Postural state modulation of cortical balance reactions

by

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Author's Declaration

I hereby declare that I am the sole author of this thesis. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners.

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Abstract

Safe and effective walking is a crucial part of daily human life, but the number of injuries and resulting financial burden from falls during walking is increasing. As a result, it continues to be important to advance understanding of dynamic balance control to improve approaches to rehabilitation and minimize fall risk. The control of stability during dynamic tasks poses a particularly complex challenge to the central nervous system (CNS) as the control of balance is performed under the changing mechanical, sensory and central states. Emerging work has a revealed the potential importance of cortical contributions to the control of stability particularly in response to moments of induced instability (perturbations). A cortically-evoked potential, the N1 response, is a discrete probe that is used to assess cortical contributions to stability and is most often used to study balance control in static contexts. Towards an understanding of dynamic balance control, it is necessary to study changes in the N1 during changes in movement isolated from other dynamic control processes. The influence of varying CNS state due to movement on cortical responses has not been evaluated. The current work assesses the response of N1 potentials during changes in pre-perturbation state evoked by different pre-perturbation leaning postures. This was used to manipulate the relative amplitude of perturbation by changing the starting position of the centre of mass (COM) with respect to the base of support. Higher threat conditions occurred when the perturbation led to movement of the COM towards the already loaded side (greater threat of instability) as compared to COM movement towards the unloaded side (low threat). It was hypothesized that pre-perturbation leaning would amplify N1 responses compared to equal-weight stance. A second hypothesis was that high threat conditions would increase the N1 compared to low threat conditions. The results supported the second hypothesis, that changes in cortical and muscle activity were related to characteristics of the threat rather than pre-perturbation changes in excitability of the N1. The effect of postural state on balance reactions was observed in response latency where leaning, regardless of perturbation direction, was associated with delayed N1 potentials compared to equal-weight stance. Scaling of cortical and muscle responses across tasks indicated that changes in posture are resolved at the onset of perturbation and reactive balance control accounts for such threats alongside the perturbation. Study designs investigating dynamic changes in posture versus the static postures used here may further explain the nature of pre-perturbation state modulation.

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Chapter 1: Background

1.0 Importance of walking

Injuries from falls in the elderly has been previously estimated to cost over $6 billion every year in Canada (Parachute, 2015), resulting in extreme economic burden as well as psychological distress. The majority (61%) of these fall-related injuries occur during walking (Public Health Agency of Canada, 2014), thus a further understanding of the control of dynamic tasks such as gait is necessary. The capacity to walk is a primary determinant of functional independence and important determinant of quality of life (Nutt, Marsden, & Thompson, 1993). Disordered walking is a common consequence of neurologic and musculoskeletal disease or injury and can also be associated with aging. The underlying cases of challenges to walking, as denoted later, are numerous and as a result, recovery outcomes after gait rehabilitation are challenged by this complexity (Hicks & Ginis, 2008; Said, Goldie, Patla, Sparrow, & Martin, 1999). There is a continued need to advance fundamental understanding of the control of human bipedal walking so as to inform more targeted and effective techniques to improve disordered walking.

Human gait has evolved to become very efficient and safe at the cost of a high demand on the central nervous system (CNS) for control. Compared to other species, humans have a high center of mass and a smaller base of support from our upright posture and bipedal stance (Bruijn & van Dieën, 2018; Winter, 1995). Two fundamental control demands associated with gait are the need to control progression and the challenge to control stability which is particularly difficult in bipedal postures. One feature that makes the control of stability challenging during walking is the complexity introduced by ongoing movement in which the CNS, musculoskeletal, and environmental states change moment to moment. This in turn complicates the transformation necessary to detect and respond to challenges to upright stability. A primary focus of the current study is to advance understanding on changes in state to CNS control of stability with the longer-term objective of advancing understanding of the control of stability when walking.

Stability can be defined as maintaining the relationship between the center of mass and the base of support (Winter, 1995) and stability control can be considered static or dynamic. Static control involves maintaining the position of the center of mass (COM) within a fixed base of support (BOS) in the absence of external perturbations or internally generated movement. Measuring static balance control is typically assessed by measuring postural sway or a proxy of sway over a period of time. Postural sway, or an excursion of the COM, is counteracted by internally generated "corrective forces" that is represented by the measurement of the center of pressure (COP). The COP represents the sum of muscle forces acting to maintain the location of the center of mass within the BOS which is typically associated with the boundaries of the feet (Gurfinkel, 1974; Soames & Atha, 1982; Thomas & Whitney, 1959; Winter, Patla, & Frank, 1990). One can measure static control by assessing center of pressure excursion or COM sway when someone is standing still. The postural sway that occurs during static control reflects the continuous control of stability to maintain the position of the COM relative to the BOS (Gurfinkel, 1974; Thomas & Whitney, 1959). In contrast dynamic stability is distinguished by the control of stability in response to external perturbations or large amplitude internally-generated perturbations (e.g. motion of the body and/or limbs) (Chan, Jones, & Catchlove, 1979; Chan, Jones, Kearney, & Watt, 1979; Winter, Patla, & Frank, 1990). During dynamic balance control, the CNS controls both the COM and BOS to maintain stability. The control of the size and location of the BOS as a strategy to maintain stability has been referred to as change-in-support reactions (Maki & McIlroy, 1997). The act of walking is a prototypical example of dynamic stability control. For example, the sub-task of progression, where muscles of the legs, torso, and upper body (Bruijn, Meijer, Beek, van Dieën, 2010; Kibushi et al., 2018; Meyns, Bruijn, & Duysens, 2013) coordinate to propel the body in a direction, introduces a backdrop of movement that serves to both challenge and maintain stability. The control also involves a purposeful excursion of the COM beyond the BOS which, by definition, introduces instability (Jian, Winter, Ishac, & Gilchrist, 1993).

1.1 The control of gait and dynamic stability control

Human gait is a very complex behaviour to study as it involves integration of multiple networks: locomotor rhythm control, step placement and dynamic balance control. There is some contribution from passive dynamics that enable gait to be efficient such that muscle activity is

relatively small given the complexity of control across many joints and the amplitude of movement generated (Nashner, 1980). An active contribution from the CNS is required to control limb movements for progression, for stabilization of body segments as well phasic and tonic contractions needed to control upright stability. This control is believed to be principally determined by somatosensory information arising from foot contact (Bancroft & Day, 2016; Bruijn et al., 2018; Duysens, De Groote, & Jonkers, 2013; Lyon & Day, 1997), however, additional CNS processing not dependent on foot contact such as vision (Patla, 1997; Patla, Prentice, & Gobbi, 1996) makes it difficult to disentangle the CNS events that allow for healthy gait. Towards an understanding of dynamic control systems, the interactions between multiple networks and their individual parameters are a necessary course of study. One area of interest is the ease at which stability is achieved during gait despite the continuous CNS interactions for forward progression of the body.

Quantifying CNS contributions to balance control during movement is challenging, as dynamic stability control will overlap with the control of progression. To mitigate the challenges of interpretation, task conditions that prioritize the "goal" of the CNS in a given moment are used such as the introduction of transient perturbations. Many types of perturbations can be used to evoke flexible compensatory motor strategies that are coordinated across multiple limbs, and account for anticipatory adjustments (Nashner, 1980; Prince et al., 1994), indicating a distributed control system accounting for multiple inputs and contexts. It is understood that a very sophisticated system controls and integrates balance control processes alongside multiple concurrent modulators of CNS activity.

1.2 Locomotor rhythm control (Central pattern generators)

Locomotor rhythm control is comprised of coordinated, multi-limb motor actions that allow for progression during gait. These actions form cyclic patterns in muscle activity specific to each type of gait (e.g. running vs. walking). Execution of these "gait cycles" has been attributed to multiple spinal interneuron circuits (Brown, 1911) called central pattern generators or CPGs. The current understanding of locomotor rhythms is largely from indirect evidence in animal models.

Animal models

Experimental evidence for spinal control over locomotor rhythms has been speculated from as early as the 18th century (Clarac, 2008), but our current understanding of CPGs is derived from early experiments by Thomas Brown on the decerebrate cat. It was found that deafferentation and a complete lesion of the thoracic spinal cord do not prevent cyclic movement of the hind legs, and thus the pervasive pattern of flexion vs. extension between limbs is central in origin (Brown, 1911). The type of gait evoked in spinalized animals is not limited to walking, for example the spinalized cat can also trot and gallop (Sherrington, 1910). Similar control is seen in other species including fish that, despite having no "leg" limbs, generate an oscillating pattern of muscle activity from the spinal cord for the purpose of progression through swimming (Grillner, Perret, & Zangger 1976). Thus, locomotor CPGs can be understood as a central network capable of generating spontaneous locomotor patterns in the absence of sensory feedback.

This is not to say that locomotor rhythms are entirely a spinal task. Centripetal modulation, or sensory feedback entering the spinal cord from the periphery, is a known modulator of locomotion. Centrifugal modulations are also relevant, such as visual feedback. Both centripetal and centrifugal modulation are constantly modulating excitability of spinal cord networks and play an important role in the success of locomotor movement (Armstrong, 1988).

Centripetal modulation

Evidence for centripetal control over locomotion in animals is prominently featured through perturbations during gait. During treadmill walking in the cat, the interruption of swing phase by a metal bar causes a stereotyped motor response to recover and no disruption to the rhythm of muscle activity in future steps. Cutaneous anesthesia of the limb contacting the metal bar results in no evoked response in EMG of nearby intact muscles or changes in behavioural kinematics (Wand, Prochazka, & Sontag, 1980). Similar results are observed with other stimuli applied to the skin (Forssberg, 1979). These responses must be mediated through cutaneous mechanoreceptor inputs to CPG networks.

Both cutaneous stimulation and passive leg extension of a spinalized animal can also evoke stepping responses similar to natural stepping (Sherrington, 1910). These movements

display phase-dependence in kinematics between flexion and extension during evoked stepping. This further highlights the continuous changes in spinal excitability with phase of movement, or phase-dependent modulation of locomotor movements (Forssberg, 1979; Sherrington, 1910).

Centrifugal modulation

Descending modulation has a profound effect on elements of locomotion, despite not necessarily recruiting the pattern of muscle activity. Stimulation to the mesencephalic locomotor region in the brain stem increases walking speed in the rat (Skinner & Garcia-Rill, 1984), and with sufficient stimulation, changes in locomotor pattern such as from a walk to a trot. Similar effects can be seen with stimulation of the medioventral medulla, even after surgical removal of the mesencephalic locomotor region (Atsuta, Garcia-Rill, & Skinner, 1990). This could be interpreted as a threshold effect where, upon reaching a certain level of excitability, spinal interneuron recruitment is altered via changes in excitation and inhibition and the overall spontaneously generated activity is now subjected to a new pattern of activation and muscle recruitment.

Human studies

Characterizing CPG networks in humans has proven to be a difficult and contentious task (Illis, 1995). No direct measure of CPG activity has been found, although indirect evidence supports their existence (Bussel et al., 1988; Calancie et al., 1994; Gurfinkel et al., 1998). Case studies in spinal cord injury patients have electrically-evoked a largely ineffective but rhythmic pattern of muscle activity when measured with EMG (Bussel et al., 1988; Calancie et al., 1994). Furthermore, evidence of centripetal modulation is seen with additional stimulation of flexor reflex afferents mechanically or electrically (Bussel et al., 1988). This could be attributed to a partially preserved CPG network, and similar phenomena have been documented in healthy participants (Gurfinkel et al., 1998) as well as infants using the mechanical stimulation of a treadmill (Thelen, 1986). Effective gait-like movements in humans have not been electrically evoked in upright stance thus far, even in healthy individuals. This may be due to the demands of balance control being a critical component of gait but not intrinsically contained within the stimulated CPG networks.

1.3 Step placement

Gait is goal-directed with the objective of travelling to a location, for some distance, or for a period of time. CNS networks involved in locomotion must be capable of progression in an appropriate direction or heading and consider feedback and feedforward modulation from changes in a dynamic environment. Directing step placement requires visual information and has been associated with involvement of the cerebral cortex. Challenges to cat locomotion such as crossing over an obstacle in view (Beloozerova & Sirota, 1993a; Drew, 1988) or across a horizontal ladder (Amos, Armstrong, & Marple-Horvat, 1990; Beloozerova & Sirota, 1993a; Favorov et al., 2015) are associated with increased firing rate in the motor cortex related to motor planning and execution. Further research attributes this to a greater parietal network integration of multiple sensory inputs (Beloozerova, 2003; Drew, Kalaska, & Krouchev, 2008; Drew & Marigold, 2015; Lajoie, Andujar, Pearson, & Drew, 2010) that involves contributions of the posterior parietal cortex with or without vision. This activity in the motor cortex is well described to conduct through pyramidal neurons (Armstrong & Drew, 1984; Beloozerova & Sirota, 1993b; Drew, 1988; Favorov et al., 2015; Stout & Beloozerova, 2013), which are a major component of the corticospinal tract that would synapse to spinal networks. Brain stem contributions, specifically the rubrospinal system, are also present during precision stepping tasks and may play a role in regulating descending motor cortex activity as well as inter-limb coordination (Lavoie & Drew, 2002).

