Postural Control of the Head During Whole Body Translations

By

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Dedication

This work is dedicated to my mother who adores me, to my father who has always believed in me, to my dogs who never fail to bring a smile to my face, to my daughter who kicked in my belly while I wrote it, and to my husband – without whom the sun would seem to shine less bright.
Curriculum Vitae

The author was born in New Orleans, Louisiana on March 27, 1982. She attended Rensselaer Polytechnic Institute from 1999 to 2003, and graduated with a Bachelor of Science degree in 2003. She came to the University of Rochester in the Fall of 2003 and began graduate studies in Biomedical Engineering. She received a Dean’s Fellowship in 2003 and NIH F31 Ruth Kirchstein National Research Service Award Pre-doctoral Fellowship in 2006. She pursued her research in the area of vestibular research under the direction of Professor Gdowski and received the Master of Science degree from the University of Rochester in 2007.
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I’d also like to acknowledge the direction and guidance the members of my committee provided over the years: Ed Freedman, PhD; Scott Siedman, PhD; Marc Schieber, PhD MD; and the chair of my dissertation committee Bill O’Neill, PhD.

I’d like to acknowledge the support of the many lab members who served as my coworkers over the years. There are too many to name all of them but Eric Brown, Vivek Khandwala, Jaimee Reynolds were fellow graduate students whose help I have greatly appreciated.

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Abstract

In primates, the head neck system can be thought of as a large mass that is located distally from the trunk atop the flexible cervical spinal column. This most basic mechanical relationship of the head and the body affords us with the ability to change the head’s position with respect to the body with many degrees of freedom. This ability, however, has its drawbacks. When the whole body is moved, the head/neck system can function like that of an inverted pendulum. Consequently, if uncontrolled the mass of the head could result in undesirable and involuntary movement relative to the trunk. Such, head movements could unintentionally change its orientation in space compromising our ability to utilize sensory signals for spatial localization (vision and hearing). They also have the potential to be injurious to the spinal column. The central nervous system is thought to employ several reflexes that contribute to the overall stability of the head/neck system. Both the anatomy and fundamental physiology of these pathways are well known, yet remarkably little is known about how they function when the body is translated in space. The goal of this dissertation was investigate the role that vestibular sensory information plays in controlling the head when the body is translated in space. Specifically, we asked: How does the brain use vestibular information to control the forces on the head that occur during whole body translation? This dissertation takes an approach to answer this question; beginning at the level of overall behavior, moving up to muscle activation with underlies that behavior, and finally the central nervous system mechanisms that could activate musculature in more natural circumstances. Our results show that the central nervous system does indeed actively control the head during whole body translation and serves to reduce forces on the head which could in turn reduce the size of head movements and protect the neck from injury. These results are profoundly different from the behavior of the CNS during whole body rotation and represent a significant difference in postural control of the head during translation.
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Chapter 1 - General Introduction

1.1 General Summary of Experimental Work

In primates, the head neck system can be thought of as a large mass that is located distally from the trunk atop the flexible cervical spinal column. This most basic mechanical relationship of the head and the body affords us with the ability to change the head’s position with respect to the body with many degrees of freedom. This ability, however, has its mechanical challenges. When the whole body is moved, the head/neck system can function like that of an inverted pendulum. Consequently, if uncontrolled the mass of the head would result in undesirable and involuntary movement of relative to the trunk during movement of the body (Figure 1-1). Such inertially driven head movements could unintentionally change its orientation in space compromising our ability to utilize sensory signals for spatial localization (vision and hearing). They also have the potential to be injurious to the spinal column (Siegmund, Brault et al. 2000; Siegmund, Sanderson et al. 2002). The central nervous system is thought to employ several reflexes that contribute to the overall stability of the head/neck system (Wilson 1988). Both the anatomy and
physiology of these pathways are well known, yet remarkably little is known about how they function when the body is translated in space (Wilson and Schor 1999). This type of movement is characteristic of many movements of daily life, including gait (Xiang, Yakushin et al. 2008). For instance, a person walking down the street reading a sign might want to stabilize his head relative to earth to help the eyes stabilize the image of the sign on the retina. However, if this person were to suddenly stop short to avoid a car he would need to quickly stabilize his head relative to his trunk to maintain his balance and to reduce the torque exerted on the neck due to movement of the head relative to the body. In one circumstance head movement is produced, in the other it is minimized. Essentially there are two functional motifs that must be dynamically controlled in order to produce the correct movement at the correct time. In each of these scenarios, there is a variety of sensory information available to the central nervous system that can be utilized to control and produce postural adjustments reflexively to achieve a behavior. These sensory signals arise from many modalities including vestibular end organs, visual information from the retina, and proprioceptive signals from the body (Berthoz, Graf et al. 1992).

The fundamental goal of this work was to investigate these mechanisms in non-human primates that have a head/neck system that is biomechanically similar to that of humans. In the dissertation that follows, I have focused on investigating the role of sensory information that originates from the vestibular end organs and how it is processed downstream at the first synapses in the vestibular nucleus of the brainstem during linear translations of the whole body. Thus, the objective of my
research was to address the question: How is vestibular sensory information used in
reflexively controlling head on trunk movements that are produced when the whole
body is translated?

To answer this question, an approach was designed in order to characterize
vestibular sensory information in the context of the effect of neck muscle torque on
inertially driven forces exerted on the head, the pattern of muscle activation with
underlies those forces, and the activity of vestibular nucleus (VN) neurons. We have
chosen to use squirrel monkeys as our experimental animal model for several reasons.
The neck musculature is more closely related to that of humans in comparison to
other mammalian species (Graf, de Waele et al. 1995). In addition, the vestibular
system of squirrel monkeys has been extensively studied from the level of vestibular
afferents (Goldberg and Fernandez 1971; Goldberg and Fernandez 1975; Goldberg
and Fernandez 1975), to their targets in the vestibular nucleus (VN) (Wilson and
Yoshida 1969; Wilson 1975; Schor and Miller 1981) and finally to their targets in the
spinal column (Boyle and Pompeiano 1979; Boyle and Pompeiano 1980; Minor,
McCrea et al. 1990; Boyle 1993) where they contribute to the body’s overall posture.
In some regards, the approach taken here is an extension of how these reflexes have
been investigated for rotations of the whole body (McCrea, Strassman et al. 1987;
Gdowski and McCrea 1997; McCrea, Gdowski et al. 1999; Gdowski, Boyle et al.
2000; McCrea and Gdowski 2003). Vestibular reflexes that function maintain the
head’s orientation during whole body rotations have been studied extensively in terms
of biomechanics (Goldberg and Peterson 1986; Keshner, Cromwell et al. 1995;
Keshner and Peterson 1995) and modes of neck muscular activation (Keshner, Baker et al. 1992; Killian and Baker 2005). Additionally the sensory signals carried by vestibular nucleus neurons during vestibular simulation (Goldberg and Fernandez 1975; Schor and Miller 1982; Schor, Miller et al. 1984; Schor, Miller et al. 1985; Gdowski and McCrea 1997; Gdowski and McCrea 1999; Gdowski, Boyle et al. 2000) as well as during the execution of reflexes (Gdowski and McCrea 1999) have been characterized. Comparatively less is known about the physiology of similar vestibular reflexes that are activated when the whole body is translated in space. These reflexes are thought to exist based on the anatomical and physiological identification of pathways primarily in cats (Uchino, Sasaki et al. 1997; Uchino, Sato et al. 1997; Uchino, Sato et al. 2001). However, the primary function of these reflexes when they are evoked during translations of the whole body is not well understood. This is partly because of the technology needed to translate the subjects and the complexity of the head movements that are produced during translational stimulation. With the advent of new technologies we have been able to overcome most of these difficulties in our laboratory.

**Chapter 2 - Biomechanical Study of the Head and Neck During Whole Body Translation**

As shown schematically in Figure 1-1, when the whole body is translated the basic principles of physics of the head and neck dictate that the will head rotate in the opposite direction as the direction of translation. Figure 1-1 shows an example of a lateral bending neck movement that results during side-to-side translation of the
whole body. Translations of the whole body in different directions will result in different types of head movements. This is because the center of mass of the head is offset from the shoulders and neck. For example, a translation in the forward direction would result in a head movement that creates neck extension. Where as, translation in the side direction would create a lateral bending movement of the head, and an effective roll movement of the head. All head movements result in a force on the head that is related to the kinematics of the head movement. In response, the CNS can activate neck muscles that exert reactive torque on the head that has the effect of reducing the size of the head movements and the force on the spinal column. The CNS can also activate neck muscles in a way such that the overall stiffness of the neck is increased. Different neck muscles are capable of exerting torques on the head in different directions (Vasavada, Li et al. 2001; Vasavada, Peterson et al. 2002). Similarly, neurophysiologic studies of the VN have shown that neurons are preferentially maximally active during the side-to-side direction of translation (Dickman and Angelaki 2002). Thus, it might be expected that the CNS response to translations of the whole body could be different in different depending on the direction of translation in the horizontal plane.

The primary aim of the studies in Chapter 1 was to address two fundamentally important questions: 1) Is an active response produced by the CNS that modifies the biomechanical forces and torques exerted on the head when the whole body is translated and 2) Is this response different in different directions of translations? We hypothesized that the existing feedback system is activated such that
CNS reduces torques on the neck during whole body translation ostensibly to stabilize the head relative to the trunk. Furthermore this study had a secondary aim, to characterize the patterns of muscle activation that underlie the CNS response. We hypothesized that vestibular sensory information would be the primary sensory information used by the CNS to drive the reduction in torque during whole body translation and that this reduction in torque would be due to neck musculature activation ipsilateral to the direction of translation. While a CNS response that functions to reduce torque on the neck and protect it from injury may seem intuitive and essential, remarkably all studies in humans to date have reported no definitive evidence for an active process that protects the neck during whole body translation.

To accomplish these aims we employed the use of both biomechanical and electromyographic experimental techniques. Additionally, in order to determine the importance of vestibular sensory information we used a surgical technique involving a total bilateral labyrinthectomy. This eliminated vestibular sensory information and allowed us to assess the CNS response in its absence. The biomechanical technique we used employed a system in which the animal’s head was fixed to a three-dimensional force transducer. This transducer was used to record the force produced on the head during whole body translations as a function of direction in the horizontal plane. One goal in these experiments was to determine how vestibular information is used to modify the forces on the head during whole body translation. A second goal was to determine if the forces exerted on the head are dependent on the direction of translation. In general, we observed that the peak force exerted on the head was
reduced with respect to the force expected based on the inertia of the head in all animals. The forces were also found to be smaller during side-to-side translations than during fore-aft translations. In addition, the forces were larger in animals after labyrinthectomy (i.e. the elimination of vestibular sensory signals). The necessity of vestibular sensory information to both the reduction of force on the head overall and to the amplification of this reduction when translations are in the side-to-side direction suggests two things. First, that the process is an active one generated by the CNS and second, that vestibular sensory information is driving this response from the CNS. These results support our hypothesis that vestibular sensory information drives a CNS response that activates neck musculature to reduce the force exerted on the head. However, these results do not give any insight into the muscular activation patterns that are produced.

We implanted chronic electromyographic electrodes on the splenius muscles of one animal in order to assess what muscular activation patterns were produced by the CNS. The patches were implanted on the splenius muscles because they have been shown to be activated when producing torques on the neck in the direction of right/left lateral bending (Vasavada, Peterson et al. 2002). Muscles related to lateral bending neck movements were of particular interest to us since our biomechanical results suggested that the reduction in forces on the head were spatially biased towards translations in the side-to-side direction. These side-to-side whole body translations produce lateral bending type head movements (shown schematically in Figure 1-1). We hypothesized that neck muscles would be activated during translation
such that the net direction of torque produced by the muscles would oppose the head movements that would occur passively due to whole body translation. However, our results suggest that rather than a specific activation of neck muscles unilaterally to generate torques that oppose the passive force exerted on the head by inertia, a more generalized strategy of co-contracting neck muscles on both sides of the neck was employed. These results are consistent with patterns of activation that would be expected based on prior anatomical studies (Wilson and Schor 1999).

Chapter 3 – Neurophysiologic Study of Sensory Signals in the Brainstem

In Chapter 3, we evaluate how other sensory signals might contribute to neck reflexes when the body is translated in space. The sensory signals that are produced during whole body translation differ depending upon whether or not the head moved with respect to the trunk during the translation. More specifically, we investigated how proprioceptive signals related to the head’s movement with respect to the trunk contribute to the output of the VN pathway. For example, first consider the situation when the body experiences a side-to-side perturbation and the whole body moves without the head changing its orientation with respect to the trunk. This condition is much like the stimuli used in the experiments conducted in Chapter 2. In this circumstance, which we call *outcome 1*, the primary sensory signal available to stabilize the head’s position with respect to the trunk is the vestibular signal originating from the otolith end organs that encodes the linear acceleration of the head in space ($a_{lb}$). However, if the head does move with respect to the trunk (*outcome 2*), the situation is more complex. In outcome 2, vestibular signals as well...
as proprioceptive signals are produced as a consequence of the head’s movement with respect to the trunk (Figure 1-2, pink). In outcome 2, there is a rotational vestibular component due to the head’s rotation with respect to the trunk that originates from the semi-circular canals ($\alpha_{rh}$). There is also a tangential acceleration component produced by the head on trunk rotation ($a_{lh}$), because the axis of head rotation is distally located along the neck (about C5-C6 cervical segments). Finally, there is a third vestibular component related to the tilt of the head with respect to gravity sensed by the sacculus endorgan. In addition to vestibular signals, there are several sources of proprioceptive signals that could be utilized to modify the output of the vestibular pathways. These signals can arise from muscle spindles (Hulliger 1984), golgi tendon organs (Lund, Richmond et al. 1978), and pacinian corpuscles (Berthoz, Graf et al. 1992) located in the neck musculature that are activated with the head moves with respect to the trunk. The signals from proprioceptive sources are conveyed indirectly to the vestibular nucleus (VN) in the brainstem. Vestibular and proprioceptive signals have been shown to converge on individual neurons on the VN and to have very specific relationship in terms of both signal strength and temporal characteristics (Gdowski and McCrea 2000).

The primary aim of the study in Chapter 3 was to characterize the convergence of vestibular information related to translation of the whole body, rotation of the whole body, and proprioceptive information related to movement of head relative to the trunk. We initially hypothesized that when proprioceptive information and vestibular information converged on the same neurons, the response
to each sensory signal would be similar in gain and out of phase so that the response to proprioceptive stimuli would cancel the response to vestibular stimuli during a whole body translation that resulted in an inertially driven head movement. To evaluate this hypothesis, the activity of VN neurons was characterized during the same stimuli used in the first two studies as well as during stimuli that were designed to be similar to those experienced during a whole body translation during which the head was free to move. Our results suggest that translational information from otolith end organs and rotational information from semicircular canals converges in the vestibular nucleus on approximately 50% of the neurons we recorded from in awake behaving squirrel monkeys. Finally, our results show that in general, when neurons sensitive to translation and/or whole body roll receive proprioceptive input, the sensitivity of those neurons to proprioceptive input is small. This low sensitivity to proprioceptive input suggests that proprioceptive input plays a different role during translations and roll head movements than it is during whole body rotations in yaw. We hypothesized that this is primarily due to the different function of the VCR in translation compared to the function of the VCR during roll, which we demonstrated in our behavioral experiments. This smaller proprioceptive signal, relative to the strength of the vestibular signal, allows for larger vestibular output during translation and may be important to maintain of the head’s position relative to the trunk.
1.2 Background and Context

**Vestibular pathways involved in controlling the head**

The CNS is thought to reflexively control head orientation in response to movements of the body. This control is in part, through the neural pathways that carry vestibular information from the sensory endorgans through the brainstem, to regions of the spinal cord that activate neck musculature (Figure 1-3). These pathways could be important in controlling the head’s movement when the whole body is translated and the anatomical presence of these pathways in part forms the basis of our hypothesis in Chapter 2.

Vestibular sensory signals originate from the vestibular labyrinth located in the inner ear. The labyrinth consists of two types of sensors to detect head movements, the semi-circular canals and the otolith end organs. These three semi-circular canals are more or less orthogonally arranged to detect rotational acceleration of the head in three planes. The afferent fibers arising from the semicircular canals are of two types: regular and irregular. In general the regular afferents have firing rates that are roughly in phase with rotational velocity while the irregular afferents have firing rates that are closer in phase to rotational acceleration (Goldberg and Fernandez 1971; Goldberg and Fernandez 1971; Boyle, Goldberg et al. 1992). Linear acceleration signals are transduced by structures in the vestibular labyrinth that are collectively called the otolith endorgans. There are two otolith end organs referred to as the utricle and the saccule. When the head moves in space, the peripheral
vestibular system can detect these movements relative to gravity and evoke neck muscle activity through pathways shown in Figure 1-3. When neck muscles are activated in response to vestibular sensory information through these pathways that response is commonly referred to as the vestibulocollic reflexes (VCR). The anatomy and physiology of these pathways form the neural substrate of the vestibular collic reflex. Those activated by the canals are referred to as the rotational VCR (rVCR) and those activated by otoliths are referred to as the translational VCR (tVCR).

Most of the studies of the neural substrate of the vestibulocollic reflex have focused on vestibulospinal pathways, specifically on the short-latency pathways between the vestibular labyrinth and neck motoneurons. Both disynaptic and trisynaptic excitatory and inhibitory connections between the vestibular labyrinth and neck motoneurons have been shown in cats (Wilson and Yoshida 1969; Ezure and Graf 1984 May.). From the VN, axons of both excitatory and inhibitory vestibulospinal neurons project axons bilaterally down the lateral and medial vestibulospinal tracts (LVST and MVST) and terminate in cervical spinal cord (Wilson and Melvill Jones 1979; Donevan, Neuber-Hess et al. 1990; Donevan, MacDonald et al. 1992; Shinoda, Sugiuchi et al. 1994; Shinoda, Sugiuchi et al. 1997; Wilson and Schor 1999). These vestibulospinal pathways are not the only pathway capable of conveying vestibular information to the cervical spinal cord. It has also been shown that neurons within the reticular formation of the brainstem receive vestibular input from the vestibular nucleus. Reticular neurons have been shown to
project down the reticulospinal pathways to the cervical spinal cord, and thus may also function in parallel with vestibulospinal pathways (Ladpli and Brodal 1968).

The details of the patterns of synaptic projections between the brainstem and neck motoneurons are different for neurons receiving input from the semicircular canal and for neurons receiving input from otolith endorgans. Each of these anatomical pathways provide an essentially direct connection from the vestibular labyrinth to motor neurons in the cervical spinal cord and are thought serve as the neural substrate of vestibulocollic reflexes (VCR). Each has been shown to alter head orientation in space in response to vestibular stimulation (Wilson and Schor 1999).

The VCR in response to whole body rotations has been described in humans (Guitton, Kearney et al. 1986; Keshner, Woollacott et al. 1988; Keshner, Hain et al. 1999), non-human primates (Gdowski, Belton et al. 1996; Gdowski and McCrea 1999; Gdowski and McCrea 1999), cats (Fukushima, Pitts et al. 1979; Peterson, Bilotto et al. 1981; Bilotto, Goldberg et al. 1982; Darlot, Denise et al. 1985; Goldberg and Peterson 1986; Keshner, Baker et al. 1992), pigeons (Gioanni, Rey et al. 1984; Dickman and Angelaki 1999), and frogs (Dieringer and Precht 1982; Dieringer 1987). However, despite all of this work describing how the head is stabilized reflexively, understanding how the head is stabilized during passive movements of the whole body is complicated by the fact that the movement of the head could be context dependent. In some contexts it might be beneficial to an organism for its head to be stabilized relative to space. For example, a primate sitting on a branch that is swaying in the wind might want to stabilize its head relative to space in order to keep
gaze fixed on an insect located on the ground. However, if that same primate’s goal was to not fall off the branch, then stabilization of the head relative to the trunk would function to better maintain balance.

