Published in final edited form as:
J Vestib Res. 2012 ; 22(1): 11–15. doi:10.3233/VES-2012-0442.

Responses evoked by a vestibular implant providing chronic stimulation

Lara A. Thompson[3,4], **Csilla Haburcakova**[1,3], **Wangsong Gong**[1,3], **Daniel J. Lee**[1,2], **Conrad Wall III**[1,4], **Daniel M. Merfeld**[1,2,3,4], and **Richard F. Lewis**[1,2,3,4]

[1]Department of Otology and Laryngology, Harvard Medical School, Boston MA

[2]Department of Neurology, Harvard Medical School, Boston MA

[3]Jenks Vestibular Physiology Laboratory, Massachusetts Eye and Ear Infirmary, Boston MA

[4]Health Sciences and Technology, Harvard University and Massachusetts Institute of Technology, Cambridge, MA

Abstract

Patients with bilateral vestibular loss experience dehabilitating visual, perceptual, and postural difficulties, and an implantable vestibular prosthesis that could improve these symptoms would be of great benefit to these patients. In previous work, we have shown that a one-dimensional, unilateral canal prosthesis can improve the vestibulooccular reflex (VOR) in canal-plugged squirrel monkeys. In addition to the VOR, the potential effects of a vestibular prosthesis on more complex, highly integrative behaviors, such as the perception of head orientation and posture have remained unclear. We tested a one-dimensional, unilateral prosthesis in a rhesus monkey with bilateral vestibular loss and found that chronic electrical stimulation partially restored the compensatory VOR and also that percepts of head orientation relative to gravity were improved. However, the one-dimensional prosthetic stimulation had no clear effect on postural stability during quiet stance, but sway evoked by head-turns was modestly reduced. These results suggest that not only can the implementation of a vestibular prosthesis provide partial restitution of VOR but may also improve perception and posture in the presence of bilateral vestibular hypofunction (BVH). In this review, we provide an overview of our previous and current work directed towards the eventual clinical implementation of an implantable vestibular prosthesis.

Keywords

vestibular; vestibular prosthesis; implant; vestibulooccular reflex; psychophysics; balance; posture

1. Introduction

The vestibular labyrinth senses angular and linear head motion and head orientation with respect to gravity. This information contributes to postural control, percepts of head orientation and motion, and the VOR that stabilizes images on the retina. When the

---

Corresponding author: Lara A. Thompson, Massachusetts Eye and Ear Infirmary, 243 Charles Street, Boston MA 02114 Tel: 617 573-6491; Fax: 617 573 4154 lthomps@mit.edu.

vestibular end-organs are damaged, these normal processes are impaired. Patients with vestibular deficits therefore experience disequilibrium and ataxia, abnormal percepts of head orientation and motion (vertigo, spatial disorientation), and visual difficulties (blurriness and oscillopsia). Since both the underlying peripheral vestibular deficits and the resultant symptoms are often poorly responsive to available modes of therapy, the development of vestibular prostheses has become an area of considerable interest.

A vestibular prosthesis requires a sensor to transduce the physical parameters normally sensed by the damaged end-organ, and a method to provide this information to the brain through some form of stimulation. Two general approaches have been developed to provide sensory information about head motion and orientation to the brain – direct electrical stimulation of vestibular nerve afferents, and non-vestibular (or sensory substitution) stimulation using tactile or auditory feedback. We have focused on the former approach, and have developed a canal prosthesis that senses angular head velocity and provides this information to the brain by stimulating canal afferent nerves with implanted electrodes. Since the polarities of all hair cells in each canal cristae are aligned, afferent activity in each associated nerve fiber modulates in a similar manner during head rotation, and we can approximate this effect by modulating the frequency of stimulation provided by the electrode. Direct vestibular nerve stimulation therefore allows one to encode head angular velocity in the afferent nerve in a reasonably physiologic manner. Conversely, in the maculae of the otolith organs the polarities of the hair cells are not aligned and hence electrical stimulation of otolith afferents would not approximate the complex modulation in macular afferent activity that occurs in response to shifts in gravito-inertial force (GIF). For these reasons, we are concentrating at present on developing and testing a three-dimensional canal prosthesis that senses head rotation about all three cardinal axes and stimulates all three semicircular canals in one ear.

