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HIGHLIGHTED TOPIC | *Neural Control of Movement*

Probing the human vestibular system with galvanic stimulation

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Fitzpatrick, Richard C., and Brian L. Day. Probing the human vestibular system with galvanic stimulation. *J Appl Physiol* 96: 2301–2316, 2004; 10.1152/jappphysiol.00008.2004.—Galvanic vestibular stimulation (GVS) is a simple, safe, and specific way to elicit vestibular reflexes. Yet, despite a long history, it has only recently found popularity as a research tool and is rarely used clinically. The obstacle to advancing and exploiting GVS is that we cannot interpret the evoked responses with certainty because we do not understand how the stimulus acts as an input to the system. This paper examines the electrophysiology and anatomy of the vestibular organs and the effects of GVS on human balance control and develops a model that explains the observed balance responses. These responses are large and highly organized over all body segments and adapt to postural and balance requirements. To achieve this, neurons in the vestibular nuclei receive convergent signals from all vestibular receptors and somatosensory and cortical inputs. GVS sway responses are affected by other sources of information about balance but can appear as the sum of otolithic and semicircular canal responses. Electrophysiological studies showing similar activation of primary afferents from the otolith organs and canals and their convergence in the vestibular nuclei support this. On the basis of the morphology of the cristae and the alignment of the semicircular canals in the skull, rotational vectors calculated for every mode of GVS agree with the observed sway. However, vector summation of signals from all utricular afferents does not explain the observed sway. Thus we propose the hypothesis that the otolithic component of the balance response originates from only the pars medialis of the utricular macula.

balance; standing; reflex; posture

GALVANIC VESTIBULAR STIMULATION (GVS) has been used for over a century as a means to discover and then look at the function of the vestibular system. In his 1820 dissertation, Bohemian physiologist Johann Purkyne (81) reported that a galvanic current flowing through the head upset balance and equilibrium. Eduard Hitzig (46), starting his experiments as an army doctor during the Franco-Prussian war, noted that nystagmus was one consequence of applying an electric current to the brains of dogs and humans, including the exposed brain of one wounded soldier. Thus we have the first evidence that the two motor outputs of the vestibular system can be driven by a galvanic stimulus. It was Josef Breuer (8) who finally demonstrated the vestibular origin of these phenomena by combining galvanic stimulation with labyrinthectomy in animals. The first description of its perceptual output may have come much earlier, in 1790, from Alessandro Volta himself (103). In between putting the electrodes of his newly invented battery in his ears and his subsequent collapse, he briefly experienced the sensations of an explosion

inside his head, spinning, and the sound of boiling tenacious matter. The spinning was likely the manifestation of vestibular stimulation and the boiling either auditory stimulation or the sound of flesh boiling. The explosion needs no further explanation: a pile of 30–40 Zn/Ag elements generates ~30 V! Hitzig and Breuer also came across the perceptual phenomenon, but they were more specific about their experiences. Camis (10) reported that these gentlemen put “the two electrodes to the two mastoid processes, and experienced a sensation of falling towards the side of the cathode.”

As its early history shows, the GVS technique is very simple. The electrodes are now placed on the mastoid processes rather than in the ears. Just a switch and a battery are needed, 6 V is more than enough, although for experimental applications, the stimulus is usually delivered by a controlled current source at levels of ~1 mA. The stimulus is most commonly delivered with an anodal electrode on the mastoid process behind one ear and a cathodal electrode behind the other ear, i.e., bilateral bipolar GVS. However, other configurations are bilateral monopolar GVS with electrodes of the same polarity at both ears and a distant reference electrode and unilateral monopolar GVS with a stimulating electrode at just

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one ear. When the small current flows for 1 or 2 s, it causes a person to sway if they are standing or perceive illusory movements if they are not. The simplicity of the technique, however, belies the complexity of the body response it evokes.

The virtual signal of head movement produced by GVS has a potent effect on whole body motor control, evoking reflex electromyographic responses and a highly organized balance response involving the entire body. However, these responses are not hard wired but are very sensitive to the task at hand, the balance and orientation of the body, and the information coming from all other sensory sources. We therefore believe that a balance system organizes a whole body response to the vestibular signal. It seems that the balance system interprets the GVS-evoked input as a real head movement in space, one that was unplanned and one that came from a movement of the body. Such an input represents a threat to balance to which the balance system must respond.

Apart from its simplicity, GVS is attractive as a tool to probe vestibular function and the balance system because it delivers a pure disturbance at the receptor level, uncomplicated by inputs to other sensory channels. At least in its early stages, it reveals the operation of the balance system to a pure vestibular perturbation. The purpose of this paper is to consider the available data on human balance responses to GVS in light of the physiology and anatomy of the vestibular organs and to draw some conclusions about the nature of the afferent vestibular signal evoked by GVS and how it produces its effects on human balance.

VESTIBULAR ELECTROPHYSIOLOGY

There have been no direct recordings from human vestibular afferents; therefore, we can only reckon their behavior by data obtained from a wide range of species. Of extreme value here is the elegant research and detailed electrophysiological data of Jay Goldberg and colleagues, which include primate afferent responses to GVS.

Kinetic Stimuli

Discharge rates. In all species studied, the vestibular primary afferent neurons, which innervate the cristae and maculae, discharge spontaneously at rest when no stimulus is applied. This means that, with rate coding, a neuron can respond to accelerations in both directions. Spontaneous discharge rates vary across species. Mean rates of 13 s^{-1} have been reported in stingrays (63), $30\text{--}40 \text{ s}^{-1}$ in rats and guinea pigs (14, 16), $45\text{--}55 \text{ s}^{-1}$ in chinchillas (38), $\sim 65\text{--}90 \text{ s}^{-1}$ in squirrel monkeys (28, 40), and $90\text{--}115 \text{ s}^{-1}$ in macaque monkeys (15).

Regularity. Primary afferents can be classified as regular or irregular according to the pattern of their resting discharge (28, 39, 40), although this may be more a convenience of description, as regularity is more a continuum than discrete populations (4, 37). The degree of regularity or automaticity of a neuron is determined by a combination of the size of its afterhyperpolarization relative to the size and rate of its excitatory postsynaptic potentials (EPSPs).

Sensitivity. Afferent firing rates increase or decrease depending on amplitude and direction of an imposed acceleration. For the squirrel monkey, this dynamic range is $0\text{--}300 \text{ s}^{-1}$ at about the $65\text{--}90 \text{ s}^{-1}$ resting discharge rate, with an average gain or sensitivity of $2 \text{ s}^{-1} \text{ per deg} \cdot \text{s}^{-2}$ for the semicircular canals and

$33 \text{ s}^{-1}/\text{g}$ for the otolith organs (27, 40). On average, irregular neurons have slightly lower tonic rates than regular neurons but are more sensitive to acceleration stimuli and have shorter refractory periods than regular neurons. The response of regular units is predominantly tonic; that of irregular units tends to be more phasic. Responses are greater for excitatory than for inhibitory stimuli, particularly for irregular units. As might be expected in a system where a continuous discharge is modulated, there does not appear to be a threshold value in these responses; they are continuous about the resting values. Adaptation in the primary afferents with a sustained acceleration stimulus is mixed. In some units, adaptation is clear, particularly to inhibitory stimuli, whereas many units show no adaptation. Adaptations of behavioral responses, such as the vestibuloocular reflex, are greater than adaptations seen in the afferent or vestibular nuclei, implying that much of the adaptation occurs further down the reflex pathways (14).

Primary afferent projections. As with the other senses, vestibular afferent pathways show a great deal of convergence. Each primary afferent innervates many hair cells (26, 31), and the secondary vestibular neurons of the vestibular nuclei receive input from many primaries. There is some correlation between the physiological properties of the primary afferents and the morphology of the target neurons. Large secondary neurons are innervated by irregular afferents with more terminal boutons almost exclusively, whereas small neurons are innervated by both types of afferents. Firing of secondary neurons is not secure, and summation of many EPSPs is necessary (53). Regular units tend to be smaller and have localized dendritic connections centrally, whereas the irregular units are large and influence a large dendritic area (26, 30, 85). The point to be made here is that the macula is not simply an array of transmitting receptors but is concerned with significant complex and adaptive processing of the raw hair cell signal, analogous to the retinal processing of optical signals [see Ross (83) for review].

Projections of the vestibular nuclei. The secondary vestibular neurons of the vestibular nuclei project to many areas of the central nervous system (CNS), including the oculomotor nuclei, the spinal cord, and the flocculus of the cerebellum (45), as well as a thalamocortical pathway.

Even by the level of the secondary neuron, there is convergence of afferents from the semicircular canals and otolith organs (23, 51) and from otolith afferents from both sides of the striola and both sides of the head (100, 102). Thus spinal-projecting neurons of the lateral vestibular nucleus respond optimally to movement in directions such as pure roll that are not encoded by any single canal (51), and a higher level of spatial tuning increases the direction specificity of secondary otolith neurons to linear acceleration (2). Also at this level, there is a large convergence of afferents from the neck (52, 112) so that a complex descending output of these neurons can come from a mix of signals denoting head on body and head in space. This convergent input from the semicircular canals and otolith organs seen onto spinal-projecting secondary neurons is infrequent for oculomotor-projecting neurons (86, 101, 114, 115).

