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**Human torsional eye movements in response to visual,
mechanical and vestibular stimuli**

Seidman, Scott Howard, Ph.D.

Case Western Reserve University, 1993

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**HUMAN TORSIONAL EYE MOVEMENTS IN RESPONSE TO
VISUAL, MECHANICAL AND VESTIBULAR STIMULI**

by

SCOTT HOWARD SEIDMAN

Submitted in partial fulfillment of the requirements
for the degree of Doctor of Philosophy

Thesis Advisor: R.J. Leigh, M.D.

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May, 1993

CASE WESTERN RESERVE UNIVERSITY

GRADUATE STUDIES

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HUMAN TORSIONAL EYE MOVEMENTS IN RESPONSE TO VISUAL, MECHANICAL AND VESTIBULAR STIMULI

Abstract

by

SCOTT HOWARD SEIDMAN

Systematic study of eye rotations in the torsional plane has recently been made possible by the magnetic search coil technique. I postulated that because visual demands are less stringent in the torsional than in the horizontal or vertical planes, the neural control of torsional eye movements might be simpler than that of horizontal or vertical movements, necessitating modification of current ocular motor models.

I began with two projects to investigate the influence of visual stimuli on torsional eye movements. In the first, I measured torsional eye movements during a perceptual illusion known as the motion after-effect, and found this illusion to be independent of torsional eye movement. The second project measured the effect of visual inputs on the gain of the torsional vestibuloocular reflex (VOR). I found that visual stimuli could negate but not enhance the

torsional VOR. Thus, torsional eye movements were less influenced by visual or perceptual images than were horizontal or vertical movements.

I used these findings and results from other laboratories to develop and test a simplified model for the torsional VOR. I performed two experiments that would enable me to modify a current model of the horizontal VOR to better suit the torsional system. First, I quantified the dynamics of the ocular muscles and orbital tissue in torsion by mechanically displacing the eye and observing the time course of its return to resting position following release. The eye returned more rapidly from a position of extorsion than from a position of intorsion. I then investigated the central nervous system's contribution to the torsional VOR, testing the efficacy of the velocity-to-position neural integration of vestibular signals. The time constant of the neural integrator was typically 3 sec in the torsional plane, while it was greater than 20 sec in the horizontal plane.

I conclude that torsional eye movements have different properties from horizontal and vertical movements. These simplified features reflect less exacting visual demands. Because of this simplicity, torsional eye movements may prove to be a valuable research tool.

The weaver-god, he weaves; and by that weaving is he deafened, that he hears no mortal voice; and by that humming, we, too, who look on the loom are deafened; and only when we escape it shall we hear the thousand voices that speak through it.... Ah, mortal! then, be heedful; for so, in all this din of the great world's loom, thy subtlest thinkings may be overheard afar.

Herman Melville, *Moby Dick*

To Mary Ann

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I would also like to thank Dr. J. Fouke, my academic advisor, who guided me through a cohesive program of study. At times, she provided gentle encouragement, but did not hesitate to crack the whip when necessary. For this I am grateful. Her careful reviews were invaluable in the completion of this document.

Dr. C.W. Thomas provided me with valuable incentive to try and link eye movements to perceptual phenomena by his "rediscovery" of the motion after-effect. Of the three studies presented in this dissertation, this one was the

most enjoyable.

For the work presented in Chapter 4, the major portion of this dissertation, I am indebted to Dr. G. Saidel, Chairman of the Biomedical Engineering Department, for sharing his insight on optimal parameter estimation techniques, without which this work would not have been possible. I am also grateful for the lengthy communications with Dr. D. Straumann and Dr. Qing Yue of Zurich, in which the unpublished results of their experiments on rhesus monkeys were made available to me, and to Dr. H. Goldstein for his lessons on the ocular motor plant.

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CHAPTER 1

INTRODUCTION

Teleology

In order to maintain clear vision, it is necessary to prevent images from slipping on the retina. Visual acuity degrades rapidly when retinal image slip exceeds about $4^\circ/\text{sec}$ (Westheimer and McKee 1975). To prevent this from occurring, most vertebrate species have developed an ocular motor system to keep vision clear and stable during movement of either the organism or of objects of interest (Walls 1961). During natural activity, such as locomotion, head movements are often faster than the $4^\circ/\text{sec}$ threshold required for high visual acuity (Grossman et al. 1988; King, Seidman, and Leigh 1992). To overcome the detrimental effects on vision that head movements of this velocity can cause, it is necessary to hold gaze (i.e., eye position in space) fairly stable. Towards this end, two ocular motor reflexes have evolved: the vestibulo-ocular reflex (VOR) and the optokinetic reflex (OKR).

The OKR acts in response to large-field slip of images on the retina, such as occurs during sustained self-rotation. When such slip is detected, the OKR causes the eyes to move in the same direction and so minimizes slip. The VOR also acts to minimize retinal slip. This reflex, however, is not visually mediated, and will even function in complete darkness. In response to an angular rotation of the head, the VOR causes the eyes to move oppositely to the head, thus keeping the position of the eyes in space relatively constant. For this reflex to function, there must be some sensor that can accurately measure angular head rotations. The semicircular canals of the inner ear meet this requirement, and serve as the transducers of angular head velocity for the VOR.

Since the OKR stabilizes images on the retina using only visual inputs, one might ask: why do we need a non-visually mediated reflex to carry out this job of visual stabilization? Why are the OKR and other visual tracking mechanisms unable to do the same job as the VOR? After all, many of the species that need a VOR also have accurate visual tracking responses. Visually mediated responses have the advantage of not requiring a whole separate transducer. Why did the semicircular canals need to evolve?

The answer to these questions lies in the relative latencies of the VOR and the OKR. Visual processing is quite slow. At least 70 ms pass between light falling on the retina and the eye movements that result (Gellman, Carl and Miles 1990). Most visually mediated ocular motor responses have latencies well over 100 ms. (Carl and Gellman 1987). A delay of this magnitude clearly

would degrade vision during high frequency head rotations such as those occurring during locomotion and other natural behaviors (King, Seidman and Leigh 1992). The VOR, however, is a much faster mechanism, showing latencies of less than 16 ms. (Maas et al. 1989). Therefore, the VOR is the only reflex that is well suited to compensate for head rotations of high frequency, while vision can help out during prolonged, low-frequency rotations.

As one might expect, the loss of the VOR has disturbing effects on vision, especially during locomotion. One physician anonymously reported on the loss of his own VOR following damage to his semi-circular canals. The effects on his vision were pronounced (J.C. 1952). In his own words:

"During a walk I found too much motion in my visual picture of the surroundings to permit recognition of fine detail. I learned that I must stand still in order to read the lettering on a sign."

He also described disturbances in his vision caused by the rather small head movement generated by the beat of his heart. This demonstrates the necessity of the VOR for clear vision during normal behavior.

The VOR is studied for a variety of reasons. One reason is its relatively simplicity as compared to musculo-skeletal reflexes. For example, the effector organ of the VOR, the eye, is a never-changing mass. Therefore, the VOR has no need to respond to mechanical considerations such as changing weight or varying moment arms. Experimental evidence suggests that there is no stretch reflex in the extra-ocular muscles (Keller and Robinson 1971). In addition,

since every cell involved in the VOR resides within the cranial vault, it is relatively simple to record from these neurons in functional animal preparations.

Angular head and eye movements are fully realized in three degrees of rotational freedom. No significant translations of the eye occur, and so it is simple to describe and measure movements. To characterize a system completely it is necessary to fully represent both the input and the output. The VOR is particularly well suited for these types of measurements.

In addition to these advantages, the study of the VOR is beneficial to the clinician. Improved understanding of vestibular function can aid in the diagnosis and treatment of various neurological and vestibular disorders.

The function of the VOR in the horizontal plane has been studied in detail for the past 20 years, but rotations in the vertical and torsional directions have received less attention. To maintain clear vision the VOR must sense and react to head movements in all three dimensions. To meet this requirement, there are 3 near-orthogonal canals in each inner ear. The planes of these canals closely correspond to the pulling directions of the muscles of the eye; thus, the eye is able to move in three rotational directions: horizontally, vertically, and around the line of sight. My studies concentrate on this latter type of response, the torsional VOR.

Anatomy and Physiology

As mentioned before, the semicircular canals of the inner ear (i.e., the

vestibular labyrinth) serve as the transducers of angular head movements. There are three semicircular canals in each inner ear. They lie in approximately perpendicular planes, enabling the transduction of head movements in three dimensions. Each canal consists of a lumen containing *endolymph*, and a sail-like *cupula* at one end.

The actual conversion from head rotation to neural signal takes place in two steps. First, head rotation causes the endolymph in the canal to move. This, in turn, causes movement of the cupula, thus stimulating the *hair cells*, that lie in its base. These specialized hair cells sense shear of their processes, or *cilia*, and are the site of mechano-neural transduction. Movements of cilia of these cells increase or decrease the tonic discharge rate of the *vestibular nerve*.

The actual behavior of the VOR is heavily dependant on the mechanical dynamics of the semicircular canals. Steinhausen (1933), who studied these properties in the pike, was the first to demonstrate the existence and functional importance of the cupula. The geometry of the canal, with its lumen diameter much smaller than its overall radius of curvature, dictates that endolymph movement in the canal is proportional to head *velocity*. The cupula behaves like a spring moving through a viscous fluid. Steinhausen showed the combination of these two effects cause the canal to behave as an overdamped torsion pendulum. For the frequency range of natural head movements, 0.5-5.0 Hz (King, Seidman, and Leigh 1992), this behavior results in the presentation of a high-pass filtered version of head velocity to the nervous system.

The output of the VOR is eye rotations. Eye movements are determined by the actions of three antagonistic pairs of muscles, each of which move the eye in their primary planes of action. The medial and lateral recti move the eye horizontally, while the superior and inferior recti are primarily responsible for vertical eye movements with additional influence from the superior and inferior obliques. Torsion is achieved mostly through action of the superior and inferior obliques, though the superior and inferior recti also influence torsional position.

The *elementary vestibulo-ocular reflex* is a 3-neuron connection between the semicircular canals and the ocular motor plant. The vestibular signal is carried on the vestibular nerve to the vestibular nucleus. The neural signal for the horizontal VOR is carried on interneurons that synapse with neurons in the abducens nucleus. The abducens nucleus contains motoneurons that project to the lateral rectus. This pathway contains two synapses and three neurons. For this reason, the elementary VOR is known as a *three neuron arc* (Szentágothai 1950). For the horizontal VOR to cause the medial rectus muscle to contract requires an extra neuron: the abducens internuclear neurons that project to the oculomotor nucleus via the medial longitudinal fasciculus.

By itself, this simple pathway is not sufficient to compensate for natural head movements. Further neural processing is required. In particular, the low-frequency response of the semicircular canals is not good enough to keep vision clear during prolonged head movements. The brain makes an effort to extend the low-frequency range.

If one records from neurons in the vestibular nucleus, it becomes apparent that the neural response to a step in head velocity lasts longer than is dictated by the mechanical properties of the canals. This phenomenon has become known as *velocity storage* (Cohen et al. 1981) and is manifest behaviorally by nystagmus that lasts two to three times longer than would be predicted by the mechanical properties of the cupula. In effect, the duration of the vestibular response is prolonged by the actions of a neural pathway that demonstrates positive-feedback characteristics. It has been suggested that this processing is carried out to help the ocular motor system obey Newton's First Law of Motion (Rademaker and Ter Braak 1948). Although the neural mechanism of velocity storage has not been well described, it appears that commissural pathways between the left and right vestibular nuclei are responsible for the prolongation of the canal signal (Katz et al. 1988; Katz et al. 1989). It has also been shown that visual inputs have access to the velocity storage mechanisms in the vestibular nucleus (Waespe and Henn, 1977). So, in the vestibular nucleus, the brain synthesizes its best estimate of head velocity from both vestibular and visual information.

In addition to velocity storage, further neural processing is still necessary to maintain clear vision during normal activity because of the mechanical properties of the orbital contents (i.e., the ocular motor plant). This is made necessary by the behavior of muscles. Muscles require *position* commands to hold a given position because of elastic forces that tend to pull the eye back to resting position. However, the vestibular system carries a representation of head

velocity. Therefore, an interface between the nervous system and the eye muscles that performs a mathematical integration is required to hold eccentric gaze. This interface is known as the *neural integrator* (Skavenski and Robinson 1973; Cannon and Robinson 1987).

It has been suggested that this neural integration is carried out via a network of neurons that laterally inhibit each other (Cannon and Robinson 1985). Thus, each neuron is connected to other neurons by an inhibitory connection. These other neurons, in turn, inhibit the original neuron. Since two inhibitions are occurring, this configuration actually exhibits a fairly stable positive feedback behavior.

For horizontal eye movements, it has been shown that this neural integrator is located in the nucleus prepositus hypoglossi and adjacent medial vestibular nucleus (Cannon and Robinson 1987). When this area is lesioned, monkeys are unable to hold eccentric gaze position in the horizontal plane. It has been suggested by similar lesion studies that vertical and torsional neural integration mainly take place in the interstitial nucleus of Cajal (Crawford, Cadera, and Vilis 1991).

The Model

The behavior of the horizontal VOR has been well described in the form of various mathematical models (Raphan, Matsuo, and Cohen 1979; Robinson 1977). For my investigations, I used Robinson's model of visuo-vestibular interaction in the horizontal plane (Fig. 1-1). There are several advantages in creating such a model. For example, each ocular motor subsystem is represented separately, providing insight that aids in the investigation of each individual element. Much of the research that follows can be considered to be tests of various elements in this model.