As preliminary steps towards the goal of future clinical application, we have examined and characterized eye movement responses in squirrel monkeys with bilateral, lateral canal plugs, while using a one-dimensional, unilateral prosthesis to provide electrical stimulation. Eye movement features we have examined included spontaneous nystagmus, VOR gain, phase, axis, and linearity, as well as spatial characteristics of the VOR. We have also examined the effects of a one-dimensional, unilateral prosthesis that stimulated the posterior canal of a rhesus monkey with aminoglycoside-induced BVH. These effects were quantified in terms of eye movement responses (VOR gain and thresholds), percepts of head orientation (subjective visual vertical test), and posture (e.g. during quite stance and during head turns). The main goals of our current work are to expand the unilateral prosthesis to a three-dimensional vestibular implant, to characterize the effects of the prosthesis on the VOR, tilt psychophysics, and postural control in rhesus monkeys, and through this characterization to determine viability of implementation in human patients.

2. Methods

Prosthesis

The details of the prosthesis design and implementation have been previously published [1], [4], [6] and will only be described briefly here. The prosthesis provides electrical stimulation to the canal ampullary nerves. The studies described below used a one-dimensional, semicircular canal prosthesis (stimulating the lateral canal in squirrel monkey and the posterior canal in rhesus monkey). Although a one-dimensional prosthesis is described here, our current ongoing research involves implementation of a three-dimensional prosthesis to simulate all three canals in one ear.

The one-dimensional prosthesis sensed head velocity and was high-pass filtered with ~0.03Hz cutoff frequency (time constant of 5 s), meant to mirror the dynamics of a normal squirrel monkey and rhesus monkey semicircular canals. The filtered head velocity was used to modulate the current pulse rate of the stimulating electrode similar to the normal physiology of the canal and ampullary nerve. A tonic, baseline pulse rate was set at 200 or 250Hz with pulse amplitude in the range of 90–140 microamperes, 200 μs pulse duration. The rate was modulated to provide a bidirectional cue (i.e. head turns that were ipsilateral to the stimulating electrode increased the rate of stimulation while head turns that were contralateral to the stimulating electrode decreased rate of stimulation). The modulation itself was based on a hyperbolic tangent function that saturated at higher angular velocities, but was linear for mid-range velocities.

Squirrel monkey experimental methods

The squirrel monkey was characterized in three sensory states, (normal, bilateral lateral canal-plugged [1], and canal-plugged/stimulated). Eye movement measurements included spontaneous nystagmus while the squirrel monkeys were stationary and VOR recorded during sinusoidal rotation about an earth-horizontal axis at frequencies of 0.01, 0.02, 0.1, 0.2, 0.5, and 1 Hz, as well as for constant-velocity step rotations.

Rhesus monkey experimental methods

One rhesus monkey has been characterized in three sensory states (normal, BVH, and BVH aided by a one-dimensional prosthesis (BVH/stimulated)). As opposed to canal-plugging done in the squirrel monkeys, the BVH state was induced with aminoglycosides (i.e. intratympanic gentamicin and systemic streptomycin). After the monkey had completed testing in the ablated state and was receiving chronic stimulation by the posterior canal prosthesis, the BVH/stimulated state was characterized.

The experimental paradigms studied included behavioral measures such as 1) eye movements, 2) perception, and 3) posture. Eye movement measurements included determining VOR using sinusoidal rotations in similar manner to that of the squirrel monkeys. The perception paradigm was similar to the subjective visual vertical (SVV) task performed in humans, in that the rhesus monkey was trained to align an arrow with perceived earth-vertical, while undergoing either static (as in [3]) or dynamic roll-tilts. For the posture paradigm, the monkey was trained to stand on a balance platform in its natural quadrupedal stance. The monkey performed three posture tasks: quiet stance, head-turns, and roll-tilts of the support surface. During quiet stance, the monkey stood stationary in test conditions for which the support surface was varied between thin gum rubber and compliant foam, and stance width was varied between wide and narrow. For quiet stance, visual orientation cues were also varied (i.e. prominent earth-vertical information provided by a large poster of a forest and minimal orientation cues provided by a view of a small ball). During the second posture task, yaw head-turns were evoked by training the monkey to make voluntary head turns between two visual targets. For the final posture task, roll-tilts of the support surface generated with a pseudorandom ternary sequence (PRTS) were implemented in one rhesus monkey in the normal state. For the PRTS posture task, the platform tilts in the roll plane with peak-to-peak amplitudes ranging from 0.5 to 8 deg, and with frequency content ranging from 0.06 to 2.33 Hz.

3. Results

The effects of a unilateral vestibular prothesis in squirrel monkeys

Our previous work in guinea pigs [1] and squirrel monkeys [2],[3],[6] focused on chronic, electrical stimulation of lateral canal afferents and showed that a one-dimensional, lateral canal prosthesis was able to generate an electrically evoked VOR. The squirrel monkey eye movements were measured both while stationary [6] and while undergoing sinusoidal rotations about a earth-vertical axis at various frequencies and step velocity head rotations [2],[4].

