The Role of the Vestibular System in the Control of Locomotion

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January, 2023

A thesis submitted to McGill University in partial fulfillment of the requirements of the degree of masters of science.

OUTLINE

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ABSTRACT

Background: Fundamental questions in the field of motor control concern the understanding of how human movements are produced and controlled, and determining what systems in the brain are involved in this control. In our research project, we will investigate the role of the vestibular (VS) system in the control of lower limb movements at different phases of gait. We will compare the traditional view of direct programming of motor output by the brain to an alternate view based on the physical principle that the brain controls movements by changing the referent configuration of the body. According to this view, discrepancies between the actual body configuration and referent body configuration lead to muscle activation that enables the actual body configuration to move towards the referent body configuration and hence produce movement from one location to another. Also, the actual and referent leg postures can match each other at specific locomotor phases and referent (R) postures are shifted forwards in space to produce locomotion. Phases at which both actual and R postures match are marked by minimized EMG activity in multiple muscles, which are called EMG minima. Our goal was to determine the effects stimulation of the vestibular system using galvanic vestibular stimulation (GVS) has on the phase of locomotion and the rate of change in EMG minima when walking. **Methods**: Healthy subjects walked form a starting point to a designated position, about 6m apart. The participants were required to begin walking with their left leg, with GVS stimulation applied from the 5th to the 10th step. Eight optotrak markers were placed on eight bony landmarks, and 10 EMG electrodes were placed on calf muscles of both legs, as well as 2 accelerometers in order to observe leg movements. There were three conditions involving different head positions, one with head facing forward, and the other two with the head either facing left or right to produce a slight deviation with GVS stimulation. Each of these conditions were tested with eyes open or closed. Each condition had 10 trials. **Outcomes:** We did not observe any statistical significant effects of GVS on both the phase of locomotion and the rate of change of EMG minima. Also, head position did not have an effect on our outcome variables, as there was no difference between the different head position and their effect on both phase of locomotion and rate of change of EMG minima. This was true when the participants had either eyes opened or closed. **Implications:** Implication of the study is that vestibular stimulation can be found to possibly have an influence on how locomotion is controlled by helping in resetting the threshold of activation of motoneurons that helps in setting the spatial frame of reference in which muscles are primed for action.

ABSTRAIT

Contexte : Les questions fondamentales dans le domaine du contrôle moteur concernent la compréhension de la façon dont les mouvements humains sont produits et contrôlés, et la détermination des systèmes dans le cerveau sont impliqués dans ce contrôle. Dans notre projet de recherche, nous étudierons le rôle du système vestibulaire (VS) dans le contrôle des mouvements des membres inférieurs à différentes phases de la démarche. Nous comparerons la vue traditionnelle de la programmation directe de la sortie motrice par le cerveau à une autre vue basée sur le principe physique que le cerveau contrôle les mouvements en changeant la configuration de référence du corps. Selon cette vue, les divergences entre la configuration du corps réelle et la configuration du corps référent conduisent à une activation musculaire qui permet à la configuration du corps réelle de se déplacer vers la configuration du corps référent et donc de produire un mouvement d'un endroit à l'autre. De plus, les postures de jambe réelles et de jambe référente peuvent correspondre les unes aux autres à des phases de locomotion spécifiques et les postures référentes (R) sont décalées vers l'avant dans l'espace pour produire de la locomotion. Les phases auxquelles les postures réelles et R correspondent sont marquées par une activité EMG réduite dans plusieurs muscles, qui sont appelés minima EMG. Notre objectif était de déterminer les effets de la stimulation du système vestibulaire utilisant la stimulation vestibulaire galvanique (GVS) a sur la phase de locomotion et le taux de changement des minima EMG lors de la marche. **Méthodes :** Les sujets en bonne santé qui marchent forment un point de départ vers une position désignée, à environ 6m de distance. Les participants devaient commencer à marcher avec leur jambe gauche, avec une stimulation GVS appliquée de la 5e à la 10e étape. Huit marqueurs optotraks ont été placés sur huit repères osseux, et 10 électrodes EMG ont été placées sur les muscles du mollet des deux jambes, ainsi que 2 accéléromètres afin d'observer les mouvements des jambes. Il y avait trois conditions impliquant différentes positions de tête, l'une avec la tête orientée vers l'avant, et les deux autres avec la tête orientée vers la gauche ou vers la droite pour produire une légère déviation avec la stimulation GVS. Chacune de ces conditions a été testée avec les yeux ouverts ou fermés. Chaque condition a fait l'objet de 10 essais· **Résultats** : Nous n'avons observé aucun effet statistique significatif du GVS sur la phase de locomotion et le taux de changement des minima EMG. De plus, la position de la tête n'a pas eu d'effet sur nos variables de résultat, car il n'y avait aucune différence entre la position de la tête et leur effet sur la phase de locomotion et le taux de changement des minimums EMG. C'était vrai lorsque les participants

avaient les yeux ouverts ou fermés**. Implications** : L'étude implique que la stimulation vestibulaire peut avoir une influence sur la façon dont la locomotion est contrôlée en aidant à réinitialiser le seuil d'activation des motoneurones qui aide à établir le cadre spatial de référence dans lequel les muscles sont prêt pour l'action.

ACKNOWLEDGEMENT

I would like to thank my supervisor, Mindy Levin, for the guidance and support she offered me during the course of my research. I would also like to thank Anatol Feldman, who guided me and provided me with enough knowledge to understand the theory behind the referent body configuration hypothesis.

I would like to thank my laboratory member, Marie-Reine El-Hajj for her contribution in helping produce some figures and also in the entry of data used in the analysis.

Finally, I would like to thank Ali Filali, the senior biostatistician of the Centre for Interdisciplinary Research in Rehabilitation of Greater Montreal (CRIR), for his contribution in the analysis of the data used in understanding the results of our research.

List of Abbreviations

Abbreviation	Full Meaning
ADC	Analog-to-Digital Converters
BPPV	Benign Paroxysmal Positional Vertigo
BNC	Bayonet Neill-Concelman
BoS	Base of Support
CED	Cambridge Electronic Design
CN	Cranial Nerve
CNS	Central Nervous System
COP	Center of Pressure
CPG	Central Pattern Generator
EMG	Electromyography
EVS	Electrical Vestibular Stimulation
fMRI	Functional Magnetic Resonance Imaging
GVS	Galvanic Vestibular Stimulation
NDI	Northern Digital Inc.
nGVS	Noisy Galvanic Vestibular Stimulation
ODAU	Optotrak Data Acquisition Unit
RBC	Referent Body Configuration
RC	Referent Configuration
SCC	Semicircular Canal
TMS	Transcranial Magnetic Stimulation
VBI	Vertebrobasilar Insufficiency
VCR	Vestibulocolic Reflex
VOR	Vestibulo-ocular Reflex
VSR	Vestibulospinal Reflex
XcOM	Extrapolated Center of Mass

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CHAPTER 1

1.0 ANATOMY & PHYSIOLOGY OF THE VESTIBULAR SYSTEM

Have you ever wondered how you are able to effortlessly perceive the spatial position of your head and body, as well as engage information about self-motion (kinesthesia)? What about our ability to stabilize gaze, head, and posture? One very important system, the vestibular system, located in the inner ear plays a very important role in this. In this chapter, I will describe what the vestibular system is composed of, and the different processes that allows it to carry out its different functions.

The human vestibular system can be divided into three parts: the **peripheral sensory apparatus, central processor, and motor output** (Hain & Helminski, 2007). The peripheral sensory apparatus of the vestibular system consists of motion sensors that send information to integrative centers of the brainstem, cerebellum, and somatosensory cortices in the central nervous system about head angular velocity and linear acceleration (Hain & Helminski, 2007). The central nervous system receives and processes this information to estimate head and body orientation (Hain & Helminski, 2007), the central processor also consists of vestibular nuclei that directly innervate various muscles such as the extraocular, cervical, and postural muscles, which are essential for locomotor stability (Hain & Helminski, 2007). These muscles form the third part of the vestibular system and they are essential to the stabilization of gaze, head orientation and posture during movement. At the level of the spinal cord, three important reflexes are regulated: the *vestibulo-ocular reflex* (VOR), *vestibulorcollic reflex (VCR),* and *vestibulospinal reflexes* (VSRs). The VOR helps with generating eye movements that enable clear vision while the head is in motion. The VCR controls the head musculature to maintain head stability. The VSRs, help to generate compensatory body movements to synchronize head and postural movement, thereby preventing falling (Hain & Helminski, 2007).

Figure 1.1 schematically shows projections of different parts of the vestibular system to other levels of the nervous system.

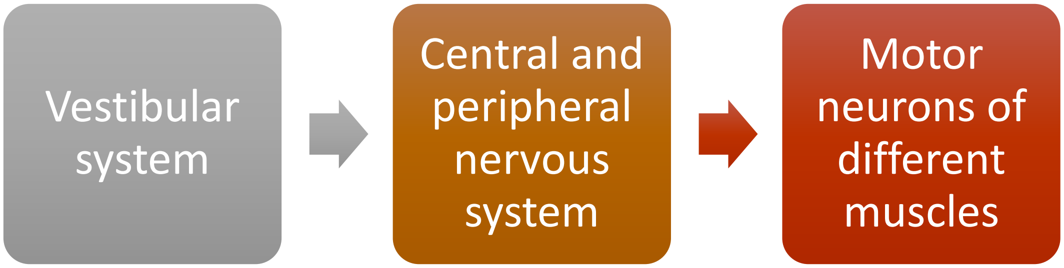

Fig 1.1 Block illustration of vestibular system organization (Hain & Helminski, 2007).

1.1 The Peripheral Sensory Apparatus

The peripheral vestibular system is the sensory portion of the vestibular system and consists of the vestibular labyrinth, as well as the hair cells, which are the motion sensors of the vestibular system. The peripheral vestibular system lies within the inner ear and is located posterior to the cochlea (Purves et al., 2004).

1.1.1 Vestibular Labyrinth

The vestibular labyrinth is the main peripheral component of the vestibular system. It is the site from which vestibular signals originate. The labyrinth is located deep within the temporal bone and lies posterior to the cochlea (Purves et al., 2004). The vestibular labyrinth is derived from the otic placode of the embryo, and it uses hair cells as its sensory organs, transducing physical motion, specifically head movement, and linear acceleration due to gravity into neural impulses (Purves et al., 2004). The vestibular labyrinth is made up of two different types of fluids with different Na^+: K^+ ratios. The endolymph, which is in the membranous labyrinth, is the innermost fluid of the vestibular labyrinth and it Na^+ poor and K^+ rich. On the other hand, the perilymph, which is the fluid that lies between the membranous labyrinth and the wall of the bony labyrinth, is similar in composition to the cerebrospinal fluid and has a higher Na^+: K^+ ratio (Purves et al., 2004). Within the vestibular labyrinth are two otolith organs and three semicircular canals (see Fig 1.2), which make up the five sensory structures of the labyrinth. The two otoliths are the **utricle** and **saccule**. The otoliths and semicircular canals have different functions. The semicircular canals comprise of the anterior, posterior, and horizontal canals, which provide information about rotation of the head, whereas the two otolith organs sense linear acceleration, as well as the orientation of the head relative to gravity (Kandel et al., 2013). At the base of each semicircular canal is a ball-like swelling called the **ampulla**, which contains hair cell extensions into the endolymph of the membranous labyrinth (Kandel et al., 2013).

The vestibular labyrinths receive their blood supply mainly from two branches of the anterior inferior cerebellar artery: the anterior vestibular artery and the posterior vestibular artery (Hain & Helminski, 2007). The anterior vestibular artery supplies blood to the utricles, the vestibular nerve, and the ampulla of the lateral and anterior semicircular canals (Hain & Helminski, 2007). The posterior vestibular artery supplies the ampulla of the posterior canal and the saccule (Hain & Helminski, 2007). It is important to note that the vestibular labyrinth is very susceptible to ischemia, with even as little as 15 seconds of blood flow cessation needed to cause excess damage to the vestibular nerve (Hain & Helminski, 2007).

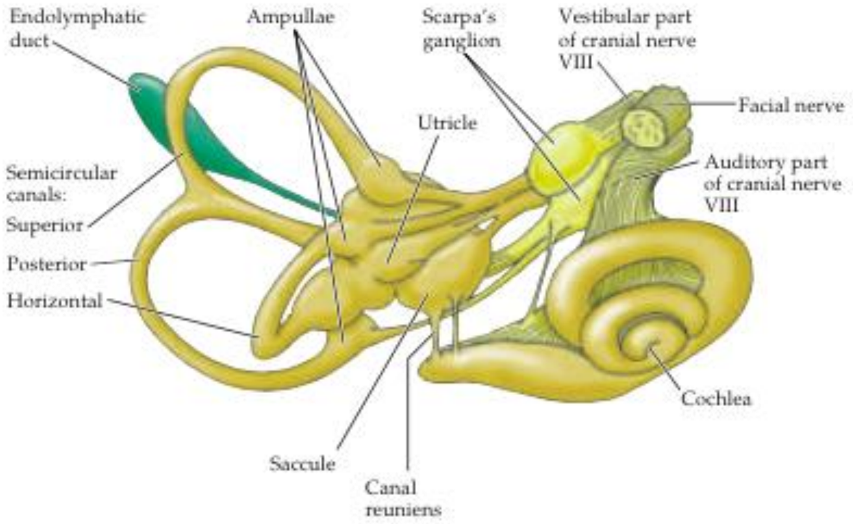

Fig 1.2 Diagram showing the anatomy of the vestibular labyrinth and its components. (Purves et al., 2004). (Copyright @ Oxford Publishing Limited. All rights reserved).

1.1.2 Vestibular Hair Cells

Throughout the vestibular system are bunches of hair cells that serve to transduce minute displacements of the head into relevant neural signals for the brain to interpret. Specifically, these hair cells are found within the five receptor organs of the vestibular system. They are very similar to the cochlear hair cells, with the main difference being the types of external stimulation they respond to.

Vestibular signals are carried from the hair cells to the brain stem by branches of the vestibulocochlear nerve (CN VIII) (Purves et al., 2004). The soma of the vestibular nerve is located in the vestibular ganglion of Scarpa, which is close to the ampulla (Kandel et al., 2013). The *superior vestibular nerve* innervates the horizontal and anterior canals and the utricle, whereas the *inferior vestibular nerve* innervates the posterior canal and the saccule. The hair cells of the ampulla rest on several supporting tissues called the *crista ampullaris*. The hair cells of the saccule and utricle are located in different regions, with the saccular hair cells located on the medial wall of the saccule and the utricular hair cells located on the floor of the utricle. As is the case with cochlear hair cells, movement of the stereocilia toward or away from the kinocilium (longest end of the hair cell) will lead to either an increase or decrease in the firing rate of the vestibular neurons, respectively. Movement of the stereocilia toward the kinocilium causes mechanically gated transduction channels to open, leading to an influx of Na^+ into the membrane, causing the depolarization and excitation of vestibular nerve fibers by releasing neurotransmitters onto them (Fig 1.3). Movement of the stereocilia in the opposite direction causes these channels to close and in the process, hyperpolarizing these hair cells with eventual reduction in vestibular nerve activity. The hair cells in each of the vestibular organs have specific orientations to which they are sensitive as we said earlier. This implies that with each movement of the head, there is deflection of hair cells to either produce excitation or inhibition of the vestibular nerve. As a result of this, the vestibular organ as a whole is responsive to displacements in all directions. For example, in a given semicircular canal, the hair cells in the ampulla are polarized in the same direction. In the utricle and saccule, the **striola** divides the hair cells into two populations based on opposing polarities.

1.2 Physiology of the Peripheral Sensory Apparatus

The sensory receptors of the vestibular system, the hair cells, are located in five different receptor organs: three semicircular canals and two otoliths. In order to understand how the vestibular system responds to mechanical stimulation associated with head movement and position, it is imperative that we describe how the hair cells in these receptor organs integrate the stimulus they receive and transduce them into neural signals that can be interpreted by the central processing areas in the brain such as specific areas of the brainstem and the cerebellum to give us information about head movement and help maintain our balance. We also need to analyze how the different receptor organs are direction specific, meaning they are most sensitive to head movement in a specific direction. The most important anatomical organs of the peripheral sensory apparatus are the three semicircular canals, as well as the two ololith organs: the utricle and the saccule. These organs are very important for the physiological function of the peripheral sensory apparatus.