**Neural Substrate of the rVCR**

Insight into the function of the vestibulocollic reflex can be drawn from the functional organization of the pathways that underlie it. The first important work that demonstrated a direct connection between the semicircular canals and neck muscles was performed by Suzuki and colleagues (Suzuki and Cohen 1964). They electrically stimulated the semicircular canal nerves and showed head movements in response to canal stimulation. This same technique was later used to investigate the pathways from the semicircular canals to the spinal cord. Shinoda and colleagues showed that pathways from semicircular canals to neck motoneurons was not a simple one-to-one connection from specific canals to specific muscles; a typical neck motoneuron was found to receive bilateral input from all 3 semicircular canals (Shinoda, Sugiuchi et al. 1994; Shinoda, Sugiuchi et al. 1996). The results of Shinoda’s work as well as several others (Wilson and Maeda 1974; Fukushima, Pitts et al. 1979; Uchino, Isu et al. 1990; Sugiuchi, Izawa et al. 1995) are summarized in Table 1-1 adapted from Wilson and Schor (1999).
The results of these studies show that the patterns of neck motoneuron activation generated by electrical stimulation of the semicircular canals are broad, but they are also consistent with findings from studies evaluating the functional role of the rotational VCR. Characterization of the VCR in terms of functional connections has been shown by either electrically or naturally stimulating canals in combination

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<td>OCS&lt;sup&gt;c&lt;/sup&gt;</td>
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<td><strong>Rotators</strong></td>
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<td>SCM&lt;sup&gt;a,e&lt;/sup&gt;</td>
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<td>OCI&lt;sup&gt;b,d&lt;/sup&gt;</td>
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<td>LC&lt;sup&gt;d,e&lt;/sup&gt;</td>
<td>n.t.</td>
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Table 1-1 Predominant connections from semicircular canals to neck motoneurons. EP Excitatory synaptic potential, IP inhibitory synaptic potential, BIV biventoer cervicis, COMP complexus, MULTI cervical multifidus, RCP rectus capitis posterior, SPL splenius, OCS obliquus capitis superior, LONG longissimus capitis, SCM sternocleidomastoid, OCI obliquus capitis inferior, LC longus capitis, HOR horizontal canals, ANT anterior canals, POS posterior canals, n.t. not tested. Reproduced from (Wilson and Schor 1999).
with an assessment of the resultant head movements and/or neck muscle activation. For example, Suzuki and Cohen showed that when the anterior canals were stimulated electrically, which mimicked a pitch rotation of the head, the animals snout was raised (Suzuki and Cohen 1964). Additionally, Goldberg and Peterson (1986) showed unilaterally specific neck muscle activation during yaw head movements. In their study, when the head was rotated contralateral neck muscles were activated (Goldberg and Peterson 1986). This result supports the notion that the rotational rVCR for horizontal movements of the body results head movement that stabilizes the head in space to compensate for initially driven movements of the head due to whole body rotation. However, this stabilization may function differently when the VCR is evoked by translation (tVCR).

Furthermore, despite the fact that these rVCR pathways seem to be organized such that they could produce the patterns of muscle activation that have been shown during functional activation of the vestibular system, there is also evidence that these pathways by themselves are not sufficient to produce the dynamics of the reflex. Ezure and Sasaki (1978) showed that at low frequencies (0.01 – 0.5 Hz) there was a phase lag between the response of second-order vestibular neurons and the response of neck motor units. They suggested that this phase lag could not be due to a short-latency vestibulospinal pathway and suggested the presence of a neural integrator in the vestibulocollic reflex arc. This neural integrator could produce a response in phase with position that would be required to account for their observations of the horizontal VCR. Other groups performed experiments in which they sinusoidally
polarized the vestibular afferent fibers and noted that second-order vestibulospinal neurons fired approximately in phase with the sine wave without the phase lag that Ezure and Sasaki found on the muscle (Wilson and Melvill Jones 1979; Peterson, Fukushima et al. 1980). These results collectively demonstrate that disynaptic pathways are not sufficient to account for the dynamics of the horizontal canal-evoked VCR because the pathway requires a neural integrator that is not present on the second-order neurons (Wilson and Schor 1999). The vestibulospinal pathway however is not the only contributor. Reticulospinal pathways could serve that function.

Additionally, research into the effect that passive head movements have on the function of vestibular reflexes has shown that the dynamics of vestibular reflexes changes during these movements. These experiments have also shown that firing behavior of vestibular nucleus neurons is modulated by proprioceptive input (Lund and Broberg 1983; Peterson, Goldberg et al. 1985; Gdowski and McCrea 2000). These results tell us that, despite the seeming simplicity of the di/trisynaptic pathways, it is clear that the output of the VCR in a functional context could be much more complicated than the anatomy suggests. This result means that the VCR must be studied not only at the level of neural activation patterns in the brainstem but also studies must examine the functional output of the VCR. In chapter 3, the experiments we carried out were on the neurophysiological underpinnings of the rotational reflexes as they are evoked during whole body translation. However, the studies
discussed Chapter 2 of this dissertation are aimed at describing the not the rVCR, but the experiments focus on evoking the tVCR from a functional behavioral standpoint.

**Neural Substrate of the tVCR**

There is considerable evidence that sensory signals related to otolith endorgans affect how the head moves during whole body translation suggesting the existence of a translational vestibulocollic reflex (tVCR). This reflex could be evoked in a scenario that we referred to as outcome 1, which is shown Figure 1-2. The head does not move relative to the trunk and thus the only vestibular signal available for use in stabilization is the linear acceleration signal. The two otolith endorgans are arranged in the labyrinth so that the saccule transduces vertical acceleration and the utricle transduces accelerations in the horizontal plane. Direct di- and tri- synaptic connections have been shown between utricular and saccular afferents and neck motoneurons. The patterns of these connections are shown in Table 1-2, which summarizes the work from many authors (Ikegami, Sasaki et al. 1994; Uchino, Sasaki et al. 1997; Uchino, Sato et al. 1997) and is reproduced from Wilson and Schor

<table>
<thead>
<tr>
<th>Muscle</th>
<th>Utriculus</th>
<th>Contra</th>
<th>Sacculus</th>
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<tr>
<td>Extensors Dorsal Rami</td>
<td>EP</td>
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<tr>
<td>Flexor Longus Capitis</td>
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<td>Rotator Sternoideomastoid</td>
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<td>EP</td>
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Table 1-2: Predominant connections from otolith receptors to neck motoneurons.

Afferent fibers from the otolith endorgans synapse on neurons in the VN (Uchino, Sasaki et al. 1997; Uchino, Sato et al. 1997) and have axons that target the spinal cord at the cervical level (Perlmutter, Iwamoto et al. 1998; Perlmutter, Iwamoto et al. 1998).

In a broad sense, it appears that connections from the utricle to neck flexors and extensors are bilaterally reciprocal and those from the sacculus are bilaterally symmetrical (Bolton, Endo et al. 1992; Ikegami, Sasaki et al. 1994; Uchino, Sasaki et al. 1997; Kushiro, Zakir et al. 2000). Functionally, this broad characterization of connection from the otolith end organs to neck motoneurons can be summarized as follows. The utricle senses mostly accelerations in the horizontal plane; these accelerations would cause head movements that alter the orientation of the head with respect to both gravity and the trunk. During a side-to-side translation in the horizontal plane, activation of neck extensors and flexors driven by utricular stimulation would allow the reorientation of the head and maintenance of upright posture of the head on the trunk. Meanwhile, the sacculus senses mostly vertical acceleration, head movements in response to vertical movements of the whole body are generally in pitch. Connections from the sacculus are comprised of excitatory connections to bilateral neck extensor muscle motor neurons and inhibitory connections to the bilateral neck flexor muscle motor neurons. This organization allows the neck extensor muscles to fulfill an antigravity function during vertical upward accelerations.
Indeed these connections do appear to be able to support the hypothesized function of the tVCR when the otoliths are stimulated naturally. Schor and Miller (1981) showed that in response to lateral tilts in the decerebrate cat, dorsal neck extensor muscles on the side tilted up were activated. They also showed that contralateral neck muscles on the side tilted down were suppressed, as suggested by bilaterally reciprocal connections from the utricle. This suggests that the tVCR when activated during tilt, would reorient the head with respect to space. Additionally in response to vertical linear accelerations of the decerebrate cat, the response of the splenius was bilaterally symmetrical as suggested by the bilaterally reciprocal connections from the sacculus. (Lacour, Borel et al. 1987). This result also suggests an ability of the tVCR to reorient the head and maintain an upright head in space.

**Quantification of the Functional Output of the VCR**

There is really only one way to study the behavioral effects of the VCR and that is to allow the head to move with respect to the trunk when the stimulus is delivered. However, this paradigm is complicated because the vestibular sensory system is not the only sensory system stimulated in this circumstance. In order to isolate the effects of vestibular sensory information from the effects of neck proprioceptive information and other types of sensory signals, many investigators have fixed the head relative to the body (i.e. prevented neck rotation). These kinds of open loop studies are useful for determining the effects of vestibular information in the absence of other sensory signals, but they do not allow the reflexes to affect actual head on trunk movements. This experimental design limitation prevents studies using
an open loop condition to really achieve a comprehensive representation of the effects of reflexive control of head movement. Studies that elicit a closed loop type of reflexive head stabilization achieve a more comprehensive picture of the effects of reflexive control of head movement. However, it is more difficult to identify the effects of vestibular sensory information in the presence of other sensory signals.

Goldberg and Petersen (1986) used EMG methods to quantify muscle activation, head movements, and torque produced by the neck acting on the head as metrics of the VCR. This metric is important because it describes muscle excitation with respect to the mechanical properties of the head/neck plant (i.e. stiffness and viscosity properties). The torque measured is the sum of the torque due to the contraction of all muscles bilaterally that are activated reflexively or voluntarily and the passive mechanical properties of the neck. Net torque is also an important metric to measure during vestibular stimulation because it can be measured in both open loop and closed loop systems, which allows the isolation of the effects of vestibular sensory information from proprioceptive sensory information. In the studies we discuss in Chapter 2 of this dissertation, we have designed an experimental setup that uses net force as the primary metric of the output of the translational VCR. Force, like torque used by Goldberg and Peterson (1986), is a measure of the overall forces due to the contraction of all muscles bilaterally that are activated and the passive mechanical properties of the head and neck. The system we designed measured the net force during open-loop conditions where the effect of vestibular sensory information could be isolated.
The Sequence of Vestibular Signals Produced During Translation of the Body

Head stabilization during translation of the whole body can be thought of as a sequence of two separate lines of defense that help maintain the head’s orientation with respect to the trunk during whole body translation. The first line of defense is the utilization of the initial linear acceleration signals to produce muscular activity that prevents the head’s rotation from ever occurring. The vestibular signal in this instance is the same as outcome 1 in Figure 1-2. However, if this system were inadequate, such that a head on trunk rotation was produced during whole body translation, then a second process could be activated. This second line of defense would be activated by vestibular sensory signals arising from the semicircular canals as a result of the rotation of the head with respect to the trunk. In this instance the vestibular signal would be equivalent to the signal shown in outcome 2 in Figure 1-2.

Many investigators have attempted to characterize how much head stabilization occurs during whole body translations (Kumar, Narayan et al. 2000; Vibert, MacDougall et al. 2001; Siegmund, Sanderson et al. 2002; Keshner 2003; Siegmund, Sanderson et al. 2003; Siegmund, Sanderson et al. 2003; Keshner 2004; Kumar, Ferrari et al. 2004). There is some evidence to suggest that a translational VCR might be important for gaze stabilization and heading during locomotion (Hirasaki, Moore et al. 1999; Imai, Moore et al. 2001; Imai, Moore et al. 2001). Other work has been done focused on characterizing head stabilization in humans during whole body translation (Vibert, MacDougall et al. 2001; Keshner 2003;
Keshner 2004). However, despite the fact that anatomically direct connections between the otolith endorgans and neck motoneurons have been shown, the behavioral response properties of otolith evoked collic reflexes during whole body translation have been difficult to evoke in closed loop conditions (Keshner 2003).

The VCR is most commonly described as producing compensatory head movements in response to rotational vestibular simulation (Ezure and Sasaki 1978; Ezure, Sasaki et al. 1978; Goldberg and Peterson 1986). However, this function is not easily observed when the body is translated in space because muscles are minimally activated at short latency. This inconclusive evidence is one reason why investigators have suggested that the tVCR has been difficult to elicit in response to translation. However, there are several pieces of evidence that suggest that perhaps the functional consequence of the rotational VCR is not to produce head movements during translation but rather to reduce rotational head movements. For example, the head movements produced during translations by bilaterally labyrinthine-deficient subjects tended to have higher peak accelerations in comparison to control subjects. These findings suggest that the vestibular pathways may function to reduce, rather than increase, the amplitudes of inertially-driven head movements produced during linear translations (Keshner 2003).

Furthermore there is neurophysiologic evidence that vestibular mediated responses to translation in the horizontal plane may be spatially biased. One study which characterized the best direction of neurons in the VN sensitive to translation in the horizontal plane noted 70% of neurons with best directions within 30° of side to
side translations (Angelaki and Dickman 2000). A figure reproduced from this work is shown in Figure 1-5. The result suggests that response of the tVCR might be biased towards side-to-side translations.

**Functional Convergence of Vestibulocollic Reflexes and Cervicocollic Reflexes**

In the beginning of this chapter we outlined two outcomes that would be possible regarding head movements when the whole body was translated in the horizontal plane and in the previous sections of this chapter we discussed the relevant background which led to our hypotheses regarding the role vestibular sensory information on postural head control during whole body translations. However, as we have mentioned, vestibular sensory information is not the only source of sensory information in outcome 2. Proprioceptive information regarding the head’s movement relative to the trunk is produced. Stimulation of neck muscle receptors has been shown to have profound effects on the posture of the trunk and limbs (Magnus 1924; Roberts 1978) and to activate powerful vestibulospinal reflexes that help to maintain a stable relationship between the head and trunk (Boyle and Pompeiano 1980; Kasper and Thoden 1981; Wilson, Yamagata et al. 1990). Furthermore, postural reflexes evoked by neck proprioceptive stimulation, including the cervicocollic reflex (CCR), have been shown to play an important role in compensating for the loss of vestibular reflexes in labyrinth deficient animals (Peterson, Baker et al. 1988) and humans (Keshner 2003). It is hypothesized that the contribution or gain of the CCR might increase in response to the loss of vestibular
sensory information. Consequently there could be a connection between vestibular reflexes and those activated by proprioceptive information.

The rotational VCR and CCR are thought to work cooperatively to counteract inertially drive head movements during whole body rotations in yaw (Goldberg and Peterson 1986; Lacour, Borel et al. 1987; Keshner, Cromwell et al. 1995; Peng, Hain et al. 1996; Keshner, Hain et al. 1999; Peng, Hain et al. 1999) and to inhibit most, but not all, ipsilateral neck muscles (Shinoda, Sugiuchi et al. 1993; Shinoda, Sugiuchi et al. 1994; Shinoda, Sugiuchi et al. 1997). This results in counter-rotation of the head with respect to the stimulus (Ezure and Sasaki 1978; Ezure, Sasaki et al. 1978; Goldberg and Peterson 1986). When the head counter-rotates, the ipsilateral neck muscles are stretched, activating the CCR, which produces torque in the direction opposite to the torque produced by the rotational VCR. This activation pattern has prompted the hypothesis that the two reflexes act antagonistically to stabilize the head’s inertia with respect to the trunk during rotation. This hypothesis was indirectly tested in cats by adding inertia to the head and measuring the head movements that were produced during whole body rotation (WBR) (Goldberg and Peterson 1986). Changing the head’s inertia had minimal consequences on head movement kinematics during low frequency WBR (Goldberg and Peterson 1986). These observations were later confirmed in humans (Keshner, Hain et al. 1999). Furthermore, studies conducted in our laboratory in squirrel monkeys have demonstrated the ability of proprioceptive information to modify head movements during whole body rotation. Reynolds and Gdowski (2008) conducted experiments in which the inertia of the
animal’s head was increased and demonstrated that an increased gain of the CCR could potentially compensate for this inertial increase and alter the resulting head movements (Reynolds, Blum et al. 2008). The results from all of these experiments demonstrate the importance of information related to the head’s movement with respect to the trunk in the regulation of reflexes that stabilize the head in response to whole body rotation. These results also underscore the importance in our study of characterizing the proprioceptive signals in the VN in order to fully understand activity of that nucleus during a head free whole body translation. Based on the hypothesized function of the rVCR and the CCR it seems that rather than operate antagonistically, these reflexes would work synergistically during head rotations produced during translation (outcome 2). Both the rVCR and the CCR are thought to activate muscles ipsilaterally with respect to the direction of translation.

**Proprioceptive Signal Processing in the Vestibular Nuclei**

Proprioceptive information can regulate head movements both by having a direct effect on neck motoneurons in the spinal cord and by conveying sensory information to the vestibular nucleus of the brainstem (Ezure, Sasaki et al. 1976; Ezure, Fukushima et al. 1983). Neck proprioceptive signals within the VN likely arise from many sources. The vestibular nuclei, particularly the lateral and descending vestibular nuclei and area X, receive direct spinal inputs (Corbin and Hinsey 1935; Pompeiano and Brodal 1957; Edney and Porter 1986; Neuhuber and Zenker 1989). In addition, several cerebellar regions project to the vestibular nuclei (e.g. the vermis, the flocculonobular lobe, and fastigial nucleus) and receive input
from spinal-cerebellar pathways (Eccles 1974; Furuya, Kawano et al. 1975; Akaike 1983; Noda, Sugita et al. 1990; Robinson, Phillips et al. 1994). The role of transcerebellar pathways in conveying proprioceptive signals to vestibular neurons during head movements and locomotion is well documented. Additional signals could also arise from cortical pathways (Guldin, Akbarian et al. 1992; Akbarian, Grüsser et al. 1993; Fukushima 1997). These signals arising from this wide variety of sources have sufficient computational power to affect the processing of vestibular signals in the VN.

The first work to characterize neck proprioceptive signals in the VN of the awake squirrel monkey was conducted by in laboratory of Bob McCrea (Gdowski and McCrea 1999; Gdowski and McCrea 2000). Their work showed that neck proprioceptive signals in the VN might be instrumental in shaping the output of pathways controlling the vestibulocollic reflexes. Figure 1-7 shows a comparison of vestibular (A) and neck proprioceptive (B) sensitivities for two VN neurons. Neck proprioceptive inputs were assessed by rotating the body while holding the head stationary in space (passive neck rotation; PNR). Responses obtained during this condition were compared to those obtained during whole body rotation (WBR) In many cases, neck proprioceptive signals were antagonistically matched to vestibular signals so that they functioned to reduce the vestibular responses during imposed head-on-trunk rotations (see combined vestibular and proprioceptive stimulation: HTR Figure 1-7). However, it is important to note the reports of neck proprioceptive signals within the VN have varied (Sadeghi, Mitchell et al. 2009). Studies in cats
squirrel monkeys (Saimiri sciereus) (Gdowski and McCrea 2000), and the cynomolgus monkey (M. fascicularis) (Sadeghi, Mitchell et al. 2009) have reported that many vestibular nuclei neurons carry neck proprioceptive signals that were identified during body rotation while the head was held stationary in space. Such neck proprioceptive signals were found to combine destructively with vestibular signals when the head was rotated with respect to the trunk. Studies of larger non-human primates (rhesus monkey, M. mulatta) have reported that few if any VN neurons have such signals (Roy and Cullen 2001; Sadeghi, Mitchell et al. 2009). The Cullen group has hypothesized that these differences between species are due to the fact that rhesus macaques are terrestrial and not arboreal (Sadeghi, Mitchell et al. 2009). However, given the similarities between rhesus macaques and squirrel monkeys in terms of other aspects of the rotational VCR and compensation after canal plugging (Raphan, Imai et al. 2001; Cohen, Xiang et al. 2009), it would be very surprisingly if the VCR and CCR had different functional role in squirrel monkeys and rhesus macaques.