In humans, similar tasks are also used to elicit increased cortical involvement during walking for motor planning and visuomotor integration. Single pulse TMS-evoked motor responses are modulated during walking with visually-cued steps, where the pattern of modulation is phase-dependent to the gait cycle (Schubert, Curt, Colombo, Berger & Dietz, 1999). Stimulus-evoked responses without visually-cued steps demonstrates a smaller effect (Schubert, Curt, Jensen, & Dietz, 1997), indicating that inputs from the cortex are weighted more heavily for modification of gait, where the motor response indicates a transient probe for cortical involvement in walking. Continuous data such as electroencephalography (EEG) measurements during balance beam walking further support these findings (Sipp, Gwin, Makeig, & Ferris, 2013). These changes in cortical activity are also associated with an increase in spinal

excitability when approaching an obstacle (Haefeli, Vögeli, Michel, & Dietz, 2011), which follows the expected relationship of cortical influence through the corticospinal tract.

Additional insight to the control of step placement comes from dual-task gait studies. Secondary tasks like talking (Chen et al., 1996; Holtzer et al., 2011) or memorizing (Lindenberger, Marsiske, & Baltes, 2000) increase cortical activity and impair walking performance. These decreases in performance are magnified in older adults as well (Chen et al., 1996; Hollman et al., 2007). Similarly, impairments in cognitive function affect spatiotemporal measures of gait and clinical test performance further even when compared to age-matched controls (Bond & Morris, 2000; Hausdorff, Balash, & Giladi, 2003; Montero-Odasso et al., 2012; Sullivan et al., 2000; Yogev-Seligmann, Hausdorff, & Giladi, 2008; Yogev et al., 2005).

1.4 Central Nervous System Control of Balance

Animals

Balance control during gait has proven to be difficult to study because it is not localized to any specific region of the CNS. Spinalized animals with no supraspinal inputs used in locomotion studies are incapable of balancing despite intact locomotor rhythm control. Mesencephalic cats can are capable of walking but will fail goal-directed adaptations such as passing a wall or obstacle (Shik & Orlovsky, 1976). It should be noted that no study has observed spontaneous or electrically evoked locomotor activity to the level of purposeful, coordinated gait-like movements without externally stabilizing the subject. Furthermore, despite some success after locomotor training in New World monkeys, similar paradigms to induce stepping have very limited success in Old World monkeys which share more evolutionary characteristics with humans (Vilensky & O'Connor, 1997). Intact animals capable of balancing demonstrate the involvement of the cortex for multiple locomotor tasks (Beloozerova & Sirota, 1993a, 1993b; Beloozerova & Sirota, 1988; Armstrong & Drew, 1984; Lajoie et al., 2010; Drew, 1988; Drew & Marigold, 2015) that may be in part due to cortical involvement in balance control.

Humans

The control of balance in humans also appears dependent on a distributed control system involving many regions of the CNS. This emerges from evidence of balance and gait among the

elderly and specific patient populations such as the various roles of sensory information (Spear, 1993; Goh, Morris, Lee, Ring, & Tan 2017; Laurence & Michel, 2017) and neurodegenerative disease affecting numerous behaviours (Kido et al., 2010; Wolfson, 2001). There is also increasing evidence of the importance of contributions from cortical regions during the control of gait and posture in humans. The cortex has become an important region of the CNS to study in gait because of well understood functions like motor control and sensory integration. Recent research supports multiple potential roles for cortical input during walking (Hamacher, Herold, Wiegel, Hamacher, Schega, 2015; la Fougère et al., 2010), and validates previous observations from pathological conditions that affect the cortex such as stroke (Said et al., 1999).

Changes in the demand to balance control are associated with changes in activity in the cortex as measured by frequency content of EEG recordings (Bruijn, van Dieën, & Daffertshofer, 2015; Sipp et al., 2013). Mechanical challenges posing different demands to balance control such as walking uphill also reveal changes in cortical activity including gait phase-dependence in alpha (8 – 12 Hz) and beta (13 – 30 Hz) frequency bands (Bradford, Lukos, & Ferris, 2015). Carrying objects or weights is also associated with hemodynamic changes to the prefrontal cortex (Clark, Rose, Ring, & Porges, 2014) that imply changes in motor planning or coordination to stabilize the object/weight during movement. There is a phase-dependence of changes in cortical frequencies, specifically increased beta activity during loading shifts (heel strike and toe off), and lower power in midstance and midswing (Bruijn et al., 2015). Externally stabilizing participants amplified this pattern in both the sensory and motor regions of the cortex, which has been interpreted as a decrease in motor control of walking related to reduced mediolateral COM displacement during double-support phase weight shifts (Bruijn et al., 2015). Phase-dependence in the nervous system is already well established to occur in spinal networks (Capaday & Stein, 1986) and leg muscles in walking (Schubert et al., 1999, 1997), possibly meaning that these methodologies are measuring a similar phenomenon related to distributed network control of gait. Balance control in dynamic tasks can thus be understood as the contribution of multiple events integrated throughout the CNS relying in part on corticospinal pathways to link complex responses to muscular control.

1.5 Cortical control of dynamic balance

Dynamic balance control requires the control of the COM relative to the BOS. Exerting control over this relationship is accomplished by various muscles and includes both capturing the COM in the BOS, but also intentionally separating them to propel the body (Jian et al., 1993). Coordinating the neuromuscular system to achieve such stability requires integration of multiple factors outside of muscle recruitment to control the COM such as visual feedback related to the environment and motor planning (Maki & McIlroy, 2007). Walking as a dynamic balance control task poses an intriguing problem where instability is necessary for propulsion but re-stabilization may potentially never be accomplished (Jian et al. 1993; MacKinnon & Winter, 1993). This purposeful instability of gait has been previously described in multiple ways such as: a "throw-and-catch" model (Lyon & Day, 1997) where instability is internally generated for propulsion to move the leg and body forwards and then corrected at footfall, or changes in spatiotemporal-related afferent information dominate the underlying cortical activity (Knaepen, Mierau, Fernandez Tellez, Lefeber, & Meeusen, 2015). Previous literature describes multiple potential roles for cortical involvement in gait (Bancroft & Day, 2016; Duysens, De Groote, & Jonkers, 2013) but the interpretation of physiological data from the cortex during gait is often superficial with respect to the behaviour or mechanisms involved. Specifically, our interpretation of cortical data often considers a notable emerging waveform or transient event within a complex signal comprised of numerous sub-tasks such as balance control. While the cortex is likely to be intricately involved in the control of stability during dynamic tasks, there is a need for confirmation of the relationship between stability and underlying cortical activity in these tasks.

EEG and functional near-infrared spectroscopy (fNIRS) have been used to evaluate mechanical and cognitive challenges to balance during stance, treadmill, and overground walking (Wittenberg, Thompson, Nam, & Franz, 2017). The advantage of EEG is the high sampling rate and temporal resolution, in the order of milliseconds. Physiologically, the signal captured in EEG experiments is believed to be largely driven by summations of post-synaptic potentials on the large pyramidal neurons in the 5^{th} cortical layer (Buzsáki, Anastassiou, & Koch, 2012; Petsche, Pockberger, & Rappelsberger, 1984). These neurons also compose the corticospinal tract, which descends from motor and somatosensory cortices to synapse directly to alpha motor neurons in the ventral horn of the spinal cord. While the temporal precision of EEG

is excellent, spatial resolution is limited (Buzsáki et al., 2012) and the ability to resolve the contributions of a given set of EEG signals to different processes (e.g. balance control and step placement) is challenging with conventional study designs.

Recent work exploring the role of cortex during walking emphasizes the motor cortical contributions to muscle activity during gait (Artoni et al., 2017; Petersen, Willerslev, Conway, & Nielsen, 2012; Roeder, Boonstra, Smith, & Kerr, 2017). These findings suggest that the cortex is highly involved in steady-state walking. Despite the strength of previous studies in describing intra-step cortical dynamics in both temporal and frequency domains (Roeder et al., 2017), the specific role of this descending control is not yet understood. Many recent studies are exploiting advances in technology and analysis to maximize ecological validity (i.e. measure natural walking), however this approach comes with a loss of experimental control. Alternate paradigms trying to reveal the cortical contributions to walking include cycling to limit balance control (Jain, Gourab, Schindler-Ivens, & Schmit, 2013) and changes in sensory feedback such as ischaemic nerve block (Dietz, Quintern, & Berger, 1985), but the fundamental challenge is disentangling the various control mechanisms during walking.

There is evidence that cortical responses evoked during more constrained experimental conditions, (e.g. standing), may reflect activity during walking. For example, the stimulus-evoked balance response of the cortex in walking is similar to perturbation-evoked potentials (PEPs) used in stance (Dietz, Quintern, & Berger, 1984; Dietz et al., 1985a). It is speculated that balance control networks are shared between various tasks and as a result exploring cortical control in standing conditions will inform understanding in more dynamic conditions (e.g. walking). The current study will assess balance reactions in standing as a probe to advance future work to understand cortical involvement related to stability during walking.

1.6 Reactive balance control

Balance perturbations have been used extensively to understand reactive balance control. Introducing a challenge to stability evokes very rapid and accurate responses including automatic postural responses in muscles to recover the COM, and limb movements to expand the BOS and shift the COM (Maki & McIlroy, 1997; McIlroy & Maki, 1993). These reactions are incredibly flexible, accounting for mechanical characteristics of the perturbation (Ting & Macpherson, 2004; Winberg, 2018), ongoing tasks at perturbation onset (Weerdesteyn, Laing, & Robinovitch,

2012; Van Ooteghem, Lakhani, Akram, Miyasike-daSilva, & McIlroy, 2013) sensory information outside of the perturbation (Zettel, McIlroy, & Maki, 2002; Lakhani, Miyasike-daSilva, Vette, & McIlroy, 2013; Akram, Miyasike-daSilva, Van Ooteghem, & McIlroy, 2013), and even task instruction (McIlroy & Maki, 1993; McIlroy & Maki, 1999). Balance reactions can be classified into two strategies: a fixed-support strategy where the response does involve limb movement, and a change-in-support strategy where the upper or lower limbs move to restabilize the body (Maki & McIlroy, 1997). The stabilizing approach is fundamentally different, where fixed-support reactions generate joint torques to correct for displacement of the COM in contrast with change-in-support reactions that reposition the BOS to capture the COM. Both strategies share many aspects of control however such as similar response latencies despite the increased complexity required for stepping or grasping (a full comparison can be seen in Maki & McIlroy, 2007). As well, both strategies can be evoked from the same amplitude of perturbation, indicating that fixed-support and change-in-support are not simply a difference in the sensory correlates of instability (McIlroy & Maki, 1993). Muscle responses to perturbation of stability during walking have been well characterized (Nashner, 1980) and may in part represent the corticospinal control of reactive balance control. Perturbations delivered to the feet of a walking participant induces a large change in the typical pattern of EMG independent of which direction the foot/lower limb was moved (Nashner, 1980). The movements related to this EMG activity are stereotypical and share many features with perturbations delivered while standing, implying a strong relationship between underlying processes related to balance reactions (Nashner, 1980). Further research found the earliest EMG responses to have a latency of 70 ms following the perturbation and clearly preceded major cortical potentials, although an initial cortical positivity, the P1, was found before EMG responses (Dietz et al., 1985a). Along with cortical responses, the amplitude of muscle activity gradually decreased and latency remained similar over the course of an experiment (Dietz et al., 1985a).

1.7 Perturbation-evoked Cortical Activity

Quick and appropriate responses to unexpected balance perturbations are critical for many activities of daily life such as walking. These compensatory balance reactions are capable of organizing incredibly complex movements given the very speed at which they occur (Maki & McIlroy, 2007), and account for contextual differences such as amplitude or direction of perturbation. Classically, balance reactions were considered automatic and mediated by networks

originating in the spinal cord (Berger, Dietz, & Quintern, 1984), but there are many studies now revealing the contributions of the cortex to the recovery of balance following a perturbation in both humans (Bolton, 2015; Payne, Ting, & Hajcak, 2019; Varghese, McIlroy, & Barnett-Cowan, 2017) and animals (Beloozerova, Sirota, Orlovski, & Deliagina, 2005; Beloozerova, 2003).

Reactive balance control has been linked to widely distributed networks using paradigms such as floor translations and lean-and-release perturbations. EEG has been primarily used to quantify this neural activity as it captures the temporal dynamics of the cortex before, during, and after the instability while simultaneously permitting a participant's unrestrained movements to recover from the perturbation. Time-locking of the balance perturbation to the EEG signal (an approach generally referred to as event-related potential or ERP analysis) allows for the measurement of time-locked cortical activity linked to the perturbation and balance reactions. Using this technique, previous research has described PEP waveforms measured after the onset of a balance perturbation (Varghese et al., 2017). PEPs are believed to represent network-level activity underlying sensory and motor processing of balance perturbations and responds to changes in task conditions. PEPs are known to involve a reorganization of network activity such that perturbation onset induces a phase-locking of EEG signals rather than a transient post-perturbation event that could be explained through movement artifact or time-locked noise (Varghese et al., 2014). There are multiple components of this waveform related to timing and polarity (i.e. positive vs. negative time-series EEG activity).

