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Orientation adaptation of eye movement–related vestibular neurons due to prolonged head tilt

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Abstract

Sixteen neurons, including vestibular-only (VO), eye–head velocity (EHV), and position–vestibular-pause (PVP) neurons sensitive to head tilt were recorded in the rostromedial and in superior vestibular nuclei. Projection of the otolith polarization vector to the horizontal plane (response vector orientation [RVO]) was determined before and after prolonged head orientation in side-down position. The RVO of VO neurons shifted toward alignment with the axis of gravity when the head was in the position of adaptation. PVP neurons had similar changes in RVO. There were also changes in RVO in some EHV neurons, but generally in directions not related to gravity. Modeling studies have suggested that the tendency to align RVOs with gravity leads to tuning of gravity-dependent angular vestibular ocular reflex (aVOR) gain changes to the position of adaptation. Thus, coding of orientation in PVP neurons would contribute significantly to the gravity-dependent adaptation of the aVOR.

Keywords

adaptation; monkey; VOR; gravity

Introduction

Work on the adaptation of the gain of the angular vestibular ocular reflex (aVOR) has shown that head orientation relative to gravity during adaptation is an important context for how changes in gain are distributed as a function of head position.^{1–5} For example, when the horizontal aVOR gain is decreased while left side down (LSD), the maximal gain changes occur in LSD. As the head is reoriented toward right side down (RSD), the gain changes are gradually decreased and the gain of the aVOR returns to normal. How these changes are coded centrally is still not known, but, it is necessary to understand this mechanism because of the way in which central canal-related neurons code the otolith input.

Sensitivity of the primary otolith afferent can be uniquely described by a single polarization vector,^{6,7} which can be estimated by a response vector orientation (RVO), which is a projection of the polarization vector to the horizontal plane.⁸ Central vestibular neurons

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Conflicts of interest

The authors have no conflicts of interest to declare.

receive convergent inputs from several otolith afferents, which make their RVO uncertain^{9–11} and subject to adaptation.

We recently demonstrated that RVO adaptation occurs after prolonged (two hours) side-down tilts in canal-related central vestibular-only neurons (VO).¹² This orientation adaptation did not occur in otolith-only related neurons,¹³ indicating that otolith-related signals are processed differently by canal-related and otolith-only neurons, whereas both may receive otolith-related inputs from multiple primary afferents. The purpose of this study was to determine whether vestibular neurons, which project to oculomotor nuclei, and, therefore, are neurons of the aVOR loop, also have orientation adaptation.

Methods

Experiments were performed in three cynomolgus monkeys (*Macaca fascicularis*). The experiments conformed to the guide for the care and use of laboratory animals and were approved by the Institutional Animal Care and Use Committee. Surgical procedures were performed under anesthesia and in sterile conditions. Procedures were performed in two stages. First, a head mount was implanted on the skull to provide painless head fixation in stereotaxic coordinates during testing.¹⁴ At a second surgery, two three-turn coils were implanted on the left eye. One coil measured the horizontal and vertical components of eye position. Another coil, placed approximately orthogonal to the frontal coil, was used to measure the torsional component of eye position.⁴ Units were recorded by varnish-coated 80- μ m-tungsten electrodes in rostral medial vestibular and superior vestibular nuclei.^{12,15} Canal-related inputs were determined by oscillation of the animal about spatial vertical or horizontal axes, with various orientation of the animal to the axis of oscillation.¹⁶ Sensitivity to static tilt was determined by tilting the animal by 30° about the spatial horizontal axis for 40 seconds and then returning it back to upright. The animal orientation in yaw was changed by 15° and the tilt was repeated. Each unit was tested with yaw orientation during tilt varying over 180°. The firing rate during the last 20 seconds of tilt was measured.

The orientation of equivalent acceleration of gravity in head coordinates ($\hat{a}_g$) was determined for each tilt as shown in Figure 1(A: insets). When the animal is tilted backward, $\hat{a}_g = 0^\circ$ (along the occipito-nasal axis); when tilted RSD, $\hat{a}_g = 90^\circ$ (along the intro-aural axis); when tilted nose down, $\hat{a}_g = 180^\circ$; and in LSD, $\hat{a}_g = 270^\circ$. The firing rate was plotted as a function of $\hat{a}_g$. Maximal sensitivity ($S_{\max} = \text{RVO}$) was the peak value of the cosine fit to the data.^{8,12} If the lateral canal-related input was dominant, the animal was placed side-down and the horizontal aVOR was decreased for two hours. If the vertical canal-related input dominated, then the vertical aVOR was adapted in side-down position. It was previously demonstrated that side-down positioning rather than adaptation of the aVOR was a driving force for orientation adaptation of VO neurons.¹² We assumed that orientation adaptation of the other neuronal classes was similarly accomplished due to head orientation.

