Human Otolithic Function Before and After Unilateral Vestibular Neurectomy

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Abstract — One index of otolith function is the so-called oculogravic "illusion" that during centrifugal stimulation a small luminous bar, fixed with respect to the observer, appears to be roll-tilted by the same amount that the observer feels to be roll-tilted. Many patients undergoing therapeutic unilateral vestibular nerve section show the illusion symmetrically for left and right roll-tilts prior to the operation, but at testing one week after vestibular nerve section show a large asymmetry: they perceive the illusion when the resultant force is directed toward their intact ear, but they perceive a much reduced illusion when the force is directed toward their operated ear. This roll-tilt perceptual response asymmetry appears similar to the asymmetrical horizontal semicircular canal vestibuloocular responses for symmetrical but opposite head accelerations that these same patients exhibit for values of head angular accelerations in the natural range (Ewald's second law), and the present paper suggests that a version of Ewald's second law may apply to the otolithic system: specifically, that there is a response asymmetry for linear accelerations. Anatomical and physiological evidence concerning such an otolithic asymmetry is reviewed.

Keywords — otolith; torsion; oculomotor; vestibular; vestibular compensation; oculogravic illusion; ocular counterrolling; Ewald's second law; labyrinthectomy.

Introduction

In this paper we review some of the effects of unilateral vestibular neurectomy on otolith functioning and integrate these results with recent evidence from studies of central otolith-related neurons after unilateral vestibular neurectomy.

I. The Oculogravic Illusion

Consider a person seated upright 1 meter from the axis of rotation of a human centrifuge which is revolving at a constant angular velocity. The person is subject to a resultant linear acceleration the magnitude of which depends on the centrifuge angular velocity and the orientation of which is determined by the orientation of the person with respect to the radius. If the person is seated with head erect and his interaural axis parallel to the radius of the centrifuge the resultant linear acceleration vector is directed along the interaural axis towards the outermost ear; in this configuration the resultant vector rotates around the person's naso-occipital (X) axis (see Figure 1A & B). The stimulus is a linear acceleration and the conventional assumption, which we will also follow in this paper, is that linear acceleration is transduced by the
otolithic receptors in the inner ear. Since the otoliths function as inertial accelerometers, it is convenient to use the direction of the centrifugal acceleration in representations of the stimulus such as Figure 1, since this direction predicts the direction of bending of the otolithic receptor hair cells. For comparison Figure 1 C & D show the stimulus situation during a simple roll-tilt in a normal 1 g environment. In both cases the subject experiences roll-tilt corresponding to the angle \( \alpha \).

We wish to contrast the oculomotor and perceptual responses to such a stimulus by normal healthy subjects with the responses of patients before and after unilateral vestibular neurectomy.

At rest (0\(^\circ\)/s) a small (9\(^\circ\)) dimly illuminated bar attached to the subject's chair but rotatable in his frontoparallel plane, can be set to be aligned with the subject's perceived gravitational horizontal in the otherwise totally darkened room. Normal subjects set such a bar to the gravitational horizontal with surprising accuracy: the standard deviation of their settings being around only 1\(^\circ\). They are so accurate that settings consistently outside 2\(^\circ\) from the true gravitational horizontal probably indicate pathology.

Note carefully that for normal subjects this accurate setting will cause the image of the bar to fall close to the horizontal meridian of the retina. During constant velocity rotation (at, e.g., 150\(^\circ\)/s; resultant angle of 34\(^\circ\)) the observer is subject to the altered resultant force and has the overwhelming sensation that his head and body has been tilted en bloc (rolled) around his X-axis. If his right ear is outermost, then he feels that he has been tilted such that the right ear is down. If the visible bar is re-presented at this time, then its image will continue to fall close to the horizontal meridian of the retina, since the observer's head has not moved. Since the observer judges that his head and body has been tilted and yet the bar has stayed in exactly the same relationship to his retina, the necessary perceptual consequence is that the visible bar has been tilted in the same direction and by the same amount as the person judges himself to have been tilted. Consequently, when asked to return the bar to the gravitational horizontal, the angle through which the subject rotates the bar is an indicator of the magnitude of the roll-tilt that the person perceives (\( \alpha \) in Figure 1A; see also Figure 2).