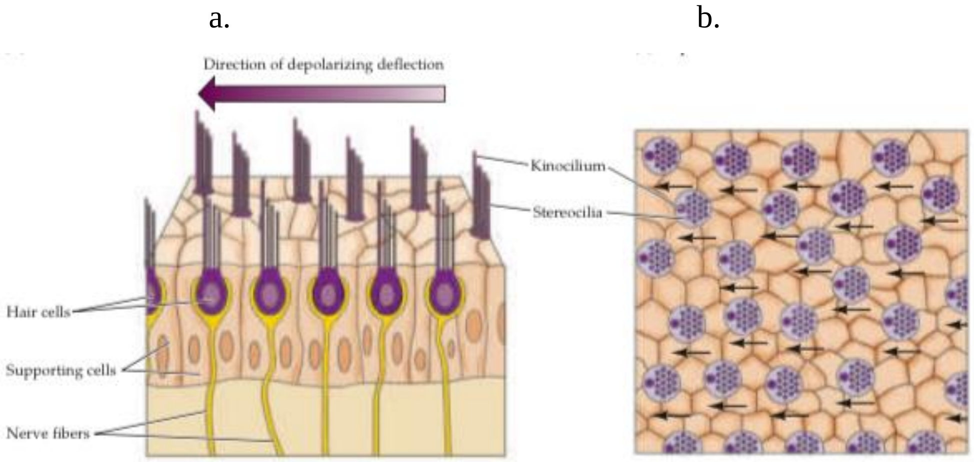

Fig 1.3 a.) Vestibular hair cells shown attached to nerve fibers. **b.)** Directional depolarization of hair cell upon deflection due to mechanical stimulation. (Purves et al., 2004). (Copyright @ Oxford Publishing Limited. All rights reserved).

1.2.1 The Semicircular Canals

Consider a car that moves in a circular path without a change in its speed. This car is described as moving with a constant angular velocity. Now, if a car was to move along the circular path with a non-constant velocity, then the car will be said to be undergoing angular acceleration, α. Angular acceleration is the rate of change in angular velocity. The unit of angular acceleration is $rads^{-2}$

$$\alpha = \frac{\Delta\omega}{\Delta t}$$

where, α is the angular acceleration, $\Delta\omega$ is change in angular velocity, and Δt is the change in time.

Angular acceleration also occurs when an object experiences a change in the rate of rotation about its axis. The head therefore undergoes angular acceleration when it tilts or turns about the axis of the neck, same as when the body rotates, and also during locomotion (Serway & Jewett, 2014). How then do we recognize when the head undergoes angular acceleration? This is the role of the three semicircular canals. These canals help us detect head rotations that arise from angular accelerations of the head and report their magnitudes and directions to the brain (Kandel et al., 2013).

The semicircular canals are tubes which are roughly semicircular in shape found in the membranous portion of the labyrinth. At the base of each semicircular canal is a bulbous expansion called the **ampulla**. This ampulla houses the **crista** in which the hair cells of the semicircular canals are housed (Purves et al., 2004). Overlying each crista, is a flexible diaphragmatic membrane called the **capula** that seals the ampulla from the adjacent vestibule (Purves et al., 2004). In the case of the vestibular system, when the head begins to rotate, the vestibular labyrinths move along the same direction of the rotation of the head. However, the endolymph within the canals lag behind and rotate in a direction opposite to that of the head (Kandel et al., 2013). One reason the vestibular organs detect accelerations of the head is due to this relative motion of the endolymph within the ampulla which creates pressure on the capula, causing it to move back and forth (Zabolotnyi & Mishchanchuk, 2020). Movement of the capula causes simultaneous movement of the hair cells, altering their membrane potentials and thereby changing the rates at which the vestibular nerves fire and relay information to the brain (Kandel et al., 2013). The stereocilia in the ampulla are arranged in such a way that flow toward the capula is excitatory for the horizontal canals, whereas flow away from the capula is excitatory for both the anterior and posterior canals (Zabolotnyi & Mishchanchuk, 2020).

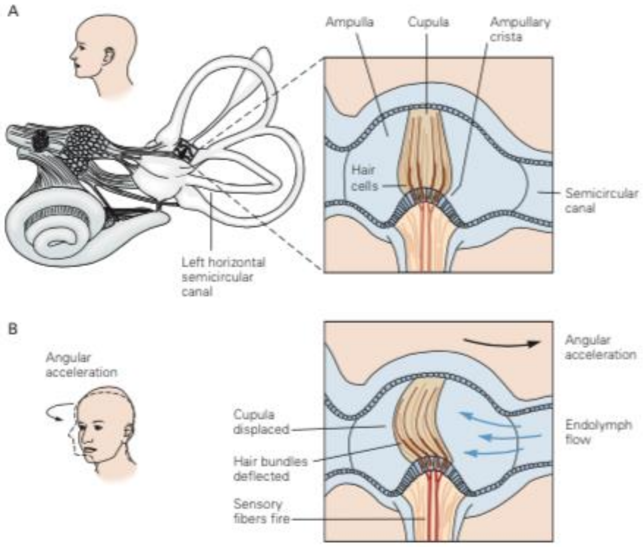

Figure 1.4 Displacement of the capula following head movement. (Kandel et al., 2013) (Copyright @ McGraw-Hill Professional Publishing. All rights reserved).

Linear acceleration causes equal deflections on the capula that causes little to no response from the hair cells of the canals. Hence, the semicircular canals do not sense any information concerning linear acceleration (Hain & Helminski, 2007). The semicircular canals also play an important role, though indirectly, in helping stabilize the gaze during head movement. By providing sensory input about the head velocity, the semicircular canals enable the vestibulo-ocular reflex (VOR) to generate eye movements that match the velocity of head movement (Hain & Helminski, 2007). This action by the VOR enables the eyes to remain still in space during head movement, thus providing us with gaze stabilization (Hain & Helminski, 2007).

Each semicircular canal operates in unison with a partner located on the contralateral side of the head with their hair cells aligned in opposite directions (Zabolotnyi & Mishchanchuk, 2020). There are three such pairs: the pair of horizontal canals, the left anterior and right posterior pair, and the right anterior and left posterior canals pair (Fig 1.5). Head rotations cause displacement of the capula in opposing directions for the two coplanar pairs, causing opposite changes in the firing rates of the vestibular nerves in the canal pairs (Kandel et al., 2013). Specifically, the hair cells in the canal towards which the head is turning are depolarized, while those on the contralateral side are hyperpolarized (Hain & Helminski, 2007). For example, when the head moves to the left, the capula is pushed toward the kinocilium in the left horizontal canal, and the firing rate of the axons of the left vestibular nerve increases. On the other hand, the capula in the right horizontal canal is pushed away from the kinocilium, with a resultant decrease in the firing rate of the related neurons on the right side (Kandel et al., 2013). This is true for all the canals, where the pair whose activity is reduced is the one in the plane of the rotation, while the one whose activity is increased is the one on the side toward which the head is turning (Kandel et al., 2013).

Each semicircular canal is maximally sensitive to rotations along its plane. The horizontal canal is oriented in the horizontal plane, and thus is most sensitive to rotations in that plane (Kandel et al., 2013). The anterior and posterior canals are also oriented more vertically, around 45 degrees from the sagittal plane. Each of the canal planes are also close to the planes of the extraocular muscles, allowing relatively easy connections between sensory neurons and motor outputs. The pair of horizontal canals lie in the pulling plane of the lateral and medial rectus muscles. The left anterior and the right posterior pair lies in the pulling plane of the left superior and inferior rectus and right superior and inferior oblique muscles. The right anterior and left posterior pair occupies the opposite pulling plane to that of the left anterior and right posterior pair.

1.2.2 The Otolith organs

We just explained how the semicircular canals are important in sensing angular accelerations such as head rotations, now let us examine another form of acceleration, linear acceleration and how this is sensed by the body. Linear acceleration is the rate of change in velocity of a moving object without a change in direction (Serway & Jewett, 2014). Linear acceleration involves either an increase or decrease in velocity of an object in a linear manner.

$$\text{Linear Acceleration} = \frac{\Delta \nu}{\mathrm{T}},$$

where $\Delta\nu$ is change in velocity and T is time taken.

The otolith organs, which include the saccule and the utricle are involved with sensing linear acceleration as well as static orientation of the head with respect to gravity (Khan & Chang, 2013). The hair cells of the otolith organs are contained in the macula. The utricle contains approximately 30,000 hair cells, whereas the saccule contains approximately 16,000 hair cells (Kandel et al., 2013). Above the hair cells is a gelatinous layer on which lies a fibrous structure called the **otolithic membrane**, which has dense particles of calcium carbonate called **otoconia** embedded in them

(Khan & Chang, 2013). The otoconia contributes in making the otolithic membrane heavier than surrounding structures. As a result of this, when the head tilts, gravity causes a shift in the membrane relative to the sensory epithelium (Khan & Chang, 2013). This resulting shearing motion between the otolithic membrane and the macula causes a displacement of the hair bundles, leading to an alteration in the activity of the hair cells, generating an action potential in them (Holstein, 2012). Just like the semicircular canals, the otoliths are also able to respond to motion in all three dimensions. However, unlike the canals, which have one sensory organ per axis of angular motion, the otoliths have only two sensory organs for three axis of linear motion (Holstein, 2012). Considering an individual in an upright position, the saccule is in the parasagittal plane and can sense linear acceleration is the occipitocaudal axis, whereas the utricle is horizontally oriented and senses lateral acceleration in the interaural axis mainly (Kingma & Van de Berg, 2016). One notable sort of movement to which the utricle responds to is tilt. For example, as the head is tilted laterally, shear forces are exerted upon the utricle, which causes it to become excited. However, the shear forces acting on the saccule are lessened. This is also experienced when the head is tilted forward or backward. The saccule, therefore, responds to movements of the head in the vertical plane, while the utricle responds to movements of the head in the horizontal plane. Both otolith organs contain a striola consisting of small otoconia, serves in dividing each otolith organ symmetrically (Kandel et al., 2013). Due to this symmetrical organization, the hair cells on the opposite side of the striola have opposing morphological polarizations. Thus, a tilt along the axis of the striola will excite the hair cells on one side while inhibiting the hair cells on the other side (Kandel et al., 2013). It is important to note that in the utricular macula, the kinocilia point towards the striola, while in the saccular macula, they point away from the striola.

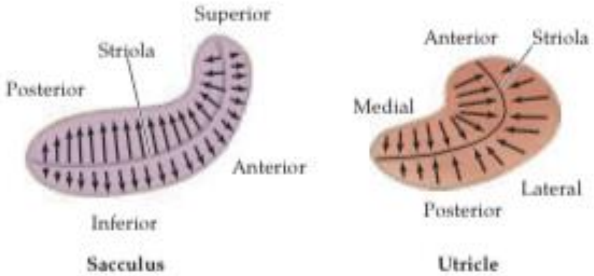

Fig 1.5 Structure of the saccule and utricle (Purves et al., 2004). (Copyright @ McGraw-Hill Professional Publishing. All rights reserved).

The structure of the otolith organs enables them to sense both static displacements such as tilting of the head, as well as transient displacement caused by translational movements of the head (Holstein, 2012).

The nerve fibers innervating the otolith organs have a steady and relatively high firing rate when the head is upright. The change in the firing rate occurs due to movement and this can be either sustained or transient, signaling either absolute head position or linear acceleration (Purves et al., 2004). An example of this is shown in Figure 1.7. The responses of the vestibular nerve fibers of the otolithic organs were recorded from axons in a monkey that was seated in a chair that could be tilted for several seconds to produce a steady force. In the first part of the figure, we see that the axons will fire at a high rate when the head is tilted. This firing rate remains constant for as long as the tilting force remains constant. Thus, such neurons encode the static force being applied to the head (Fig 1.7A) (Purves et al., 2004). Conversely, when the head is tilted in the opposite direction, these same neurons will respond accordingly by decreasing their firing rate, and this rate of firing also remains constant as long as the tilting force is constant (Fig 1.7B) (Purves et al., 2004). Just like with the semicircular canals, hair bundles orientation within the otolith organs enables them to be able to transmit information about linear acceleration in every direction the body moves.

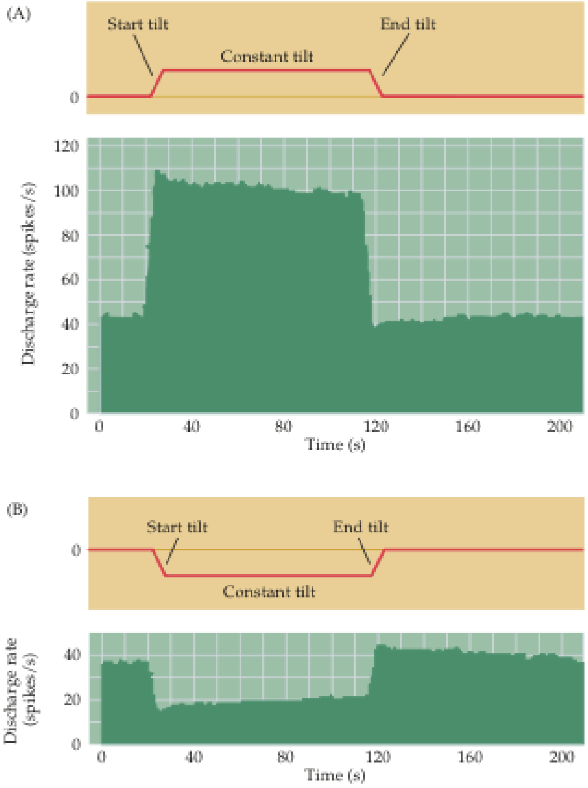

Fig 1.7a and b Responses of a vestibular nerve axon from an otolith in response to tilt. (Copyright @ Oxford Publishing Limited. All rights reserved).

1.3 The Central Pathways of the Vestibular System

The organs of the peripheral sensory apparatus that make up the vestibular system are mostly located in the inner ear and play a big role in sensing information about head position, particularly with regards to linear and angular acceleration. On the other hand, the central pathways of the vestibular system mostly comprise of the vestibular nerves and areas of the brain such as the brainstem and cerebellum and how they play a role in combining vestibular and non-vestibular signals to achieve both gaze and postural stability, kinesthesia, and spatial orientation.

1.3.1 Vestibular Nerve

Information about linear and angular acceleration, is received by the hair cells of the vestibular organs and then relayed to the brain through the vestibular nerves. Vestibular nerves are bipolar neurons that transmit afferent signals from the vestibular labyrinths to the brainstem (Kingma & Van de Berg, 2016). The vestibular nerves project to the ipsilateral brainstem from the vestibular ganglion to the vestibular portion of the cranial nerve VIII to the four vestibular nuclei located on the brainstem (Kingma & Van de Berg, 2016). These vestibular nuclei serve to integrate signals from the vestibular organs with signals from the spinal cord, cerebellum and visual system. Another target of vestibular afferent is the cerebellum. The cerebellum serves in monitoring vestibular action and adjusting central vestibular processing.

1.3.2 Vestibular Nuclei

The vestibular nuclei or the vestibular nucleus complex consists of four major nuclei that are located mainly in the dorsal portion of the pons and the medulla in the brainstem (Hain & Helminski, 2007). These nuclei help integrate signals from the spinal cord, cerebellum, and visual system and they project these signals to the central processors such as the cerebellum, the thalamus, and also the oculomotor nuclei (Hain & Helminski, 2007). The four major vestibular nuclei are the medial, lateral, superior, and descending nuclei. These nuclei have different cytoarchitectures, which account for their functional differences (Hain & Helminski, 2007).

The superior and medial vestibular nuclei receive fibers predominantly from the semicircular canals and they project fibers to the oculomotor centers and to the spinal cord. These vestibular nuclei are predominantly concerned with affecting the (VOR) (Kandel et al., 2013). Neurons in the medial vestibular nucleus are excitatory, whereas those in the superior vestibular nucleus are mainly inhibitory (Kandel et al., 2013). The lateral vestibular nucleus also receives fibers from the Semicircular canals and otolith organs and projects mostly into the lateral vestibulospinal tract, mainly acting to control postural reflexes (Kent et al., 2010). Lastly, the descending nuclei receive mainly input from the otolith and projects to the cerebellum and the reticular formation (Hain & Helminski, 2007). Additionally, the descending vestibular nuclei also send projections to the contralateral vestibular nuclei and the spinal cord. This vestibular nucleus helps integrate vestibular signals with motor information from the central nervous.

Two important brain regions that are important in making sense of vestibular projections from the vestibular nuclei are the thalamus and the cerebellum.

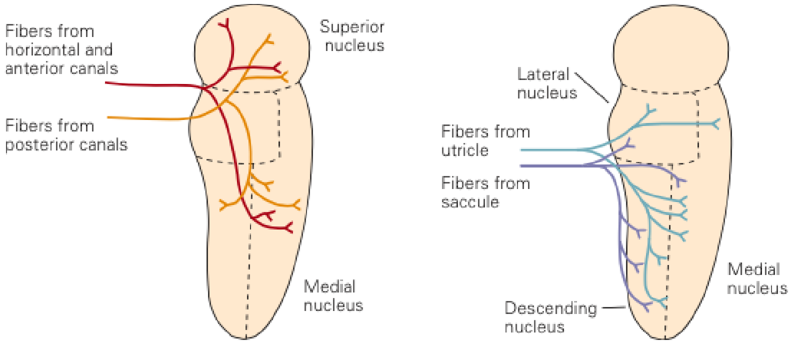

Fig 1.7 Anatomy of the vestibular nuclei that project information to the central processors (Kandel et al., 2013) (Copyright @ McGraw-Hill Professional Publishing. All rights reserved).