The RVOs determined before and after adaptation were compared. For neurons that have eye position sensitivity, the sensitivity was determined using multiple linear regression (MLR) and subtracted from the neuronal instantaneous frequency. Periods when firing rate declined to zero because of eye movements in the inhibitory direction were detected and eliminated from further analyses. Saccades were determined using a maximal likelihood algorithm,¹⁷ and intersaccadic intervals were also eliminated from the analyses.

EHV or PVP neurons were classified based on previous descriptions.^{18,19} EHV neurons had sensitivity to eye and head velocity in the same direction. They burst with saccades in one direction and paused with saccades in the alternate direction. PVP neurons respond to eye and head velocity in the alternate direction. PVP may pause during saccades in a particular

direction. Some EHV and PVP neurons had eye position sensitivity in the same direction as eye velocity sensitivity.

Results

All eight PVP neurons received convergent input from the vertical canals: five from the ipsilateral and three from the contralateral side. Five (5/8) PVP neurons also received convergent input from the lateral canal: four from ipsilateral and one from the contralateral side. Two (2/4) VO neurons received vertical canal-related input from the ipsilateral side. Lateral canal-related inputs were seen in all four neurons (three contralateral, one ipsilateral). Three (3/4) EHV neurons received vertical canal-related input: one from ipsilateral and two from the contralateral side. All the EHV neurons had convergent input from either ipsilateral (2/4) or contralateral (2/4) lateral canals.

Sensitivity changes of typical PVP neurons for static tilt is shown in Figure 1. Before adaptation, the maximal sensitivity ($38.7 \text{ imp}^*/\text{s/g}$) occurred when $\hat{a}_g = 198^\circ$ (Fig. 1A). This is indicated by a gray vertical line. Thus, the RVO of this neuron was 198° before orientation adaptation (Fig. 1A, open symbols) and changed to 144° (black vertical line) after two hours of being RSD. The RVO had maximal sensitivity of $17.5 \text{ imp}^*/\text{s/g}$. In spatial coordinates, the RVO was 108° from $\hat{a}_g$ before adaptation (Fig. 1B, gray arrow), but only 54° after adaptation (Fig. 1B, black arrow). The same neuron is shown in Figure 2A-5. Changes in RVO of the other PVP neuron were even larger with the same tendency to align RVO with acceleration of gravity in position of adaptation (Fig. 2A-2). Changes were observed in the other six recorded PVP neurons, which had a tendency to align with the positive or negative axis of gravity (Fig. 2A). Similar orientation adaptation was also observed in four VO neurons (Fig. 2B).

Different patterns of orientation adaptation were observed for EHV neurons (Fig. 2C). One unit (Fig. 2C-1) had its RVO align with $\hat{a}_g$ after adaptation. A second unit (Fig. 2C-2) had its RVO orthogonal to $\hat{a}_g$ before adaptation, but changes in RVO overshoot $\hat{a}_g$ after adaptation. A third unit had no changes in RVO (Fig. 2C-3). A fourth unit had its RVO aligned with $\hat{a}_g$ before but not after adaptation. On average, the angular displacement of the RVO from the axis of gravity for PVP neurons was 83° before adaptation, but only 24° after adaptation ($P = 0.005$). For VO neurons, it was 78° before and only 17° after adaptation. For both groups, these changes in orientation were significant ($P = 0.003$). For EHV neurons, however, the angular displacement of the RVO from $\hat{a}_g$ did not change significantly (76° before and 72° after adaptation; $P = 0.905$).

There were some changes in sensitivity to tilt after adaptation in all neuronal classes, increasing in some neurons and decreasing in other neuron classes. On average, sensitivity to tilt of PVP neurons before and after adaptation was $20.4 \pm 10.4 \text{ imp}^*/\text{s/g}$ and $16.2 \pm 9.9 \text{ imp}^*/\text{s/g}$, respectively ($P = 0.42$). Average sensitivity to tilt of VO neurons was $25.2 \text{ imp}^*/\text{s/g}$ before and $17.4 \text{ imp}^*/\text{s/g}$ after adaptation ($P = 0.23$). Average sensitivity of EHV neurons was $25.2 \text{ imp}^*/\text{s/g}$ before adaptation and $17.4 \text{ imp}^*/\text{s/g}$ after adaptation ($P = 0.43$).

