 2018). Thus, it is possible that slow breathing may also affect the neuromuscular response to postural perturbations in older adults.

The purpose of this study was to determine: 1) the effect of slow breathing on HR and SBP response following surface support postural perturbations in older adults; and 2) the effect of slow breathing on lower limb muscle onset latency and burst amplitude during surface support postural perturbations in older adults. It was hypothesized that slow breathing would enhance the HR and SBP response post-perturbation compared to spontaneous breathing. It was also hypothesized that muscle onset activation would be delayed and not change with slow breathing and muscle burst amplitude would be higher and would not change with slow breathing, compared to that previously found in young adults.

5.2 Methods

Twenty community-dwelling adults (9 female; age 68.5 (6.7) yrs; height 170.0 (12.9) cm; weight 73.9 (13.0) kg over the age of 60 years completed this study. All participants considered themselves to be healthy and were absent of any uncontrolled neurological disorders, respiratory diseases, cardiovascular diseases, and musculoskeletal disorders. Participants were not excluded for taking medication, such as beta-blockers. Participants did not consume any food and caffeinated or alcoholic beverages for a minimum of 4 hours and did not participate in any strenuous physical activity for 12 hours, before the scheduled appointment. Pre-screening of the participants' health history and medication screening was completed to ensure participants did not report any

uncontrolled health issues as outlined in the study's inclusion criteria. The study was approved by the University of Western Ontario Health Sciences' Research Ethics Board (#110471) and conformed with the Declaration of Helsinki (World Medical Association, 2013). All participants provided written consent prior to their participation.

5.2.1 Experimental Protocol

To assess ambulatory balance, the CB&M scale (Howe et al., 2006) was performed. The CB&M consists of various standing balance tasks, such as single-legged standing, unilateral hopping, walking down a set of stairs, etc., that are known to decline in performance with age (Zbarsky et al., 2010). The test comprised of 19 balance tests scored on a scale from 0 to 5, where higher scores reflected successful completion of the task. The SEBQ-2 was used to rate 25 breathing-related symptoms and their severity (Courtney & van Dixhoorn, 2014), as higher scores can predict respiratory illness and dysfunction (Mitchell et al., 2016).

Participants stood on a treadmill (GRAIL; Motekforce Link, Amsterdam, Netherlands) facing a 180-degree virtual reality screen, projecting an image of an open grass field with cobble stone path, located 2.5 m in front of the treadmill. Participants wore an upper body safety harness, that did not provide any body weight support, while standing. A familiarization period was performed and served two purposes; it allowed participants to experience treadmill-induced perturbations and allowed the researchers to determine the perturbation intensity that would be chosen for each participant. An application created in the GRAIL software D-flow was used to trigger treadmill perturbations (300 ms) in increasing intensity. The maximum intensity in which the participant was able to consistently regain balance without stepping or grasping the handrails was chosen for the perturbation tasks (mean velocity 0.3 (0.1) $m \cdot s^{-1}$ and peak velocity 0.6 (0.1) $m \cdot s^{-1}$).

Following the familiarization period, a 5-min quiet stance (QS) period while standing upright was performed to measure resting cardiovascular parameters. Two postural perturbation tasks were then completed in random order, separated by a 5-min rest. The perturbation tasks were completed while spontaneously breathing (SPON) and

while slow breathing (SLOW) at six breaths per minute. In the SLOW task, participants followed a visually guided breathing metronome projected onto the virtual reality screen that instructed them to inhale for 4 s and exhale for 6 s. Breathing at six breaths per minute was chosen because breathing at this frequency can couple the cardiac baroreflex with respiration and enhance blood pressure and HR fluctuations (Russo et al., 2017). Participants must have felt comfortable following the metronome before the SLOW task began. Perturbation tasks consisted of 25 brief, posteriorly directed accelerations of the treadmill belts, with pseudorandomized timing (8-12 s) between trials. After each QS, SPON, and SLOW task, participants were asked to rate their perceived state anxiety on a scale from 0 ("No Anxiety") to 10 ("Most Anxious you have ever felt") and rate their perceived stability on a scale from 1 ("Completely Stable") to 10 ("About to Fall"). Similar protocols have been used to examine the effect of postural perturbations on cardiovascular response (Siedlecki et al., 2022b; Study Two) and the effect of slow breathing on EMG activity of the lower limb (Siedlecki et al., 2022a) during perturbations.

5.2.2 Data Collection

Cardiovascular and respiratory data were collected using a 3-Lead Bio AMP ECG (ADInstruments, Bella Vista, Australia), a finger cuff with brachial Finometer sphygmomanometer (Finapres Medical System, Amsterdam, The Netherlands) placed on the right arm, and a Pneumotrace II respiratory belt transducer over the xiphoid process (UFI, Morro Bay, California, USA). An arm sling was worn around the right arm to restrict movement of the blood pressure cuffs.

Muscle activity was recorded with a wireless surface EMG system (Trigno^{TM} with Avanti bipolar sensors, Delsys, Inc., Natick, Massachusetts, USA) from five lower limb muscle groups (quadriceps, QUADS; medial hamstring, MH; gastrocnemii, GASTROC; soleus, SOL; and tibialis anterior, TA) unilaterally on the right leg. For the QUADS muscle group, individual sensors were placed on the rectus femoris, vastus medialis, and vastus lateralis, and for the GASTROC muscle group, the individual sensors were placed on the medial and lateral gastrocnemius. It was confirmed that the individual muscles within each group responded similarly (there was no statistical difference in muscle onset

latency and amplitude) before they were grouped. Prior to sensor application the skin was cleaned with rubbing alcohol.

5.2.3 Cardiovascular Response Calculations

5.2.3.1 Blood Pressure and Heart Rate Response

The beat-to-beat SBP and HR tracings were derived from blood pressure and electrocardiogram tracings sampled at 1000 Hz (Powerlab 8/35; ADInstruments, Bella Vista, Australia). The treadmill belt velocity of each belt was recorded through a Phidget Analog 4-output #1002_0B (Phidgets, Inc., Calgary, AB, Canada) and the signals were imported into Spike2 v.8.13 (Cambridge Electronic Design Limited, Milton, England), along with the beat-to-beat blood pressure and HR data. The blood pressure and HR data were down-sampled to 50 Hz and a 12 s window starting 4 s prior to the onset of the perturbation was selected for each trial. Trials containing artifacts in the SBP and HR tracings were excluded. The individual trials were averaged for each participant within each perturbation task. Data from the entire five minutes of quiet standing were used for the QS period. The cardiovascular data from one participant were excluded due to persistent artifacts.

One-dimensional statistical parametric mapping (1-D SPM) analyses were used to determine statistical differences in mean HR and SBP between perturbation tasks post-perturbation (0 s to 8 s) using an open source spm1d-package (spm1d.org, T. Patasky) in MATLAB 2019b (MathWorks Inc., Natick, MA, USA). A t-test was performed on the residuals of the continuous mean HR and SBP response between perturbation tasks over an 8 s time series for each voxel (400 data points), creating a t-curve over the function of time. Random field theory was utilized to determine the critical t-value (threshold) and calculate specific p-values for each cluster of data above the critical t-value. Thus, any supra-threshold clusters signified statistically significant differences between the means of two 1-dimensional signals (Adler & Taylor, 2007). Statistical parametric mapping allows for a single statistical test to be applied over an entire time series while minimizing type 1 error (Pataky et al., 2013), providing advantages over traditional scalar

extractions. We have previously used 1D-SPM to identify differences in HR and SBP response during postural perturbations (Study Two).

5.2.3.2 Cardiac Baroreflex Calculations

Cardiac baroreflex sensitivity was estimated using beat-to-beat physiological R-R interval (the distance between R-peaks in an electrocardiogram and is inversely related to HR) and SBP data. Signal artifacts in the raw data were corrected using interpolated data one cardiac cycle before and after the missing data point. The cBRS was estimated in the time domain, using the sequence method (Parati et al., 2000) in MATLAB 2019b. For the QS period, the sequence method was applied to the beat-to-beat R-R interval and SBP data from the entire period. During the perturbation tasks, the sequence method was applied to the time period (1 to 8 s) following the onset of each perturbation (+ 0.4 s if the onset occurred between 2 heart beats) to estimate cBRS post-perturbation. We have used this approach to estimate cBRS following similar postural perturbations previously (Siedlecki et al., 2022b). A lag of 0 beats was selected a priori because the average R-R interval in each task was less than 775 ms (Blaber et al., 1995). A sequence was defined as three or more consecutive cardiac cycles where R-R interval and SBP jointly increased or decreased, and there was a minimum change of 4 ms in R-R interval and 1 mmHg in SBP. Only sequences that had regression lines with $r^2 > 0.85$ were used. The average of the slopes from all sequences within the selected time periods determined the cBRS (Bertinieri et al., 1985).

5.2.4 Electromyography Calculation

The EMG signals were collected by Power 1401, 16-bit data acquisition interface, with Spike2 v8.13 (Cambridge Electronic Design Limited, Milton, England) using DelsysTalk at 2000 Hz, and all EMG analyses were performed using the same Spike2 v8.13 software. The onset of each perturbation was identified using threshold crossing set at mean plus two standard deviations of the 500 ms velocity signal epoch measured before the perturbation. The EMG signals were band-pass filtered (10-500 Hz), full-wave rectified and averaged for 1.5 s with 0.5 s prior to the perturbation onset.

The EMG baseline was defined as a 500 ms epoch prior to the perturbations. Subsequently, the EMG burst was identified when EMG amplitude exceeded 1.5 times the EMG baseline, the average rectified value (ARV) EMG amplitude was calculated for 200 ms after the burst onset and then divided by the EMG amplitude during baseline. The onset of the EMG burst for each muscle was determined by threshold crossing set at two standard deviations above the mean baseline EMG. Muscle activation latency was calculated as the time difference between the onset of the burst and the onset of the perturbation. The muscle activity was calculated using a 60 s sample during QS and compared to EMG baseline to assess muscle preactivation. See Siedlecki et al. (2022a) for more information. The EMG data from the QUADS and TA from one participant and the EMG data from the SOL from another participant were excluded from the analysis because of consistent artifacts. Figure 10 illustrates the EMG data analysis from a representative sample.

