THE VESTIBULO-OCULAR REFLEX OF HYPERGRAVITY RATS

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INTRODUCTION The vertebrate vestibular system detects linear (otolith organs) and angular (semicircular canals) acceleration. The function of the otolith system is twofold, 1: perception of linear acceleration of the head, and 2: assessment of the spatial orientation of the head relative to the vector of gravity. Because of the latter function, a change of gravity will affect the vestibular input which, in turn, may have a wide range of serious physiological effects, for instance on ocular reflexes. The function of the vestibulo-ocular reflex (VOR) is to stabilize the visual image on the retina. Measurement of this VOR provides a method to investigate the (processing within the) vestibular system.

Discrimination between gravity and linear acceleration, caused by movement of the head, is not possible. Therefore, information from the otolith system must be constantly compared with additional information from other sensory systems in order to solve the inherent ambiguity between tilt and translation. In this processing, cues from the semicircular canals also play a role.

During parabolic flight, experiments can be performed at altered gravity levels for brief periods of time. On earth, the only effective possibility to manipulate gravity for longer periods of time is a centrifuge. Together with experiments in weightlessness during orbital flight, these methods form useful tools to investigate the influence of gravity on physiology. In our laboratory, rats have been kept inside a centrifuge at 2.5g during their entire life-span (i.e. including gestation).

EXPERIMENTS The horizontal component of the VOR has been measured from immobilized rats spending their entire life-span, including gestation, at a hypergravity (HG) level of 2.5g, and from controls living at normal gravity (NG). Eye position was recorded (under IR illumination) in response to a horizontal rotatory stimulus while the vertical acceleration component (gravity) was varied. Measurements were made under normal gravity, and on board of an airplane at 0 and 1.8g during parabolic flight. Horizontal rotation was applied either as an angular velocity step (from 90?/s to standstill in one second after 60 s of constant velocity), or as a sinusoidal oscillation (f=1/6 Hz, amplitude=90?; or f=1/12 Hz, amplitude=180?).

Angular displacement of the eye between the start of deceleration at t=1s and t=4s was determined (Fig. 1). The average response of HG rats to such a velocity step was 2.9?1.7? versus 13.1?5.6? for NG rats (p<0.005).

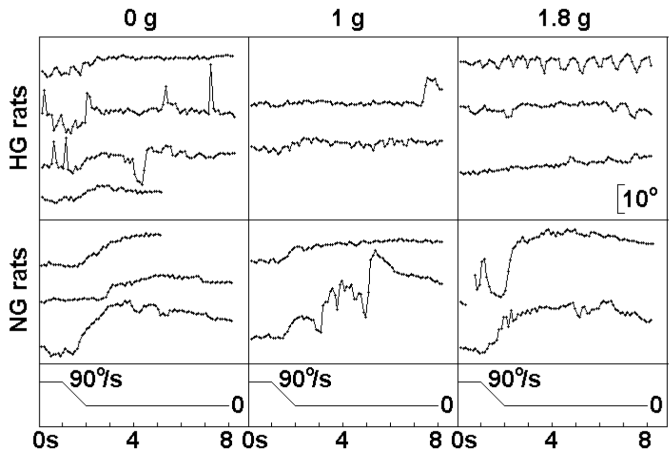

Figure 1: Horizontal eye movement in response to a velocity step at three different gravity levels of a number of HG and NG rats. Responses of HG rats are smaller.

When stimulated with an oscillating horizontal rotation, the VOR of HG rats was also reduced (Fig. 2). Gain (i.e. the ratio of response and stimulus amplitude) of HG rats is 0.078?0.035 (mean?SD) versus 0.141?0.062 for NG animals (p<0.05). The phase of the response is shifted by -40? (p<0.005).

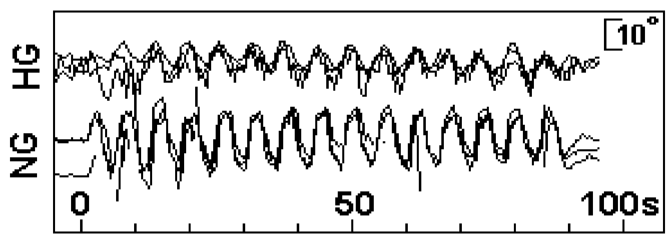

Figure 2: Horizontal compensating eye movements (at 1g). Responses of 3 HG and 3 NG rats to slow sinusoidal oscillation (f=1/6 Hz; stimulus not shown) have been superimposed. Responses of HG rats are smaller and shifted in phase by ?40?.