This model describes the vestibular system, the optokinetic system, and their interactions. Beginning at the bottom of the figure, and working our way upwards, the head velocity signal is transduced by the semicircular canals. As discussed above, the geometry and mechanics of the canals is such that a high-pass filtered version of head velocity is the input to the nervous system. Following this initial signal conditioning, velocity information is passed directly to the ocular motor neurons which, in turn, cause movement of the eye.

Head velocity information transduced by the semicircular canal enters a positive feedback loop known as "velocity storage". This positive feedback, that adds directly to the signals generated by the canal, has the effect of perseverating the canal response. Therefore, velocity storage enables the vestibular system to better compensate for prolonged rotation of the head, improving the overall low-frequency response of the system.

Figure 1-1

Model of visuo-vestibular interaction in the horizontal plane. The inputs to this model are head velocity, $\dot{H}$, and the velocity of the visual environment with respect to the subject, $\dot{W}$. The outputs are eye velocity, $\dot{E}$, and gaze velocity, $\dot{G}$. $\dot{H}$ is transduced by the semicircular canals, which are modeled as a high-pass filter with time constant T_c , and then multiplied by the VOR gain, G . This information then enters the positive-feedback velocity storage loop, which contains a low-pass element with time constant T_0 and a feedback gain element, K . In this loop, vestibular information combines with optokinetic input, full-field retinal slip ($\dot{W}-\dot{G}$). The model's best estimate of head velocity is thus $\dot{H}'$. This estimate then passes through the ocular motor plant to produce $\dot{E}$. $\dot{G}$ is simply the sum of eye velocity and head velocity.

Although the plant can be simply described as an amplifier with a gain of 1, as it is in this model, this is somewhat misleading. The nervous system receives and processes head velocity information but the eye muscles must receive position commands to function correctly. To meet this physiological requirement, there is an interface between the vestibular portions of the brain stem and the eye muscles. This interface, which will be described in more detail at a later time, effectively integrates velocity information and overcomes any lag elements inherent in the plant. For the horizontal eye movements described by this model, this interface is so well-matched that we can ignore plant mechanics, justifying the representation of the plant as a follower (Robinson 1981). However, plant dynamics in the torsional plane have not been extensively studied; anatomical differences prevent us from assuming that the behavior is the same as in the horizontal plane.

The optokinetic system comprises the visual portions of this model of visuo-vestibular interaction. As described previously, this system takes full-field visual information from the retina, and uses this information to produce eye movements that compensate for retinal slip. As noted above, optokinetic inputs project to the vestibular nucleus where they sum with inputs from the semicircular canals (Waespe and Henn 1977). During prolonged head rotations, after the vestibular signal has died away because of canal dynamics, retinal slip information still causes optokinetic eye movements. On examination of this

model, one can see that all this visual information must pass through the velocity storage loop before being presented to the plant. The dynamics of the optokinetic response tend to support this configuration (Cohen, Matsuo and Raphan 1977).

In preliminary work, I have shown that velocity storage does not exist for torsional vestibular eye movements in humans (Seidman and Leigh 1989). This allows me to simplify the model greatly; the velocity storage loop may be removed. Furthermore, the optokinetic system is weak in the torsional plane (Morrow and Sharpe 1989; Collewijn et al. 1985; Cheung and Howard 1991). Therefore, visual inputs to the model may be ignored for torsional movements.

Research Goals

There are reasons to predict that the dynamic properties of the torsional VOR may be simpler than those of the corresponding horizontal and vertical systems. My prediction that the torsional VOR might be quite simple lies in the nature of the visual demands that are placed on torsional eye movements. It is important to remember that the eye movements that are studied have evolved for the sole purpose of aiding vision (Walls 1962). With this in mind, I asked the question, "How accurately must torsional eye movements be controlled to prevent degradation of vision?" The answer seems to be, "Not very accurately at all."

Why should the visual demands placed on the VOR in the torsional plane be less than those placed on the VOR in the horizontal and vertical planes? In the horizontal and vertical systems, one of the main functions of the VOR is to keep the image of a target on the fovea, the area of highest photoreceptor density on the eye. For torsional eye movement systems, this is unnecessary. A movement of the eye or head around the line of sight will not displace an image from the fovea. This can best be conceptualized by the simple analogy of a point of light that falls on the exact center of a circle. If the circle is then rotated about its center, the point of light will still fall on the center of that circle. If we were to place a photoreceptor at this center point, the rotation described will not cause a change of output in that receptor. The geometry also dictates that during torsional disturbances, image slip on the retina will be worst in the periphery of the visual field. Images falling in this region are usually not where our attention is directed. In fact, photoreceptor density is quite low at peripheral locations on the retina. It is quite likely, therefore, that much larger disturbances in torsional gaze position might be tolerated by visual systems than for horizontal or vertical gaze.

Even when the eyes are "at rest" in the absence of head rotations, fixation mechanisms seem weakest in the torsional plane. This weakness manifests itself as constant wandering eye movements of fairly large magnitude in the torsional plane (standard deviation of gaze position= 0.18°), as opposed to horizontal (standard deviation= 0.11°) and vertical movements (standard deviation= 0.10°)

during fixation, which rarely leave the target by more than $1/2^\circ$ (Ott, Seidman and Leigh 1992; Ferman et al. 1987). This variation in torsional baseline position is normal, and does not appreciably degrade vision. Since this weaker control of torsional fixation is clearly tolerated by visual systems, perhaps control of the torsional VOR might be similarly lax.

Even higher perceptual mechanisms, such as stereo perception, seem to tolerate considerable anomaly in the torsional plane under certain conditions. Cyclofusional disparities, the torsional misalignment of images on each retina, occur during normal vision (Bishop 1978; Kertesz and Jones 1970). It has been shown that torsional eye movements cannot compensate for these disparities. Although these disparities can get much larger than horizontal and vertical disparities, and even exist in two directions at the same time, they apparently do not interfere with normal stereo vision.

Taking these geometrical, behavioral, and perceptual considerations into account, it seems that the torsional VOR need not be controlled as rigorously as the horizontal and vertical VORs. If this assertion is true, perhaps a very simple, "bare-bones" torsional vestibulo-ocular reflex is sufficient to maintain high-acuity vision during natural behavior. My preliminary investigations of the VOR tend to confirm this hypothesis.

My current research of the torsional VOR takes two main directions. I have performed a number of experiments to show the simplicity of the torsional VOR, allowing us to modify a current model of horizontal visual-vestibular

interaction to describe torsional eye movements. In addition, I have conducted an experiment in perceptuo-motor interaction, that takes advantage of the simplicity of torsional eye movements to draw conclusions that were difficult to make during a corresponding horizontal investigation.

The Experiments

My preliminary work involved the presentation of velocity-step stimuli to the torsional vestibular system (Seidman and Leigh 1989). I found that the overall time constant of the torsional VOR was < 5 sec. This time constant is approximately equal to the time constant of the semicircular canal, and is indicative of no perseveration of the canal signal. Hence, I concluded that velocity storage was absent in the torsional plane. I then set out to gather data to support the hypothesis that visual inputs have little direct effects on torsional eye movements. In particular, I studied perceptual illusions known as motion after-effect and VOR cancellation in the torsional plane. It will be demonstrated that the small effect of visual input to the torsional eye movement systems can, in some cases, make the torsional VOR a more appropriate research tool than corresponding horizontal and vertical systems.

In Chapter 2, I present data on eye movements during motion after-effect (MAE), the illusory reversal of target direction following prolonged target movement in a constant direction (Holland 1965; Wohlgenuth 1911). Eye

movement systems have never been formally eliminated as a possible mechanism of this illusion (Masland 1969). When vertical and horizontal eye movement systems are stimulated by large-field targets, the velocity storage loop is charged up (see model of Fig. 1-1). In addition to causing eye movements, velocity storage is involved in the perception of self-rotation. Perhaps, somehow, velocity storage can be responsible for MAE. Strong fixation mechanisms in the horizontal and vertical planes would tend to mask any eye movements that occur during MAE. In the torsional system fixation mechanisms are weak (Ott, Seidman, and Leigh 1992). In addition, velocity storage in this plane is weak or absent (Seidman and Leigh 1989), and therefore cannot cause MAE. These two factors combine to make the torsional eye movement system ideal for the study of eye movements during MAE.

In Chapter 3, I present an experiment on the reduction of the gain of the torsional VOR in response to visual feedback in the torsional plane. This experiment also takes advantage of the weakness of visual tracking mechanisms in torsion. In the horizontal and vertical planes, smooth pursuit mechanisms serve to cancel vestibular eye movements during tasks that require combined eye-head tracking (CEHT) (Huebner et al. 1992; Lisberger 1990). Since there is no smooth pursuit mechanism in the torsional plane (Robinson 1982), and the optokinetic response is feeble, any reduction in the gain of the torsional VOR cannot be due to a cancellation by these mechanisms, and must therefore be caused by a parametric reduction in VOR gain (Leigh et al. 1989). To see if and

to what extent such a reduction exists, I presented human subjects with a visual display which moved as a function of torsional head rotation. This situation is somewhat analogous to CEHT in the horizontal and vertical planes. If, in fact, the gain of the torsional VOR can be reduced in this manner, then torsional eye movement systems are ideal for the study of the parametric reduction of VOR gain without the complicating factor of visual cancellation. I also investigated the ability of these visual inputs to enhance the torsional VOR.

More research was necessary to further adapt Robinson's model of the horizontal VOR to the torsional system. Towards this end, in Chapter 4 I investigate the interface between the nervous system and the extra-ocular muscles with a series of two experiments. As mentioned previously, in the horizontal plane this interface serves to integrate the velocity commands present in the nervous system to provide the position commands the muscles need for proper function. This interface also has the effect of canceling out the dynamics of the plant so they do not interfere with eye movements. The function of this interface for torsional eye movement systems has yet to be investigated.

To investigate this interface, the first experiment was performed to characterize the dynamics of the ocular motor plant in the torsional plane. Similar experiments have been carried out in the past for horizontal behavior. Consideration of the anatomy of the extra-ocular muscles that cause torsional movements would suggest that the visco-elastic properties of the plant in the torsional plane differ from those in the horizontal plane. In particular, the

superior oblique muscles, which are the major intorters (i.e., the top of the eye going towards the nose) have a very different anatomy from the inferior obliques, the muscles that pull the eye to a position of extorsion. The superior oblique has a longer tendon than other eye muscles, that passes through the trochlea before its insertion point on the eye.

In this experiment, the eye was released from positions of forced duction. The time course with which the eye returned to resting position was then determined using optimal parameter estimation techniques.

After characterizing the plant dynamics, I was then able to begin a second experiment on the nervous system-plant interface, the neural integrator. I administered position steps around the line of sight to the head, stimulating the torsional VOR. Parameter estimation techniques were then used to characterize the neural integrator.

The Equipment

For all of my experiments, it was necessary to measure angular displacement of the eyes, and possibly the head. Towards this end, I used the magnetic scleral search coil technique (Robinson 1963; Collewijn 1977). This system (CNC Engineering, Seattle, WA) employs 6-foot Helmholtz coils to generate alternating magnetic fields. These fields induce currents in coils of wire embedded in a Silastic ring, that is placed on the eye, surrounding the cornea

(Skalar, Delft, The Netherlands). Eye movements can be measured via the gain of the induced coil signal (Robinson 1963), or, when using a rotating magnetic vector, by the phase of the induced coil signal as compared to a stationary reference coil (Collewijn 1977). This system uses both methods. Head movements can be measured using the same system by simply fixing a scleral coil to the forehead. Using this system, rotations can be measured with an accuracy of 0.05° . Although this system has been used for many years, the measurement of torsional eye movements using these techniques is fairly recent (Collewijn et al. 1985).

Data were collected with a 16-bit A/D board in a PC-based system (Data Translation, Marlborough, MA). Prior to digitization, data were filtered with a cutoff frequency less than half the digitization rate using 4-pole maximally flat analogue filters (Krohn-Hite Corporation, Avon, MA) to prevent aliasing. Other equipment, which was necessary for individual experiments, will be described later.

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CHAPTER 2

EYE MOVEMENTS DURING MOTION AFTER-EFFECT

Abstract

Using the magnetic search coil technique, we measured torsional eye movements in four male subjects during and after rotation of a visual display around the line of sight. During rotation of the display, subjects developed a torsional nystagmus with slow-phases in the direction of target rotation that had a typical gain of < 0.01 . Upon cessation of display motion, subjects experienced a motion after-effect (MAE) in the direction opposite prior target rotation, which persisted for > 15 sec. During this MAE, slow-phase eye movements of low velocity were in the same direction as the MAE, but did not persist as long as perceptual effects. In separate experiments, horizontal eye movements were recorded during horizontal stimulus motion; during MAE, no eye movements occurred due to stronger fixation mechanisms. We conclude that MAE is not caused by retinal slip of images, but MAE and the accompanying eye movements

might be produced by shared or similar mechanisms.

Introduction

The motion after-effect (MAE) is an illusory motion perception that follows the viewing of a moving target. After the target stops moving, it appears to move in the opposite direction (Holland 1965; Wohlgenuth 1911). This phenomenon, for historical reasons, is also known as the waterfall effect. Eye movements during MAE have not been measured, although there has been speculation as to their presence and effects (Masland 1969).

A popular stimulus for the study of MAE has been a rotating spiral. According to Cavanagh and Favreau (1980), one justification for this particular stimulus has been that rotation of a target around the line of sight involves stimulation of all directions equally, giving rise to the assumption that the eyes do not move during stimulation. This is thought to rule out eye movements as an artifactual cause of the MAE. The eyes, however, are perfectly able to move about the line of sight during this type of stimulation (i.e. torsional, or cyclorotatory eye movements), and therefore the veracity of this assumption requires investigation.