Discussion

This study demonstrates that, similar to VO neurons,¹² PVP neurons with static otolith sensitivity change their RVO toward direction of $\hat{a}_g$ in the position of adaptation. The angular changes of the RVO were comparable to those obtained for VO neurons.¹² In contrast, changes in RVO of EHV neurons, even when they occurred on average, were unrelated to $\hat{a}_g$ in the position of adaptation.

Previous studies of gain changes of the aVOR after adaptation in tilted positions have identified two components of adaptation: a global component, which is independent of head position, and a localized component, which is maximal in the position of adaptation and is decreased for other head orientations.^{2–4,20} We have modeled the gravity-dependent adaptation with a neural net²¹ that incorporates these features. Further studies showed that the tuning was dependent on the oscillation amplitude with regard to gravity; small amplitudes produced sharp tuning, whereas the tuning became wider when the amplitude of head oscillation with regard to gravity increased.²² Preliminary modeling studies indicate that orientation adaptation could be responsible for tuning of aVOR gain changes to the position of adaptation and regulating the coordination of the gravity-independent and gravity-dependent components.²³ We have extended this model by incorporating neurons that adapt their polarization vector orientation, and simulations show that they play a critical role in the coordination of the two components of aVOR gain adaptation.²³ Thus, our model predicts that central vestibular neurons change their sensitivity such that their RVO adapts toward the direction of $\hat{a}_g$, which would contribute to gravity-dependent adaptation.

This study shows that PVP neurons contribute to gravity-dependent adaptation by changing the orientation of their polarization vectors. Previously, we had shown that their sensitivity also varies in association with aVOR gain as the head is moved away from the position of adaptation, indicating that these neurons also code the gravity-dependent component of aVOR adaptation.²⁴ In contrast, changes in sensitivity of EHV neurons were similar in all head orientations,²⁴ and their RVOs were not altered in specific relation to gravity. Thus, PVP neurons could be associated with the neural net elements that are involved with the governing of orientation adaptation and the gravity-dependent component of adaptation. EHV neurons could be the neurons that produce the gravity-independent component of aVOR adaptation.

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References

1. Yakushin SB, Raphan T, Cohen B. Context-specific adaptation of the vertical vestibuloocular reflex with regard to gravity. *J Neurophysiol.* 2000; 84:3067–3071. [PubMed: 11110833]
2. Yakushin SB, Bukharina SE, Raphan T, et al. Adaptive changes in the angular VOR: duration of gain changes and lack of effect of nodulo-uvulectomy. *Ann NY Acad Sci.* 2003; 1004:78–93. [PubMed: 14662450]
3. Yakushin SB, Palla A, Haslwanter T, et al. Dependence of adaptation of the human vertical angular vestibulo-ocular reflex on gravity. *Exp Brain Res.* 2003; 152:137–142. [PubMed: 12879171]
4. Yakushin SB, Raphan T, Cohen B. Gravity specific adaptation of the vertical angular vestibulo-ocular reflex—dependence on head orientation with regard to gravity. *J Neurophysiol.* 2003; 89:571–586. [PubMed: 12522203]
5. Yakushin SB, Xiang Y, Raphan T, Cohen B. The role of gravity in adaptation of the vertical angular vestibulo-ocular reflex. *Ann NY Acad Sci.* 2005; 1039:97–110. [PubMed: 15826965]
6. Fernandez C, Goldberg JM. Physiology of peripheral neurons innervating otolith organs of the squirrel monkey. I. Response to static tilts and to long duration centrifugal force. *J Neurophysiol.* 1976; 39:970–984. [PubMed: 824412]
7. Fernandez C, Goldberg JM, Abend WK. Response to static tilts of peripheral neurons innervating otolith organs of the squirrel monkey. *J Neurophysiol.* 1972; 35:978–997. [PubMed: 4631840]
8. Schor RH, Miller AD, Tomko DL. Responses to head tilt in cat central vestibular neurons. I. Direction of maximum sensitivity. *J Neurophysiol.* 1984; 51:136–146. [PubMed: 6319622]

