Keeping balance in space

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Introduction

On earth integration of sensory information from the vestibular system, the optokinetic system and the proprioceptors is necessary to maintain balance and a stable retinal image ("multisensory integration" hypothesis). In space the sensory information provided by the otolith organs is absent or very small due to the lack of gravity (microgravity). Here, on earth, we studied the influence of gravity and the consequences of gravity perception loss on eye movements using a mutant mouse lacking otoconia, which serve as the gravito-inertial loading of the otolith organs (*tilted* mouse, *tlt*).

These mice provide us with a model that allows us to study the interaction between inputs from otolith, semicircular canals and the retina in the control of eye movements.

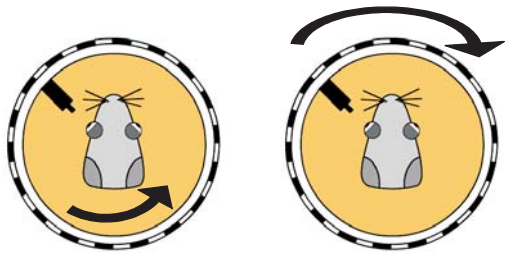
Methods

Thirteen *tlt* mice and seventeen control mice, identified by using the swimming behavioral test, were used in this study. Eye movements were induced either vestibularly by rotating the mouse in the dark (Fig. 1A) or optokinetically (Fig. 1B). These stimuli were delivered at frequencies between 0.2 and 1 Hz with amplitudes of ± 5 degrees. The induced eye movements were recorded with the video eye-tracking device of Chronos Vision. Various paradigms were used to dynamically stimulate only the semicircular canals (yaw VOR - Fig. 2A and vertical roll VOR - Fig. 2B) or both the otolith organs and the semicircular canals (horizontal roll VOR - Fig. 2C). Static stimulation of the otolith organs was elicited by positioning the mouse at different roll angles. Furthermore, semi-thick slices of otolith organs were cut to investigate otoconia and hair cells of control and *tlt* mice.

Figure 1

A
Vestibulo-ocular reflex

B
Optokinetic reflex



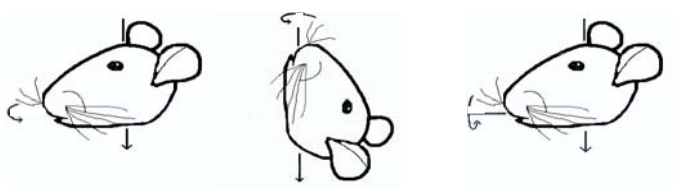
Video eye movement recording apparatus with table rotating sinusoidally during vestibular stimulation and drum rotating sinusoidally during optokinetic stimulation.

Figure 2

A
Yaw (Y)

B
Vertical roll (Rv)

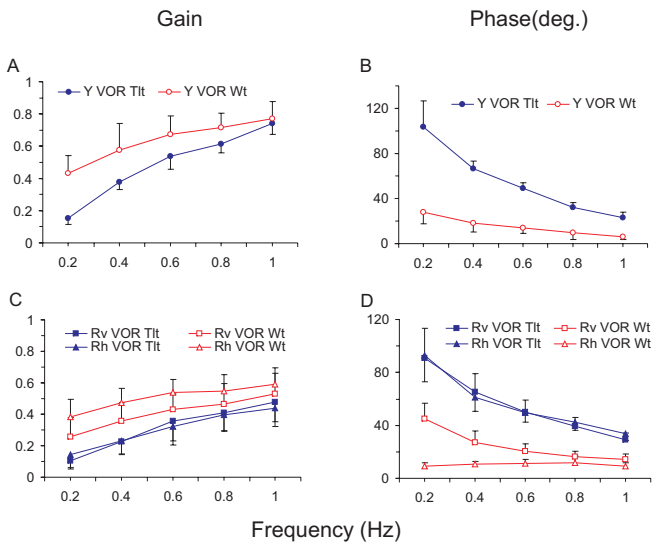
C
Horizontal roll (Rh)



Paradigms used during eye movement recordings. In yaw and vertical roll paradigms only the semicircular canal are dynamically stimulated, whereas in horizontal roll the semicircular canals and otolith organs are dynamically stimulated.