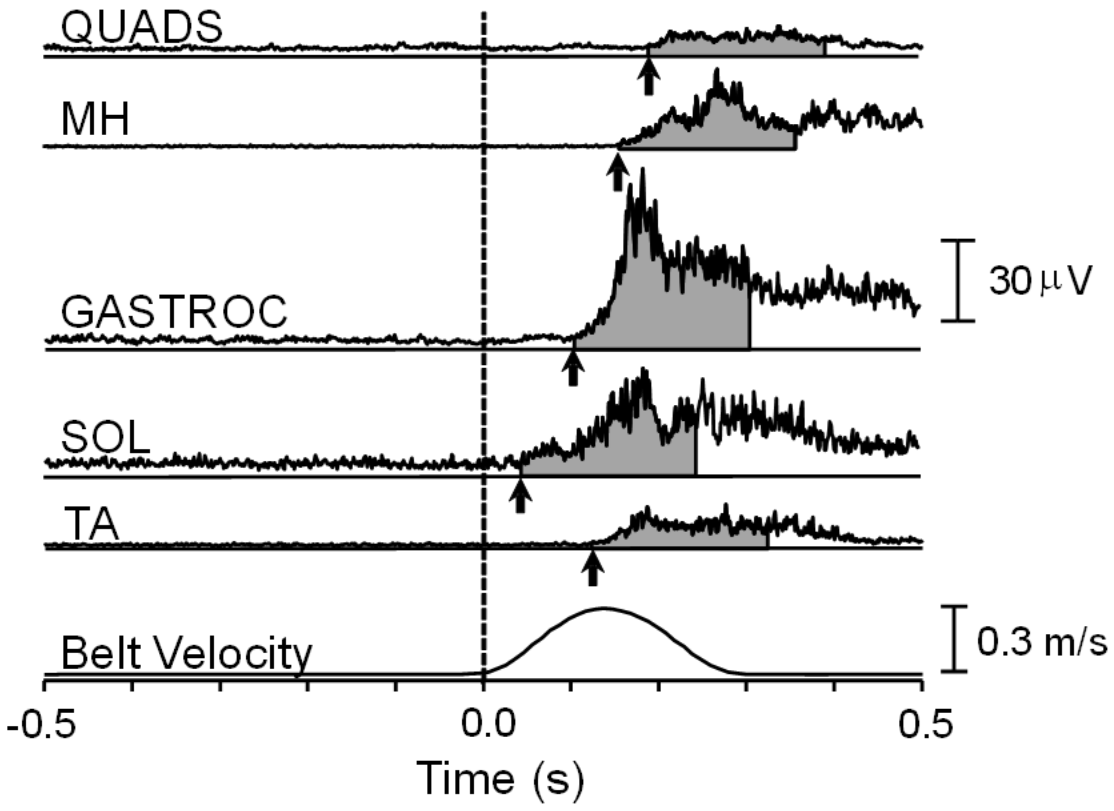

Figure 10. The electromyography (EMG) recordings from a representative participant in the spontaneous (SPON) breathing task. The EMG data are averages of 24 perturbations in the rectus femoris (representing the quadriceps muscle group; QUADS), medial hamstrings (MH), medial gastrocnemius (representing the gastrocnemii muscle group; GASTROC), soleus (SOL), and tibialis anterior (TA). The perturbation onset (dashed vertical line), EMG onset (arrow), and area (grey shaded) where average rectified value amplitude was calculated, are shown.

5.2.5 Statistical Analysis

Statistical analyses were performed with SPSS v.25 (IBM Corp, Armonk, New York) and MATLAB. The data are presented as mean (standard deviation). An alpha level of $p < 0.05$ was used to denote statistical significance, unless stated otherwise. To identify if statistical differences occurred between tasks (QS, SPON, SLOW) in perceived state anxiety or perceived stability scores, Friedman tests followed by Wilcoxon signed-rank tests were performed. A Bonferroni correction of $p < 0.016$ was set to denote significance in the post-hoc analysis. A 1D-SPM was applied to an independent sample t-test to compare SBP response post-perturbation (0 s to +8 s)

between perturbation tasks (SPON and SLOW). As HR data were not normally distributed, a non-parametric 1D-SPM (1D-SnPM) was used to compare HR response post-perturbation between perturbation tasks. Separate one-way repeated measures ANOVAs were performed to determine the effect of task (QS, SPON, SLOW) on cBRS characteristics. A Bonferroni post-hoc analysis was selected to identify where the significant difference had occurred.

A two-way repeated measures MANOVA was conducted to compare EMG measures (latency and burst amplitude) between task (SPON and SLOW) and muscle group (QUADS, MH, GASTROC, SOL, TA). Univariate analyses (two-way repeated measures ANOVAs) were used as post-hoc analyses to determine the differences between tasks and muscle group. A Bonferroni correction (corrected $p < 0.025$) was chosen to denote significance. Muscle activity data pre-perturbation were not normally distributed, and Friedman tests were performed to evaluate the differences between task (QS, SPON, SLOW). Wilcoxon signed-rank tests were performed if statistical significances were found. A Bonferroni correction of $p < 0.016$ was used to signify significance.

5.3 Results

Participants achieved CB&M scores (86.6 (9.6)) that were at or above previously recorded values in healthy adults between 60-79 years of age (Zbarsky et al., 2010). Participant SEBQ-2 scores (4.0 (5.7)) were also below the threshold (27/75) for respiratory impairment (Kiesel et al., 2017). Respiratory rate was recorded during QS (15.7 (3.3) breaths per minute), SPON (18.6 (3.3) breaths per minute), and SLOW (6.1 (0.3) breaths per minute) tasks and indicated participants were able to successfully follow the breath-guided metronome. The mean HR and SBP during QS was 82 (15) bpm and 135 (15) mmHg, respectively.

5.3.1 Perceived Anxiety and Stability Score

The mean perceived state anxiety (n=20) and perceived stability (n=20) scores were measured during QS (0.7 (0.8); 1.5 (1.1)), SPON (1.7 (1.2); 2.5 (1.5)), and SLOW (2.0 (1.9); 2.2 (1.1)) tasks, respectively. There was a significant difference in perceived

state anxiety scores between tasks (χ^2 (2) = 12.603, p = 0.002). Completion of the perturbation tasks significantly increased perceived state anxiety in both the SPON (Z = -2.865, p = 0.004) and SLOW (Z = -2.719, p=0.007) tasks when compared to QS, while there was no difference in anxiety scores between perturbation tasks (Z = -0.852, p = 0.394). Similarly, perceived stability was significantly affected throughout the study (χ^2 (2) = 16.217, p < 0.001). Participants perceived their stability to decrease during both the SPON (Z = -3.14, p = 0.002) and SLOW (Z = -2.754, p = 0.006) tasks compared to QS, yet there was no difference between the perturbation tasks (Z = -1.303, p = 0.193).

5.3.2 Cardiovascular Response

The SnPM analysis found a supra-threshold cluster (t* = 2.478) in HR between SPON and SLOW tasks (Figure 11A). During SLOW, HR was significantly elevated at 7.42 s to 8.00 s (p = 0.020) compared to SPON post-perturbation. The SPM identified two supra-threshold clusters (t* = 2.757) in SBP between SPON and SLOW tasks (Figure 11B). The SBP was significantly elevated at approximately 0 - 1.26 s (p = 0.042) and 1.78 s to 8.00 s (p = 0.001) in SPON compared to SLOW post-perturbation.