9. Angelaki DE. Spatio-temporal convergence (STC) in otolith neurons. *Biol Cybern.* 1992; 67:83–96. [PubMed: 1606247]
10. Angelaki DE, Dickman JD. Spatiotemporal processing of linear acceleration: primary afferent and central vestibular neuron responses. *J Neurophysiol.* 2000; 84:2113–2132. [PubMed: 11024100]
11. Dickman JD, Angelaki DE. Vestibular convergence patterns in vestibular nuclei neurons of alert primates. *J Neurophysiol.* 2002; 88:3518–3533. [PubMed: 12466465]
12. Eron JN, Cohen B, Raphan T, Yakushin SB. Adaptation of orientation vectors of otolith-related central vestibular neurons to gravity. *J Neurophysiol.* 2008; 100:1686–1690. [PubMed: 18497367]
13. Eron JN, Cohen B, Raphan T, Yakushin SB. Adaptation of orientation of central otolith-only neurons. *Ann NY Acad Sci.* 2009; 1164:367–371. [PubMed: 19645928]
14. Yakushin SB, Reisine H, Büttner-Ennever J, et al. Functions of the nucleus of the optic tract (NOT). I. Adaptation of the gain of the horizontal vestibulo-ocular reflex. *Exp Brain Res.* 2000; 131:416–432. [PubMed: 10803411]
15. Yakushin SB, Raphan T, Büttner-Ennever JA, et al. Spatial properties of central vestibular neurons of monkeys after bilateral lateral canal nerve section. *J Neurophysiol.* 2005; 94:3860–3871. [PubMed: 15987758]
16. Yakushin SB, Raphan T, Cohen B. Spatial properties of central vestibular neurons. *J Neurophysiol.* 2006; 95:464–478. [PubMed: 16192336]
17. Singh, A.; Thau, GE.; Raphan, T.; Cohen, B. Detection of saccades by a maximum likelihood ratio criterion. *Proceedings of the 34th Ann. Conf. Eng. Biol;* Houston, TX. 1981.
18. Scudder CA, Fuchs AF. Physiological and behavioral identification of vestibular nucleus neurons mediating the horizontal vestibuloocular reflex in trained rhesus monkeys. *J Neurophysiol.* 1992; 68:244–264. [PubMed: 1517823]
19. Tomlinson RD, Robinson DA. Signals in vestibular nucleus mediating vertical eye movements in the monkey. *J Neurophysiol.* 1984; 51:1121–1136. [PubMed: 6737024]
20. Yakushin SB, Xiang Y, Raphan T, Cohen B. Spatial distribution of gravity dependent gain changes in the vestibulo-ocular reflex. *J Neurophysiol.* 2005; 93:3693–3698. [PubMed: 15689386]
21. Xiang Y, Yakushin SB, Cohen B, Raphan T. Modeling gravity-dependent plasticity of the angular vestibulo-ocular reflex (aVOR) with a physiologically-based neural network. *J Neurophysiol.* 2006; 96:3349–3361. [PubMed: 16971684]
22. Storozh O, Xiang Y, Raphan T, et al. Spatial distribution of gravity-dependent gain changes in the angular VOR (aVOR) induced by oscillation at different amplitudes. *Soc Neurosci Abstr.* 2005; 35:391.
23. Xiang Y, Yakushin SB, Cohen B, Raphan T. Modeling the effects of large amplitude gravity-dependent gain adaptation of the angular vestibulo-ocular reflex (aVOR). *Ass Res in Otolaryngol.* 2011; 34:336.
24. Kolesnikova OV, Raphan T, Cohen B, Yakushin SB. Coding of gravity-dependent and -independent adaptation of the angular vestibulo-ocular reflex (aVOR) by central vestibular eye movement-related neurons. *Ass Res Otolaryngol.* 2011; 34:337.

Figure 1.

Determining RVO before and after prolonged head orientation RSD. (A) Neuronal sensitivity obtained from PVP neuron before (open symbols) and after (filled symbols) a head orientation RSD for two hours. Sensitivities (ordinate) were plotted as a function of direction of acceleration of gravity in head coordinates (abscissa). Dashed and solid curves are cosine fit through the data. Vertical lines are plotted through the peak fitted values obtained before (gray) and after (black) adaptation. Insets below approximate head orientation for corresponding accelerations of gravity. (B) Polar plot for RVO obtained for the neuron shown in (A) before (gray arrow) and after (black arrow) orientation adaptation.

Figure 2.

Representative changes in RVO after orientation adaptation for PVP (A), VO (B), and EHV (C) neurons. RVO's before adaptation are shown by gray arrows and after adaptation by black arrows.