The major potential is a negativity (N1) which is the most studied component occurring around 80-160 ms after perturbation onset. The N1 is primarily interpreted as trial-averaged peak EEG amplitude in frontocentral areas following a perturbation (Quant, Adkin, Staines, & McIlroy, 2004; Quant, Maki, & McIlroy, 2005; Maki & McIlroy, 2007) . Response latency characterized as the time to peak appears invariant when tested across task conditions and stimulus amplitudes (Mochizuki, Sibley, Cheung, Camilleri, & McIlroy, 2009). Topographic measures reveal the N1 to be a frontocentral potential occurring between 90 and 150 ms after the onset of a perturbation. There remains considerable debate regarding the role of the N1 responses and the associated generators. It was originally proposed that the N1 may be related to sensory information of conflict generated by unexpected disturbances to balance (Quant et al., 2004;

Quant et al., 2005; Maki & McIlroy, 2007). Supporting evidence comes from manipulating task conditions through increases in perturbation amplitude (Mochizuki, Boe, Marlin, & McIlroy, 2010; Staines, McIlroy, & Brooke, 2001), or changes to posture such as walking (Dietz et al., 1984) which modulate N1 peak amplitudes. Efforts to localize the N1 response to a single dipole suggest the medial frontal gyrus and supplementary motor area rather than areas associated with error or conflict detection (Marlin, Mochizuki, Staines, & McIlroy, 2014). Follow up work considering multiple generators with functional connectivity analysis indicates that many areas over the entire sensorimotor region of the cortex are involved (Varghese, 2016).

The exact role of the N1 remains debated (Adkin et al., 2008; Marlin et al., 2014; Varghese, Beyer, Williams, Miyasike-daSilva, & McIlroy, 2015; Varghese et al., 2014), though it can be understood as a reflection of evoked cortical processes related to instability. In the absence of a perturbation, challenging stances increasing mediolateral COP displacement are associated with amplified cortical potentials resembling the N1 (Varghese et al., 2015), and may be evidence of a continuous monitoring phenomenon that manifests in other tasks with stability challenges. These documented changes in the N1 presuppose that control conditions are stable where evoked responses are caused entirely by mechanical characteristics of the perturbation, but many non-perturbation factors that interact with stance may confound our interpretation of cortical responses.

Factors that Influence N1 Characteristics

Critical to the current study is an understanding of the factors that influence cortical excitability as measured by the amplitude of the N1 response. Characteristics of the N1 in dynamic balance control are determined both by characteristics of the perturbation, and state interactions related to the current context (Jacobs & Horak, 2007; Maki & McIlroy, 2007). The latency of the N1 is largely invariant across many studies, with the few changes reporting longer latencies in gait compared to stance (Dietz et al., 1984), and in subjects with a muscular pathology (Dietz, Quintern, Berger, & Schenk, 1985). As well the topographic representation remains constant with a frontocentral distribution (Varghese et al., 2014; Marlin et al., 2014; Mochizuki et al., 2009; Adkin, Quant, Maki, & McIlroy, 2006). In contrast the amplitude of the N1 response is highly modifiable. Much like other sensory-evoked potentials (such as non-perturbation-evoked N1 responses), there is clear evidence of additional influences unrelated to

sensory information generated by the perturbation. For example, perturbation predictability heavily attenuates N1 amplitude (Adkin et al., 2008), while arousal related to the potential threat of a fall amplifies the N1 (Sibley, Mochizuki, Frank, & McIlroy, 2010). These changes may be indicative of prior engagement in balance control networks that affects the excitability and amplitude of PEP waveforms. Progress in our understanding of reactive balance control may therefore be importantly determined by quantifying or controlling for additional factors present at the time of a perturbation.

Perturbation characteristics

The amplitude of perturbation is a primary determinant of the PEP amplitude (Mochizuki et al., 2010; Staines, McIlroy, & Brooke, 2001), specifically the N1 component. It should be noted that the scale of this relationship does not appear to be linear and may be indicative of physiological limitations in resources available to amplify the response. While changes in maximum displacement and velocity are associated with balance reactions, particularly the behavioural characteristics, it is most likely that initial events like acceleration, form the sensory component evoking initial responses (Mochizuki et al., 2010; Staines et al., 2001; Starr, McKeon, Use, & Burke, 1981). Modifying perturbation characteristics with respect to how they impact the body (e.g. perturbations delivered to one leg) and overall direction of perturbation do not appear to affect early cortical responses including the N1 (muscle responses are consistently direction and limb specific), although opposing perturbations delivered simultaneously to each leg increase N1 amplitude (Berger, Horstmann, & Dietz, 1990) and may indicate a summation of multiple destabilizing events at the level of the cortex.

State and context

Current state can be defined as the modification of neural network excitability due to changes in context (Jacobs & Horak, 2007) and may be achieved through both centripetal and centrifugal pathways. Modulation of the N1 related to state changes occur independently of perturbation characteristics, where the same mechanical sensory information from a balance perturbation can evoked different responses. Changes due to the environment, such as standing at a height (Sibley et al., 2010), amplify N1 responses. This was not statistically associated with electrodermal measurements of autonomic responses (i.e. anxiety) but could be argued to be related to the “consequential threat” of a fall at height vs. on the ground. Modulations to inhibit

motor neuron recruitment due to this threat have been observed at the level of the spinal cord (McIlroy et al., 2003). Another task is the blocked stepping paradigms where reactive stepping is modified due to environmental constraints or task instructions. In these paradigms the step constrained by task instructions is significantly slower demonstrating the flexibility of reactive control (Maki & McIlroy, 1997; McIlroy & Maki, 1993). Perturbation predictability is strongly associated with an attenuation of the N1 (Adkin et al., 2008; Dietz et al., 1985; Mochizuki et al., 2010). With successive predictable trials, this attenuation continues to the point that the N1 cannot be distinguished from background EEG activity. The continuous adaptation of cortical responses is evidence of distinct changes in cortical networks independent of the motor response or perturbation.

Another factor relevant to movement or dynamic tasks is postural state, which specifically refers to the CNS activity modulated by a change in posture, or as a consequence of the movements that change posture (Nashner, 1980). Postural state includes both posture and the task demands of motor activity associated with posture, for example, narrow foot stances amplify the N1 compared to normal width, but no changes are associated with wide stances (Dimitrov, Gavrilenko, & Gatev, 1996). This may be due to modification of mechanoreceptor discharge at the feet and lower limbs due to the overall posture but may also reflect postural state changes in balance control networks due to instability occurring prior to the perturbation.

Overall, many task conditions modulate the N1 amplitude. Factors that increase N1 amplitude involve either the magnitude or potential consequence of a perturbation. This can be explained through the perspective of N1 processes as being related to detection and consequential threat (Adkin et al. 2008, 2006; Mochizuki et al., 2010), where the response is considered largely context-dependent. Continuous tasks where the N1 serves as a discrete probe have been done previously with cognitive dual-tasking (Little & Woollacott, 2014; Omana Moreno, 2017; Quant et al., 2004) where the N1 decreases, potentially as a result of limited cortical resources due to engagement with the secondary task. Similar experiments with movement as the continuous task have shown similar results, though this is not well understood.

1.8 Perturbation Evoked Reactions

Response mechanisms

Ischaemic nerve block of the afferent nerve in the leg did not affect either EMG or EEG (Dietz et al., 1985), making these responses unlikely to occur from cutaneous receptors. Furthermore, responses were preserved in a patient with vestibular dysfunction, and were also occurring prior to movement of the head (Dietz et al., 1985), although a potential role for vestibular input is debated (Staines et al., 2001). Regardless, the N1 is preserved in seated perturbation tasks that do not involve head movement or vestibular afferents. These findings imply that the generation of muscle responses in response to an imposed instability are driven by changes in non-cutaneous afferents, and potentially independent of vestibular afferent discharge, such as effector-based afferents like the golgi tendon organs and muscle spindles. The N1 is modified by factors that do not affect the EMG response, and thus these two physiological markers likely represent different processes evoked simultaneously. It is possible that cortical responses represent some combination of afferent processing, detection of instability, initial motor responses, and motor planning related to current body posture. EMG likely represents some subset of activity in the greater PEP waveform, locally-driven responses, (e.g. stretch reflex), and contributions from additional regions such as the brain stem that descends through corticospinal tracts to motor neurons for the purpose of movements to regain stability.

Changes in evoked cortical activity are independent of changes in compensatory muscle activity to regain balance. Increases in perturbation predictability profoundly decrease N1 amplitudes with little effect on EMG at the tibialis anterior (TA) (Adkin et al., 2006; Jacobs et al., 2008). Perturbations while sitting elicited faster EMG responses in the anterior deltoids than standing responses in the TA, yet N1 characteristics were statistically similar in both tasks (Mochizuki et al., 2009). Furthermore, the N1 has no lateralized components across the cortex regardless of lower or upper limb reactive responses (Mochizuki et al., 2009) unlike the so-called "motor homunculus" organization at the primary motor cortex. Thus, the role of the N1 appears to be a generalized response to incoming sensory information associated with threats to stability. Despite the latency being similar to the onset of EMG in a reactive response, muscle activation patterns may be determined by processes not related to the N1.

Compensatory muscle activity in the calf may be initially driven by cortical responses such as the early components of the PEP (e.g. the P1). P1 potentials are known to occur before EMG responses and speculated to be sensory processing of instability (Dietz et al., 1985a; Starr et al., 1981). In this view, discrepancies between EMG and later EEG responses around the timing of the N1 could be interpreted as the combination of: 1) continuing afferent inputs to the cortex from the perturbation, and 2) efferent motor responses for stability. This is supported by functional connectivity measures of the N1, which describe a distributed and heavily interconnected pattern of activity loosely centered on the Cz location (Varghese, 2016). Areas with higher connectivity, such as the primary motor and somatosensory cortices, would contribute sensory and motor information respectively to the N1 at the same time. Accounting or controlling for ongoing motor activity and incoming sensory information could provide insight into state characteristics influencing network-level dynamics of reactive balance control revealed through the N1 potential.

1.9 Postural state as a modulator of cortical balance responses

Our current understanding of balance reactions is driven by experimental task demands affecting the CNS and/or behavior at the time of perturbation, however, the influence of pre-perturbation state is largely unknown (Mochizuki, Boe, Marlin, & McIlroy, 2017). An example of this is walking where postural state changes under the pressures of a continuous requirement for stability and monitoring of posture during phases of movement. The influence of this pre-perturbation instability has not been quantified during balance reactions despite supporting evidence in both stance (Dimitrov et al., 1996) and walking (Bruijn et al., 2015; Sipp et al., 2013). Faster walking elicits greater cortical activity than a control speed during a cognitive task (Wagner, Makeig, Gola, Neuper, & Müller-Putz, 2016), which may reflect contributions from both balance control and cognitive networks that are known to interact for reactive balance responses (Omana Moreno, 2017). Additionally, previous research paradigms on elements of gait such as cadence (Bulea et al., 2015) or sensory feedback (Wagner, Solis-Escalante, Scherer, Neuper, & Müller-Putz, 2014) may have unintended consequences to balance control. For example, increased cadence affects the control of balance such that the foot is in contact with the ground for a shorter period of time, and the CNS must control for a rapid lateral weight shift between stance legs in this period. The consequence of postural state in gait is difficult to

quantify because of the multiple potential sources of cortical involvement. As a result, the functional implications of previous research investigating changes in the N1 during gait (Dietz et al., 1984; Quintern, Berger, & Dietz, 1985) are not well understood and the role of the cortex remains ambiguous.

Multiple studies establish a link between state characteristics and the perturbation-evoked N1 potential. Dual-task studies have revealed a decline in N1 response that suggests a link to attentional resource allocation (Little & Woollacott, 2014; Maki & McIlroy, 2007; Mochizuki et al., 2017) and follows similar results from behavioural measures (Brown, Shumway-Cook, & Woollacott, 1999; Norrie et al., 2002). Increased arousal related to fear of falling demonstrates an increased N1 response independent of autonomic influence that may relate to emotional processing (Sibley et al., 2010). Perturbation predictability strongly attenuates N1 amplitudes and, along with changes in background cortical activity, is associated with anticipatory modulation of balance networks (Adkin et al., 2008). Many state characteristics are associated with changes in context surrounding a perturbation, however, postural state as a modifier of CNS excitability has also been linked to changes in evoked responses (Nashner, 1976; Nashner, 1980) with supporting evidence specific to the cortex (Bruijn et al., 2015; Dimitrov et al., 1996; Sipp et al., 2013; Slobounov et al., 2008; Varghese et al., 2015)

Changes in postural state manifest in both amplification and attenuation of the N1. Balance challenges such as narrow stance show an increase in N1 amplitude when compared to normal or wide stance attributed to an increase in sensory information related to instability (Dimitrov et al., 1996). These findings were discussed as resulting from somatosensory changes but may involve top-down modulation related to changes in stability or maintaining the stance as a task. On the other hand, N1 responses to seated perturbations are statistically similar to standing (Mochizuki et al., 2009) leading to the understanding that reactive responses are generalizable across some postures and not others. This generalizability could be explained by summations of cortical activity lacking a specific response to every possible manipulation of posture. Such specificity would likely manifest in single cell recordings and different measures sensitive to somatosensory changes accompanying posture such as the Hoffman reflex. Postural state as a change in the context of how perturbations interact with the body remains a candidate to increase cortical excitability given evidence of COM position influencing cortical involvement

through unprompted postural sway (Varghese et al. 2015) and voluntary COM displacement (Slobounov et al. 2008).