All of the experiments in primates discussed above, which characterize proprioceptive input in the VN, examined these signals in the context of whole body rotations and head rotations on the trunk in yaw. In chapter 3, we aim to describe the relationship between vestibular and proprioceptive signals in the VN that would be observed during head on trunk rotation produced during side-to-side translation. As shown schematically in Figure 1-2, during a head free whole body translation there are
vestibular signals related to the roll head movements, the whole body translation, and proprioceptive signals related to the roll head movement relative to the trunk. Based on these results, we hypothesize in chapter 3 that proprioceptive signals resulting from roll head movements with respect to the trunk will destructively combine with vestibular signals, similar to the results from prior studies using squirrel monkeys in yaw and unlike the results from prior studies using rhesus macaques.
1.3 Summary

The goal of this dissertation was investigate the role of vestibular sensory information in controlling head on trunk movement during whole body translation. These postural responses stimulated by whole body translation have been historically difficult to elicit in animals models. Several different systems were designed that allowed us to study these reflexes during translations in the horizontal plane in both open and closed loop paradigms. Squirrel monkeys were used as our animal model. In our first study (Chapter 2), we use a novel system that employed the use of a three dimensional force transducer to measure the forces exerted on the head during translation. The force transducer quantified the force against a fixed substrate; this allowed us to examine a net response resulting from presumably of two components: a CNS component related to the translational VCR and a biomechanical component due to the head’s inertia. To separate these components, we performed a labyrinthectomy in one animal in order to quantify the forces on the head during translation before and after the loss of vestibular sensory signals. The concept of characterizing the VCR in the context of force is similar to Goldberg and Petersen’s work (1986), which characterized the torque exerted by the neck. By measuring force we were able to characterize the overall effect of both force due to passive biomechanics of the head and neck including the inertia of the head and force due to active contraction of neck muscles. Furthermore, the tuning of directions of maximum activation vectors of translation sensitive neurons in the VN to the side-to-
side direction of translation as well as the spatial tuning of neck muscles activation patterns suggests that the functional output of the VCR in translation may also be spatially tuned. This first study addressed the central question: Does vestibular information influence the biomechanical forces exerted on the neck by the head during whole body translation and if so is this effect spatially biased to whole body translations in particular directions in the horizontal plane?

Force however is not necessarily linked to specific neck muscles. The resulting force is due to both physiologic properties of the muscles themselves and due to the anatomical arrangement of muscles in the neck. Additionally, it does not provide information about the details of how the muscles are activated in order to exert force on the head. Thus, in this study we also measured the activation of neck muscles during whole body translation in one animal. During these experiments the animal’s heads were fixed relative to the trunk, to eliminate other sensory stimuli during whole body translation. Recordings of the muscle activity from chronically implanted EMG patch electrodes were obtained during whole body translation. In this study two questions were addressed: 1) Does the vestibular system activate neck muscles during whole body translation? 2) What types of activation patterns are produced, and are they used to control the forces on the head during these translations?

There are several different neural mechanisms that can be utilized for driving muscle activation. The short latency pathways from the vestibular nucleus seem the most likely candidate. In our second study (Chapter 3) we investigated the neural
activity that might have a role in activating neck muscles. We recorded from single neurons located in the vestibular nucleus of two animals. However, vestibular information conveyed to the VN is not the only source of sensory information during a translation when the head is allowed to move with respect to the trunk (outcome 2). Proprioceptive sensory information potentially also plays a role in control of the head during whole body translation. Proprioceptive information from the neck is conveyed to vestibular nucleus neurons, and integrates with vestibular signals to contribute to the overall control of head movement. Thus in our second study (Chapter 3) we ask: How do vestibular nucleus neurons dynamically combine different vestibular signals and proprioceptive signals that occur during whole body translation? Is the processing of proprioceptive signals and vestibular signals the same as during yaw head movements produced during horizontal rotation?

The purpose of this thesis work was to determine how vestibular sensory information is used by the CNS to control the head during whole body translation. Specifically, we asked: How does the brain use vestibular information control the forces on the head that occur during whole body translation? This thesis work takes a novel approach to answer this question; beginning at the level of overall behavior, moving up to muscle activation which underlies that behavior, and finally to the central nervous system.
Figure 1-1 Schematic drawing of head movements during translation: A) Shows the head and shoulders in a neutral position when the body is not moving. B) When the body is translated to the left, because of the mass of the head and biomechanics of the neck the subject’s head would counter rotate in roll to the right.
Figure 1-2 Outcomes of whole body translation: A) outcome 1 – the vestibular signals produced during whole body translation with the head fixed relative to the trunk is equal to the linear acceleration of the whole body B) Vestibular and proprioceptive signals produced during whole body translation with the head free to move on the trunk. Vestibular signal is equal to the combination of linear acceleration of the whole body + rotational acceleration of the head relative to the body. Additionally, a proprioceptive signal is also generated. There is also a centripetal acceleration that is small and omitted from this simplification. Symbols include: $a_{lb}$ - whole body linear acceleration, $a_{lh}$ - linear acceleration of the head, $p_n$ - rotational position of the head relative to the trunk, and $\alpha_{rh}$ – rotational acceleration of the head relative to the trunk. Blue arrow – translation of body from the animal’s right to its left.
Figure 1-3 Short latency reflex pathway of the vestibular system: Flowchart of reflex pathways from vestibular endorgans to neck muscles.
Figure 1-4 Flow chart of the pathways that allow proprioceptive information to effect head movements: 1) Cervicocollic pathway (stretch reflexes). 2) Indirect contribution through convergence of processed proprioceptive signals on vestibular pathways.
Figure 1-5 Best direction and gain of neurons responsive to translation in the horizontal plane: Figure is modified from Angelaki and Dickman (2000). Responses are shown on a polar plot where angle is the direction of translation and radius is the gain. Horizontal axis corresponds to side-to-side translation and the vertical axis corresponds to fore-aft translation.
Figure 1-6 Changes in the CCR gain evoked by modifying the inertia of the head: Shown are raw and averaged data records obtained before (A), during (B) and after (C) the inertia of the head was modified by adding mass to the head free system producing a 36 fold change in inertia (ΔI = 36.4 x IHF). In each condition, the head was initially free to move. The vertical line in the raw data records denotes the time at which the head was quickly restrained so that the head was stationary in space. The head was stabilized in space for several cycles, released, and then repeated. The records at the bottom are the average response of the first few cycles after the head was stabilized. A large change in torque was observed after the inertia of the head was increased (B) in comparison to the torque produced before the inertia was increased (A). (Reynolds, Blum et al. 2008)
Figure 1-7: Vestibular and neck proprioceptive interactions for two mVN neurons. Shown are (A₁-C₁) a neuron with stronger vestibular input and (A₂-C₂) a neuron with nearly equivalent vestibular and neck proprioceptive input. Two stimulus frequencies are shown. Shown: WBR (A₁₂), passive neck rotations (PNR; B₁₂) and forced head on trunk rotations (HTR; C₁₂). The dashed traces in C₁₂ are the linearly regressed fit to the data. WBR – Whole Body Rotation; PNR - Passive Neck Rotation; HTR- Forced Head Rotation. \( \dot{H}_s \) – Head in space velocity; \( \dot{H}_t \) = Head on trunk velocity (Gdowski and McCrea 2000).
Chapter 2: The Use of Vestibular Signals in Controlling the Forces Produced on the Head During Whole Body Translation

2.1 Introduction

Multiple sensory modalities have been known to be important in postural reflexes since the early 1900s (Magnus 1924; Wilson 1975). A particularly important set of reflexes is collic reflexes which function to maintain the head’s posture with respect to the trunk. The collic reflexes have been extensively studied in response to whole body rotation (Keshner and Peterson 1988; Keshner, Cromwell et al. 1995; Keshner and Peterson 1995), but far less is known about how these reflexes function during linear translations of the body (Siegmund, Sanderson et al. 2002; Keshner 2003; Siegmund, Sanderson et al. 2003; Siegmund, Sanderson et al. 2003; Keshner
Although many animals studies have shown that central neurons are sensitive to whole body translation few have studied these responses in the context of neck reflexes (Angelaki 1992; Angelaki, Bush et al. 1993). The majority of what is known about collic reflexes is based on responses during whole body rotations in which horizontal head rotation has been studied (Goldberg and Peterson 1986; Keshner and Peterson 1995; Gdowski and McCrea 1999; Gdowski and McCrea 1999). The rotational dynamics of collic reflexes have been extensively studied in animal models including squirrel monkeys (Goldberg and Fernandez 1971; Goldberg and Fernandez 1971) and the decerebrate cat (Wilson and Yoshida 1969; Wilson and Maeda 1974; Goldberg and Peterson 1986). These studies have provided the basis of our understanding of the mechanisms by which vestibular and proprioceptive sensory information is conveyed centrally and peripherally to produce neck muscle activity to counter-rotate the head in response whole body rotation. Rotational collic reflexes could be functionally important during daily activities such as gait (Raphan, Imai et al. 2001). Despite these efforts, the contribution of vestibular signals related to linear translation remains unknown.

One reason these collic reflexes have not been extensively studied is because the head movements they evoke during lateral translation involve lateral bending of the spinal column and consequently they are much more difficult to quantify. One technique used in the past was to quantify the rotational torque exerted by the head and neck when it is prevented from moving with respect to the trunk during whole body rotation (Goldberg and Peterson 1986). The net mechanical torque that was
quantified during rotation was thought to represent a linear combination of the passive torque produced by the inertia of the head, and the active torque produced by the rotational vestibulocollic reflexes. Here we have used an equivalent mechanical technique for quantifying the contribution of the translational vestibulocollic reflexes evoked during linear translation of the whole body in space. In our case, the three-dimensional force transducer was used to quantify the force exerted on the head during linear translation. This represents a combination of the passive force produced by the inertia of the head, and the active force produced by the translational vestibulocollic reflexes. Using this measure we were able to demonstrate that linear vestibular signals are actively utilized to control the head’s movement.

The CNS can utilize a variety of sensory signals including vestibular information and proprioceptive information to govern the overall movement of the head with respect to the trunk. There are several physiologic mechanisms that can underlie this active component of the head and neck response. Vestibular and proprioceptive sensory information is conveyed centrally to the cortex and can be used to drive voluntary responses of neck muscles. Additionally, reflexive responses driven by both vestibular and proprioceptive signals can be evoked through central pathways that convey information from the peripheral sensors, to the brainstem, and to the cervical motor nuclei that produce neck muscle activation. Proprioceptive signals can also be used to activate spinal reflex pathways by evoking reflexes such stretch reflexes in neck muscles. (Peterson, Goldberg et al. 1985; Wilson, Schor et al. 1986; Manzoni 1988; Wilson and Schor 1999).
One of the major difficulties in studying reflexive head movements has been to tease apart how each of the sensory modalities is used throughout the execution of a reflex. Even if one could separate out the contributions of a specific sensory modality, it would be difficult to identify which pathway caused the response because many parallel pathways share common sensory modalities (Gdowski and McCrea 1999; Gdowski, Boyle et al. 2000; Gdowski, Belton et al. 2001). One way to simplify the problem is to create contexts in which one of the sensory modalities is not activated. For example, proprioceptive signals related to head on trunk rotation are minimally produced if the head is not permitted to move with respect to the trunk during whole body translation. In this open loop context, only vestibular signals can be used to generate neck muscle activity. This vestibular-evoked activity presumably contributes to the forces exerted on the device used to restrain the head from moving with respect to the trunk. Based on this principle, we have used the forces exerted by the head and neck during whole body translation as a method for assaying collic reflexes evoked by only vestibular signals associated with linear translation. In this chapter, we address the fundamental question: is there an active response of the head and neck when the body is translated?

We were able to further use this technique to determine if linear vestibular signals are utilized to the same extent when the body is translated in different directions. There are several lines of evidence that suggest linear reflexes could be activated differently depending on the direction of translation. At the single unit level, neurons have been found to be maximally activated during specified directions
of translation. The responses of these neurons are spatially tuned and as a population are biased to side-to-side translations (Dickman and Angelaki 2002). At the level of muscle activation, each neck muscle has been found to be tuned towards exerting force on the head in a particular direction (Vasavada, Li et al. 2001). At the behavioral level, postural stabilization during whole body translation in cats has also been shown to be spatially tuned towards increased stabilization during the side-to-side directions of translation (Horak, Shupert et al. 1994). Taken together these results suggest that the translational VCR in squirrel monkeys may also exhibit directional dependent behavior during translations in the horizontal plane. In this chapter we aim to answer a second fundamental question: is the active component of the head stabilization sensitive to the direction that the body is translated? By answering these two fundamental questions we address what role vestibular sensory information plays towards driving an active component of the head and neck response during whole body translation.

To further address these issues we performed a bilateral labyrinthectomy on a single animal and repeated our experiments. This allowed us to evaluate responses in the absence of vestibular sensory signals and to determine the magnitude of the effect that vestibular information plays in stabilizing the head. Finally, we implanted an electromyographic (EMG) patch electrode on the left splenius muscle of a different single animal in order to confirm the activity of neck muscles during our experimental paradigm. The EMG recordings provided a direct measure of the muscle activation that underlies the active component of force during translation and
demonstrates more directly the presence of a mechanism that utilizes vestibular information to stabilize the head with respect to the trunk during whole body translation.
2.2 Materials and Methods

*Surgical Preparation*

The University Committee for Animal Resources at the University of Rochester approved all surgical and experimental procedures. The animals were housed under conditions that comply with National Institutes of Health standards as stated in the *Guide for the Care and Use of Laboratory Animals* and the Association for Assessment and Accreditation of Laboratory Animal Care International.

Five adult male Squirrel monkeys were used in this study. Each animal was surgically prepared for chronically recording forces exerted on the head during linear translation. All surgeries were carried out under sterile conditions under 3% isoflurane anesthesia. A dental acrylic cap was rigidly connected to the cranium of each animal by implanting small stainless steel screws into the skull. A keyed bolt was placed stereotaxically within the dental acrylic cap so that the head could be connected to the experimental apparatus with a head orientation that was pitched 15° downward. In squirrel monkeys, this head orientation places the horizontal canal in alignment with the earth horizontal plane of the experimental apparatus. The head bolt was placed on the cap along the sagittal suture on the most caudal aspect of the occipital bone.

In a separate surgery, a bilateral labyrinthectomy was carried out in one animal to lesion the vestibular endorgans. A retroauricular approach was used in which the boney labyrinth was gradually drilled through the otic capsule. When the
perilymphatic space was entered, a micropick was used to undermine the sacculus and sever its nervous innervation. The same procedure was then carried out for the utriculus, and semicircular canals. In this particular case, a unilateral labyrinthectomy was carried out prior to the experiments conducted in this study. The animal was first studied as a unilaterally lesioned subject and then the other side was lesioned to complete the bilateral labyrinthectomy.

One animal was also surgically prepared for electromyographic recordings from neck muscles. An incision was made on the lateral aspect on the left dorsal side of the animal’s neck. The neck muscles were bluntly dissected into layers to reveal the splenius muscle. A small silicon patch with embedded bipolar steel electrodes was sutured onto the splenius muscle. Each pair of electrodes was composed of two stainless steel Teflon coated wires which were barred to expose a 2mm long portion of wire spaced 2 mm apart. Each electrode was sutured perpendicular to the splenius muscle striations of the splenius and the lead was run subcutaneously to the skull cap and soldered to a permanent pin connector.

**Experimental Setup**

In all experiments, the animals were seated on a chair within a box in order to maintain an upright posture. The orientation of animal’s head was held in a neutral position that was defined as having the head facing forward relative to the upper torso and pitched 15° nose downward. Movements of the animal’s whole body were delivered by placing the box and animal on a multi-axis rotator and translator (Figure 2-1A). In all experiments, the animals were translated with their head and trunk both
fixed rigidly to the chair. This was accomplished by having each animal wear a customized jacket that was connected to the chair in order to maintain the animal’s orientation with respect to the experimental apparatus. Drawstring straps were used to attach the animal’s jacket to a V-shaped back plate. The animals were attached to the back plate at both shoulders and around the hips to minimize trunk movement with respect to the chair. All experimental paradigms were conducted in the dark to minimize visual contributions to the responses that were recorded. Animals were continuously monitored using an infrared camera system located in the recording room.

The vestibular stimulator (Acutrol Inc.) consisted of three motors that were used to rotate the animal around earth horizontal and earth vertical axes as well as translate along a sled that was aligned with an earth horizontal axis. The animal could be translated or rotated in any direction by first positioning the body on the apparatus. This was accomplished by mounting the animal’s chair in the center of a sundial that permitted the rotation the animal’s whole body with respect to the axis of translation or rotation (Figure 2-1B). The animal was first oriented so that side-to-side motion was produced (Figure 2-1C). This orientation is referred to as 0°. Similarly, the orientation for fore-aft translation is denoted as 90°. Movements of the experimental apparatus were monitored using outputs from the Acutrol control system (acceleration, velocity, and position) of the apparatus.

A miniature quartz-based tri-axial piezoelectric force transducer (Kistler, model 9317B) was used to measure three orthogonal components of force. The dc-
drift associated with each sensor was eliminated using a conditioning circuit (Kistler) with a nulling amplifier. The transducer was initially mounted on a block so that each of the three sensors could be tested and calibrated by measuring gravitational force with the block in different orientations. After the transducer was calibrated it was oriented on the experimental apparatus so that one sensor measured forces in the fore and aft direction (z), the second sensor measured forces in the right to left (side-to-side) direction (x), and the third sensor measured forces in the upward and downward directions (y). The transducer was positioned so that positive values of force corresponded to forward, leftward, and upward directions. The calibration of the transducer was verified after it was put on the experimental apparatus by placing a fixed mass (0.25 lb.) at the location where the head was later attached. The force produced by the fixed mass was then measured while the apparatus was sinusoidally translated in space (2Hz, 0.5 G). The transducer was then rotated 90° on the experimental apparatus using the sundial and the calibration procedure was repeated. For verification purposes, the measured force was compared to the theoretical force computed from the mass and system acceleration. Transducer linearity was also tested by translating at different amplitudes of acceleration and by placing the sundial at 45° in order to activate two sensors simultaneously and equally during linear translation.

A standalone data acquisition system (National Instruments system, PXI) connected to a PC via TCP-IP was used throughout experiments to acquire data and to control movement of the experimental apparatus. The acquisition system included:
analog inputs and outputs (16 bit), and digital input and output lines. Software for controlling the NI system and experimental apparatus was developed in a LabView RT environment. All analog signals including feedback signals and forces were low pass filtered (Bessel, 200 Hz cutoff), and recorded using the analog inputs of the NI system (sampling rate: 500 Hz). The EMG activity of muscles were differentially pre-amplified and filtered (x5000, DC-1.0KHz) using an eight-channel electromyography system (AMT-8, Octopus, Bortec Biomedical Ltd.). The analog signals of EMG activity were rectified, low pass filtered (Bessel, 200 Hz cutoff), and recorded using the analog inputs of the NI system (sampling rate: 500 Hz).

**Experimental Paradigms**

A sequence of experimental paradigms was completed in order to quantify the forces exerted on the head when the whole body was translated along the earth horizontal plane in all directions about the vertical axis of the body. The first experimental paradigm was designed to quantify the responses to sinusoidal translation. Initially, the apparatus was oriented to produce side-to-side translations of the animal’s whole body in space with sled motion (i.e. sundial set to 0°). The animal then experienced 0.5G peak acceleration sinusoidal translations over a range of stimulus frequencies (0.5-4Hz). The orientation of the animal was incrementally changed (15° on the sundial) and the translation paradigm was repeated six times until the sled produced translations in the fore and aft directions (i.e. sundial set to 90°). A total of seven experimental runs were conducted. This permitted 14 directions to be directly tested (i.e. positive acceleration for forward directions and
negative for backward directions). For all directions of translation, the force output was tested for symmetry. It was found in each case that the peak force in the positive direction was equivalent to the peak force in the negative direction.