1.3.3 Thalamus

The thalamus is a structure within the brain whose main function is to serve as a relay center for both motor and sensory information to the cerebral cortex. All the vestibular nuclei project to the ventral posterior and ventral lateral nuclei of the thalamus, which then project to the primary somatosensory area of the cortex (Purves et al., 2004). Vernon Mountcastle demonstrated that electrical stimulation of the vestibular nerve in cats could evoke activity in the primary somatosensory cortex and in the parietal association cortex (Purves et al., 2004).

Single cell recordings in animals have shown that these areas in the thalamus also receive visual and somatosensory inputs (Kandel et al., 2013). This helps in the facilitation of the integration of all relevant sensory information for the perception of motion and orientation (Kandel et al., 2013). It is important to note that vestibular and visual areas of the cortex have reciprocal connections that help in the resolution of contradictory vestibular and visual inputs.

1.3.4 The Cerebellum

Although the cerebellum is not required for vestibular reflexes, these reflexes become less fluid and ineffective with lesions to the cerebellum (Holstein, 2012). The cerebellum plays a major role in monitoring motor action and adjusting the central processor response to the feedback it gets. There are reciprocal connections between the vestibular nuclear complex and the cerebellum. The cerebellar projections to the vestibular nuclear complex are mostly inhibitory in nature (Holstein, 2012). The major areas in the cerebellum receiving vestibular input are the flocculus and the ventral paraflocculus (Kandel et al., 2013). Also, most of the cerebellar vermis responds to stimulation of the vestibular nuclei (Kandel et al., 2013). The cerebellar flocculus helps in adjusting and maintaining the gain of the VOR (Kandel et al., 2013). Thus, the flocculus and paraflocculus help in maintaining the VOR. The cerebellar nodulus is another area in the cerebellum that helps adjust the duration of VOR responses and also processes input from the otolith (Hain & Helminski, 2007). Patients with lesions to the cerebellar nodulus show gait ataxia and often have nystagmus (Hain & Helminski, 2007).

1.4 Motor Output of the Vestibular System

Information received by the vestibular system through the excitation of vestibular hair cells in the otoliths and semicircular canals travels through vestibular afferents to vestibular nuclei in the brainstem and then this information is relayed to central processors in the brain to help make sense of them and effect appropriate actions in order for us to keep our balance and know our body position in space. In order to ensure this, the processed vestibular information has to be relayed to the desired muscles that help ensure balance and locomotion.

One of the main muscles that receives output from the central processors are the eye muscles. These muscles play an important role in the VOR. The output neurons of the VOR are the ocular motor nuclei, which drive the extraocular muscles (Fife, 2010). The semicircular canals affect the action of the extraocular muscles, whose pulling direction lies in about the same plane as those of the SCCs. Excitatory and inhibitory pathways of the VOR connect each of the three pairs of SCCs to the four extraocular muscles. Leftward head rotation will cause excitation of hair cells in the left horizontal canal, exciting neurons that evoke rightward eye movement. The muscles excited by this canal include the ipsilateral medial rectus and the contralateral lateral rectus, while the ipsilateral lateral rectus and the contralateral medial rectus muscles are inhibited. Neurons that are excited in the process include the right abducens nucleus and the nucleus prepositus hypoglossi.

1.5 Vestibular Reflexes

Important characteristics of vestibular system function are the vestibular reflexes. The three main vestibular reflexes are the VOR the vestibulospinal reflex (VSR), and the VCR.

1.5.1 The Vestibulo-ocular reflex (VOR)

The VOR normally acts to help in maintaining a stable gaze during motion of the head. This reflex has two components to it. The angular VOR that is mediated by the SCCs, and the linear VOR that is mediated by the otoliths. The former helps compensate for rotations, while the later compensates for translations (Hain & Helminski, 2007). One way to investigate how the VOR works is by looking at rightward movement of the head. When you turn your head to the right, endolymphatic fluid displaces the capula to the left. The hair cells in the right of the cristae begin to increase their firing rate in proportion to the velocity of head movement, while those at the left side of the cristae reduce their firing rate. The vestibular nerve relays information about the firing rates of the hair cells on either side of the cristae to neurons of the medial and superior vestibular nuclei and the cerebellum. This causes the neurons in these regions to regulate their firing rates. Excitatory impulses are transmitted through white matter tracts in the brainstem to the oculomotor nuclei, which activates the ipsilateral medial rectus and the contralateral lateral rectus. Simultaneously, the left lateral rectus and right medial rectus muscles contract, while the left medial rectus and right lateral recuts muscles relax, causing a lateral compensation of eye movements towards the left, the direction opposite to head movement. If the eye and head velocities are incongruent, the cerebellum will act to adjust VOR by sending projections to the vestibular nuclei in order to modify the firing rate of neurons within the vestibular nuclei to reduce error.

1.5.2 The Vestibulospinal Reflex (VSR)

The purpose of the VSR is to help stabilize the body. Actually, the VSR consists of an assembly of several reflexes that are named according to the timing (dynamic vs tonic) and sensory input (canal vs otolith) (Purves et al., 2004). There are several ways in which the VSR helps in stabilizing the body. Consider when the head is tilted to one side, for example the left, both the otoliths and the canals are stimulated. Endolymphatic fluid causes deflection of the capula, and the hair cells within the otolith are deflected, since this is linear acceleration (Purves et al., 2004). This deflection of hair cells causes the activation of the vestibular nerve and vestibular nuclei. Impulses are then transmitted through the lateral and medial vestibulospinal tracts to the spinal cord. Extension is induced on the side to which the head is inclined, and flexion is induced on the opposite side (Kandel et al., 2013).

1.5.3 The Vestibulocolic Reflex (VCR)

The VCR is mainly important in stabilizing the head by acting on the neck muscles. This reflex helps produce head movement that counters the movement sensed by the otoliths or SCCs. However, details pertaining to the pathways mediating this reflex are yet to be elucidated.

1.6 Vestibular Disorders

Vestibular disorders occur due to disturbances in the body's balance system due to peripheral or central causes (Thompson & Amedee, 2009). The symptoms of peripheral and central vestibular disorders often overlap and can be very well differentiated via the help of a physical exam. Symptoms include vertigo, nausea, vomiting, intolerance to head motion, nystagmus, postural instability and unsteady gait. Vestibular neuritis and ischemic stroke of the posterior fossa, which contains the brainstem and the cerebellum, are the most common peripheral vestibular dysfunctions and central vestibular dysfunctions, respectively. Some of the relevant vestibular disorders are discussed below.

Benign paroxysmal positional vertigo (BPPV) is one of the most common causes of vertigo. In BPPV, there is a brief period in which the patient experiences mild to severe dizziness. BPPV usually occurs when calcium crystals in the inner ear are dislodged from their normal position to somewhere else in the inner ear (Nunez et al., 2000). It can occur in people of all ages, but it is most common in people 50 or older.

Vestibular neuritis is an inflammatory disorder that is caused by viral infection of the vestibular nerves in the vestibular system. It is common in people of all ages. Some of the symptoms include sudden and severe vertigo, balance difficulties, and dizziness. These symptoms can last several days, and they usually improve gradually without treatments (Strupp et al., 2004).

Ménière's disease is another vestibular disorder. This is caused due to an abnormal amount of endolymph fluid in the inner ear that can be due to viral infection, abnormal immune response or improper fluid drainage to anatomic abnormality (Minor et al., 2004). Symptoms include recurring episodes of vertigo, hearing loss, as well as tinnitus. It is typically common in people between the ages of 20 and 40 years old.

Vertebrobasilar insufficiency (VBI) is due to reduction in the flow of blood to the vertebral and basilar arteries, which are arteries that supply blood to brain structures like the brainstem, occipital lobes, and cerebellum (Thompson & Amedee, 2009). Smoking, obesity, high lipid levels, and being over 50 years old are all risk factors for the disease. Some of the symptoms of VBI include, loss of balance and coordination, vertigo, double vision, and numbness in the hands or feet.

Cerebellar infarcts are some of the least common strokes and occur due to blockage or bleeding of a blood vessel that carries blood to the cerebellum. Some of the symptoms include poor coordination, abnormal reflexes, vertigo, and uncontrollable eye movement.

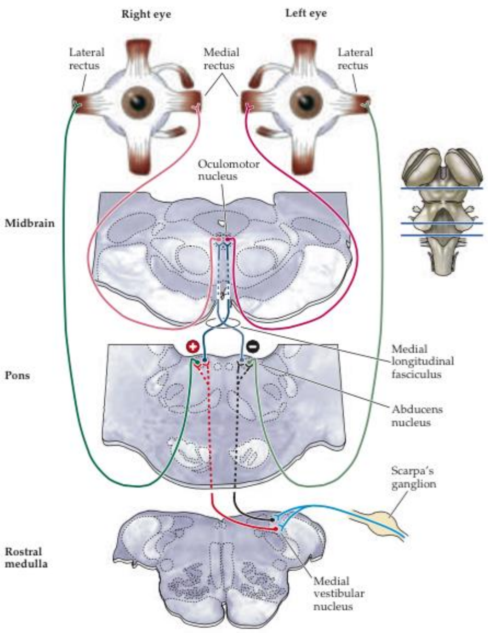

Fig 1.8 Diagram showing connection between structures involved in the vestibulo-ocular reflex (VOR) (Purves et al., 2004) (Copyright @ Oxford Publishing Limited. All rights reserved).

CHAPTER 2

2.0 THE VESTIBULAR SYSTEM AND BALANCE

The vestibular system's ability to regulate balance is very important to us since it helps us maintain stability in our environment by avoiding fall every time we experience disturbances by external forces acting on us. It is however important to note that balance is not the sole responsibility of the vestibular system, as the visual system, somatosensors and proprioceptors all contribute to help maintain balance of the body.

2.1 Biomechanics and Neuroscience of Balance

Balance, along with orientation, are the two components of posture. Control of these components is crucial for everyday activities. Balance involves active resistance to external forces that act on the body (Kandel et al., 2013). Because the body is made up of several segments that are linked together by joints, this makes the body mechanically unstable. In order to maintain balance, the nervous system must control the position and motion of the body's center of mass. The center of mass is the point at which the net effect of gravity acts on the body (Winter et al., 1990). The location of the center of mass on the body is not fixed, but is dependent on the postural orientation. The force of gravity acting on the body is opposed by the ground reaction force, and the ground reaction force occurs at a point on the ground called the center of pressure (Latash, 2012). To maintain balance while standing, the body needs to keep the downward projection of the center of mass within the base of support, an area defined by those parts of the body in contact with the environment (Fujimoto et al., 2015). Because the body is constantly in motion, the center of mass continually moves about with respect to the base of support (BoS) (Meyer & Ayalon, 2006). It is important to note that balance in humans can be described in two forms; static balance, which is the ability of the body to maintain the base of support with minimal movement, and dynamic stability, which is the ability to perform tasks while still maintaining the body in equilibrium (Winter et al., 1990). Standing upright requires antigravity support and also maintaining balance, requiring us to continuously make motor corrections to remain upright due to the downward pull of gravity (Arntz et al., 2019). These two actions to maintain upright stance are controlled by different areas of the nervous system, as they are differentially affected in certain pathological conditions (Arntz et al., 2019). Antigravity support is the tonic action of muscles that generate force against the ground to keep the limbs extended and the center of mass at the appropriate height (Kandel et al., 2013). However, this tonic activation of antigravity muscles is not sufficient to maintain balance. Balance control has also been explained using the equilibrium point hypothesis as two subsystems that function hand-in-glove. The first subsystem determines a referent position of the body with respect to which the equilibrium of the body is to be maintained, and the second subsystem helps shift the body to maintain equilibrium about the preselected referent point (Zatsiorsky & Duarte, 2000). In their attempt to confirm this hypothesis, Zatsiorsky and Duarte (2000) conducted an experiment in which they asked subjects to stand upright on a 40 by 80cm force platform for 30s with their eyes open. The participants were asked to maintain the same posture for the entirety of the trial while center of pressure (COP) and ground reaction forced were acquired. The COP movement was partitioned into time series using two techniques: rambling-trembling decomposition and gravity line decomposition. They found that there was a positive correlation between trembling trajectory and the difference between COP and gravity line. They also found a negative correlation between rambling trajectory and horizontal force. What they concluded was that during quiet standing the body sways due to rambling, caused by the migration of the referent point, and trembling, deviation away from that referent point (Zatsiorsky & Duarte, 2000).

When the body experiences a sudden disturbance that causes it to be destabilized, it uses various strategies to maintain its center of mass within its base of support. One of such strategies involves the base of support remaining fixed relative to the support surface. As such, the feet remain in place while the body rotates about the ankles back to the upright position (Fig. 2) (Kandel et al., 2013). In other strategies, the base of support is moved or enlarged (Kandel et al., 2013). One such strategy is the hip strategy where the hips are swayed to help counteract perturbation, moving the center of gravity around to keep it over the base of support (Fig 2.1) (Latash, 2012). Older views of motor control focused exclusively on the trunk and proximal limbs as the main postural effectors (Nashner & McCollum, 1985). However, there is evidence that other groups of muscles from the neck and trunk, legs and arms can act as postural muscles depending on the body parts in contact with the environment and the biomechanical requirements of equilibrium. Automatic postural responses to sudden disturbances of the body have both temporal and spatial features (Kandel et al., 2013). Rapid recruitment of muscles must occur following the onset of disturbance. Humans have long latencies of postural responses because of their large bodies and longer signal conduction distances from the sensory receptors to the central nervous system and then to the leg compared to smaller animals such (Kandel et al., 2013).

The main aspect of stability in which we are interested when it concerns locomotion is dynamic stability. Locomotion, with particular emphasis on walking and running are essential to humans, as they help us with the ability to move from place to place and also enable us to perform a lot of vital tasks. Therefore, it is important that while we are performing such tasks, we avoid all sorts of instability that might lead to fall. This is particularly important as we become older, as dynamic stability eventually reduces and the frequency of falls increases.

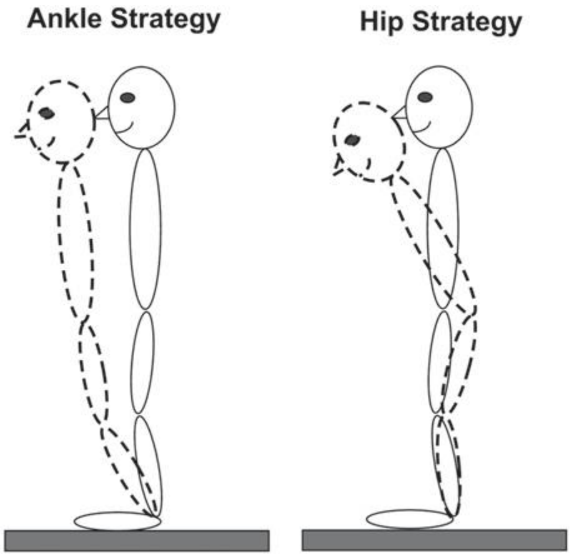

Fig 2.1 Illustration showing both the hip and ankle strategies used by humans to maintain balance (Latash, 2012) (Copyright @ Elsevier Science & Technology. All rights reserved).

How does the vestibular system contribute in setting dynamic stability that helps us in locomotion? In dynamic stability, both the base of support and the center of mass are in motion. Momentum control of this center of mass is an important factor in dynamic stability. For static stability, the condition fulfilled for balance to be maintained is for the vertical projection of the center of mass to be within the base of support. However, Pai and Patton (1997) and Iqbal and Pai (2000), showed that this condition is insufficient to fulfil the conditions of dynamic stability. They pointed that the velocity of the center of mass also had to be taken into account. This is because even when the center of mass is above the base of support, if the velocity of the center of mass is directed outwards of this base of support, balance may not be possible to achieve (Pai and Patton, 1997). Importantly, balance can also be achieved if the center of mass is outside the base of support, but its velocity is directed towards it. The center of mass and its velocity can be called the position of the extrapolated center of mass (XcoM) (Pai and Patton, 1997). Therefore, we can say that the condition for dynamic stability is when the XcoM is confined within the base of support (Hof et al., 2005). The center of pressure is also important in the maintenance of balance. The location of the center of pressure, especially prior to the first step, contributes to a person's ability to maintain their balance after a perturbation (Fujimoto, et al., 2015). The base of support boundaries is considered as stability limits within which we maintain our balance by rapidly moving our center of pressure to keep our center of mass from leaving the base of support (Hof et al., 2005; Winter et al.,1995). Lugade et al. (2011) went further to investigate how the trajectory of the center of mass changed in relation to the ever changing base of support throughout the gait cycle in healthy young adults, healthy elderly adults and elderly fallers. What they observed was that at heel strike, even though young adults and elderly fallers had similar base of support areas, they were able to control their center of mass in such a way that the distance from the base of support boundaries along the direction of the center of mass velocity was significantly greater for young adults than in the elderly fallers. These examples show that how fast and how far the center of pressure moves with respect to the base of support is greatly important in dynamic balance control (Lugade, et al., 2011). Fujimoto et al. (2015) showed that this functional limit of the base of support, which is the area utilized for center of pressure movement is significantly decreased with aging. This might be a possible explanation as to why older adults have more difficulty in controlling their balance and avoiding falls effectively, compensating by taking more recovery steps compared to younger people who are better able to control their center of pressure location (Mille et al., 2013).