As mentioned before, there is some debate over the meaning of perturbation-evoked N1 responses. Many experimental paradigms evoke N1 responses, thus the N1 was considered to arise purely from sensory events and scale to characteristics of the perturbation itself. Evidence directly refutes this idea through changes in excitability of cortical networks and electrodermal responses independent of perturbation parameters (Sibley et al., 2010). State characteristics are an important modifier of the N1, but many factors that may be interpreted as state changes have not been studied directly or at all. Towards an understanding of the cortical involvement in balance control, disentangling the parameters that create or influence N1 responses is an important goal.

Postural state as a modifier of cortical excitability explains previous findings and expands our understanding of the control of dynamic tasks. When viewed as a challenge to stability, cortical activity during gait appears to reflect BOS changes between single and double support phases (Bruijn et al., 2015; Knaepen et al. 2015). As a result, previous literature manipulating posture in stance may be expressing these same stability changes and their associated neural consequences. These consequences are observed but undefined, and capturing the mechanisms underlying postural state modulation through gait-like tasks may reveal the meaning of cortical contributions to gait. PEP responses as an expression of cortical excitability driven by context and task therefore provide an opportunity to probe cortical activity specific to the influence of postural state.

Experimental paradigms using movement as a task may be influenced by the effects of changing posture on the CNS control of balance. It is possible that the results from many interventions, even tasks as simple as quiet standing, are not independent of the ongoing balance control (e.g. postural sway). The effects of postural sway can be seen in task demands eliciting instability preceding a perturbation with increased amplitudes around the timing of the N1 (Dietz, et al., 1984; Dimitrov et al., 1996). A possible mechanism could be amplified responses of balance control networks due to ongoing balance control demands. This postural state-related amplification would be independent of the sensory input from the perturbation itself, and thus

controlling posture and thereby sensory information at the time of a perturbation may reveal an association between state and the N1 potential.

One such means of controlling posture and the related sensory consequence is through voluntary leaning and repositioning of the COM to the lateral limits of stability. Cortical activity related to maximal voluntary dynamic leaning has demonstrated a clear increase in activity compared to an upright stance control (Slobounov et al. 2008) and may represent different postural states arising from the COM approaching limits of stability. Similar findings have been seen in walking where cortical activity during the single-support phase (COM is normally at or exceeding the lateral limits of stability) is modulated by task demands (Bruijn et al., 2015; Seeber, Scherer, Wagner, Solis-Escalante, & Müller-Putz, 2014; Sipp et al. 2013; Wagner et al. 2012), though again this model has not been applied to the N1.

Another factor to consider with postures that shift the COM such as leaning, is the interaction of the posture with the perturbation. Changes in postural state through leaning paradigms have the advantage of potentially changing the events leading to reactive responses, specifically, perturbations can constitute many different levels of relative amplitude depending on posture at the onset of the perturbation. While the literature continues to investigate modulators of the N1, a leaning paradigm enables the disentangling of factors previously studied in isolation of each other: perturbation parameters as a somatosensory input to the CNS, postural state caused by leaning, and interactions of these two factors expressed as relative perturbation amplitude.

1.10 Objectives and Hypotheses

The purpose of this thesis is to advance the understanding of cortical involvement during dynamic balance control to eventually inform understanding of the control of balance during walking. The cortex is known to be involved in the control of balance, and cortical activity is modulated by numerous task conditions. During walking these intertwined factors limit one's ability to determine the specific nature of cortical control of balance. Our understanding of cortical activity during gait is unclear, and an important first step is to understand the nature of postural state in balance control. It is proposed that the ability to assess the nature of cortical contributions to dynamic balance control during walking will require initial understanding of the factors that mediate cortical activity during changes in posture. To advance the understanding of

cortical contributions to dynamic stability control, this thesis aims to characterize changes in N1 potentials due to postural state at the onset of a perturbation. In the current study we use changes in static lean, altering the position of the COM with respect to the BOS, to introduce variation in the relative perturbation amplitude or potential threat depending on the direction of perturbation. In this study direction of perturbation is unknown and we set out to determine if possible changes in postural state, associated with static lean towards the stability limits, would result in increased cortical excitability (N1 response). Evidence of postural state changes, linked to pre-perturbation lean, would provide evidence that the CNS monitors potential challenges to stability to enhance control for unexpected movement of instability. We hypothesize that pre-perturbation changes in posture, specifically positioning the COM at the lateral limits of the BOS will be associated with amplified N1 potentials compared to equal weight stance for the same perturbation characteristics. We also hypothesize that, during a voluntary lean, perturbations shifting the COM past the limits of stability will increase N1 amplitudes compared to perturbing the COM towards the midline of the body – further within the limits of stability (Figure 1).

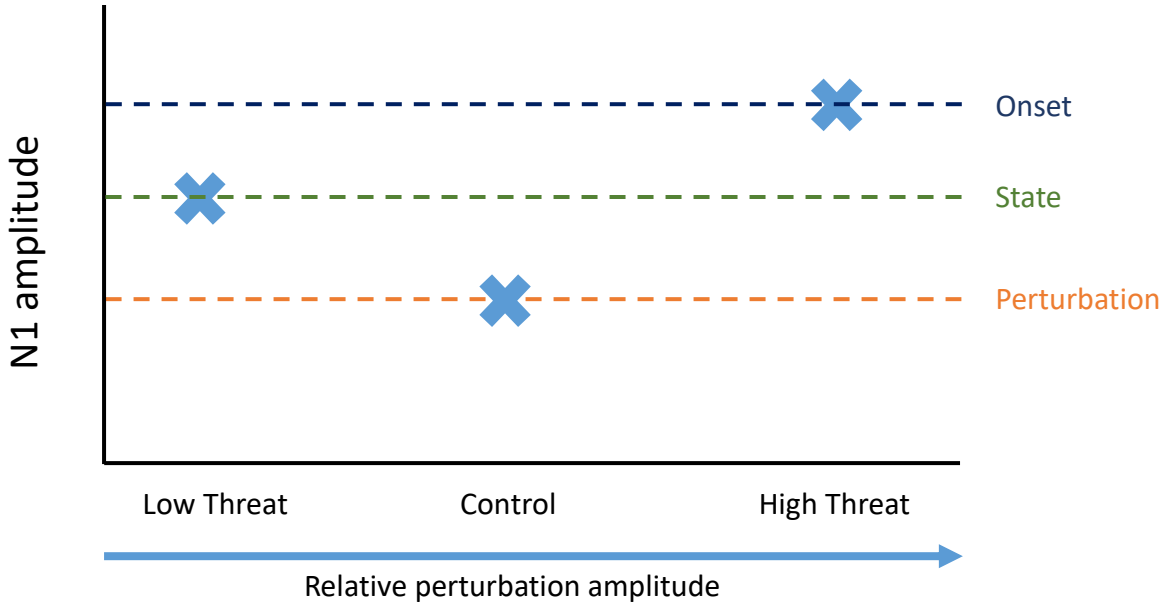

Figure 1. Hypothesized results of N1 amplitude across conditions with similar absolute perturbation amplitudes. The orange dashed line indicates the excitability of the N1 during the control or equal weight stance in this study, the green dashed line indicates the increased excitability hypothesized from leaning, and the dark blue dashed line indicates further increased excitability hypothesized from increased relative perturbation amplitude.

Potential Significance

Towards the long-term goal of understanding cortical control of dynamic stability (eg. during walking), this work intends to describe cortical responses to a change in postural state during static task conditions which helps to mitigate some the confounding factors present in dynamic tasks. Specifically, the aim of this thesis is to study the effects of current posture and motor activity generated to achieve pre-perturbation posture on cortical excitability in balance control. By isolating responses from phasic movement such as gait, current postural state can be studied while avoiding motor control related to progression, leaving only state and sensory processing as possible modulators. Previous literature supports postural states involving a change in stability as a modulator of cortical activity, though this relationship has not been directly measured relative to an imposed instability (Dimitrov et al., 1996; Varghese et al., 2015). This research may explain associations between balance control and cortical activity seen in older adults, where atrophy and declines in dynamic stability are well established to occur (Brody 1955; Salat et al., 2004; Woollacott, Shumway-Cook, & Nashner, 1986).

Chapter 2: Methods

2.0 Participants

Twelve young, healthy students (23.1 ± 4.3 years old, 6 male, 6 female) from the University of Waterloo were recruited to participate in this study. All participants self-reported as right foot dominant and engaged in some form of moderate or intense exercise weekly. Participants were excluded if they had current or previous musculoskeletal or neurological disorders. The study was approved by the University of Waterloo Research Ethics Board.

2.1 Task

A custom-built servomotor translating platform (Sidac Automated Systems Inc., Toronto, ON) was used to perturb balance in participants. Input perturbation parameters were 0.5 m/s^2 acceleration and 0.25 m/s velocity occurring over 0.1 m displacement. All perturbations were single translations to the right or left (randomized and counterbalanced) to perturb mediolateral control of stability. Actual measured perturbation characteristics were identical between left and right translations with onset peak values of approximately 1 m/s^2 acceleration and 0.25 m/s velocity occurring over 0.1 m displacement, and a deceleration peak of 2 m/s^2 approximately 500 ms after peak acceleration. This intensity was a level that would evoke fixed support but not compensatory stepping reactions. This level was initially determined during pilot data collection and confirmed for each subject.

A fully randomized design was used across 6 task conditions: 3 tasks (different stance positions) and 2 perturbation directions for a total of 6 task conditions. The stance conditions in included: 1) Control (equal weight stance); 2) Lean left (≥80% weight on left limb) and 3) Lean right (≥80% weight on right limb). As noted direction of perturbations were either left or right for a total of 6 possible task conditions. A total of 6 blocks of 15 trials were collected (90 trials total) fully randomized across stance and direction within blocks.

The combination of perturbation direction and stance position led to the 3 different task categories (each with 30 trials collected):

1) Control (equal weight and left or right perturbation),

2) High threat (lean left and perturbation to right, lean right and perturbation to left),

3) Low threat (lean left and perturbation to left, lean right perturbation to right).

In High Threat and Low Threat conditions, participants executed a voluntary lean of at least 80% bodyweight (determined by forceplate data) to the left or right while both feet remained in full contact with the floor. 15 trials of each combination of lean and perturbation direction were measured and collapsed into the Low Threat (COM perturbed towards midline) or High Threat (COM perturbed outside of BOS limits) conditions. Control trials consisted of 15 perturbations to the left and right each. Participants stood barefoot with the same initial foot position; 17 cm between the heels and external rotation of 14 degrees measured on the long axis of the foot (McIlroy & Maki, 1997).

Trials were up to 12 seconds in duration where the timing of platform movement occurred randomly between 2-7 seconds after the start of a trial. Two minutes of rest were given between each block, with more rest granted upon request. For all trials, participants were instructed to stand comfortably with arms relaxed at their side and eyes fixated on a target 3 meters in front of them. Participants were made aware of the balance perturbations and were instructed to respond any way they feel is appropriate to maintain balance.

2.2 Measures

Electroencephalography

Thirty-two channel EEG (Compumedics Neuroscan, Charlotte, NC) was used to record cortical activity with a sampling rate of 1000 Hz. EEG cap placement followed the international 10-20 system with dual-mastoid referencing and channel impedance was reduced to below 5 kOhms. Data was stored offline for analysis.

Using EEGLAB (Delorme and Makeig, 2004) each block of data was band-pass filtered (linear phase FIR filter, 66000 order) at 0.05 – 50 Hz defined as the edge of the passband, epoched around the delivery of the perturbation (-0.5 to 1 seconds), then visually inspected for artifacts. Independent component analysis was used on epoched data to remove noise components related to eye blinks or movement, EMG and ECG contamination, and uncharacteristic high voltage shifts that may represent movement-related artifact. After further inspection, remaining components were projected back to the scalp, baseline corrected, and averaged across trials by condition. From visual inspection, one channel (Oz) was removed from

subject 1, and two channels (T8 and T7) were removed from subject 9. One trial was removed due to pre-perturbation movement in subject 10 but was noted and recollected in the same session. The N1 is identified from trial-averaged data as the first major negativity after the onset of perturbation from the Cz channel for each condition. N1 latencies were computed at time to peak from perturbation onset.