A different sequence of experimental runs was used to quantify the EMG activity when the whole body was translated along the earth horizontal plane in different directions with respect to the head and trunk orientation. The stimulus used in these experiments was a position shift paradigm where the sled was moved 20cm, with a peak velocity of 100 cm/s, and a peak acceleration of 0.5G. This stimulus was timed so that the peak velocity was reached only instantaneously before the sled began to decelerate. The stimulus was delivered at unpredictable time points by randomizing the interval between each translation and unpredictable direction by randomizing which direction the sled moved in each trial. Initially, the apparatus was oriented to produce side-to-side translations of the animal’s whole body in space with sled motion (i.e. sundial set to 0°). The orientation of the animal was incrementally changed (45° on the sundial) and the translation paradigm was repeated two times until the orientation of the animal on the sled produced translations in the fore and aft directions (i.e. sundial set to 90°).

**Data Analysis**

The kinematic data of the sled (position and velocity) and force data (x, y, and z directions simultaneously) from the load cell during sinusoidal translations were recorded over at least 10 stimulus cycles. Each direction of force was cyclically averaged with respect to stimulus frequency and fit with a sinusoid to determine the
magnitude of the force in each direction. A resultant vector was computed from the three directional magnitudes for each experimental condition.

In some of the figures, normalized force is shown. Peak force was normalized by the peak force recorded in the fore-aft direction. The fore-aft direction was chosen since it was in most cases the largest force recorded. This process was done so that spatial asymmetry could be quantified and compared across the population as a function of direction. Two statistical analyses were performed to assess spatial asymmetry. A two-way ANOVA was used to examine the effect of direction of translation on peak force measured as well as animal. This analysis was done using the normalized forces for all animals in the population. Additionally, the response of each animal for each direction of translation, before the peak force was normalized, was fit with an ellipse and the major and minor axes of each best-fit ellipse were used to calculate the eccentricity of the ellipse using the following equation:

\[ e = \sqrt{1 - \left(\frac{b}{a}\right)^2} \]

In this equation, \( e \) is the eccentricity, \( a \) is the major axis of the ellipse, and \( b \) is the minor axis. Eccentricity provides a measure of the asymmetry of the 2D force data.

**EMG Analysis**

Peak time and onset time of EMG records were calculated with pre-filtered data. Peak time was considered to be the time of the maximum value. Onset time was determined by finding the first EMG value after the onset of sled movement that was two standard deviations above noise on the electrode when the table was stationary.
To determine the noise level, 2 seconds of activity from the recording electrode was averaged and the standard deviation was determined. This activity was recorded while the table was stationary, the animal was calm, and the investigator could detect no voluntary EMG activity. The point in time when the EMG signal rose above two standard deviations over the average of the noise was used as the onset time of EMG activation. EMG records were then filtered with a simple moving average filter over 20 time points.
2.3 Results

Forces Measured During Linear Translation

Four animals were translated sinusoidally with the head and body oriented in the earth-horizontal plane. An example of the analysis procedure for forces recorded from the force transducer is shown in Figure 2-2. The cyclically averaged raw data from 2Hz sinusoidal translations of an animal at 0°(side-to-side), 45°, and 90°(fore-aft) is shown along with the sinusoidal fits that were applied to the averages. Force measured in the side-to-side direction of the animal is shown on the top row, and force measured in the fore-aft direction of the animal is shown in the middle row. Each column corresponds to a direction of translation in the horizontal plane. The bottom row shows the magnitude of the resultant vector. The third force axis was not included because it was perpendicular to the plane of translation and showed a constant 1 G force reading during all stimulations. The peak of the vector combination of the sine fits of two axes that lie in the horizontal plane was used to assay directional sensitivity. This value is shown graphically as the peak of the fit of the plots on the bottom row of Figure 2-2. The force exerted on the head was quantified for a sinusoidal whole body translation stimulus at frequencies (2 Hz, 0.5 G) in which voluntary mechanisms phase locked to the stimulus are not thought to exist (i.e. cancellation of the VOR).
Directional sensitivity of forces exerted on the neck during whole body translation

The net force was quantified as a function of the direction of translation along the horizontal plane. Translations were executed first in side-to-side directions (denoted as 0°). The peak net forces recorded during each direction of translation for each animal are shown in Table 2-1. The overall peak force varied from animal to animal. This variance could be due to many factors (e.g. differences in head mass), which are reviewed in the discussion section.

<table>
<thead>
<tr>
<th></th>
<th>0° (side to side)</th>
<th>15°</th>
<th>30°</th>
<th>45°</th>
<th>60°</th>
<th>75°</th>
<th>90° (fore-aft)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subject S</td>
<td>0.19 lbs</td>
<td>0.20 lbs</td>
<td>0.25 lbs</td>
<td>0.26 lbs</td>
<td>0.33 lbs</td>
<td>0.36 lbs</td>
<td>0.33 lbs</td>
</tr>
<tr>
<td>Subject E</td>
<td>0.15 lbs</td>
<td>0.17 lbs</td>
<td>0.18 lbs</td>
<td>0.18 lbs</td>
<td>0.19 lbs</td>
<td>0.20 lbs</td>
<td>0.22 lbs</td>
</tr>
<tr>
<td>Subject B</td>
<td>0.15 lbs</td>
<td>0.16 lbs</td>
<td>0.18 lbs</td>
<td>0.20 lbs</td>
<td>0.21 lbs</td>
<td>0.21 lbs</td>
<td>0.21 lbs</td>
</tr>
<tr>
<td>Subject G</td>
<td>0.21 lbs</td>
<td>0.23 lbs</td>
<td>0.24 lbs</td>
<td>0.25 lbs</td>
<td>0.26 lbs</td>
<td>0.27 lbs</td>
<td>0.26 lbs</td>
</tr>
</tbody>
</table>

Table 2-1: Peak force measured for each subject in each stimulus direction before normalization.

Although the net force varied across animals, its magnitude was consistently dependent on the direction of translation. The smallest peak forces were observed during the side-to-side (0°) direction of translation for each animal. Similarly, the largest peak forces were observed during translations in directions that were close to the fore-aft direction (75 - 90°) for each animal. Normalization was chosen to characterize the relative directional sensitivity of peak forces across the population. The peak force observed in the fore-aft direction was used to normalize the peak force for each direction. This normalization was chosen because the largest forces were typically observed in the fore-aft directions. The normalization results in a
percentage with respect to the force observed in the fore-aft direction. The normalization value for each animal is the fore-aft measurement shown in Table 2-1. Figure 2-3 shows the normalized peak force experienced on the head during translations as a function of direction along the horizontal plane for each of the four animals. If the forces exerted on the head were the same during translations in all directions (as would be expected for an inanimate mass) the plots would be circular with a value of 1. The plot for each of the animals was elliptical and deviated from circularity where the force decreased by 12-24% for side-to-side translations relative to fore-aft translations.

Several statistical tests were performed to determine if this asymmetry was significant. First, the population was analyzed as a whole using normalized force data. The mean normalized force for the entire population at each direction of translation is shown in Figure 2-4. The error bars in this figure denote the upper bound of the 95% confidence interval on the mean. We performed a two-way ANOVA on this data where the nominal variables were direction of translation and individual animal. This analysis determines whether the normalized force was significantly affected by either the individual animal, the direction of translation, or both (p<0.05). Results of this analysis show that there was a significant effect of direction of translation on the observed force (p=0.03) but not a significant effect of individual differences between animals (p=0.4). We expected this result as we normalized forces in order to remove the effects of animal individuality from the results. We also performed paired t-tests to compare each direction of translation
with the side-to-side direction of translation. This analysis determined that 90°, 75°, and 60° were significantly different from 0° (p<0.05), while the other directions were not.

<table>
<thead>
<tr>
<th></th>
<th>Major Axis (a)</th>
<th>Minor Axis (b)</th>
<th>Eccentricity (e)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subject S</td>
<td>0.31 lbs</td>
<td>0.18 lbs</td>
<td>0.81</td>
</tr>
<tr>
<td>Subject E</td>
<td>0.23 lbs</td>
<td>0.18 lbs</td>
<td>0.62</td>
</tr>
<tr>
<td>Subject B</td>
<td>0.22 lbs</td>
<td>0.17 lbs</td>
<td>0.64</td>
</tr>
<tr>
<td>Subject G</td>
<td>0.24</td>
<td>0.22</td>
<td>0.40</td>
</tr>
</tbody>
</table>

Table 2-2 Eccentricity of best fit ellipses of peak force for each animal: The force data from each animal was fit with an ellipse before it was normalized. The major and minor axes of these best fit ellipses are reported in the table above along with the eccentricity of that ellipse.

Furthermore, forces for each animal as shown in Table 2-1 were plotted as polar plots and then fit with an elliptical function. Each of these fits yielded the size of the major and minor axis. These measures were used to calculate the eccentricity of the ellipse. The results of this analysis yielded eccentricities of 0.84, 0.62, 0.64 and 0.40. If the ellipse were a perfect circle, the eccentricity would have been equal to 0. Each one of these measurements indicates a substantial deviation from circularity. Both this analysis, and the two-way ANOVA quantitatively demonstrate the spatial bias in the force results that is apparent in on the polar plots.

The deviation from circularity was consistent in all animals indicative of an active process. A circular plot would have been expected if such a process did not
exist, because the mass of the head is constant and produces the same magnitude of force regardless of the stimulus direction. It was not possible to discern if the putative active process enhanced the forces produced during fore-aft translation or minimized the forces during side-side translation. Either type of active mechanism would result in the asymmetries observed in Figure 2-3 and shown with the analysis discussed above.

**Relationship between the direction of force and the direction of translation**

We looked for further evidence of an active process by comparing the direction of force that was observed with the direction of the stimulus. In the absence of an active process, the force produced during translation would be expected to be in the same direction as the stimulus. If an active process were present it could produce force in any direction with respect to the stimulus. Consequently, the net force observed during experiments would be the vectorial combination of the passive force due to the mass of the head and the force due to the active process. We compared the direction of the net force with the direction of the stimulus for all stimulus directions (Figure 2-5A). In all cases, a linear regression between the direction of the net force with the direction of the stimulus produced an average slope of $0.90 \pm 0.02$ (degrees/degrees) and an average y intercept of $8.5^\circ \pm 2.3^\circ$. This suggests that if an active process was evoked it either produced forces that were significantly weaker than the passive forces produced by the mass of the head, or the force vector that was evoked by the process was nearly in the same direction as the stimulus.
Temporal relationship between the force produced and the stimulus

If there were no active processes, the peak force produced during translation would also be expected to be in phase with peak acceleration. An active process could disrupt this relationship if it utilized sensory signals that were not in phase with linear acceleration, or if there was a considerable time lag in the response of the process. We evaluated this possibility by computing the relative phase difference between when the peak force was produced (\( \Theta_F \)) and the peak acceleration of the stimulus (i.e. \( \Theta_S-\Theta_F \)). The phase difference is plotted as a function of the direction of translation for all animals in Figure 2-5B. On average across all animals and all directions of translation, the phase difference was small, 0.51° ±3.78°. A linear regression was carried out for all animals and the average slope for all animals was 0.02 ± 0.001 (degrees/degrees). Like the prior analysis for the direction of force, these results support the conclusion that if an active process was evoked it produced forces that were significantly weaker than the passive forces produced by the mass of the head. Alternatively, the active process could have a short time lag resulting in only a small phase difference between the force produced and stimulus acceleration.

Frequency Dependency of Forces

An active process might also be expected to be sensitive to the stimulus frequency. A fundamental question was whether the force asymmetry observed in Figure 2-3 was also dependent on the stimulus frequency. To address this question, we quantified the forces produced over a range of stimulus frequencies (0.5 Hz to 3.36 Hz; in quarter octave increments, with a peak acceleration of 0.25 G). Only the fore-
aft direction and the side-to-side direction were investigated, because those were the
directions that most readily demonstrated directional asymmetry. A lower peak
acceleration was used in these stimuli in order to allow for a larger frequency range to
be tested using the same stimulus amplitude.

In this case, the force at each frequency was normalized the same force used
to normalize the forces in Figure 2-3. The top Figure 2-6 shows the normalized peak
force measured for all subjects at each stimulus frequency in the fore-aft direction of
translation and the black line shows the same thing for the side-to-side direction of
translation. The peak force measured during the side-to-side direction of translation
was always smaller than the peak force measured during the fore-aft direction of
translation. However the difference between fore-aft direction and the side-to-side
direction was more apparent for the low stimulus frequencies. The difference
between the side-to-side and fore-aft directions at the 2hz frequency at this stimulus
amplitude (0.25 G) is on average 15%, which was similar to the 18% difference that
was measured at the previous stimulus acceleration (0.5 G). However, at the lower
stimulus frequency (0.5 Hz) the difference between the peak force measured during
side-to-side translations and the peak force measured during fore-aft translations was
on average 40%. For each direction of translation, we performed a two-way ANOVA
to determine whether there was a significant effect of individual animal, frequency of
the stimulus, or both. For the fore-aft direction there was no significant effect of
individual or frequency of stimulus (p>0.05). However for the side-to-side direction
there was a significant effect of frequency of stimulus (p<0.001) but not individual
animal \( (p > 0.05) \). This result means that during fore-aft translation, the frequency of the stimulus does not significantly affect the forces measured while during side-to-side translation the force measured is significantly affected by the direction of translation, trending towards decreasing force at lower frequencies.

**Effect of Labyrinthectomy on Force Magnitude**

In order to more directly assess the utility of the vestibular system in actively regulating torque on the neck and force on the head, we conducted a complete labyrinthectomy to eliminate all vestibular sensory signals. The labyrinthectomy was completed in a single animal that already had a unilateral peripheral vestibular lesion five years prior. We performed another labyrinthectomy in the opposite ear in order to eliminate all vestibular sensory information. The forces exerted on the head during translation were recorded on days 1, 3, 7, and 45 post labyrinthectomy in order to quantify the effect and recovery from vestibular sensory loss.

Figure 2-7 shows the raw and cycle averaged force during side-to-side sinusoidal translations \( (2\text{Hz}, 0.5 \text{G}) \) recorded the day before and the day after the labyrinthectomy. The results indicate that the forces exerted on the head were greatly increased after the removal of all vestibular sensory information. The peak force exerted during translation on day 1 post labyrinthectomy increased to 0.18 lbs. This was a 189\% increase from recordings prior to the labyrinthectomy (0.095 lbs).

The peak force measured during sinusoidal translations in all directions in the horizontal plane is shown in Figure 2-8. The stimulus direction is shown on the x-axis and the peak force measured (lbs) on the y-axis. The blue line shows the peak force
measured for each direction of translation before the labyrinthectomy and the red lines (in various shades) show the peak forces measured for each direction after the labyrinthectomy. These results showed that the force measured in each direction significantly increased after the labyrinthectomy. More importantly, that the peak forces measured did not recover to their pre-labyrinthectomy levels over 45 days postoperatively. An unpaired t-test was used to compare the pre-labyrinthectomy data for all directions of translation with all post-labyrinthectomy data (all days, all directions). A statistically significant difference (p<0.0001) was found between the pre and post labyrinthectomy forces measured.

Figure 2-9 shows the same before and after data in polar plot. The post-op data was averaged over all of the data collection sessions after labyrinthectomy. The solid lines in Figure 2-9 shows the results from the day prior and an average of all days post labyrinthectomy. The eccentricity of best-fit ellipse of the before labyrinthectomy data was 0.11 and eccentricity of best-fit ellipse of the average of all post labyrinthectomy data was 0.09. Since both values were close to 0 it was not possible to conclude that there was any asymmetry of forces demonstrated in this subject.

Fore-aft movements produced forces of 0.16 lbs and similarly those produced during side-to-side movements were 0.17 lbs. After post-op day 45 the animal was euthanized and weight of the head was determined to be 0.155 kg. We estimated the force exerted on the neck based solely on the mass of the head and the stimulus acceleration. The animal’s head mass was determined directly by measuring the weight of the animal’s head after post-mortem removal from the body. This estimate
is plotted as a dashed line in Figure 2-9. AS can be seen in Figure 2-9, the force estimate from the head’s mass nearly coincided with the force observed post-op for all directions of translations. This is indicative of the absence of any active process that utilizes vestibular information.

_Neck Muscle Activity Evoked by Whole Body Translation_

Thus far we have presented biomechanical evidence of active control of the head with respect to the neck for which vestibular sensory information was thought to be utilized. The next set of experiments was conducted to more directly assay the active process controlling the head by recording the electromyographic activity of neck muscles.

The top half Figure 2-10 shows raw EMG records recorded during a side-to-side translation of the animal. The blue line in the top graph shows the position of the sled over time, and the green line is the filtered, rectified, and smoothed EMG signal from the patch on the left splenius muscle. The animal was translated along a side-to-side direction. The record of EMG activity in the top half of Figure 2-10 shows the activity both in response to the sled movement, and voluntary EMG activity independent of sled motion. In order to determine if there was any EMG activity that was induced by the sled movement, the epochs of this top graph that contain the movement of the sled were expanded and are shown in the bottom half of Figure 2-10. The pink bars in the top half of Figure 2-10 indicate the portions of the whole record that are shown below. The red traces in the bottom half of Figure 2-10 are the acceleration of the sled 0.5 peak G). The sled acceleration was shown in these plots to
help identify the onset of whole body translation. The four plots on the bottom half of the figure shows that the activity of the left splenius muscle was elicited between 20 ms and 45 ms after the onset of acceleration of the whole body. We can also see from these traces that left splenius muscle activity was elicited when the direction of translation was both leftward (positive) and rightward (negative). Peak EMG activity for each block in order was 0.23 mV, 0.26 mV, 0.19 mV, and 0.24 mV. There was not a significant difference (unpaired t-test; p<0.05) between the average peak EMG activity observed during leftward-directed translation compared to rightward-directed translation. This suggests that neck muscles on both sides of the neck were activated in response to translations in both directions.

**Directionality of EMG Activity**

We have shown that forces were reduced more during side-to-side translations than during fore-aft translations. We questioned whether the splenius muscle was specifically activated more during side-to-side translations. To address this question, we repeated the experiments shown in Figure 2-10 in the side-to-side direction (0°), 45° between side-to-side (0°) and the fore-aft direction (90°). The bottom half of Figure 2-11 shows the average EMG recording from the left splenius muscle averaged over all of the translations in each of the three directions and the top half of Figure 2-11 shows sled position over time. The red in the bottom half of the figure represents the average EMG recording during side-to-side translations (between 5 and 8 repetitions). Similar to the results shown in Figure 2-10, there was a peak of EMG activity (0.48 mV) during side-to-side translations approximately 25 ms after the
onset of movement of the whole body. Additionally, during the 45° translations there was also a peak EMG activity (0.24mV) calculated approximately 25 ms after the onset of movement, however the average peak was 50% smaller during the 45° direction of translation. However, during the fore-aft translations, shown in blue in the bottom half of Figure 2-11, there was no discernable peak within 75 ms of the onset of movement. These results suggest that the splenius muscle may be activated more robustly during side-to-side directed translations.
2.4 Discussion

The overall goal of this study was to determine if and how vestibular sensory information is used to modify the forces exerted on the head during whole body translation. It has been well established that vestibular sensory information is used to activate neck muscles in response to whole body rotations to stabilize the head in space and in turn stabilize gaze (Ezure and Sasaki 1978; Ezure, Sasaki et al. 1978; Peterson and Goldberg 1982). However, the role of vestibular information to stabilize the head in response to whole body translations is physiologically poorly understood. The system we used to characterize the role of vestibular information during translation recorded the forces on the head during passive translations of the whole body with the animal’s head fixed relative to the trunk. By fixing animal’s head relative to the trunk and delivering our translational stimuli in complete darkness, we were able to isolate vestibular contributions by minimizing the sensory information coming from other sensory modalities.