This is the so-called "oculogravic illusion" and it was extensively studied by the USAF group at Pensacola, Florida, from 1949 to 1967 (1-3; see (4) for a review). There is no "illusion"; there is only an accurate perception of the direction of the resultant force. Although the stimulus will cause both somato-
sensory and vestibular stimulation, the effect clearly depends mainly on vestibular function since early investigators demonstrated that individuals without vestibular sensory input do not experience roll-tilt sensation to nearly the same extent as normal subjects. We have confirmed this by showing that 2 patients with bilateral vestibular nerve section show only about one-third the magnitude of the results of normal subjects (Figure 3).

Normal healthy subjects show settings very close to the angle of the resultant vector (α in Figure 1) and have symmetrical perceptual responses for symmetrical but oppositely directed linear acceleration stimuli (Figure 3; (5)).

We addressed the simple question: using this oculogravic task, what is the effect of unilateral vestibular neurectomy on roll-tilt perception. Specifically do these patients show symmetrical responses for symmetrical but oppositely directed linear acceleration stimuli? We answered this question by testing patients one day before and at various intervals from one week to one year after unilateral vestibular neurectomy (UVD) for the treatment of Meniere's disease, intractable paroxysmal vertigo, or small acoustic neuromas, and 21 of these patients were tested before as well as after operation. The vector was directed toward either their intact or their operated ear (see Figure 4).

There is a clear result. In every patient tested there is asymmetrical roll-tilt perception after operation. For resultant vectors directed to the normal ear, the response was in the normal range or close to it. However, if the resultant vector was directed to the operated ear, then the same magnitude of roll-tilt was not experienced. In other words, patients underestimate the magnitude of the roll-tilt when the resultant is directed towards their operated ear. At testing one week after operation, this difference is large (averaging 18.8° for a resultant of 26°—in other words, a 72% asymmetry), but over time the asymmetry decreases (that is, compensates see Figure 5). Even at testing 1 y after operation, there remains a small perceptual asymmetry consistent with the side of the vestibular neurectomy (see Figure 5).

There were some attempts in the early 1950s to test a few patients with unilateral vestibular function on the oculogravic test with very variable results (6,7). We consider that the variable results in those studies were due to the following reasons: there was no preoperative measure of roll-tilt perception; the small number of patients (only 6 in comparison to the total of 33 we have studied);
II. S. Curthoys et al was originally demonstrated by the asymmetry of the nystagmus response of the pigeon to equal magnitude but oppositely directed stimuli. Recent oculomotor behavioral evidence (10) has confirmed Ewald's second law in humans, using physiological angular accelerations and measuring horizontal compensatory eye movements.

The anatomical and physiological evidence since the time of Ewald has shown the basis for his second law: uniform semicircular canal receptor morphological polarization in the crista, uniform afferent directional preference, but an asymmetry of physiological response for symmetrical acceleration stimuli by both primary canal afferents and secondary neurons. Recordings from semicircular canal primary afferents show that all afferents are excited by angular accelerations which cause hair cell deflection in one particular direction. Angular accelerations in the opposite direction result in hair cell deflections in the opposite (inhibitory) direction and a reduction in neural response (11,12).

The asymmetrical oculogravic results show that in the otolithic system there is an asymmetry of response to symmetrical linear acceleration stimuli that is analogous to the asymmetry of semicircular canal response to symmetrical angular acceleration stimuli. Can the asymmetrical response to linear acceleration stimuli be explained in terms similar to those used to explain the asymmetry of the canal response? We consider that the present
result suggests that the otoliths are also subject to a version of Ewald's second law, and we explore this idea below in conjunction with Figure 6.

We contend that the asymmetry we have measured reflects the asymmetry in the anatomy and the physiology of primary and secondary otolithic neurons. Firstly, unlike the cristae, the receptor morphological polarization in the utricular and saccular maculae is

Figure 4. Schematic illustration of roll-tilt stimulation of a patient who has had a left vestibular neurectomy. The resultant vector can be directed towards the intact ear (a laterally directed roll-tilt stimulus) or towards the operated ear (a medially directed roll-tilt stimulus). The insets show the resolution of the stimulus vectors in relation to the otolithic receptors.

