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TORSIONAL VESTIBULO-OCULAR REFLEX MEASUREMENTS FOR IDENTIFYING OTOLITH ASYMMETRIES POSSIBLY RELATED TO SPACE MOTION SICKNESS SUSCEPTIBILITY.

Robert J. Peterka, Ph.D.

Good Samaritan Hospital & Medical Center
Clinical Vestibular Laboratory
1040 N.W. 22nd Ave., N010
Portland, OR 97210

ABSTRACT

Recent studies by Diamond and Markham[1,2] have identified significant correlations between space motion sickness susceptibility and measures of disconjugate torsional eye movements recorded during parabolic flights. These results support an earlier proposal by von Baumgarten and Thümler[3] which hypothesized that an asymmetry of otolith function between the two ears is the cause of space motion sickness. It may be possible to devise experiments that can be performed in the 1 g environment on earth that could identify and quantify the presence of asymmetric otolith function. This paper summarizes the known physiological and anatomical properties of the otolith organs and the properties of the torsional vestibulo-ocular reflex which are relevant to the design of a stimulus to identify otolith asymmetries. A specific stimulus which takes advantage of these properties is proposed.

INTRODUCTION

Attempts to predict motion sickness susceptibility, and in particular space motion sickness susceptibility, have been generally unsuccessful. Many factors which play a role in motion sickness have been identified. These factors include receptor system physiology, neural coding of sensory information about body orientation in space, oculomotor and postural control reflexes, the perception of motion and orientation, and the interaction between motor behavior and perception. However, the correlations of these factors with motion sickness susceptibility are weaker than desired, and there has been poor transference of predictions of susceptibility from one setting to another.

Recent studies by Diamond and Markham[1,2] have identified a strong correlation between prior history of space motion sickness susceptibility in astronauts and their eye movement asymmetries identified during parabolic flights. Specifically, Diamond and Markham measured torsional eye position (ocular counterrolling) in both eyes at rest in a 1 g environment, and in the 0 g and 1.8 g periods during parabolic flight trajectories. With the 1 g measurements serving as a reference, they identified the existence of small disconjugate torsional eye positions in 0 g and 1.8 g conditions. The greater the difference between the disconjugate eye positions in the 0 g and 1.8 g conditions, the greater the likelihood that the astronaut had experienced motion sickness symptoms while on shuttle flights. Among those who had

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experienced motion sickness, the severity was correlated with the magnitude of the difference between 0 g and 1.8 g disconjugate eye torsion.

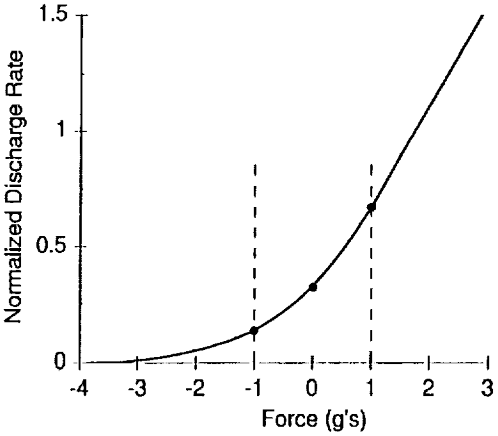
An asymmetry of otolith function between the two ears may be the cause of the torsional asymmetry. However, Diamond and Markham were not able to identify an ocular torsion asymmetry in any subject during roll tilts made in a 1 g environment, including subjects who had identifiable asymmetries in the 0 g and 1.8 g conditions. A reasonable explanation for this is that in the terrestrial environment, otolith function asymmetries are well compensated by central nervous system mechanisms which effectively mask the existence of the asymmetry.