The force measured by the transducer during our experiments was the net force representing the vector combination of forces due to the passive biomechanics of the head/neck plant and forces generated actively by the contraction of neck muscle. It was not possible to directly separate these components to specifically identify the active component of force. Despite this limitation, it was possible to use overall net force as an assay of the significance of the active component during linear translation. The results showed a spatial asymmetry with respect to the peak forces produced as a function of the stimulus direction in the horizontal plane. Based on
Newton’s Laws, when a mass is accelerated it produces an opposing force equal to
the product of the object’s mass and the acceleration regardless of the direction of
translation. Thus, if the forces measured were only due to passive properties of the
head/neck plant the peak force measured would have been expected to be the same in
all directions. No asymmetry in forces would have been observed as a function of
direction of translation. The asymmetry is indicative of an active mechanism that
exerts force on the head differently for different directions of translation. Presumably
the component of the force measured that is actively produced is due to neck muscle
contractions that exert force on the head. However, it was not possible to know from
these biomechanical force measurements alone what the role of vestibular sensory
information was because it was not possible to separate the absolute effect of the neck
muscle contractions from the net forces that were measured. For example, neck
muscles could have been activated and contracted in a manner that reduced the
passive biomechanical force on the head during side-to-side translation or in a manner
that increased the force on the head during fore-aft translations. Additionally, it was
not possible to determine exactly what the role vestibular sensory information played
in producing active generation of force exerted on the head. Since we did not know if
the force measured was due only to passive biomechanics, it was not possible to tell
whether the active process was increasing the forces during fore-aft translation or
decreasing the forces on the head during side to side translation.

A bilateral labyrinthectomy was performed on a single animal to address how
the forces changed in the complete absence of vestibular sensory signals. The data
shown in Figure 2-8 and Figure 2-9 show the results of the same series of horizontal translation performed before and after complete labyrinthectomy. These results show that the peak forces measured before labyrinthectomy were 40% lower than peak forces measured after labyrinthectomy. Although the labyrinthectomy was conducted in only one animal the results indicate in intact animals that vestibular sensory signals provide the CNS with information that is used to reduce forces on the head during whole body translations.

The results of the EMG recordings from the left splenius muscle during whole body translations also support the hypothesis that the head was stabilized during translation in a manner that would function to reduce head movements on the trunk. Figure 2-10 shows that the left splenius muscle was activated during both leftward-directed and rightward-directed side-to-side translations. The natural extension of this result is that the right splenius muscle would have also been activated during translations in both directions. Thus, these results support that the CNS used a strategy that co-contracted muscles on both sides of the neck during whole body translation. The outcome of such a strategy would be to increase the stiffness of the neck, which would in turn reduce motion of the head during whole body translation. Indeed, the forces never recovered to their pre-labyrinthectomy levels. This is consistent with a complete permanent loss of vestibular information. Adaptation could not have occurred in our experiments (i.e. proprioceptive) because other sensory signals were minimized in our experiments. However, the method of stabilization demonstrated in the EMG recordings, and the stabilization demonstrated
in the load cell recordings are different. In fact this con-contraction would not be expected to reduce the forces on the head during the head-fixed conditions of the first experiments. It’s possible that different strategies are employed because the stimuli were different in the two experiments. Despite the possible differences between head stabilization strategies the end results of both strategies would be the same. Movements of the head with respect to the trunk would be reduced. It is possible both strategies were used because it was not possible to determine if muscle activity was exactly the same on both sides of the neck.

The reduction in forces on the head that is shown in our studies is indicative of a different mode of head stabilization strategy compared to what has been described during horizontal plane whole body rotations. When head stabilization has been investigated in rotation in both humans (Keshner, Cromwell et al. 1995; Keshner and Peterson 1995; Keshner 2000) and animals (Goldberg and Peterson 1986; Gdowski and McCrea 1997; Gdowski and McCrea 1999) it is most commonly described as producing compensatory head movement in the opposite direction as the rotation, functioning to help stabilize gaze. Head movements produced when the whole body is translated have been investigated by several groups because of their putative roles during gait (Raphan, Imai et al. 2001) and in potentially reducing the risk of whiplash injuries that occur during automobile accidents (Kumar, Ferrari et al. 2004; Kumar, Ferrari et al. 2004). They have also been investigated in laboratory environments during translation of the body in the fore-aft and side-to-side directions (Vibert, MacDougall et al. 2001; Keshner 2003; Keshner 2004). In particular, the
study by Keshner et al (2003) showed that head movements produced during whole body translation of labyrinth deficient human subjects have been shown to have higher peak accelerations in comparison to control subjects. These results are consistent with our results in that higher forces were observed to be exerted on the head of labyrinthectomized animals.

Taken together our results suggest that head stabilization in whole body translation might serve to reduce rather than produce head movements. This, at first, might seem like a very different mode of head stabilization than we normally think of based on studies done in rotation. However, our results are consistent with anatomy and physiology studies described in Chapter 1. It has remained unclear whether postural control of the head during translation served to help prevent whiplash injuries by reducing head movements or to inadvertently contribute to the occurrence of whiplash injuries by producing head movements (Vibert, MacDougall et al. 2001). Our results suggest that the former is the more likely mode of head stabilization utilized during translation where the vestibular reflexes serve to reduce the force on the head and in turn to reduce overall head movements with respect to the trunk. This mode of stabilization of the head could be useful towards maintaining balance, and in protecting the fragile anatomical structures of the neck from distraction injuries, such as whiplash.

The results also demonstrate that not only is vestibular sensory information providing information to the CNS which reduces forces on the head during whole body translations, but that this reduction in forces was asymmetrical and more
effective for translations in the side-to-side direction. In Figure 2-3, we showed that the peak forces on the head were reduced during side-to-side translations compared to fore-aft translations for all animals. This result suggests that the 12-20% reduction in force that occurs during side-to-side translations when compared to fore-aft translations results because of an increase in the output from vestibular pathways in those directions. This behavioral result reflects neurophysiologic evidence that demonstrates an increased presence of neurons responsive to lateral directed motion compared to neurons responsive to fore-aft directed motion among otolith-only neurons and otolith canal convergent neurons in the vestibular nuclei of macaques (Angelaki and Dickman 2000; Dickman and Angelaki 2002). This same spatial tuning of otolith sensitive neurons in the vestibular nuclei has also been shown in other animal models such as decerebrate cats and rats (Schor, Lakshminarayanan et al. 1984; Schor 1988; Bush, Perachio et al. 1993). The similarity between the spatial asymmetry of vestibular driven head stabilization and the directional preference of neurons in the vestibular nuclei suggests that the asymmetry measured in our studies may originate form properties of neurons in the vestibular nuclei.

In general, the results suggest that vestibular evoked collic reflexes could be important to normal activities such as locomotion. It is well known both vestibular and proprioceptive sensory signals are used to maintain the body’s stability throughout locomotion (Brandt and Dieterich 1993; Hollands, Sorensen et al. 2001; Vallis and Patla 2004). Additionally, with vestibular loss, it has been shown that gait instability occurs, specifically as a result of lateral motion of the body and altered
percept of body tilt (Allum, LB et al. 2008). This gait instability could be due in part to the need to maintain vision aligned with the spatial horizontal during forward heading locomotion in order to maintain balance (Xiang, Yakushin et al. 2008). The linear translations of the whole body that occur during locomotion cause rotations of the head relative to the body due to the biomechanics of the head/neck plant. The vestibular ocular reflex (VOR) can compensate for rotations of the head by counter rotating the eyes primarily in pitch and yaw in order to maintain gaze stability. When the head rotates in pitch and in yaw the gain of the VOR is near unity and thus gaze is effectively stabilized. However, the VOR is not as well suited to compensate for head rotation in roll. The gain of the VOR in torsion or roll is maximally 0.6 in monkeys and in humans (Crawford, Cadera et al. 1991; Henn, Straumann et al. 1992). Thus, in order to keep vision aligned with the spatial horizontal during locomotion, it would be advantageous to stabilize head relative to the trunk and prevent excessive roll head movements and minimize the utilization of the torsional VOR.

The studies of the role of vestibular sensory information during locomotion really underscore the importance of vestibular pathways in the maintenance of stability throughout locomotion. Furthermore, they also suggest that vestibular pathways play a particularly important role in controlling roll head movements and medial lateral postural sway during locomotion (Grasso, Glasauer et al. 1996; Grasso, Assaiante et al. 1998; Raphan, Imai et al. 2001; Dunbar, Badam et al. 2004). This data is the first evidence in animals that demonstrates the importance of vestibular signals during side-to-side motion and may explain why neurophysiologic pathways
through the vestibular nuclei are biased in their sensitivity towards this direction of motion.
2.5 Conclusions

The results of this study point towards an otolith evoked head stabilization response that reduces the forces exerted on the head during whole body translations in the horizontal plane. We have also shown that this response is more active during translations in the side-to-side direction. This type of head stabilization is different from what has often been described during whole body rotation. The key difference between the translation and rotation responses is that during whole body rotation, the vestibular response evokes compensatory head movements in the opposite direction of rotation. The otolith evoked postural response actively reduced forces on the head. The end result of this would be to reduce head movements relative to the trunk during a head free whole body translation. This mode of head stabilization, to our knowledge, has never before been demonstrated physiologically in animals.
Figure 2-1 Experimental Set-up for Chapter 2: A) Photograph of vestibular stimulator. Arrow shows direction of translation. B) Diagram of animal seated in primate chair wearing a jacket to restrain trunk movement relative to the chair. The chair was placed in the center of a sundial that could rotate as shown by the arrow. This allowed the animal to be translated in any direction relative to its body. The force transducer was connected to both the primate chair and to the animal’s head bolt. C) Diagram showing the side-to-side (left), 45° (center), and fore-aft (right) directions of translation.
Figure 2-2 Demonstration of computational methods in Chapter 2: The top 2 rows show the cycle averaged force data from a single animal during whole body translations (solid lines) along with the sinusoidal fits of each average (dotted lines). The bottom row shows the dimensionless magnitude of the vector combination of both the cycle average data (solid lines) and sinusoidal fits (dotted lines) of the top 2 rows. Each column is a different direction of translation, as shown by the diagrams at the top of the figure. All recordings were collected during 2 Hz, 0.5 G peak acceleration translational sinusoids. This data from Subject G.
Figure 2-3 Polar plot of peak forces measured during horizontal plane translation: A polar plot of normalized peak force as a function of all directions of translation during 2 Hz 0.5G peak acceleration sinusoidal translations. Peak forces were measured in the horizontal plane for 4 animals. Peak force values were normalized to peak force measured during fore-aft direction (90°). Orange dots indicated directions of translation that were actually tested. Directions without orange dots duplicates of the corresponding directions in other quadrants.
Each bar shows the mean normalized force for all four animals at each direction of translation. Error bars denote the upper bound of the 95% confidence interval. Since force was normalized for each animal to the force measured during the 90° (fore-aft) translation direction, the normalized force for each animal was equal to 1 for the 90° direction. Hence, there is no error bar shown for this direction of translation.
Figure 2-5 Direction and phase of peak forces: A) The calculated direction of the peak force measured as a function of direction of translation for all four animals. B) The phase difference in degrees between the stimulus and the force measured as a function of direction of translation for all four animals. In both plots, 0° is side to side translation and 90° is fore-aft.
Figure 2-6 Frequency dependency of peak forces: Normalized peak force measured during side-to-side (bottom plot) and fore-aft (top plot) for all 4 animals over a range of stimulus frequencies (0.5 Hz to 3.36 Hz, in quarter octave steps). Forces were normalized to the same normalization value used to normalize forces in Figure 2-3.
Figure 2-7 Raw recordings of force before and after labyrinthectomy: Forces exerted on the head during side-to-side whole body translation (2Hz, 0.5G) when the head was not permitted to rotate with respect to the trunk. Forces before and immediately after labyrinthectomy (blue and red) are shown. Sled acceleration (green). Raw data records on left, cycle-averaged records on right. Records from Monkey C.
Figure 2-8 Effect of labyrinthectomy over time: Peak force measured before labyrinthectomy (blue) and days 1, 3, 7, and 45 after labyrinthectomy during sinusoidal translations with a frequency of 2Hz and a peak acceleration of 0.5G.
Figure 2-9 Effect of labyrinthectomy on peak forces: Peak force (not normalized) measured during sinusoidal translations with a frequency of 2Hz and a peak acceleration of 0.5G on the day before (blue) and the average of days 1, 3, 7, and 45 after (red) labyrinthectomy during whole body translations in the horizontal plane. Predicted force values based on the mass of the head (0.155 kg) for a completely passive system are shown as the black dotted line. Red dotted lines show +/- one standard deviation of the mean of average post-labyrinthectomy response. Orange dots indicated directions of translation that were actually tested. Directions without orange dots duplicated with respect to the corresponding directions in other quadrants.
Figure 2-10 EMG activity during position shift stimulation in the side-to-side direction: Top trace shows 25 of EMG activity from the left splenius muscle (green line) and sled position over time (blue line). The shaded red epochs in the top graph are magnified in the 4 plots across the bottom. Each of these 4 plots shows left splenius EMG activity (green) sled acceleration (red), and slide position (blue). Data shown is from Monkey E.
Figure 2-11 EMG activity during position shift stimulation in the horizontal plane: EMG Top portion shows sled position over 0.5 seconds of an example shift. The bottom portion shows rectified, filtered, and smoothed EMG activity recorded from the left splenius muscle during position shifts in the side-to-side direction (red), 45° direction (green), and fore-aft direction (blue). Orange dots indicated peak of EMG after onset of stimulus.
Chapter 3: Convergence of Proprioceptive and Vestibular Sensory Information in the Vestibular Nucleus

3.1 Introduction

In the previous chapter, the results underscored the importance of the role that the vestibular pathways have in controlling inertially produced roll head movements during lateral translation of the whole body. We showed that the forces exerted on the head was reduced during whole body translations. This observation was shown to be directionally asymmetric and more active during translations in the side-to-side direction. Additionally, the lack of intact vestibular pathways was found to result in larger forces exerted on the head during translation. The requirement that intact
vestibular pathways be in place implies that the neural mechanisms that underlie this response are contained within these pathways. The goal of the work discussed in this chapter was to characterize these neural mechanisms by recording the extracellular responses of single neurons in the vestibular nucleus of the brainstem. The vestibular nucleus was chosen because it is the first synapse where afferent information from otolith end organs and semicircular canals converge in the brainstem. Some of these neurons ascend to cortical regions through thalamic pathways and some neurons project to the spinal cord where they are involved in reflexive control of posture. Furthermore, many neurons in the VN also receive indirect sources of proprioceptive input. Thus, this region has signals related to “outcome 1” and “outcome 2”. How these signals converge, dictates how the overall reflexes are governed to control head movements. The goal of these recordings was to characterize how sensory information converges within the vestibular nuclei and to understand how they might contribute to the postural control of the head during whole body translation.

Since the results we detailed in Chapter 2 showed that postural collic reflexes are more active during side-to-side direction of translation, we focused on recording the responses of neurons that were sensitive to side-to-side translations of the whole body. During a whole body translation in a real-life scenario, such as outcome 2, the result is head movement with respect to the trunk. In this scenario, the vestibular system would sense both the side-to-side translation of the whole body relative to space as well as the roll head movement relative to the trunk that would be generated
as a result of the biomechanics of the head and neck plant. The roll movement of the head relative to the body, produces proprioceptive signals that convey relevant information about movements of the head with respect to the trunk. Neurons in VN are likely to be active throughout the entire sequence of events that occur during whole body translation and convey an integrated response consisting of signals from otoliths, canals, and proprioceptive sources. Recording these neurons provides evidence of when reflex pathways are active and gives insight into how these signals might be used for reflexive control of head movement.

As was discussed in Chapter 1, semicircular canals provide information representing rotational motion of the head in space and the otolith endorgans provide information representing linear translation of the head in space. Recording studies that employed the use of electrical stimulation, have attempted to understand how information from semicircular canals and otoliths converge on single neurons in the vestibular nucleus of the brainstem (Wilson 1972; Ono, Kushiro et al. 2000; Uchino, Sato et al. 2001). These studies suggested that 30-40% of VN neurons respond to stimulation from both otoliths and canals. However, studies which used direct translation and rotation of the head while recording from single units in the VN have shown a higher prevalence of neurons with converging input from canals and otoliths (Markham and Curthoys 1972; Bush, Perachio et al. 1993; Dickman and Angelaki 2002).

Neck proprioceptors provide information about the movement of the head relative to the trunk rather than movement the head in space. The cervicocollic reflex
is a stretch reflex whose input comes from proprioceptive signals. The CCR has been shown to have an important role in compensating for the loss of vestibular function in both animals and humans (Peterson and Goldberg 1982; Horak, Shupert et al. 1994; Maurer, Mergner et al. 1998). The additional presence of neck proprioceptive signals on vestibular nucleus neurons is well documented in a variety of species (Pompeiano and Barnes 1971; Boyle and Pompeiano 1980; Anastasopoulos and Mergner 1982; Gdowski, Boyle et al. 2000; Gdowski, Belton et al. 2001; Gdowski, Duarte et al. 2006). These signals have been shown to provide information about both static and dynamic head-on-trunk movement to secondary vestibular neurons (Fuller, Lin et al. 1988 Jan.; Manzoni, Pompeiano et al. 1998). When the head is rotated on the trunk in yaw, these signals have been shown to be primarily antagonistic to vestibular signals during passive head-on-trunk rotation (Boyle and Pompeiano 1980; Anastasopoulos and Mergner 1982; Gdowski and McCrea 2000). However, little is known as to how these signals converge in awake primates during lateral bending movements that are commonly produced when the whole body is translated. The primary goal of this study was to characterize the patterns of convergence of vestibular signals and proprioceptive signals during roll plane rotations of the head relative to space and of the body relative to the head.
3.2 Materials and Methods

The University Committee for Animal Resources at the University of Rochester approved all surgical and experimental procedures. The animals were housed under conditions that comply with National Institutes of Health standards as stated in the *Guide for the Care and Use of Laboratory Animals (2003)* and the Association for Assessment and Accreditation of Laboratory Animal Care International.

*Surgical Preparation*

Two adult squirrel monkeys were surgically prepared for chronic recordings of single-units. Surgeries were carried out under sterile conditions with 3% isoflurane anesthesia. A dental acrylic cap was rigidly connected to the cranium of each animal by implanting small stainless steel screws into the skull. A keyed bolt was stereotaxically placed within the dental acrylic cap so that the head could be connected to experimental apparatus with a head orientation that was pitched 15° downward. In squirrel monkeys, this head orientation placed the horizontal canal in alignment with the earth horizontal plane of the experimental apparatus. The head bolt was placed on the cap along the sagittal suture on the most caudal aspect of the occipital bone.

*Experimental Recording Conditions*

In all experiments, the animals were seated on a chair within a box in order to maintain an upright posture. Movements of the animal’s whole body in space were
delivered by placing the box containing the animal on the vestibular apparatus that had a multi-axis rotator and translator (Figure 3-1A). The vestibular apparatus (Acutrol Inc.) consisted of three motors that were used to rotate the animal around earth horizontal and earth vertical axes as well as translate along a sled that was aligned with an earth horizontal axis. The animals could also be translated along an axis parallel to an earth horizontal axis (straight arrow in Figure 3-1). The animals were translated with their head and trunk fixed both rigidly attached to the chair (no head-on-trunk movements were permitted). All animals wore a jacket that was connected to the chair in order to control the animal’s trunk orientation with respect to the experimental apparatus. The animal’s jacket was connected to the chair by attaching the jacket to a V-shaped back plate with drawstrings. The drawstrings tightly connected the animal’s jacket to the V back plate at both shoulders and around the animal’s hips. This was done to minimize any trunk movement with respect to the chair. All experimental paradigms were conducted in the dark to minimize visual contributions to the responses that were recorded. Animals were continuously monitored using an infrared camera system located in the recording room.