Modulation of the horizontal VOR by vertical acceleration components has been shown to be species dependent (4). Therefore, we have also measured the VOR of rats during parabolic flight. Modulation of the horizontal VOR was observed only in the response of HG rats which appeared to be reduced during 1.8g (10). Sometimes, NG rats showed a small nystagmus superimposed to their sinusoidal eye response; the response of HG rats never showed a nystagmus.

DISCUSSION Immobilized animals are easily startled by external disturbances causing blinking, closing of the eye, or sudden voluntary eye movements. Because anticipation of a velocity step by the animal is impossible, discrimination between vestibular-induced and other eye movements is difficult. Also, a velocity step is always preceded by a long period of constant velocity (allowing adaptation of the semicircular canal system). During parabolic flight, therefore, this type of stimulus appears an inefficient use of the available time. Continuous stimulation (e.g. with sinusoidal oscillation) proved to be more efficient.

Ontogenetic development of the vestibular system at 2.5g does not result in a complete loss of vestibular functioning. Even development at 0g appears to have relatively moderate effects on the peripheral vestibular sensory organs (5).

However, an altered gravity level during gestation has significant effects on vestibular-related behaviour (6,8,9). The present study shows that vestibular induced compensatory eye reflexes are also affected by the gravity level during development. Probably, these changes with respect to behaviour and compensatory eye movements mainly find their origin in some sort of neurological adaptation. Structural neuronal effects of altered gravity have been reported for the number of synapses on the otolith organs (7), and in the vestibular nucleus (1,3). These modifications will not leave subsequent integration processes which lead to particular reflexes or behaviour unaffected. Depending on the plasticity of a specific system, these modifications may be irreversible or not.

During prenatal development, the initial neuronal connections between vestibular sensory system and the oculomotor system are established (2). Only when the eyes open (12-16 days after birth), vestibular induced oculomotor activity can be optimized for its function of stabilizing images on the retina by visual feedback. This postnatal maturation of the VOR will also be affected by the conditions within a centrifuge. These conditions also include the Coriolis forces which the animals experience when they move freely around. For the effect of altered gravity conditions on ocular reflexes, most questions with respect to plasticity of the system and the occurrence of critical periods during development still remain unanswered.

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REFERENCES

1. Bruce LL, B Fritzsch. The development of vestibular connections in rat embryos in microgravity. J Gravit Physiol 4: P59-62, 1997.
2. Curthoys IS. The vestibulo-ocular reflex in newborn rats. Acta Otolaryngol 87: 484-489, 1979.
3. Johnson JE, WR Mehler, J Oyama. The effects of centrifugation on the morphology of the lateral vestibular nucleus in the rat: a light and electron microscopic study. Brain Res 106: 205-221, 1976.
4. de Jong HAA, WJ Oosterveld. Rotation test in the weightless phase of parabolic flight. Aviat Space Environ Med Suppl 58: A253-A256, 1987.
5. Lychakov DV. Structure of vestibular receptor-organs and animal behavior in microgravity. J Evol Biochem Physiol 34: 364-385, 1998.
6. Ronca AE, JR Alberts. Effects of prenatal spaceflight on vestibular responses in neonatal rats. J Appl Physiol 89: 2318-2324, 2000.
7. Ross MD. Morphological changes in rat vestibular system following weightlessness. J Vestib Res 3: 241-251, 1993.
8, Sondag HNPM, HAA de Jong, WJ Oosterveld. Altered behaviour in hamsters conceived and born in hypergravity. Brain Res Bull 43: 289-294, 1997.
9. Wubbels RJ, HAA de Jong. Vestibular induced behaviour or rats born and raised in hypergravity. Brain Res Bull, 52: 349-356, 2000.
10. Wubbels RJ, HAA de Jong. The horizontal vestibulo-ocular reflex of hypergravity rat at different gravity levels. Neurosci Lett, 303: 5-8, 2001.