THE USE OF ALTERED GRAVITY AS A TOOL TO UNDERSTAND NEUROVESTIBULAR MECHANISMS IN VERTEBRATES

R. Boyle, Y. Popova, and J. Varelas
NASA Ames Research Center, Moffett Field, CA 94035 USA.

Vertebrates sense gravito-inertial acceleration by mechanoreceptors (hair cells) in the otolith structures of the inner ear. These structures consist of ciliated sensory hair cells surmounted by biomineral grains of calcium carbonate ($CaCO_3$) called otoconia that provide mechanical loading of hair cell cilia. Changes in their high density can alter the hair cells' sensitivity to acceleration and orientation with respect to gravity. A widely considered mechanism by which the animal responds to a chronic change in amplitude of gravity is a change in weight-lending otoconia. Hair cells are synaptically coupled to the vestibular nerve afferents that convey the signals into the brain. Synapses are modifiable in strength and numbers, and thereby can be an additional target to adjust the sensation as the gravity load changes. Here, we present the results obtained in 2 species exposed both to µG and HG. Adult toadfish, *Opsanus tau*, were exposed to µG in 2 short-duration shuttle missions and to 1.4 – 2.24G [resultant] centrifugation for 1-32 days; re-adaptation was studied following 1-8 days after return to 1G. Results show a biphasic pattern in response to 2.24G: initial hypersensitivity, similar to that observed after µG exposure, followed by transition to a significant decrease at 16-32 days. Recovery from HG exposure is ~ 4-8 days. Two major pieces of information are still needed: vertebrate hair cell response to altered gravity and impact of longer duration exposures on sensory plasticity. To address the latter we applied electron microscopic techniques to image otoconia mass obtained from 1) mice subjected to 91-days of weightlessness in the Mouse Drawer System (MDS) flown on International Space Station, 2) mice subjected to 91-days of 1.24G centrifugation on ground, and 3) mice flown on 2 short-duration orbital missions. Images indicate a clear restructuring of individual otoconia, suggesting deposition to the outer shell. Images from their HG counterparts indicate the converse - an ablation of the otoconia mass. For shorter duration exposures to weightlessness on 13-day shuttle missions mice otoconia appear normal. Despite the permanence of 1G in evolution the animal senses exposure to a novel, non-1G, environment and adaptive mechanisms are initiated - in the short term compensation is likely confined to the peripheral sensory receptors, the brain or both. For longer exposures structural modifications of the endorgan may also result.

In µG, it is argued, the organism counters the loss of gravity by increasing $CaCO_3$ production, thereby increasing otolith mass, as a means to increase "system gain". In hypergravity (HG), the converse is argued. Here, we present the results obtained in 3 species exposed both to µG and HG. Adult toadfish, *Opsanus tau*, were exposed to µG in 2 short-duration shuttle missions and to 1.24 – 1.73G centrifugation for 1-32 days; re-adaptation was studied following 1-8 days of 1G. Results show a biphasic pattern in response to 1.73G: initial hypersensitivity, similar to that observed after µG exposure, followed by transition to a significant decrease at 16-32 days. Recovery from HG exposure is ~ 4-8 days. Next, we examined directly the responses of statocyst receptors in the land snail after exposure to μG on two unmanned Russian Orbital missions and at 1.24G. Similar to vertebrate afferents snail receptors increased their sensitivity to tilt after μG exposure, and decrease it after 16-32 days of HG. Two major pieces of information are still needed: vertebrate hair cell response to altered gravity and impact of longer duration exposures on sensory plasticity. To address the latter we applied electron microscopic techniques to image otoconia mass obtained from 1) mice subjected to 91-days of weightlessness in the Mouse Drawer System (MDS) flown on International Space Station, 2) mice subjected to 91-days of 1.24G centrifugation on ground, and 3) mice flown on 2 short-duration orbital missions. Images indicate a clear restructuring of individual otoconia, suggesting deposition to the outer shell. Images from their HG counterparts indicate the converse - an ablation of the otoconia mass. For shorter duration exposures to weightlessness on 13-day shuttle missions mice otoconia appear normal. Despite the permanence of 1G in evolution the animal senses exposure to a novel, non-1G, environment and adaptive mechanisms are initiated - in the short term compensation is likely confined to the peripheral sensory receptors, the brain or both. For longer exposures structural modifications of the endorgan may also result.

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