Electromyography

Biopolar EMG (TMSi, Oldenzaal, The Netherlands) was used to record muscle activity and monitor for anticipation prior to perturbation with a sampling rate of 1024 Hz. The skin was cleaned to reduce impedance below 20 kOhms, and electrodes were placed in accordance with SENIAM guidelines on the peroneus longus and tibialis anterior bilaterally. Data was stored offline for analysis.

Using MATLAB, data was downsampled to 1000 Hz for time series comparison with other data. Prior to all analysis, data were band-pass filtered (-3 dB response at passband edges of 25 - 450 Hz; linear phase dual-pass FIR filter, 1000 order), epoched around the onset of the perturbation (-2 to +1 seconds). After full wave rectification, EMG responses were averaged for each combination of direction and condition for a total of 6 means per muscle (3 conditions by 2 directions) and 24 means per subject before calculating response latency and amplitude.

Onset of muscle activity is defined here as an increase in voltage +5 SD greater than the mean of the last 100 ms before the perturbation (Mochizuki, Sibley, Esposito, Camilleri, & McIlroy, 2008). Visual inspection of the onset latency was done to ensure accuracy and manual adjustment was necessary in 23 trials. Integrated EMG (iEMG) was used to characterize EMG amplitudes following the perturbation using cumulative trapezoidal integration. EMG amplitude was calculated as the total iEMG value for 200 ms after the onset of muscle activity (Sibley et al. 2010). For statistical analysis, iEMG results were collapsed into the loaded and unloaded leg relative to direction of instability (e.g. if the COM is perturbed to the left via a rightward translation, the left leg is loaded), this was applied to both the leaning and Control tasks. For representative figures, EMG was smoothed using a 100 Hz low pass dual-pass Butterworth filter.

Average EMG was very low during Low Threat conditions and onset latency was not consistently identified using the criteria mentioned and thus amplitude and latency is not

reported for Low Threat in the present study. Similar issues were present in the Control condition of 5 subjects (10 means missing out of 96 Control means; 9 peroneus longus, 1 tibialis anterior). Another 2 means were removed from 1 subject, both from peroneus longus in Control condition, for having extreme latencies (656 and 369 ms after perturbation onset). Remaining values were used to compute statistics.

CNS Arousal

Galvanic skin response (GSR) was collected as a means of quantifying differences in arousal related to the threat posed by each condition. After skin preparation, Ag-AgCl electrodes were filled with a conductive paste and placed on the middle phalange of the first/index and third/ring finger. Data were sampled at 1000 Hz and stored offline for analysis. Due to technical difficulties GSR was collected for 5 out of 12 participants, and 1 of the 5 collected did not have evoked responses.

Using MATLAB, GSR data was low pass filtered (-3 dB response at 5 Hz; linear phase dual-pass FIR filter, 2000 order) and epoched around the delivery of the perturbation (-2 to + 5 seconds). Response latency, duration, and amplitude were extracted from epoched data.

2.3 Statistical Analysis

Alpha level was set at $p = 0.05$ for significance. One-way repeated measures ANOVAs were used to compare N1 amplitude and N1 latency across the 3 main tasks. A two-way repeated measures ANOVA was used to compare between leg (loaded vs. unloaded), and task (Low Threat vs. Control vs. High Threat) for iEMG amplitude. A three-way repeated measures ANOVA was used to compare between muscle (TA vs. PL), leg, and task for EMG onset latency. A post hoc Tukey test was used to investigate significant effects. Due to the repeated measures design and missing data in the Control condition for 6 subjects, the remaining 6 subjects were used in comparisons across Control and High Threat.

Two planned contrasts of N1 amplitude were performed for the mean of High Threat and Low Threat compared to control, and High Threat vs. Low threat. A post hoc Tukey test was used to compare N1 latencies across tasks. All statistical calculations were performed using R (R Core Team 2018) using the car package (Fox & Weisberg 2019), nlme package (Pinheiro et al. 2019), and the emmeans package (Lenth 2019).

Chapter 3: Results

3.0 Perturbation characteristics

The platform control or model acceleration profile was maintained constant throughout the study. The control signal was a period of increased and constant acceleration (500 ms in duration) and then a shorter (approximately 300 ms in duration), higher amplitude deceleration phase. This is represented by the dashed line displayed in Figure 2. The actual acceleration, measured from an accelerometer mounted on the platform, is provided in the dark line overlaying the idealized control waveform. As can be noted the actual acceleration of the platform deviated considerably from the control waveform. Figure 3 provides the initial acceleration profile. This initial platform motion is what evokes the balance reactions and cortical responses (latencies occurring approximately 150 to 200 ms after onset of acceleration). As a result, the initial peak acceleration (labelled X on Figure 3) is used to express the amplitude of the perturbation as it relates to the current responses. It should be noted that, in spite of the complexity of the acceleration waveform, the initial aspects of the acceleration were highly reproducable trial to trial in this and previous studies (Winberg 2018).

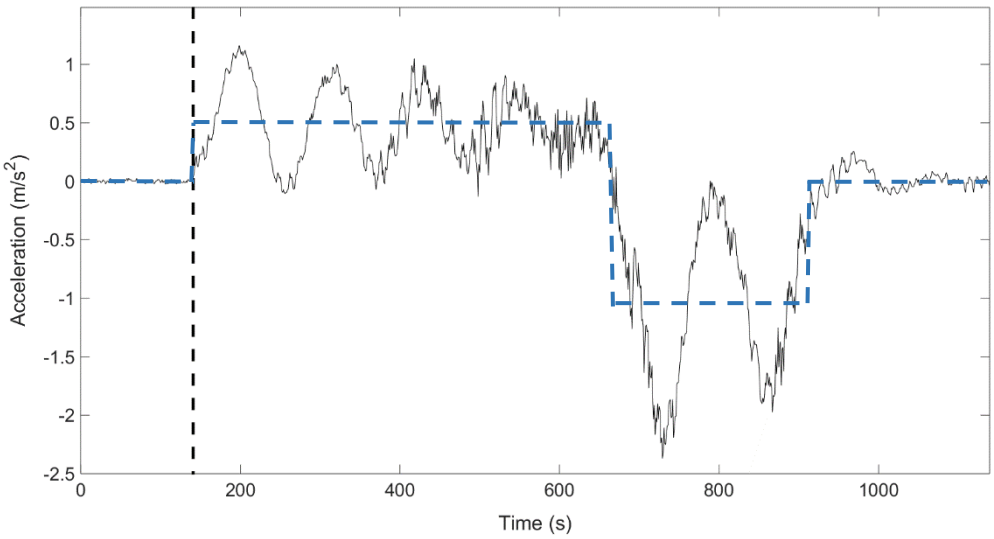

Figure 2. Actual platform acceleration plotted over time (dark line) from a single trial. Perturbation onset is denoted as the black dashed line. The blue dashed line represents the control signal for the platform motion.

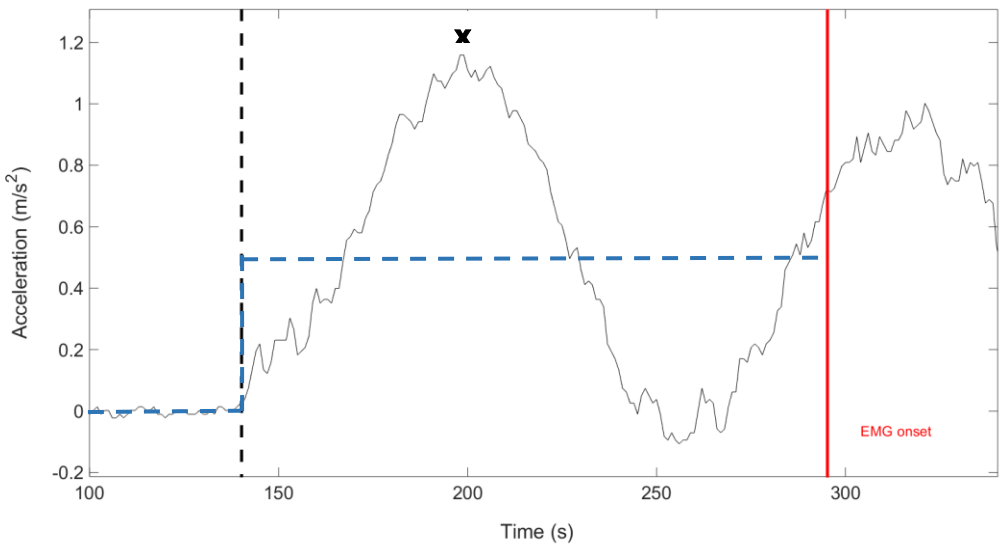

Figure 3. Initial actual platform acceleration (cropped from data shown in Figure 2) to display the initial acceleration events. The blue dashed line represents the associated control signal.

This applied perturbation evoked expected electromyographic and electroencephalographic reactions to the perturbation. Figure 4 provides a sample of average data from 1 subject in the High Threat task condition.

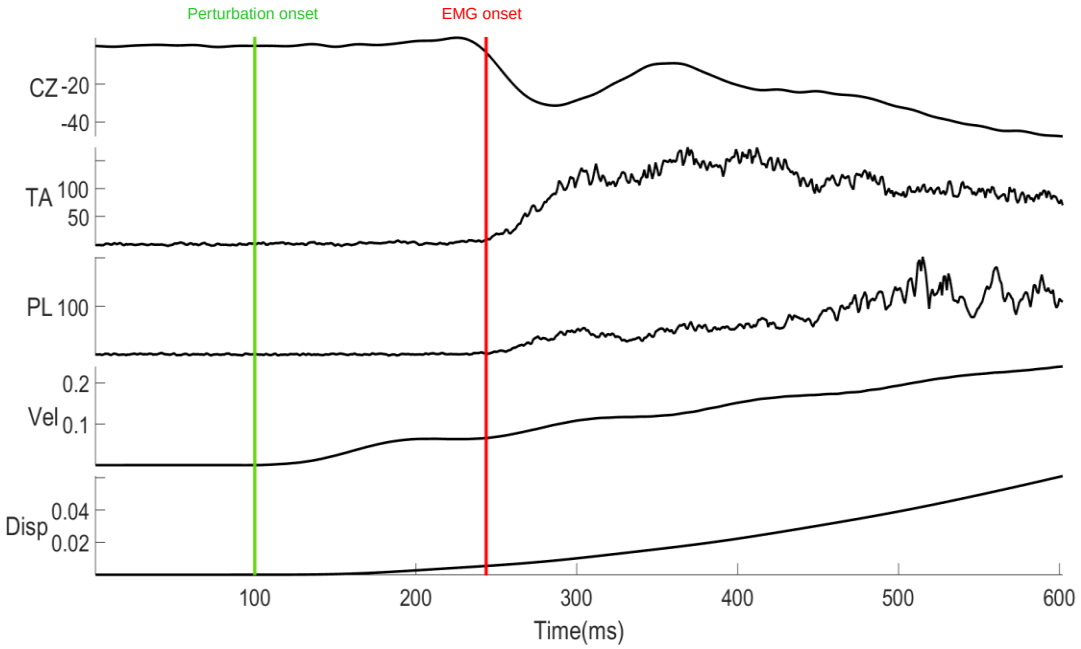

Figure 4. Average responses to perturbation for the High Threat task from a single subject (30 trials). Platform motion is displayed as both velocity (Vel – m/s) and displacement (Disp – m). Average muscle activity from tibialis anterior (TA) and peroneus longus (PL) of the right (mV). Event-related cortical potentials are displayed for the Cz electrode site (μV). Average onset of perturbation, determined from platform acceleration, is denoted by the green line. Onset of EMG from the tibialis anterior is shown by the red line.

3.1 N1 responses

Amplitude

There was a significant main effect of condition on N1 amplitudes ($F(2,22) = 27.159$, $p<0.001$) (Figure 5). Planned contrasts of N1 amplitude indicate that leaning overall is not different from Control ($F(1,11) = 0.014$, $p=0.907$), and High Threat is significantly larger than Low Threat ($t(11) = -6.9396$, $p<0.001$). Post hoc testing indicates that Low Threat is smaller than Control ($t(11) = 3.588$, $p = 0.0045$) and High Threat is larger than Control ($t(11) = 3.781$, $p=0.0028$) (Figure 6). Relative to the Control condition, the grand averaged N1 amplitude was attenuated to 73% in the Low Threat condition and amplified to 128% in the High Threat condition.