We also have shown that when the prosthesis was activated while the squirrel monkeys were stationary the nystagmus produce by the high tonic rate of stimulation attenuated rapidly to near normal baseline within one day, and reversed when the prosthesis was turned off. The strength of the nystagmus lessened when these on-off cycles were repeated, and the reduction in nystagmus during high-frequency electrical stimulation appeared to have components due to both adaptation and habituation [5].

Our previous studies [2],[4],[6] also examined horizontal eye movements recorded while the squirrel monkeys underwent sinusoidal rotations about an earth-vertical, yaw axis. We found that the VOR gradually increased over time and this increase was augmented by repeatedly cycling the stimulation between the off and on states. Despite the increase in gain, there was no evidence that VOR time constant increased over time. In addition to increased gain, the rotational axis of the VOR improved during chronic stimulation as did its symmetry.

Although these studies were conducted with unilateral stimulation, we also investigated bilateral stimulation. By stimulating both lateral canals simultaneously, the interaction between two stimulating electrodes either in or out of phase was determined [2]. We found that the two stimulated canals interacted in an essentially linear manner, which suggests that one advantage of a bilateral prosthesis would be to produce a larger VOR gain than a unilateral prosthesis, given the normal “push-pull” interaction noted in these bilateral studies.

The effects of a unilateral vestibular prosthesis in rhesus monkeys

In the rhesus monkey one posterior canal was stimulated with the prosthesis, and we found that the VOR gain, when rotated in the plane of the instrumented posterior canal, increased modestly in the BVH animal. Static tilt perception, measured with the SVV task, also improved during prosthetic stimulation. More specifically, for static roll tilts, the perceived tilt error (the difference between actual vertical and vertical that the rhesus monkey indicated) was close to zero for the normal state but increased substantially in the BVH state. However, when the rhesus monkey was in the BVH/stimulated state the perceived tilt error was reduced and the animal's perception of vertical became closer to normal.

In our preliminary posture experiments, the vestibular prosthesis showed only moderate effects. For quiet stance, the normal rhesus monkey showed increased trunk (roll) sway for the more difficult test conditions (i.e. foam support surface with narrow-stance width), and this sway further increased after bilateral vestibular ablation. However, in the BVH-stimulated state, there was no significant reduction in body sway. This finding could indicate that one-dimensional stimulation may not be adequate for quiet stance posture. However, prosthetic stimulation in the BVH state did result in a modest decrease in body sway for the head turn task. Lastly, roll-tilts of the platform surface using a PRTS stimulus were done for the normal rhesus monkey and will be conducted for the BVH and BVH/stimulated states. In the normal animal, trunk sway showed saturation with increasing stimulus amplitude similar to that seen in normal humans [7].

4. Discussion

Our findings demonstrate that VOR is markedly diminished in ablated monkeys but can improve when the animals receive chronic prosthetic stimulation. That is, the prosthesis was able to partially restore canal cues needed to drive a functioning VOR. Future work includes restoration of three-dimensional canal rotation cues by a three-dimensional prosthesis (i.e. electrical stimulation in each canal). The hypothesis is that the brain will utilize these three dimensional cues to restore angular VOR in three-dimensions.

Vestibular contributions to postural control and perceived head orientation appear to depend, at least in part, on the brain's estimate of the direction of the gravitational vector. While this parameter is transduced by the otoliths and other extra-vestibular graviceptors, these sensors provide information about an inherently ambiguous parameter, the vector sum of gravity and linear acceleration. There is considerable evidence that rotational information provided by the canals is used by the brain to disambiguate these gravito-inertial cues and that canal inputs thereby directly affect estimated head orientation. Eye movement studies in humans indirectly support this hypothesis, and our recent findings in rhesus monkeys confirm that estimates of head orientation, reflected in the SVV response, are directly affected by canal rotational cues. Since rotational information derived from the canals appears to directly influence estimates of head orientation, providing prosthetic rotational cues may improve the brain's ability to estimate the relative orientation of the gravitational vector in patients with deficient canal and otolith function, either directly or by synthesizing with extra-vestibular (e.g. tactile or visceral) graviceptive cues or residual otolith inputs, resulting in improved postural control and spatial orientation.

