# Just two weeks in orbit causes changes in eyes

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Animal Enclosure Modules similar to the one shown here, being inspected by Mission Specialist Tracy Caldwell, Ph.D., and Pilot Charles Hobaugh aboard Space Shuttle Endeavor (STS-118), are used to study animals in low gravity conditions. Scientists are reporting mice traveling aboard STS-133 showed evidence of ocular nerve damage and changes in eye gene expression. Credit: NASA

Just 13 days in space may be enough to cause profound changes in eye structure and gene expression, report researchers from Houston

Methodist, NASA Johnson Space Center, and two other institutions in the October 2013 issue of *Gravitational and Space Research*.

The study, which looked at how low gravity and radiation and oxidative damage impacts mice, is the first to examine eye-related gene expression and cell behavior after spaceflight.

"We found many changes in the expression of genes that help cells cope with oxidative stress in the retina, possibly caused by radiation exposure," said Houston Methodist pathologist Patricia Chévez-Barrios, M.D., the study's principal investigator. "These changes were partially reversible upon return to Earth. We also saw optic nerve changes consistent with mechanical injury, but these changes did not resolve. And we saw changes in the expression of DNA damage repair genes and in apoptotic pathways, which help the body destroy cells that are irreparably damaged."

Since 2001, studies have shown astronauts are at increased risk of developing eye problems, like premature age-related macular degeneration. Experts suspect the cause is low gravity, heightened exposure to solar radiation, or a combination of the two.

In Nov. 2011, a NASA-sponsored Ophthalmology study of seven astronauts showed that all seven had experienced eye problems after spending at least six months in space. Doctors saw a flattening of the back of the eyeball, folding of the choroid (vascular tissue behind the retina), excess fluid around and presumed swelling of the optic nerve, or some combination of these.

High-energy radiation from the Sun can cause nasty, extremely damaging chemical reactions in cells, collectively called oxidative stress. Earth's atmosphere reflects or absorbs much of this radiation and is, ironically, a much better shield than the thick metal hulls of space

shuttles and the International Space Station.

Damage to eyes isn't merely a long-term health issue for some astronauts back on Earth—it could interfere with future missions in which any loss of focus or vision makes it difficult for humans to complete long missions, such as round-trip travel to Mars (12 to 16 months) or to the moons of Jupiter (about two years). If both radiation exposure and gravity loss are to blame, one solution to save astronauts' eyes might be a spacecraft with a more protective hull and inside, a spinning hamster wheel that simulates gravity similar to those envisioned by futurist author Arthur C. Clarke and realized in Stanley Kubrick's film, 2001: A Space Odyssey.

To determine the impact of radiation exposure on eyes, Chévez-Barrios and lead author Susana Zanello, Ph.D., a space life scientist at NASA Johnson Space Center, examined mouse retinal gene expression on the 1st, 5th, and 7th days following a 13-day trip aboard space shuttle Discovery (STS-133), measuring indicators of oxidative and cellular stress. The researchers also examined the eyes and surrounding tissues for broad changes in structure and shape that could relate to low gravity. They maintained two controls on Earth—one in which mice were kept in the same general conditions as those aboard the shuttle, and one in which mice were maintained in typical, Earth-based care facilities.

Mice returning to Earth showed immediate evidence of oxidative stress in their retinas. But the increased expression of six oxidative stress response genes appeared to return to normal by the seventh day on Earth. An indicator of oxidative stress in the cornea was also elevated one day after mice had returned from orbit, but returned to near-normal levels by the seventh day.

"This suggests oxidative stress in the retina and lens are at least partially reversible under the circumstances of the experiment," Chévez-Barrios

said. "This was after a relatively short time in orbit. We don't know if damage caused by longer periods of oxidative stress will be more severe. Only more studies with longer exposure times may help answer this question."

In the mice that had been to orbit, the researchers also found an increase in beta-amyloid in their optic nerves, and this increase persisted after seven days on Earth. Beta-amyloid is associated with traumatic brain injury in humans, and was not detected in the mice that remained on Earth. The researchers also found an increased number of glial cells—cells that respond to injury—in the optic nerves of mice that had been to space. It is not known whether the deposit of beta-amyloid and increased glial cells were caused by sustained low gravity or during the trips to or from Earth orbit. The researchers also found orbiting mice were expressing elevated levels of caspase-3 in the retinal pigment epithelium. Caspaces are enzyme precursors that help the immune system destroy damaged cells in a process called apoptosis. Abnormalities of the epithelium are associated with development of age-related macular degeneration.

Chévez-Barrios and colleagues found changes in cell and tissue shape and fluid balance similar to what has been reported from previous studies, specifically studies of astronauts who had experienced optic nerve changes.

The study described in the *Gravitational and Space Research* paper was small—18 mice in nine different condition groups. Space is limited aboard orbital missions.

"We say in the paper these results should be thought of as preliminary, like a pilot study," Chévez-Barrios said. "We think our results are plausible based on what we know from previous studies of structural changes and damage caused by oxidative stress and changes in the eyes

of astronauts returning to Earth, but additional experiments are needed to confirm what we are reporting about gene expression, cellular behavior and mechanisms of damage."

Chévez-Barrios also said the strain of mice used in the study are known to be unusually sensitive to light, and that the severity of oxidative, cellular, and tissue problems her group saw would probably be milder in healthy human eyes.

Provided by Houston Methodist