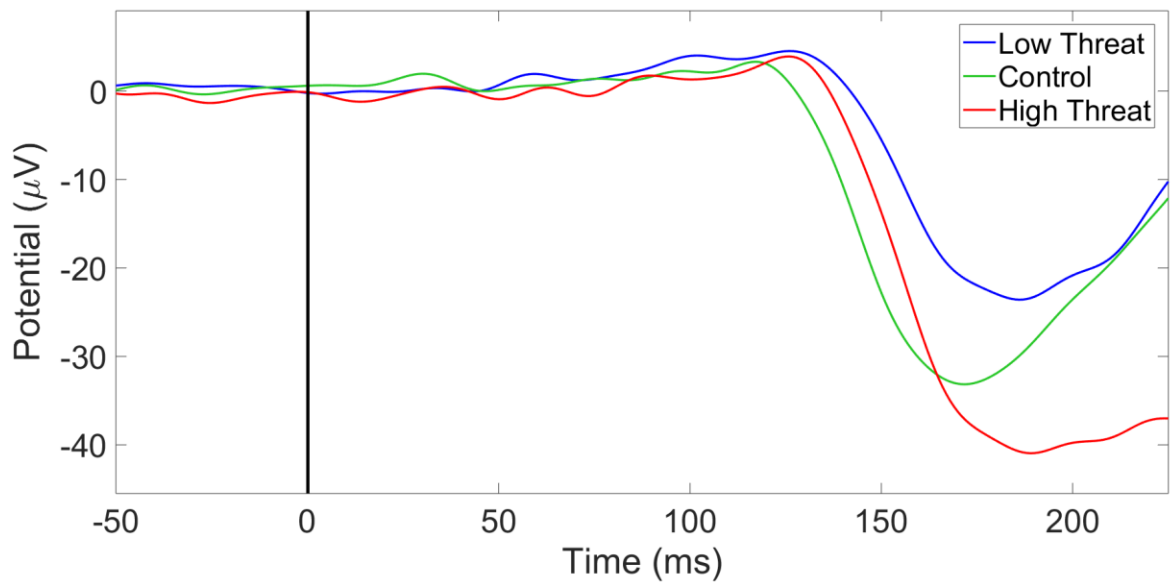

Figure 5. Grand average N1 waveform for all subjects plotted by task condition. 0 ms vertical black line indicates onset of perturbation.

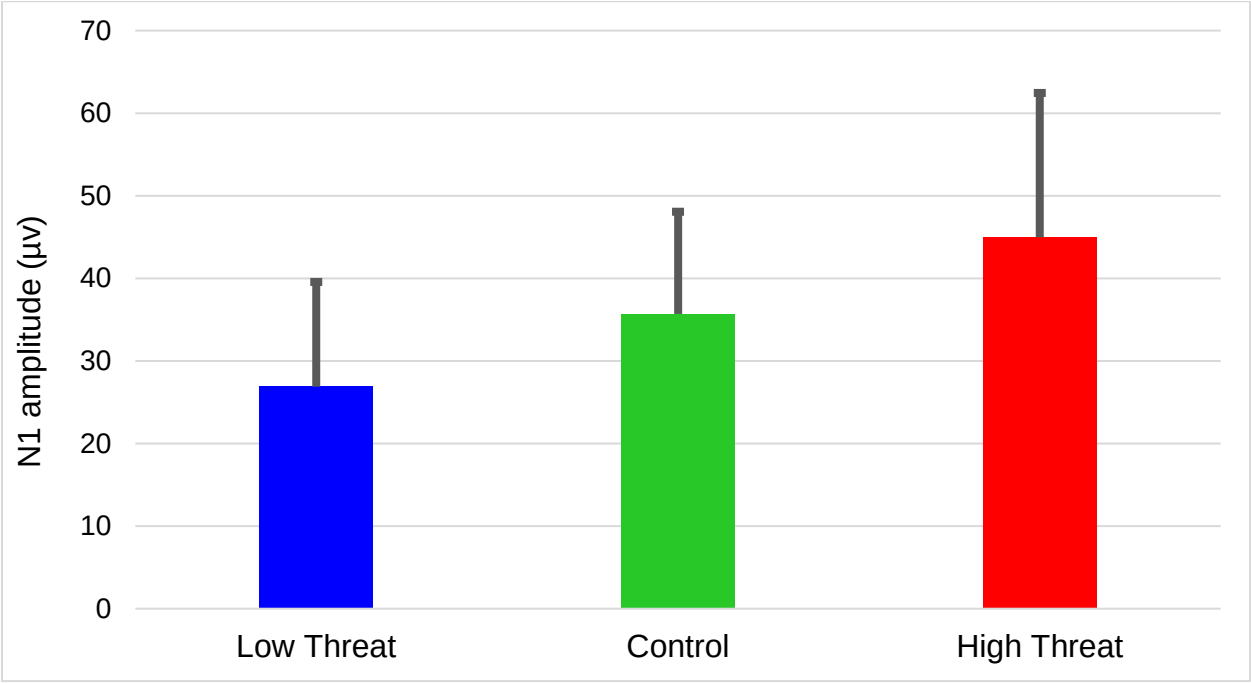

Figure 6. Grand average N1 amplitude from all subjects plotted by condition. Error bars represent standard deviation.

In addition to the grand averages displayed in Figure 5 the average N1 amplitude measured within each subject and for High and Low threat task conditions are displayed in Figure 7. The data presented is displayed as the average N1 amplitude for Low or High Threat conditions compared to the Control N1 amplitude (difference score). Positive values indicate a larger N1 compared to Control and negative differences indicate a smaller average N1 response to Control. Noteworthy from this data is that in 10 of 12 subjects the N1 amplitude for the High Threat was greater than the Control trials. In two of the subjects (5 and 6) they had very similar Control and High Threat N1 amplitudes with the High Threat being slightly smaller. For the Low Threat condition, all 12 subjects had smaller N1 responses for Low Threat as compared to Control.

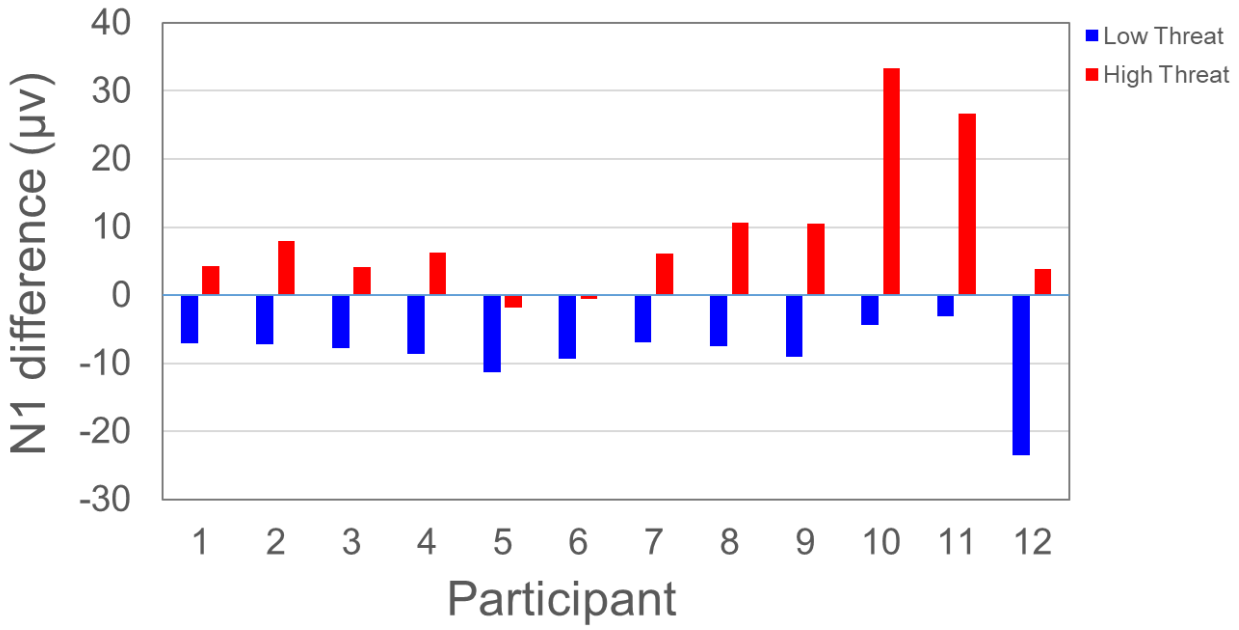

Figure 7. Average difference scores of N1 amplitude from High and Low Threat task conditions minus Control displayed for each subject individually. Positive values indicate a less negative (smaller) N1, negative values indicate a more negative (larger) N1.

Latency

Averaged N1 latencies measured from perturbation onset were significantly different by condition ($F(2,22) = 21.21$, $p<0.001$). Overall, the control task condition was characterized by a shorter latency (170.7 ± 14.4 ms) as compared to the Low Threat (182.8 ± 13.8 ms) ($t(11) =$

5.445, p < 0.001) and High Threat (183.7 ± 12.7 ms) (t(11) = 5.818, p < 0.001). There was no significant difference between Low and High threat (t(11) = 0.373, p = 0.9265). Note that such task related differences in N1 latency is also evident when comparing grand averages displayed in Figure 5.

Topographic Distribution

The topographic distribution of cortical activity compared over time and across tasks is displayed in Figure 8. Noteworthy from this figure is the frontocentral activity associated with the N1 response was consistent across the different task conditions. The differences in amplitude have been noted previously, this specific data reinforces the idea that the underlying topographic representation was similar across tasks with the highest mean activity occurring at the Cz and Fcz electrode sites. This is represented approximately at the 180 ms time window shown on Figure 8.

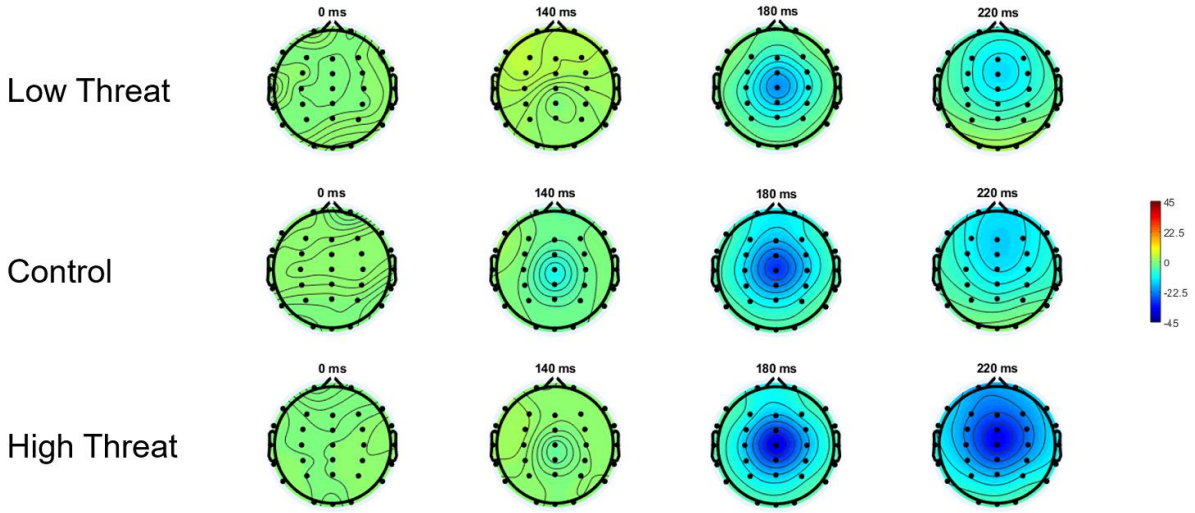

Figure 8. Grand average topographic distribution of perturbation evoked cortical activity from all subjects plotted for each task condition and for specific time points relative to onset of perturbation. 0 ms = Onset of perturbation, 140 ms = approximate onset of N1, 180 ms = approximate peak of N1 response.

3.2 EMG responses

As noted, data is not presented for Low Threat condition due to the difficulty in quantifying the average EMG due to the small amplitude. As a result, comparisons are restricted

to High Threat and Control trials. iEMG comparisons from the two-way repeated measures ANOVA reveal a significant main effect of Task ($F(1,5) = 196$, $p<0.001$), and Leg ($F(1,5) = 114.8$, $p<0.001$) indicating that 1) High Threat responses are larger than Control, and 2) In the High Threat condition, loaded leg responses are larger than unloaded leg.

A three-way repeated measures ANOVA for EMG latency demonstrates a main effect of Task ($F(1,5) = 8.16$, $p = 0.036$) and Leg ($F(1,5) = 14.48$, $p = 0.283$). No effect of Muscle was observed for response latency ($F(1,5) = 1.4$, $p>0.05$). Results indicate similar onset latencies for all combinations of task and leg (grand average 146.01 ± 9.67 ms) except for the unloaded leg in the Control task (both muscles, grand average 164.92 ± 14.96 ms) as shown in in Figure 9.