Diamond and Markham's results support a theory put forward by von Baumgarten and Thümler[3]. This theory postulates that an asymmetry of otolith function between the two ears exists in some subjects and causes the neural activity arising from the otolith organs in one ear to be unequal to activity of the other ear. In order to compensate for this imbalance and provide for normal vestibular function under terrestrial conditions, the central nervous system generates a central neural tone that corrects for the asymmetry. When the subject enters a 0 g environment, the unweighting of the otolith organs in the two ears produces a shift in the peripheral neural tone to new levels. The continued presence of the central compensatory tone in the 0 g environment results in an effective imbalance of otolith function, possibly leading to the development of motion sickness symptoms. The theory of von Baumgarten and Thümler is additionally supported by the results of Lackner et al.[4]. Lackner's results actually did show a correlation between asymmetric ocular torsion measured in 1 g and motion sickness susceptibility on parabolic flights. The correlation, however, was not large enough to allow accurate prediction of motion sickness susceptibility.

More sensitive tests for asymmetrical otolith function have been proposed by Wetzig et al.[5]. Wetzig measured tilt perception and ocular torsion during constant velocity vertical-axis rotations in which the subject's orientation with respect to the rotation axis varied so as to deliver asymmetric centrifugal accelerations to the two ears. Experiments on a limited number of subjects revealed results consistent with the existence of asymmetric otolith responses. In addition, disconjugate torsional eye movements were observed indicating that the otolith organ in a given ear exerts a stronger influence on ipsilateral as compared to contralateral eye movements. This observation tends to support the recent results of Diamond and Markham, and indicates that binocular measurements of ocular torsion could improve the sensitivity of tests of asymmetric otolith function. Although Wetzig's experiments were well conceived, the magnitude of the differential acceleration applied to the two ears was small, about 0.07 g, possibly decreasing the likelihood that otolith asymmetries could be reliably measured.

In this paper we describe an alternative test stimulus that has the potential of more reliably identifying the existence of asymmetric otolith function. The design principles for creating an appropriate stimulus are described. Since our knowledge of the CNS processing of otolith signals is not sufficient to predict the success of any given stimulus, experiments will be necessary to evaluate the efficacy and efficiency of alternative approaches.

Figure 1. A typical otolith afferent stimulus - response function relating the otolith afferent discharge rate to the component of linear acceleration acting along the afferent's most sensitive axis of stimulation (adopted from Fernández and Goldberg[6]).



STIMULUS DESIGN PRINCIPLES

A reasonable set of principles for the design of stimulus and measurement techniques capable of detecting the existence and quantifying the magnitude of asymmetric otolith function are as follows:

1. The stimulus should be based on the known physiology of the otolith receptors.
2. The stimulus should provide a linear acceleration stimulus that is as large as possible and will produce a differential effect on the two otolith organs.
3. The stimulus should be novel in the sense that subjects would not typically be exposed to the stimulus in everyday life. (This would limit the likelihood that CNS compensatory mechanisms have masked the effects of asymmetric otolith function.)
4. For practical purposes, the stimulus and measurement techniques should not be so exotic as to require equipment not currently available.

PHYSIOLOGICAL PROPERTIES

Otolith Nonlinear Force-response Properties

Otolith afferent neural responses show significant nonlinear response properties[6]. Figure 1 shows a typical stimulus-response characteristic curve of an otolith afferent nerve fiber for a linear acceleration acting along the most sensitive axis, the polarization vector, of the afferent. The stimulus-response curves vary from afferent to afferent in their horizontal and vertical shift and scale factors, but the general nonlinear shape is consistent. On average, the 0 g point is located on a very nonlinear portion of the stimulus response curve.

For the utricular otolith organs, which to a first approximation lie in a horizontal plane when the head is in an upright position, the gravity vector exerts an ineffective compressional force on the utricular hair cells, and most afferents will be biased near the 0 g points on their stimulus response curves. When the head is rolled 90° so that one ear is directed downward, otolith afferent fibers whose polarization vectors are oriented toward the downward ear will be biased to the steeper +1 g point on their stimulus-response curves, and