The static psychophysics results in the rhesus monkey indicated that chronic, one-dimensional stimulation can improve the perception of upright. In the BVH state, the perception of head orientation was less accurate than normal due to loss of rotational and graviceptive cues. However, the prosthetic rotational information provided to the posterior canal helped to generate a more accurate percept of head orientation. Future work includes restoration of three-dimensional canal rotation cues by a three-dimensional prosthesis and testing dynamic as well as static percepts of head orientation during roll tilt. After three-dimensional canal rotational cues are chronically re-introduced with the canal prosthesis, we hypothesize that the brain will learn to use this information to make more accurate perceptual estimates of head orientation.

For quiet stance posture, the one-dimensional prosthesis had no clear effect while sway evoked by head-turns was moderately reduced. During quiet stance, the rhesus monkey did not make large head movements and was most likely relying primarily on graviceptive (otolith) cues. For the ablated state, there was an increase in trunk roll for all test conditions due to hair cell damage of the canals and otoliths. However, it was unclear if the response was shifted towards normal when the BVH monkey was chronically stimulated with the prosthesis. Since the monkey was likely relying primarily on graviceptive cues to orient itself during this task, one hypothesis is that that the canal information provided by the prosthesis was not utilized. Also, the animal may not have had sufficient time to adapt to chronic stimulation, however, this proposition would need to be tested by determining the time course of adaptation associated with both the ablation and prosthetic stimulation. Another presumption is that there was inadequate information provided by stimulating only one canal and that a greater shift towards normal may be seen with three-dimensional stimulation. When the monkey executed larger velocity voluntary head turns towards visual targets, there was a slight reduction in body sway for the BVH/stimulated state. This could be due to the ability of the monkey to make use of the partially restored canal information.

The results for the normal rhesus monkey tested with the PRTS protocol indicated that trunk sway saturated as the amplitude of the platform tilt increased. This finding was similar to that seen in normal humans [7] and is attributed to sensory reweighting, that is, the tendency for the normal rhesus monkey to weigh vestibular cues more heavily for the larger platform tilts, orienting more towards the earth-vertical and less towards the orientation of the support surface. We hypothesize that, like vestibulopathic humans, the ablated rhesus monkey will not exhibit this same sway saturation, and thus, will have a linear relationship between platform tilt and trunk sway. The prosthesis may restore sufficient vestibular cues such that these postural responses are shifted more towards normal in the BVH/stimulated monkey.

5. Conclusions

We have shown that a vestibular prosthesis can provide meaningful stimulation of vestibular afferents in ablated non-human primates, and we observed both improvement in VOR and in percepts of head orientation. Though only modest effects on posture were observed in preliminary experiments using the one-dimensional prosthesis, the implications of these results are still being characterized. We hypothesize that the effects of a three-dimensional prosthesis on the VOR, perception, and postural control will produce greater shifts towards normal than the one-dimensional prosthesis. In summary, these studies demonstrate the potential utility of a vestibular prosthesis to improve the quality of life for human patients who have severe vestibular loss.

Acknowledgments

This work is supported by NIH/NIDCD grants DC8362 and DC3066, DC008167, and European Commission 225929.

References

1. Gong W, Merfeld DM. System design and performance of a unilateral semicircular canal prosthesis. IEEE Trans on Biomed Eng. 2002; 49(2):175–181.
2. Gong W, Haburcakova C, Merfeld DM. Vestibuloocular responses evoked via bilateral electrical stimulation of the lateral semicircular canals. IEEE Trans on Biomed Eng. 2008; 55(11):2608–2619.
3. Lewis RF, Haburcakova C, Merfeld DM. Roll tilt psychophysics in Rhesus monkeys during vestibular and visual stimulation. J Neurophysiol. 2008; 100:140–153. [PubMed: 18417632]
4. Lewis RF, Haburcakova C, Gong W, Merfeld DM. Vestibuloocular reflex adaptation investigated with chronic motion-modulated electrical stimulation of semicircular canal afferents. J Neurophysiol. 2010; 103:1066–1079. [PubMed: 20018838]
5. Merfeld DM, Gong W, Morrissey J, Saginaw M, Haburcakova C, Lewis RF. Acclimation to chronic constant-rate peripheral stimulation provided by a vestibular prosthesis. IEEE Trans on Biomed Eng. 2006; 53(11):2362–2372.
6. Merfeld DM, Haburcakova C, Gong W, Lewis RF. Chronic vestibulo-ocular reflexes evoked by a vestibular prosthesis. IEEE Trans on Biomed Eng. 2007; 54(6):1005–1015.
7. Peterka RJ. Sensorimotor Integration in Human Postural Control. J Neurophysiol. 2008; 88(3): 1097–1118. [PubMed: 12205132]