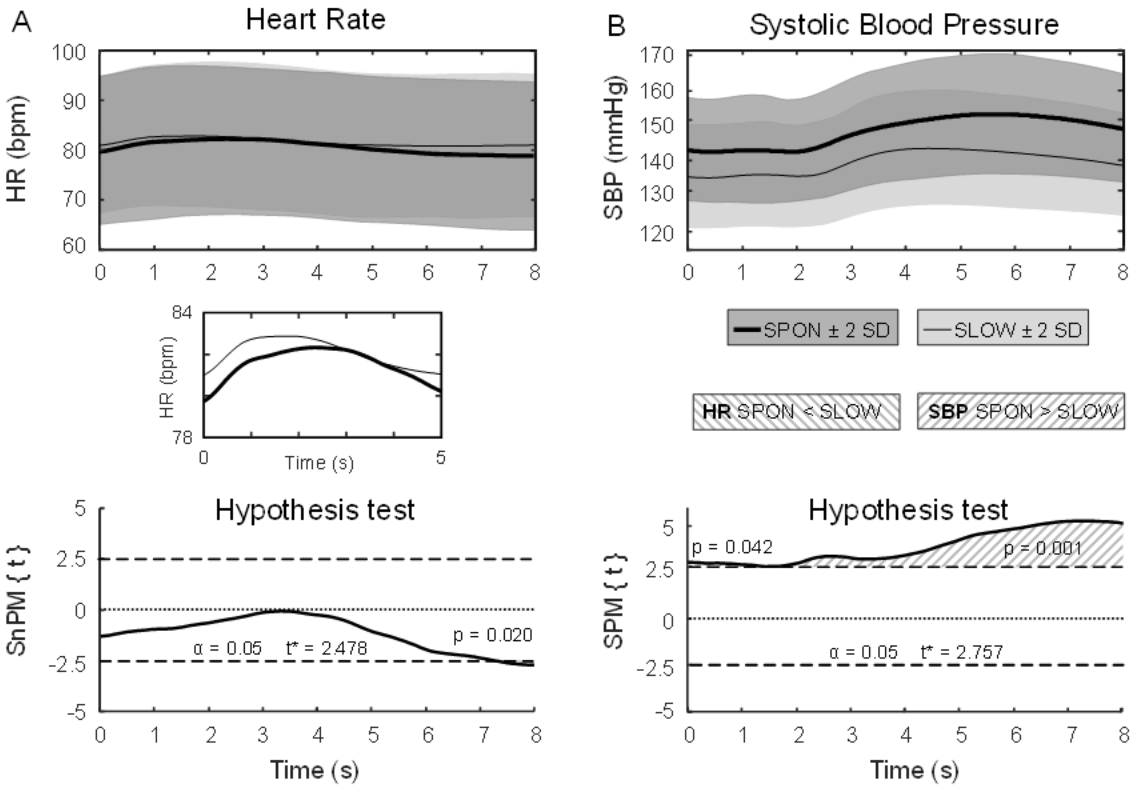

Figure 11. Heart rate (HR; A) and systolic blood pressure (SBP; B) in spontaneous (SPON) and SLOW breathing perturbation tasks and the hypothesis test for the statistical non-parametric map (SnPM; t; left) and statistical parametric map (SPM; t; right). In the top panels, the mean and 2 SD for SPON (thick black line with darker grey shaded area) and SLOW (thin black line with lighter grey shaded area) are shown. A panel illustrating a zoom in on mean HR without SD during the initial HR response can be found in the middle panel. In the bottom panels, the SnPM/SPM (solid line) and the critical threshold (dashed line) values are presented. For HR (A) the critical threshold was exceeded from 7.42 to 8.00 s (grey shading) with a supra-threshold cluster of $p = 0.020$. For SBP (B) the critical threshold was exceeded between 0 and 1.26 s and between 1.78 and 8.0 s with supra-threshold clusters (grey shading) of $p = 0.042$ and p = 0.001, respectively.

5.3.3 Baroreflex Sensitivity

The characteristics of cardiac baroreflex sequence analysis between QS, SPON, and SLOW tasks can be found in Table 7. There was no difference in cBRS between tasks (F (2, 36) = 0.947, $p = 0.397$). There were differences in the length of sequence (F (2, 36) = 8.374, $p = 0.001$) and the percentage of up-sequences (R-R interval and SBP increased; F (2, 36) = 5.719, $p = 0.007$) between tasks. There was no difference in the length of sequence between QS and SPON ($p = 1.00$), while the length of sequence was

significantly longer in SLOW compared to QS (p = 0.017) and SPON (p = 0.015). The percentage of up sequences was significantly elevated in SPON (p = 0.014) and SLOW (p = 0.017) compared to QS, while there was no difference between perturbation tasks (p = 1.00).

Table 7. The cardiac baroreflex characteristics from the sequence analysis during quiet stance and perturbation tasks

Characteristics	QS	SPON	SLOW
Gain (ms/mmHg)	4.1 (2.6)	3.7 (2.7)	4.2 (3.5)
Length (# of RRIs)	3.6 (0.4)	3.6 (0.4)	4.1 (0.6)* ±
Up Seq (%)	47 (8)	73 (32)*	68 (26)*
Seq / Pert (%)	-	64 (23)	61 (27)

Data presented as mean (SD); QS: quiet stance; SPON: spontaneous breathing; SLOW: slow breathing; RRI: R-R interval; Up Seq: sequences where both RRI and systolic blood pressure are increasing; Seq / Pert: ratio between the number of sequences to the number of perturbation trials, n = 19. * represents a significant difference from QS at $p < 0.05$; ⁺ represents a significant difference from SPON at $p < 0.05$.

5.3.4 Electromyography

The MANOVA found a significant interaction effect between *task* and *muscle group* (F (8, 134) = 2.288, p = 0.025; Wilks' Λ = 0.774) on the combined dependent variables (e.g., muscle onset latency and EMG burst amplitude). The multivariate analysis also found statistically significant differences in neuromuscular response on *task* (F (2, 16) = 12.674, p = 0.001; Wilks' Λ = 0.387) and *muscle group* (F (8, 134) = 17.183, $p < 0.001$; Wilks' Λ = 0.244).

5.3.4.1 Muscle Latency

The EMG latency for all muscle groups can be found in Figure 12. The univariate analysis indicated a statistically significant effect of *task* (F (1,17) = 26.417, $p < 0.001$) and *muscle group* (F (4, 68) = 14.420, $p < 0.001$) in muscle onset activation following a perturbation. The onset of muscle activation was shortened in the SLOW compared to the SPON task. The EMG latency was longer in the QUADS and MH muscle groups compared to the GASTROC (p = 0.031, $p < 0.001$) and SOL (p = 0.001, $p < 0.001$), but

not in the TA (p = 1.00, p = 1.00), while there was no difference in EMG latency between QUADS and MH (p = 1.00). The TA onset muscle activation was longer than SOL (p = 0.013), but not different from GASTROC (p = 0.22). The EMG onset latency was significantly shorter in the SOL compared to GASTROC (p = 0.01). However, there was no significant interaction effect between task and muscle group (F (4, 68) = 2.469, p = 0.092) in EMG latency.

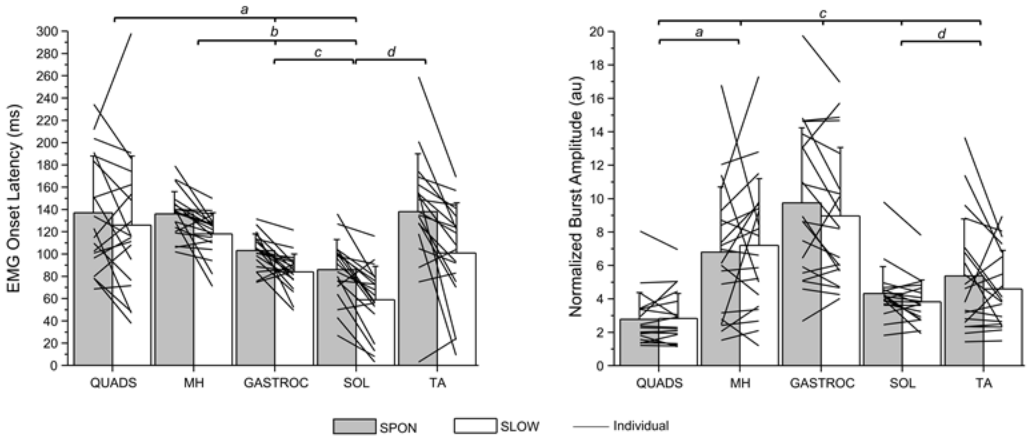

Figure 12. Muscle onset latency post-perturbation (left) and normalized electromyography (EMG) burst amplitude for 200 ms from the onset of muscle activation following a postural perturbation (right) in SPON (grey) and SLOW (white) breathing tasks. Data are shown as group mean and SD (bars) with lines connecting individual participant's values between tasks in each muscle group. QUADS; quadriceps: MH; medial hamstring: GASTROC; gastrocnemii: SOL; soleus: and TA; tibialis anterior. *a,* indicates significant difference from QUADS; *b* significant difference from MH; *c* significant difference from GASTROC; *d* significant difference from SOL; $p < 0.05$ for all comparisons done on combined SPON and SLOW data for each muscle.

5.3.4.2 Burst Amplitude

Muscle burst amplitude for all muscle groups normalized to baseline can be found in Figure 12. The univariate analysis found a statistically significant effect of *muscle group* on muscle burst amplitude (F (4, 68) = 20.242, $p < 0.001$). The EMG amplitude of the GASTROC was significantly greater than the QUADS ($p < 0.001$), MH (p = 0.008), SOL (p = 0.001), and TA (p = 0.001) muscle groups, while the EMG amplitude of the MH was significantly greater than the QUADS (p = 0.002), but not significantly different from the SOL (p = 0.072) and TA (p = 0.117). The TA had a significantly greater burst

amplitude compared to the QUADS (p = 0.028), while there was no difference between SOL and TA (p = 1.00), and SOL and QUADS (p = 0.386). There was no significant interaction effect between *task* and *muscle group* (F (4, 68) = 2.005, p = 0.154) and effect of *task* (F (1, 17) = 0.912, p = 0.353) on EMG amplitude. The effect of slow breathing on burst amplitude varied across muscle groups and participants. In one participant, slow breathing increased the burst amplitude across all muscle groups and decreased in another participant across all muscle groups, while the burst amplitude response in most participants was mixed.

5.3.4.3 Electromyography Pre-Activation

The EMG activity was not significantly different between the tasks in QUADS (χ^2 (2) = 5.147, p = 0.076), MH (χ^2 (2) = 0.329, p = 0.848), GASTROC (χ^2 (2) = 1.544, p = 0.462), SOL (χ^2 (2) = 5.787, p = 0.055), and TA (χ^2 (2) = 3.547, p = 0.17) muscle groups (Table 8). Thus, the participants were not increasing the EMG activation in advance of the perturbation.

Table 8. The muscle activity during quiet stance and prior to the perturbation tasks

	EMG Activity (μV)		
Muscle group	QS	SPON	SLOW
QUADS (n=19)	4.0 (3.4)	5.1 (3.9)	4.3 (2.6)
MH (n=20)	2.7 (3.0)	2.6 (1.8)	2.5 (1.8)
GASTROC (n=20)	3.1 (1.3)	3.1 (1.4)	3.1 (1.1)
SOL (n=19)	4.6 (2.0)	4.4 (1.7)	4.4 (2.8)
TA (n=19)	2.8 (2.1)	3.5 (2.6)	3.4 (1.8)

Data presented as mean (SD); EMG: electromyography; QS: quiet stance; SPON: spontaneous breathing; SLOW: slow breathing; QUADS: quadriceps; MH: medial hamstring; GASTROC: gastrocnemii; SOL: soleus; TA: tibialis anterior.