At the secondary neuron level, there is also temporal filtering of the vestibular signal. The transduction mechanics of the semicircular canals act as a low-pass filter so that the afferent canal signal largely resembles an angular velocity response. The process, known as velocity storage (82), is a further

neuronal filtering or integration, so that, even at very low frequencies, the vestibular secondary neuron's response is related to angular velocity. A similar filtering exists for otolith signals. Whereas primary afferents respond in proportion to linear acceleration, most central otolith neurons respond in proportion to linear velocity (2). This is particularly so at low frequencies (<0.5 Hz), which are most significant for balance control.

Vestibular cortex. In monkeys, small areas of the somatosensory cortex, within area 3a, receive bilateral vestibular projections (75), and small areas of the parietal cortex, area 2v, receive mostly contralateral vestibular projections (36). The ventral-posterior and lateral-posterior nuclei of the posterolateral thalamus are the thalamic areas concerned with this vestibular sensory function and cortical projection (50).

There is also a cortical efferent limb. In cats, stimulating cortical cells in area 2, and less so area 3a, affects the discharge of most ipsilateral vestibular-nucleus neurons with spinal projections that respond to sinusoidal tilts. They were either facilitated, inhibited, or a mixture of the two. Thus these areas should be able to modulate vestibular reflexes acting on the neck and limbs (113).

Galvanic Stimuli

Site of action. Galvanic stimuli are still effective when the labyrinth is excised, but typical responses are not seen after section of the eighth cranial nerves (80, 92). The modulation by GVS of primary afferents occurs no further central than Scarpa's ganglion because the effects can be recorded in these neurons (14). Goldberg et al. (41) showed that cathodal GVS applied in the perilymphatic space and anodal GVS applied to the afferent nerve fiber at a more proximal point both caused excitatory responses. This is consistent with the spike trigger zone of the primary afferent being the point of GVS action as both stimuli will cause an outward depolarizing current at this trigger site. Thus GVS can be considered to modulate the hyperpolarization of the neuroepithelia of the cristae and maculae. These findings imply that GVS bypasses the transduction mechanism of the hair cells. It should be possible to distinguish peripheral vestibular lesions from more central lesions by comparing vestibular responses to galvanic and kinetic stimuli.

Irregular afferents affected. About three-quarters of primary afferents are regular firing (4, 37), and anatomically they make strong connections to both vestibulospinal and vestibuloocular output pathways of the vestibular nuclei (45). However, it is the irregular primary afferents that respond to GVS, whereas regular units are only slightly modulated even by large stimulus currents (25, 37, 41). Spinal-projecting secondary neurons are innervated more by irregular afferents, whereas oculomotor-projecting neurons receive more from regular afferents (45), although these variations are <20% each side of an even split. Cerebellar-projecting units are intermediate. Because the irregular units carry the GVS signal, we would expect the GVS signal to be relayed to all CNS areas that receive vestibular projections. Furthermore, as sensitivity of afferent units to GVS and kinetic stimuli parallel one another by virtue of the underlying electrophysical properties of the units (37, 41), the CNS distribution should reflect that of naturally occurring vestibular afferent signals. This probably applies equally to afferents regardless of their canal or otolith origin. Anodal and

cathodal GVS affect the discharge of semicircular canal afferents in the same way as ipsilateral and contralateral angular accelerations, and GVS responses are the same for afferents from the otolith organs and the semicircular canals (63).

Phasic and tonic responses. For the entire population, the GVS-evoked afferent discharge rate is not constant over time with a maintained stimulus current; however, on an individual basis, the discharge pattern varies. Several records show adaptation of firing rate during maintained GVS after a step change of the stimulus current (41, 58, 63). Adaptation, or a phasic response that subsided to baseline over 1–2 s, was seen in 7% of the primary units and 23% of the secondary units that Courjon et al. (14) recorded from in the rat. Most other units had a tonic pattern of discharge for the duration of the stimulus. In agreement with this phasic response, when sinusoidal GVS is applied, there is some phase advance in the modulated afferent signal by 14 deg at the primary level and a further 25 deg at the secondary unit along with a modest increase in gain across the physiological frequency range (25).

Central effects. With the body immobilized during functional magnetic resonance imaging, GVS at intensities that produce illusions of movement activates the cerebral cortex near the temporoparietal junction, the central sulcus, and the intraparietal sulcus (60, 61). These areas, PIVC and areas 3aV and 2v, correspond to the "vestibular cortex" in monkeys.

Galvanic vs. kinetic stimuli. Can we equate galvanic and kinetic stimuli? In the squirrel monkey, afferent responses to GVS applied in the perilymphatic space range from 0 to nearly 300 s^{-1} in an almost linear manner for currents between $70\text{ }\mu\text{A}$ cathodal and $70\text{ }\mu\text{A}$ anodal (41). This should represent the dynamic range of the system. Angular accelerations of the order of $\pm 150\text{ deg/s}^2$ are required to obtain responses across the same dynamic range (40). We can assume therefore that these values represent the equivalent dynamic ranges for afferent discharge and angular acceleration. What we don't know is the relationship between current density at the organ produced by percutaneous GVS and the much smaller perilymphatic stimulus currents.

Consider three responses to percutaneous transmastoid GVS in human subjects: one ocular, one postural, and one perceptual. GVS at 2 mA produces ocular torsion with a tonic response of 4–12 deg/s and a phasic response of 0.67–2 deg/s² (87). In a subject without sensation mediated by large fibers from the neck down, GVS between 0.5 and 1.5 mA produced a continuous compensatory roll of the trunk and head at ~ 1 –2 deg/s (18). Percutaneous GVS of ~ 1 mA produced perceptions of body rotation that subjects matched to actual accelerations of 2–3 deg/s² (34). Assuming that discharge rates are equivalent for humans and monkeys, each observation indicates that the commonly used 1-mA current would produce an afferent response equivalent to perhaps no more than 2% of the dynamic range. Although as experimenters we often wish for a bit more gain from our stimuli, it is probably fortunate that there is sufficient insulation here to prevent us accessing to the full dynamic range of this system.

Let us choose an approximate scaling of afferent response to stimulus, say 1 mA gives a 4 s^{-1} response, and apply it to each vestibular signal. From the data of Ref. 40, the average gain, or sensitivity, of vestibular responses to kinetic stimuli is 2 s^{-1} per $\text{deg}\cdot\text{s}^{-2}$ for semicircular canal afferents and $33.3\text{ s}^{-1}/\text{g}$ for otolith afferents. Thus, with 1 mA GVS, a single afferent fiber

would signal angular acceleration of 2 deg/s² if it innervated the semicircular canals and either linear acceleration of 1.18 m/s² (0.12 g) or 28.4 deg tilt if it innervated the utricular macula. However, these are not the net population signals because each fiber signals movement in a different direction. A vector sum based on the morphology of the receptor organs is necessary to calculate a resultant. That summation is considered in the next section.

In many ways, the physiological and morphological properties and connectivity within the afferent vestibular system appear to form a continuum. However, it is one with much diversity. Thus the different associations of physiological properties, morphologies, and connections might provide for different aspects of vestibular sensation and vestibular control, a hypothesis presented in detail by Goldberg (37).

VESTIBULAR ANATOMY

Unlike natural stimuli, GVS has no direction. The entire population of susceptible afferents are affected regardless of the alignment of the hair cells that they innervate. The direction sensitivity of the semicircular canals is obtained by resolving head movement into three vectors. All hair cell receptors in the crista of each canal are aligned along the circumferential axis of the canal and have the same directional sensitivity. The anatomic orientation of the canals therefore determines the direction of these three vectors. Within the otolith organs, the hair cells are aligned in a multitude of directions across the macular surfaces. Spatial encoding of the entire population response provides directional sensitivity. Thus, to look at the effects of GVS on the semicircular canal system, we can consider the net effect on only three canal vectors. For the otolith organs, we have to consider a vast array of vectors from the otolith hair cells because the net GVS response will come from the histological pattern of cell orientation within the neuroepithelial surface.

Semicircular Canals

The semicircular canals sense angular acceleration and velocity of the head. Three canals on each side of the head are approximately orthogonal (11). The horizontal canals respond maximally to yaw. The anterior and posterior canals are oriented vertically at ~45 deg to the sagittal axis, so that both canals respond to pitch and roll movements. The mirror symmetry of the canals across the head means that, for natural stimuli, the two horizontal canals provide similar, although inverse signals. Thus yaw rotation of the head to the left increases the firing of afferents from the left horizontal canal but decreases the firing rate from the right horizontal canal. This push-pull arrangement about the tonic discharge rate will improve the amplitude and directional sensitivity of the canal system. The other canals operate similarly as the anterior canal is aligned with the contralateral posterior canal.