Figure 5. Summary of results from 33 patients compared to 31 normal subjects at 10°, 17°, and 26° roll-tilt stimulus angles, before, 1, 3, 12, and 24 weeks after unilateral vestibular neurectomy. Shaded areas show 2-tailed 95% confidence intervals for normal subjects. Top row: Absolute values of perceived roll-tilt angle; open symbols show settings for stimuli directed toward the intact ear; filled symbols show settings for stimuli directed towards the operated ear. The large asymmetry present 1 w after operation has decreased by 3 w, but is still abnormal at all stimulus levels even 24 w after operation. Bottom row: Asymmetry in roll-tilt perception fails to decrease much after 3 weeks postneurectomy.
not uniform. Flock and others have shown that in the utricle and saccule, receptor hair cells on one side of the striola are all polarized in one direction, whereas hair cells on the other side of the striola are polarized oppositely (13,14). However, there is not an equal division: in the utricle, for example, there are more receptor cells preferring ipsilaterally directed linear accelerations than contralaterally directed linear accelerations (13). Correspondingly, recordings from otolith primary afferents show that individual neurons have a directional preference or polarization axis along which the afferent neuron can be optimally stimulated (15). More neurons prefer ipsilaterally directed linear accelerations than contralaterally directed linear accelerations (13). For any particular otolith primary afferent, systematically increasing the magnitude of the linear acceleration stimulus in the preferred direction systematically increases the firing rate of the afferent. However, systematically increasing the magnitude of the linear acceleration stimulus in the opposite direction (or nonpreferred) direction drives the neuron to a low, saturated firing rate (1976, for example, their Figure 5B). The result is that the output of many primary otolithic afferents is asymmetrical for symmetrical linear accelerations, just as the output of many semicircular canal afferents is asymmetrical for symmetrical angular accelerations (11) (see Figure 6).

For semicircular canal second-order neurons, the asymmetry of response is even more marked than at the primary level; most second-order canal neurons have a lower resting rate and a higher sensitivity to angular accelerations than their primary counterparts and are consequently even more easily silenced by "off-direction" accelerations than primary neurons. This asymmetry of neural response has been noted by many investigators (for example, references 16,17). It has been referred to as a threshold cut-off, and most algorithms for calculating gain of second-order canal neurons ignore the cut-off and calculate gain just for the "on-direction" or some extraplated value. We contend that this nonlinear property is an important mode of canal operation. It seems that a number of central otolithic neurons exhibit a similar nonlinearity of response, a nonlinear operation similar to that of the otoliths themselves. Figure 6. To show in schematic summary the anatomical, physiological, and behavioral evidence for Ewald's second law in the semicircular canal system (top row) and to suggest the parallel anatomical, physiological and behavioral evidence for a comparable principle for the otoliths (bottom row). Top row: The anatomical evidence is that the crista has a uniform morphological polarization of the receptor hair cells. The "canal neuron" represents second order neuronal responses where sensitive neurons with low resting rates show a small decrease in firing (that is, are silenced) by accelerations in the "inhibitory" direction but can increase to large values for excitatory accelerations. The ocular motor response summarizes the results of compensatory eye movements in human patients after UVD causing either ampullofugal ("inhibitory") endolymph flow to the left in this schematic) or ampullopetal ("excitatory") endolymph flow to the right in this schematic (9). When physiological levels of stimulation are used, these patients show a marked and permanent asymmetry in ocular motor response. Bottom row: The utricular macula does not have a uniform morphological polarization, but there is a predominance of receptors polarized toward the ipsilateral side. This predominance is reflected in the predominance of primary afferents preferring ipsilateral linear accelerations. The utricular neuron represents a primary otolithic neuronal response (redrawn from reference 15, Figure 5B), to show that even at the level of the otolithic primary afferent there is a marked asymmetry of response to left as opposed to right directed roll-tilt stimuli. Similar patterns of nonlinear otolith response patterns have been demonstrated more centrally (for example, reference 18, Figure 5; reference 19, Figure 2). The perceptual response is a redrawing of the results of Figure 5 with the operated side on the left and the intact side on the right. The perceptual result shows a reduced sensitivity for roll-tilt stimuli directed towards the lesioned side (shown as left) in comparison to the response to the intact side (shown as right).
response (compare, for example, reference 18). In addition, most investigators have reported that a predominance of lateral vestibular nucleus (LVN) neurons is excited by ipsilateral ear down tilts (Duensing and Schaefer's α neurons) in comparison with neurons excited by ipsilateral ear up tilts (Duensing and Schaefer's β neurons; references 18-24). Thus both the anatomical and physiological evidence shows that the otolith system of each labyrinth is asymmetrical in its operation commencing from the peripheral afferent response, and this evidence provides the basis for explaining the Ewaldian asymmetry in roll-tilt perception demonstrated in patients after UVD.