The vestibular system plays an important role in the regulation of balance. The vestibular system, via the action of the semicircular canals and the otolith organs help in detecting linear acceleration, deceleration and rotational accelerations of the head (Kent et al., 2009). Vestibular afferents from both the otoliths and the semicircular canals project ipsilaterally, via cranial nerve VIII, where they end up in the vestibular nuclei and later project to the reticular formation (Abzug and Peterson, 1973). The vestibular afferent projections that end up in the vestibular nuclei provide multisensory input that help in distinguishing between self versus external motion, as well as activating and modulating postural reflexes and balance (Arntz et al., 2019). The vestibular nuclei is able to control balance via two descending pathways to the spinal cord, the lateral and the medial vestibulospinal tracts. Axons of the medial tract travel in the medial longitudinal fasciculus and terminate in the upper cervical regions of the spinal cord, innervating upper-body musculature, especially those of the neck. Thus, this circuitry is essential for the rapid control of vestibular reflexes and neck postural changes related to head orientation (Arntz et al., 2019). The lateral vestibulospinal tract contains fibers that descend ipsilaterally and innervate multiple levels of the spinal cord, providing the capacity to modulate spinal motoneuron activity across segments (Abzug and Peterson, 1973). Electrical stimulation of lateral vestibular nuclei evoked an increase in extensor motoneurons excitability while accentuating inhibitory effects on the flexor motoneurons. This facilitation of vestibulospinal inputs on extensors suggests that this pathway provides some level of extensor tone to achieve vertical support against gravity (McCall et al., 2017). In addition, the vestibular system also helps coordinate movements of the head with those of the eyes, the trunk and the limbs helping to reduce incongruence between these systems and reducing the risk of imbalance (Kent et al., 2010). Vestibular signals encoding head movements in space as well as the orientation of the body relative to gravity contributes in activating muscle activity that is required to stand and maintain upright posture. This encoding occurs within a fixed gravito-inertial reference frame. This is particularly evident in the absence of visual cues (Dakin and Rosenberg, 2018). Marsden et al. (2003) showed that adding or reducing body load alters vestibular evoked postural responses, whereby the rate of force production increases with loading and reduces with unloading. This can also be observed in asymmetric standing postures, suggesting that load-related afferent feedback of gravity can influence the processing of vestibular signals for the control of balance (Marsden et al., 2003). Vestibular evoked muscle responses were also found to be greatest when the direction of the vestibular disturbance was aligned with the balance direction in subjects who were standing and restricted in a single plane (Forbes et al., 2016). Most of these vestibular disturbances evoke stereotypical muscle and whole body postural corrections to maintain upright balance, especially when standing (Nashner and Wolfson, 1974). This provides evidence that stimulation of the vestibular system influences muscle activity to maintain balance. Arntz and colleagues specifically conducted a study to see whether changes in otolith driven signals of gravity caused a modification in the vestibular evoked muscles responses for standing balance. They varied the load and the gravity conditions independently of each other by either loading the body downward at 1.5 and 2 times the body weight or exposing subjects to brief periods of micro (0.05g) and hyper-gravity (1.8g). What they found was that there was a reduction in the relative contribution of the vestibular system to balance control in conditions where the vestibular cues of gravity varied mostly in the microgravity (Arntz et al., 2019). Additionally, they observed that vestibular evoked responses were still observed in all conditions following electrical vestibular stimulation. This implied that even in the absence of vestibular signal of gravity, the vestibular clues provided by the load were still able to elicit a reaction from the otolith organs to help in maintaining balance (Arntz et al., 2019). The vestibular system also helps provide a sense of self-motion, activates and modulates postural reflexes that help in the maintenance of vertical support and control of balance (Mackinnon, 2018).

As we know, the otolith organs and the semicircular canals in the vestibular system help inform the nervous system about how much the body is tilted with respect to gravity and also whether the body is experiencing any rotational movement, respectively. The vestibular system is not essential in providing information about the timing of balance reactions. However, it is essential in influencing the directional tuning of postural responses, providing information about the orientation of the body relative to gravity in order to maintain equilibrium (Kandel et al., 2013).

Several studies, past and present, have illustrated in diverse ways how the vestibular system can be shown to have a role in balance. Initially, along with the cochlea, all organs in the inner ear were thought to participate in the processing of auditory signals, and thus contributing to hearing. The first scientist to establish that the vestibular system in the inner ear played a role in balance or equilibrium was French neurologist Marie-Jean-Pierre Flourens in 1842 (Desai & Dua, 2014). In a series of experiments on pigeons, he observed that cutting the semicircular canals in these pigeons produced abnormal head movements and that the plane of the movement was always the same as that of the canal that was injured. Importantly, also, he noticed that hearing in these pigeons was not affected when he damaged their canals, but was completely abolished when he damaged their basilar papilla, which is the bird's cochlea (After Flourens, several others over the years were able to perform more studies to ascertain these facts of the role of the vestibular system in balance. In I892 German physiologist, J.R. Ewald was able to show changes in muscle tone and postural reflexes as a result of unilateral vestibulectomy (Ewald, 1892). This was additional evidence of the role of the vestibular system in balance. Winter (1989) and Rothwell (1994) described the control of balance and locomotion to be provided by systems across the caudal-to-rostral extent of the neuraxis, which include the visual system, vestibular system, and the somatosensory system. They describe these systems as having five primary goals: (1) maintaining the vertical support of the body against gravity; (2) maintaining balance by keeping the center of mass within the base of support; (3) providing postural stability appropriate for specific tasks; (4) control foot trajectory; and (5) help attenuate transmission of acceleration of the head to stabilize both visual and vestibular apparatus.

In the present day, several methods have been utilized to study the vestibular system and its effect on the control of balance. The most popular of such methods is called Galvanic Vestibular Stimulation (GVS), which involves stimulating the mastoid processes with electrical current in order to activate neurons of the vestibular system. In a study identifying the effects of GVS on human walking, it was found that GVS caused deviations in the anodal direction in the trajectory of movements especially in the first three steps following stimulation. Additionally, this GVS effect was seen to be more pronounced when the eyes were closed than when they were open (Fitzpatrick, et al., 1999). Also, short duration GVS (4mA, 20ms) delivered bilaterally to the mastoid processes I was shown to evoke balance responses in muscles of the lower leg when participants were standing still with their head facing forward (Son, et al., 2008). Additionally, Peterka and Benolken (1995) have suggested that visual and somatosensory inputs provide dominant sources of afferent information during stance, while the vestibular system was thought to have less important role. This leads us to question if reducing visual input while stimulating the vestibular system will enhance the vestibular role in balance and locomotion. Noisy GVS (nGVS), which is another form of GVS with the only difference being that it uses white-noise current stimulation rather than unidirectional current stimulation used in conventional GVS (Matsumoto et al., 2021) has also been used to improve vestibulospinal function in patients with bilateral vestibulopathy (Schniepp et al., 2018). In one study involving healthy elderly adults suffering from frequent falls due to increased center of pressure sway away from the base of support, noisy GVS was used to stimulate the vestibular system in order to improve balance. What was found was improvement in center of pressure sway, especially in subjects with eyes open. They also found that the effect of this nGVS on reduction of center of pressure sway was persistent even after the end of the stimulation (Inukai et al., 2018; Inukai et al., 2020). Iwasaki et al. (2014) also showed a similar decrease in the center of pressure sway of subjects who stood on a foam rubber with eyes closed while receiving nGVS. GVS effects on the vestibular system and its effect on balance was also shown in children with cerebral palsy disorder. The aim was to investigate if stimulation of the vestibular system using GVS would help improve their balance. The children received GVS for two sessions per week for a total of 12 sessions. Results showed the children were able to change and control their center of pressure displacement faster, consequently, managing their balance better (Hosseini et al., 2015).

One fundamental question regarding GVS action on neuronal cell population in the vestibular system is how does GVS act on otolith and semicircular canal hair cells. The answer to these questions have been ambiguous. Several studies have shown that galvanic currents influence the discharge of otolith and semicircular canal nerve afferents in humans, as well as guinea pigs and monkeys (Goldberg et al., 1984; Fitzpatrick and Day, 2004; Kim and Curthoys, 2004). However, different approaches have been used to achieve this goal such as inserting stimulus electrodes unilaterally or bilaterally into the perilymphatic space of the semicircular canals (Ezure et al., 1983), or noninvasively attaching them to the neck for transmastoidal stimulation in humans (Fitzpatrick and Day, 2004). At low intensity, GVS has been shown to activate irregular vestibular afferents, with higher stimulus intensities leading to activation of regular afferents (Kim and Curthoys, 2004). However, there is still no definitive experimental proof for the cellular substrates that are activated by GVS. In some cases, researchers assume it is the vestibular afferents, while in other clinical research, vestibular hair cells have been seen to be activated by GVS (Aw et al., 2013). Several studies have reported contradictory results in a study by Cohen et al. (2012), where high frequency electrical stimulation of the vestibular system excited mainly otoliths rather than semicircular canal afferent neurons, due to the fact that otolith related behavioral responses were observed. This was because in their experiments, the sensations of head rotation that are responses unique to semicircular canal stimulations, were not experienced. Conversely, using binaural bipolar GVS, Fitzpatrick and colleagues investigated the effect of this stimulation on the semicircular canals of their subjects. To minimize the activation of the otolith, they made the axis of rotation collinear with the midline between the ears. GVS in this experiment was found to produce a sensation of rotation, and not translation (Fitzpatrick et al., 2002). In another study, the effect of head pitch on GVS-evoked balance responses were examined. Strong sway responses were observed when the head was upright, but when the head was tilted down the main balance response was abolished, leaving a small transient sway. These observations appear to have a consistent otolith stimulation response. However, close examination of the results suggested that these responses were not compatible with anatomical properties of otolith organs. This raises the possibility that trans-mastoidal current may also stimulate non-vestibular pathways to produce motor output (Reynolds & Osler, 2012). GVS is primarily interpreted by the brain as head roll, which is consistent with activation of semicircular canal afferents, while indication of its activation of sensation of linear acceleration or sensation of tilt, which are indicative of otolith activation, are less clear (St George and Fitzpatrick, 2011).

Previous studies have reported preferential activation of primary vestibular afferents that innervate the horizontal semicircular canals and the otoliths. Using constant current GVS with electrodes applied both on the mastoid and the tensor tympani muscles of the middle ear of guinea pigs, and responses from single primary vestibular neurons were recorded. What they reported was that tensor tympani GVS was more effective than surface GVS and cathodal stimulation resulted in an increase in firing compared to anodal stimulation. They finally found no evidence for preferential activation of horizontal semicircular canals and otoliths compared to other vestibular afferents (Kim & Curthoys, 2004). GVS therefore activates both primary otolithic neurons as well as primary semicircular canal neurons. Additionally, Holstein et al. (2012) described regions in the rat brain that were activated by GVS. Holstein and colleagues used c-Fos labeling in order to show brain regions that were active during this stimulation and what they found was that some regions that were previously thought to be involved in vestibular evoked behavioral responses, were not expressing this c-Fos label. Some of these regions were the vestibulo-spinal and vestibulo-colic neurons of the vestibular system (Holstein et al., 2012). An explanation as to why this might be the case is that c-Fos protein is not expressed in neurons that are tonically inhibited, which is the case of vestibulo-ocular neurons that receive substantial inhibition from cerebellar Purkinje cells (Holstein et al., 1999). One important factor that is not being taken into account in the analyses of these results is the context in which the galvanic stimulation was carried out. One such context is the presence of vision, which is known to affect the results of vestibular stimulation on the vestibular system, depending on whether there was full light (good vision) or darkness (reduced vision) (MacDougall et al., 2002). This is important because it brings forward the importance of context and also highlights the fact that when the context in which the stimulation occurs is changed, it also leads to changed behavior. Another contextual variable that is important in vestibular stimulation is head position (Kennedy & Inglis, 2002). Now one more question that can be asked is if contextual changes effect is the same for both otolith and semicircular canal responses. There is evidence that both the otolith (Gianna et al., 2000) and semicircular-ocular responses can be suppressed or enhanced by by influence from the vestibulo-ocular reflex. Thus, here we see that both the semicircular canals and the otoliths are activated by GVS, depending on the circumstances in which the experiments are carried such as the stimulus used, the electrodes, and how the responses are measured. In a study examining the effects of both the otolith organs and the semicircular canals on human balancing reflexed following GVS, the contextual variable of head position was used. In one condition, participants received GVS stimulation when the head was upright, and in another condition the participants received stimulation with the head bent forward. Upright head position predicts that GVS-evoked canal signal will lead to lateral head rotation and otolith signal will lead to lateral tilt or acceleration. In the head bent forward condition, canal activation is indicated by body spin about the vertical axis, whereas otolith signal was indicated by lateral body motion (Cathers, et al., 2005). What they found was that when the head was upright, GVS evoked large body sway in the direction of the anode electrode. However, this was not the case in the head bent forward condition. Additionally, in the head upright condition, GVS evoked both short and medium latency EMG responses of opposite polarities. This medium response was abolished during the head bent forward condition (Cathers, et al., 2005). The results of this study show that GVS indeed evokes separate otolithic and canal reflexes, with both participating in the maintenance of balance in independent and separate ways. However, there is still no definite way to uniquely stimulate one or the other separately. A prospective study that might be interesting to observe in order to determine the effect GVS has on each of these organs might be to use optogenetics in which either the otolith organs or the semicircular canals are suppressed while the other is activated, and the response to GVS is measured.

2.2 Other Sensory Systems involved in Balance Control

Although the vestibular system plays a major role in the control of balance, it is not the only system in the body that contributes to the ability to maintain balance. Balance is controlled via a multisystem interaction with contributions from the visual system, the somatosensory system, and some areas of the central and peripheral nervous systems. These sensory systems provide information to the nervous system that is used to establish an internal schema of the body's motion and how it relates to the external environment (Mackinnon, 2018). This description represents the internal model view of motor control. Another view that can be used to explain balance control is the referent body configuration hypothesis, where stimulation of the sensory, proprioceptive and vestibular systems causing a perception of instability will lead to a shift of the referent body configuration to a new location. This causes a difference between the actual and referent configuration and primes the body to advance to the new equilibrium position in order to restore balance. Additionally, because vestibular receptors are in the head, they provide information about acceleration of the head but not the entire body and as a result, the vestibular system may find it hard to distinguish between head tilting on a stationary body and head tilt due to entire body rotation at the ankles (Kandel et al., 2013). As such, the vestibular system relies on information from other sensory organs in order to control and regulate balance. It is important to note that the contribution of each sensory modality to balance changes according to the task at hand. In some instances, such as when standing on a firm surface, subjects tend to rely more on their somatosensory activation to control balance. On the other hand, when the support is unstable, subjects depend more on vestibular and visual information (Kandel et al., 2013). All these sensory modalities converge at multiple levels of the neuraxis to influence balance control.

2.2.1 Vision

Visual input plays an important role in balance regulation in that it provides information about motion information both centrally and peripherally. It also helps reduce body sway and provides stabilizing cues especially when attempting a new balancing task (Kandel et al., 2013). For example, people who do skating rely on vision to maintain stability while spinning by fixing their gaze on a point in the visual field. However, because visual processing is too slow, it is not very effective in affecting balance control in the advent of a sudden disturbance. The visual system also plays a great role in anticipatory postural adjustment to maintain balance, especially in voluntary tasks where it assists us in carrying actions like placing our feet in the right places when walking over obstacles while still maintaining our balance. In a study analyzing judo athletes, Paillard et al. (2002) showed that they were more dependent on visual information to control their posture and had better balance when their eyes were opened than when they were closed. Similarly, Romero-Franco et al. (2012) looked at the effect of a proprioceptive training program on the ability of sprinters to control their center of mass and what they found was improvement in balance of these athletes when they performed the training with their eyes opened rather than with their eyes closed. The importance of vision can also be seen in studies that compared the ability to control balance between children who had visual impairment compared to children without visual impairment. The results from this studies showed that children with visual impairment performed worse in both static and dynamic balance tasks than those without visual impairment (Haibach et al., 2011). Furthermore, Zylka, et al. (2013) showed that young girls with visual impairments were able to control their balance when sitting, standing and walking. However, their ability to control their balance was very low when their base of support was narrowed, or in situations in which their center of pressure was shifted towards their base of support boundary. In contrast, another study showed that in the absence of vision, people who were born with total blindness might have developed superior proprioceptive and vestibular reactions as these subjects showed better postural control than subject who were blindfolded (Juodzbaliene & Muckus, 2006). It should be noted that the visual system on its own cannot regulate balance control since it does not properly distinguish between self motion from object motion, providing ambiguous feedback that might lead to instability (Kandel et al., 2013). As such, through connections with the vestibular system through both the dorsal and ventral stream of vision, the visual system and vestibular system interact to maintain posture stability and balance.