The hair cell neuroepithelium, or crista, is within an ampulla at the end of each canal with the cilia embedded in a gelatinous cupula that occludes the ampulla. The hair cells are oriented according to the plane of the canal. Figure 1 shows the orientation of the hair cells relative to the three canals (labeled a, p, and h) and the utricle (labeled u). A single hair represents the orientation of all cells in the crista, with the kinocilium drawn as the thick line at one end of the array of stereocilia. As

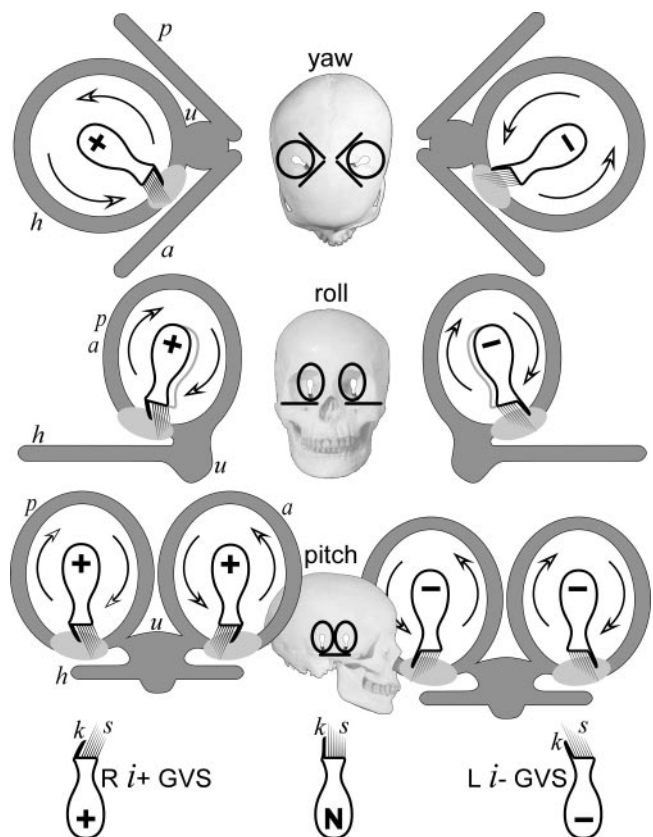


Fig. 1. Model of semicircular canal responses to galvanic vestibular stimulation (GVS). Plan, front, and side views of model orthogonal labyrinths show the directions of the yaw, roll, and pitch signals evoked by GVS. The hair cells of the cristae, represented by a single hair cell, have specific orientations with respect to the canal and the utricle (u), and this determines the directions of the virtual rotation that they signal when excited or inhibited by GVS. *Left:* right labyrinth stimulated with anodal current (i+). The central nervous system will interpret the reduced afferent firing produced by anodal GVS as rotation in the direction (arrows) that would normally deflect the stereocilia (s) away from the kinocilia (k). Thus the horizontal canal (h) signals yaw toward the contralateral ear. The anterior (a) and posterior (p) canals, superimposed in the front view, both signal roll to the contralateral side, but the anterior canal also signals backward pitch and the posterior canal forward pitch. *Right:* cathodal GVS (i-) to the mirror-reversed canals on the other side would produce yaw and roll signals in the same direction but pitch in the opposite direction.

the crista moves with the head, the cupula and stereocilia are deflected by the inertial reaction force of the endolymph. Deflection in the direction of the kinocilia, as shown for the left labyrinth in Fig. 1, depolarizes the afferent fiber and increases its firing rate above tonic levels. The arrows in Fig. 1 show the natural rotational stimuli that would produce these excitatory responses. When the stereocilia are deflected away from the kinocilia, shown for the right labyrinth, hyperpolarization reduces the firing rate.

GVS will alter the firing pattern of canal afferents in a way that has no natural rotational equivalent. Cathodal GVS will increase the firing rate of all responsive afferents, regardless of their direction specificity. Thus, for the horizontal canal, this would signify a natural yaw with the nose moving toward the ipsilateral, or cathodal, side (Fig. 1, left horizontal canal). The same increased firing induced by cathodal GVS in afferents of the anterior and posterior canals will signify ipsilateral ear-down roll, and the signals from both canals should add (Fig. 1,

left of roll; the canals overlap in this view). Because they are aligned at 45 deg to the sagittal axis of the skull, the anterior canal will also indicate nose-down pitch and the posterior canal a similar nose-up pitch (Fig. 1, left of pitch). These opposing signals have no natural equivalent and should cancel because they are equal in size and opposite in direction. Thus, considering all three canals, the pattern of afferent discharge evoked by GVS will signal rotation with yaw and roll components relative to the plane of the vestibular apparatus. Furthermore, the roll component should be larger than the yaw component because of the vector addition of signals from both vertical canals.

By hyperpolarizing the afferents, anodal GVS will decrease the firing rate of all responsive afferents, regardless of their direction specificity. This means that for each canal anodal and cathodal stimulation will produce signals of rotation in opposite directions. Anodal responses are shown for the right canals in Fig. 1. The directions are reversed horizontally because of the mirror symmetry of the canals on either side of the head.

To complicate matters, the canals are not aligned in the plane of the head and are not quite orthogonal so they will not add and cancel quite as neatly as this model suggests. The entire canal structure tilts backward by ~ 30 deg from the head horizontally, and this gives the horizontal canals a roll component at the expense of yaw. The vertical canals develop a yaw component at the expense of roll, while maintaining sensitivity to the pitch component. Fortunately, however, we can calculate the vector for each canal because their planar relationships relative to Reid's stereotactic line (inferior orbital rim to auditory canal) have been accurately measured (7). From these data, Fig. 2 shows the GVS angular acceleration unit vectors (right-hand rule) for each canal. Considering these as unit vectors means that we are assuming that the same stimulus will produce equally sized responses from each canal. The vectors are oriented for anodal stimulation on the right and cathodal on the left, that is, bilateral bipolar GVS.

The lateral view shows the vector components of GVS angular acceleration signals in the sagittal plane for each canal (α_p , α_a , α_h) and their resultant (α_r). Thus, for example, anodal GVS produces from the right horizontal canal a signal of rotation about an axis that is directed mostly upward, slightly backward, and slightly laterally (α_h , marked by asterisk in Fig. 2). The resultant vector of the three right canals is largely backward with smaller upward and lateral components. The vectors for cathodal GVS on the left side will have identical vertical and sagittal components but inverted lateral components. Summing vectors from both sides, we predict that bilateral bipolar GVS will evoke an afferent signal of rotation about an axis in the sagittal plane directed backward and slightly upward (mean of 18.8 deg) from Reid's line. When the head is in the normal anatomic upright position, Reid's line is nearly horizontal. Thus, during normal upright standing, the afferent discharge evoked by bilateral bipolar GVS will signal roll with a small yaw component, both directed toward the cathodal electrode as shown by resultant vector $L \pm R$ in Fig. 2.

The length of the canal affects canal sensitivity because the longer the canal, the greater the pressure that the endolymph exerts on the cupula (70, 76, 96). The human canals differ in size (11): the posterior canal is the longest (18–22 mm), then the anterior (15–20 mm), and finally the lateral (12–15 mm). The nervous system may need to calibrate the signals from

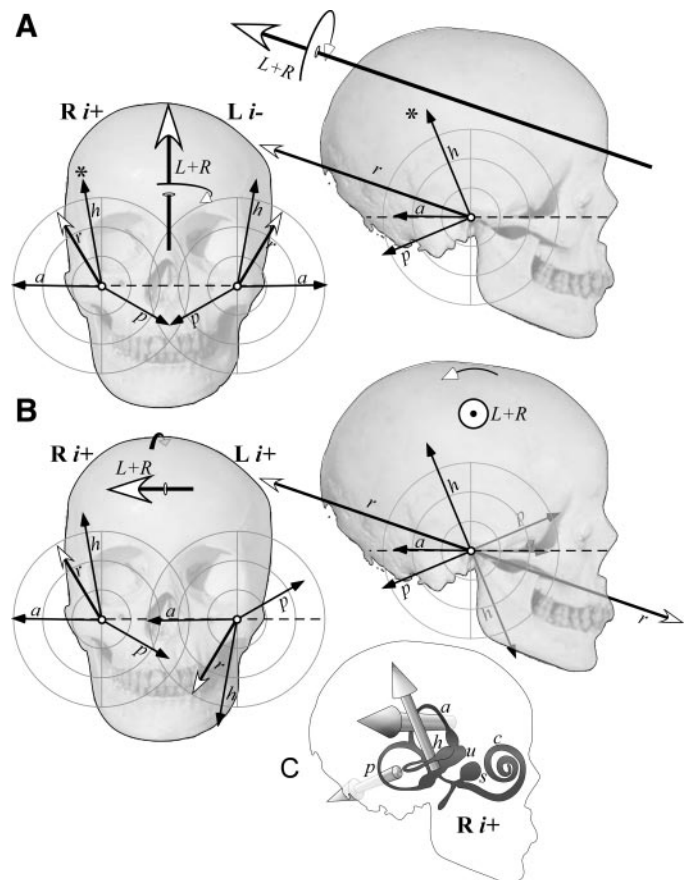


Fig. 2. Vector summation of semicircular canal responses to GVS. Vectors of unit amplitude are plotted orthogonal to the plane of each canal (a , p , and h), referenced to Reid's stereotactic plane (broken line). Lateral and vertical components are in the front view; sagittal and vertical components are in the lateral view. The resultant vectors (r) for each labyrinth are shown as white arrows. The vector sums of the resultants from each side are the large white arrows ($L+R$), and the curved arrow shows the right-hand rule representation of the vector direction. **A:** Bilateral bipolar GVS, anode right. The canal vectors are superimposed in the lateral view. GVS vectors sum to produce a large roll component and a yaw component. The pitch components cancel. **B:** bilateral unipolar GVS, anodal. The canal vectors are in opposite direction in the lateral view. GVS vectors in roll and yaw cancel, leaving a small residual pitch vector, directed backward for anodal current. **C:** three-dimensional sketch of the right anodal GVS vectors for each canal, to assist orientation. *See text for explanation.

each canal to produce a constant spatial representation. For example, if the shorter length of the horizontal canal means a smaller signal, it would need to be "amplified" so that yaw is represented on the same scale as the movements signaled by the other canals. How much would this process affect the net GVS canal vector? Redoing the calculations after the unit vectors are scaled inversely with the canal length produces a net vector that is angled backward and upward by 27.1 deg from Reid's line. The signal is still mostly roll toward the cathode, but the yaw component is slightly larger.