It has been shown by Collewijn, Van der Steen, Ferman and Jansen (1985) and by Morrow and Sharpe (1989) that torsional optokinetic nystagmus (OKN) and optokinetic after-nystagmus (OKAN), although low in gain, do occur

when a subject is exposed to a full-field visual stimulus rotating around the line of sight. If OKAN occurs when the target stops, then the retinal slip caused by the OKAN would be in the appropriate direction to cause an apparent reversal of target motion. This would suggest that MAE is, at least in part, due to drift of images on the retina, i.e., "retinal slip."

MAE can also be induced by sustained visual motion in the horizontal plane, but the properties of horizontal fixation and pursuit differ greatly from the torsional case.

Our goals, therefore, were to (1) observe eye movements during torsional and horizontal MAE and (2) to determine if MAE was caused by retinal slip following the motion of the target. Some of these findings have been presented in abstract form (Seidman et al. 1990).

Methods

Four male human subjects, ages 24-43, were studied. All gave informed consent. Two subjects were myopes, one of whom habitually wore contact lenses; none wore corrections during the experiments.

Torsional and horizontal rotations of one eye were recorded using a 'double-loop' silastic search coil (Skalar, Delft, the Netherlands) and 6-foot field coils (CNC Engineering, Seattle, WA) that employed a rotating field in the horizontal plane and an alternating field in the torsional plane (Seidman and

Leigh 1989). The search coil was precalibrated on a protractor device prior to placement on the subject's eye. The measurements of eye position were 98.5% linear over an operating range of $\pm 20^\circ$. The standard deviation of the noise of our coil system was less than 1 minute of arc. The crosstalk artifact on the torsional channel produced by horizontal or vertical rotations was $\leq 0.025^\circ$ torsion per degree of horizontal or vertical movement. Crosstalk of this magnitude did not effect our results. Data were filtered (0-40Hz) using 4-pole maximally flat filters (Krohn-Hite Corporation, Avon, Massachusetts) and digitized at 100 Hz using a 16-bit data acquisition board (Data Translation, Marlborough, Massachusetts) installed in an IBM PC-AT computer.

Because the torsional eye movements produced by our stimuli were small in magnitude, instantaneous eye velocity was estimated at approximately 75 instances during each trial using an interactive program. This provided a convenient method to view slow-phase direction.

Visual targets were generated using an IBM PC-AT with a dedicated board used to create the images. These images were recorded directly to videotape. A 19" monitor was used to present the stimuli to the subjects. The monitor was placed outside of the magnetic field, and was thus approximately three feet from the subject. At this distance, the monitor subtended $> 30^\circ$ of the visual field of the subject, who viewed the display binocularly.

Two different groups of stimuli were generated. The first group consisted of circular targets that incorporated 8 or 16 alternating light and dark

sectors with a fixation spot in the center and rotated around the line of sight with angular velocities of $60^\circ/\text{sec}$ or $90^\circ/\text{sec}$ (Fig. 2-1A). Although this stimulus is not a spiral, MAE is still elicited, and the torsional optokinetic system is stimulated without the presence of complicating linear components. Subjects were requested to fixate upon the center of the rotating display. The second group consisted of 8 or 16 alternating vertical light and dark bars, with a central fixation spot (Fig. 2-1B). These targets moved to the right, and, at the viewing distance of 3 ft, had linear velocities of $6^\circ/\text{sec}$ or $9^\circ/\text{sec}$. Neither the torsional or the horizontal stimuli elicited circularvection (CV) in any subjects.

Subjects reported perceptions of motion through use of a continuous potentiometer, which they were asked to rotate at a velocity matching the apparent velocity of the display stimulus. This signal was filtered and digitized in the same manner as the eye position signal.

The stationary target was presented on the monitor for a period of 20 sec. At the end of this time period, the target started to move, and continued to do so for 20 sec. The target then stopped moving, but remained visible for a further 60 sec. Data collection began approximately 10 sec prior to target movement, and continued for 60 sec.

Figure 2-1

Typical visual stimuli, which were displayed on a video monitor: (A) torsional and (B) horizontal.

A

B

Results

Typical responses are shown in Figure 2-2, while the responses of all subjects are summarized in Table 2-1. During rotation of the circular targets, all subjects signalled stimulus motion and developed a torsional nystagmus with slow-phase eye movements going in the same direction as the target. The gain of the slow phases of this nystagmus was low, with a steady-state value usually <0.01 . Peak slow-phase velocity, occurring near the onset of target motion, tended to be slightly higher in gain.

Upon motion cessation of the circular target, all subjects reported an illusory reversal in the direction of target motion, or MAE. This illusory motion persisted for a median time of 20.9 sec (range: 16.0 to >33.9 sec). During this period slow-phase eye movements also reversed direction, with one subject actually developing torsional nystagmus. This reversed nystagmus was usually of lower velocity than that developed during target rotation, and declined to zero in a median time of 12.6 sec (range 5.6 to 26.9 sec, Fig. 2-2A).

Horizontal eye movements were monitored during torsional trials, and were found to deviate $<2^\circ$ from the center of the target with velocities $<2^\circ/\text{sec}$. These movements would be expected to produce $<0.05^\circ$ and $<0.05^\circ/\text{sec}$ of crosstalk artifact on the torsional channel, which is too small to bias our results. During horizontal target motion, subjects developed a small horizontal nystagmus, once again with slow phases in the same direction as the target. The steady-state gain of the slow phases of this nystagmus was low

Figure 2-2

Typical responses to torsional and horizontal motion stimuli. Lower traces show eye position (line) and instantaneous estimates of eye velocity (crosses). Upper traces show perception, as reported by subjects with a continuous potentiometer. (A) Torsional motion stimulus of $180^\circ/\text{sec}$ and (B) horizontal motion stimulus of $9^\circ/\text{sec}$, followed by fixation on center of still target. Note reversal of slow-phase direction following cessation of target movement in (A) and the lack of a reversal in (B).

A

B

TABLE 2-1

EYE MOVEMENT AND PERCEPTION CHARACTERISTICS						
SUBJECT	TARGET			POST-MOVEMENT DURATION (sec)		GAIN PEAK/STEADY STATE
	MODE	SECTORS	VELOCITY (deg/sec)	PERCEPTION	EYE MOVEMENT [†]	
1	T	16	60	21.0	17.2	0.01/ <0.01
		16	90	24.6	19.6	<0.01/ <0.01
		8	60	>33.9	26.9	0.01/ <0.01
	H	16	6	12.6	†	0.72/0.20
		16	9	23.7	†	0.87/0.08
2		8	6	27.6	†	0.57/0.15
	T	16	60	23.3	17.5	0.04/ <0.01
		16	90	17.7	12.1	0.06/ <0.01
		8	60	18.0	5.6	0.04/ <0.01
	H	16	6	5.9	†	0.70/0.11
3		16	9	6.9	†	0.55/0.11
		8	6	6.8	†	0.70/0.15
	T	16	60	18.7	6.9	0.04/0.02
		16	90	20.8	13.2	0.03/ <0.01
		8	60	16.0	7.5	0.03/ <0.01
4		16	6	†	†	†
		16	9	11.8	†	0.79/0.33
		8	6	17.1	†	0.62/0.13
	T	16	60	24.9	10.0	0.03/0.01
		16	90	†	20.8	0.02/ <0.01
		8	60	†	11.3	0.03/ <0.01
	H	16	6	5.4	†	0.05/0.03
		16	9	5.0	†	0.04/ <0.01
		8	6	5.0	†	0.08/0.07

T = torsional

H = horizontal

† = not applicable (suppressed by fixation, see text)

‡ = not measured

GAIN = optokinetic gain during target motion

(mean=0.125) presumably because of the suppression of OKN by fixation mechanisms.

Following horizontal target movement, subjects experienced a small, short-lived MAE that was reported to be less compelling than torsional MAE. The MAE lasted for a median time of 11.5 sec (range 5.0 to 27.6 sec). Reversal of horizontal nystagmus did not occur following cessation of target motion (Fig. 2-2B).

Discussion

We have shown that there are eye movements associated with torsional MAE. These eye movements are present both during and after the motion stimulation. During stimulation, torsional eye movements were in the same direction as the motion stimulus. Following stimulation, the eye movements reversed direction. The torsional eye movements during the perception of illusory motion were not in the direction that would have produced the retinal slip necessary to cause the perception. Therefore, we conclude that retinal slip is not responsible for MAE. Although there are small eye movements during horizontal motion stimulation, there are no horizontal eye movements during the MAE. This difference between torsional and horizontal MAE may be due to the strength of the horizontal fixation system: gaze stability during fixation of a stationary target is much less precise torsionally than horizontally (Ferman et al.

1987).

The reversal of eye movements during torsional MAE may be linked to the illusory reversal of the direction of the visual stimulus. Similar observations have been made by Brandt, Dichgans and Büchele (1974) for horizontal eye movement during CV, in which a reversal in the direction of CV is accompanied by a reversal in slow-phase eye movement. However, since "velocity storage" in the human torsional optokinetic-vestibular system is weak or absent (Morrow and Sharpe 1989; Seidman and Leigh 1989), this mechanism is unlikely to contribute to eye movements during MAE.

Another possibility is that the reversal of torsional eye movements that occurs during MAE may reflect the activity of secondary visual areas in cerebral cortex that encode both torsional visual stimuli and eye movement signals (Graziano, Andersen and Snowden 1990; Newsome, Wurtz and Komatsu 1988).

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CHAPTER 3
THE TORSIONAL VESTIBULO-OCULAR REFLEX
CAN BE CANCELED BUT NOT ENHANCED
BY VISUAL STIMULI

Abstract

We measured torsional eye movements in four human subjects during roll rotations of the head. During head rotation, various degrees of visual feedback were provided by a large-field, randomly spotted visual display that rotated proportionally to torsional head velocity. The visual feedback varied by integer values between -1 to 3 times the velocity of the head. It was found that by rotating the visual display 3 times as fast as the head, and in the same direction (i.e. 3 times visual feedback gain), the gain of the torsional VOR could be reduced by as much as 80%. The reduction of VOR gain was greatest for the higher values of visual feedback gain. I was unable to increase the gain of the torsional VOR by rotating the visual display in a direction opposite to the head.

The results suggest that the mechanism by which the gain of the torsional VOR is modulated by visual stimuli is unrelated to visual tracking mechanisms, such as smooth pursuit and optokinetic nystagmus, that respond to retinal image slip.

Introduction

The VOR serves to hold gaze stable during angular rotations of the head, thereby maintaining clear and stable vision during natural activity such as locomotion. Visual tracking mechanisms, particularly smooth pursuit, keep images of moving targets on the fovea, so as to maintain high-acuity vision. During natural behavior it is rare, however, that tracking of a moving target is carried out solely with eye movements. Usually, a moving target is tracked with a combination of eye and head movements. This behavior is known as combined eye-head tracking (CEHT).

The VOR acts to hold gaze steady. During CEHT, however, gaze must constantly change to track the moving target, and keep its image close to the fovea. Therefore, vestibular eye movements induced by head rotation during CEHT need to be negated.

There are two hypotheses as to how the VOR can be overridden during CEHT. The first hypothesis is that the gain of the VOR is parametrically reduced during CEHT. The second asserts the existence of an internal signal that is summed with the VOR signal in a manner which cancels it out; the prime

candidate for the generation of such a signal is the smooth pursuit system. In fact, both mechanisms may contribute. It has been demonstrated for horizontal eye movements in both monkeys and humans, that smooth pursuit cancels 70% or more of vestibularly induced eye movements (Huebner et al. 1992; Lisberger 1990) while approximately 30% is accomplished by a parametric reduction in VOR gain (Huebner et al. 1992).

To investigate the mechanisms operating in the torsional plane, I carried out experiments on torsional eye movements which are analogous to CEHT in the horizontal plane. Smooth pursuit is nonexistent in the torsional plane (Robinson 1982), thus, any reduction in VOR gain must be through a parametric reduction, as opposed to a cancellation by another signal. Although the reduction of the torsional VOR has already been demonstrated in humans (Leigh et al. 1989), our experiments encompassed a wider range of visual feedback, resulting in a greater reduction in torsional VOR gain than previously reported.

Methods

Torsional eye and head movements were measured in four subjects using the magnetic search coil technique, and digitized for later analysis. Subjects 1 and 3 were emmetropes. Subject 2 was a myope who habitually wore contact lenses (-5 OS) and subject 4 was a myope who habitually wore spectacles (-3 OD). Subjects did not wear corrections during experiments.

Our search coil system employs 6-foot Helmholtz coils (CNC Engineering, Seattle, WA) and double-loop silastic scleral coils (Skalar, Delft, the Netherlands).

To perform this experiment, it was necessary to design and build a visual stimulator which functions in the torsional plane. To meet our needs, certain design criteria had to be met. First, it was necessary to be able to use head velocity as a command signal for our stimulator. In addition, the amount of magnetic materials in the visual stimulator had to be kept to a minimum so as not to interfere with our coil system.

The heart of our torsional motion stimulator (TMS) was a 103 oz-in servo-motor with an integral tachometer (EG&G Torque Systems, Watertown, MA, Model 3515) and a matching linear servo-amplifier (EG&G Torque Systems, Model CO502) shown in Figure 3-1. To prevent the motor from operating at speeds below its optimal range, motor output was stepped down by a 50:1 worm gear reducer (Hampton Power Products, Portland, OR).