2.2.2 Somatosensory System

Our somatosensory system, via the action of proprioceptive receptors found on our joints, muscles, and tendons, provides the nervous system with information about the movement of body segments and their relationship with the base of support (MacKinnon, 2018). This also contributes to the conscious awareness of our body location in space. This knowledge is obviously very important for the regulation of balance. The muscle spindles in our muscles encode muscle length and rate of muscle stretch. They provide nervous system information about the relative position and motion of the joint. Another proprioceptive receptor called Golgi tendon organs, particularly those in the lower-limb extensor muscles are important in sensing the forces to resist forces such as gravity and imposed loads, regulating the activity required for maintaining vertical support and postural stability. The cutaneous receptors on the feet provide feedback about the base of support, the direction, level and the rate of load bearing, as well as the compliance and geometry of the support surface. Qiu and colleagues (2012) showed that enhancing somatosensory information through the use of textured insole surfaces actually helped in improving the balance by reducing postural sway in older adults, especially in conditions where they stood on foam surfaces with their eyes closed. Similarly, in another study using low-level electrical noise applied to the knees to enhance the sensitivity of the somatosensory system, the balance performance was characterized using a force platform to measure the displacement of the center of pressure under the subject's stance foot. Improved balance was defined as reduction in postural sway as observed by decreases in the center of pressure measures. What the researchers found was that this application of electrical noise to the knee was effective in reducing postural sway and improving balance in elderly people (Gravelle et al., 2002). Shumway-Cook and Horak (1986) suggested that because the nervous system can only rely on one sensory modality at a time for orientation and balance information, the somatosensory information from the feet in contact with the support surface were the preferred sensory input.

2.2.3 Central Vestibular System

Apart from the visual, vestibular and somatosensory systems, other parts of the nervous system contribute to the control of balance. The cerebellum plays an important role in influencing orientation and balance via the outputs of two regions: the vestibulocerebellum and the spinocerebellum (Kandel et al., 2013). These two regions are connected with the vestibular nuclei and reticular formation. Neuroanatomical studies have shown that lesions to the spinocerebellum result in excessive postural sway that is worse when the eyes are closed, suggesting a deficit in balance control (Kandel et al., 2013). Brainstem regions are equally sites of sensory input integration and as such play an important role in the generating the internal model of the body used in maintaining balance. Additionally, the medial and lateral vestibulospinal tracts that originate from the vestibular nuclei, along with the medial and lateral reticulospinal tracts originating from the reticular formation of the pons, play an important role in postural stability and balance. Lesions to these areas have been associated with profound ataxia and loss of balance (Kandel et al., 2013). Cutaneous signals that convey information about the base of support are conducted along the fast conducting dorsal column medial lemniscal pathway to end up in the contralateral thalamus in the brain (MacKinnon, 2018). Substantial sensory conduction delays or lesions to the dorsal columns can lead to abolition of kinesthesia which is greatly associated with instability of posture and gait (MacKinnon, 2018).

The vestibular system is one of the primary components of the nervous system that is responsible for maintaining equilibrium and balance of the body both during static and dynamic situations. Consequently, any dysfunction of the vestibular system, both peripheral and central, is likely to cause a major disruption in the body's ability to remain stable. In general, the clinical manifestation of vestibular dysfunction is loss of balance ipsilateral to the affected vestibular nuclei (Kent, et al., 2010). There is enough evidence from pathology that can be used to show involvement of the vestibular system in certain aspects of the control of balance and equilibrium. Peripheral vestibular disorders are those that affect the vestibular structures of the inner ear, such as the otolith organs, semicircular canals, vestibular labyrinths (Strupp & Brandt, 2013). Some disorders of the peripheral vestibular system include vestibular neuritis, labyrinthitis, bilateral vestibular loss and Meniere’s disease. Bilateral vestibulopathy symptoms can be mimicked following selective bilateral semicircular canal lesion without any involvement of central vestibular structures such as the brainstem and cerebellum (Chen & Malmagyi, 2018). The main symptoms involved in bilateral vestibulopathy are unsteadiness when walking or standing. This provides another evidence of the importance of the semicircular canals in balance control. Central vestibular disorders are those that involve lesions or dysfunctions of areas such as the cerebellum, vestibular nuclear complex, and reticular activating system of the brainstem (Brandt & Dieterich, 2017). Some of the symptoms that occur due to central vestibular dysfunctions include imbalance, difficulty in controlling postural sway, falls (Thompson & Amedee, 2009).

In conclusion, the vestibular system plays an important role in the control of balance by providing information that is necessary to keep the center of mass within the base of support. Stimulation of the vestibular system has also been shown to improve balance both when standing and walking. Additionally, the contribution of the visual system, the somatosensory system, and the central vestibular system such as the cerebellum and reticular formation in the brainstem have shown to be important in controlling different aspects that are important to balance control.

CHAPTER 3

3.0 LOCOMOTION AND THE VESTIBULAR SYSTEM

3.1 Mechanisms of Locomotion

Locomotion can be described as a combination of various movements of body segments together performed by an organism is order to change location from one place to another. Locomotion is very important for animals as it serves various survival purposes such as search for food and shelter, fleeing from predators, and carrying on with their day to day activities. Various types of locomotion include crawling, walking, running, swimming, etc. The predominant manner in which we humans tend to locomote is walking. The manner in which we walk is called gait. Gait is characterized by repetitive sequences of limb movements to propel the body forward while maintaining balance at the same time (Kharb et al., 2011). This repetitive sequence of limb movement is called the gait cycle. More specifically, the gait cycle can be described as the period of time between any two identical phases of the walking cycle (Ayyappa, 1997). Initial contact of the heel to the ground known as heel strike is generally considered as the onset of the gait cycle, even though any event could be selected as such (Ayyappa, 1997). By definition then, the gait cycle can be defined as the period of time between two successive heel strikes. Each gait cycle comprises of two phases: the stance phase and the swing phase. The stance phase of the gait cycle includes events such as heel strike, support, and toe-off. The swing phase, is the phase in which the leg is propelled forward and consists of leg lift and swing. The swing phase begins when the foot is lifted from the floor (toe-off) (Kharb et al., 2011). There is a period during the gait cycle where both feet are in contact with the ground, called the double support phase. This phase occurs both at the end and the beginning of the stance phase (Ayyappa, 1997). It is important to note that as the velocity of locomotion increases, such as during fast walking or running, the double support time decreases. As shown in Figure 3.1, the phases of locomotion between the left and right leg during the gait cycle alternate and only correspond to each other during the double support phase.

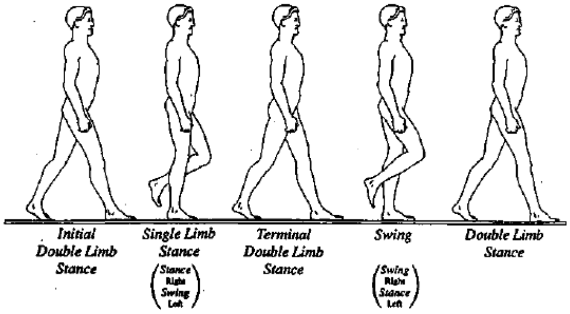

Fig 3.1 Events of the gait cycle beginning with the double support phase (Ayyappa, 1997). (Copyright @ Wolters Kluwer Health, Inc. All rights reserved).

Walking and running in humans is characterized by out-of-phase movements of the two legs and of the two arms. While the contralateral leg and arm move in phase, the ipsilateral leg and arm move out of phase (Latash, 2012). The importance of arm movements during human locomotion has been suggested to be for the minimization of trunk rotation, which is important for the stabilization of head orientation in space. It equally contributes to the stability of both vestibular signals and gaze (Latash, 2012). This lack of arm movement is an important pathological sign in bradykinesia, which is a disorder that can be seen in patients suffering from Parkinson’s disease (Latash, 2012). Indeed, locomotion is a relatively simple task to perform but is controlled by complex mechanisms that involve integration of various body segments to produce a smooth change in location from one place to another. In walking and running, our leg muscles are most active, especially during the stance phase where they serve three distinct functions: help support the body by opposing the downward pull of gravity, generate progression by helping in forward acceleration of the body, and controlling mediolateral balance during each step (Pandy & Andriacchi, 2010). The five most important muscles that perform these functions according to model calculations are the gluteus maximus and gluteus medius, the vasti, soleus, and the gastrocnemius (Pandy & Andriacchi, 2010). Whereas the gluteus maximus, gluteus medius and vasti function more to provide support in the first half of the stance phase, the soleus and the gastrocnemius are more involved in the lifting and acceleration of the center of mass in the second half of the stance phase (Pandy & Andriacchi, 2010).

Compared to other species in the animal kingdom, human locomotion is very unique in that it is more of a learned process than the maturation of various inborn reflexes (Inman, 1966). We can see this evidence with infants who during the course of their experimentation with walking have their first steps characterized with a lot of faltering steps and falls. Very quickly however, they learn how to become more stable and precise with their movements (Inman, 1966). Popova, working with Bernstein, described the mechanism of walking in growing children. In this study, she noted that the characteristic pattern of adult locomotion was not achieved until about 7 to 9 years of age. Before then, the children experiment with their neuromusculoskeletal system, adapt the displacement of various body segments to changes in body proportions, and also develop improved neural controls (Popova, 1935). This can explain the large diversity in locomotion patterns between humans. The development of adult gait from infant stepping is gradual, and it is dependent upon the growing integration of supraspinal, intraspinal and sensory control (Forssberg, 1999). In human locomotion, in the absence of internal or external factors, the body tries to integrate motion of the various segments of the body and control muscle activity in order to minimize energy required for each step (Inman, 1966). A study performed by Ralston (1958) showed that energy expenditure was higher when individuals walked either slower or faster, and was at a minimum when the participants were told to choose their own walking speed. During locomotion, there is transfer of energy from potential energy when the body is displaced up and down to kinetic energy when the body moves forward. This transfer of energy between kinetic and potential energy within the body helps conserve and minimize energy expenditure by the muscles (Inman, 1966).

Several attempts have been made to understand and explain the mechanisms involved in energy minimization and increased stability in healthy gait patterns. According to Saunders and colleagues (1953), there are six determinants of gait that if absent, will lead to an increased cost in energy consumption during locomotion, also leading to inadequate gait patterns, which they called compass gait (Saunders et al., 1953). They believed that locomotion was the translation of the center of gravity through space along a path where the least amount of energy would be expended. The six determinants of gait according to Saunders et al. (1953) included pelvic rotation, pelvic tilt, stance-phase knee flexion, knee and ankle interaction, foot-ankle mechanisms, and lateral displacement of the pelvis. In summary, the role of these different joint actions was thought to enhance walking economy by reducing the displacement of the body center of mass in the different axes of motion (Kuo & Donelan, 2010). However, research using kinematic data obtained from vertical trunk displacements during normal walking have shown that both pelvic tilt and stance-phase knee flexion have little to no effect on the magnitude of the trunk's vertical displacement during walking as was previously thought by Saunders and colleagues (Gard & Childress, 2000). Additionally, several studies have argued that the reduction in the displacement of the body center of mass during walking instead leads to increased energy expenditure rather than a reduction in energy expenditure (Massaad et al., 2007; Gordon et al., 2009; and Ortega & Farley, 2005). This implies that contrary to what was suggested by Saunders et al. (1953), minimization of center of mass displacement during walking is not necessarily desirable.

Another theory that attempted to explain the mechanics of locomotion along with the six determinants is the inverted pendulum theory. This theory suggests that the stance leg can be viewed as an inverted pendulum swinging about the ankle joint of the supporting leg, while the swing leg can be viewed as a pendulum swinging about the hip joint (Latash, 2012). This theory does well to explain the potential conservation of mechanical energy involved in locomotion, in that any change in kinetic energy will be transformed into gravitational potential energy, leading to no work performed by the muscles. In order words, this theory attempts to suggest that walking requires little to no work or force applied (Kuo, 2007). However, this theory fails to explain why walking costs energy or the reason why longer and faster steps require a different amount of work than shorter and slower steps (Kuo & Donelan, 2010). Another shortcoming of this theory is its inability to explain energy generation and absorption, as well as the different patterns of muscle activation during walking (Latash, 2012).

Expanding from the inverted pendulum approach to explain the biomechanics of locomotion, another model considers how the passive dynamics of the legs with little active control can influence the entire gait cycle. This model, called the dynamic walking model, was introduced by McGeer (1990). In his study, he demonstrated using both computational simulations and two-legged machines, that walking could occur even on level ground with minimal active energy input (McGeer, 1990). In a subsequent study, new machines with knees were developed to expand on the original work from McGeer, where knee extension was passively stopped to maintain the stance leg in full extension and prevent knee hyperextension. The logic was to induce passive support of the body weight so that the single limb support phase could be produced with no need for active control. He concluded from his observations that the principles of dynamic walking could also apply in passive situations (McGeer, 1990). Other studies have shown that rather than passive leg dynamics producing gait, muscles actually do more positive work during human locomotion. This implies that muscles act to prevent the dissipation or loss of energy during human locomotion (DeVita et al., 2007). Several studies suggested that level walking produced net muscle work of zero and did not explain any difference in net positive and negative muscle work in ascending versus descending walking. DeVita et al. (2007) in their study with thirty-four healthy human adults walking while maintaining a constant average velocity on level ground and while ascending or descending a ramp, showed that muscle work was more biased towards positive work (energy generation) over energy dissipation (negative work) in all walking conditions. Additionally, it was found that the net positive work done during ascending walking was more than during descending walking (DeVita et al., 2007). However, they were cautious with their interpretation of the results stating that further tests were necessary to see how the environment, population, and form of locomotion could affect these findings. This implies that there must be a central processor that integrates both internal (muscle and joints) and external (environment) properties in order to ensure that locomotion proceeds fluidly.

3.1.1 Computational Model of Locomotion

The control of locomotion has been a subject of debate for over half a century, with the role of the brain in this control being the central matter of this debate. For the most part, the leading theory of motor control used to explain movement and locomotion has been the internal model theory, which is part of the broader computational model. According to the computational theory of motor control, the brain controls locomotion by directly changing biomechanical variables such as force, angles, and torques that influence muscle activity in order to achieve the goal of the task (Wolpert, 1997). There have been several studies that have described the computational approach of movement. Many of these studies have tried to explain movements through the use of robotics and engineering. Computational models mostly involve the quantitative description of both the mechanical actions of muscles as well as the brain commands that activate these muscles for action (Flash & Sejnowski, 2001). The body is seen as a system whose inputs are the motor commands that originate from the central nervous system, which is considered the controller (Wolpert, 1997). Knowing the various inputs that are emanating from the brain can help determine the future behaviour of the system (Wolpert, 1997). Some studies using the computational approach have suggested that the brain controls movement and locomotion by coding for low-level parameters such as muscle force directly (Scott, 2000). Additionally, others have suggested that cortical neurons do not code for the force of a particular muscle, but for that of group of muscles, firing rate of these cells increases in proportion to movement of the muscles in the preferred direction of these neurons (Todorov, 2000). In order to perform a movement or in our case in order to walk from one place to another, the individual must first locate the target and survey the environment, there must be coordination of multi-modal proprioceptive signals, and then motor commands can be generated that drive the muscles of the legs or arms to action (Flash & Sejnowski, 2001). Cognisant of this, the computational model has tried to explain each step of the process, from motor planning, to motor prediction and learning. Because movements to achieve a specific goal, such as moving the arm to reach a cup can be performed in a variety of ways, the question now becomes how does the brain select the best possible alternative from the numerous degrees of freedom available? The computational approach explains that motor planning is achieved as the brain selects the best possible alternative such as the necessary joint angles, the actual velocity profiles, and the path that the hand should move along from the infinite number of alternatives available to perform the task (Wolpert, 1997). One computational approach that explains this better is the optimal control model which suggests that every possible movement solution has a cost associated to it, and the movement solution with the lowest cost is the one selected as the plan to perform to achieve the goal, which might be walking, running, or moving the arm (Bryson & Ho, 1975). The proposed optimal control cost-function of movements have been explained using two main models, which are the kinematic based and dynamic based models. The cost function in kinematic based models takes into account the geometric and time-based properties of motion such as the position, the joint angles, the velocities, and accelerations of the feature performing the movement. The dynamic based model for its part is more concerned with joint torques, the different forces acting on the effector, and the muscle commands that drive those effectors to action (Wolpert, 1997).