Otolith Organs

The otolith organs, utricle and saccule, sense linear acceleration of the head in space or the equivalent change in the gravitational acceleration vector when the head is tilted. The macula of each organ contains 20,000–30,000 hair cells ar-

rayed across an approximately planar surface. The cilia of the hair cells are embedded in a gelatinous membrane made denser than the surrounding endolymph by the inclusion of calcium crystals or otoconia. When gravito-inertial forces move the membrane, the stereocilia are deflected. As they bend toward the kinocilium, they increase the firing rate of the associated afferent fibers; when they bend the other way, they decrease it.

The plane of the utricular macula is inclined backward from the horizontal by ~ 30 deg and slopes away laterally by ~ 10 deg (48, 72), approximately in the plane of the horizontal semicircular canal. Thus the utricular afferents predominantly signal lateral and sagittal components of head acceleration. The saccular macula is aligned with the sagittal plane and therefore its afferents signal vertical and anteroposterior components of head acceleration. The maculae are ellipsoid rather than strictly planar (48, 71, 72) with the utricular macula concave up and the saccular concave medially. This means a greater spread in the directions of movement that can be detected from each organ. However, the effect is relatively small; for the purpose of estimating an average otolith vector, only the planar orientation will be considered here.

The hair cells are aligned over the surface of the maculae in an orderly fanlike pattern so that the optimal direction response for each hair cell is related to its position on the macular surface. Figure 3 illustrates the alignments of the otolith maculae and their hair cells. On either side of a striola that divides the utricular macula into the pars medialis (also known as pars interna) and pars lateralis (also known as pars externa), the hair cells are aligned in opposite directions so that the kinocilia are always toward the striola. Thus, for any imposed acceleration, one set of cells will maximally increase and another will maximally decrease their resting discharge rates. With the kinocilia toward the striola, ipsilateral acceleration, or contralateral tilt, will increase the firing of pars lateralis units and decrease it from pars medialis units. The hair cells of the saccular macula have their kinocilia directed away from the striola saccular. Thus upward acceleration will increase firing from the pars externa and decrease firing from the pars interna.

Real acceleration causes direction-related differences in firing rates across the afferent population. We assume that the CNS performs the equivalent of a vector summation on the responses of the entire array of hair cells to derive a meaningful representation of direction and amplitude of the acceleration. GVS, in contrast, will have the same effects on all susceptible afferents without favor for any direction. The vector sum will now be determined by the position and alignment of the striola on the macular surface, as this determines the number of units that signal different directions. If the hair cell population is exactly balanced so that the net anterior, left, and down vectors cancel the net posterior, right, and up vectors, then GVS will produce a zero net vector from the otolith organs. However, the populations are not exactly balanced. In guinea pigs and squirrel monkeys, the utricular striola is closer to the lateral edge, making the pars medialis larger than the pars lateralis (29, 59). In agreement with this, contralateral linear acceleration, or ipsilateral ear-down tilt, increases the firing rate of more than half of the utricular afferents in squirrel monkeys and cats (27, 62). The prevailing direction is the other way in chinchillas, in which the pars medialis makes the smaller 40% contribution (30).

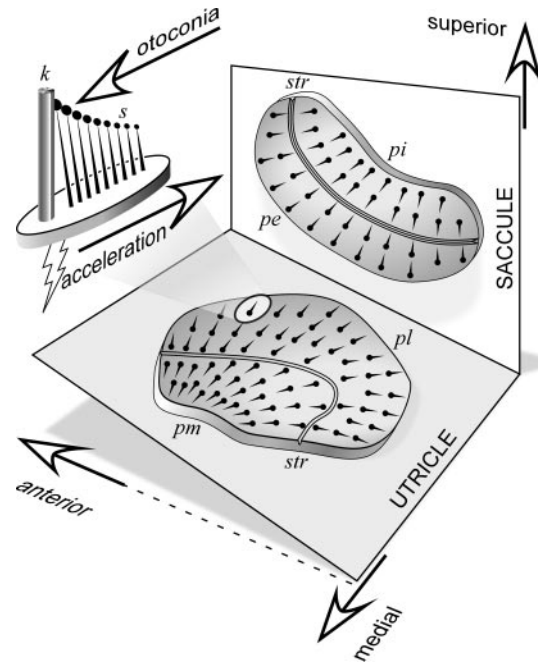


Fig. 3. Orientation of the maculae of the utricle and saccule. In head coordinates, the saccular macula is in a vertical plane aligned anteroposterior. The utricular macula is mostly horizontal plane but with a backward tilt. The fanlike alignments of the hair cells on the macula surface are depicted with the kinocilia (*k*) at the thick end and stereocilia (*s*) at the thin end. Each hair cell responds optimally to acceleration in the direction of its alignment, increasing firing rate when the stereocilia are deflected toward the kinocilium. Thus linear acceleration of the head from kinocilium toward stereocilia will cause an increase in discharge. A striola (*str*) divides each macula into two regions of reversed hair-cell polarity, so that when all afferents of a macula are excited or inhibited, the net signal will be determined by the relative weighting of each region. *pe*, Pars externa; *pi*, pars interna; *pl*, pars lateralis; *pm*, pars medialis. [Adapted from drawings by Spoendlin (93).]

A recent detailed study of 43 human macula utriculi by Tribukait and Rosenhall (99) shows a much more even balance of the pars medialis and pars lateralis areas: 47% medialis to 53% lateralis. Based on this human utricular direction sensitivity and the relative changes in firing rates for acceleration and galvanic stimuli (40, 41), Fig. 4 shows the expected firing pattern of utricular afferents that signal lateral acceleration or tilt. These are shown for the head stationary and level (Fig. 4A), accelerating laterally (Fig. 4B), and stationary during bilateral bipolar GVS (Fig. 4C). The bars represent the signal amplitude (rate \times sensitivity) of pars medialis and pars lateralis. The net acceleration signal, shown as the black bar, is the vector sum of the four signals. When the head is stationary, the firing from each side cancels and there is a zero net signal (S_0). Acceleration to one side increases the discharge of pars lateralis on that side and pars medialis on the other side, whereas it decreases the discharge of the complementary sides of the utriculi. Thus vectorial combination of the four signals gives a large signal of the acceleration (S_A).

Cathodal GVS increases the firing rate of utricular afferents innervating both sides of the striola. The imbalance of hair cell alignment leaves a net response that would normally indicate acceleration to cathodal side. On the contralateral macula, anodal GVS will produce a much smaller imbalance that would normally indicate acceleration to the anodal side. Summing the net signals from both sides leaves a signal that would indicate

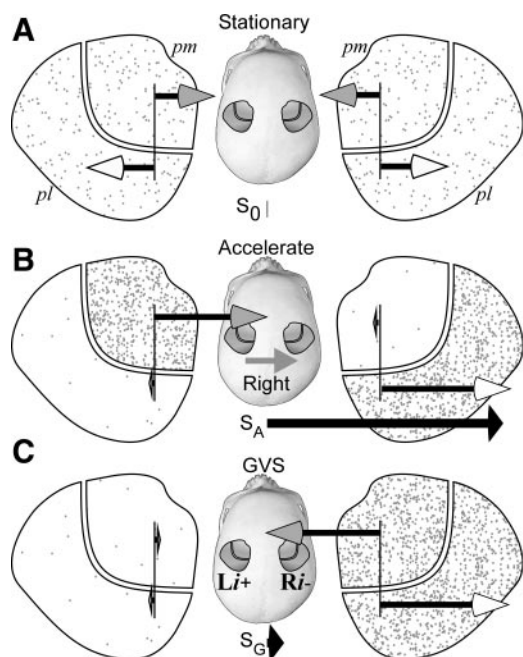


Fig. 4. Summation of the lateral components of utricular signals. The utricular maculae with the head for orientation are shown. *A*: with the head stationary and level, all afferents will maintain their tonic discharge (dot density). Thus the pars lateralis and pars medialis produce acceleration signals in opposite directions, indicated by the white and gray arrows respectively. Because pars lateralis is slightly larger than pars medialis, the net signal from the utricular macula will be a small lateral acceleration. However, the signal from the contralateral macula cancels this, resulting in a net acceleration signal of zero (S_0). *B*: when exposed to a lateral acceleration toward the right, or tilt to the left, the discharge from the left pars medialis and the right pars lateralis increases and that of the left pars lateralis and right pars medialis decreases. Thus both sides sum to produce the large net acceleration signal (S_A). *C*: on the left, anodal GVS decreases the firing rate of the pars medialis and the pars lateralis afferents. Cathodal GVS on the right increases the firing of the entire population. On each side of the head, the signals almost cancel. Only the small size discrepancy between the pars medialis and pars lateralis populations results in a small net acceleration signal (S_G).

a small acceleration toward the cathodal side. Thus bilateral bipolar GVS should produce a utricular firing pattern consistent with a natural stimulus of linear acceleration toward the cathodal side or tilt toward the anodal side (Fig. 4, S_G). However, GVS will produce only a small net acceleration signal because, for each utricle, the pars medialis and lateralis signals will nearly cancel with vector summation. We estimate that, for equivalent changes in discharge rates, the GVS response would only be $\sim 6\%$ of the acceleration response (Fig. 4, compare S_A with S_G). Furthermore, GVS applied to one side only will cancel in this way without involving the contralateral utricle, so that no form of GVS, monopolar or bipolar, unilateral or bilateral, can be expected to produce a large afferent signal from the otolith organs. This is a very different situation from the semicircular canal responses to GVS where there is no cancellation of roll and yaw signals.