II. Ocular Counterrolling (OCR)

Does unilateral vestibular neurectomy cause a comparable asymmetry of another otolithic-related response—ocular counterrolling (OCR)? The literature on this question is not clear because there have been comparatively few studies and some of the reports have included the results from every patient measured, irrespective of the patient's prior history, diagnosis, or treatment. The definitive answer to this question will come from the results of patients comparable to the patients reported above, where all patients receive the same surgical procedure, in which the entire vestibular nerve has been surgically cut for the removal of small acoustic neuromas which have not affected the brainstem. This known surgical section is in contrast to the older and much more indefinite procedure of labyrinthectomy (see above). The most clear-cut results will come from studies comparable to the ones we have described for the oculogravic illusion; the same patient is tested both shortly before and shortly (one week) after vestibular neurectomy, and OCR responses of all patients had been within the normal range preoperatively. There are very few data which meet these criteria. Those that come closest show that OCR is smaller for tilts toward the operated side than for comparable tilts toward the intact side: unilateral vestibular neurectomy of one healthy rhesus monkey (25); all 6 unilateral vestibular neurectomy patients of Kanzaki and Ouchi (26); and 13 of the 14 neurectomy patients reported by Nelson and House (27) all showed smaller OCR for tilts towards the operated side than for comparable tilts to the intact side. Other evidence is not consistent with this pattern (28, 29), but fails to satisfy the criteria specified above. This important question and the related question of the recovery of OCR response after unilateral vestibular neurectomy (otolithic compensation) require further investigation.

III. Ocular Torsion

Recently we have shown that UVD in human patients causes a maintained torsion of both eyes; the upper poles of both eyes roll towards the lesioned side and the magnitude of this torsion decreases over time (30; Curthoys et al. unpublished observations). While there is likely a contribution of vertical canal afferents to this phenomenon, it is equally likely that otolithic deafferentation has a large role, since electrical stimulation of one otolithic nerve causes both eyes to tort away from the stimulated side (31,32).

IV. Relation of the Effects to Neural Data

The following outlines how imbalance of otolithic activity could result in the responses we have observed. We presume that with the patient's head erect the two lateral vestibular nuclei (LVN) will each receive afferent input from the spontaneously active otolithic afferents and that there will be approximately equal neural activity in each LVN by virtue of the equality of the afferent input and the indirect, predominantly functionally excitatory, commissural interaction between the two LVNs (15,33). In the lateral vestibular nuclei of intact cats, the evidence points to a predominance of roll-tilt sensitive neurons being excited by ipsilateral side down and inhibited by ipsilateral side up (Duensing and Schaefer's α neurons; references 18-24). Thus both the anatomical and physiological evidence shows that the otolith system of each labyrinth is asymmetrical in its operation commencing from the peripheral afferent response, and this evidence provides the basis for explaining the Ewaldian asymmetry in roll-tilt perception demonstrated in patients after UVD.
response type) (18–22). Consequently, as the head is rolled to the left, more cells in the left LVN will be active than in the right LVN. Following a unilateral vestibular neurectomy on the right side, there are fewer of the roll tilt-sensitive cells in the right LVN, and the average resting rate of all cells in the right LVN decreases (24). This uniform decrease in resting activity means that with head erect there will be an imbalance between the two LVNs in terms of the total neural activity, with the result that the average neural activity of the left LVN will be greater than the average activity of the right LVN, corresponding, we suggest, to the imbalance that occurs in a normal animal during roll head tilt toward the left ear. The direction of maintained ocular torsion is consistent with this. In an intact animal if the head is rolled towards the left (resulting in a left LVN superiority), then the eyes counterroll in the head by a few degrees to the right. Here, after right unilateral neurectomy (resulting in a left LVN superiority), the eyes roll in the head toward the right (see Figure 7).