5.4 Discussion

This is the first study to explore the effects of slow breathing on the cardiovascular and postural systems following postural perturbations in older adults. The main findings of the current study reveal that slowing the respiration rate affected

primarily SBP responses to perturbation. Slow breathing, when compared to spontaneous breathing, resulted in the modulation of muscle onset latency but not muscle burst amplitude during a postural perturbation.

5.4.1 Cardiovascular Response Following Postural Perturbations

Following a postural perturbation, HR rapidly increased and began recovering while blood pressure increased regardless of respiratory rate. The recovery of HR (R-R interval increasing) while SBP was increasing indicated baroreflex engagement secondary to the initial cardiac response. We have reported similar hemodynamics in young adults while spontaneously breathing (Siedlecki et al., 2022b; Study Two).

Slow breathing did not alter the initial HR response compared to spontaneous breathing. It should be noted that HR was higher in the SLOW task compared to SPON between 7-8 s post-perturbation, however, it is unlikely that this difference is physiologically meaningful to the task. The lack of an effect of SLOW breathing on HR in older adults was unexpected because slow breathing enhances vagal control of the heart (Russo et al., 2017; Vidigal et al., 2016). It is possible that the emotional state of the participant might have engendered the homogenous response in HR. We have previously reported higher perceived state anxiety scores that were accompanied with larger HR modulation during more challenging perturbations (Study Two). In the current study, perturbation intensity was identical, and participants reported comparable state anxiety and perceived stability scores between perturbation tasks. Increased parasympathetic activity while slow breathing reduces anxiety and may even be more beneficial in older adults (Magnon et al., 2021). However, slow breathing, when combined with postural perturbations, did not affect state anxiety. Thus, similar perceived state anxiety scores between perturbation tasks may partially explain the lack of difference in HR response.

Another possible explanation is due to age-associated changes to the cardiovascular system. The HR response to cardiovascular stress is blunted with age (Klein et al., 2020; McCrory et al., 2016) as there is a lessened parasympathetic effect on the myocardium in older adults than in younger adults (Karavidas et al., 2010). To compensate, older adults tend to modulate blood pressure mostly through peripheral

vascular resistance rather than cardiac adaptation (Laitinen et al., 2004). A lesser reliance on HR to modulate cardiac output and mean arterial pressure is accompanied with lower resting cBRS (Monahan, 2007). A lower cBRS in older adults is thought to be due to stiffened arterial walls lessening the sensitivity of baroreceptors to fluctuations in blood pressure (Li et al., 2018). The cBRS in quiet stance in the current study was relatively decreased compared to younger adults during similar perturbations (Siedlecki et al., 2022b), suggesting that cardiac baroreflex was inhibited in the current study.

The effect of slow breathing on SBP was more prominent. Slow breathing resulted in lower SBP compared to uncontrolled breathing throughout most of the post-perturbation period. The difference in SBP may be caused by parasympathetic dominance driven by slow breathing, lowering SBP (Russo et al., 2017). Between 1-2 s post-perturbation, there was briefly no difference in SBP between perturbation tasks around the time when HR reached its peak. This could indicate that SBP began rising slightly earlier in SLOW.

The modulation of cBRS following postural perturbations has been reported previously. We reported elevated cBRS after postural perturbation compared to quiet standing (Siedlecki et al., 2022b) and proposed that the elevated cBRS improved the stabilization of arterial blood pressure when the body was perturbed. In the current study, the sensitivity of the cardiac baroreflex was unaffected by perturbations.

Despite age-associated impacts on vagal control of the heart, slow breathing is more effective in enhancing vagal control of the heart in older adults when compared to younger adults (Magnon et al., 2021). Slow breathing can acutely enhance vagal outflow in older adults (Magnon et al., 2021), thereby reducing blood pressure and HR, and increasing cBRS (Zou et al., 2017). Surprisingly, cBRS was unaffected by a reduction in respiratory rate in older adults.

Baroreflex curves may be useful in understanding the cardiovascular changes reported in the current study. Baroreflex resetting is a phenomenon that explains the adaptation of the cardiac baroreflex during exercise. For example, performing physical exercise resets the baroreflex curve upwards and rightwards as elevated HR and arterial

pressure are required to meet the cardiovascular demands placed on the body (Fadel & Raven, 2012; Raven et al., 2019). Another possible explanation for the hemodynamic response is the creation of a new baroreflex curve that only shifted leftwards (reduced SBP) while slow breathing, without affecting the steepness of the curve (same cBRS gain). The impact of slow breathing on the cardiac baroreflex suggests that the dominance of the sympathetic and parasympathetic nervous systems on the heart favour the parasympathetic over the sympathetic nervous system (Russo et al., 2017). Thus, metronome guided slow breathing can affect blood pressure, although HR remained unaffected in the initial cardiac response after a postural perturbation, and the effect on cBRS might be limited.

5.4.2 Neuromuscular Response after Postural Perturbations

There was a faster onset of muscle activation but no change in muscle burst amplitude in lower limb musculature while slow breathing following a postural perturbation in older adults. These findings are not in agreement with a young adult population (Siedlecki et al., 2022a). In young adults, it was found that both muscle onset latency and muscle burst amplitude decreased while slow breathing. The benefits of a shortened onset latency can lead to a more efficient neuromuscular response during periods of postural instability (Afschrift et al., 2016). This is especially important in older adult populations who are prone to delayed reaction times following a perturbation (Martelli et al., 2017).

Slow breathing did not result in any change in muscle burst amplitude post-perturbation whereas slow breathing reduced muscle burst amplitude following perturbations in young adults (Siedlecki et al., 2022a). This is likely due to age-related adaptations to postural responses. Older adults use a greater percentage of the maximum voluntary contraction (Arsenault et al., 2022; Tsai et al., 2014) and have greater center of mass excursions to maintain upright standing compared to young adults (Henry & Baudry, 2019). The lack of muscle amplitude modulation in older adults may act as a protective response, as older adults require greater muscle force to maintain balance.

The cardio-postural integration model described by Garg and colleagues (2014b) may partially explain why muscle burst amplitude was not affected by slow breathing during perturbations. The relationship between the cardiovascular and postural control systems has been observed in older adults (Garg et al., 2014a; Verma et al., 2017; Verma et al., 2019). Verma et al. (2017) proposed two pathways, a non-baroreflex pathway that drives blood pressure regulation because of changes in skeletal muscle activity, and a baroreflex pathway that controls postural sway and muscle activity because of blood pressure fluctuations. The authors posited that there is greater dependence on the non-baroreflex pathway than the baroreflex pathway with aging. This suggestion is in accordance with previous literature in which EMG activity was elevated during upright standing in older adults compared to their young counterparts (Masterson et al., 2006). It is possible that older adults in the current study were favouring the non-baroreflex pathway to regulate blood pressure. This possibility is supported by our finding that muscle burst amplitude was not reduced with slow breathing in older adults, unlike our previous findings in young adults (Siedlecki et al., 2022a). Additionally, cBRS was unaffected by the perturbation tasks, indicating older adults did not increase their reliance on the baroreflex to regulate blood pressure following a perturbation. Thus, older adults in the current study would have required similar muscle activation while slow breathing to counterbalance the unchanged cBRS to regulate blood pressure.

Another possible explanation for slow breathing not affecting muscle burst amplitude is the large variability in the response in older adults. Greater variability in postural control has traditionally been linked with aging (van Emmerik & van Wegen, 2002). In the current study, slow breathing affected burst amplitude similarly across all muscle groups in only two participants. A mixed response was found in the remaining participants indicating inter- and intra-individual differences in how older adults' response to postural perturbations while slow breathing.

5.4.3 Limitations

The novel findings of the study are apparent, though there were limitations. The perturbations were not synchronized to a respiratory reference, which may have contributed to additional variability in the cardiovascular variables. An additional

limitation was not monitoring the movement of the COM because greater COM and center of pressure excursions in older adults have been identified (Massion, 1994). Tracking COM would allow for an examination as to whether shortened latency had any influence on COM control in a population with impaired balance.

5.5 Conclusion

This study found cardiovascular and neuromuscular responses to a postural perturbation were modulated while slow breathing. Reducing respiration rate to 6 breaths per minute altered primarily the blood pressure response, with limited effects on HR and the sensitivity of the cardiac baroreflex compared to spontaneous breathing. Additionally, slow breathing only affected the modulation of muscle onset latency and not muscle burst amplitude.

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Chapter 6

6 Discussion

This dissertation highlights the effects of postural perturbations on the cardiovascular system and the neuromuscular response to slow breathing. The major findings of the four research studies are as follows. Study One illustrated central- and reflex-mediated hemodynamic regulation post-perturbation. A primary centrally mediated tachycardia was followed by a secondary cardiac baroreflex engagement that led HR recovery while blood pressure rose. The primary HR response scaled with intensity, while SBP and cBRS were unaffected by perturbation intensity. Study Two attempted to ascertain the function of a feedforward mechanism during postural perturbations. Despite the timing of postural perturbations being known, there was no anticipatory cardiovascular response from HR and SBP prior to the perturbation similar to what was found using perturbations with unknown timing. However, the effect of state anxiety may contribute to the scaling effect of tachycardia post-perturbation. Study Three identified that breathing at six breaths per minute shortened muscle latency and decreased EMG burst amplitude post-perturbation compared to spontaneous breathing in young adults. Study Four built upon the foundations of the previous three studies in young adults exploring our findings in an older adult population. Older adults were able to maintain standing balance with a similar cardiovascular response pattern to postural perturbations as young adults, yet with lower SBP with slow breathing. While slow breathing, the muscle latency shortened but EMG burst amplitude in lower limb musculature in older adults was not affected.

6.1 Effects of external perturbations on cardiovascular response

Collectively, the data showed that cardiovascular modulation occurs when balance is perturbed, regardless of age. Immediately following the onset of the perturbation, a rise in HR was observed which peaks approximately 1-2 s later, while SBP elevation lags behind HR and peaks 4-6 s post-perturbation. The HR and SBP

responses to perturbations were similar to that of handgrip exercise (Cechetto & Shoemaker, 2009).