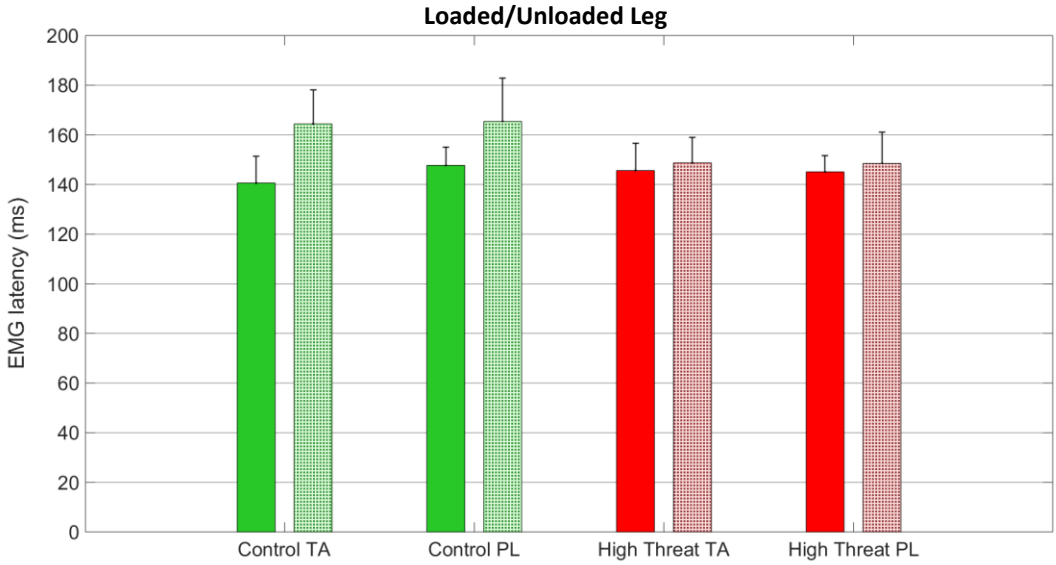

Figure 9. Grand average EMG onset latencies from all subjects plotted by task conditions and leg. Solid bars are loaded leg, faded bars are unloaded leg, direction relative to COM perturbation. TA = tibialis anterior; PL = peroneus longus. Error bars represent standard deviation.

iEMG amplitude was significantly larger overall for High Threat vs. Control, and amplitude was also higher in the loaded leg compared to the unloaded leg for High Threat only (Figure 10).

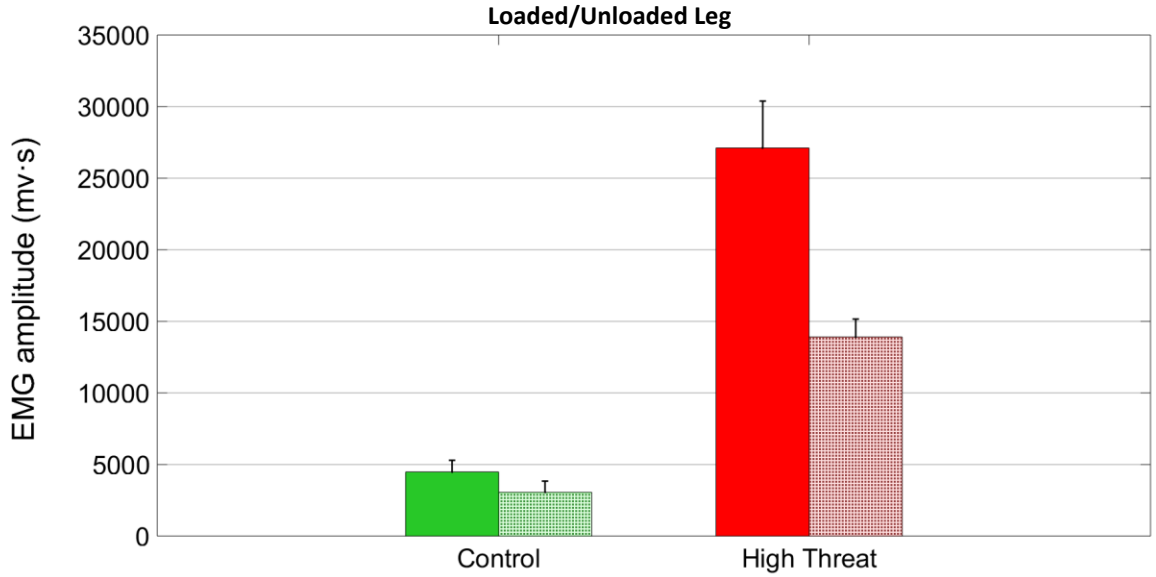

Figure 10. Grand average tibialis anterior iEMG from all subjects plotted by task condition and leg. Solid bars are loaded leg, faded bars are unloaded leg, direction relative to COM perturbation. Error bars represent standard deviation.

Peroneus Longus

Similar to tibialis anterior, iEMG amplitude was significantly larger for High Threat vs. Control, and amplitude was higher in the loaded leg compared to the unloaded leg for High Threat only (Figure 11).

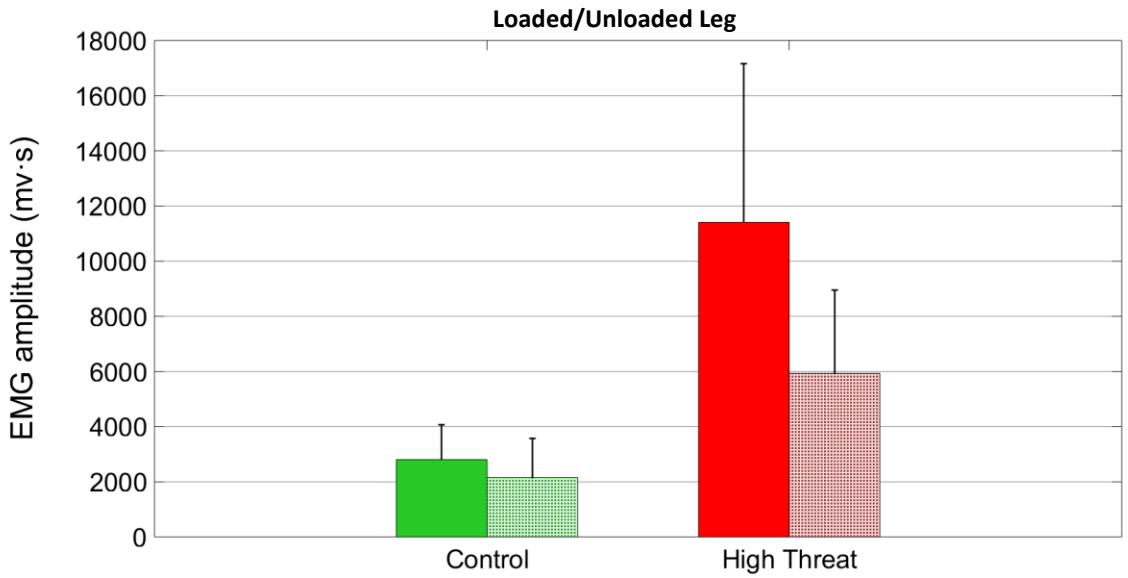

Figure 11. Grand average peroneus longus iEMG from all subjects plotted by task condition and leg. Solid bars are loaded leg, faded bars are unloaded leg, direction relative to COM perturbation. Error bars represent standard deviation.

3.3 GSR responses

GSR data was complicated by the perturbation waveform in this study, making interpretation of the signal challenging. The polyphasic platform acceleration appears to manifest as a continuous stimulus at the level of skin conductance (Figure 12). Previous work looking at electrodermal responses in reactive balance control report the response onset latency as approximately 2 seconds after perturbation onset (Sibley et al., 2010). In the current study GSR response onsets were similar (approximately 1800 ms compared to the previous study reporting a grand mean of 2045 ± 129 ms). Of the 5 participants with GSR measured, 4 participants had no clear observable responses and/or significant artifacts related to the perturbation and because of this the data was not analyzed. A difference can be visually observed in response amplitude such

that High Threat is larger than Control and Low Threat with no difference between Control and Low Threat, but no testing was performed.

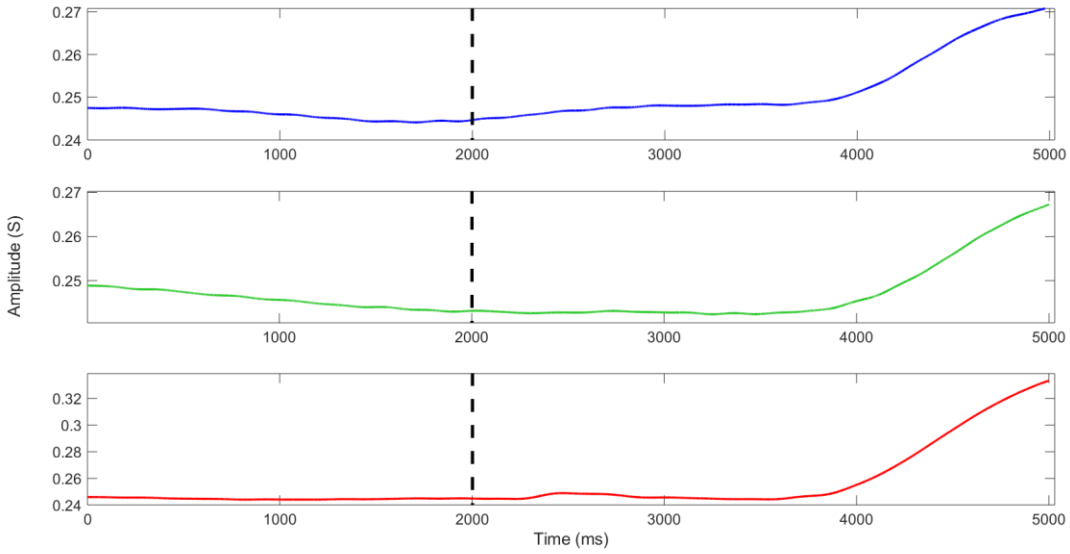

Figure 12. Example GSR responses across conditions. Data generated from task averages (30 trials per line) from one subject and ordered top to bottom as: Low Threat, Control, High Threat. The black dashed line represents onset of perturbation.

Chapter 4: Discussion

4.0 Discussion

The current study set out to determine whether changes in pre-perturbation postural lean evokes changes in relative perturbation amplitude depending on the direction of perturbation, resulting in differential cortical excitability (N1 response) to the applied perturbation. It was anticipated that, even though the direction of perturbation was unpredictable, individuals would adopt a pre-perturbation postural set that would be differentially weight the potential threat of perturbation based on the COM position relative the BOS. It was proposed that evidence of direction specific differences in N1 response amplitude would be reflective of such a setting of postural state based on potential threat to stability. The current study did reveal differences in N1 response amplitude comparing between different pre-perturbation stance positions. Overall there was a significant difference between N1 responses when comparing the relative amplitude of

threat. It was noteworthy, however that there was no significant difference comparing between pre-perturbation lean and equal-weighted stance independent of relative amplitude.

4.1 Latency of responses

The latency of initial EEG and EMG responses, while consistent across participants, was unique in this study as a direct result of the perturbation waveform. Typically the N1 response is 80-150 ms (Varghese et al., 2017) while the ankle EMG response is between 70-100 ms (Diener, Horak, & Nashner, 1988). The onset of EMG and N1 responses in this study was not similar at about 155 ms for EMG and 175 ms for EEG which is much later than many previous studies. One factor that contributes to these differences is the time between onset and peak acceleration of 60 ms in this study. The discrepancy of this data to previous work highlights the need for an improved understanding of how the CNS detects balance perturbations and characteristics of the transformation between mechanical inputs to tissue and subsequent physiological responses.

Differences in latency between EEG and EMG responses have been documented before and is proposed to be a result of differential sensory processing for each response (Payne, Hajcak, & Ting, 2019). The statistically shorter latency of tibialis anterior activity in High Threat compared to Control is the opposite of the effect seen in N1 response latencies, which may arise from such processing differences. Longer latency cortical responses could be a result of increased conduction distance and time to involve the cortex as opposed to balance reactions typically evoked at the level of the brain stem. It is possible that both leaning tasks have slower N1 latencies due to changes in postural state affecting conduction time through changes in the number of synapses/neurons involved.

Another explanation is that differences in latency between EMG and EEG is how timing is determined. Unlike EMG latency, the onset of N1 timing is not a measure of the start of change in cortical activity but rather the peak activity. In this regard they are not equivalent representation on onset. In fact, the latency of peak amplitude in N1 response can be influenced by the amplitude of the response, assuming similar initial slope of activity, and as a result the large amplitude of the High Threat condition has an expected increase in peak latency as a product of a higher amplitude and not as a reflection of the timing of processing events.