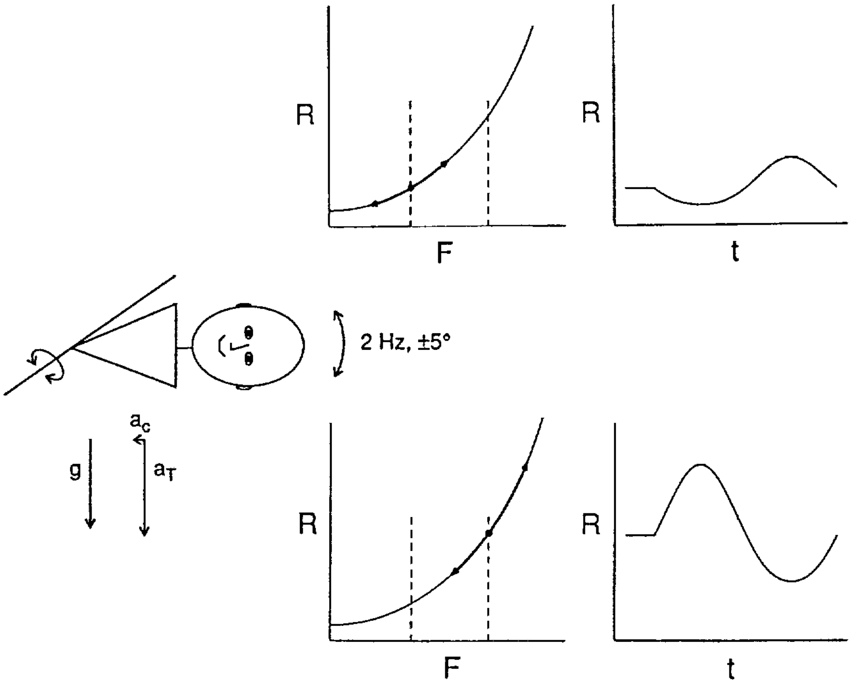


Figure 2. Otolith afferent neural responses (R versus t) predicted during subject-on-side low amplitude, high frequency sinusoidal oscillations about an earth-horizontal axis with the subject's head displaced from the rotation axis. Most utricular otolith afferents in the upper ear will be biased toward the -1 g operating point on the stimulus-response curves (R versus F), and in the lower ear toward the +1 g operating point.

afferents with oppositely directed polarization vectors will be biased to the flatter -1 g point. With the head in this ear-down orientation, any linear acceleration applied along a vertical axis (collinear with gravity) would therefore produce very different responses in the afferents with oppositely oriented polarization vectors. Specifically, afferents biased toward +1 g would have larger resting discharge rates and show larger modulations in neural activity (larger gains) than afferents biased toward -1 g.

Asymmetrical Otolith Morphology

Fernández and Goldberg[7] identified asymmetries in the distribution of polarization vectors within the otolith organs of the squirrel monkey. Specifically for the utricles, about 75% of the afferents had polarization vectors that were generally oriented toward the lateral direction. This asymmetry means that when a subject is oriented with one ear directed downward, most utricular afferents in that downward ear are biased toward their +1 g operating points and most utricular afferents in the opposite ear toward their -1 g operating points. If a linear acceleration collinear with gravity is applied, on average the utricular otolith responses arising from the downward ear should be quite different from those from the upward ear (Figure 2).