The explanation of the reduction in roll-tilt sensitivity for stimuli directed towards the operated ear is more problematical. Neuronal recordings in cats show that in the LVN on the lesioned side there is a very large drop in the number of responsive neurons and a large drop in the average resting rate of cells that can be recorded. Similar but less dramatic changes occur on the LVN on the intact side. In consequence, a roll-tilt stimulus directed towards the lesioned side may elicit a smaller total output from the LVN on the operated side after neurectomy in comparison with the same stimulus directed towards the intact side. This reduced neural output in comparison with the intact side may contribute to the asymmetry we have observed.

**SCHEMATIC REPRESENTATIONS OF LATERAL VESTIBULAR NUCLEI ACTIVITY**

1. **DURING ROLL-TILT STIMULATION**

   ![Schematic 1](image1)

   **RLVN**

   ![Schematic 2](image2)

   **LLVN**

   ![Schematic 3](image3)

   **RLVN**

   ![Schematic 4](image4)

   **LLVN**

   **L = R**

   **L > R**

2. **AFTER UNILATERAL VESTIBULAR NEURECTOMY**

   ![Schematic 5](image5)

   **RLVN**

   ![Schematic 6](image6)

   **LLVN**

   ![Schematic 7](image7)

   **RLVN**

   ![Schematic 8](image8)

   **LLVN**

   **L = R**

   **L > R**

**Figure 7.** To contrast schematically the overall pattern of neural activity in the left LVN and right LVN change during roll-tilt stimulation as opposed to the changes following UVD. Both roll-tilt stimulation to the left and unilateral right neurectomy result in a predominance of left LVN activity over right LVN activity. The predominant firing rate shown in each inset is as deduced from published results of single neuron recording studies in the LVN primarily in cats (see text).
The Use of Patients and the General
Experimental Paradigm

We have attempted to minimize the difficulties in drawing conclusions about normal function from the results of tests on patients, by testing the same patient preoperatively and postoperatively and comparing these patient data with data from normal subjects. However the preoperative performance of some patients was affected by the pathology for which they were operated; in some patients even at the preoperative measurement the neuroma may have already caused a partial neurectomy and possibly even compensation by virtue of the slow progressive loss of vestibular afferents. Such factors probably contribute to the large variation between patients measured at 1 week post operation. On the other hand, there were a number of patients whose preoperative performance was not detectably different from normal healthy subjects on this test. The pattern of results on the oculogravic illusion for all patients was similar.

Conclusion

Unilateral vestibular neurectomy results in asymmetrical otolith function as measured by the oculogravic test. We suggest that this result reflects an inherent asymmetry of the otolithic system such that the otoliths are subject to a version, albeit a weaker version, of the same law, Ewald's second law, to which the semicircular canals are subject. This asymmetry of ocular motor and perceptual effects appears to be consistent with the anatomical and neural results at both the primary afferent and vestibular nucleus level showing physiological evidence for an asymmetry of otolith functioning. The progressive recovery of the asymmetrical response after operation suggests that some otolithic symptoms recover after vestibular damage, just as some static canal symptoms recover — that there is a process of otolithic compensation as well as one of canal compensation (34).

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REFERENCES

5. Dai MJ, Curthoys IS, Halmagyi GM. Linear acceleration perception in the roll plane before and after unilateral vestibular neurectomy. Exp Brain Res. [In press].