In these experiments, the animals were only rotated around an axis parallel to an earth horizontal axis (shown as the dotted line in Figure 3-1A). This rotation allowed movements of the animal’s body and head only in the coronal plane. The location of this axis, relative to the animal, was determined empirically for each animal and is described below. The animals were seated in the chair and the axis of rotation was moved sequentially in 0.25 inch steps from a position 0.5 inches from
the level of the C2 vertebra to the C6 vertebra. In each position, the investigator evoked voluntary roll head movements by the animal. When the roll axis was centered in close proximity to C5, the animals readily generated voluntary head movements in roll. These head movements were the largest in magnitude over the range of the axis positions tested. Once the position of the axis was determined for each animal, that position was used throughout all experiments. In the two animals used in these experiments the distance from the interaural axis of the animal to the location of the roll axis was 5.08 cm and 4.92 cm.

In order to deliver specific controlled stimulation, the bolt on the animal’s head was fixed to a rod assembly behind the animal (Figure 3-1B). The rod assembly allowed two types of stimulation to be delivered depending upon its configuration. The animal’s head could be fixed with respect to the trunk or fixed in space while the trunk was rotated with respect to the head. Whole body translation (WBT) stimulation was produced with the animal’s head fixed relative to its trunk so that the movements of the head and trunk were the same while the animal was translated in the side-to-side direction. Whole body rotation (WBR) stimulation was produced with the animal’s head fixed relative to its body while the body was rolled about the empirically determined axis described above. Finally, passive neck flexion extension (PNFE) stimulation was delivered while the animal’s head was fixed relative to space and its body was rotated underneath his head. A potentiometer was aligned coincident with the axis of rotation of the animal so that roll rotation of the animal’s head with respect to the trunk could be quantified. The dynamic range of both WBR
and PNFE stimulation was limited (±40°) by the apparatus. All analog signals including linear translation position and velocity, rotational position and velocity of the animal’s body, and rotational angle of the animal’s head relative to trunk were recorded in the same manner as discussed in Chapter 2.

Extracellular recordings from single VN neurons were recorded using epoxy-coated tungsten microelectrodes (4-7 MΩ impedance, FHC Corp.). Electrodes were placed in a protective 23 gauge guide tube that were advanced together into the brain through the dura, cerebellar cortex, and cerebellar tentorium. The electrode was then advanced out of the guide tube and into the cerebellum and finally into the vestibular nuclei with a remote controlled hydraulic microdrive. During the advancement of the electrode, side-to-side interaural WBT (Figure 3-2B) and WBR (Figure 3-2A) were used as search stimuli in order to identify brain regions sensitive to vestibular stimulation. These stimuli were effective for neurons located within the vestibular nucleus. Neural activity was amplified and filtered (500Hz to 4kHz, Bak). Action potentials were recognized with a spike template match algorithm (Alpha Omega, Inc.) and recorded as a digital event using the real-time clock of the data acquisition system. The data acquisition system recorded analog signals and digital events at a sampling rate of 500 Hz. Spike times were used to calculate instantaneous spike rate for individual neurons (method described below).

**Experimental Procedure**

The responsiveness of each cell was first evaluated by the investigators for sensitivity to eye movements. When a cell was isolated from the noise, visual stimuli
were presented to the animal to evoke both smooth pursuit eye and saccadic eye movements in several directions. Units were qualitatively examined for sensitivity to eye movements and if any response related to eye movements was observed, the unit was not studied further. No quantitative analysis was carried out to evaluate eye movement sensitivity and consequently some neurons included in this chapter could have had minimal eye movement sensitivity.

Once a unit was determined to have no sensitivity to eye movements, it was studied during three different stimulus conditions including: 1) whole body translation (WBT) along an axis aligned with the coronal plane of the animal and parallel to an earth horizontal axis, 2) whole body rotation (WBR) about an axis aligned with the sagittal plane of the animal and located approximately at the level of the C5 vertebra, and 3) PNFE (proprioceptive neck flexion/extension) about the same axis as WBR (Figure 3-2C). The WBT stimulus consisted of sinusoidal translations (1 Hz; either 0.25 G or 0.125 G), the WBR stimulus consisted of sinusoidal rotations (1 Hz; 25°/s), and the PNFE stimulus consisted of sinusoidal rotations (1 Hz; 25°/s).

**Data Analysis**

All data analyses for this study were performed using IGOR Pro (Wavemetrics Inc.). Instantaneous firing rate was computed by building a histogram of the number of spikes found during each 0.002 second interval (corresponding to the sampling rate of 500 Hz used analog signals) over the course of the stimulus. The histogram was filtered with a moving average filter with a window size of 0.04 seconds, similar to that carried out in other studies (Dickman and Angelacki, 2002).
Spike rate was then calculated by dividing the number of spikes in each bin by the width of the bin (0.04 seconds) yielding a spike rate having dimensions of spikes per second. Instantaneous spike rates were then cycle by cycle averaged with respect to stimulus velocity for WBR and acceleration for WBT. The gain and phase of the response were calculated by fitting the averaged spike rate histogram with a sine function with the frequency of the curve fitting equation fixed to the stimulus frequency (Figure 3-3). For WBT stimuli, the response gain was expressed as sp/s/G and phase of the response was expressed in degrees relative to stimulus acceleration. For WBR stimuli, the response gain was expressed as sp/s/°/s and the phase of the response was expressed in degrees relative to stimulus velocity. For PNFE stimuli, the response gain was expressed as sp/s/°/s and the phase of the response was expressed in degrees relative to stimulus velocity. In all cases, phases were calculated with respect to ipsilateral movement. The gain of the response to specific stimuli is also referred to as the neuron’s “sensitivity”. These analytic methods have been used in several previous studies (McCrea, Chen-Huang et al. 1996; Gdowski and McCrea 1997; McCrea and Chen-Huang 1999; Gdowski, Boyle et al. 2000). Neurons that were sensitive to WBR stimuli were thought to receive semi-circular canal input and neurons that were sensitive to WBT stimuli were thought to receive otolith input. It is important to note that the only stimulus directions tested in this study were whole body rotation in roll and whole body translation in the side-to-side direction. Neurons sensitive to side-to-side translations and lateral roll are the most likely
neurons that contribute to the signal processing of reflexive head movements produced in that direction.

**Sensitivity to WBR stimuli**

The classification of neurons was based on the sensitivity to rotational and translational stimuli. Additional analytic techniques were employed because the rotational axis was distal (approx. 5 cm) from the interaural axis. This axis could not be readily changed while engaged in the recording of neurons. Consequently, this experimental position placed the vestibular endorgans off-axis from the center of rotation. As such, both canals and otolith endorgans were activated by off-axis WBR stimuli. An analytic technique was developed to determine which vestibular endorgans (canal and/or otolith) contributed to the response. In this analytic technique, the goal of the technique was to determine if the response was due to only canal input. The gain of the canal contribution to the neuron’s response to off-axis WBR stimulation was estimated assuming a linear relationship in combining the two signals such that:

\[ DR_{wbr} = A \omega + B l \]

In this equation \( DR_{wbr} \) is the instantaneous firing rate of the neuron during off-axis WBR stimuli (sp/s), \( A \) is the gain of the neuronal response due to canal contribution (sp/s/°/s), and \( \omega \) is the rotational velocity during WBR stimulus (°/s). The values of \( B \) and \( l \) were both calculated specifically for this analytic technique. \( B \) is the calculated gain of the neuronal response to linear velocity and is calculated based on the neuronal response to the WBT stimulus and \( l \) is the estimated
instantaneous linear tangential velocity at the level of the interaural axis (cm/s).
Throughout the chapter the neuronal response of a neuron to WBT stimulus is
expressed relative to the stimulus acceleration (sp/s/G), however for this analytic
method it was necessary to also calculate the gain of the neuron with respect to linear
velocity (sp/s/cm/s).

The value of \( l \) is calculated for the entire WBR stimulus cycle by multiplying
the rotational velocity, \( \omega \), by the distance from the rotational axis to the interaural
axis, \( r \). This resulted in a calculated instantaneous linear velocity \( l \), at the level of the
interaural axis. This instantaneous velocity was multiplied by the gain of the
neuronal response to during WBT, \( B \), to get the estimated instantaneous firing rate of
the neuron due to the otolith contribution at all time points during the WBR stimulus.
A bin-by-bin subtraction of this estimated firing rate was the subtracted from the
recorded firing rate of the neuron during the WBR stimulus and the resultant response
was fit with a sinusoid. The gain of the resultant response is referred to as the
corrected WBR gain.

**Neuron Classification**

Responses to a stimulus were considered to be significant if the gain was
above a minimal threshold (0.15 sp/s°/s for both WBR and PNFE, and 50 sp/s/G for
WBT). For rotational stimuli, each neuron was classified according to Duensing and
Schafer (1958) where Type 1 was assigned for responses in phase with ipsilateral
rotation (phase between 270° and 90°), and Type 2 was assigned for responses in
phase with contralateral rotation. Neurons were then further classified as being either
**Histological Reconstruction**

After completion of all experimental recordings, electrolytic lesions were placed at the location of tracks have neurons sensitive to vestibular stimulation. Electrolytic lesions were done by administering DC current of 1 mA for 5-10 seconds. Lesions were used for confirming that recordings were located in the VN. After lesions were completed euthanasia was performed. This was done first by sedating the animals with ketamine and xylazine. The animals were then given pentobarbital sodium trans-cardially and perfused with 10% NBF solution. The brains were then removed, sectioned (40μm thick), mounted on slides, and counterstained. A standard nissel stain was used to stain the sections. Sections were microscopically visualized at 50x to indentify electrolytic lesions within the VN. The lesions were then utilized to anatomically map the physiologic recordings based on the grid locations of the track penetrations within the recording chamber. The anatomical map was constructed by correlating the histology with a squirrel monkey brain atlas. A top-down view was constructed from the atlas by indentifying the borders of the structures in coronal sections and mapping the extent of the structure in the horizontal plane which was approximately coincident with the penetration plane of the recording chamber.
3.3 Results

Anatomical Location of Neurons

One hundred and nine neurons were recorded in the VN in two animals. The approximate location of these neurons was determined using a histological reconstruction. An example of a stained section is shown in Figure 3-4. The slice shown in this figure also shows the electrolytic lesions that were made in a single track in order to localize recording tracks within the VN. This track was approximately in the center of all the recording tracks that resulted in neurons responsive to vestibular stimuli. One lesion was located at the location of the most dorsal neuron in the track (lesion duration: 5 s of DC current). A second lesion was located at the most ventral neuron in the track (lesion duration: 5 s of DC current). A third lesion was the largest and was located in the middle of the vestibular sensitive region (lesion duration: 10 s of DC current) within the vestibular nuclei. Using the calibration line of the microscope and an atlas of the squirrel monkey brainstem, an approximate location for this section was determined to be 3 mm posterior to AP 0. Using the borders of the medial and lateral VN marked on the atlas, an approximate top down map of the VN was constructed. Using the position of recording tracks relative to the lesions, as well as the approximated position of the lesions, an approximate top down recording location map was constructed for each animal. The maps for each animal were superimposed and the approximate recording locations are shown on a single map in Figure 3-5. The majority of the neurons were recorded in
the medial aspects of the LVN. A smaller percentage of neurons were located in the MVN. The recording chambers, unfortunately, prevented recording from the most lateral aspects of the LVN.

**Vestibular Responses – WBR and WBT responses**

Neurons responded with a variety of responses to rotational and translational stimuli. Figure 3-6 shows the different response categories that were observed. Units were considered responsive to WBR stimulus based on the corrected WBR gain of each unit (for details see methods). 88 of 109 units (80.7%) were responsive to the WBR stimulus and were considered to be rotationally sensitive. 83 of 109 units exhibited sensitivity (76.1%) to the WBT stimulus.

Each neuron was classified as one of 3 types in terms of vestibular input including: canal-only, otolith-only, and convergent neurons. Examples of the responses of each of these types of units to both WBR (left column) and WBR (right column) stimulation are shown in Figure 3-6. Units that were sensitive both to WBR stimuli and WBT stimuli were classified as convergent neurons. Units that had only WBR responses were classified as canal-only. Finally, units with only WBT responses were classified as otolith-only units. Overall 43.12% (47/109) units responded to only one type of vestibular stimulation (i.e. either canal-only or otolith-only).
All units were categorized as either type 1 or type 2 based on the corrected WBR gain and phase. The polar plots in Figure 3-7 show the gain (along the radial axis) and phase (as angulations) for each unit responsive to the WBR stimulus. These plots also identify which units were classified as Type 1 (open symbols) or Type 2 (closed symbols). Furthermore the *canal-only* units are shown in Figure 3-7A and the *convergent* units are shown in Figure 3-7B. The population of WBR sensitive neurons was split roughly evenly into type 1 (48 units) and type 2 (40 units) categories. Canal-only and convergent neurons with type 1 responses to WBR tended to be more sensitive than those with type 2 responses. This is consistent with the two populations looking equidistant from the origin in the polar plots in Figure 3-7. The average type 1 response gain of a neuron sensitive to WBR was $0.65 \pm 0.51$ sp/s/°/s while the average type 2 response gain was $0.51 \pm 0.33$ sp/s/°/s (Table 3-1). However, the difference between the gains of type 1 and type 2 responses was not statistically significant (using unpaired t-test; $p>0.05$). The response of these neurons to WBR stimulation typically phase led whole body velocity with an average phase type 1 responses of $353^\circ \pm 41.3^\circ$ and for type 2 units it was $173^\circ \pm 37.2^\circ$.

The polar plots in Figure 3-8 show the gain (along the radial axis) and phase (as angulations) for each unit responsive to WBT stimulus. These plots identify which units were classified as Type 1 (open symbols) or Type 2 (closed symbols). Furthermore, the *otolith-only* units are shown in Figure 3-8A and the *convergent* units are shown in Figure 3-8B. Neuronal response types during WBT stimulation also were split roughly evenly between type 1 responses (39) and type 2 responses (44).
In the case of WBT sensitive units, type 2 units tended to be more sensitive than type 1 units. The average gain of WBT type 1 response was $191.6 \pm 158.7 \text{ sp/s/G}$ and type 2 response was $246.9 \pm 130.0 \text{ sp/s/G}$. Similar to WBR responses the gains of these two populations was also not statistically significant (using unpaired t-test; p>0.05).

Unlike WBR responses, WBT responses tended to lag stimulus acceleration. The average phase for type 1 units was $44^\circ \pm 37.8^\circ$ and for type 2 units it was $233^\circ \pm 18.8^\circ$. The majority of these neurons fell about the $45^\circ$ - $225^\circ$ line in Figure 3-8. In some rare cases, neurons were found in phase with velocity ($90^\circ$ - $270^\circ$) in Figure 3-8.

**Vestibular Responses – Canal-Only and Otolith-Only Neurons**

Units were also evaluated with respect to their classification as canal-only, otolith-only, and convergent. Twenty-six of the single units were classified as canal-only neurons based on their response to 1Hz WBR stimulation. The average gain of canal-only units was $0.83 \pm 0.55 \text{ sp/s/°/s}$, which was significantly higher than the average WBR gain of the convergent units (unpaired t-test; p<0.01). Most of the

<table>
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<th>N</th>
<th>Gain</th>
<th>Phase</th>
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<tbody>
<tr>
<td>WBR Type 1</td>
<td>48</td>
<td>$0.65 \pm 0.51$</td>
<td>$353^\circ \pm 41.3^\circ$</td>
</tr>
<tr>
<td>WBR Type 2</td>
<td>40</td>
<td>$0.51 \pm 0.33$</td>
<td>$173^\circ \pm 37.2^\circ$</td>
</tr>
<tr>
<td>WBT Type 1</td>
<td>39</td>
<td>$191.6 \pm 158.7$</td>
<td>$44^\circ \pm 37.8^\circ$</td>
</tr>
<tr>
<td>WBT Type 2</td>
<td>44</td>
<td>$246.9 \pm 130.0$</td>
<td>$233^\circ \pm 18.8^\circ$</td>
</tr>
</tbody>
</table>

Table 3-1: Gain and phase for all neurons that were sensitive to each vestibular stimulation type. WBR gains shown in this table are corrected for influence of translational signal. Standard errors are shown.
canal-only units had ipsilateral semicircular canal input; 20 units had type 1 responses and only 6 units had type 2 responses (Figure 3-7A).

Twenty-one units recorded in this study were classified as otolith-only units. Otolith-only units were not as heavily weighted as canal-only units towards ipsilateral inputs. Of the otolith-only units, 12 units had ipsilateral responses and 9 units had contralateral responses (Figure 3-8A). The average gain of otolith-only units was 153.80±87.01 sp/s/G, which was significantly lower than the WBT sensitivity of convergent units (unpaired t-test; p<0.05).

**Vestibular Responses -- Convergent Neurons**

Units were classified as convergent units if the unit responded to both WBR and WBT stimulation (Figure 3-7B and Figure 3-8B). Each convergent neuron was classified as having a type 1 or type 2 response to both WBR and WBT stimuli. As shown in Table 3-2, neurons that were classified as convergent had all 4 possible combinations of response to WBR and WBT stimuli. Convergent units represented more than half of the total units recorded (62/109; 57.8%). The average gain of convergent units was 0.54±0.35 sp/s/°/s for the WBR stimulus and 242.05±151.27 sp/s/G for the WBT stimulus.

Based on the responses to both WBR and WBT stimuli, convergent neurons could be further split into two broad categories. The first category was referred to as convergent-convergent units and consists of those units with convergent input from the same side (i.e. units that had a type 1 WBR response and a type 1 WBT response or a type 2 WBR response and a type 2 WBT response; see Figure 3-9B). The second
category was referred to as convergent-mixed response units. These units had convergent input from different sides (i.e. units with a type 1 WBR response and a type 2 WBT responses or a type 2 WBR response and a type 1 WBT response; see Figure 3-9A and C).

The majority of the population of convergent neurons received ipsi-ipsi or contra-contra input. (42/62; 68.9%). Of those units 40.4% (n=17) had convergent responses sensitive to the ipsilateral movements and 59.5% (n=25) had convergent responses sensitive to the contralateral movements. Twenty units of the 62 with convergent vestibular input (32.2%), received either contra-ipsi or ipsi-contra input. These units were evenly split with 10 units responding to contralateral otolith and ipsilateral canal stimulation (contra-ipsi) and 10 units responding to ipsilateral otolith and contralateral canal stimulation (ipsi-contra). There were no significant differences in WBR or WBT sensitivity between neurons ipsi-contra input or contra-ipsi input (unpaired t-test, p>0.05).

**Proprioceptive Responses**

Neck proprioceptive signals have been reported on VN neurons in the squirrel monkey during rotations of the body around the head in the yaw plane (Boyle and Pompeiano 1980; Gdowski and McCrea 2000). Proprioceptive stimuli (PNFE) in this

<table>
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<tr>
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<th>WBR Type 1</th>
<th>WBR Type 2</th>
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<tr>
<td>WBT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type 1</td>
<td>16</td>
<td>11</td>
</tr>
<tr>
<td>Type 2</td>
<td>10</td>
<td>25</td>
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Table 3-2: Response types of units with convergent vestibular input from both canals and otolights.
study were carried out at 1 Hz as body roll about an axis near the C5 vertebra while the head was held stationary in space. This condition minimized vestibular stimulation while producing proprioceptive stimulation. Our search stimulus to locate neurons was WBR and WBT. Consequently, only neurons that responded during vestibular stimulation were tested for response sensitivity to the proprioceptive stimulus. An example unit response to PNFE stimulation is illustrated in Figure 3-10. The average response of this neuron was 0.48 sp/s/°/s when the trunk was rotated and the head was held stationary in space. This response was in phase with trunk velocity with a phase difference of 40°. Overall, 63 neurons (63/109; 57.68%) were responsive to PNFE stimulation with a threshold greater than 0.15 sp/s/°/s. The average gain of these units overall was 0.32±0.16 sp/s/°/s.