Neuroimaging studies have identified close relationships between cardiovascular and cortical function. Wong and colleagues (2007) found elevated HR response to handgrip exercise resulted in the deactivation of the ventral medial prefrontal cortex, a structure associated with parasympathetic activity. Cechetto and Shoemaker (2009) also reported a delayed blood pressure response following a 2 s handgrip. The delay in blood pressure corresponded with increased left insular cortex activity when the task was completed. The left insular cortex is said to assist in parasympathetic control (Williamson et al., 1997). These findings suggest a primary centrally mediated tachycardia, followed by a secondary baroreflex response, occurs following mild, yet brief muscle contractions. However, without experimentally manipulating cortical activity, the mechanism modulating the initial HR and SBP response in postural perturbations remains speculative.

We were able to successfully estimate cBRS during cardiovascular recovery following a postural perturbation. Explanations for the cardiovascular changes observed in this study could be illustrated with models of the baroreflex curves (Figure 13). A baroreflex curve is comprised of a sigmodal curve with SBP on the x-axis and R-R interval/HR on the y-axis. The operating point, which represents the sensitivity of the baroreflex (cBRS). The centering point is located at the steepest point on the baroreflex curve (Raven et al., 2006). At rest, the operating point for HR and SBP regulation is located near the centering point. In this model, when the operating point moves away from the centering point, an outcome would be a lowering of cBRS (Figure 13A). A possible explanation for the increase in cBRS in young adults with perturbations could be the movement of the operating point along the same baroreflex curve. However, the initial increase in HR following a postural perturbation occurred while SBP remains unaffected. Thus, this explanation fails to account for the observations in this dissertation.

The second possible explanation for the increased cBRS is the creation of a new and steeper baroreflex curve during perturbations (Figure 13B). Specifically, the current

accepted model for baroreflex resetting during dynamic exercise marks the movement of the curve upwards and rightwards (Fadel & Raven, 2012; Raven et al., 2019). This resetting could include a steeper slope of the curve as well. Following a postural perturbation, an upward resetting of the baroreflex curve during the initial cardiovascular response would account for the rapid HR response without a change in SBP, while the recovery of the data can be accounted for by an additional rightward shift. Therefore, the baroreflex resetting model accounts for the changes or lack thereof, in blood pressure and HR as well as a greater cBRS.

The concept of cBRS as applied to rapid events such as those used in the current studies generally is believed to relate to a withdrawal of parasympathetic restraint of HR. This mechanism would account for the rapid onset and recovery of HR responses observed here. In our older adult participants, slow breathing depressed SBP throughout the majority of the post-perturbation period compared to spontaneous breathing. Thus, the entire baroreflex curve only shifted leftwards to a new position during SLOW, keeping the operating point near the centering point and not impacting cBRS compared to SPON (Figure 13C). However, we were unable to specifically measure either the parasympathetic or sympathetic arms of cardiac baroreflex regulation.

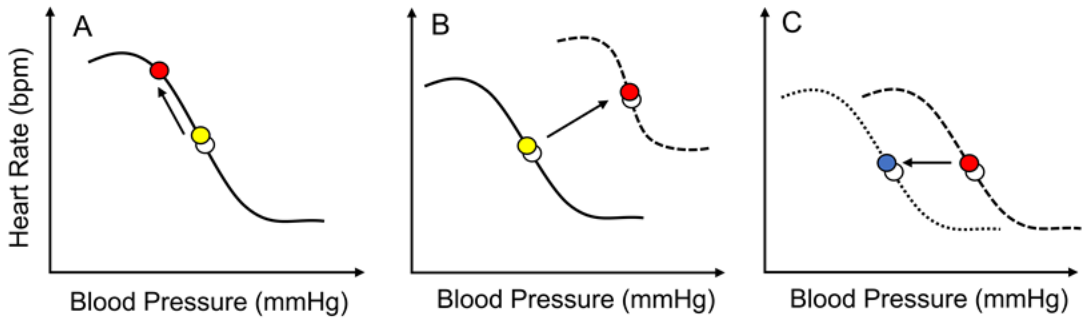

Figure 13. Schematic representation of the baroreflex curves during quiet stance (solid line) and perturbations while spontaneous breathing (dashed line), and slow breathing (dotted line). (A) The operating point at quiet stance is close to the centering point and moving throughout the perturbation protocol on a single baroreflex curve; (B) the baroreflex is resetting to a new baroreflex curve between quiet stance and perturbation *in younger adults*, and (C) during perturbations the baroreflex is resetting between spontaneous and slow breathing *in older adults* with operating point remaining close to the centering point. The yellow dots represent the position of the operating point during quiet stance, the red and blue dots represent the location of the operating point during perturbations while spontaneous and slow breathing, respectively, and the white dots represent the position of the centering point.

There are three ways in which the cBRS is shown to be dependent on age. First, while engagement of the cardiac baroreflex occurred post-perturbation, the modulation of cBRS appeared to be age group specific. In Study One, cBRS was significantly elevated in young adults during the perturbation conditions compared to quiet standing. When similar perturbations were delivered in older adults (Study Four), cBRS was unaffected.

Second, resting cBRS in the young adults (8.5 ms/mmHg) was relatively higher compared to older adults (4.1 ms/mmHg) in the current studies. These resting cBRS values corroborated those reported in young (Bringard et al., 2017; Xu et al., 2017) and older adult literature (Milan-Mattos et al., 2018). Age-associated decline in arterial compliance (Avolio et al., 1985) may be responsible for depressed cBRS in older adults. Because baroreflex activation is sensitive to arterial stretch, reduced arterial compliance inhibits baroreceptor stimulation to changes in blood pressure. However, lower resting cBRS in older adults does not guarantee that the modulation of cBRS is affected. When testing the dive reflex, where the head is submerged underwater, the bradycardia response is preserved with age (O'Mahony et al., 2000). In contrast, during a central hypovolemic

stress test that replicates central blood loss, a greater hypotensive response has been observed, suggesting an impaired rapid acceleration of HR (Shi et al., 2000).

Third, slow breathing did not affect cBRS following post-perturbation in older adults. Slow breathing can elevate cBRS in older adults similar to that seen in young adults when the cardiac baroreflex is simulated with neck pressure (Radaelli et al., 2004). In contrast, Maddens and colleagues (1987) suggested impaired parasympathetic modulation of HR with natural aging while deep breathing. The HR modulation impairment was more noticeable when accompanied with unexplained syncope in the older adult population (Maddens et al., 1987). Thus, it is possible that age-associated differences in cBRS in this dissertation were due to the inability to modulate cBRS in older adults.

6.2 Effect of slow breathing on neuromuscular response

The effect of slow breathing on the neuromuscular response was reported. Interestingly, the influence of breathing at six breaths per minute was age dependent. The muscle onset latency during surface support translations in our current studies was consistent with past literature in young (Horak & Nashner, 1986) and older adult populations (Arsenault et al., 2022). Relative to our young adult population, muscle onset latency was longer in older adults (Table 9). This is not surprising as a recent meta-analysis found that older adults had longer muscle onset latency, when compared to young adults, regardless of perturbation type (Phu et al., 2022). Reductions in information processing speeds are the likely cause of the delayed reaction times observed in older adults (Lockhart, 2008).

Table 9. Muscle onset latency (ms) between young and older adults during perturbations while spontaneously or slow breathing

	Task			
	SPON		SLOW	
	Young	Old	Young	Old
QUADS	127 (35)	137 (51)	117 (33)	126 (62)
MH	121 (21)	136 (20)	114 (26)	118 (19)
GASTROC	88 (18)	103 (15)	74 (24)	84 (16)
SOL	66 (19)	86 (27)	55 (21)	59 (30)
TA	97 (24)	138 (52)	94 (28)	101 (45)

Data presented as mean (SD) for the averaged spontaneous (SPON) and SLOW breathing perturbations between young and older adults; QUADS: Quadriceps; MH: Medial hamstring; GASTROC: Gastrocnemii; SOL: Soleus; TA: Tibialis anterior

The CNS favouring energy efficiency over postural stability has been described previously (Afschrift et al., 2016). The concept suggests that the mechanical effort required to maintain balance can affect postural strategy selection. Earlier muscle onset while slow breathing may enhance the efficiency of the CNS to maintain balance when perturbed. A more energy efficient response to a perturbation may be especially important in older adults who already have a delayed response to a perturbation. An earlier muscle onset time would allow for the recapture of the COM sooner and perhaps without needing to take a step to regain balance.

Slow breathing resulted in a reduced EMG burst amplitude in the young adults but not the older adults. However, during maximum voluntary contraction paradigms the effect of slow breathing was an increase of the EMG activity (Barbosa et al., 2015; Barbosa et al., 2013), not a decrease. This finding indicates that respiratory and motor systems interact, and respiratory motor interactions are task specific and may be dependent on the primary objective of the task. For instance, if the outcome of the task is to generate as much force as possible, such as with a maximum voluntary contraction,

slow breathing increases muscle force production when compared to spontaneous breathing (Barbosa et al., 2013). In the event of a postural perturbation, the primary objective is to maintain stability. Applying the concept of energy efficiency to explain the effect of reduced EMG burst amplitude while slow breathing may be of interest. The EMG amplitude is higher when the timing of a perturbation is unknown compared to perturbations that can be anticipated (Kaewmanee & Aruin, 2022), suggesting that the mechanical effort required to regain balance after perturbations can be less when the timing is known than when unknown or that the burst is anticipatory and reduces the COM movement. Thus, perhaps slow breathing can be utilized when regaining balance while being more energy efficient (reduced burst amplitude).