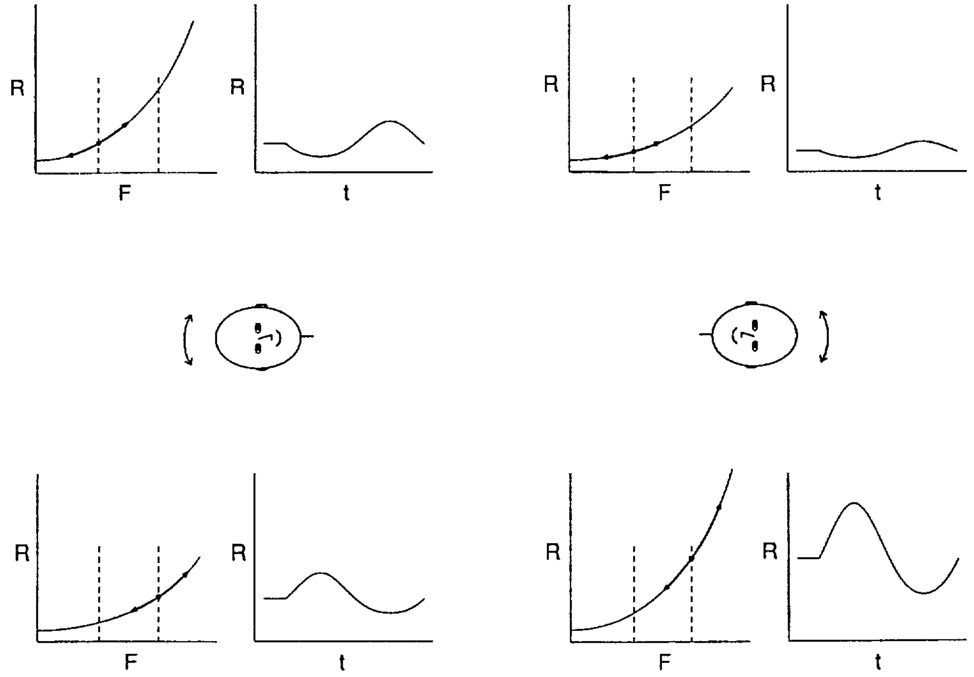


Figure 3. Prediction of utricular otolith afferent responses in a subject with asymmetric otolith function represented by different slopes for the stimulus-response curves (R versus F) in the two ears. The stimulus-response curve for the subject's right ear has a lower slope than the left ear. The identical low amplitude, high frequency, sinusoidal eccentric axis oscillations with the subject oriented with right ear down (left side plots) versus left ear down (right side plots) result in very different patterns of utricular otolith activity (R versus t) in the two head orientations.

Asymmetric otolith function

The theory of asymmetric otolith function postulated by von Baumgarten and Thümler[3] can be expressed in terms of the otolith stimulus-response characteristic curves. A reasonable interpretation is that, on average, the slopes of the stimulus-response curves differ between the two ears, possibly due to differences in the effective otoconial mass. If a subject were tested with a vertical oscillating linear acceleration, first with one ear oriented downward, then with the other ear oriented downward (Figure 3), the otolith responses generated in the two head positions would be quite different. One would expect these differences to be reflected in differences in VOR eye movements.

Torsional VOR

A linear acceleration stimulus can evoke horizontal, vertical, or torsional VOR eye movements depending upon the direction of the acceleration[8]. Early experiments which measured ocular counterrolling in response to static tilts with respect to gravity showed only low

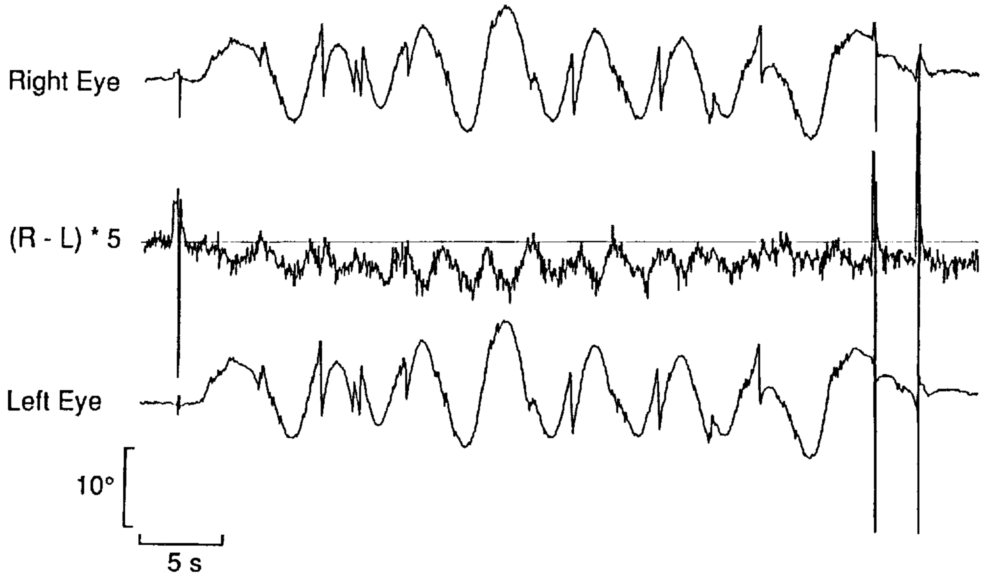


Figure 4. Binocular recordings of torsional eye movements in response to a sinusoidal roll tilt stimulus (0.2 Hz, ±20°) about an earth-horizontal axis with head on axis. Torsional measurements were derived from video recordings. Systematic differences between right and left eye torsion were observed (center trace). Large spikes are eye blink artifacts.