All units responsive to PNFE stimulation were classified as type 1 or type 2 based on the response properties (see methods for details). Furthermore, the vestibular response properties of these units were used to further divide PNFE responsive neurons into 3 categories: Canal-only + PNFE, Otolith-only + PNFE, and Convergent + PNFE. The polar plots in Figure 3-11 show the gain (along the radial axis) and phase (as angulations) for each unit responsive to PNFE stimulus. These plots also show which PNFE responses were classified as Type 1 (open symbols) or Type 2 (closed symbols). The canal-only + PNFE units are shown in Figure 3-11A. The otolith-only + PNFE units are shown in Figure 3-11B, and the convergent + PNFE units are shown in Figure 3-11C. Of the 63 units responsive to PNFE stimulation, 32 units were classified as type1 units because the PNFE response of these units was in
phase with body movements toward the ipsilateral ear and 31 units were classified as type 2 units because the response was in phase with body movements toward the contralateral ear. Type 1 units had an average gain of 0.32±0.15 sp/s/°/s and phase of 328°±46° (with respect to stimulus velocity), while type 2 units had an average gain of 0.32±0.17 sp/s/°/s and phase of 80°±55° (with respect to stimulus velocity; shown in Table 3-3).

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<tr>
<th>PNFE</th>
<th>N</th>
<th>Gain</th>
<th>Phase</th>
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<tr>
<td>Type 1</td>
<td>32</td>
<td>0.32±0.15</td>
<td>328°±46°</td>
</tr>
<tr>
<td>Type 2</td>
<td>30</td>
<td>0.32±0.17</td>
<td>80°±55°</td>
</tr>
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Table 3-3 Response Properties of Neurons Sensitive to PNFE Stimulation: Gain and phase for all neurons that were sensitive to PNFE stimulation. Standard errors are shown.

All vestibular categories (canal-only, otolith-only, and all convergent types) were sensitive to PNFE stimulation. Of the units that were sensitive to PNFE, most were also sensitive to WBR (52/63; 82.5%). 40 of these units received convergent canal and otolith input and 12 received canal only vestibular input (9 Type 1: 3 Type 2). The remaining 11 units that were sensitive to PNFE in the roll plane were classified as otolith-only and only responded to WBT. These units were evenly split with 5 units receiving ipsilateral otolith input (type 1) and 6 units receiving contralateral otolith input (type 2).

**Neck proprioceptive signals and their relationship to vestibular signals**

In general, for most of the neurons that were sensitive to both WBR and PNFE, the sensitivity to PNFE was weaker (69.2%; 36/52). Figure 3-12 shows the
relationship between the gain of the PNFE response and the uncorrected WBR response. The uncorrected WBR response was used because we hypothesized that the proprioceptive signal on these neurons would be related to the combination of otolith and canal driven activity present on the same neurons during off-axis WBR. In our study no such relationship was observed (Figure 3-12). In each case, a linear trend line had small slopes with low $r^2$ values indicating little correlation between PNFE and WBR gains. For the PNFE + canal-only units the slope was 0.09 and the $r^2=0.01$ (Figure 3-12A), for the PNFE + otolith-only units the slope was 0.19 and the $r^2=0.001$ (Figure 3-12B), and finally for PFNE + convergent units the slope was -0.08 and the $r^2=0.06$ (Figure 3-12C). If the PNFE and WBR gains of each unit type had been well matched, neurons would have resided along the unity line (grey lines in Figure 3-12) and the slopes of the trendlines would have been near 1, and the $r^2$ values would also be near 1.

We further evaluated if the phase of the PNFE response was related to the phase of the WBR response. Figure 3-13 shows the relationship between the phase of the WBR response vs. the phase of the PNFE response for each neuron responsive to both stimuli. No orderly relationship between the phases of the WBR and PNFE responses was observed for these neurons. Again the linear trendline indicated this lack of a relationship having small slopes and low $r^2$ values. However, despite this lack of a relationship there were several neurons that resided near the unity line (grey line Figure 3-13), indicating that the PNFE and WBR response were perfectly out of phase. These few neurons were evaluated further. In general, it did seem that the
gains of the PNFE and WBR responses of these neurons were also similar; indicating that despite the existence of a general relationship, several neurons did have well matched gains and had completely out of phase responses to WBR and PNFE stimulation.

Despite the fact that the relationship between PNFE responses and WBR responses on individual neurons was not orderly, we carried out a vector addition of the WBR and PNFE fits on an individual neuron basis. When this was done it was determined that a total of 5 units of the 52 units that were sensitive to both PNFE and WBR had combined responses that would be attenuated to below threshold values (uncorrected WBR gain less than 0.15 sp/s/°/s) when uncorrected WBR and PNFE responses were added. This is a smaller number than reported in other studies using squirrel monkeys. However, we did find that even though only 5/52 units were attenuated completely, 24 of the 52 units had a response during WBR stimulation that would be attenuated by the addition of the PNFE response when the head was rotated on the trunk. This result suggests that despite the fact that there was not a simplistic relationship between the proprioceptive and vestibular sensitivity in the frontal plane, proprioceptive information was acting to diminish the vestibular response in 55.77% of the units we recorded that were sensitive to both sensory modalities.
3.4 Discussion

The primary goal of the work was to characterize the convergence of proprioceptive sensory information from neck proprioceptors and vestibular sensory information from the canals and otoliths during roll head movements. In order to accomplish this goal, we recorded from 109 non-eye-movement related neurons in the vestibular nucleus of 2 alert squirrel monkeys. However, as a secondary goal we first characterized the response properties of these neurons to canal and otolith input. Similar work has been conducted before by Dickman’s group (Dickman and Angelaki 2002). This work was conducted in rhesus macaques and characterized the otolith + canal convergence of neurons in the VN by responses to horizontal plane translation of the whole body and yaw whole body rotation. However, despite these fundamental differences in terms of both the animal model used and how canal + otolith convergence was characterized, our results are similar to those obtained the study by Dickman’s group (Dickman and Angelaki 2002). Most of the neurons recorded in our study were in the lateral part of the VN and along the border of the lateral and medial parts of the VN and most of the neurons received convergent otolith and canal input. This result is consistent with results presented in Dickman’s study (Dickman and Angelaki 2002). Their work showed that most convergent neurons were recorded in the same area of the VN. Furthermore, the proportion of neurons in the population characterized as canal-only, otolith-only, and convergent was similar in both our work and theirs. Finally, their work also tested the sensitivity of their otolith sensitive neurons to static roll tilts of the animal, and found that vestibular information related
to whole body static roll often converged with vestibular information related to horizontal plane whole body translation.

However, in the work conducted by Dickman’s group, neurons were classified as type 1 or 2 based on their response to WBR stimuli in yaw. In our work we classified units as type 1 or 2 based on both WBR stimuli in roll and WBT stimuli during side-to-side translations. This difference in classification methods led us to indentify 20 units with convergent canal + otolith input that had incongruent type classifications (referred to as convergent-mixed response units). This incongruent type classifications means that these units respond to whole body translations in one direction and roll head movements in the opposite direction. This response is particularly interesting because whole body translation results in an inertially driven counter roll of the head. When the whole body translation and counter rotation of the head happen at the same time, neurons with incongruent type classifications would have an enhanced firing rate. This enhancement in firing rate may be important to the simultaneous activation of the rVCR in roll and the tVCR in translation.

Despite the interesting vestibular convergence patterns observed in the neurons we recorded, the primary goal of this work was to characterize the convergence of vestibular and proprioceptive information in the VN. Our results show that most vestibular neurons in the squirrel monkey vestibular nuclei that process whole body rotations signals also process signals related to the movement on head relative to the trunk, is consistent with previously published results (Gdowski and McCrea 2000). Some studies in other species have generally shown that neck
movement signals combine antagonistically in a linear manner with vestibular signals on the same neurons (Rubin, Liedgren et al. 1977; Kasper and Thoden 1981; Fuller, Lin et al. 1988 Jan.). However other studies have shown little of this type of convergence (Cullen, Roy et al. 2001). Our results show that proprioceptive information from neck movements in the roll plane would interact antagonistically with vestibular information if the two responses were combined linearly. However the relationship was not as orderly or as well matched was previously been reported in squirrel monkeys during yaw rotations (Gdowski and McCrea 2000).

There are several reasons that could account for these differences. The first reason may simply be due to the nature of the head movement we applied. The animal’s heads in our study were fixed to a rod behind the animal’s head and the body was moved under the animal with the center of rotation located at approximately the level of the C5 vertebra. This location was selected as the point of rotation because size of head movements evoked about this point were the largest. However, a natural head movement in roll relies on neck flexion/extension along several cervical vertebra. Additionally, proprioceptive signals that originate from stretch receptors arise from numerous neck muscles that span multiple joints that are all stretched in complex combinations when the head moves naturally with respect to the trunk. The relatively low gain of the proprioceptive signals we recorded in our study may simply be due to the fact that we did not produce neck flexion/extension across the vertebra as would have been produced in completely head-free circumstances.
However, the main difference between our study and other studies in squirrel monkeys was that those studies focused on head-on-trunk movements and whole body rotations in yaw. In yaw, vestibulocollic reflexes have been shown to produce compensatory head movements that reduce the head velocity in space in response to whole body rotation. This reduction in head velocity in space tends to reduce the vestibular drive and represents a negative feedback loop. However, results from Gdowski and McCrea show that the firing rate of many secondary vestibulospinal pathway neurons was not proportionally reduced with decreases in head velocity in space (Gdowski and McCrea 1999; Gdowski, Boyle et al. 2000). These investigators hypothesized that proprioceptive inputs, by cancelling out the vestibular signal related to head rotation on the trunk, contributed to the ability of the secondary vestibular neurons to remain sensitive to trunk in space velocity. However, the vestibulocollic reflex that produces a compensatory movement of the head in roll during side-to-side whole body translation has not been observed in squirrel monkeys.

When the whole body is translated in the side-to-side direction, the tVCR is activated. However, the tVCR does not likely function alone in controlling the head’s movement. As the head rolls during whole body translation the rVCR is activated. The combined activities of the tVCR and rVCR are to reduce head-on-trunk movement. This helps in gaze stabilization. The torsional vestibulo-ocular reflex (tVOR), which counter rotates the eyes in response to roll movements of the head, has been shown to have a much lower gain than the horizontal vestibulo-ocular reflex (approximately 0.6). The lack of a VOR suitable to stabilize the retinal image in
response to head movements in roll may be a fundamental reason that the function of
the rVCR and tVCR may be to stabilize the head relative to the trunk during whole
body translation. This different function of the rVCR in roll compared to the rVCR in
yaw may also be one reason why proprioceptive processing is different when the two
reflexes are evoked. It may be important to head stabilization during side-to-side
translation that the rVCR be evoked maximally, and thus proprioceptive processing
that cancels out the drive for this reflex would be undesirable.

Despite these limitations, the results discussed in this chapter greatly improve
our understanding of CNS response to whole body translation. Both vestibular and
proprioceptive responses measured in the vestibular nucleus were similar, but
fundamentally different from responses measured during whole body rotation and
head on trunk rotation in yaw. The proprioceptive results, if confirmed by
experiments using more natural head movements, could indicate that during whole
body translation in the side-to-side direction, it is more important for the CNS to have
head on trunk information than to have head in space information. The vestibular
responses measured were also fundamentally different, and could underlie the
completely different head stabilization strategy that we showed in Chapter 2 is
employed by the CNS during whole body translation. In summary, we have
demonstrated that signal inputs and processing in the vestibular nucleus during whole
body translation in the side-to-side direction and during head rolls, is fundamentally
different from the processing that takes place during whole body and head rotation in
yaw.
Figure 3-1 Experimental setup for Chapter 3: A) Photograph of vestibular simulator. Straight arrow across the bottom shows axis of translation and curved arrow at the top shows direction of rotation. Dotted line shows axis about which rotation occurred. B) Side view of the animal seated in a primate chair. Dotted line shows axis of rotation aligned empirically to the determined best axis of rotation. Animal’s head bolt was rigidly attached to a rod that could be fixed relative to the primate chair (fixed relative to the animal’s body) or fixed relative to the room (fixed relative to space). C) “x” shows where axis of rotation was approximately located.
Figure 3-2 Experimental stimuli used in Chapter 3: The 3 stimuli used in this study shown schematically A) Whole Body Off-Axis Rotation B) Whole Body Translation C) Passive Neck Flexion/Extension.
Figure 3-3 Examples of neural processing methods: Plots on the left show 8 seconds of firing rate (green bars) of two different neurons in response to rotation and translation along with the stimulus (red lines). Plots of the right side of the figure show the cycle-by-cycle averaged firing rates (green bars) and stimulus (red lines) along with the sinusoidal fits to the firing rates (blue dashed lines). The scale for the left axis of both plots in each row is shown as the left axis on the left plot. The right axis of both plots in each row is shown as the right axis on the right plot. Neuron in the top row is: #68; monkey G; track 12; WBR gain: 1.38 sp/s°/s; equation of the sine fit of the averaged spike rate $23.49 + 27.63 \sin(6.28x - 1.55)$. Neuron in the bottom row is #31; monkey G; track 7; WBT gain: 250.8 sp/s/G; equation of the sine fit of average spike rate $65.73 + 36.31 \sin(6.28x - 0.87)$. 
Figure 3-4 Photograph of coronal histological section from monkey G: Photograph of a histological section showing lesion. Section was determined to be approximately located at p3 by use of anatomical landmarks and squirrel monkey brain stem atlas. Arrows indicated the location of the 3 electrolytic lesions. The dashed line shows the midline.
Figure 3-5 Top-down map of approximate recording track locations:

An approximate map of vestibular nucleus and locations of cellular recordings from both animals. This map was constructed based on the histologic reconstruction. Symbols on the map show approximate locations of 60 neurons. Neurons of the same type found in approximately the same location are not marked. A Squirrel monkey atlas was used to locate the approximate anatomical location of lesions. Tracks were placed on the map relative to the lesion location. MVN: Medial Vestibular Nucleus LVN: Lateral vestibular nucleus. The top of the map is rostral and the left of the map medial.
Figure 3-6 Three types of vestibular responses: Left column are responses to WBR with cycle average firing rate (green bars), firing rate fit (black dashed line) and stimulus velocity (red lines) and the right column are responses to WBR with cycle average firing rate (green bars), firing rate fits (black dashed lines), and stimulus acceleration (red lines). Each row shows a single neuron response. A. Canal-only neuron, #66 monkey G track 12. Corrected WBR gain: 1.01 sp/s/°/s; WBT gain: 21.76 sp/s/G. B. Convergent neuron, #26 monkey S track 3. Corrected WBR gain: 0.75 sp/s/°/s; WBT gain: 256.02 sp/s/G. C. Otolith-only neuron, #31 monkey G track 7. Corrected WBR gain: 0.09 sp/s/°/s; WBT gain: 250.88 sp/s/G.
Figure 3-7 WBR stimulation response properties: Gain and phase of the neuronal response in each neuron deemed sensitive to WBR. Gain is expressed as sp/s°/s and is shown along the radial axes as distance from the center. Phase is expressed in degrees (°) and is calculated relative to ipsilateral stimulus velocity. Black squares are type 2 units and black open squares are type 1 units classified as canal-only. Black circles are type 2 units and black open circles are type 1 units classified as convergent. Type 1 units are those with responses in phase with ipsilateral velocity or acceleration and are defined as units with a phase from 270° to 90°.

Units on the other side of the circle are classified as type 2 units. A. 19 type 1 and 7 type 2 canal-only units. B. 29 type 1 and 33 type 2 convergent units.
Figure 3-8 WBT stimulation response properties: Gain and phase of the neuronal response in each neuron deemed sensitive to WBT. Gain is expressed as sp/s/G and is shown along the radial axes as distance from the center. Phase is expressed in degrees (°) and is calculated relative to ipsilateral stimulus acceleration. Black squares are type 2 units and black open squares are type 1 units classified as canal-only. Black circles are type 2 units and block open circles are type 1 units classified as convergent. Type 1 units are those with response in phase with ipsilateral velocity or acceleration and are defined as units with a phase from 315° to 135°. Units on the other side of the circle are classified as type 2 units. A. 12 type 2 and 9 type 2 otolith-only units. B. 27 type 1 and 35 type 2 convergent units.
Figure 3-9 Three types of convergent vestibular responses: Left column plots show cycle averaged firing rate (green bars), firing rate sinusoidal fit (black dashed line), and stimulus velocity (red line) during to WBR. Right column plots show cycle averaged firing rate (green bars), firing rate sinusoidal fit (black dashed line), and stimulus acceleration (red line) during to WBT. Each row shows the responses from a single neuron. A. Convergent-mixed neuron with Type 1 WBR response and Type 2 WBT response. Neuron #108 monkey G track 15. Corrected WBR gain and phase: 0.23 sp/s/°/s and 19°; WBT gain and phase: 167.9 sp/s/G and 265°. B. Convergent-convergent neuron with Type 2 WBR response and Type 2 WBT response. Neuron #26 monkey S track 3. Corrected WBR gain and phase: 0.75 sp/s/°/s and 195°; WBT gain: 256.0 sp/s/G and 248°. C. Convergent- mixed neuron with Type 2 WBR response and a Type 1 WBT response. Neuron #105 monkey G track 15. Corrected WBR gain and phase: 0.39 sp/s/°/s and 200°; WBT gain and phase: 396.7 sp/s/G and 265°.
Figure 3-10 Raw and cycle average PNFE response: Plots show 8 seconds of firing rate (green bars) of a single neuron in response passive neck flexion (PNFE). Plots on the right side of the figure show the cycle-by-cycle averaged firing rates (green bars) and stimulus (red lines) along with the sinusoidal fits to the firing rates (black dashed lines). Neuron #113 monkey S track 20. Gain of PNFE response was 0.48 sp/s/°/s. Equation of sine fit to cycle averaged response was 31.36 + 12.272* sin (6.28* x +.71).
Figure 3-11 PNFE response properties: Gains and phases of the neuronal response to PNFE stimulation. Gain is expressed as sp/s/°/s and is shown about the radial axis as the distance from the center. Phase is expressed in degrees (°) and is calculated relative to ipsilateral stimulus velocity. Black open squares and black squares show canal-only + PNFE units. Black open circles and black circles show otolith-only + PNFE units. Black triangles and black open triangles show convergent + PNFE units. All open symbols are type 1 units and all filled symbols are type 2 units. A. Shows 4 type 1 and 8 type 2 neurons with PNFE and canal-only WBR responses. B. Shows 4 type 1 and 7 type 2 neurons with PNFE and otolith-only WBR sensitivity. C. Shows 20 type 1 and 20 type 2 neurons with PNFE and convergent WBR responses.
Figure 3-12 Relationship between WBR and PNFE response gains: Trendline for each plot is shown as dashed line, and unity line is shown as a grey line. Units were classified as Type 1 or 2 by WBR response. A. Gain of uncorrected WBR response plotted against the gain of PNFE response for neurons responsive to PNFE and classified as canal-only. Slope and intercept of trendline are 0.0856 and 0.2321 respectively; $r^2 = 0.01$. B. Gain of uncorrected WBR response against gain of PNFE response of neurons responsive to PNFE and classified as otolith-only. Slope and intercept of the trendline are 0.185 and 0.213 respectively; $r^2 = 0.0001$. C. Gain of uncorrected WBR response against gain of PNFE response of neurons responsive to PNFE and classified as convergent. Slope and intercept of the trendline are -0.0872 and 0.372 respectively; $r^2 = 0.06$. 
Figure 3-13 Relationship between WBR and PNFE response phase: Trendline for each plot is shown as dashed line, and unity line is shown as grey line. Units were classified as Type 1 or 2 by WBR response. A. Phase of uncorrected WBR response plotted against the phase of PNFE response for neurons responsive PNFE and classified as canal-only. Slope and intercept of trendline are -0.33 and 276.81 respectively; $r^2 = 0.20$. B. Phase of uncorrected WBR response against phase of PNFE response of neurons responsive to PNFE and classified as otolith-only. Slope and intercept of trendline are 0.06 and 257.5 respectively; $r^2 = 0.0028$. C. Phase of the WBR response against phase of PNFE response for neurons responsive to PNFE and classified as convergent. Slope and intercept of the trendline are 0.0071 and 239.34 respectively; $r^2 = 0.003$. 