Table 10. Electromyography burst amplitude (μV) between young and older adults during perturbations while spontaneously and slow breathing

	Task			
	SPON		SLOW	
	Young	Old	Young	Old
QUADS	2.9 (1.5)	2.8 (1.6)	2.1 (0.9)	2.8 (1.5)
MH	5.8 (2.9)	6.8 (3.9)	4.6 (2.4)	7.2 (4.0)
GASTROC	8.6 (3.6)	9.7 (4.5)	8.7 (3.7)	9.0 (4.1)
SOL	4.9 (2.3)	4.3 (1.6)	4.8 (2.2)	3.8 (1.3)
TA	5.0 (2.8)	5.4 (3.4)	4.2 (2.7)	4.6 (2.3)

Data presented as mean (SD) for the averaged spontaneous (SPON) and SLOW breathing perturbations between young and older adults; QUADS: Quadriceps; MH: Medial hamstring; GASTROC: Gastrocnemii; SOL: Soleus; TA: Tibialis anterior

Breathing at six breaths per minute did not affect the EMG burst amplitude in older adults. This finding contradicts the concept of the CNS favouring energy efficiency because older adults were using similar EMG burst amplitude to regain balance regardless of breathing rate. It should be noted that EMG burst amplitude was relatively similar between young and older adults during the perturbation tasks, although larger

bursts in the MH muscle group were found in older adults (Table 10). A possible explanation for this lack of effect on muscle burst amplitude is that older adults use a greater percentage of their maximum muscle force (Arsenault et al., 2022; Tsai et al., 2014). Maximum voluntary contractions were not measured in the dissertation; however, the muscle pre-activation data during perturbation tasks indicated older adults relied more on the QUADS and less on the SOL than their younger counterparts (Table 11). This finding, coupled with the lack of difference in EMG burst amplitude between age groups suggests older adults used a greater percentage of their force- an observation consistent with previous literature (Arsenault et al., 2022). This is likely due to the decreased muscle mass that is associated with natural aging (Roman-Liu, 2018). Thus, the CNS not modulating muscle burst amplitude in older adults while slow breathing could act as a protective response to avoid risk of a fall.

Table 11. Muscle preactivation (μV) during perturbation tasks between young and older adults

	Task			
	SPON		SLOW	
	Young	Old	Young	Old
QUADS	2.7 (1.7)	5.1 (3.9)	2.1 (1.1)	4.3 (2.6)
MH	2.4 (2.3)	2.6 (1.8)	2.0 (2.0)	2.5 (1.8)
GASTROCS	3.9 (2.1)	3.1 (1.4)	3.3 (1.9)	3.1 (1.1)
SOL	6.3 (2.8)	4.4 (1.7)	6.1 (2.9)	4.4 (2.8)
TA	2.5 (1.3)	3.5 (2.6)	2.3 (1.1)	3.4 (1.8)

Data presented as mean (SD) for the averaged spontaneous (SPON) and SLOW breathing perturbations between young and older adults; QUADS: Quadriceps; MH: Medial hamstring; GASTROC: Gastrocnemii; SOL: Soleus; TA: Tibialis anterior

Muscle activation patterns in the lower limb followed a distal to proximal activation pattern. Additionally, posterior muscle groups were activated prior to anterior muscles. Posteriorly translated belt accelerations require posterior muscle activation to

counteract the anterior acceleration of the COM. The older adults in Study Four displayed similar muscle activation patterns to the young adults in Study Three. The muscle activation patterns resembled an ankle strategy (Horak & Nashner, 1986) in both age groups. Furthermore, slow breathing did not influence the overall postural strategy of distal to proximal activation.

6.3 Cardiovascular and postural control interactions

The interaction between cardiovascular and postural control systems has been reported. The cardio-postural integration model suggests that the cardiovascular, postural control and musculoskeletal systems interact with one another (Garg et al., 2014). Recent literature has identified a functional role between cardio-postural interactions during upright balance (Verma et al., 2019; Xu et al., 2020). For example, the contraction of skeletal muscles induced by postural sway combats the pooling of blood in the lower limbs (Garg et al., 2013). Similarly, center of pressure excursions and mean sway velocity increase while standing upright when regulation of blood pressure is impaired (Xu et al., 2020). The findings of these studies highlight the possible interactions between the cardiovascular and postural control systems in blood pressure regulation.

Our findings support the cardio-postural integration model. We found that in addition to postural perturbations affecting the cardiovascular system, manipulating the cardiovascular system with respiration can also affect the motor system's response to postural perturbations. An interesting observation of the cardio-postural integration model as presented by Garg and colleagues (2014) is that the subsystems are visually represented as three equally sized subsystems suggesting that the three interacting subsystems contribute equally to cardiovascular and postural control. However, we have demonstrated that cardiovascular and neuromuscular responses can act independently from one another. Garg et al. (2014) also highlighted that the cardiovascular control is secondary to maintaining postural control. Thus, we suggest that a more appropriate illustration of the cardio-postural interaction should reflect the cardiovascular control subsystem visually smaller than the postural control and musculoskeletal systems. This reweighting would indicate a smaller role of the cardiovascular system in postural control compared to the other systems.

Anticipatory responses in the cardiovascular system were not present in Study Two. This is an interesting finding because anticipatory neuromuscular responses in postural control during external perturbations have been reported (Pollock et al., 2017). The cardiovascular system is capable of producing an anticipatory response to stationary cycling (Krogh & Lindhard, 1913; Miyamoto et al., 2022), and walking and running (Eldridge et al., 1985) tasks. However, the presence of an anticipatory cardiovascular response may depend on the task because posture tasks, such as head-up tilt (Patel et al., 2018) and transitions from supine to standing (Borst et al., 1982), are absent of anticipatory responses. Therefore, the findings of the dissertation illustrate the complex interactions of the cardio-postural system during postural perturbations.

6.4 Future Directions

Further research is required to understand the interaction between cardiovascular, respiratory and motor systems as well as mechanisms underlying these systems. Future studies would benefit from triggering perturbations in-phase with respiration. Cardio-respiratory coupling, called respiratory sinus arrhythmia, affects the rhythmic fluctuations in HR and is dependent on respiratory phase. During expiration, cardiac vagal efferent fibers fire more strongly and evoke bradycardia, while lung inflation inhibits cardiac vagal outflow, increasing HR during inspiration (Yasuma & Hayano, 2004). Additionally, breathing can also mechanically affect blood pressure via pressure gradients in cavities located in the trunk and torso (Rowell, 1986). Triggering a perturbation in-phase with respiration would permit the onset of perturbations to be synchronized with HR and SBP, limiting the variability in HR and SBP at perturbation onset.

Improving the generalizability of our results would benefit from three changes to the experimental protocol. First, breathing at six breaths per minute can be a challenging task, especially if prolonged. Identifying whether other breathing rates can cause similar neuromuscular effects would allow for general application of controlled breathing to investigate the impact on postural control. Volitional breathing corresponds with cortex activation in the motor cortex, premotor cortex and supplementary motor areas (McKay et al., 2003), suggesting controlled breathing may also affect neuromuscular responses to

stimuli. Controlled breathing at 15 breaths per minute can have similar effects as slow breathing on EMG activity (Rodrigues et al., 2018) and motor-evoked potential amplitude and latency (Ozaki & Kurata, 2015). The findings of such studies may provide evidence that controlled breathing, rather than the frequency of breathing, may influence the respiratory-motor interaction.

Second, the movement of the support surface made the center of pressure response from the muscle activation difficult to distinguish. Force plates for human movement analysis provide accurate measurements of the ground reaction forces used for center of pressure calculations when mounted rigidly. However, when using an instrumented treadmill to apply perturbations, the ground reaction forces exerted by the tested subject are added to the inertial and gravitational forces measured during perturbations as a result of the rotation and translation of the platform in which the force plates are positioned. This leads to errors in calculated center of pressure and additional analytical methods are necessary to assess the reactive component of center of pressure. In our analysis we applied a second order low-pass Butterworth filter with a cut-off frequency of 6 Hz, which is typically used for the inverse dynamic analysis of walking (van den Bogert et al., 2013). However, there are additional methods developed to compensate for the inertial distortions, but they require calibration procedures at the time of data collection that we did not perform. Functional changes in postural control have been reported previously, as center of pressure deviations are increased while slow breathing in standing (Rodrigues et al., 2018). Identifying functional changes in addition to muscle changes could determine the therapeutic value of slow breathing on balance performance.

Lastly, investigating the transferability of our findings to other forms of external perturbations would be important. Selection of a perturbation type in future studies should reflect real-world scenarios because the postural response to perturbations triggered during gait (Fukuda et al., 2022) and the hemodynamics during dynamic exercise (Yadav & Bagi, 2018) differ compared to the surface support translation perturbations used in the current studies. Therefore, a loss of balance during dynamic movement may produce different findings to surface-support translations.

6.5 Conclusion

The findings of the dissertation provide evidence that cardiovascular modulation occurs when standing is perturbed and supports the notion that the cardiovascular, respiratory and motor control systems share a complex interaction during postural perturbations. The studies in this dissertation identified that standing perturbations evoked a HR and SBP response that was regulated by central and reflex mechanisms. When respiration was manipulated, slow breathing was also found to affect muscle onset latency in young and older adults and EMG burst amplitude in only young adults.

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Appendix: Ethics Approval

Western Research

Date: 19 March 2018

To: Dr. Jayne Garland

Project ID: 110471

Study Title: Regional Activation of Plantarflexor Muscles during Standing Balance

Application Type: HSREB Initial Application

Review Type: Delegated

Meeting Date / Full Board Reporting Date: 17/Apr/2018

Date Approval Issued: 19/Mar/2018

REB Approval Expiry Date: 19/Mar/2019

Dear Dr. Jayne Garland

The Western University Health Science Research Ethics Board (HSREB) has reviewed and approved the above mentioned study as described in the WREM application form, as of the HSREB Initial Approval Date noted above. This research study is to be conducted by the investigator noted above. All other required institutional approvals must also be obtained prior to the conduct of the study.