amplitude torsional responses[9]. This led to the conclusion that the torsional component of VOR was unimportant relative to the horizontal and vertical components. However more recent results have shown that the gain of the torsional VOR during roll rotations (vertical canal and otolith stimulation) is comparable to that of the horizontal and vertical components[10,11], particularly at higher stimulus frequencies[12]. Therefore alterations of otolith function associated with 0 g conditions could have a significant influence on torsional VOR dynamics, possibly contributing to increased sensory conflict and leading to motion sickness.

The torsional VOR has some unusual properties that could make it particularly useful as a measure related to otolith function. In comparison to horizontal and vertical VOR, the torsional VOR is less influenced by visual information and is less influenced by conscious attempts to modulate the reflex amplitude by imagining earth-fixed or subject-fixed targets during motions in the dark[13]. The direction of gaze and the vergence angle of the eyes are known to influence the gain of the horizontal and vertical VOR[14], but not the gain of the torsional VOR. Finally, some linear accelerations, such as those along an interaural axis, are known to evoke torsional eye movements that are not compensatory in the sense that they do not serve to stabilize gaze in space[8]. The fact that this non-compensatory VOR exists, suggests that it is an artifact of an unusual force environment, and as such is likely to have escaped the actions of CNS mechanisms that might otherwise mask the effects of asymmetric otolith function. Therefore, the use of a stimulus that evokes torsional VOR eye movements as an indirect indicator of otolith function is likely to be less influenced by uncontrolled experimental variables which confound horizontal and vertical VOR responses.

A CANDIDATE STIMULUS

With minor modifications to available equipment, we propose to deliver a low amplitude, high frequency, roll rotational stimulus (±5°, 2 Hz) to subjects positioned with head about 0.8 m off-axis and oriented in both the right and left ear down positions. This stimulus produces an oscillating tangential acceleration with a peak value of 1.1 g acting essentially collinear with gravity, and with only a small centripetal acceleration with peak amplitude of 0.1 g. Unfortunately a rotational stimulus also stimulates the vertical semicircular canals. The vertical canal responses, however, should be identical in both the right and left ear down positions, so that any difference in VOR responses in the two positions should be attributable to asymmetric otolith function.

One would expect this stimulus to evoke both torsional and horizontal VOR eye movements. The torsional component would be driven by both otolith and vertical canal stimulation and the horizontal component probably would be driven by the interaural tangential linear acceleration. From the work of Paige[15], it is reasonable to expect that the gain of the horizontal component would depend upon vergence angle, and therefore it will be important to record eye movements binocularly in order to account for this variable. In addition, binocular recordings will allow detection of disconjugate torsional eye movements which might be an additional indicator of the presence of asymmetric otolith function.

We have recently begun binocular video recordings of eye movements with off-line computer analysis of horizontal, vertical, and torsional eye position using image processing techniques similar to those described by Clarke et al.[16]. An example of binocular recordings of torsional eye movements evoked by a head-on-axis roll rotation about an earth-horizontal axis is shown in Figure 4. The torsional eye movements produced by this mild stimulus (0.2 Hz, ±20°) showed some small disconjugacy such that at maximum excursions of torsion, which typically occurred at maximum tilt positions, the intorting eye moved farther than the extorting eye. Given the mild nature of this stimulus, it would be surprising if the disconjugate torsion was the result of otolith asymmetry. Rather, orbital mechanics of the eye may be a contributor to disconjugate torsional eye movements, and therefore could be a confounding factor in the search for measurements reflecting otolith asymmetries.

CONCLUSION

We will shortly begin experiments using the stimulus described above, and will additionally measure torsional responses to rotational stimuli designed to replicate the work of Wetzig et al. (1990). If the two experiments give corresponding results, this will provide strong evidence for the existence of asymmetric otolith function in a normal population, and will motivate the application of these results to prospective studies of space sickness susceptibility in astronauts.

ACKNOWLEDGMENT

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