4.2 Modulation of N1 amplitude

The perturbation-evoked N1 is believed to be generated by similar processes to muscular balance reactions through sensory information, in particular the group I and II afferents (Dietz et al., 1984, 1985). More recent investigations into the relationship of initial cortical and muscle responses confirm this relationship although with different scaling to perturbation amplitude (Payne et al., 2019b). Previous attenuation of the N1 with posture changes, namely during gait, likely does not involve the same influence on CNS networks observed here. Lower N1 amplitudes during gait are associated with group II afferents and gating of group I afferents, similarly a general attenuation effect can be seen during movement on spinal networks that would mediate these afferents before reaching the cortex (Capaday & Stein 1986). It is possible that due to the single perturbation magnitude used, multiple N1 responses are related to expectation of the perturbation being different between Leaning and Control. Rather than the CNS preparing for the worst possible outcome (High Threat) and setting the CNS state to reflect that, modulation of the N1 is potentially a result of the sensory experience combined with an internal comparison of experience with the Control perturbations. A confound to this interpretation is habituation to the perturbation where the initial few trials may contain larger reactions due to novelty. Single trial analysis would be a logical next step to quantify changes over time and link them to well documented trial to trial changes in arousal such as GSR, EMG and COP reactions (Sibley, Mochizuki, Lakhani, & McIlroy, 2014; Maki & McIlroy, 2007; Quant et al., 2004; McIlroy & Maki, 1999; Nashner, 1976; Nashner, 1980; Winter, 1995; Smith, Jacobs, & Horak, 2012; Payne et al., 2019b; Quintern et al., 1985). Single trial analyses are challenging in the EEG domain due to the presence of random noise, from either biological or non-biological sources, and a lack of a ground-truth signal to ideally quantify such noise. Efforts have been made to describe trial-to-trial changes in the N1 (Mierau, Hülsdünker, & Strüder 2015; Payne et al., 2019b) suggesting that peak potentials demonstrate purposeful adaptation independent of this noise.

One major contributor to the increases in N1 amplitude observed is likely related to somatosensory processing of instability. In a floor translation paradigm, the initial sensory event involves a shearing action from the movement of the platform to mechanoreceptors on the sole of the foot. Changes in somatosensory information that modulate cortical responses would be driven by interactions of the participants posture sensed through skin, joint, and muscle mechanoreceptors with the initial mechanical characteristics of the perturbation. Perturbation-

evoked instability sensed through cutaneous receptors of the foot are relevant for balance control (Kavounoudias and Roll 1998) and in this thesis are similar across stances, however, muscle and joint mechanoreceptor activity sensing the leaning posture may alter the excitability of ascending pathways to the brain. Further work is necessary to disentangle the relative contributions of different modulating mechanisms to cortical balance reactions.

Inherent subject differences in N1 amplitude have not been studied, but it is possible there are relevant phylogenetic or ontogenetic differences in information processing (Tan 2018). Anecdotally, differences in behavioural response were observed such that taller participants made smaller compensatory movements overall, which has been studied directly with respect to the N1 (Payne et al., 2019b) and is likely one of many individual characteristics contributing to reactive responses.

4.3 Differences in relative perturbation amplitude

Pre-perturbation postural state

In previous work investigating changes in cortical activity during leaning, modulation was associated with motor control in maximal voluntary swaying which has some similarities to the current study (Slobounov et al. 2008). When cortical activity is time-locked to the peak of voluntary sway in any direction, there is a clear modulation of activity both at the peak and mediolateral directions evoked the largest change in cortical activity. This change could correspond to the interaction of the COM and BOS, specifically that approaching the limits of stability engages cortical networks related to balance control and this is reflected in data time-locked to position. A similar explanation applies to changes in pre-perturbation stability linked to BOS changes that amplify N1 responses (Dimitrov et al., 1996), but results were not attributed to stability by the authors. Grand average responses revealed a similar difference between wide stance (potentially low threat) and narrow stance (potentially high threat) conditions, but no difference between wide stance and control (Dimitrov et al., 1996). These results do not directly contradict each other as the characteristics of the perturbation differed. Dimitrov et al. (1996) used a sudden ankle dorsiflexion via platform tilt (similar to antero-posterior perturbations) vs. the mediolateral floor translations used in this thesis. Furthermore, while one perturbation was used to generate multiple unique responses in the previous study, the role of postural state was not disentangled due to multiple foot configurations (footwear not specified). In the present

study, one standardized foot position was used across all participants and multiple cortical waveforms were still evoked implying that some component of the modulation seen in narrow stance may be related to instability and not posture itself.

Cortical responses to threat

A comparative study of pre-perturbation postural state and relative amplitude to evoke responses is novel to this study, where proposed modulation of the N1 from COM and BOS interactions during leaning was not supported. It was proposed that this sensory information would result in a constant threatened state of instability, however this was not reflected in the Low Threat condition. The effect of posture is still observed in response latencies implying that postural state was changed but amplitude characteristics were resolved at perturbation onset. The changes observed do support other findings surrounding amplitude of perturbation. Changes in "consequential threat", such as instability at a height, amplify the N1 similar to this study (Sibley et al. 2010), however, all perturbations were in a predictable direction towards the edge of a raised platform and therefore would be classified as "High Threat". The lack of Low Threat or perturbing away from the edge of a raised platform makes it difficult to interpret if pre-perturbation arousal is linked to amplified N1 responses or whether the consequence of a perturbation off of a platform is driving changes in the N1. Based on this data, it is proposed that cortical networks involved in reactive balance control are primarily a result of events occurring at perturbation onset and do not clearly reflect changes in pre-perturbation state. Postural state changes such as the absolute position of the COM do not appear to change pre-perturbation activity or evoke activity interpreted as a preparatory change in N1 networks, rather the perturbation organizes a temporally urgent response related to information present at perturbation onset. This re-organization of cortical activity indirectly supports a partial phase-resetting mechanism to explain the generation of cortical balance reactions that is revealed through frequency and connectivity changes (Varghese, 2016; Varghese et al., 2014).

Perturbation amplitude scaling to the N1 has already been observed (Staines et al., 2001; Mochizuki et al., 2010; Payne et al., 2019b), which is replicated in this study as an interaction of COM and BOS rather than differences in kinematic parameters. While parameters are different in this study, kinematic profiles were similar across multiple trials and initial events did not show large deviations from an ideal waveform (Winberg, 2018). Changes in N1 amplitude did not

reflect state changes, but it cannot be ignored that the largest responses still occurred with a change in postural set. Furthermore, leaning evoked a slightly slower response than equal weight stance, possibly highlighting a role for unpredictable direction of perturbation to affect N1 latencies not observed in previous studies where changing direction of perturbation typically has no meaningful consequence.

The topographic map of the N1 was similar across tasks indicating that changes in posture and relative amplitude or threat did not affect spatial representations of the N1 (Figure 8). There are some differences in the spatial distribution of cortical activity after the N1 in the High Threat condition. Given that the distribution is similar and stepping responses were evoked in every participant in this condition, it may be inferred that post-N1 activity reflects cortical involvement to plan and execute stepping. Given the wide distribution of N1 networks, activities such as motor planning are likely to engage similar networks.

4.4 Between-Subject Differences

While previous work manipulating posture (Dimitrov et al., 1996) did not comment on individual means contributing to group observations, the present study found no consistent relationship of control to either Low Threat or High Threat N1 amplitudes for every participant (Figure 7). Between-subject differences in baseline evoked excitability did not scale with relative amplitude. Characteristics of an individual that contribute to the excitability of cortical-evoked responses are lightly studied and generally unreported in balance control and should be addressed in future work. It should be noted that postural state as a modulator of evoked responses is not limited to relative amplitude and N1 responses may not demonstrate a relationship to significant changes in posture, such as the differences between seated and standing perturbations that report similar N1 amplitudes (Mochizuki et al., 2009). Many factors are different between these postures as the delivery of the perturbation affects different areas of the body initially, such as the back in a chair vs. the feet when standing and considering that perturbation parameters for each task were not reported we cannot confidently relate to evoked potentials measured in that study. To describe potential differences across multiple studies, a thorough effort to parameterize kinematic and kinetic variables relating perturbation parameters and their consequence to the body for the purpose of comparisons across paradigms and responses would be necessary.

Personal characteristics of subjects such as height appear to contribute to N1 responses (Payne et al., 2019b) and were not measured in this study. For a thorough description of the sensory events that generate reactive responses, accounting for how each individual is being perturbed mechanically is recommended and allows for a more thorough discussion of state modulation.

4.5 Limitations

One explanation of these findings is that the threat posed by this paradigm is insufficient to create the expected state change in N1 amplitude. Compared to the threat used in previous studies such as standing at a height, this paradigm was unique in that COM position was directly manipulated rather than the consequence of the perturbation. In healthy young adults, it may be that these static changes in posture are not threatening enough to the CNS, and sensory information from loading the body at the limits of stability does not induce a change in state. The example GSR data (figure 12) suggests that no notable change in baseline arousal was observed between tasks, however, the limited data in both GSR and EMG responses makes it difficult to infer the role of state modulation, which control centers are affected (e.g. muscle recruitment vs. cortical activity), and the scaling of relative perturbation amplitude across these control centers.

The acceleration characteristics of the perturbation used in this study are different from previous studies (Figure 2). It is assumed here that reactive responses are primarily determined by the onset characteristics of acceleration (Figure 3), which strongly resembles some previous studies. One concern of the data comes from the additional sensory information from oscillations through the rest of the perturbation. Events during one perturbation can influence reactive balance control in future trials, such as an expectation or prediction of future perturbation characteristics (Lakhani et al., 2013). Should the state of the CNS be informed by sensation of the oscillations in platform acceleration, it could be expected that some trial-to-trial variability of response characteristics includes accounting and habituating to these oscillations.

Individual events contributing to changes in stability may confound these results, namely ongoing movement associated with naturally occurring postural sway. While changing absolute COM position through voluntary leaning was not directly associated with changes in cortical responses in this work, the direction and speed of typical postural sway may have a similar effect to the Low Threat and High Threat task used here. For example, sway to the right side of the

body could be greatly exaggerated by a floor translation perturbing the body further to the right. A goal of this work was to eliminate or account for the influence of dynamic events that might confound our interpretation of postural state affecting cortical excitability, and the data does indicate that absolute position related to threat posed by a perturbation is relevant to the N1 potential. In many previous studies of the N1 potential some movement occurs in the form of postural sway, which normally does not reflect a threat to stability but may involve movement of the COM prior to and at the time of the perturbation. This confound is not always a concern, such as in lean-and-release paradigms where posture is fixed, but future research should still address pre-perturbation events such as postural sway as a potential modulator of N1 responses.

A challenging aspect of this study revolved around identifying the initial reactive muscle activity in the Low Threat condition. The goal of measuring muscle activity in this study was to confirm the relative threat of each condition, and to capture automatic postural responses. While peroneus longus is related to lateral stability of the ankle via eversion, the task of leaning will increase activity during the baseline period. Combined with a Low Threat perturbation, the difference between evoked responses and an active baseline period is difficult to disentangle, hence exclusion of Low Threat trials from EMG analysis. In the future, a more appropriate muscle to describe lateral reactive balance control would be muscles acting on the hip, specifically the gluteal muscles. The muscles measured may also be contributing to significantly different functions, where tibialis anterior prominently contributes to stepping while peroneus longus is generally associated with lateral ankle stability. While amplitude scaling is similar across muscles, the magnitude of tibialis anterior may be exaggerated by stepping responses rather than postural corrections occurring in the High Threat condition. As well, peroneus longus activity may simply be a reflection of co-contraction to stabilize the ankle. The purpose of muscle activity and how behaviour was affected in this paradigm is unclear without additional data such as COP/COM changes related to muscle activity.

Typically, EMG amplitudes are normalized to interpret changes in voltage relative to maximal voluntary contraction. In this study, the effects of relative perturbation amplitude were clearly reflected in changes of motor unit activity measured at the skin and so changes between conditions are considered valid. For comparison to previous work EMG normalization is an appropriate and a useful tool to strongly describe the evoked magnitude of task differences.

Another approach that could be used is normalization by task, essentially percentage voltage change between each perturbation amplitude, which would likely reduce variably although not necessarily improving the understanding of the evoked muscle potentials measured.

Chapter 5: Conclusion

5.0 Conclusions and future directions

Pre-perturbation changes in posture affecting the relationship of the COM to the BOS do not appear to modulate N1 responses. Evoked activity is clearly modulated by relative perturbation amplitude arising from posture at the onset of instability. These results demonstrate that cortical involvement in balance control may be primarily dependent on sensory feedback mechanisms rather than state changes in network activity. In the absence of events like postural sway (present in the control condition) or voluntary COM movement (present in dynamic tasks like walking), absolute COM position is likely not a continuous modulator of N1 amplitudes or cortical excitability during balance reactions.

The findings from this data imply that the cortical control of dynamic tasks is in part dependent on the demands for stability at the onset of instability within that task. This has important consequences for the design of tasks in future studies that may unintentionally introduce instability. Relevant to the aims of this thesis, walking may be a task where changes in postural state are required to maintain mediolateral stability during progression. There is a need for constant monitoring of posture and precise control to ensure the COM travels efficiently and without errors. Towards the future study of walking, an important follow up is the introduction of dynamic events and non-static COM control. Study designs manipulating an ongoing task have revealed aspects of cortical involvement between balance control and cognitive processing (Omana Moreno, 2017; Little & Woollacott, 2014; Quant et al., 2004), and in a similar vein intentional movement of the body/COM alongside a balance perturbation may further reveal cortical contributions towards the control of dynamic tasks.

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