Since the tachometer in this servo-system was an integral part of the motor, and not placed on the output shaft, it was important to keep the output shaft and all couplings somewhat rigid. However, the output shaft was required to be long in order to keep the motor out of our magnetic field, and it could not be metal, as this would also distort the field. It is difficult to simultaneously meet both of these requirements, and material for the output shaft had to be carefully selected. After trying various plastic shafts and finding them

Figure 3-1

Mechanical diagram of TMS. Motor and integral tachometer (tach) were stepped down by a gear reducer, to which the visual display was connected by a shaft. Figure is not to scale.

unsatisfactory, I decided to use a 4-foot length of 3/4-inch diameter linen-filled Phenolic rod because of its torsional rigidity.

For couplings between the servo-motor and gear-reducer, and between the gear reducer and output shaft, Lovejoy products (Dowersgrove, IL) were used. These couplings afforded certain advantages over similar products. They allowed us to link shafts of differing diameters, and the inserts used for cushioning the mechanical connections could be changed to vary the stiffness of the coupling. In between the motor and the gear reducer, a rubber insert was used. This was primarily to protect the motor from damage due to shaft misalignment. Rigidity was not an issue at this linkage, because the gear reduction greatly reduced any backlash or mechanical deformation. Between the reducer and the output shaft, however, rigidity was required, and a urethane insert was used in the linkage. All mechanical connections were keyed with aluminum bar stock to prevent slippage.

The output shaft was supported by two ball-bearings mounted in pillow blocks. Our visual display, a 70 cm diameter, randomly-spotted disk, which was constructed from foam-core paper, was attached to the output shaft with a plastic hub. This connection was also keyed with aluminum bar stock.

The whole assembly was mounted on a 4'x2' sheet of 3/4-inch plywood to prevent mechanical deformation. This was, in turn, mounted to a rolling, height-adjustable table to make the TMS maneuverable.

The subjects' torsional head position was measured in real time. This

signal was passed through a 4-pole maximally flat, low-pass filter with a cutoff frequency of 40 Hz, and then fed to an analog differentiator to yield head velocity in real time (Fig. 3-2). This signal was then passed through a variable gain amplifier, and used as a command signal for the servo-amplifier.

The stimulus display was moved up to the subject, until it was no further than 15 cm from the subject's face, subtending more than 70° of the visual field. The subject was then instructed to roll his head in an ear-to-shoulder fashion at approximately 0.5 Hz while viewing the center of the display, which was marked with a red spot. The display rotated at positive or negative multiples of torsional head velocity, according to the settings on the variable-gain amplifier, and provided different amounts of visual feedback to the subject. For our experiments, the target moved with gains varying by integer values between -1 to +3 with respect to torsional head velocity. In addition, the gain of the torsional VOR was also determined in darkness (i.e., no visual feedback).

During this experimental protocol, head and eye position were digitized at 100 Hz following analog filtering at 40 Hz. with a 4-pole, maximally flat filter to prevent aliasing. Data were acquired for 40 sec. intervals. Data were collected once for each subject at each feedback level.

Figure 3-2

Functional diagram of control of TMS. Head position was measured by the magnetic system, whose output was differentiated in real time (d/dt) to yield a velocity signal. Velocity was amplified by a variable gain (G), and passed to the servo-amplifier (servo-amp), which employed a tachometer in a negative-feedback arrangement. This controlled the motor which turned the visual display.

Data Analysis

Head and eye position were digitally differentiated using a two-point, central difference algorithm to yield head and eye velocity. Saccades were then interactively removed from the eye velocity record (Barnes 1982). Since spectral techniques were used to analyze our data, the points removed during saccades were replaced using cubic spline interpolation techniques.

Gain was calculated using the Welch periodogram technique (Bendat and Piersol 1986; Grossman et al. 1989). At least 20 sec (i.e., 2000 points) of head velocity and eye velocity were divided into overlapping 256-point epochs. The Fast Fourier Transform (FFT) of each epoch was calculated, then all the FFT's for each signal were averaged to provide estimates for the Fourier Transforms of the input, head velocity, and for the output, eye velocity. From these transforms, I computed the auto-power spectral density of the input and of the output, and the cross-power spectral density (see Appendix I). Coherence was then calculated. Gain was estimated as a function of frequency by the ratio of the auto-power spectral density of the output to the auto-power spectral density of the input. Thus, gain and coherence as a function of frequency were estimated. The gain and coherence for frequencies less than 0.75 Hz are reported.

Results

Results from one subject are shown in Figure 3-3, and cumulative results are shown in Table 3-1. In all subjects, the visually enhanced VOR (i.e., no target motion with respect to the head) was of greater gain than the VOR in the dark. Subjects were not able to further increase VOR gain with visual stimuli. In fact, for two subjects, VOR gain actually decreased by more than 25% when the display rotated in a direction opposite to that of the head. When the display rotated in the same direction as the head, gain was decreased in all cases, with the most reduction for three out of four subjects occurring when the display moved 3 times as fast as the head (the largest visual feedback). The greatest reduction in gain observed was 80% from the visually enhanced VOR and 70% from the VOR in the dark. Coherence was > 0.95 in 80% of our trials, and never went below 0.85, showing a high degree of linearity in the torsional VOR.

Discussion

I conclude that the gain of the torsional VOR can be reduced but not increased by viewing a display that moves relative to the head during active head roll. Since smooth pursuit is nonexistent for torsional eye movements (Robinson 1982), and the optokinetic response is feeble (Collewyn et al. 1985; Morrow and Sharpe 1989; Cheung and Howard 1991), the reduction in gain of the VOR cannot be attributed to visual mechanisms. The decrease in gain for subjects 2

Figure 3-3

Representative results from subject 1 with visual feedback gain of (A) $\times -1$, (B) $\times 0$, (C) $\times 1$, and (D) $\times 2$. Positive gain indicates display rotation in the same direction as head rotation. Note decreased VOR gain for higher positive values of visual feedback.

A

B

C

D

TABLE 3-1
TORSIONAL VOR GAINS FOR VARIOUS VISUAL FEEDBACK GAINS

	Visual Display Feedback Gain					
Subject	×-1	×0	×1	×2	×3	Dark
1	0.67	0.62	0.27	0.18	0.12	0.42
2	0.57	0.78	0.35	0.42	0.28	0.42
3	0.36	0.51	0.39	0.42	0.22	0.40
4	0.63	0.65	0.56	0.53	0.54	0.62

and 3 during a stimulus which would result in an enhancement of VOR gain in the horizontal system indicates a suppression mechanism responsive to the magnitude of visual-vestibular nonagreement, regardless of direction. These properties differ considerably from those of eye movements in the horizontal plane, in which VOR gain is reduced mainly through cancellation by a smooth pursuit signal. While the mechanisms by which the gain of the torsional VOR is reduced remain unknown, suppression, nonvisual cancellation, proprioceptive, and predictive mechanisms are possible explanations for the observed responses. It is possible that the neural control of these eye movements is effected at a level as low as the vestibular nuclei.

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CHAPTER 4
DYNAMIC PROPERTIES OF THE HUMAN VESTIBULO-OCULAR
REFLEX DURING HEAD ROTATIONS IN ROLL

Abstract

The dynamic properties of the human vestibulo-ocular reflex (VOR) during roll head rotations were investigated in three human subjects using the magnetic search coil technique. The properties of the torsional VOR were compared with those of the horizontal VOR, and differences were related to the contributions of the extraocular muscles and orbital tissues (ocular motor plant), and of the central nervous system.

The purpose of the first experiment was to quantify the behavior of the ocular motor plant in the torsional plane. The subject's eye was mechanically displaced into intorsion, extorsion or abduction, and then released; the dynamic course of return of the eye to its resting position was measured. The eye returned more rapidly from a position of extorsion than from a position of

intorsion in all three subjects; the mean predominant time constant of this return was 210 ms from intorsion, 83 ms from extorsion, and 217 ms from abduction. The results of this experiment were implemented in a mathematical model of the torsional ocular motor plant in humans.

The purpose of the second experiment was to determine the contribution of the central nervous system to the torsional VOR, specifically to quantify the efficacy of velocity-to-position integration of the vestibular signal. Position-step stimuli were applied with subjects' heads erect or supine. Position-step stimuli were also used to test the horizontal VOR. After a position-step stimulus, the eye drifted back to its resting position in the torsional plane but, in the horizontal plane, the eye held its new position. No disconjugacy of torsional eye movements was observed, implying that the brain may have compensated for any asymmetrical properties of the ocular motor plant. To interpret the responses, we used models for the horizontal and torsional VOR, and estimated the optimal values of the model's parameters. The time constant of the velocity-to-position neural integrator was smaller (typically 2 sec) in the torsional plane than in the horizontal plane (> 20 sec).

The main conclusion of this study is that the dynamic properties of the torsional VOR differ significantly from those of the horizontal plane, with little "neural integration" of the signal from the labyrinthine semicircular canals. We hypothesize that the incomplete integration of vestibular signals for the torsional VOR reflects different (and lesser) visual demands placed on this reflex

compared with the horizontal VOR.

Introduction

The vestibulo-ocular reflex (VOR) permits clear vision of the environment during head perturbations by generating eye rotations that largely compensate for head movements. The horizontal VOR has been widely investigated, and it has been possible to quantify the contributions to this reflex of the labyrinthine semicircular canals, the neural pathways, and the mechanical properties of the orbital tissues (reviewed by Robinson 1981; Wilson and Melville Jones 1979). Thus, by studying the relationship between head rotation and the discharge characteristics of vestibular nerve afferents, Fernandez and Goldberg (1971) were able to determine the transfer function of the semicircular canals. Robinson (1964) studied the dynamic course of eye movements during saccades and isotonic movements, and proposed a transfer function to describe the mechanical properties of the ocular motor plant. Skavenski and Robinson (1973) measured the relationship between abducens motoneurons and vestibular eye movements and applied the aforementioned descriptions of the semicircular canals and ocular motor plant to deduce the contribution that the brain makes to the VOR. They determined that an integration of the head velocity signal emanating from the semicircular canals was necessary in order for the brain to generate the observed vestibular eye movements.

With the development of reliable methods to record torsional eye rotations (Collewijn et al. 1985), it has become possible to measure the dynamic properties of the VOR during roll head rotations. Several studies have shown that the properties of the torsional VOR differ from those in the horizontal or vertical planes. For example, the gain of the torsional VOR is only about 50% of the corresponding values for the horizontal and vertical planes (Ferman et al. 1987a; Seidman and Leigh 1989). Furthermore, in humans, the torsional VOR lacks the "velocity storage" property that perseverates the horizontal VOR during sustained rotation (Seidman and Leigh 1989). To date, however, no study has attempted to determine the relative contributions of the vestibular organ, brain, and orbital tissues to the dynamic properties of the torsional VOR. Using a similar deductive approach to that applied to the horizontal VOR, we investigated the properties of the torsional VOR with two experiments. In the first experiment, we mechanically displaced the eye in the torsional plane and measured its return to resting position; this enabled us to quantify the dynamic properties of the ocular motor plant for intorsional and extorsional eye rotations. Using this information, and prior descriptions of the vestibular organ, we were able to conduct a second experiment that consisted of measuring the VOR using position-step stimuli. This allowed us to determine the efficacy of neural integration of vestibular signals in the torsional plane.

To interpret our data, we made use of a mathematical model of the VOR that incorporated transfer functions for the semicircular canals, the central neural

pathways, and the ocular motor plant (Fig. 4-1); this model was adapted from that presented by Robinson (1981). Note that the input to this model is head velocity, and the output is eye position. Because velocity storage is absent in the torsional plane (Seidman and Leigh 1989), and the torsional optokinetic responses are very weak (Collewijn et al. 1985; Morrow and Sharpe 1989; Cheung and Howard 1991), we were able to use a simplified description of the vestibular input and to assign published values to its parameters. The dynamic properties of the ocular motor plant are unknown for torsional eye movements. Since electrophysiologic studies have attested to the reliability of a two-pole, one-zero plant model in the horizontal plane (Robinson 1964; Robinson, Kapoula and Goldstein 1990; Fuchs, Scudder and Kaneko 1988), we chose the same model for our torsional studies. The results of Experiment 1 were used to determine the optimal values of the parameters of this plant model for torsional eye movements. To describe the brain's contribution to the torsional VOR in our model, we used three pathways: a direct pathway, a neural integrator, and a "slide" pathway (Robinson et al. 1990). Each pathway incorporated a gain element (Fig. 4-1). The results of the position-step experiment were used to estimate the optimal values of parameters of the three neural pathways, especially the time constant of the velocity-to-position neural integrator.

Figure 4-1

A model of the torsional vestibulo-ocular reflex. Model input is head velocity, $\dot{H}$, and output is eye position, E . Head velocity, is transduced by the semicircular canals (described as a high-pass filter with time constant T_c). The latency of VOR is τ , and its common gain is g . The vestibular signal projects to ocular motoneurons (OMN) through three separate pathways: a direct pathway, a "slide" pathway with gain g_s and time constant T_s , and integrated pathway with gain g_i . The leaky integrator is approximated by a low-pass filter with time constant T_i . Note that as T_i becomes large, the integrator becomes perfect. The signals of all three pathways are summed at OMN, and passed to a two-pole, one-zero representation of the ocular motor plant (detailed in Figure 4-2). The Laplace operator is denoted by s .

Methods

Three healthy men, aged 25, 30 and 45 years served as subjects for both experiments. All three gave informed consent for the experimental procedures which were approved by our Institutional Review Board. Subject 1 was a myope who habitually wore spectacles (OD -3.00, OS -1.75), subject 2 was a myope who habitually wore contact lenses (-5 diopters, OU) and subject 3 was an emmetrope; no refractive corrections were worn during experiments. No subject was taking any medication.