A. Canal–Only Units

B. Otolith–Only Units

C. Convergent Units
Chapter 4 : General Discussion

4.1 Introduction

A fundamental goal of the work discussed in this dissertation was to characterize how the central nervous system could control movements of the head relative to the body during passive translations of the whole body. In Chapter 2, we described our approach to achieving this goal from a behavioral perspective. We showed that during whole body translation of an animal, an active response from the central nervous system was generated and this response reduced the net forces exerted on the head. We hypothesized that an active CNS response like this, would serve to limit head movement in the scenarios where the head was allowed to move during whole body translation. We also showed that this response was most readily elicited during side-to-side directions of whole body translations.
These results taken together suggest one particularly novel conclusion: that during whole body translation vestibular mediated postural control of the head is geared towards to reducing movements of the head relative to the trunk during movements of the whole body, especially in the side-to-side direction. However, the experiments that led to this conclusion were all conducted in animals whose heads were not permitted to move relative to their bodies. This experimental limitation affected the robustness of the conclusions that we could draw from this work. While a head fixed preparation has many advantages, primarily the isolation of vestibular sensory information, it does not allow us to measure the end behavioral result of the tVCR, which would be to prevent or control head movements.

In order to try and understand better what our results might mean in terms of head movements that would result from whole body translations, we built a simple inverted pendulum model of the passive biomechanics of the head and neck complex. Using this model we were able to investigate how much head movement relative to the trunk might be expected during whole body translations similar those we used as stimuli. We also used the model to evaluate the overall effect of an increase in stiffness of the neck would be on head movement during WBT.

Furthermore, a better understanding of the kinematics of head movements that might be produced due to whole body translations may help us contextualize the results of our behavioral and single unit studies. In these studies, we attempted to understand how vestibular nucleus neurons respond and process the information that would arise from several sensory modalities during a whole body translation if the
head were free to move. The results of this modeling effort can give us an approximation of how the head would move in roll during stimulations similar to the ones used in our behavioral experiments.
4.2 Biomechanical Model of the Head and Neck in the Frontal Plane

Our simple mechanical head movement model is a basic frontal plane second order lumped parameter system model that only approximates the passive biomechanics of the head and neck. We selected a frontal plane model because the behavioral results shown in Chapter 2 show a spatial asymmetry to the tVCR that was biased to the side-to-side direction of translation. This direction of translation would result in a frontal plane head movement as demonstrated in outcome 2 in Figure 1-2. A frontal plane model allows head movements specifically this direction of translation to be approximated while keeping the complexity of the model itself manageable. The model we implemented is shown in block diagram form in Figure 4-1 and is adapted from work published by Pedrocchi’s group (Pedrocchi and Ferrigno 2004). Specifically, Pedrocchi’s group models the roll head movements produced in response to rotational acceleration of the head. The model shown in Figure 4-1 is our version of the model, adapted to predict roll head movements as a result of linear acceleration of the head.

The block diagram in Figure 4-1 shows that there are four main mechanical contributions considered head inertia, neck stiffness, neck viscosity, and the action of gravity on the mass of the head. The model includes the gain block $1/J$ where $J$ represents the moment of inertia of the head. The inverse is multiplied by the output of the summer block in order convert net torque to rotational acceleration of the head.
The moment of inertia coefficient, $J$, was calculated using an elliptical assumption for head shape:

$$ J = \frac{m(a^2 + b^2)}{5} $$

In this equation, $a$ is the major axis of the ellipse and $b$ is the minor axis of the ellipse.

Measurements were made of a single animal’s head post mortem and these measurements were used to approximate the major and minor axes of this elliptical approximation. In this case the major axis $a$ was measured from the top of the animal’s implant down the midline of the bottom to the center of the animal’s chin and was measured to be 3.2 cm. The minor axis $b$, was measured from either side of the head at approximately level of the animal’s ear canals and was found to be 2.2 cm. Head mass was approximated as $m=0.09$ kg based on the post mortem weight of the animal’s head. Thus, the value for $J$ used in this modeling effort was $2.71 \times 10^{-4}$ kg*cm$^2$.

The stiffness of the neck in terms of only the passive biomechanics, depends mostly on muscle elongation and biological characteristics of other tissues involved in the movement (Zangemeister, Lehman et al. 1981). Stiffness is expressed in this model as:

$$ H_{\text{stiffness}} = K_s * \theta $$

In which $K_s$ representing stiffness of tissues of the neck was assumed to be equal to 0.5 N m/rad for frontal plane head rotation (Zangemeister, Lehman et al. 1981) and $\theta$ was the angular position of the head relative to the trunk.
However, the value for the parameter $K_s$ from the work by Zangemeister et. al. (1981), was obtained on a completely relaxed neck. The total overall stiffness of the neck could be greatly increased by co-contraction of neck muscles. The value of $K_s$ was varied in the model to analyze the effect of co-contraction of neck muscles.

The model also includes a block, $H_{\text{visc}}$ representing the viscosity of physical structures of the neck such as muscles, ligaments, joints, tendons, connective tissues, and joints. The viscosity parameter is expressed as:

$$H_{\text{visc}} = B \dot{\theta}$$

In this case, $B$ was determined by Pedrocchi et al (2004) by fitting experimental head movement data from several different experimental paradigms with their model. The value of $B$ for frontal plane movements of the head was determined to be $1.707 \text{ N m s/rad}$ and $\dot{\theta}$ is the velocity of the head with respect to the trunk.

The last element of the mechanical model is the gravity block that represents the effect of the earth’s gravitational field on head movements. The equation in this block is:

$$H_{\text{gravity}} = mgl\sin(\theta)$$

Where $m$ is an approximation of head mass (0.09 kg) and $g$ is acceleration due to gravity. The value for $l$, 5.08 cm, is equal to an estimate, based on measurements from several animals, of the distance from the approximate interaural axis to the approximate location of C5. This measurement was used frequently in Chapter 3 to find the linear tangential component of rotational velocity that occurred at the level of the vestibular endorgans. We estimated the center of mass of the head to be near the
interaural axis, and used this measurement in our modeling efforts as well. Due to the biomechanical arrangement of the head relative to the neck, the effect of gravity on the head is dependent on the position of the head with respect to the body. Thus, the mass of the head and gravity are multiplied by the sine of the head’s position relative to the body.

The model was implemented in Simulink in Matlab (Mathworks, Inc.). The input to the model was sinusoidal linear acceleration of the head with a amplitude of 0.5 G. The frequency was varied across the range of 0.5 Hz to 4 Hz. The acceleration input was multiplied by the cosine of the head’s position (\(\cos(\theta)\)), the mass of the head (\(m\)), and the distance of the head from the shoulders (\(l\)) in order for it to be transformed to represent tangential torque on the animal’s head. The output of the model (\(\theta\)) was the angle between the midline axis of the head and the horizontal axis that goes through the shoulder blades. During simulated sinusoidal whole body translation, the output of the model was the predicted head movements based on the biomechanical properties of the head and neck. The amplitude of the predicted head movements was expressed relative to the frequency of the whole body translation in Figure 4-2. This plot represents an estimate of head movements that might be expected during the sinusoidal whole body translations similar to those used as stimulation in our experiments.

In general, predicted head movements were fairly small in size. The peak head movement predicted at 2 Hz was 0.54° in amplitude, which means the total head movement was about 1°. However, during a 1Hz stimulation of the same peak
acceleration the predicted head movement is five times larger with a total head movement of $5.12^\circ$. This non-linear relationship between the size of predicted head movements and frequency of the stimulus may account for the non-linear relationship between force exerted on the neck and frequency shown in Chapter 2. If the purpose of a vestibular driven postural response were to restrain movements of the head with respect to the trunk, it would likely be more important for lower frequency stimuli. At low frequencies the model predicted larger head movements.

We also used the model to investigate the effect of an increase in neck stiffness on the size of head movements. Figure 4-3 shows the amplitude of predicted head movements at three different values for stiffness (0.5, 2, and 4 N*m/rad). Not surprisingly, when neck stiffness was increased, the amplitude of the predicted sinusoidal head movements was decreased. The effect is also more profound at the lower frequencies of stimulation, and this may be another reason why force reductions in the experiments in chapter 2 were shown to be greater at lower frequencies. This effect of increasing overall neck stiffness on decreasing head velocity has also been shown during experimental conditions in human subjects. Simoneau and colleagues (2008) examined the effect of increasing pre-loads on the head on overall stiffness of the neck and peak head angular velocity after an abrupt force perturbation. These investigators found that increasing the pre-load on the neck increased overall neck stiffness and resulted in corresponding decreases in head velocity after force perturbations.
These results from this modeling effort suggest that increasing neck stiffness would be one available strategy to stabilization the head relative to the trunk during whole body translations. However, the results of our modeling also seem to show that it would be difficult for an increase in stiffness alone to reduce head movements completely. Failure to eliminate head movements would result in a counter rotation of the head in roll relative to the trunk and would allow the rVCR to act to stabilize the head during whole body translation. Thus, these results underscore the importance of understanding the rVCR that is activated when the head counter rotates in roll during whole body translation.
4.3 General Summary

The purpose of this dissertation was to determine how vestibular sensory information is used by the CNS to control the head during whole body translation. Specifically, we asked: how does the brain use vestibular information control the forces on the head that occur during whole body translation? We took an approach to answering this question; beginning at the level of overall behavior, moving up to muscle activation with underlies that behavior, and finally the central nervous system mechanisms that could activate musculature during whole body translation.

In the behavioral work, we demonstrated that there is an active response of the CNS during whole body translation that serves to reduce forces on the head. This result is notable because it is very different than the response of the CNS during whole body rotation in yaw, which has much more frequently been studied. During whole body rotation in yaw, the CNS is thought to produce compensatory head movements in order to stabilize the head in space. However, in translation we found instead that the CNS seems to reduce the size of head movements relative to the trunk in order to stabilize the head with respect to the trunk. This different functional response of the CNS is interesting because it could useful to stabilize the head during normal daily activities when the head is accelerated linearly, such as during gait.

The experiments we conducted did have a few experimental limitations. A direct way to measure the tVCR would have been to measure muscle activation direction during a head-fixed whole body translation. This would allow the measurement of the output of the tVCR while see isolating vestibular information as
the primary source of sensory information available to the CNS. However, we were unable to obtain high quality EMG signals. This may have been a result of the type of electrodes that we used or possibly it could be related to the inflammatory response to those electrodes that prevented the transduction of good EMG signals. It is also possible that the inability to collect high quality EMG signals was related to the predictability of the stimuli used and that experiments that employ more unpredictable stimuli would be more readily able to elicit EMG activity. In order to improve upon the understanding of how the tVCR functions during whole body translations, experiments that capture better quality EMG signals from all neck muscles would be necessary. Furthermore, other types of translational stimuli should be used to reduce the animal’s ability to predict the stimuli. Much work that focuses on the tVCR in humans has used both unpredictable stimuli and EMG recordings. This work has been conducted by Keshner and colleagues (2001, 2003). However, further research is necessary to fully understand activation of the tVCR in humans.

Furthermore, the ultimate measure of output of the reflex that we were seeking to characterize during these behavioral experiments (tVCR) would be head movements. However by fixing the head relative to the trunk we did not allow those head movements to occur. Thus we were forced make inferences about the function of the tVCR based on other indirect parameters (force exerted on the head). We chose to fix the head relative to the trunk not only because it allowed the isolation vestibular sensory information as the primary sensory input to the CNS but it also allowed isolation of the tVCR from the rVCR. As we have described, whole body
translation leads to head movements as a result of the biomechanics of the head and neck. The head movements that are produced generate rotational vestibular signals that can be used to activate the rVCR. Thus experimental paradigms that allow the head to go free during whole body translation are likely activating both the tVCR and the rVCR rendering it difficult to separate the individual function of the two reflexes.

In our experiments conducted in the VN we attempted to understand the activation patterns of neurons that might underlie a head control strategy that reduced head movements. In this work, we found many VN neurons that responded to whole body translation in the side-to-side direction. The response of these neurons alone would seem like it would be enough to generate tVCR response that we measured in Chapter 2. However, historically the tVCR has been shown to be a relatively small reflex, and our work confirmed that the tVCR evoked during the stimuli used would not alone be enough to stabilize the head relative to the trunk. Thus for this part of the work, we also investigated how the signals that drive the rVCR evoked in roll and proprioceptive signals related to movement of the head relative to the trunk converge.

In this work we determined first, that most neurons that are responsive to whole body translation in the side-to-side direction also responded to whole body rotation in the roll plane. This convergence of vestibular information was not unexpected and makes sense given how linked a whole body translation in the side-to-side direction and a head counter roll are related biomechanically.

The dynamics of how these signals converged varied across the population of neurons recorded. Some neurons coded for whole body roll in the same direction as
translation, and some for whole body roll in the opposite direction as translation. However, one particular class of convergent neurons seemed quite interesting in the context of head movements produced during whole body translation. These were the neurons that coded for whole body translation in one direction, and whole body roll in the opposite direction. A head roll, in the opposite direction of whole body translation is exactly the head movement that would be produced during a head unrestrained whole body translation. During this type of head unrestrained translation, these neurons would first receive excitatory signals related to the whole body translation, and then when the head started counter rotate, it would receive excitatory signals regarding the head’s counter roll. When these signals combined on these neurons, the magnitude of the firing rate would be increased during the head’s counter roll.

It is possible to imagine a postural system that serves to control the head that as a first line of defense, activates neck musculature in response to any whole body translation and attempts to reduce forces on the head, and perhaps to reduce the size of, or prevent a head movement entirely. Neurons that have convergent input regarding head roll and head translation that are in opposite directions, could serve as a second line of defense to prevent head injury or control head movements during activities like gait. These neurons in response to the inevitable head movement generated by head-neck biomechanics, would increase their firing rate, and thus could drive an increase in neck muscle activation and amplify the response.
However, experiments to confirm this hypothesis would need to characterize the functional connections between neurons in the VN and neck musculature. Documentation of this connection would be necessary in order to determine if these neurons are actually the ones that underlie this response. Furthermore, this was not the only type of convergent neuron that we observed. Other neurons responded to whole body roll and whole body translation in the same direction. The response of these neurons would be decreased in the head unrestrained case when the head began to counter roll. This provides a counter example to the processing we discussed above thus is it hard to make a definitive conclusion regarding the convergence of vestibular information on signal units and their relationship to functional convergence of the rVCR and tVCR.

Our work also analyzed the proprioceptive inputs to the vestibular nucleus related to head roll relative to the trunk. The expectation of these experiments was that proprioceptive signals would be similar in gain and out of phase with head roll vestibular responses, based on what has been previously reported for neurons sensitive to yaw body rotations and yaw head on trunk rotation (Gdowski and McCrea 1997; Gdowski, Boyle et al. 2000). If the signals were well matched in this way, than the vestibular signals would be cancelled out by the proprioceptive signals effectively eliminating vestibular information necessary to activate the rVCR in roll. However, this was not what was observed. Instead we found that proprioceptive responses due to head on trunk roll were in general small in gain and not related to vestibular responses during whole body roll. It is possible that the phase relationship...
was also not orderly. However, the small gain of these responses rendered it difficult to accurately determine the response phase (Seidman, Telford et al. 1998). There might be several other reasons why the gain and phase of proprioceptive and vestibular information regarding head roll were not well matched. A few of these reasons are related to the experimental conditions. It is possible that the type of head roll we created in our study was not sufficient to generate large proprioceptive responses on these neurons. Despite the fact that we attempted to create as natural a head movement relative to the animal’s trunk as possible, natural movements of the head in roll are complex. The stimuli we used, while generating a head movement in roll, rotated about a single center and thus were not identical to naturally evoked lateral bending neck movements. Natural head movements in primates are complex, involving many muscles, ligaments, and joints; each of which is capable of providing proprioceptive information to the CNS. It is possible that our experimental setup simply did not allow us to fully examine the proprioceptive inputs to the vestibular nucleus. We also may not have been producing head movements of the correct sizes or correct dynamics. We used only one frequency and velocity of head movements. These were chosen to match the frequency and velocity of the translation, but it is possible that the head movements evoked during whole body translation would have much different dynamics.

It is also possible that proprioceptive responses and vestibular responses of neurons in the VN related to head roll relative to the trunk are not well matched for good computational reasons. A well-matched proprioceptive signal that cancels out
the rotational vestibular signal, as seen in experiments in head yaw, may not be useful for reducing head movements relative to the trunk produced during whole body translations. Our behavioral experiments demonstrate that the tVCR alone is not sufficient to eliminate roll head movements to zero. Thus, when the whole body is translated and the rVCR evoked when the head counter rotates may be vital to maintaining head position relative to the trunk.

In order to fully explore these questions, experiments could be conducted that recorded from vestibular nucleus neurons during more natural passive and active head movements in roll. It is difficult to imagine an experimental set up that would allow this type of head movement to be created, but it is likely necessary to conclusively determine how proprioceptive information in roll is processed in the vestibular nucleus.

Ultimately, despite the limitations of this work, our results have certainly gone a long way towards answering the questions that were posed. We have determined that the CNS response to whole body translation is to reduce the size of head movements. We have shown that the patterns of information received during whole body translation and roll in the vestibular nucleus converge in new and unexpected ways. We have also shown that proprioceptive information could have a different role in the grand scheme of sensory processing during a head unrestrained whole body translation. Our results suggest that this role is different than sensory processing observed during head unrestrained whole body rotations in yaw. Our results at every stage have shown that the response of the CNS to whole body
translation is fundamentally different than the response to whole body rotation and that this response may play a large role in head stabilization during gait.
Figure 4-1 Mechanical model of head and neck: Block diagram of biomechanical model from Chapter 4. This figure shows a box diagram of the simple inverted pendulum model of head biomechanics in the frontal plane. $\theta$: head angle relative to shoulders; $\dot{\theta}$: rotational velocity of the head; $\ddot{\theta}$: rotational acceleration of the head; $H_{\text{stiffness}}$: stiffness of neck; $H_{\text{visc}}$: viscosity of neck; $H_{\text{gravity}}$: effect of gravity on head movements; $J$: moment of inertia of the head; $m$: mass of the head; $g$: 9.8 m/s$^2$; $l$: distance of interaural axis from C5.
Figure 4-2 Frequency response of mechanical model: Predicted head movements based on biomechanical model. The predicted amplitude of the sinusoidal head movements. The model was run for several frequencies of whole body translation and predicted sinusoidal head movement responses of varying amplitude. These amplitudes are shown relative to the frequency of whole body translation. \( K_s = 0.5 \text{ N}\cdot\text{m/ rad}; B = 1.707 \text{ N}\cdot\text{m/ s/ rad}; m = 0.09 \text{ kg} \)
Figure 4-3 Predicted head movements varied with neck stiffness: Predicted head movements with varying stiffness from biomechanical model. The predicted amplitude of the sinusoidal head movements. The model was run for various frequencies of whole body translation at different stiffness and predicted sinusoidal head movement responses of varying amplitude. These amplitudes are shown relative to the frequency of whole body translation.
Bibliography