In the computational approach, neural mechanisms can mimic the input and output characteristics, as well as their inverses, of the motor apparatus (Kawato, 1999). In order for limb movements to be adapted to the different possible forces that might act on them, internal representation of these forces are formed in the brain (Pierella et al., 2019). The computational model argues that because fast and coordinated movements cannot be executed solely under feedback control since is a slow process, the brain also needs to acquire an inverse model of the body part to be controlled via motor learning, so that after this, motor control can be executed in a purely feed-forward manner (Kawato, 1999). In other words, just as neural mechanisms can be used to predict motor outputs, these same motor outputs can be used to determine the exact neural mechanisms that initiated them. This model assumes a linear relationship between neural activation and motor output. The major origin of this theory has been from robotics. The site in the brain thought to be responsible for the forward models of the limb is the cerebellum (Ito, 2002). Functional magnetic resonance imaging (fMRI) studies have also shown that the cerebellum is activated when individuals held objects with the tips of their index finger and thumb (Tamada et al., 1999). They used this as an explanation of the presence of the internal model forward activity in the cerebellum. Additionally, through the use of computer simulations based on the feedback-error-learning theory, it has been suggested that changes in neural codes and learning acquisition of the inverse dynamics model can be reproduced by knowing the synaptic plasticity of Purkinje cells in the cerebellum (Kawato, 1999). Jordan and Rumelhart (1992) introduced the concept of distal learning where the learner had to find a mapping from the desired outcomes when performing an action in order to achieve a desired outcome as a way of learning of forward and inverse models of actions. They suggested that the subject began by forming a predictive forward model by associating actions to distal outcomes, which is learned by exploring the different outcomes associated with particular action choices. Once the forward model was learned, it could be used to guide the learning of the inverse model that can be used to predict the action needed to achieve the distal outcome (Jordan & Rumelhart, 1992).

However, this approach to the control of movement and locomotion has several shortcomings. One of these involves the fact that this model does not explain how we are able to avoid falling by transferring equilibrium from one point in space to another (Feldman et al., 2011). Additionally, computational models do not provide any solution to the posture-movement problem, which is a fundamental concept in motor control. According to the computational model, the body changes from a stable posture to movement by suppressing reflexes that are active to maintain postural stability (Powers, 2010). Holst and Mittelstaedt (1950), had a different viewpoint by asking how it was possible for people to move from one stable point to another without triggering these posture stabilizing reflexes (Von Holst, 1950; Powers. 2010; Latash, 2012 pages 57-58). Another shortcoming of the computational approach is that it treats the relation between neural mechanisms that activate motor neurons and the corresponding motor outputs that ensue as a linear relationship. There is evidence suggesting that this might not be the case. Some studies have shown that several different neural activations can lead to the same motor outcome due to redundancy in the neural circuitry innervating the motor neurons. As such, predicting either the neural mechanisms that produce motor outcomes or the reverse might not be possible.

3.1.2 Referent Configuration Hypothesis Model

One theory that provides a more plausible explanation for the posture-movement problem, while explaining how the body changes from one stable posture to another without triggering posture-stabilizing mechanisms, is the referent body configuration (RBC) hypothesis (Feldman et al. 2011). The referent body configuration theory uses the physical approach perspective that considers the interaction of the body and the physical world to provide explanations for movements. According to the referent body configuration hypothesis, the central nervous system (CNS) controls movement and locomotion by resetting the spatial threshold at which α-motoneurons in the muscles are activated and by changing the referent equilibrium position of the body from one location in space to another (Zhang et al., 2018). In other words, to elicit gait, the CNS shifts the referent body location to a new location in the environment. This also offers an explanation to the posture-movement problem. According to the referent configuration (RC) hypothesis, the posture-movement problem is solved by shifting the referent equilibrium position of the body from one location in space to the other. Because the body wants to maintain equilibrium, the actual position is now considered as a deflection from the equilibrium point, which is now set at a different location in space (referent position), which is the desired position where the body wants to be. Movement occurs in order to reset the body's equilibrium. Additionally, difference between the actual and referent body configurations primes the muscles for action. The recruitment of motor units occurs when the difference between actual (x) and threshold (λ) muscle lengths is positive, (i.e., $x-\lambda \geq 0$; Zhang et al., 2018). Therefore, the difference between the actual body configuration and the referent body configuration is what primes the body for action, resulting in a forward shift in the body that produces locomotion (Figure 3.2). The rate of change of this difference between the actual and referent body configurations also influences the change in the speed of movements (Latash et al., 2010). The spatial positions at which the actual and referent body configurations are equal, are indicated by minimal muscle activation, called EMG minima (St-Onge & Feldman, 2004)

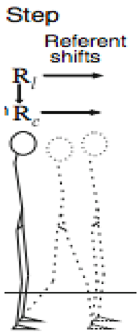

Fig 3.2 Locomotion as explained by the referent body configuration hypothesis (Feldman et al. 2011)

The referent body configuration theory originated from the work done by Asatryan and Feldman (1965) who found that changing a specific parameter called the threshold position of motoneurons, which is the position at which muscles are silent but ready to be recruited for action when stretched was fundamental in the control of posture and movement. In addition, Feldman and Orlovsky (1972) performed electrical stimulation of the pyramidal tracts in decerebrated cats and found that signals from higher brain areas such as primary motor cortex (M1) were able to influence the threshold limb position. Despite not being the predominant theory to explain the role of the nervous system in control of movement this theory has attracted much attention. This has led to a great deal of research that has helped establish this theory as a significant contributor to the present knowledge we have about motor control and the role of the nervous system. In an attempt to argue against the referent body configuration hypothesis, Gomi and Kawato (1996) argued that under equilibrium-point control the net moments driving the arm during movement are the product of the stiffness of the joint and the difference between the actual movement trajectory and the equilibrium-point trajectory (Kistemaker et al., 2007). In order to reconstruct the equilibrium-point trajectory, they first estimated the stiffness K and the damping B of the neuromuscular system by subjecting their subjects to controlled musculoskeletal system perturbations. Then these parameters together with the inertia, I, of the second-order-mass spring damping (KBI) model were optimized to achieve a best fit between perturbation responses observed experimentally and the KBI-model’s responses. They then used the estimated stiffness, damping and inertia, and the measured kinematics to calculate the equilibrium points (Kistemaker et al., 2007). From this they concluded that the equilibrium-point trajectories did not resemble the actual movement trajectories. However, in their study, Kistemaker and colleagues (2006) using a musculoskeletal model of the arm to explore the feasibility of equilibrium-point control for fast arm movements and found that responses of the musculoskeletal model to perturbations were similar to the actual movement produced by human subjects (Kistemaker et al., 2007). This prompted them to conclude that rejection of the equilibrium-point control theory by experimentally estimating stiffness using a KBI-approach and reconstructing equilibrium-point trajectories was unjustified (Kistemaker et al., 2007). They argued that this was because the estimated stiffness based on the KBI model used in most of the studies to reject the equilibrium-point hypothesis was different from the actual stiffness of the musculoskeletal model they used (Kistemaker et al., 2007).

Muscle activity obtained from EMG and corresponding neuronal activity in the cortex have been shown to correlate with overall characteristics of motor tasks such as the magnitude, velocity, and direction of movement (St-Onge & Feldman, 2004). This hinted at the ability of the nervous system to influence some global factors or properties of the system to control all muscles in a coherent manner. One such global factor that has been explained as influencing the activity of functionally diverse muscles in the coactivation (C) command, which occurs as a result of a change in the thresholds of activation of motoneurons of opposing muscle groups (Feldman & Levin, 1995). The activation threshold of a muscle can be defined as the joint angle that separates the zone in which motor units of the muscle are silent and the zone in which they begin to be recruited. The angular zones in which these groups are activated may overlap or not, depending on the values of the threshold angles for opposing muscle groups acting at the same joint. This will result in either coactivation (C>0) or co-silence (C<0) zones (St-Onge & Feldman, 2004). The concept of the activation threshold can also be generalized in such a way that we can have a generalized threshold that is the configuration of the body at which all skeletal muscles may reach their individual recruitment thresholds (Feldman & Levin, 1995). This configuration was considered as the referent (R) configuration with which the actual configuration of the body is to be compared. They suggested that the difference between both configurations was a global factor that influenced all muscles of the body and that the R configuration was modified by the nervous system to elicit movement of any kind (St-Onge & Feldman, 2004). The view of the referent configuration hypothesis is that biomechanical, afferent and central interactions between neuromuscular elements tend to minimize the difference between the referent and actual configurations of the body or body segment. In certain instances, during movement, both configurations might match each other, leading to minimization of the EMG activity of all muscles involved in the movement, which is identified as EMG minima. The referent body configuration hypothesis further suggests that neural factors, rather than mechanical factors are responsible for this EMG minimization in the activity of multiple muscles. In order to verify these, St-Onge and Feldman (2004) carried out an experiment where they analyzed the EMG patterns of several functionally diverse muscles of the legs, trunks and arms during jumping and stepping in place. What they found was that there was a global EMG minimum in the activity of all muscles that was observed when the participants were at the apex of the jump (St-Onge & Feldman, 2004). They also found another minimum near the point of transition of the body from flexion to extension leading to a jump (Figure 3.3). Similar EMG minima were found during stepping where they observed that EMG minima usually occurred near the beginning and end of the stance phase, as well as during maximum elevation of the foot (St-Onge & Feldman, 2004). These results led to the confirmation of the hypothesis that neural factors were responsible for the minimizing of EMG activity during movements.

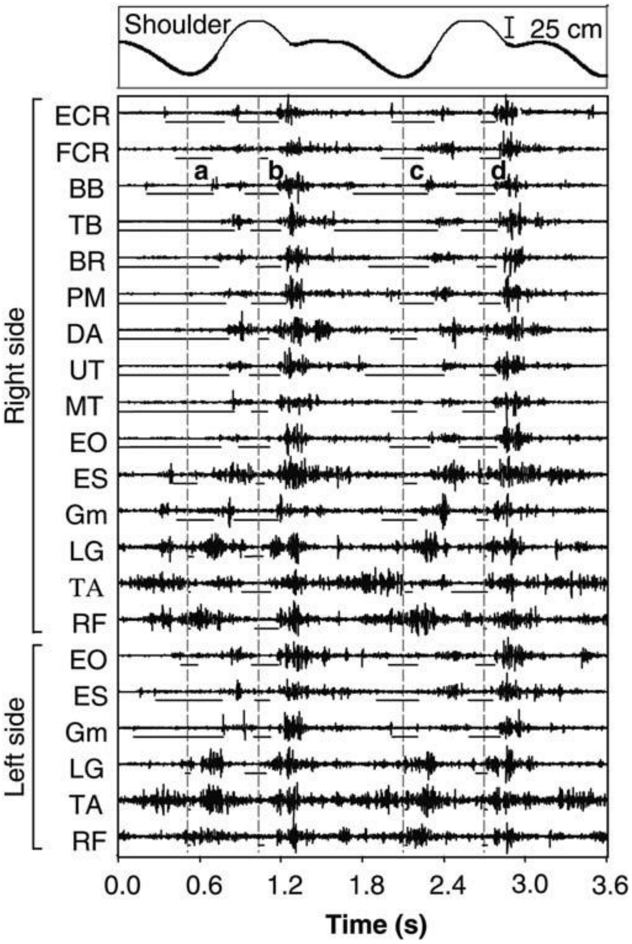

Fig 3.3. EMG activity of all muscles during jumping activity. The light vertical lines illustrate points of EMG minima (St-Onge & Feldman, 2004).

Every movement we perform entails taking into account both internal and external forces that act on the body to maintain equilibrium while performing these movements and one important force that has to be overcome or balanced is the gravitational force. Feldman (2015) suggested that for whole body actions, only the referent configurations that resulted in actual configurations that were appropriately oriented in the gravitational field were used to control posture and movement, therefore suggesting the efficiency by the nervous system in regulating movement. Feldman (2015) went on to explain that during quiet standing, since the center of mass was in front of the ankle joints, there was a small gravitational torque that caused the body to lean slightly forward from the referent position (Feldman, 2015). Because of this deviation of the actual body configuration from the referent configuration, this causes the ankle extensors to be activated, leaning the body slightly forward until active and passive muscle forces begin to balance the gravitational force. This leads to a slight forward lean of the body with respect to the vertical (Mullick et al., 2017). To intentionally lean the body forward, the referent body configuration has to be moved forward to bring it closer to the actual body configuration, causing an increase in the activation threshold of ankle extensors and other antigravity muscles. Because of this increase in the threshold, the activity of these muscles will drop, and the unbalanced gravitational force would cause the body to lean forward again to create a difference between the actual and referent configurations, leading to a re-stretching of ankle extensors and antigravity muscles (Mullick et al., 2017). This explanation can also be extended to explain locomotion as to how the body is able to move forward and backward and how the nervous system indirectly controls the parameters necessary for that to happen. In order to test this hypothesis, Mullick et al. (2017) conducted an experiment in which they subjected participants to three tasks: in the first task, participants stood on a horizontal surface. In the second task, the subjects were asked to lean forward intentionally while standing on a horizontal surface and in the last task, they were asked to rhythmically lean their body. In the 3rd task, what they found was that at certain positions of the body, the actual and body configurations overlapped, resulting in minima in muscle activity, confirming that movement of the body can be explained using the referent body configuration hypothesis and did not have to be pre-programmed (Mullick et al., 2017). Descending brain pathways, especially the corticospinal pathway has been found to influence the neurophysiological variables that are responsible for resetting the threshold position at which muscles were silent but ready to be recruited. This was first established in a study of tonic electrical stimulation of the pyramidal tract in decerebrated cats by Feldman and Orlovsky (1972). A study by Raptis et al. (2010) attempted to verify if active changes in wrist position would lead to threshold position resetting and also tested the role played by the corticospinal pathway, as well as other descending pathways, in effecting threshold position resetting and setting the spatial frame of reference in which the neuromuscular periphery is constrained to work (Raptis et al., 2010). They established that if the corticospinal pathways were involved in threshold position resetting, then the steady state of the pathway should change with a transition to the new position, and this changed threshold position should be maintained after the movement offset, even if the activity of the α-motoneurons at the new position return to the level of activity before movement onset (Raptis et al., 2010). On the other hand, if the corticospinal pathway was instead involved in direct programming of motor activity, then corticospinal excitability should return to the pre-movement level if the muscle activity returns to pre-movement levels (Raptis et al., 2010). To test this hypothesis, subjects were asked to perform wrist movements from an initial extended position of the wrist joint to a final flexed position and vice versa. A torque motor was used to compensate for passive wrist muscle forces so that muscle activity of the wrist muscles was equalized at each position and transcranial magnetic stimulation (TMS) was applied at each wrist position. What they found was that in response to mechanical perturbations, the excitability of motoneurons was similar at the two wrist positions, with the same TMS eliciting a wrist extensor contraction in the extended wrist position and a flexor contraction in the flexed wrist position (Raptis et al., 2017). This study provided evidence that the corticospinal pathway and possibly other descending pathways played a role in resetting the threshold position for muscle action.

The control of locomotion has also been explained by looking at central pattern generators (CPG). This was first demonstrated by Graham Brown in 1911 by showing that there were CPGs in locomotor-like EMG activity when proprioceptive reflexes were absent following deafferentation (Brown, 1911). According to various studies, the CPG elicits coordinated rhythmical activity of numerous muscles of the body, while also controlling the reflex influences on this activity by facilitating or inhibiting α-motoneurons at specific phases of locomotion (Feldman et al., 2021). These CPGs can also have their phase shifted due to reflex reactions to perturbations, establishing the importance of these CPGs in phase resetting of locomotion (Feldman et al., 2011). Studies of the H-reflex by Capaday and Stein (1987) and other reflex responses of motoneurons at different phases of locomotion gave shown that muscle activity during normal human gait is basically produced by the CPG with less contribution of proprioceptive reflexes, with the contribution of CPG to locomotion being phase dependent (Feldman et al., 2021). Feldman went on to illustrate that some important features of parametric control of body segments are similar to how external objects in the environment act i using an example of a stone thrown in the air. In this example, he explains that whether the parameters are changed or not, they do not influence the causality inherent in physical or physiological laws but influence how these laws are manifested. In the case of the stone thrown in the air, motion of a stone obeys the second law of Newton regardless of the mass of the stone (Feldman et al., 2021). This point gives us perspective into how the nervous system can indirectly influence motion using parametric control of the threshold at which muscles are activated and for the nervous system to equally allow all components of the body to manifest their natural physical and physiological properties without any internal representation of such properties (internal models) (Feldman et al., 2021). Additionally, the nervous system can also help change the threshold activation of muscles and use sensory feedback such as sound, vision, and kinesthesia to report that the targeted equilibrium point has been reached (Feldman et al., 2021).