Torsional, horizontal and vertical movements of each subject's non-dominant eye were recorded using a double-loop scleral search coil (Skalar, Delft, the Netherlands). The 6-foot field coils (CNC Engineering, Seattle, WA, U.S.A.) employed a phasic measurement system in the horizontal plane (Collewijn 1977) and an amplitude system in the torsional and vertical planes (Robinson 1963). The search coil was precalibrated on protractors prior to placement on the subject's eye. The measurements of eye movement were >98% linear in all planes over an operating range of $\pm 20^\circ$. Crosstalk on the torsional channel from horizontal movements was $<0.025^\circ$ torsion per degree of horizontal rotation. The eye was anesthetized with topical proparacaine prior to coil insertion. Subjects wore the coil for periods of time which were always less than 30 minutes.

Experiment 1

The subject viewed a spot of light projected from a laser onto a tangent screen at a distance of approximately 1.3 m with his non-dominant eye. The other eye was occluded with a sheet of white, opaque paper at a distance of about 5 cm. A site on the temporal conjunctiva of the viewing eye was then anesthetized with topical lidocaine. Using ophthalmic forceps, the eye was gently grasped at the anesthetized site, and displaced in the torsional plane, either intorsionally or extorsionally, or abducted in the horizontal plane. The eye was then released, and its movement back to resting position was recorded. Coil voltage signals were digitized at 1 kHz following analogue filtering at 200 Hz to avoid aliasing. This "forced duction" procedure was conducted twice in each direction for subject 1, and three times in each direction for subjects 2 and 3. A total of 6 trials had to be discarded because of the presence of blinks or saccades early in the response.

Using non-linear parameter estimation techniques, data were fit to the plant component of the model shown in Fig 4-1. The mechanical equivalent for this one-zero, two-pole model, and the corresponding equation for eye position are shown in Fig. 4-2. The forced duction of the eye is considered to be an initial condition placed on the model. Therefore, the return of the eye is described by this model to be a double-exponential decay to resting position, shown by the equation:

$$E = Ae^{-\frac{c}{T_{01}}} + Be^{-\frac{c}{T_{02}}}$$

Where E = Eye position

Although this equation appears to have four parameters that may vary, there is an added constraint which dictates that $A+B$ =total deflection. This constraint reduces this equation to a three-parameter model.

For parameter estimation, we used a commercially available FORTRAN subroutine known as NL2SOL (Dennis, Gay and Welsch 1981a; 1981b), that has been applied previously to models of the ocular motor system (Huebner, Saidel and Leigh 1991). This routine is provided with a residual array (i.e., a point-by-point array which shows how the model's prediction differs from the actual data) and a Jacobian matrix (i.e., a matrix of sensitivities, showing how the prediction would change in response to a change in each parameter). It is the task of the estimation routine to minimize the sum-squared of the residual array. This quantity will be referred to as the error function. Using the information provided by the residual array and the Jacobian matrix, the routine modifies the parameter values iteratively until they converge. In this first experiment, the estimation was simplified because the output variable and sensitivities could be expressed in closed form (see equation above and Appendix II); thus, the residuals and Jacobian matrix could be calculated directly.

Data were prepared for estimation using an interactive software package (Asyst Software Technologies, Rochester, N.Y., U.S.A.). The time of release

Figure 4-2

This model is the mechanical equivalent to the plant in the model of Figure 1. It consists of two parallel visco-elastic elements arranged in series. The equation shown describes eye position resulting from the zero-input, initial condition case of the forced duction (i.e., return of the eye to resting position after it is released subsequent to being mechanically displaced). E = eye position, F = applied force, r_i = viscosity, k_i = elasticity, and $i = 1, 2$. (Adapted from Robinson 1964 and Robinson et al. 1990).

$$E = Ae^{-t/Te1} + Be^{-t/Te2}$$

Where $A + B = \text{Total Duction}$

$$\text{and } Te_i = r_i / k_i$$

of the eye from forced duction was determined, and then any DC offset was removed. Naturally occurring drift in torsional eye position (Ferman, Collewijn, Jansen and van den Berg 1987b; Ott, Seidman and Leigh 1992) sometimes made it difficult to determine precisely the resting position. In these cases, we defined resting position to be where the velocity of torsional eye movements first went to zero following the release from forced duction. After preparation in this manner, data were then stored in a file to be analyzed by NL2SOL, which attempted to provide estimations for A , T_{e1} (the larger plant time constant), and T_{e2} (the smaller time constant).

Generally, the first 500 data points (i.e., the first 500 ms of data) were included in the estimation procedure. To help guarantee isotonic conditions, however, all data following blinks and saccades were discarded, and fewer points were used in these cases.

The algorithm usually converged to a final solution within 12 iterations. NL2SOL provides a variance/covariance matrix for each estimation, which is based on the Jacobian matrix. The diagonal elements of this matrix provide an indication of the precision of the estimate for each individual case (Huebner et al. 1991). It should be noted that the precision of the estimation is calculated under the assumption that the model is correct (Meyers 1990). Therefore, the precision of the estimation is not an indication of goodness of fit. For example, if the goal were to fit data which describes a line perfectly to the equation $y=ax+bx+c$, the error function might become quite low, indicating a good fit.

The precision of the estimates of a and b would be poor, however, due to multicollinearity of these two parameters, even though the quantity $(a+b)$ might be estimated with high precision.

Experiment 2

Coil linearity was the same as for Experiment 1. Rotation of the vestibular chair in the magnetic field caused a minor artifact in the search coil signals, which is most likely due to the pickup of offset position signals as described by Kasper, Hess, and Dieringer (1987). To correct for this artifact, which was linear with chair position, the search coils were mounted on the chair and both were rotated in the magnetic field, referencing the coil signals to true angular chair position signalled by a 12-bit optical encoder mounted within the chair (BEI Motion Systems, Cincinnati, OH). In this way, the artifact was carefully measured prior to each experimental run, and was subsequently removed. Subjects wore the search coil on the same eye that was studied in Experiment 1; the other eye was occluded with a patch. They also wore a search coil firmly attached to their foreheads to measure head position. Subjects sat in a vestibular chair with their faces oriented towards the ceiling, as previously described (Seidman and Leigh 1989). By the use of a plumb line, the eye of the subject wearing the search coil was located as close as possible to the center of rotation of the chair. Foam pads were placed to one side of each subject's head to help in centering the eye, as well as behind the subject's back for comfort.

The subject's head and body were then firmly fixed to the vestibular chair using restraints. Reid's line (Blanks, Curthoys and Markham 1975) was always greater than 70° from earth horizontal. To minimize the effects of Listing's Law (Ferman, Collewyn, and van den Berg 1987b), the visual axis of the subjects was held close to the axis of rotation of the chair by asking the subjects to view an earth-fixed light-emitting diode, 50 cm above their heads, which blinked with a duration of 2 ms at a frequency of about once per second, thereby minimizing retinal slip information. Prior to the beginning of each experimental run, the subject was slowly stepped to points within $\pm 30^\circ$ from starting position, and gaze was allowed to come to a final resting position. The eye always returned to a gaze position very near zero, showing that our methodology tended to minimize Listing's eye movements.

Position-step head rotations (range $5\text{-}30^\circ$) were then applied, moving the chair by hand; stimuli were applied in a non-predictable manner. This stimulus was selected since we were particularly interested in measuring gaze holding at the end of the head rotation, i.e., maximizing sensitivity to the parameter of primary interest, and in minimizing the effects of saccades. As control experiments, the ocular responses to self-generated horizontal (yaw) and torsional (roll) position-step stimuli were studied, as the subjects sat with their heads erect and imagined the location of a target 1.3 m in front of them in a dark room. During these experiments with the head erect, subjects 1 and 2 wore scleral search coils on both eyes to measure the conjugacy of the eye movements.

During each of 30 or more trials applied to each subject, coil voltage signals were sampled at either 1 kHz or 500 Hz, following analog filtering at 40 Hz. Trials contaminated with blinks or saccades were discarded.

Parameter estimation techniques were then used to fit our data to the models shown in Fig. 4-1. As described by Robinson et al. (1990), the two-zero, one-pole model of the plant requires three pathways to simulate horizontal saccadic data: a direct pathway from the semicircular canals, an integrated pathway containing a leaky integrator modeled as a low-pass filter with time constant T_i , and a pathway containing a "slide" component, which has been described in our model as a low-pass filter with a time constant of 100 ms. Thus, our model has 10 parameters, as follows:

τ	VOR latency
T_c	canal time constant
g	common gain
g_i	integrator gain
T_i	integrator time constant
g_s	slide gain
T_s	slide time constant
T_{e1}	plant pole 1
T_{e2}	plant pole 2
T_z	plant zero

Note that g represents an internal gain common to the three VOR

pathways, and not the overall gain of the VOR response. The VOR gain is dependent on all the model's parameters.

Estimation of 10 parameters presents a computational problem, and the results of such a large estimation may be difficult to interpret. However, certain simplifications may be made. Towards this goal, τ , the VOR latency, was fixed at 8 ms, a minimum value demonstrated for the horizontal VOR by Maas, Huebner, Seidman and Leigh (1989). T_e was set at 7.0 sec, as estimated by Cohen et al. (1981). T_s was fixed at a value of 100 ms (Robinson, Kapoula and Goldstien 1990). Finally, since T_{e2} represents a high-frequency zero in plant behavior, this time constant should not strongly influence our results, and was fixed at a value of 7 ms (Robinson, Kapoula and Goldstein 1990). In addition, T_{e1} was fixed at the average values estimated for each subject during Experiment 1. For those trials in which the eye was carried to a position of extorsion (intorsion), the time constant found for the return from a position of extorsion (intorsion) was used in the estimations, since this phase of eye movements dominated the response. These simplifications leave us with a model in which 5 parameters are allowed to vary.

The position-step stimuli were chosen to enhance sensitivity to T_t , since this was our primary interest. These were, in fact, not perfect steps in the mathematical sense, and therefore lack high-frequency components which would increase the sensitivity of other parameters, such as T_z .

In an effort to further simplify the parameter estimation procedure, we

attempted to eliminate the slide component of this model altogether. While this worked sufficiently well in approximately 50% of our trials, in some cases the error function of the estimation was increased by a factor of 10 or more. Therefore, these attempts were abandoned.

Although the 5-parameter model described above was chosen for these estimations, the choice of model did not greatly affect the estimate of T_i , the time constant of the neural integrator, despite possible increases in the error function. The use of a different model, such as one in which the slide pathway was omitted, or a model in which T_{ei} was fixed at the same value for both intorsions and extorsions, did not change the estimate of T_i by more than one second, and does not significantly change our conclusions. In addition, we also tried fixing the value of T_z at 92 ms, the value reported for the horizontal plant (Robinson, Kapoula and Goldstein 1990), also with little effect on the estimate of T_i . Thus the 5-parameter model was used for all subsequent estimations of parameters for the torsional system.

For estimations of horizontal position-step data, one further simplification was possible. Since plant dynamics in this plane have been well studied, we were able to fix the value of T_z to the previously reported value of 92 ms (Robinson, Kapoula and Goldstein 1990), reducing to four the number of parameters to be estimated. The long time constant of the plant was fixed at the values measured during Experiment 1 for each subject. In addition, because of the effects of velocity storage in the horizontal plane, the canal signal is

perseverated (Cohen et al. 1981). To account for this effect, the canal time-constant in our model was replaced with the time constant of the decaying eye velocity due to a $60^\circ/\text{sec}$ velocity step in the dark. This value was measured to be 25 sec for subject 1, 14.5 sec for subject 2, and 13 sec for subject 3.

While the actual functioning of NL2SOL for Experiment 2 did not differ from that during Experiment 1, the implementation of the parameter estimation routine was different. Due to the varying nature of the input (each stimulus was unique) there is no closed-form solution to this model, and the predicted outputs must be calculated by numerically integrating the differential equations describing the system. NL2SOL was provided with initial guesses of parameter values that were passed to ACSL (Mitchell and Gauthier Associates, Concord, MA), a numerical simulations package, which used parameter values to calculate eye position, as well as the five sensitivity functions. This information was passed to a file for use by NL2SOL, which used it to update the current parameter values. The process continued until convergence criteria were met. The differential equations describing our model output and its sensitivity functions are derived in Appendix II.

To obtain realistic solutions, it was necessary to put constraints on parameter values. Gains and time constants were not permitted to assume negative values. To prevent floating-point errors from occurring during calculation of the sensitivity functions, we assigned minimum values of all parameters to be 0.0001. In addition, we did not permit T_1 to take on values

greater than 200 sec.

Since this estimation process is a minimization problem involving 5 variables, it was quite possible that the procedure would converge to a local minimum, yielding unreliable estimates. To avoid this pitfall, a 3-parameter estimation which was more tolerant to poor initial guesses of parameter values, was first run to provide sound starting points for our 5-parameter estimations. This simplified model incorporated a one-pole plant and omitted the slide pathway. The results of this estimation were then passed as the starting points to our estimation routine.

The coefficient of variation (CV%) was used to assess precision of the estimations of parameter values (Huebner, Saidel, and Leigh 1991). This is the ratio of the standard deviation of each estimated parameter (taken from the diagonal of the variance/covariance matrix of each estimation) to the estimated value of the parameter. The coefficient of determination, R^2 , was used to assess goodness-of-fit of individual subject responses by the optimized model. This statistic represents the proportion of variation in the response data that is accounted for by the model (Meyers 1991).