Documents Approved:

Document Name	Document Type	Document Date	Document Version
CB&M	Other Data Collection Instruments	15/Dec/2017	1
Comments about E-mail	Email Script	07/Feb/2018	1
Poster	Recruitment Materials	26/Feb/2018	2
Regional Activation Protocol	Protocol	02/Mar/2018	2
Regional Muscle Activation in Balance Tasks Information Letter and Consent Form	Written Consent/Assent	02/Mar/2018	2
Self Evaluation of Breathing Questionnaire V2	Paper Survey	13/Nov/2017	

Documents Acknowledged:

Document Name	Document Type	Document Date	Document Version
References - Ethics	References	26/Feb/2018	2

No deviations from, or changes to, the protocol or WREM application should be initiated without prior written approval of an appropriate amendment from Western HSREB , except when necessary to eliminate immediate hazard(s) to study participants or when the change(s) involves only administrative or logistical aspects of the trial.

REB members involved in the research project do not participate in the review, discussion or decision.

The Western University HSREB operates in compliance with, and is constituted in accordance with, the requirements of the TriCouncil Policy Statement: Ethical Conduct for Research Involving Humans (TCPS 2); the International Conference on Harmonisation Good Clinical Practice Consolidated Guideline (ICH GCP); Part C, Division 5 of the Food and Drug Regulations; Part 4 of the Natural Health Products Regulations; Part 3 of the Medical Devices Regulations and the provisions of the Ontario Personal Health Information Protection Act (PHIPA 2004) and its applicable regulations. The HSREB is registered with the U.S. Department of Health & Human Services under the IRB registration number IRB 00000940.

Please do not hesitate to contact us if you have any questions.

Sincerely,

Western Research

Date: 25 September 2018

To: Dr. Jayne Garland

Project ID: 110471

Study Title: Regional Activation of Plantarflexor Muscles during Standing Balance

Application Type: HSREB Amendment Form

Review Type: Delegated

Meeting Date / Full Board Reporting Date: 02/Oct/2018

Date Approval Issued: 25/Sep/2018

REB Approval Expiry Date: 19/Mar/2019

Dear Dr. Jayne Garland ,

The Western University Health Sciences Research Ethics Board (HSREB) has reviewed and approved the WREM application form for the amendment, as of the date noted above.

Documents Approved:

Document Name	Document Type	Document Date	Document Version
Amendment Revised Information Letter and Consent Form	Consent Form	19/Sep/2018	3
Revised Protocol	Protocol	01/Sep/2018	3

Documents Acknowledged:

Document Name	Document Type	Document Date	Document Version
Summary of Changes	Summary of Changes	19/Sep/2018	1

REB members involved in the research project do not participate in the review, discussion or decision.

The Western University HSREB operates in compliance with, and is constituted in accordance with, the requirements of the TriCouncil Policy Statement: Ethical Conduct for Research Involving Humans (TCPS 2); the International Conference on Harmonisation Good Clinical Practice Consolidated Guideline (ICH GCP); Part C, Division 5 of the Food and Drug Regulations; Part 4 of the Natural Health Products Regulations; Part 3 of the Medical Devices Regulations and the provisions of the Ontario Personal Health Information Protection Act (PHIPA 2004) and its applicable regulations. The HSREB is registered with the U.S. Department of Health & Human Services under the IRB registration number IRB 00000940.

Please do not hesitate to contact us if you have any questions.

Sincerely,

Patricia Sargeant, Ethics Officer on behalf of Dr. Joseph Gilbert, HSREB Chair

Note: This correspondence includes an electronic signature (validation and approval via an online system that is compliant with all regulations).

Western Research

Date: 8 May 2019

To: Dr. Jayne Garland

Project ID: 110471

Study Title: Regional Activation of Plantarflexor Muscles during Standing Balance

Application Type: HSREB Amendment Form

Review Type: Delegated

Meeting Date / Full Board Reporting Date: 21/May/2019

Date Approval Issued: 08/May/2019

REB Approval Expiry Date: 19/Mar/2020

Dear Dr. Jayne Garland ,

The Western University Health Sciences Research Ethics Board (HSREB) has reviewed and approved the WREM application form for the amendment, as of the date noted above.

Documents Approved:

Document Name	Document Type	Document Date	Document Version
Recruitment Poster 2	Other data collection forms	11/Apr/2019	1

REB members involved in the research project do not participate in the review, discussion or decision.

The Western University HSREB operates in compliance with, and is constituted in accordance with, the requirements of the TriCouncil Policy Statement: Ethical Conduct for Research Involving Humans (TCPS 2); the International Conference on Harmonisation Good Clinical Practice Consolidated Guideline (ICH GCP); Part C, Division 5 of the Food and Drug Regulations; Part 4 of the Natural Health Products Regulations; Part 3 of the Medical Devices Regulations and the provisions of the Ontario Personal Health Information Protection Act (PHIPA 2004) and its applicable regulations. The HSREB is registered with the U.S. Department of Health & Human Services under the IRB registration number IRB 00000940.

Please do not hesitate to contact us if you have any questions.

Sincerely,

Patricia Sargeant, Ethics Officer on behalf of Dr. Joseph Gilbert, HSREB Chair

Note: This correspondence includes an electronic signature (validation and approval via an online system that is compliant with all regulations).

Western Research

Date: 17 December 2020

To: Dr. Jayne Garland

Project ID: 110471

Study Title: Regional Activation of Plantarflexor Muscles during Standing Balance

Application Type: HSREB Amendment Form

Review Type: Delegated

Meeting Date / Full Board Reporting Date: 12/Jan/2021

Date Approval Issued: 17/Dec/2020

REB Approval Expiry Date: 19/Mar/2021

Dear Dr. Jayne Garland ,

The Western University Health Sciences Research Ethics Board (HSREB) has reviewed and approved the WREM application form for the amendment, as of the date noted above.

Documents Approved:

Document Name	Document Type	Document Date	Document Version
Amendment Information Letter and Consent Form	Consent Form	15/Dec/2020	4
Data Collection and Recording Sheet	Other Data Collection Instruments	15/Dec/2020	1
Health History	Paper Survey	15/Dec/2020	1
Amendment Protocol	Protocol	15/Dec/2020	4

Documents Acknowledged:

Document Name	Document Type	Document Date	Document Version
Summary of Changes	Summary of Changes	15/Dec/2020	1

REB members involved in the research project do not participate in the review, discussion or decision.

The Western University HSREB operates in compliance with, and is constituted in accordance with, the requirements of the TriCouncil Policy Statement: Ethical Conduct for Research Involving Humans (TCPS 2); the International Conference on Harmonisation Good Clinical Practice Consolidated Guideline (ICH GCP); Part C, Division 5 of the Food and Drug Regulations; Part 4 of the Natural Health Products Regulations; Part 3 of the Medical Devices Regulations and the provisions of the Ontario Personal Health Information Protection Act (PHIPA 2004) and its applicable regulations. The HSREB is registered with the U.S. Department of Health & Human Services under the IRB registration number IRB 00000940.

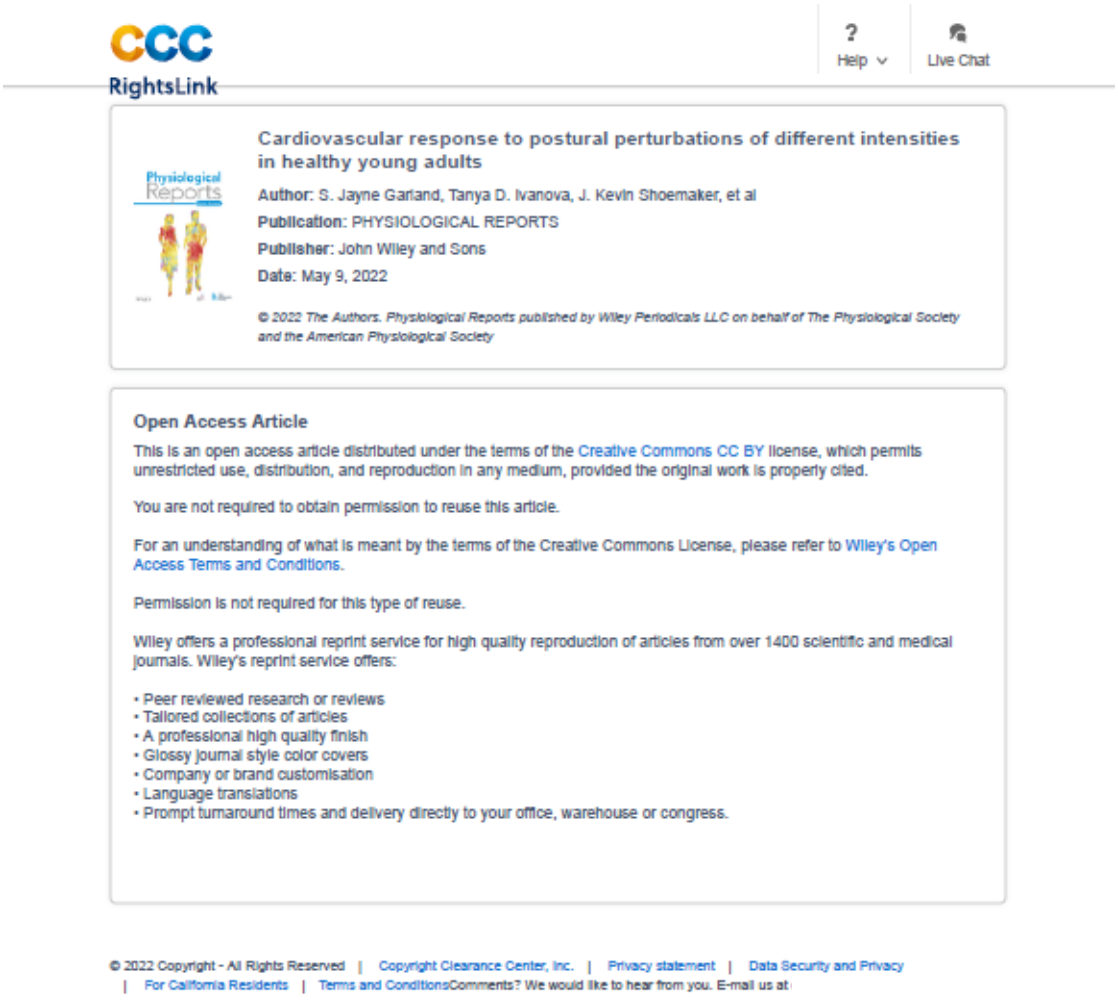
Please do not hesitate to contact us if you have any questions.