This analysis can now be extended to consider the two dimensions of the utricular surface. Tribukait and Rosenhall (99) measured the areas of the macula utriculi that correspond to eight different compass directions of the striola and used these to calculate an average sensitivity for anteroposterior as well as mediolateral accelerations. Their results indicate that the utricle should be 25% more sensitive to lateral acceleration

than medial acceleration and 38% more sensitive to posterior acceleration than anterior acceleration. They also calculated the direction of maximal excitatory sensitivity for pars lateralis as lateral, 29.7 deg posterior, and for pars medialis as medial, 22.5 deg anterior. These represent the directions of the population-weighted vector. If we assume that, on average, the spontaneous and GVS-evoked firing rates of macular afferents are not direction specific, scaling these vectors by the firing rate will give the vector signal represented by the afferent population firing. In Fig. 5A, these are plotted for the left and right macula utriculi for the neutral or resting discharge condition and for anodal and cathodal GVS. The resultant of the pars medialis and pars lateralis vectors are shown as the thick white arrows. *Vector dN* is drawn for the stimulus conditions and represents the difference between the GVS afferent signal and the neutral or resting signal. These show that cathodal stimulation evokes signals of posterolateral acceleration from each utricle, whereas anodal stimulation evokes signals of anteromedial acceleration.

These net GVS utricular vectors from each side are added in different combinations to predict the total GVS utricular signal for every combination of stimulus polarity delivered either unilaterally or bilaterally. Figure 5B shows the resultant vectors for bilateral anodal (*vector $b+$*), unilateral anodal (*vector $u+$*), bilateral bipolar (*vector bb*), unilateral cathodal (*vector $u-$*), and bilateral cathodal GVS (*vector $b-$*). Thus this model predicts that 1) bilateral bipolar GVS will produce a signal of acceleration toward the cathodal electrode or tilt toward the anode, 2) bilateral unipolar GVS will produce a forward acceleration signal, or backward tilt, with anodal current and the opposite for cathodal current, and 3) unipolar GVS will produce a signal of oblique acceleration, contralateral and forward for an anodal electrode or ipsilateral and backward for a cathodal electrode.

The saccules respond to sagittal and vertical acceleration. The striola of the saccule is approximately along the center line of the macula so that GVS-evoked signals from each side of the striola will largely cancel each other. There are no data available on the hair cell populations for the saccular macula; therefore, it is not possible to determine whether a residual acceleration signal is expected. A net saccular GVS signal could affect the total anteroposterior acceleration signal from the otolith organs but not the lateral acceleration signal. Any net vertical signal is probably not significant for normal balance.

BALANCE RESPONSES

GVS produces a signal of head movement that has a potent effect on whole body motor control. In the trunk and limbs, it evokes reflex responses seen in the electromyogram (EMG), and these result in a well-organized body movement. However, the response is not hard wired. The pattern of muscle activity, hence the movement response, is exquisitely sensitive to many factors. Above all, for a response to appear in any given muscle, it is usually necessary that the muscle be engaged in a balance task. For example, the EMG responses that are evoked in leg muscles of a freely standing subject disappear when seated, even when the muscles are activated by comparable amounts in the two situations (9, 33). Similarly, if subjects cannot stabilize themselves with the legs, when standing on a

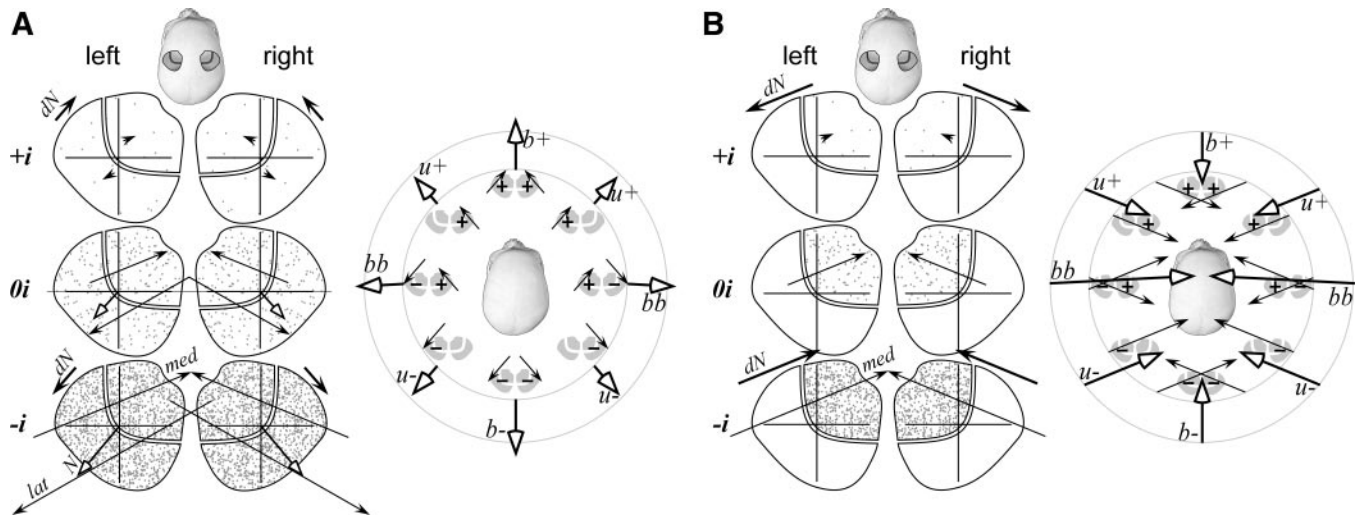


Fig. 5. Vector summation of utricular signals for different modes of GVS. *A*: acceleration vectors (N, white arrows) of the left and right utricle with anodal GVS (+*i*), neutral (0*i*), and cathodal GVS (−*i*) are calculated by summing the pars medialis (med) and pars lateralis (lat) vectors. For each condition, a net vector (dN) is calculated by subtracting the vector for the neutral (0*i*) condition (dN = 0 for 0*i*). In the wheel on the right, each combination of the left and right net vectors (thin black arrows with macula outlines) is summed to give the total utricular acceleration vectors (large white arrows). This model indicates that with unilateral GVS the utricles will signal forward and contralateral acceleration with anodal current (*u*+), or backward and ipsilateral with cathodal current (*u*−). The bilateral GVS signals will be forward with two anodal currents (*b*+), backward with two cathodal currents (*b*−), or to the cathodal side with one of each polarity (*bb*). *B*: considering only the pars medialis afferents, the same calculations show acceleration signals in the opposite directions that are generally larger and much larger for laterally directed acceleration.

wobbly board for example, and use the arm to balance by holding onto an earth-fixed support, then responses appear in arm muscles (9). The response is distributed in proportion to the load borne by each limb (68, 69), and relatively small changes in standing posture can also influence the response. Standing with the feet a few centimeters apart compared with standing with feet together, which has the effect of stabilizing the lower body (21), dramatically attenuates the leg muscle response (20).

Observations such as these lead us to conclude that the whole body response to GVS is organized by the balance system. It seems that the balance system interprets the GVS-evoked input as a real head movement in space arising from an unplanned body movement. Such an input would represent a threat to balance, and so the balance system responds with a counteraction. In reality, of course, the counteracting response is inappropriate and further destabilizing because the vestibular signal is fictitious. Nevertheless, the response, at least in its early stages, reveals the operation of the balance system to a pure vestibular perturbation.

Electromyography

After the onset of a step current, short- and medium-latency EMG responses can be observed in muscles of the upper limbs (5, 9), the trunk (1, 3), and the lower limbs (9, 33, 73, 107, 110). After a constant GVS current is stopped, equivalent but reversed “off” responses imply that these reflexes are driven by the change in the vestibular nerve discharge rate rather than its absolute level (108).

Size and direction. The short-latency and medium-latency EMG responses are in opposite directions (Fig. 6). In keeping with the effects of GVS on vestibular afferents, both increase with stimulus current (12), although it appears that a bigger stimulus is required to evoke the short-latency response than

the medium-latency response (33). Both responses are inverted in antagonist muscles if they are also active in the balance task (Fig. 6*B*). The medium-latency response is normally larger in amplitude, and its direction and size correlates with the observed pattern of whole body sway (9, 33). It is also more susceptible to changes in other sources of sensory input. For example, Britton et al. (9) observed that visual input can nearly abolish the medium-latency response without affecting the short-latency response. The earlier response can produce small segmental movements but has no effect on whole body movement (33). However, because this is a response to an abrupt nonphysiological perturbation, this does not mean that the pathways underlying the short-latency response have no role in the vestibular control of balance in normal situations.

EMG responses are seen only in muscles engaged in balance; therefore, we can assume that there is a task-dependent gating of descending vestibulospinal influences. However, in subjects lying prone, the amplitude of the soleus H-reflex is increased by 3–4% with 4-mA unilateral GVS or decreased with the opposite polarity (55), and this is influenced by turning the head to the side (54). Thus a small vestibulospinal influence can still be seen in muscles that seemingly have no role in balance control.