Results

Experiment 1

Typical responses after the eye was released from intorsion, extorsion and abduction, from one subject are shown in Fig. 4-3. The long time constant, T_{e1} , for the return from forced duction for each subject are shown in Table 4-1. The mean time constant for the return from extorsion was 83 ms, while the mean time constant for a return from intorsion was 210 ms. The mean time constant from a return from abduction was 217 ms, similar to previous reports (Robinson 1964). For each individual, the time constant for a return from extorsion was always shorter than the time constant for a return from intorsion. R^2 was greater than 0.99 for 60% of our estimations, and was only below 0.95 for one estimation.

The gain, B , of the faster exponential component of this model (T_{e2}) was most often estimated to be zero. Therefore the estimate of the faster time constant, T_{e2} , lacks meaning and precision, since it has no effect on the output. This is probably the result of our inability to identify precisely the time of release from the position of forced duction. It may also be due to a very small contribution of T_{e2} to overall eye position for our experimental protocol. With this in mind, estimates of T_{e2} are not presented.

CV% values are shown in Table 4-1 for each estimation. This value is usually below 3%, and exceeds 15% only once, showing good precision in our estimations.

Figure 4-3

Time course of the return to resting position after the eye was mechanically displaced and then released in subject 3. After the eye was released from intorsion (A) T_{ei} was 323 ms. Following return from extorsion (B), T_{ei} was 58 ms. Following abduction (C), T_{ei} was 183 ms. The solid lines show eye position, while the dashed lines show the fit to the model of Fig. 4-2. Note that in (A) and (B) the dashed line is almost totally superimposed on the data. The high-frequency sinusoidal oscillation present in the torsional data is noise, which did not influence the estimation process. Note also the two blinks and the saccade near the end of the horizontal record, C. Estimation, in this case, was performed on the data preceding the first blink.

TABLE 4-1

Long Time Constant (T_{cl}) of Return From Forced Duction			
Subject	Intorsion	Extorsion	Abduction
1	.126 CV% = 1.9	.095 CV% = 2.3	.345 CV% = 1.3
	.186 CV% = 2.3	.0705 CV% = 4.4	
2	.155 CV% = 1.6	.081 CV% = 12.0	.204 CV% = 3.1
	.134 CV% = 1.1	.086 CV% = 43	.180 CV% = 3.1
3	.325 CV% = 3.1	.146 CV% = 1.6	.183 CV% = 1.7
	.223 CV% = 2.0	.058 CV% = 0.8	
	.323 CV% = 1.9	.041 CV% = 2.7	

Experiment 2

Typical responses to position-step stimuli in the torsional and horizontal planes are shown in Fig. 4-4; note that head position has been inverted in the figures for clarity of display. It is evident that, following the horizontal stimulus, the eye is held steady at its new eccentric position; in the torsional plane, however, the eye drifts rapidly back to its resting position. The drift of the eyes back to resting position following the roll head movement suggested a deficiency of velocity-to-position integration of vestibular signals. When we estimated the optimal values of the parameters of the model shown in Fig 4-1, a consistent finding was that T_1 was always less than 6.0 sec for subjects 1 and 3, and did not exceed 2.0 sec for subject 2 (see Table 4-2A). Note also that the overall gain of the torsional response is less than for the horizontal, which is close to 1.0 (see Fig 4-4).

The coefficient of determination, R^2 , was greater than 0.96 for all estimations. Estimates of the internal parameters of our model, particularly g_s and T_z , varied more. Indeed, for some of our estimations with 5 degrees of freedom, more than one solution seems likely, and these estimates might reflect this fact. Nevertheless, the estimates of T_1 were consistently less than 6 sec in the torsional plane. The gain of the slide pathway, g_s , and the time constant of the plant zero, T_z , were not precisely estimated using the present stimuli, and might only be determined reliably through electrophysiologic methods in animal preparations.

Figure 4-4

Typical responses to position-step stimuli in the torsional (A) and horizontal (B) planes from subject 1. The solid lines show eye position, and the dashed lines show head position, which has been inverted for clarity. Note that, following the horizontal stimulus (B), the eye retains its new eccentric position; in the torsional plane (A), however, the eye drifts rapidly back to its resting position. Note also that the gain of the torsional response is less than that of the horizontal.

A) TORSIONAL

B) HORIZONTAL

Median CV%, as well as the range of CV%'s, are shown in Table 4-2 for each subject; medians and ranges are used because of the non-normal distributions. For subjects 1 and 2, CV% on the estimates of T_1 were always 5% or less, indicating precise estimations. For subject 3, CV%'s of this parameter were typically 30%, and exceeded 45% in only one case, showing fair precision of estimations. For all three subjects, the CV% for T_z , when it was estimated to be near zero, was high. This is most likely because our stimuli did not sufficiently excite the high-frequency dynamics of the VOR, and therefore this parameter was not estimated well.

In subject 1, whose T_1 was estimated to be the greatest, CV%'s of g and g_1 were always under 10%. Precision on the estimates of g_s in subject 1 was lower, with CV% values usually under 300%. For those estimations in which the CV% of g_s was above 100%, the contribution of the slide pathway was usually estimated to be negligible (i.e., $g_s < 0.1$). For subjects 2 and 3, whose time constants of integration were estimated to be small, CV%'s of the parameters other than T_1 were generally much higher. Indeed, as T_1 decreases, there is more redundancy between the direct, slide, and integrated pathways, and this largely contributes to the high CV%'s of these estimations. The significance of these low-precision estimates will be addressed in the Discussion.

The absence of drift of the eyes back to resting position after the horizontal head rotations suggested near-perfect integration of vestibular signals. When we estimated the optimal values of parameters for our model of the

TABLE 4-2
PARAMETER ESTIMATES AND PRECISIONS

TABLE 4-2A

subject		g	g _s	T _e	T _i	g _i	T _e (fixed)
1	Extorsion, n = 5						.083
	mean	.041	.11	.009	3.9	11.2	
	std. dev.	0.002	0.01	0.015	1.2	0.7	
	CV % median	4.0	45	192	1.4	4.1	
	CV % range	2.1-10.9	13.5- > 500	10.0- > 500	0.9-2.9	2.0-10.6	
	Intorsion, n = 5						.156
	mean	.077	.098	.0001	2.5	5.2	
	std. dev.	0.008	0.094	0.0	0.85	0.65	
	CV % median	3.6	66	> 500	2.8	4.0	
	CV % range	1.7-7.4	14.5- > 500	very low prec.	1.7-2.9	1.5w.6	
2	Extorsion, n = 8						.084
	mean	.012	.48	.007	0.88	27.5	
	std. dev.	.002	.79	.008	.33	6.5	
	CV % median	91	> 500	> 500	3.5	93	
	CV % range	40- > 500	80- > 500	234- > 500	0.6-4.6	52-444	

TABLE 4-2B

subject		g	g _s	T _i	g _i	T _{e1} (fixed)
1 n = 8	mean	.080	2.3	199.9	12.7	.345
	std. dev.	.007	.32	0.0	1.1	
	CV % median	1.2	2.0	49	1.0	
	CV % range	0.7-1.8	1.2-3.3	32-480	0.7-1.3	
2 n = 10	mean	.062	.42	199.9	17.9	.192
	std. dev.	.008	.24	0.0	2.4	
	CV % median	1.9	11	71	1.8	
	CV % range	0.8-3.7	2.1-74	21-150	0.8-3.5	
3 n = 4	mean	.052	0.9	199.9	17.5	.183
	std. dev.	.008	.51	0.0	2.1	
	CV % median	1.4	4.2	60	1.4	
	CV % range	0.5-2.7	1.0-17.8	15.9-103	0.5-2.6	

horizontal VOR (Table 4-2B), T_1 was always estimated to be greater than 199 sec., the maximum value allowed by our estimation. Note that because we used 1.5 sec epochs of eye movement data for parameter estimation purposes, a long T_1 (e.g., > 20 sec) would appear infinite to our method of estimation; however, the difference between estimated values of T_1 in the torsional and horizontal planes showed no overlap. For all parameters other than T_1 , CV% were under 5% for greater than 90% of all estimations. CV%'s of T_1 were larger, reflecting low sensitivity at large values of this parameter.

Figure 4-5A shows a comparison of a typical response of the torsional VOR from subject 1 (same response as shown in Fig. 4-4) and the corresponding simulation of the response by the model of the (shown in Fig. 4-1), using optimal parameters for this subject. Head position is not shown for clarity of display. Fig. 4-5B shows the corresponding information for the horizontal VOR.

We also measured the torsional VOR with the head erect. The dynamic characteristics of these responses were similar to those with the head supine, consistent with reports from other laboratories (Fischer et al. 1992). One qualitative difference of these responses from those with the head supine, was the presence of a tonic ocular counter-roll component that had a gain typically of 0.25 or less (Collewyn et al. 1985; Ott 1992). Accordingly, we did not attempt to estimate the values of parameters using these data, since our model does not attempt to account for tonic counterrolling. We did, however, examine the responses of subjects 1 and 2, who wore scleral search coils on both eyes for

Figure 4-5

(A) Comparison of a typical response of the torsional VOR from subject 1 (same response as shown in Fig. 4-4A) and the corresponding simulation of the response by the model shown in Fig. 4-1, using optimal parameters for this subject. Head position is not shown for clarity of display. (B) Simulation for horizontal VOR in the same subject (same response as shown in Fig. 4-4B). Solid lines show the actual response, and the dashed line shows the optimized model's simulated data.

A) TORSIONAL

B) HORIZONTAL

these experiments, for conjugacy of eye movements in the torsional plane in response to roll movements with the head erect. We found a high degree of conjugacy of the torsional eye movements in both subjects; an example is shown in Fig 4-6.

Discussion

We have shown that the contributions made to the dynamic properties of the torsional VOR by the orbital tissues and by the central nervous system differ considerably from those reported for the horizontal VOR. Our first finding was that the time course of return of the eye to its resting position after it was mechanically displaced and then suddenly released from extorsion was much shorter than after release from intorsion or abduction. The explanation for this asymmetrical response might be related to the unique course of the superior oblique tendon through the trochlea resulting in stiffer properties than those of the inferior oblique or medial rectus muscles. Whatever the explanation, this finding raised the question of whether the brain compensates for this asymmetry of the torsional properties of the ocular motor plant during vestibular eye movements. When we examined the torsional eye movements of two of our subjects for conjugacy, the responses were indeed conjugate (Fig. 4-6). When we used the model of Fig. 4-1 to predict the response to head roll, holding values of brain parameters constant, we found that setting the value of the plant

Figure 4-6

Demonstration of conjugacy of eye movements in the torsional plane. Torsional movements of both eyes and the head were recorded while the subject actively rolled his head in an ear-to-shoulder fashion, starting from the upright position. The response was conjugate. In addition, note that the data are similar to that occurring with the face supine (Fig. 4-4A), with the exception of a static ocular counterroll component present in this trial. Head position is inverted for clarity.

time constant T_{e1} to either 82 ms or 210 ms substantially affected the conjugacy of the response (Fig. 4-7). Two explanations seem possible. Either the brain programmed vestibular eye movements differently for each eye, taking into account the asymmetrical properties of the orbit, or the movements of the eyes after the release from forced duction during Experiment 1 did not provide an accurate description of the contribution of the ocular motor plant during active movements. Though we cannot exclude the second explanation, our simulations show that our model was able to produce conjugate eye movements by assigning appropriate values to the three neural pathways for each value of T_{e1} (See Fig. 4-7). This was reflected by the gain of the integration pathway, g_i , being estimated to be larger for extorsional trials than for corresponding intorsional trials in all three subjects, perhaps indicating an attempt by the nervous system to yoke the eyes. If the measured plant asymmetries are, in fact, corrected by neural integration, this suggests independent integrator control for each extra-ocular muscle.

Our second finding was that the integration of the vestibular signal (head velocity) by the brain was much less complete for torsional than for horizontal eye movements. Specifically, the time constant of the torsional neural integrator was typically 2 sec, compared with a much larger time constant for the horizontal system. Because we only measured gaze for 1.5 seconds after the position step, we could not estimate T_i in the horizontal plane with precision; thus, all our estimates on horizontal position steps show identical time constants

Figure 4-7

Simulated eye movements demonstrating the ability of our model to produce conjugate eye movements in the torsional plane despite asymmetries in the plant. Torsional head position (inverted for clarity) was recorded during an actual trial, and optimizations were performed to find parameters which would enable our model to reproduce the actual eye movements which were elicited. The solid line shows the simulated eye movements after the model had been optimized for $T_{e1} = 83$ ms. The dotted line shows the simulation after T_{e1} has been changed to 156 ms., with no re-optimization (i.e., other parameters remaining the same), resulting in a simulated movement that is disconjugate compared to the first simulation. The dashed line shows a third simulation following re-optimization of all parameters with $T_{e1} = 156$ ms. This simulation produces eye movements which are conjugate to the first simulation, demonstrating how the model is capable of simulating conjugate eye movements even if plant asymmetries are large. R^2 was greater than 0.99 for both optimizations.

of 199.9 sec (the upper limit of the permitted range) for the integrator. Note that when T_i becomes large, variation of this parameter affects the output progressively less (i.e., there is low sensitivity to this parameter). Therefore, our data are consistent with published values for neural integrator leak in the horizontal plane, which indicate a time constant of >20 sec (Becker and Klein 1973; Robinson et al. 1984).

As the estimates of T_i get smaller, precision in the estimates of the remaining variables declines. This probably reflects a redundancy of the three pathways in our model. Nevertheless, we are hesitant to remove any of these pathways simply to increase precision of our estimates because of the evidence supporting their contribution to horizontal eye movements, and, as has been shown, our attempts to dispense with the slide pathway often invalidated our analyses. It is also been demonstrated that it is possible to train humans to produce tonic changes in torsional eye position with torsional saccades (Balliet and Nakayama 1978). This last line of evidence suggests the potential for development of a "perfect" integrator function in the torsional plane, though whether all ocular motor signals, or just saccades, would be integrated is unresolved.