The referent body configuration hypothesis has been used to explain how the step cycle and continuous human locomotion is controlled. According to this hypothesis, during quiet standing, the ankles are in the neutral position with the feet flat on the ground, constituting the initial actual body configuration, Q*i*. Conversely, the referent configuration R of the ankles are in the virtual plantar flexion, such that the feet are virtually penetrating the ground (Fig 3.4). Because the ground is preventing the feet from penetrating the ground to reach the referent configuration of the ankles, there is a difference that is created between Q and R, causing activation of antigravity muscles like the gastrocnemius, soleus, and peroneus longus, which produce the force necessary to compensate these ground reaction forces (Feldman et al., 2021). The swing phase of the right leg is achieved by changing the referent body configuration to transfer body weight to the left leg and to move the referent posture of the right leg into flexion. The referent trajectory is formed ahead of the actual position during the swing phase, and when the phase of locomotion transfers from stance to swing, the actual and referent ankle positions sometimes coincide and match each other, resulting in a minimal EMG activity in numerous leg muscles (Feldman et al., 2021). During mid-swing, the referent toe trajectory is redirected towards the ground to provide transition of the right leg to the next stance phase, completing the gait cycle (Feldman et al., 2021).

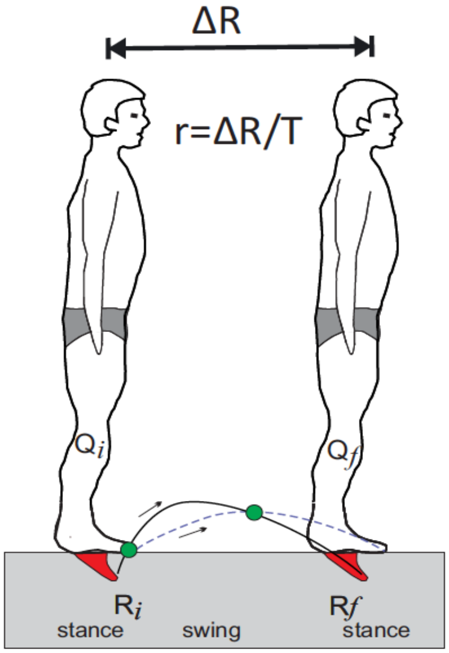

Fig 3.4 Figure displaying the configuration of the body at stance and swing phases, with the red colour displaying the inward trajectory of the referent toe configuration (Feldman et al., 2021).

3.2 Evidence of Vestibular Function in Locomotion

Concerning locomotion, the function of the vestibular system has still not been very well established. Very few studies have described the role of the vestibular system in locomotion, with most studies limiting the role of the vestibular system to stabilizing gait posture. However, there is evidence that the vestibular system contributes more than that in locomotion processes. Bent et al. (2004) found that there was a difference in vestibular regulation between upper and lower limb muscles. Using GVS, they found that vestibular regulation in the control of the head, trunk or pelvis was the same throughout the gait cycle and did not depend on when the stimulation was delivered. On the other hand, the regulation of lower body control (foot placement) by the vestibular system, was more phase dependent, with greater regulation of lower body control occurring during heel strike compared to mid swing or during toe-off. This implies that the vestibular system helped in modulating foot placement that is important in transferring the center of mass forward during locomotion (Bent et al., 2005). Additionally, by evaluating the vestibulo-ocular reflex gain (horizontal semicircular canal function) and cervical and ocular vestibular evoked myogenic potentials (otolith function), it was found that reduced horizontal semicircular canal function was associated with longer, but slower steps in healthy adults. However, the otoliths were not found to affect gait speed or stride length (Anson et al., 2018). Furthermore, it has been suggested that vestibular control of locomotion is inhibited or less active during running and more active when walking (Brandt et al., 1999). Also, noisy GVS was also found to increase the gait speed of both normal individuals and individuals with bilateral vestibular pathology (Iwasaki et al., 2018). Therefore, according to most of these studies, the vestibular system is associated with setting the pace of locomotion.

3.3 Objectives and Hypotheses

Most of the studies that have investigated the role of the vestibular system on locomotion and walking have done so using the computational approach of motor control to analyze their findings. This is problematic because the computational approach considers locomotion as a sequence of falling and catching based on biomechanical responses. On the other hand, the physical approach recognizes that muscle variables cannot be directly specified due to the nonlinearity of the system and accounts for the transfer of stability from one position to another to avoid falling (Feldman et al., 2021). Additionally, there is little literature concerning the role of vestibular structures and neurons such as semicircular canals and otolith and how they help with locomotion. The objectives and hypotheses of our study are the following:

Objectives

- To determine if stimulation of the vestibular system using GVS leads to a shift in the phase of locomotion in steps where there was GVS applied compared to steps where there was no GVS.
- To determine if there is a difference in changes between two successive EMG minima in steps with GVS compared to steps without GVS.
- To determine if head position and input from the visual system affect the degree of phase shift in locomotion and also the rate at which the referent body configuration shifts from one location to another.

Hypotheses

- The first hypothesis is that stimulation of the vestibular system will lead to shifts in the phase of locomotion, with the magnitude and direction of the shift being more pronounced in conditions where GVS is applied.
- The second hypothesis is that in steps with GVS, there will be a faster shift in the referent body configuration, implying a faster change in gait speed compared to steps without GVS.
- The third hypothesis that changes in head position will affect both the rate of change in EMG minima in steps and the phase shifts in locomotion. Additionally, conditions in which the visual system is supressed will result in a greater impact of vestibular input evidenced by higher magnitude phase shifts and slower shifts in EMG minima.

CHAPTER 4

4.0 METHODS

The research was a pilot proof of concept of the study. We conducted a 3x2x2 study using a factorial design. There were three factors in the experiment which were head position, visual condition, and GVS. The head position factor had three levels (head straight, head right, head left), the visual condition had two levels (eyes open and eyes closed) and the GVS had two levels as well (no GVS and GVS on). The combinations of these levels to form the experimental conditions are shown at the end of the paragraph. The purpose of this experimental research design was to determine the role of the vestibular system on the control of locomotion as explained by the referent body configuration hypothesis. We also wanted to determine if electrical stimulation of the vestibular system would lead to phase resetting in gait. Our independent variables were: head position, eyes open or closed, presence or absence of GVS. The dependent variables were: time difference between successive EMG minima during the gait cycle, and phase shifts during the gait cycle. We specifically used a within subject factorial design to determine how changing the different conditions of the study affected the dependent variables in the same individual. There were seven different conditions that were used to collect the data and were presented in a random order. Each of the conditions had 10 trials each. These conditions were:

- Head straight + eyes open + no GVS
- Head straight + eyes open + GVS
- Head straight + eyes closed + GVS
- Head turned to the right + eyes open + GVS
- Head turned to the right + eyes closed + GVS
- Head turned to the left + eyes open + GVS
- Head turned to the left + eyes closed + GVS

The different conditions were chosen for a variety of reasons. The first condition was the baseline condition. This condition was used to compare responses with other conditions to see if GVS produced phase resetting in the gait cycle and if it also led to a change in the rate at which the referent body configuration moves from one place in the environment to the other in order to produce gait. Head position was important when stimulating the vestibular organs that are responsible in helping us sense balance and body position. Depending on the head position, either the semicircular canals or the utricles would be activated. These organs sense different forms of body accelerations and report different aspects of body orientation to help balance the body. Therefore, it made sense that while stimulating the vestibular system, we controlled for head position in order to understand which part of the vestibular system might be playing a role in helping shift the referent body configuration to produce gait. We also aimed to determine if there was a difference in vestibular input depending on whether the participant's visual system was active or not. With visual stimulation, which was experienced when the eyes are open, postural sway was not as pronounced as when the eyes are closed, showing the compensatory influence of the visual system on posture and balance. However, when the eyes were closed, postural sway and deviation were expressed more strongly. In a study conducted by Fitzpatrick et al. (1999), vestibular stimulation of the subject when their eyes were closed produced a significant deviation from the intended path compared to when they had their eyes open. This explains why we decided to vary visual stimulation during the procedure. There are different ways to stimulate the vestibular system, some of which include electrical vestibular stimulation (EVS) and GVS. We chose GVS because of its ability to produce postural sway and also the non-invasiveness of the stimulation method. However, one inconvenience of this method is the non-specificity of the stimulation due to the use of surface electrodes placed over the mastoid. This method does not allow us to determine which specific part of the vestibular apparatus was being activated when the vestibular system was stimulated.

4.1 Participants

The participants for this study were both men and women between the ages of 18 and 30 years of age. The criteria for inclusion were: being healthy, having no history of mobility problems due to musculoskeletal or neurological injury (stroke, epilepsy), having no history of vestibular damage or dizziness, having no blindness or visual impairment that could interfere with motion ability. The participants were chosen based on convenience and availability. The recruitment of these participants was done from McGill University, Concordia University, the Jewish Rehabilitation Hospital, and using social media like Facebook. The majority of the participants were students, but some came from other walks of life in order to diversify the participant pool. There were 10 participants in the study proper (n=10), but a total of 18 participants participated in the full data collection protocol. The other 8 participants served as pilot test participants in order to properly set up our methodology. The number of subjects was a convenience sample in order to conduct this proof of concept pilot study within the time constraints of the program.

Additionally, in order to reduce attrition rate and increase chances of subject participation, the initial trials and conditions of the study were reduced from the initial 3x3x2x2 factorial study to a 3x2x2 factorial study. The number of trials per condition was also reduced from 20 to 10 trials per condition. Subject signed an informed consent form and were provided $30 compensation.

4.2 Procedure

Data collection sessions took place in the Sensorimotor Control and Rehabilitation Laboratory in the Research Centre of the Jewish Rehabilitation Hospital, Laval.

The participant was asked to walk from a starting location to an end location, which was indicated by green tape placed on the floor at opposite ends of the room at a distance of 6 meters. The participant was always instructed to begin walking with their left leg and adopt a normal walking speed. The participant was instructed to begin when hearing a verbal “go” signal. During the baseline condition, no GVS was applied. For the six remaining conditions, GVS was applied at the 5th step, which corresponds to the 3rd step of the left leg, at a time when they had achieved a steady-state locomotor velocity. For the first four steps, the Grass stimulator was turned off and switched on immediately following heel-strike for the right leg (fourth step). Because of the deviation that might be observed when GVS was applied, a research assistant was present to provide support in case the participant lost his/her balance. The duration of each GVS stimulation was 2s. Each condition had 10 trials, bringing the total number of trials to 70, barring any error in recording where trials would have to be repeated. In conditions in which the eyes were closed, there was a research assistant to tell the participant where to stop.

4.3 Data collection

4.3.1 Optotrak kinematic Sensors & Camera

The Optotrak system was used to record marker movements, kinetic and electromyographic (EMG) signals in real-time. Eight Optotrak markers were placed on the bony landmarks of the participant (Table 1). Six surface EMG (Table 2) electrodes were placed on the lower leg muscles of each leg and 2 accelerometers were placed on each lateral malleolus. Marker data was collected at 100Hz for 10s per trial.

Two Optotrak Certus 3-camera bars were used to view the marker positions at every point of the subject’s movement from starting point to the end point. The cameras were connected to the Optotrak system unit, and the Optotrak data acquisition unit (ODAU). Optotrak markers were plugged into two 3020 strobers. The Optotrak markers were taped to the different body landmarks using double-sided tape, and the two strobers were attached to a Velcro belt that was placed around the abdomen. The software NDI first principles software was used to operate the kinematic system, and a pedal was used to trigger the system recording of kinematic data in synchrony with EMG Delsys and Signal recording. A calibration cube connected to the Optotrak system unit was used to define the area of recording and to define the different axes of movement. When this was done, the calibration cube was disconnected and strober 1 was connected to the Optotrak system unit for visibility of the markers by the NDI First Principles software. In order to ensure the visibility of the Achilles tendon markers, the cameras were tilted forward at an angle of about 30°. The cameras recorded the markers as the participant walked from one end to the other end of the walking path and visibility of markers was confirmed by checking the software.

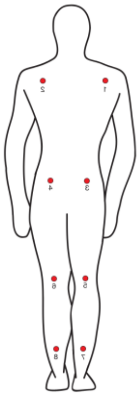

Figure 4.1. Diagram displaying the placement of markers on different body landmarks.

Table 1. Marker number and names of bony features to which they were assigned. In brackets includes the abbreviations of the bony features used throughout the research.

	Marker No.	**Body location**
Strober 1	1	Left scapula
	2	Right scapula
	3	Left posterior superior iliac spine (LPSIS)
	4	Right posterior superior iliac spine (RPSIS)
	5	Left posterior aspect of the knee
	6	Right posterior aspect of the knee
Strober 2	7	Left Achilles tendon
	8	Right Achilles tendon

4.3.2 Delsys EMG Electrodes

The EMG Delsys system (Delsys Incorporated, Natick, Massachusetts) is comprised of wireless electrodes that measure electrical activity in the muscles. We placed 5 electrodes on five different muscles of each leg, which amounted to 10 electrodes used in total. The list of the electrodes and muscles can be seen in Table 2:

Table 2. Electrode number and names of muscles to which they are assigned. In brackets includes the abbreviations of the muscles used throughout the research.

Electrode Number	**Name of muscle**
1	Left Soleus (*lSOL*)
3	Left Gastrocnemius Lateralis (*lGL*)
4	Left Gastrocnemius Medialis (*lGM*)
5	Left Tibialis Anterior (*lTA*)
6	Left Peroneus Longus (*lPL*)
7	Right Soleus (*rSOL*)
8	Right Gastrocnemius Lateralis (*rGL*)
9	Right Gastrocnemius Medialis (*rGM*)

10	Right Tibialis Anterior (*rTA*)
11	Right Peroneus Longus (*rPL*)

In addition to having EMG electrodes and markers on, participants also had accelerometers placed on their feet in order to monitor the movement of the legs and trace how the phase of locomotion shifts following GVS. Also, the data from the accelerometer was used to identify where in the step does EMG minima occur. There was one accelerometer on the left leg, which had two axes, the X and the Y axis. The right leg contained two accelerometers and each of these accelerometers represented either axis.

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Figure 4.2. EMG placement

4.3.3 Galvanic Vestibular Stimulation (GVS)

For the GVS stimulation, AgCl electrodes were placed on the mastoid processes, with the anode on the left mastoid and the cathode on the right mastoid. The intensity of the current was then tested and a choice was made based on the tolerance threshold of the participant. The accelerometer on the left ankle was connected to a Grass stimulator and served as GVS trigger whenever the left leg was in heel strike. The data collection began with the baseline condition.

The galvanic vestibular stimulation was done using a s88 Grass Stimulator (Grass Instruments Co, West Warwick, Rhode Island) (Figure 2). The stimulator was connected to a Grass SIU5 isolation unit to monitor the current, which was then connected to a Grass constant current unit. Two wires from the Grass constant current unit were connected to the mastoid of the participant, causing them to feel the stimulation. The s88 Grass stimulator also received an input connection from the accelerometer box in order to trigger it with each movement of the left leg, and was connected to ADC input 4 (channel 5) of the CED block in order to be displayed on the Signal 7 software (Cambridge Electronic Design Limited, Cambridge, England). The different parameters set for the GVS stimulation and current were: Stimulation duration-2s, voltage at 40V, current intensity between 0.5mA and 2.5mA. The current intensity was adjusted using a current adjuster on the Grass constant current unit. In each trial, there was an average of 4 stimulations.

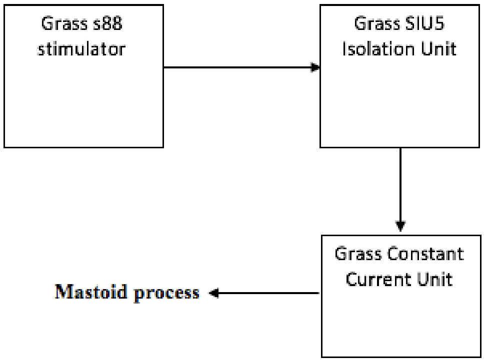

Figure 4.3 Diagram showing how the devices for vestibular stimulation were connected to each other.

4.3.4 Signal 7 Software and EMGworks Acquisition

Alongside the EMGworks Acquisition software, Signal 7 software was also used to collect EMG data. EMGworks is the software that is linked with Delsys EMG and it was used to collect EMG data directly. The EMGs were modified and set up using this software. Attached to the Delsys EMG power box was a transmission box to which a CED power3A block containing 8 channels with an extension block of 8 channels (total of 16 channels) was connected. The CED block was connected to the Delsys transmission box through 16 BNC cables from the ADC inputs of the CED block to the transmission box. This CED power3A block was linked with the Signal 7 software, which displayed the same data collected by the EMGworks acquisition software. In addition to displaying data collected from the EMG electrodes, the Signal 7 software also displayed data from the accelerometers and the s88 stimulator. Table 3 shows the channels and what they represent. Also, Figure 4 shows the different connections of the materials used in the study. The sampling frequency used for EMG and accelerometer data was 2000Hz for 10 seconds, for a total of 20000 points per frame.