Latency. The short-latency EMG responses are seen at ~40 ms in the arm and at 55–65 ms in the leg (5, 9, 33, 106). This is shown for one subject in Fig. 6*C*. With the assumption that both responses are based on the same afferent volley reaching the vestibular nuclei, the conduction velocity within the spinal cord is estimated to be ~60–80 ms^{−1}, very similar to the conduction velocities of the corticospinal tract calculated from responses to percutaneous electrical stimulation and transcranial magnetic stimulation of the motor cortex (67, 84). However, the vestibulospinal latencies are ~30 ms longer than the corticospinal latencies. The need to demodulate the modulated

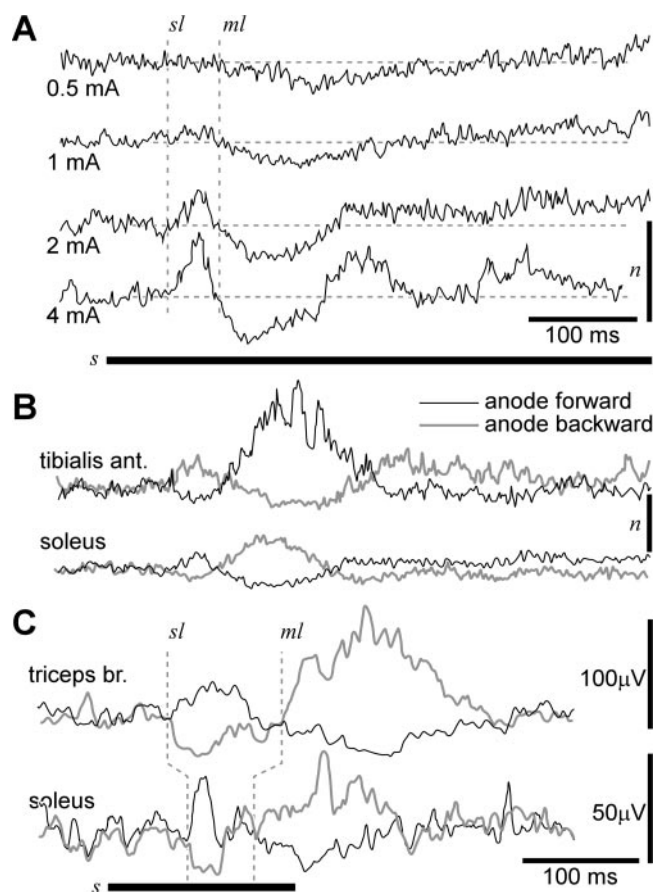


Fig. 6. Electromyographic responses to GVS. **A:** mean EMG responses (9 subjects \times 32 trials), for GVS intensities between 0.5 mA and 4 mA, recorded over soleus for bilateral bipolar GVS. The anodal electrode was on the right, and subjects had the head turned so that the right ear was forward. *Line s* is the stimulation period. *Line n* is the normalized prestimulus EMG level for each subject before averaging. Thus 4-mA GVS modulates background EMG by more than 50% in the short-latency (sl) and medium-latency (ml) responses. The medium-latency response could explain the forward sway observed in this situation. **B:** in the same format, reciprocal changes in soleus and tibialis anterior EMG are shown for 2-mA GVS of opposite polarities. Tibialis anterior was made tonically active by standing subjects on an inclined support. **C:** mean EMG responses from 1 subject (40 trials at 1 mA) for GVS of opposite polarities. *Top:* subject is balancing upright using the arm muscles, and EMG is recorded over triceps brachii. *Bottom:* subject is standing normally, and EMG is recorded over soleus. [A and B are redrawn from Fitzpatrick et al. (33), and C is redrawn from Britton et al. (9).]

firing rate of the irregular vestibular afferents could explain this central time as two pulse intervals with a mean firing rate of 70 Hz correspond to 30 ms.

The medium-latency EMG response to GVS appears at 110–120 ms in the lower limbs (5, 9, 33, 106), less than this in the paraspinal muscles (1, 3), but it is >20 ms later in the arm (9). Thus this response is not produced by the same system that appears to release immediately the shorter latency response. This and the complex nature of the GVS response suggest that the vestibular signal is processed by a balance system that uses information from many sources and produces a unified response according to the current demands for maintaining balance.

Faradic stimulation. Galvanic stimulation is the application of direct current for a long period. However, it is worth considering the effects of brief pulses of the type commonly

used to stimulate peripheral axons. When delivered for longer than the chronaxie (0.9–1.8 ms), they produce a single brief movement of the head in cats (92). In human subjects, transmastoid electrical stimulation at 5 mA for 2 ms evokes short-latency biphasic EMG responses in the ipsilateral sternocleidomastoid muscle (109) and bilaterally in the masseter muscles (22). It would appear therefore that a brief stimulus of this type produces a single synchronous activation of vestibular afferents. Irregular afferents, being closer to threshold most of the time (91), are likely to make the greater contribution to this response. This synchronization is seen when short stimuli (50 μ s) are delivered within the perilymphatic space (41) but is followed by a lengthening of the subsequent interspike interval. Thus the behavioral responses to this type of stimulus, and this might include small ocular or head movements that are commonly seen at the onset of prolonged GVS, are likely to be manifestations of synchronous recruitment of afferent fibers rather than modulation of their discharge rates.

These brief stimuli create prominent responses in the musculature of the neck and are associated with movements of the head on the trunk rather than movements of the whole body. This suggests passage to the cervical spinal cord through the medial vestibulospinal tract rather than the lateral vestibulospinal tract, which projects predominantly to the lumbosacral segments. The continuity of the medial vestibulospinal tract with the medial longitudinal fasciculus and its connections with the abducens, trochlear, and oculomotor nuclei indicate that the system concerned with stabilizing the eyes and head might respond preferentially to these stimuli.

Modulated GVS. In a few studies, the stimulus current has been delivered as continuously varying sinusoidal (13, 79) or stochastic (32, 78) waveforms of alternating polarity. Responses indicate that these stimuli modulate afferent firing by the same means as the continuous tonic stimulus. They also indicate that the neural response can extend to frequencies much higher than the normal behavioral limits of vestibular responses.

Balance Responses

When a subject stands normally with the head facing forward, the balance response to bilateral bipolar GVS is directed laterally. However, in a beautiful demonstration that revived much interest in GVS, Lund and Broberg (64) showed that the direction of the response depends critically on the orientation of the head relative to the feet (64). If the subject turns the head to face various directions in the horizontal plane, i.e., the head yaws, then the balance response is redirected so that the body moves along the interaural line. This fundamental behavior has been the premise of all subsequent studies. Figure 7 shows sway responses recorded by Pastor et al. (77) with the head turned in five different directions while the feet remained in the same alignment (77). The strong convergence of proprioceptive afferent axons from the neck onto the second-order vestibular neurons of the vestibular nuclei could underlie this remapping of the GVS response. However, it is not quite that straightforward. Lund and Broberg also showed that it does not matter how the head orientation is achieved. Whether it is by simply turning the head at the neck, turning at the trunk, or a combination of both, the response is the same. This implies that the pattern of muscle activity evoked by GVS takes into

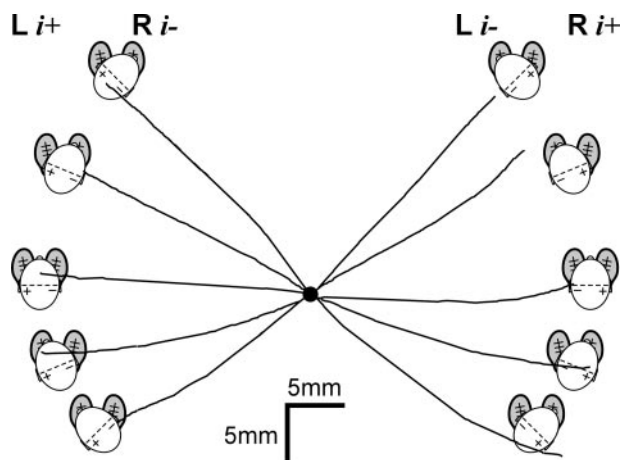


Fig. 7. Sway responses to GVS. Subjects stood still at the central point with the head turned in yaw in 1 of 5 positions (R45°, R22°, 0°, L22° L45°, where R is right and L is left), but with the feet always pointing straight ahead. Bilateral bipolar GVS at 0.5 mA of both polarities (anode left and anode right) was applied for 2 s. The whole-body sway trajectories were always along the interaural line and towards the anodal electrode. [Redrawn from Pastor et al. (77).]

account the orientation of all body segments from the head to the feet. Here it is worth noting that if, by experimental means, my perception of the direction that my head is facing is distorted, then the direction of my balance response is determined by my illusion rather than by the reality (44). Clearly, this is no straightforward conduit from vestibular afferent to muscle contraction. The transformation of the vestibular signal must be through a very elaborate system of balance control.

Coordinate transformation. This directional tuning of the GVS response reflects the operation of what is often described as a coordinate transformation. This process is absolutely essential if vestibular information is to assist balancing the whole body. The need arises because, with the vestibular organs fixed inside the skull, the hair cells can only signal head movement and, because the receptors rely on inertial forces, those signals are referenced to external gravito-inertial space. The head, however, can adopt a whole range of positions relative to the body and relative to the earth. Consider a vestibular signal of sideways movement when you are standing and facing straight ahead. It says that your body, or at least the upper part of it, is falling sideways. If, however, you were looking over one shoulder it would mean that you are falling backward or forward. Completely different patterns of muscle activation are required to arrest these different falls. To control balance, therefore, the brain has to combine vestibular information with all those other signals that tell it how the various body segments are orientated to each other.

Sensory Interactions

Sensory input from many sources other than the vestibular organs is used to maintain balance. Proprioceptive, visual, cutaneous receptors in the feet or elsewhere, receptors in the abdomen, and undoubtedly receptors in other locations can all provide information to the balance system. Although each sensory channel has different qualities in terms of resolution, bandwidth, and importance for whole body and segmental balance, the availability and sensitivity of one input can alter

the reliance placed on the others. Some of the evidence for this comes from GVS studies.