Although certain parameters in our model were estimated with low precision, the CV%'s of the estimates on T_i were consistently low. T_i is the only parameter in our model which can produce any eye movement responses to a position-step with a time constant longer than 400 ms, and is therefore

estimated in all cases with high precision. Hence, the low precision of estimates on certain parameters does not change our main conclusion - integration in the torsional plane is leaky compared to that in the horizontal plane.

Recently, Crawford, Cadera and Vilis (1991) reported that stimulation of the interstitial nucleus of Cajal in rhesus monkeys causes vertical-torsional eye movements and that pharmacological inactivation of this nucleus apparently caused impairment of the torsional integrator. In this study, the investigators used saccades to tertiary orbital positions to generate tonic changes in ocular torsion. Thus, the deficiency in torsional gaze holding might have reflected the monkey's inability to hold a sustained tertiary eye position (due to centripetal drift of the eye in the vertical plane). Unfortunately, these investigators did not assess the neural integrator for torsional eye movements using vestibular stimuli. Preliminary data from another laboratory (D. Straumann and Quing Yue, personal communication 1992) suggest incomplete integration of torsional eye velocity in rhesus monkeys, when evaluated with position-step stimuli. Caution is required, however, in comparing torsional eye movements of monkeys with humans. For example, the gain and velocity storage properties of the torsional optokinetic responses are well developed in rhesus monkeys (Schiff, Cohen and Raphan 1986) but not in humans (Collewijn et al. 1985; Morrow and Sharpe 1989; Cheung and Howard 1991).

Why should the brain's contribution to the torsional VOR differ so much from that in the horizontal plane? In order to account for the unique properties

of the torsional VOR, it is pertinent to recall that the purpose of vestibular eye movements is to maintain clear and stable vision during head movements. In the horizontal and vertical planes, this is achieved by generating eye movements that largely compensate for head movements, thereby holding images of the surroundings fairly stable on the retina, and the image of an object of interest close to the fovea. However, in the torsional plane, the situation differs. It is not clear that perfect compensatory eye movements are necessary in this plane. Consider, for example, the consequences of absent torsional eye movements during head movements in roll. Torsional eye movements are not used to hold images steady on the fovea. This can best be conceptualized by the simple analogy of a point of light falling on the exact center of a large circle. Torsional movements of this circle will not displace the light from the center. For this reason, smooth pursuit in the torsional plane is a meaningless concept (Robinson 1982). Following the same reasoning, retinal slip caused by poor control of torsional eye movements is maximal in the periphery of the visual field (Enright 1990), where photoreceptor density is low. Objects that fall in the periphery are not what our attention is directed to, suggesting that this type of retinal slip is well tolerated by perceptual mechanisms, and does not degrade vision during natural activity. Thus, from a visual standpoint, a modest VOR is probably all that is required to lessen image slip in the periphery and maintain visual acuity. Indeed, perceptual mechanisms involved in the processing of visual information appear to be better suited for handling torsional disturbances than corresponding

horizontal and vertical mechanisms. For example, the stability of torsional gaze, though much less constant than horizontal or vertical gaze (Ferman, Collewijn, Jansen and van den Berg 1987b; Ott, Seidman and Leigh 1992) does not appear to impair visual acuity or perception. When these factors are taken into consideration, it seems unreasonable to expect that the properties of the torsional VOR would be the same as those of the horizontal VOR.

Another factor that might account for the deficiency of the neural integrator for torsional eye movements is that human subjects are unable to make voluntary torsional saccades. Only after extensive training is this possible, and then it seems that the time constant of the neural integrator approaches that of the horizontal system (see for example Fig 1 of Balliet and Nakayama 1978). Theoretically, the otolithic organs might provide the signal required to hold a compensatory torsional eye position at the end of a roll head movement. However, the gain of the otolith-ocular reflexes in humans is low (Collewijn et al. 1985; Ott 1992). Furthermore, in the present study we found little difference in the dynamic properties of the torsional VOR whether the head was erect or supine during roll movements; others have reported similar results (Fischer et al. 1992). Thus, only if prolonged visual training imposes new (and unphysiologic) demands upon torsional eye movements do their properties become similar to horizontal movements (Balliet and Nakayama 1978). Interestingly, although visual stimuli induce only a weak optokinetic response (Collewijn et al. 1985; Morrow and Sharpe 1989; Cheung and Howard 1991) and cannot enhance the

fixed visual display during roll head movements (Seidman and Leigh 1992; Leigh, Maas, Grossman and Robinson 1989). The reason for this discrepancy is unclear.

In the present study, we chose to use position-step stimuli in order to deduce the properties of the neural integrator. Our reason for this choice was that we wanted to avoid quick phases of nystagmus that have the effect of "resetting" a deficient neural integrator (Skavenski and Robinson 1973; Sugie and Melvill Jones 1971). To our knowledge, position-step stimuli have not been used before to test the torsional VOR; Bello, Paige and Highstein (1991) have studied the dynamic properties of the torsional VOR of the squirrel monkey using sinusoidal stimuli. They found smaller phase shifts than our data would predict; this discrepancy, however, may be due to the presence of many saccades during low-frequency stimulation, and the small range of torsional eye movements in this species.

In conclusion, the human VOR during roll head rotations shows different properties from horizontal systems that imply simpler neural processing of vestibular signals. One reason that the VOR has been so extensively studied is that it is a simple reflex capable of motor learning. The unique properties of the VOR in the torsional plane, and the special visual demands that they serve, may provide an opportunity for studying a special case of the same reflex with considerably different characteristics.

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CHAPTER 5

ABNORMALITIES OF TORSIONAL EYE MOVEMENTS

In addition to aiding in the research of the normal ocular motor system in the torsional plane, the recent enhancements to the magnetic scleral search coil technique have also enabled quantitative descriptions of abnormalities of torsional eye movements. Previously, without accurate measurement techniques, reported abnormalities of torsional movement were of a qualitative nature. Some abnormalities even went unnoticed.

During my research, I have encountered, in our laboratory, patients with abnormalities of their torsional ocular motor systems. I present here a brief summary of such abnormalities, concentrating on those disorders that I have been able to observe personally.

Disorders of the torsional ocular motor system have received little attention, with the exception of the ocular tilt reaction (OTR), which consists of skew deviation, ocular torsion and head tilt (Dieterich and Brandt 1992;

Halmagyi, Gresty and Gibson 1979; Brandt and Dieterich 1987; Halmagyi, Brandt and Dieterich 1990; Lueck et al. 1991). Such patients also show a deviation of the subjective visual vertical, although this does not necessarily correlate with the amount of ocular torsion (Dieterich and Brandt 1992). The OTR probably reflects an imbalance of otolithic inputs. It has also been attributed to an imbalance of posterior semicircular canal inputs. Both factors may contribute to the OTR (Dieterich and Brandt 1992). Thus, lesions affecting the vestibular labyrinth, vestibular nuclei, medial longitudinal fasciculus, or interstitial nucleus of Cajal (Lueck et al. 1991) have been reported to produce the OTR. The OTR may be tonic, due to destructive lesions (e.g., in Wallenberg's syndrome) or paroxysmal, due to irritative processes.

Certain other brain-stem disorders that disrupt central vestibular pathways may cause torsional nystagmus. Examples are syringobulbia (an abnormal cavity in the brain stem), demyelination (multiple sclerosis), infarction (stroke) and posterior fossa tumors (Noseworthy et al. 1988; Weissman et al. 1991; Lopez et al. 1992). Although both peripheral vestibular and congenital nystagmus may have torsional components, nystagmus that is purely torsional implies disease of the central nervous system. In some patients with brain-stem lesions, precise measurement of the oscillations shows that vertical movements may be associated with the torsional oscillations (Weissman et al. 1991). Torsional nystagmus shows many of the features shown by downbeat and upbeat nystagmus, including modulation by head rotations, variable slow-phase waveforms and suppression

by convergence (Noseworthy et al. 1988).

I have also been exposed to abnormal torsional eye movements which are hardly evident clinically and cannot be detected without methodology such as the magnetic scleral search coil technique. For example, using this technique, the horizontal, vertical, and torsional rotations of both eyes of two patients with idiopathic superior oblique myokymia (SOM), and of the affected eye in a third patient were measured (Leigh et al. 1991). Patients with this disorder often complain of monocular "shimmering" or "jumping" in their vision. The eye movements that cause these visual disturbances are usually too small for the clinician to see with the naked eye, thus the complaints are sometimes dismissed as fanciful. Measurement during SOM episodes revealed that SOM was strictly monocular, and consisted of an initial intorsion and depression of the affected eye, and subsequent oscillations with torsional and vertical components. The peak-to-peak torsional and vertical amplitudes of the oscillations were less than 1° , but peak velocities frequently exceeded $4^\circ/\text{sec}$ in both planes. Fourier analysis indicated that a broad range of frequencies up to about 50 Hz was present during SOM episodes, indicating irregular oscillations. In addition, a superimposed larger amplitude oscillation in the range 1.5-6 Hz was also present. In conjunction with electromyographic data from other studies, these results indicate that SOM reflects spontaneous discharge of trochlear motor neurons that have undergone regenerative changes.

As another example, for the first time, a specific disorder of torsional eye

movements in a patient with a unilateral midbrain lesion has been demonstrated (Leigh et al. 1992). His right-sided lesion was associated with an ipsidirectional loss of torsional quick phases. This finding is consistent with the results of experimental lesions of the rostral interstitial nucleus of the medial longitudinal fasciculus (riMLF) in monkeys (Vilis et al. 1989), and supports the hypothesis that each riMLF generates torsional quick phases that rotate the upper pole of each eye ipsilaterally. Measurement of torsional eye movements in patients such as this individual contribute to the understanding of the anatomical substrate in the brain stem that controls torsional eye movements.

Finally, it has been possible to start to compare the effects of disease affecting the brain stem and cerebellum on the dynamic properties of torsional eye movements with those in the vertical and horizontal planes. Thus, in a recent study (Grant et al. 1992), the ability of eight normal subjects and fifteen patients with brain stem or cerebellar disease to smoothly follow a moving visual stimulus with either the eyes alone or with combined eye-head tracking (CEHT) was compared. The visual stimulus was either a laser spot (horizontal and vertical planes) or large rotating disc of the torsional motion stimulator (torsional plane,), that moved at one sinusoidal frequency for each subject. The visually-enhanced vestibulo-ocular reflex (VOR) was also measured in each plane. In the horizontal and vertical planes, it was found that if tracking gain (gaze velocity / target velocity) for smooth pursuit was close to 1.0, the gain of CEHT was similar. If tracking gain during smooth pursuit was less than about 0.7, CEHT

was usually superior. Most patients, irrespective of diagnosis, showed CEHT that was superior to smooth pursuit; only two patients showed the converse. In the torsional plane, in which optokinetic responses were weak, CEHT was much superior, and this was the case in both subjects and patients. A linear model, in which an internal ocular tracking signal canceled the VOR, was able to account for the findings in most normal subjects in the horizontal and vertical planes, but not in the torsional plane. The model failed to account for tracking behavior in most patients in any plane, and suggested that the brain may use mechanisms other than visual tracking responses to reduce the internal gain of the VOR during CEHT. These results confirm that certain patients who show impairment of smooth-pursuit eye movements preserve their ability to smoothly track a moving target with CEHT.

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CHAPTER 6

SUMMARY

In Chapters 2 and 3, I presented experiments involving the effects of visual inputs on torsional eye movements. The experiment of Chapter 2 demonstrates that eye movement systems are not responsible for the perceptual illusion known as motion aftereffect (MAE). This conclusion is made more sound because the experiment was performed in the torsional plane, where velocity storage is weak or absent (Seidman and Leigh, 1989). If velocity storage were strong during this experiment, then one might argue that the illusory motion of the target could be due to the lingering effects of the velocity storage integrator. This argument does not hold for torsional eye movements. Therefore, we can conclude that ocular motor systems are not responsible for MAE.

In addition, we noted a reversal of eye movement following the cessation of actual target motion. There is no current explanation for this reversal inherent

in models of the ocular motor system. Optokinetic systems cannot cause the observed reversal, and the target is stationary during this phenomena, so eye movements induced by retinal slip should not cause this reversal. Perhaps the reversal of eye movement is driven by higher perceptual mechanisms in the brain; the illusion of motion reversal causes the observed eye movement. Because of strong fixation mechanisms in the horizontal and vertical planes, this effect is masked.

In Chapter 3, I show that the gain of the torsional VOR can be reduced, but not enhanced, by employing visual feedback in the torsional plane. Since visual following responses are weak or absent in this plane, this gain reduction must be due to a parametric reduction in the efficacy of torsional VOR pathways, as opposed to linear superposition with visual following mechanisms. The neural mechanism by which this occurs is simply unknown, and further investigation seems indicated.

Because of the absence of visual-following mechanisms, the torsional ocular motor system is well-suited for investigation of this sort. Although this parametric gain reduction occurs during horizontal CEHT (Huebner et al., 1992), it occurs to a lesser extent, and is masked by visual following responses. While patients with deficient visual following may have good CEHT (Grant et al., 1992), indicating a parametric gain reduction, this is a pathological case, and may not easily lend itself to neurophysiological study.