Table 3. Channel numbers and channel names.

Channel Numbers	Channel Name
Channel 1	Right Accelerometer-Y axis
Channel 2	Right Accelerometer-X axis
Channel 3	Left Accelerometer-X axis
Channel 4	Left Accelerometer Y-axis
Channel 5	GVS
Channel 6	Left-Soleus (L-SOL)
Channel 7	Left- Gastrocnemius Lateralis (L-GL)
Channel 8	Left- Gastrocnemius Medialis (L-GM)
Channel 9	Left-Tibialis Anterior (L-TA)
Channel 10	Left- Peroneus Longus (L-PL)
Channel 11	Right-Soleus (R-SOL)
Channel 12	Right-Gastrocnemius Lateralis (R-GL)
Channel 13	Right-Gastrocnemius Medialis (R-GM)
Channel 14	Right- Tibialis Anterior (R-TA)
Channel 15	Right- Peroneus Longus (R-PL)

4.4 Data Analysis and interpretation

4.4.1 Phase Resetting Analysis

Analysis of the phase of locomotion and how it was affected by GVS was done with Signal 7 software. Accelerometer pulse recordings of leg movement were used to determine the phases of locomotion. A step was defined as the trough-to-trough time difference of a single accelerometer pulse. In this analysis, the first two steps, (i.e, the first step by the left and right legs) were not taken into account because the participant was assumed to be reaching their stable locomotor state. Each leg was analyzed independently. For simplicity sake, we label the step before GVS in each leg as step 1. The first step post GVS is labeled as step 2 and the next step as step 3. To determine locomotor phase, the duration of step 1 in each leg was determined, i.e., the first steps taken into consideration for the left and right legs, respectively, as well as the last steps before the application of GVS. For the left leg, the duration of the last step before GVS application was determined as the period, T, in seconds. To determine the projected phases of locomotion, time T was added to the time of onset of the first and second steps post GVS to determine the offset time of each step. This gave us the projected phase of locomotion if no change in the step cycle as determined from accelerometer data occurred. To determine the phase shift, Δt, the actual offset time of the first and second steps post-GVS was subtracted from the projected offset time of the pre-GVS step, T. To convert Δt to degrees, we used the following formula:

$$\frac{\Delta t}{T} \text{ x } 360$$

Each of the conditions was analyzed separately using accelerometer data. Data from the left accelerometer and right accelerometer were also separately analyzed. In order to better quantify the effect of vestibular stimulation on the locomotor phase shift, the predominant phase shift behavior in each condition was determined, rather than averaging the absolute values i.e., either positive phase shift (longer step) or negative phase shift (shorter step). For example, in the no head turn, eyes open condition, if the majority of trials in the first step post GVS (step 2) were positive, and those of the second step post-GVS (step 3) were negative, we averaged only the positive trials for step 2 and only the negative trials for step 3. Also, phase shifts were analyzed in terms of the magnitude of the shift (how negative or positive shifts between conditions differed) and direction (if the shift was negative or positive) relative to the first step pre-GVS. We also only analyzed the 3rd step for the eyes closed conditions because the 2nd step mostly showed little sensibility to GVS.

4.4.2 EMG Minima Analysis

Analysis of EMG minima data was used to test the hypothesis that GVS causes a change in the speed of locomotion. This was determined by comparing the time difference between two successive minima in a gait cycle without GVS to that of minima occurring in a gait cycle with GVS. A shorter time difference is synonymous with a faster change in referent body configuration and location, which can also be interpreted as faster speed of locomotion. In order to find the EMG minima, the recordings of the EMG signals were filtered (bandpass 2^{nd} order, Butterworth model at frequencies between 50 and 350Hz) and processed using LabVIEW software (version 5.1, National Instruments Corporation, Texas, USA). An EMG minimum was defined as the time at which the overall activity of all muscles in a leg was less than 5% of the maximal EMG amplitude of all leg muscles. Signal software was used to determine the time of onset of GVS.

In addition, to determine the effect of GVS on walking speed, the distance between EMG minima was determined by a MATLAB code and the walking speed of each step in cm/s was calculated.

4.4.3 Kinematic Analysis

In order to obtain appropriate results from the kinematic data collected by Optotrak, several transformations were carried out. Graph.EXE software (version 1.1.0.3, MFC Application, USA) was used to interpolate missing data. The files were exported to Microsoft Excel by the NDI first principles software. Microsoft Excel software was used to calculate the height of markers 7 and 8 with the measurement of the marker relative to the participant's heel. The files were eventually used in MATLAB (version R2019a; MathWorks, MA, USA) by a code to transform the marker distances into stick figures of the gait of the participant. The positions of the EMG minima were illustrated in the time series of the kinematic profiles of walking (Figure 4).

4.4.4 Statistical Analysis

In order to determine if the effect of GVS on the kinematics of gait according to the theory of the referent configuration of the body was significant, the time between each minimum EMG was calculated and a linear mixed model analysis of the effects of visual conditions, head position and GVS on EMG minima and phase shift was carried out to compare the different conditions. Levene’s test was carried out to determine the equality of variance in the data. Additionally, phase shifts with and without GVS were compared with a linear mixed model with post-hoc tests, and an initial *p*-value of 0.05.

CHAPTER 5

5.0 RESULTS

5.1 Effect of GVS and Head Position on the Change in Phase of Locomotion

We hypothesized that stimulation of the vestibular system using GVS would cause a shift in the phase of locomotion and that there would be a difference in the effects of head position on this shift in the phase of locomotion. Additionally, we hypothesized that conditions in which the eyes were closed would show a more pronounced shift in the phase of locomotion compared to conditions in which the eyes were open. We carried out a linear mixed model in order to compare the effect of the different head positions on phase shift and how these effects differed from each other. We analyzed the results of each leg separately.

For hypotheses 1and 3, in the left leg and the eyes open condition, there was no significant difference between the head straight (*M* = 8.121°, *SD* = 17.194), head right (*M* = 0.149°, *SD* = 26.506), and head left (*M* = 8.339°, *SD* = 25.607) in phase shift 1. In the eyes closed condition for phase shift 1, there was also no significant difference between head straight (*M* = -0.166°, *SD* = 27.460), head right (*M* = 15.628°, *SD* = 20.624) and head left (*M* = 10.660°, *SD* = 23.414). Looking at phase shift 2, a similar result was obtained as there was no significant difference in the eyes open condition between the head positions; head straight (*M* = -17.803°, *SD* = 31.137), head right (*M* = 5.125°, *SD* = 42.833) and head left (*M* = 6.116°, *SD* = 33.769). For the right leg, the results were similar as there were no differences between the effects of the different head positions on both phase shift 1 and phase shift 2 in either the eyes open or eyes closed conditions (See Table 5 for complete descriptive statistics).

Table 4. Means and standard deviations (in degrees °) for the effects of the different head positions on the phase shift in the right and left leg for eyes open and eyes closed conditions.

Eye condition	OPEN		CLOSED	
Left Leg				
GVS **Head position**	Phase shift 1	Phase shift 2	Phase shift 1	Phase shift 2
Straight	8.12° ± 17.19	-17.80° ± 31.14	-0.17° ± 27.46	-16.29° ± 36.04
Turned right	0.15° ± 26.51	5.13° ± 42.83	15.63° ± 20.62	23.58° ± 14.15
Turned left	8.34° ± 25.61	6.12° ± 33.77	10.66° ± 23.41	-6.40° ± 34.63
Right Leg				
Straight	0.83° ± 25.99	-6.25° ± 39.07	-1.88° ± 30.62	-18.55° ± 49.91
Turned right	2.65° ± 28.91	11.56° ± 41.57	8.39° ± 29.18	-14.78° ± 32.09
Turned left	8.52° ± 22.60	-11.22° ± 46.62	0.53° ± 22.66	-5.28° ± 33.71

5.2 GVS and Head Position Effect on the Change in Referent Body Configuration

For hypothesis 2 and 3 of the research, the location of the referent body configuration was represented by the time of lowest EMG activity called EMG minima. We did a linear mixed model analysis to compare the effect of the step without GVS (No GVS) to the two steps with GVS (step

2 and step 3) and we found that there were no statistically significant differences between the effects of no GVS and GVS on the change in minima in both the eyes open and the eyes closed conditions. This was true regardless of the leg analyzed. We also used a linear mixed model to compare the difference in the effects of head position on minima changes in both eyes open and eyes closed conditions. There was no statistically significant result in the eyes open condition. In the eyes closed condition for the left and right legs, there was a statistically significant difference in the effects of the head turned left when compared to the head straight in the no GVS step (see Table 6). The effects of the head straight condition on the change in minima were not statistically different from either the head turned right or the head turned left in the GVS steps (step 2 and step 3) conditions. (Fig. 5, and Fig. 5.2 below showing the graphs displaying the effects of head position on the change in minima and also how GVS affected the minima for each head position. In these figures we see there is some difference between the groups, but the large standard deviations make the results non-significant.

Figure 5: Effects of head position on the change in minima when comparing steps with and without GVS stimulation in the eyes closed condition for the right and the left leg.

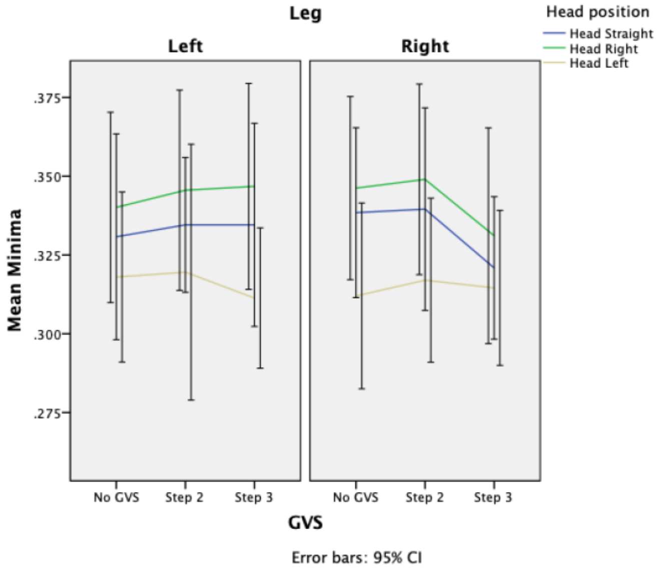

Figure 5.2: Comparison of the effects of GVS versus no GVS on change in minima when walking with different head positions separately in eyes closed condition

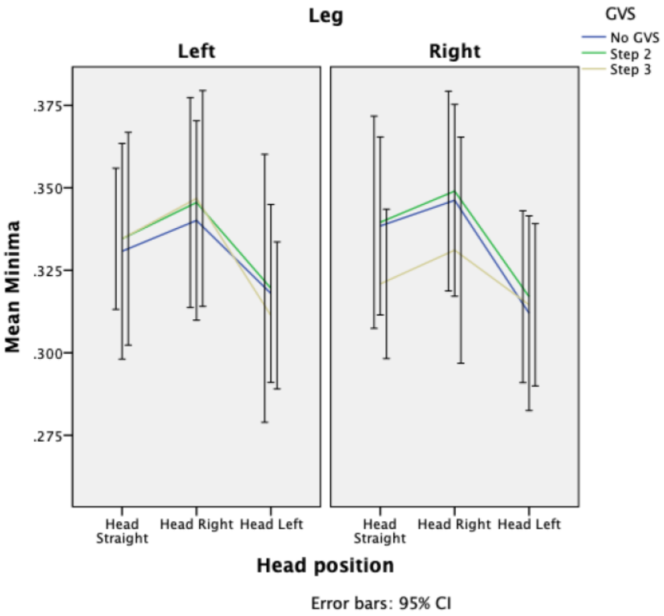

Table 5. Means and standard deviations (in ms) for the effects of head position and GVS on the change in minima during walking for each leg in the eyes open and eyes closed condition.

Eye condition	OPEN			CLOSED		
Left Leg						
GVS **Head position**	No GVS (Step 1)	GVS (Step 2)	GVS (Step 3)	No GVS (Step 1)	GVS (Step 2)	GVS (Step 3)
Straight	0.34ms ± 0.04	0.34ms ± 0.03	0.34ms ± 0.04	0.33ms ± 0.04	0.34ms ± 0.03	0.34ms ± 0.04
Turned right	0.33ms ± 0.04	0.33ms ± 0.04	0.35ms ± 0.04	0.34ms ± 0.04	0.35ms ± 0.04	0.35ms ± 0.04

Turned left	0.33ms ± 0.04	0.33ms ± 0.04	0.34ms ± 0.04	0.32ms ± 0.04	0.32ms ± 0.05	0.31ms ± 0.03
Right Leg						
Straight	0.35ms ± 0.04	0.35ms ± 0.04	0.33ms ± 0.04	0.34ms ± 0.04	0.34ms ± 0.04	0.32ms ± 0.03
Turned right	0.34ms ± 0.03	0.35ms ± 0.05	0.34ms ± 0.05	0.35ms ± 0.04	0.35ms ± 0.04	0.33ms ± 0.05
Turned left	0.33ms ± 0.03	0.34ms ± 0.03	0.35ms ± 0.04	0.31ms ± 0.04	0.32ms ± 0.03	0.32ms ± 0.03

Table 6. Table showing statistical results for the effects of head position on change in minima in both eyes open and eyes closed conditions.

	Eyes Open			Eyes closed		
	Head Straight	Head Right	Head Left	Head Straight	Head Right	Head Left
Step 1	-	-	-	-	-	p = 0.02
Step 2	-	-	-	-	-	-
Step 3	-	-	-	-	-	-

CHAPTER 6

6.0 CONCLUSION

In this study, we observed that stimulation of the vestibular system using GVS did not produce any significant change in the phase of locomotion while the participants walked with their head in different positions. However, there was a difference between the duration of the step cycle in the no GVS step compared to the steps with GVS. However, due to differences in the GVS sensitivity for different participants, ranging from 0.5mA to 2mA, the significance of the phase shift cause by GVS compared to the non-GVS step cycle might have been minimized.

In the EMG minima data, our hypothesis that the change in minima would occur due to GVS stimulation, was equally not met, as there was no significant difference between the GVS and no GVS groups. However, the different head positions affected the change in EMG minima in different ways, probably suggesting that different head positions activate different vestibular organs that can influence the rate of change of the referent body configuration.

6.1 Limitations

The small sample size and the high variability in the threshold intensity of GVS between the participants might have contributed to the inability to see a possible effect of GVS on the phase of locomotion. Because threshold intensity was based on the tolerance level of each participant, it gave rise to variability in the intensity used to stimulate each participant. In order to improve the sample size in the future, a better recruitment strategy may include running online advertisements on Facebook pages and college campuses to attract more participants. Another limitation was that the distance required for the subjects to walk was insufficient to record enough steps with and without GVS. We recorded 8 steps, with the first two steps being discarded since the participants had not yet reached a steady state, this left us with 6 steps to analyze, 3 for each leg. We believe that in order to get more convincing results, we would need a minimum of 10 steps to be analyzed, as this will enable us to have sufficient steps to compare. A larger testing room with a longer runway to allow the participants to take as many steps as possible would be one way to improve this situation in the future. Additionally, rather than only walking in a straight line, we could increase steps by requiring participants to walk with changes in direction while still ensuring that the movement is being properly monitored. This would have increased the total amount of steps and probably shown better contrast between the GVS groups. We also did not use a treadmill as a walking platform because there is no change in optic flow as compared to normal ground walking, and there is also not much variability in the pace of walking compared to walking on normal ground. Lastly, because we strapped the accelerometer on each participant's ankle using Velcro and tape, there is the possibility for slightly erroneous accelerometer data due to movement of the straps while the participants moved. In the future, it would be important to use better fixation of the accelerometers on the skin, similar to the EMG sensors to reduce the chances of error.

Therefore, we conclude that the protocol for this research study is feasible, but there is need to increase the sample size of the participants in order to reduce variability and increase the chances of seeing significant effects of our predicted variables on our outcome variables.

6.2 Implication

One implication of the study is that vestibular stimulation was found to possibly have an influence on how locomotion is controlled by resetting the threshold of activation of motoneurons that helps in setting the spatial frame of reference in which muscles are primed for action.

An additional implication is that it could potentially offer further explanation that locomotion can be explained using the referent body configuration hypothesis, which will assert that the nervous system is indirectly involved in controlling locomotion rather than directly pre-programming motor variables such as muscle force, torques, etc., that are necessary for movement to occur.

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