When visual input about body sway is available, the whole body GVS sway response gets smaller (6, 9, 64, 74, 111), and this stabilizing effect is graded depending on the richness of the visual cues (19). Loss of somatosensory input leads to a massive increase in the GVS sway response. This may happen with an unstable support surface (33, 47), with hypothermic anesthesia of the feet (65), or through peripheral neuropathy (47). With complete loss of somatosensory input, the GVS response is an order of magnitude greater (18). Conversely, the tactile cues provided by lightly touching a stable reference with the fingertip reduce the sway response (9).

These competitive effects from other sensory channels can occur through two processes. One is by influencing or selecting the initial response through gain changes in vestibular and other sensory pathways, a system something like proportional representation voting. The other effect is on terminating the developing vestibular response. At some stage in the sway response to GVS, a threshold is reached at which the balance system, getting conflicting information from other sources, says “no more” and disregards the vestibular input. This threshold may explain the common observation that some subjects seem to accept the stimulus and sway a long way, whereas others react as if fighting it with multiple corrections. Standing with the legs apart decreases the size of the GVS sway response (20) (Fig. 8), whereas decreasing it by tandem Romberg stance makes the sway response so large that it is nearly impossible to maintain balance (105). Standing on compliant surfaces, such as a piece of foam rubber, also increases the size of the sway response (33, 105). Apart from effects on sensory input, the altered dynamic coupling of muscle contraction and load with these manipulations could also influence the final tilted position of the body.

There is, however, something different and compelling about GVS as a perturbation to the balance system. It is obvious that if a physical perturbation, such as being pushed to the side, is anticipated then it can be negated by an appropriate anticipatory response. In the same way, an unexpected visual stimulus that disturbs balance has no effect when self-delivered and expected (43). GVS is different because the evoked sway response is identical for unexpected or self-delivered stimuli, and this effect does not appear to adapt with time (42). Why this should be is uncertain. It may reflect a different entry level of vestibular input to the balance system or a decoupling of the efferent signal from the reafference that comes from the sway response. The very small cortical area receiving vestibular input, compared with the vast regions allotted to visual and somatosensory sensation, may also be relevant.

Sway Profile

At the onset of stimulation, the body moves and leans toward one side; after 1 or 2 s, however, the motion stops, leaving the body tilted (49). Figure 8, redrawn from Day et al. (20), shows typical responses. All body segments contribute to the response so that, as well as leaning, the body also becomes slightly bent (20). The head tilts on the trunk, the trunk tilts on the pelvis, and the pelvis tilts with respect to the ground. In agreement with inverted EMG responses of the same size that occur when the stimulus ceases, the body segments return

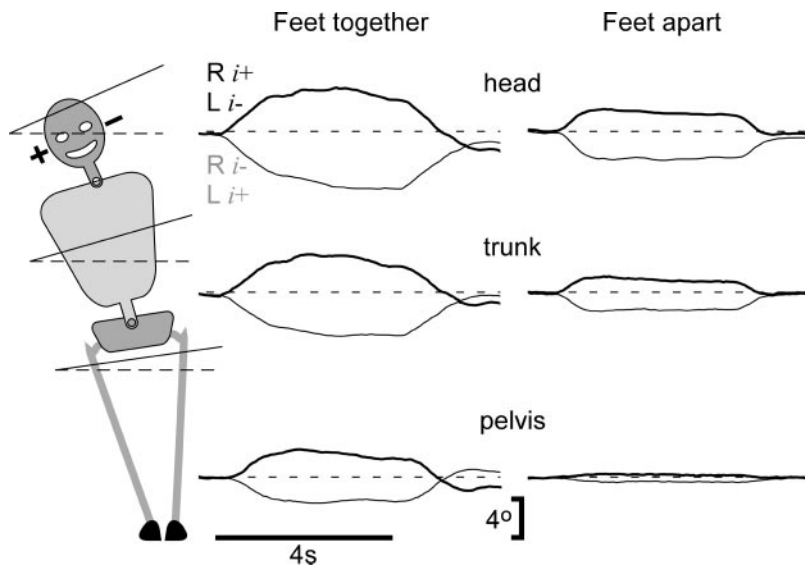


Fig. 8. Alignment of the body. Sway responses for the pelvis, trunk, and head segments for GVS at 0.5 mA, delivered during the period indicated by the 4-s timeline. The up-going traces are with anode-right GVS, and the down-going traces are with anode-left GVS. As shown on the *left*, each segment tilts on the one below it so that the greatest tilt in space is at the head. On the right, sway is greatly attenuated when standing with the feet apart, but follows the same pattern of progressive bending. Shortly after stimulus onset, the body moves toward the anodal side before reaching a steady level. When the stimulus stops, the segments straighten to their original positions. [Redrawn from Day et al. (20).]

approximately to their starting orientation (20). It is interesting to note that, until recently, this static change in alignment of the body has led researchers interested in balance control to believe that the effects of GVS are mediated through activation of the otolithic or graviceptive system, whereas those interested in ocular control have explained the GVS-evoked eye movements by activation of semicircular canal afferents.

A continuous response. At first glance, the GVS response appears to consist of a static tilt response of all body segments, as if the GVS signal was itself mimicking a static tilt of the head. The greater the stimulation current the greater the virtual tilt. However, the response to the GVS signal produces a true destabilization of the body that activates other sensory systems, producing further compensatory reactions. Thus the reduced sway seen with GVS when additional input is available or the support is stable could be explained by the earlier and more effective recruitment of these reactions, and the opposite could explain the larger responses seen when sensory input is limited or the support is compliant. This process no doubt explains the very different amounts of static tilt produced by GVS without any difference in subjects' perceptions of the alignment of the vertical (105).

This "interference" from other balance responses provides a somewhat misleading picture of the nature of the GVS signal. This is evident in the response to GVS of a "deafferented" subject, *subject IW*, who had lost all large-fiber somatosensory afferent input from his whole body below the collar line (94). Figure 9A shows this subject's responses to GVS while seated with eyes closed (18). Normal subjects, when seated, tilt the head and trunk by very small amounts during GVS. In *subject IW* it differed in two important ways. First, it was an order of magnitude larger than normal. This is not surprising in a subject with no other information about body orientation and movement. Second, and of greater relevance here, the response consisted of a continuous tilt throughout the stimulation period rather than reaching a new level of static tilt. This continuous tilting behavior can be demonstrated in healthy standing subjects by using small stimulation intensities and reducing the destabilizing effect of the response by tethering the subject's feet to the ground (104). These responses are shown in Fig. 9B.

These results show us that, when feedback from nonvestibular sensory systems is removed or made less relevant, the response remains unbridled and shows itself as a continuous tilting response.

Both studies that demonstrated the pattern of continuous sway (18, 104) showed that the response could be described accurately as the sum of step and ramp responses (Fig. 9C). Although it is possible that either the otolithic or canal signal

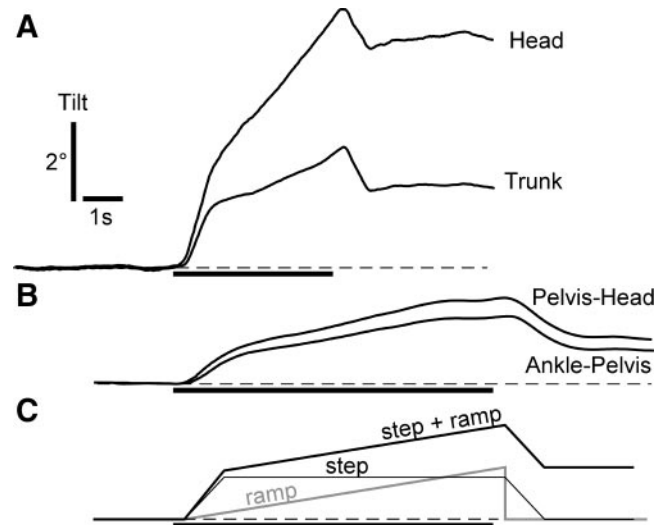


Fig. 9. Movements of the body segments. Sway responses to GVS showing continuous movement throughout the entire stimulus period. In both records, GVS at 0.5 mA was delivered for the period shown by the time line. **A:** very large responses of a subject who had lost all large-fiber sensory afferents below neck level. The data were recorded with the subject seated. After stimulus onset, there is a rapid tilt of the head and trunk that lasted for ~ 1 s, after which there is a continuous roll to the side that stops only when the stimulus is turned off. At that time, there is a rapid movement, again over ~ 1 s, in the opposite direction. The return movement stops a long way short of the original vertical position. [Data are from Day and Cole (18).] **B:** similar response profiles, although much smaller, from normal subjects standing in conditions that were designed to allow sway to occur over a long 8-s period. [Data are from Wardman et al. (104).] **C:** sway profiles of both sets of data are accurately described as the sum of a constant-velocity roll (ramp) and a step or plateau movement to the same side (step).

with appropriate processing within the nervous system could produce such a response, the most parsimonious explanation is that an otolithic signal of altered gravitational alignment produces a step response and that a semicircular canal signal of rotation produces a ramp response. When the stimulus stops, the realignment component is reversed, but the body remains in a tilted position because the movement signal simply stops rather than reverses.