Future work remains to determine the mechanisms of this torsional

suppression. Firstly, my results must be duplicated in an animal preparation in which neural recordings are possible. If a similar suppression of the torsional VOR occurs, then neurophysiological studies must be carried out to determine the location of VOR suppression. Such recordings should begin at the hair cells and continue on to the vestibular and ocular motor nuclei. Once the site of suppression is found, perhaps the mechanisms will become clear.

In Chapter 4, I show that, unlike the horizontal and vertical ocular motor systems, the ocular motor plant exhibits asymmetrical properties in the torsional plane. However, the brain seems to account for these asymmetries, producing conjugate eye movements in the torsional plane. This suggests independent control of each individual eye muscle by the ocular motor system. In addition, the efficacy of neural integration in the torsional plane is less than that in the horizontal plane. I incorporated both of these findings into a model of the horizontal VOR to better suit torsional eye movements.

Future work in animal preparations is necessary to better characterize some of the internal parameters of this model. If an asymmetry which requires neural compensation to produce conjugate eye movements exists in the torsional behavior of the ocular motor plant of the monkey, neural recordings should tell us if neural control is, in fact, different for each eye muscle.

Although we noted feeble neural integration in the torsional plane, it remains possible that the neural integrator may be improved through training, possibly explaining the results of Balliet and Nakayama (1978), in which humans

were trained to make and hold voluntary saccades in the torsional plane. If future work in which the experiments of Chapter 4 were run on subjects trained in this fashion and improvement in the efficacy of neural integration for vestibular eye movements in the torsional plane was found, then the torsional ocular motor system would afford researchers an opportunity to study motor learning of a type previously unavailable. Motor learning of a more classical type, learned VOR gain changes, might also be studied in the torsional plane. Although in this plane it is difficult to change visual feedback with lenses and prisms, as is done for research of this type in the horizontal plane, the torsional motion stimulator presented in Chapter 3 seems well-suited for this purpose.

In conclusion, I have demonstrated that the torsional ocular motor system affords advantages to researchers that are not present in horizontal systems. I have described the effects of various types of visual input on torsional eye movements, showing effects which are difficult to see in horizontal systems. In addition, I have shown that the ocular motor plant and neural integrator differ in torsional and horizontal behavior. The neural substrate for torsional eye movements is different and simpler than that for horizontal and vertical systems. These simpler properties likely reflect the less exacting visual demands placed on the torsional system. I also presented researchers with various tools with which to study torsional eye movements: the torsional motion stimulator presented in Chapter 3, and the improved model of the torsional VOR presented in Chapter 4.

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APPENDIX I

EQUATIONS FOR CHAPTER 3

Given a linear, time-invariant system with transfer function $H(f)$, input transfer function $X(f)$ and output transfer function $Y(f)$, we can estimate the input and output transfer functions in the presence of noise using the Welch Periodogram technique as described in Chapter 3. Once these estimates are obtained, we can calculate the auto- and cross- power spectral densities as follows (Bendat and Piersol 1980):

$$\begin{aligned}G_{xx}(f) &= X(f) X^*(f) \\G_{yy}(f) &= Y(f) Y^*(f) \\G_{xy}(f) &= X^*(f) Y(f)\end{aligned}\tag{I-1}$$

From the relationship

$$H(f) = \frac{Y(f)}{X(f)}\tag{I-2}$$

and by multiplying the numerator and denominator by $X^*(f)$, we see that

$$H(f) = \frac{G_{xy}}{G_{xx}}, \quad (\text{I-3})$$

which is, in fact, the optimal frequency response estimate for $H(f)$ (Bendat and Piersol 1986).

Given the coherence function defined as follows:

$$\gamma_{xy}^2(f) = \frac{|G_{xy}(f)|^2}{G_{xx}(f) G_{yy}(f)} \quad (\text{I-4})$$

the absolute error on the estimate of $H(f)$ is

$$\varepsilon (|H(f)|) = \frac{[1 - \gamma_{xy}^2(f)]^{1/2}}{| \gamma_{xy}(f) | \sqrt{2n_d}} \quad (\text{I-5})$$

where n_d is the number of overlapping segments used to estimate the periodograms (Bendat and Piersol 1986). Therefore, with a coherence of 0.9 and 20 segments, the relative error is less than 0.08.

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APPENDIX II

EQUATIONS FOR CHAPTER 4

Experiment 1

The following equations describe the output and sensitivities of the model of Figure 4-2.

$$e_{duction} = Ae^{-\frac{t}{T_{d1}}} + Be^{-\frac{t}{T_{d2}}} \quad (\text{II-1})$$

*where $e_{duction}$ = calculated eye position
during return from mechanical displacement*

$$\text{Maximum Deflection, } e_{\max} = A + B \quad (\text{II-2})$$

$$e_{duction} = Ae^{-\frac{t}{T_{d1}}} + (e_{\max} - A)e^{-\frac{t}{T_{d2}}} \quad (\text{II-3})$$

$$e_{duction} = Ae^{-\frac{t}{T_{d1}}} + e_{\max}e^{-\frac{t}{T_{d2}}} - Ae^{-\frac{t}{T_{d2}}} \quad (\text{II-4})$$

For our parameter estimations, it is necessary to calculate the partial derivative of the output variable with respect to each parameter to be estimated. This is done as follows:

$$\frac{\partial e_{duction}}{\partial A} = e^{-\frac{t}{T_{e1}}} - e^{-\frac{t}{T_{e2}}} \quad (\text{II-5})$$

$$\frac{\partial e_{duction}}{\partial T_{e1}} = \frac{At}{T_{e1}^2} e^{-\frac{t}{T_{e1}}} \quad (\text{II-6})$$

$$\frac{\partial e_{duction}}{\partial T_{e2}} = \frac{(e_{\max} - A)t}{T_{e2}^2} e^{-\frac{t}{T_{e2}}} \quad (\text{II-7})$$

$$\begin{aligned} \text{Residual } R &= e_{data} - e_{duction} \\ \text{where } e_{data} &= \text{measured eye position} \end{aligned} \quad (\text{II-8})$$

$$\begin{aligned} \frac{\partial R}{\partial \Theta_i} &= -\frac{\partial e_{duction}}{\partial \Theta_i} \\ \text{where } \Theta_i &= A, T_{e1}, \text{ or } T_{e2} \end{aligned} \quad (\text{II-9})$$

EXPERIMENT 2

To simplify the equations describing the system's output and sensitivity functions, as well as computer implementation, the plant was moved to the front

of the model, immediately following the VOR latency and the semicircular canals. This is mathematically equivalent to the model of Figure 4-1. Note that following this manipulation of our model, total eye movement is the sum of its three component pathways: the direct pathway, e_{direct} , the integrated pathway, e_{integ} , and the slide pathway, e_{slide} .

The head signal was pre-conditioned to reflect the effects of the canals and the VOR latency, as described by the following transfer function (note that capitalized state variables are Laplace transforms):

$$\frac{\dot{H}'(s)}{\dot{H}(s)} = e^{-s\tau} \frac{sT_c}{sT_c + 1}$$

where (II-10)
 τ = VOR latency, and
 T_c = canal time constant
 $\dot{H}$ = measured head velocity

Thus, in the Laplace domain, the equation for the direct pathway is

$$\frac{E_{\text{direct}}(s)}{\dot{H}'(s)} = \frac{g(sT_z + 1)}{(sT_{e1} + 1)(sT_{e2} + 1)} \quad (\text{II-11})$$

The differential equation describing this system (assuming zero initial conditions) is

$$\frac{d^2 e_{\text{direct}}}{dt^2} = \frac{gT_z}{T_{e1}T_{e2}} \frac{dh'}{dt} + \frac{gh'}{T_{e1}T_{e2}} - \frac{de_{\text{direct}}}{dt} \left(\frac{T_{e1} + T_{e2}}{T_{e1}T_{e2}} \right) - \frac{e_{\text{direct}}}{T_{e1}T_{e2}} \quad (\text{II-12})$$

This equation is of second order. We may reduce this problem for simulation purposes by substituting equation II-13, below, into equation II-12, to yield equation II-14.

$$w = \frac{de_{direct}}{dt}, \quad \text{and} \quad (\text{II-13})$$

$$\frac{dw}{dt} = \frac{gT_z}{T_{e1}T_{e2}} \frac{dh'}{dt} + \frac{gh'}{T_{e1}T_{e2}} - w \left(\frac{T_{e1} + T_{e2}}{T_{e1}T_{e2}} \right) - \frac{e_{direct}}{T_{e1}T_{e2}} \quad (\text{II-14})$$

Equations II-13 and II-14 are a pair of linked, first-order differential equations which are solvable for e_{direct} in ACSL by integrating both sides of both equations. Note that if the plant were not moved to the front of the model, this substitution would have had to be done three times, needlessly complicating our equations and requiring unnecessary computation.

Now, we calculate the sensitivity of e_{direct} with respect to g and T_z , as follows:

$$\frac{\partial w}{\partial g} = \frac{\partial e_{direct}}{\partial t \partial g} \quad (\text{II-15})$$

$$\frac{\partial w}{\partial t \partial g} = \frac{T_z}{T_{e1}T_{e2}} \frac{h'}{dt} + \frac{gh'}{T_{e1}T_{e2}} - \left(\frac{T_{e1} + T_{e2}}{T_{e1}T_{e2}} \right) \frac{\partial w}{\partial g} - \frac{1}{T_{e1}T_{e2}} \frac{\partial e_{direct}}{\partial g} \quad (\text{II-16})$$

$$\frac{\partial w}{\partial T_z} = \frac{\partial e_{direct}}{\partial t \partial T_z} \quad (\text{II-17})$$

$$\frac{\partial w}{\partial t \partial T_z} = \frac{g}{T_{e1} T_{e2}} \frac{dh'}{dt} - \left(\frac{T_{e1} + T_{e2}}{T_{e1} T_{e2}} \right) \frac{\partial w}{\partial T_z} - \frac{1}{T_{e1} T_{e2}} \frac{\partial e_{direct}}{\partial T_z} \quad (\text{II-18})$$

Note that T_{e1} and T_{e2} are fixed, and the sensitivities to these parameters need not be calculated. In addition,

$$\frac{\partial e_{direct}}{\partial g_s} = \frac{\partial e_{direct}}{\partial g_I} = \frac{\partial e_{direct}}{\partial T_I} = 0 \quad (\text{II-19})$$

Since the plant has been moved to the front of the model, e_{direct} is now the input to the slide and the integrated pathways, and the following equations result.

$$\frac{E_{integ.}(s)}{E_{direct}(s)} = \frac{g_I T_I}{s T_I + 1} \quad (\text{II-20})$$

$$\frac{de_{integ.}}{dt} = g_I e_{direct} - \frac{e_{integ.}}{T_I} \quad (\text{II-21})$$

$$\frac{\partial e_{integ.}}{\partial t \partial g} = g_I \frac{\partial e_{direct}}{\partial g} - \frac{1}{T_I} \frac{\partial e_{integ.}}{\partial g} \quad (\text{II-22})$$

$$\frac{\partial e_{integ.}}{\partial t \partial T_z} = g_I \frac{\partial e_{direct}}{\partial T_z} - \frac{1}{T_I} \frac{\partial e_{integ.}}{\partial T_z} \quad (\text{II-23})$$

$$\frac{\partial e_{integ.}}{\partial t \partial g_I} = e_{direct} - \frac{1}{T_I} \frac{\partial e_{integ.}}{\partial g_I} \quad (\text{II-24})$$

$$\frac{\partial e_{integ.}}{\partial t \partial T_I} = \frac{e_{integ.}}{T_I^2} - \frac{1}{T_I} \frac{\partial e_{integ.}}{\partial T_I} \quad (\text{II-25})$$

$$\frac{\partial e_{integ.}}{\partial g_s} = 0 \quad (\text{II-26})$$

Similarly,

$$\frac{E_{slide}(s)}{E_{direct}(s)} = \frac{g_s}{sT_s + 1} \quad (\text{II-27})$$

$$\frac{de_{slide}}{dt} = \frac{g_s e_{direct}}{T_s} - \frac{e_{slide}}{T_s} \quad (\text{II-28})$$

$$\frac{\partial e_{slide}}{\partial t \partial g} = \frac{g_s}{T_s} \frac{\partial e_{direct}}{\partial g} - \frac{1}{T_s} \frac{\partial e_{slide}}{\partial g} \quad (\text{II-29})$$

$$\frac{\partial e_{slide}}{\partial t \partial T_z} = \frac{g_s}{T_s} \frac{\partial e_{direct}}{\partial T_z} - \frac{1}{T_s} \frac{\partial e_{slide}}{\partial T_z} \quad (\text{II-30})$$

$$\frac{\partial e_{slide}}{\partial t \partial g_s} = \frac{e_{direct}}{T_s} - \frac{1}{T_s} \frac{\partial e_{slide}}{\partial g_s} \quad (\text{II-31})$$

$$\frac{\partial e_{slide}}{\partial g_I} - \frac{\partial e_{slide}}{\partial T_I} = 0 \quad (\text{II-32})$$

Now we can determine total eye movement,

$$e = e_{direct} + e_{integ.} + e_{slide} \quad (\text{II-33})$$

and

$$\frac{\partial e}{\partial \Theta} = \frac{\partial e_{direct}}{\partial \Theta} + \frac{\partial e_{integ.}}{\partial \Theta} + \frac{\partial e_{slide}}{\partial \Theta} \quad (\text{II-34})$$

where $\Theta = g, T_z, g_p, T_p$ or g_s

Finally, since we are interested in the sensitivities of the residuals,

$$R = e_{data} - e \quad (\text{II-35})$$

and

$$\frac{\partial R}{\partial \Theta} = - \frac{\partial e}{\partial \Theta} \quad (\text{II-36})$$

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APPENDIX I

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