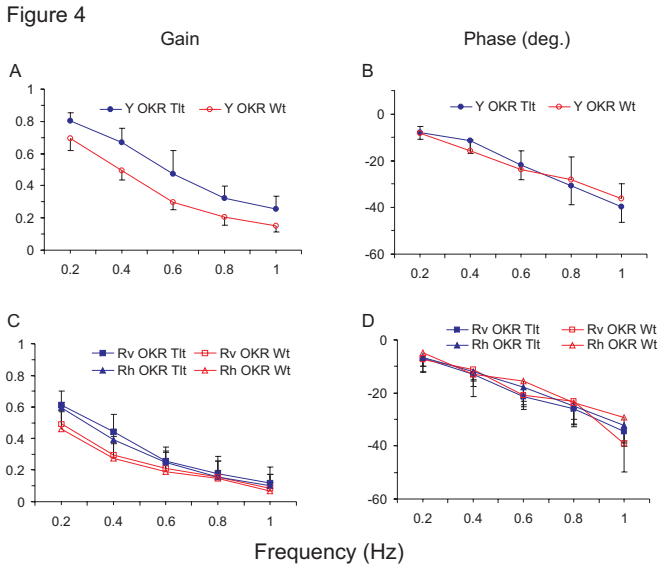
Results

Figure 3



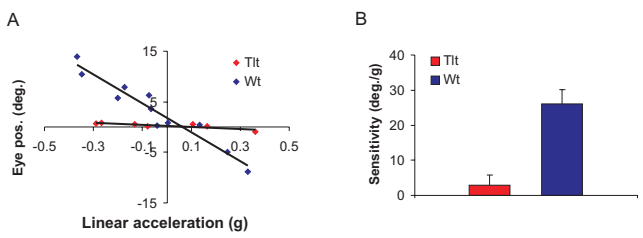
Canals mediated VOR and canals-otoliths mediated VOR. The tlt mice showed significantly lower canals mediated VOR gains (yaw - Fig. A and vertical roll - Fig. C) and significantly lower canals-otolith mediated VOR (horizontal roll - Fig. C) compared to the control mice. In all paradigms VOR phases in tlt mice were significantly higher than in control mice (Fig. B and D). In tlt mice no significant differences could be found between horizontal and vertical rolls. Although, in control mice significant differences were found between these two stimuli.

Figure 4



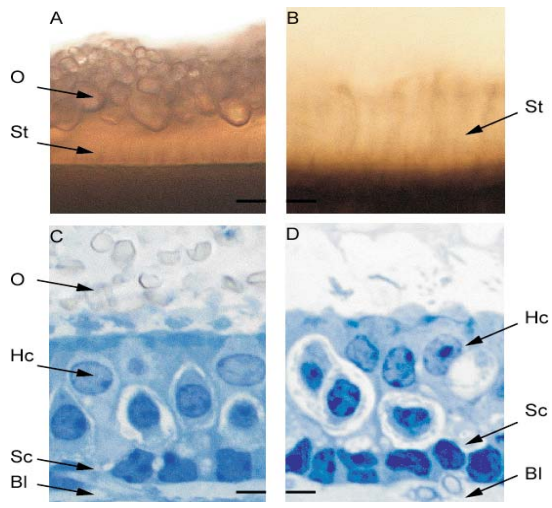
Compensatory optokinetic eye movement response. In all paradigms tested tlt mice showed significantly higher OKR gains (Fig. A and C) compared to the control mice. There were no significant differences in OKR phases between the two groups of mice (Fig. B and D).

Figure 5



Eye movement sensitivity to static roll. The eye position in respect to the head of the mouse is plotted against the sine of the roll angle (represents the linear acceleration along the interaural axis). The tlt mice showed almost no response during static roll stimulation (Fig. A). The eye movement sensitivity (degrees/g) was significantly lower in the tlt mice compared to the control mice (Fig. B) indicating that these mice do not have functional otolith organs.

Figure 6



Microscope images of whole mounts and semi-thick utricular macula. In control mice (Fig. A) there is a thick layer of otoconia (O) over the stereocilia (St) of the hair cells. In tlt mice (Fig. B) hair cells can be clearly seen, but there are no otoconia over the sensory epithelium. In semi-thick section the hair cells (Hc), supporting cells (Sc) and basal lamina (Bl) of the tlt mice (Fig. D) look similar to those of control mice (Fig. C). These results are in agreement with previous studies. Bar:10 µm.

Conclusions

- Otolith stimulation increases the gain values and decreases the phase lead of the VOR.
- *Tlt* mice compensate the lack of otoconia by increasing the gain of the OKR. The increased OKR gain is a frequency dependent compensatory mechanism, which is not influenced either by the position of the mouse or by the eye movement plane.
- These data support the "multisensory integration" hypothesis. This study clearly reveals that there is a functional synergy in the processing of otolith and optokinetic signals regarding the gravito-inertial acceleration. This mechanism might also be important for maintaining balance and stable retinal images in space.

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Photo credit: NASA

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