Sway Size

It appears from Fig. 9 that the step and ramp contributions to the total sway response are not dissimilar and, if they are otolith and canal responses, that we should expect GVS to produce signals to the balance system from the canals and otolith organs of approximately equal size. The roll signal produced by bilateral bipolar GVS (Fig. 2A) is of “physiological” magnitude in that GVS does not produce a signal from another canal that cancels a significant part of the signal. In other words, GVS produces a total signal that reflects the altered firing rates of the individual afferents in much the same way that a movement stimulus would. In contrast, the same change in the firing rate of utricular afferents would only produce a very small “nonphysiological” signal because the push-pull arrangement across the striola, which augments the signal with movement stimuli, largely cancels the GVS signal (illustrated in Fig. 5A). It does not seem sensible to accept that these large sway responses can be explained by the small imbalance in afferent populations from each side of the striola (99).

The coefficient of variation of the difference between the pars medialis and pars lateralis areas will be much larger than the coefficient of variation of the pars medialis area; we calculated 105 vs. 8% from data of Tribukait and Rosenhall (99). Thus their data indicate that, between subjects, sway amplitudes in the highest decile should be 250% that of the middle decile, whereas the lowest decile should be about the same size but in the opposite direction. Even with the inconsistencies of delivering percutaneous GVS and the different weightings that subjects may place on vestibular inputs, GVS does not produce this range of responses. What is more, in 7 of the 43 maculae studied by Tribukait and Rosenhall, the pars medialis was larger than the pars lateralis; however, among countless subjects in GVS studies, sway toward the cathodal side has never been reported.

Thus we construe that the GVS-evoked utricular signal to the balance system is much larger and less variable than can be explained by the small residual after-vector summation of the signals from the entire population of utricular afferents.

Sway direction. Probably since the observations of Hitzig and Breuer, it has been known that the polarity of the stimulating electrodes determines the direction of the responses to GVS. In a subject standing normally, the response to bilateral bipolar GVS is a movement of the body toward the side of the anodal electrode (12). Reversing the stimulus polarity causes a balance response in the opposite direction, as illustrated by the mirror responses in Fig. 7. This presumably arises because afferents previously excited by cathodal current become inhibited by anodal current and vice versa, resulting in an oppositely directed virtual head movement.

In addition to the relative sizes of otolithic and canal responses discussed above, their directions need to be considered. If both otolithic and semicircular canal signals contribute to produce the sway profiles shown in Fig. 9, then both sway responses must have the same direction. Do the GVS-evoked changes in firing of the otolithic and canal afferents account for this?

Bilateral bipolar GVS. The signal from the semicircular canals during bilateral bipolar GVS will indicate a large roll and small yaw, both toward the cathodal side (Fig. 2). Hence, the observed sway toward the anodal side appears to be the appropriate balance response. Now consider the response to a utricular signal. A signal derived by the vector summation of all parts of the utricle, as shown in Fig. 5A, will indicate a small acceleration toward the cathodal side or tilt toward the anodal side so that realignment of the body by swaying toward the cathodal side would be the appropriate response. This however is opposite the observed sway. If, however, we consider a utricular signal that is the vector summation of afferents from partes mediales only (Fig. 5B), then the signal will indicate a large acceleration toward the anodal side or tilt toward the cathode. The observed sway toward the anodal side then becomes the appropriate response.

Unilateral GVS. Further insight into vestibular function and the action of GVS comes from stimulating just one side of the head. The nonstimulating electrode is usually placed on the forehead, although it can be on more distant regions, even the arm (97). This mode of GVS evokes sway responses that have a trajectory oblique to the interaural axis rather than in line with it (66, 74, 89, 90).

The lateral component of the oblique sway produced by unilateral GVS is either toward an anodal electrode or away from a cathodal electrode and by equal amounts in each direction (90). Furthermore, vector summation of separate sway responses to oppositely directed unilateral stimuli give a resultant that is not different from the sway produced by bilateral bipolar GVS. Severac Cauquil et al. (90) reasoned that the CNS must use the discrepancy between left and right vestibular activity to orientate balance responses. The sagittal components of the oblique sway are forward when cathodal current is applied to either ear and backward when anodal current is applied.

Compare these sway responses with the expected responses of the vestibular afferents. From Fig. 2B, anodal GVS should produce a semicircular canal signal of roll away from the stimulus side and a small signal of backward pitch. The pitch component will be less than one-quarter of the roll component. We therefore expect anodal stimulation of the canals to produce a sway largely toward the stimulus side and slightly forward. Thus the afferent signal from the semicircular canals predicts the sway toward the stimulus side but not the backward sway. A small forward sway is expected. The net utricular response to anodal GVS signals contralateral and forward acceleration or ipsilateral and backward tilt (Fig. 5A). Here, both predictions of sway, away from the anodal side and forward, are wrong. Again, a utricular signal from the pars medialis only (Fig. 5B) provides the correct prediction of sway toward the anode and forward.

Another observation that supports the idea that the utricular signal could be derived from the pars medialis only is the observation by Severac Cauquil et al. (90) that the oblique

sway produced by unilateral GVS had lateral components twice as large (196%) as the anteroposterior components. This is exactly the prediction of the pars medialis model (Fig. 5B) and not the prediction of the total utricle model (Fig. 5A). Of course it is possible that sway is better detected and corrected in the sagittal plane than in the lateral plane. However, as Fig. 7 shows, the sagittal and lateral components are similar when oblique sway is produced by turning the head with bilateral GVS (77), indicating that this effect is minimal.

Bilateral unipolar GVS. The reasoning above also holds for this mode of GVS. Subjects sway forward with cathodal GVS on both sides and backward with anodal GVS on both sides. Figure 2B indicates that bilateral anodal GVS will produce a semicircular canal signal of a small backward pitch with no roll component, which means that the observed backward sway cannot be a response to the signal from the semicircular canals. As above, it cannot be explained by the total utricular signal of Fig. 5A, but it is the prediction of the pars medialis model of Fig. 5B. The pars medialis model also correctly predicts that the sagittal sway produced by bilateral unipolar GVS is less than one-half the size of the lateral sway produced by bilateral bipolar GVS (88).

Origin of the otolith signal. If we accept that the morphological data define the weighting of the utricular afferent response to GVS, from all of the above considerations we must conclude that the sway response does not come from the total utricular signal. However, the responses from just the pars medialis of the utricle (Fig. 5B) have all of the characteristics to explain the sway response. First, it is in the right direction. With anodal GVS, unilateral or bilateral, pars medialis afferents will signal backward acceleration or forward tilt and with cathodal GVS they will signal forward acceleration or backward tilt. Second, the pars medialis afferents alone will signal much larger tilts than the entire utricle because the signal is not cancelled by afferents from pars lateralis. Third, it will remain reasonably consistent between subjects. Finally, the lateral acceleration signal of the pars medialis afferents is much larger than the sagittal acceleration signal. All of these factors agree with the observed sway responses to each mode of GVS. It would, of course, be very useful to include saccular GVS vectors into the model, but detailed morphological data are not available.

There is evidence that the two regions of the utricle may be specialized to provide for different behavioral responses to tilt and translational movements. In cats, local stimulation within the pars medialis produces torsional vestibuloocular reflex (VOR) responses, whereas in the pars lateralis it evokes a lateral VOR (35). Stimulation of discrete branches of the utricular nerve produces eye movements that are either predominantly torsional or predominantly horizontal (95). Torsional movements are appropriate responses to tilt of the head, whereas horizontal movements are appropriate for lateral translation. There are also behavioral correlates to support this hypothesis of different roles for the two regions. Unilateral loss of vestibular function causes a loss of sensitivity for detecting roll toward the deafferented labyrinth but not toward the functioning labyrinth (17, 98). Because the utricular pars medialis responds to ipsilateral tilt, this is consistent with it having a dominant role in responses to tilt. An opposite response is seen with translational accelerations. With acute unilateral vestibular deafferentation, horizontal VOR responses are di-

minished or absent when the functioning utricle is accelerated medially, but they are preserved with lateral acceleration (56, 57). Thus horizontal VOR, the normal response to translational acceleration, appears to be driven by pars lateralis afferents and not pars medialis afferents. As Tribukait and Rosenhall (99) point out, these are large effects that cannot be explained by the relatively small discrepancy in afferent populations from each side of the striola.

The division of the macular surface into parts having opposite polarities therefore may be a part of the evolutionary solution to the dilemma of acceleration and gravity equivalence (24). Appropriate responses to each contingency could be ready and calibrated and then selected on the basis of the present task, behavior, and sensory inputs that resolve the signal duality.

SUMMARY AND CONCLUSIONS

The vestibular signal of head movement produced by GVS has large and predictable effects on the balance system. Electrophysiological studies show that the afferent signal for these responses can originate from both the otolith organs and the semicircular canals. By the level of the secondary neurons in the vestibular nuclei, convergence of signals from all vestibular receptors and somatosensory and cortical inputs creates a signal that is highly organized and adapted to the needed posture and balance requirements. In most situations, GVS produces a plateau-shaped sway response in which the body segments realign leaving the body bent and tilted toward the anodal electrode. The plateau shape arises because the developing sway response is arrested by a response to other conflicting sensory information. However, when that other sensory input is not available, the sway response is a continuous movement and is best described by the sum of a step and a ramp response. Consistent with the responses of vestibular primary afferents, the two components are likely to correspond with otolithic and semicircular canal responses. On the basis of the morphology of the cristae and the alignment of the semicircular canals in the skull, GVS rotational vectors can be calculated for every mode of GVS, and these agree with the observed movements. This is not so for the otolithic system in which the net GVS acceleration signal calculated by vector summation of all utricular afferents is too small, too variable, and in the wrong direction to explain the sway responses. However, the GVS-evoked sway is consistent with the balance response originating from only one part of the utricular macula, the pars medialis.

GRANTS

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