Sincerely,

Patricia Sargeant, Ethics Office on behalf of Dr. Joseph Gilbert, HSREB Chair

Note: This correspondence includes an electronic signature (validation and approval via an online system that is compliant with all regulations).

Appendix: Manuscript Permissions



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Cardiovascular response to postural perturbations of different intensities in healthy young adults

Author: S. Jayne Garland, Tanya D. Ivanova, J. Kevin Shoemaker, et al

Publication: PHYSIOLOGICAL REPORTS

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Date: May 9, 2022

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1. Grant of License

Curriculum Vitae

PATRICK SIEDLECKI

EDUCATION

Ph.D., Integrative Biosciences, Kinesiology, Western University, expected 2023.
Dissertation Advisor: Jayne Garland

M.Sc., Kinesiology, Lakehead University, 2017
Thesis Advisor: Paolo Sanzo

B.A., Kinesiology, Western University, 2015
Honours Specialization

RESEARCH EXPERIENCE

Research Coordinator, London Health Sciences Centre, 2022-Present

- Managing, organizing, and coordinating clinical trials at the Department of Paediatric Emergency Medicine and ensuring compliance with the clinical trial protocol and regulations.

Graduate Fellowship, Western University, 2017-2022

- Investigated preliminary biomechanical and electromyography analysis using CED Spike2, MATLAB, Orthotrax, and Empowerhealth research software, as well as writing and preparing manuscripts for publication.

Research Assistant, Independent Claims Ltd, 2018

- Created and managed an EndNote library, updated clinical assessment and management forms, reviewed physical medicine treatment literature, and transcribed, prepared, and reviewed independent medical evaluation documents for submission.

WORK EXPERIENCE

Graduate Teaching Assistant, Western University, 2017-2022

- Overseeing undergraduate kinesiology and health sciences' students in a laboratory setting, proctoring, and marking examinations and bellringers, and holding office hours.
- Appointments held: Functional Human Anatomy, Biomechanical Analysis of Physical Activity, Biomechanics, Exercise Neuroscience, Neuromuscular Physiology.

Graduate Teaching Assistant, Lakehead University, 2015-2017

- Supervised undergraduate kinesiology and biology students in lecture and laboratory settings. Duties included marking assignments and examinations, and proctoring.

- Appointments held: Internal Anatomy, Introduction to Human Physiology, Physical Growth and Motor Development, and Lifestyle Counselling.

Clinical Assistant, EMG London, 2014-2015
- Collaborated with an orthopaedic surgeon and physiatrist.
- Responsibilities included obtaining medical histories, performing physical examinations and modalities, and prescribing exercises in patients with chronic musculoskeletal disorders.

VOLUNTEER EXPERIENCE

Researcher, Wolf Orthopaedic Biomechanics Laboratory, 2017-Present
- Assisted with ongoing clinical research focusing on gait analysis and electrophysiological parameters.
- Experienced working with Delsys sEMG, Cortex motion analysis software, D-Flow, and BIODEX isokinetic dynamometer.

Conference Organizer, Exercise Neuroscience Group, 2022
- Aided in the planning of a conference.

Mentor, KGSA Mentorship Program, 2020-2021
- Provided co-mentorship to first year kinesiology graduate students.

Grade 12 Preview Day Presenter, Lakehead University, 2017
- Created an interactive learning environment for high school students which showcased research performed at the university.

Baseline Health Evaluator, HEAD SMART, 2014-2015
- Volunteered with the Sports Legacy Institute Concussion Evaluation branch at Western University in performing baseline concussion evaluations on young athletes.

Physiotherapy Assistant, St. Joseph's Health Centre, 2014-2015
- Organized and sterilized therapeutic supplies in the physiotherapy department.

Physiotherapy Assistant, Quattro Health and Performance, 2014
- Coordinated physical modalities and various rehabilitation treatments with a physiotherapist and registered kinesiologist.

HONOURS & AWARDS

2022 International Society of Electrophysiology and Kinesiology Travel Award ($500)

2021 Kinesiology Graduate Student Association Poster Presentation winner

2019-2020 Ontario Graduate Scholarship recipient (Western University)

2018-2019 Ontario Graduate Scholarship recipient (Western University)

2018 Society of Graduate Students Travel Subsidy ($500)

2018 Fall Graduate Student Conference Travel Award ($500)

2018 International Society of Biomechanics in Sports Travel Grant ($500 NZD)

2017 International Society of Biomechanics in Sports Travel Grant (€500)

CONFERENCES & INVITED TALKS

International Society of Electrophysiology and Kinesiology Congress | Quebec City, QC | 2022 | Poster

Exercise and Neuroscience Group Meeting | London, ON | 2022 | Oral

Own Your Future: May Conference on Teaching | Western University | 2022 | Attendee

Spring Perspectives on Teaching Conference | Western University | 2021 | Attendee

London Health Research Day | London, ON | 2021 | Poster

Own Your Future: May Conference on Teaching | Western University | 2021 | Attendee

Kinesiology Graduate Student Association Conference | Western University | 2021 | Poster

International Society of Electrophysiology and Kinesiology Congress | Nagoya, Japan | 2020 | Attendee

Canadian Society of Exercise Physiology Conference | Kelowna, BC | 2019 | Poster

Exercise and Neuroscience Group Meeting | Hamilton, ON | 2019 | Oral

3 Minute Thesis Competition | Western University | 2019 | Oral

Canadian Physiotherapy Congress | Montreal, QC | 2018 | Poster

36th International Conference on Biomechanics in Sports | Auckland, New Zealand | 2018 | Oral

35th International Conference on Biomechanics in Sports | Cologne, Germany | 2017 | Oral

Bodies of Knowledge Graduate Student Conference | Toronto, ON | 2017 | Oral

Neuroscience Research Interest Group | Thunder Bay, ON | 2017 | Oral

Research and Innovation Week | Lakehead University | 2017 | Poster

3 Minute Thesis Competition | Lakehead University | 2017 | Oral

St. Joseph's Care Group Research Showcase | Thunder Bay, ON | 2017 | Poster

St. Joseph's Care Group Research Showcase | Thunder Bay, ON | 2016 | Attendee

PUBLICATIONS

Siedlecki, P., Ivanova, T.D., Shoemaker, J.K., & Garland, S.J. (2022). The effects of slow breathing on postural muscles during standing perturbations in young adults. *Experimental Brain Research, 240*(10), 2623-2631. doi:10.1007/s00221-002-06437-0

Siedlecki, P., Shoemaker, J.K., Ivanova, T.D., & Garland, S.J. (2022) Cardiovascular response to postural perturbations of different intensities in healthy young adults. *Physiological Reports, 10*(9): e15299. doi:10.14814/phy2.15299

Siedlecki, P. (2020). Implementing team-based learning to strengthen communication skills among undergraduate kinesiology students. *Teaching Innovation Projects, 9*(1), 1-11. doi:10.5206/tips.v9i1.10316

Siedlecki, P., Sanzo, P., Zerpa, C., & Newhouse, I. (2018). End-tidal carbon dioxide levels in patients with post-concussion syndrome during neurocognitive and physical tasks compared to a normative control group. *Brain Injury*, *32*(13-14). doi:10.1080/02699052.2018.1506945

Siedlecki, P., Sanzo, P., Zerpa, C., & Newhouse, I. (2018). Effects of Walking versus Completing A Neurocognitive Task on End-Tidal Carbon Dioxide After Concussion- A Pilot Study. *ISBS Proceedings Achieve, 36*(1), 165. Retrieved from http://commons.nmu.edu/isbs/vol36/iss1/165

Siedlecki, P., Sanzo, P., Zerpa, C., & Newhouse, I. (2017). Effects of walking versus completing a neurocognitive task on breathing physiology in healthy individuals – A pilot study. In W. Potthast, A. Niehoff, & S. David (Ed.), *International Society of Biomechanics Conference Proceedings*: 35th International Conference on Biomechanics in Sports (pp. 1104-1107). Cologne, Germany: German Sport University Cologne. Retrieved from https://dshs-koeln.sciebo.de/index.php/s/CamALh9yXz0k6Vt#pdfviewer

Siedlecki, P., Sanzo, P., & Zerpa, C. (2017). The effects of neurocognitive and physical tasks on end-tidal carbon dioxide levels and respiratory rate in healthy individuals – A pilot study. *Clinical Practice, 6*(1), 1-8. doi:10.5923/j.cp.20170601.01

PROFESSIONAL SERVICE

Lakehead University School of Kinesiology campus interview student committee

PROFESSIONAL ASSOCIATIONS

Member of the College of Kinesiologists of Ontario

Student Member of International Society of Electrophysiology and Kinesiology

ACCOMPLISHMENTS

Completed Health Canada Division 5 training

Completed Good Clinical Practice training

Completed Certificate for University Teaching and Learning (Summer 2021)

Completed Teaching Mentor Program

Graduate Student Teaching Assistant nominee (Winter 2018)

New Investigator Award nominee (ISBS 2018)

Completed Advanced Teaching Program

Advanced Teaching Program certificate from Western University

Registered Kinesiologist

Dean’s Honour List (2015)

SKILLS AND ABILITIES

Proficient in Microsoft Office Suite, OWL, EndNote, Zoom

Certified Gait Real-time Analysis Interactive Laboratory (GRAIL) operator

Can perform on/off-field upper and lower extremity therapeutic taping