Space Flight Studies Explore Role of Gravity in Mammalian Development

Findings from developmental biology studies involving pregnant rats flown on the Space Shuttle are enhancing understanding of the role of gravity in mammalian development. In addition to showing that pregnancy and gestation can withstand the challenge of microgravity, the studies provide the first scientific evidence that early development of the vestibular system—which senses gravity and regulates balance—depends on the stimulus of gravity.

In humans and other mammals, normal development of senses such as sight and hearing relies on stimulation of the brain of the developing fetus or newborn infant. Nobel Prize-winning experiments in the 1960s demonstrated that without stimulation by patterned light during a crucial period of infancy, vision fails to develop normally. More recently, other researchers have shown that acoustic input during early life is critical for the normal development of hearing.

The role of gravity during mammalian development remains poorly understood, however. Because gravity is impossible to remove on Earth, the developmental consequences of the lack of a gravity stimulus can only be studied in an environment without gravity, such as space flight.

The gravity-sensing system of humans and many other animals is the vestibular system—a network of canals and fluid-filled sacs located deep in the inner ear. The vestibular system also regulates balance and orientation. The principal vestibular organs are the otoliths, which respond to changes in gravity and to linear acceleration, and the semicircular canals, which detect angular rotations of the body.

Role of Gravity in Early Development

Experiments conducted aboard the Space Shuttle have provided the first scientific evidence that the stimulus of gravity is as important to the early development of the vestibular system as light is to vision and sound to hearing. These studies were led by NASA-supported investigators Jeffrey R. Alberts, Ph.D., a psychobiologist at Indiana University, and April E. Ronca, Ph.D., a developmental biologist at NASA Ames Research Center in California.

A total of 20 pregnant rats were flown on two space shuttle missions. Both missions launched near the midpoint of the rats' 22-day pregnancy and returned to Earth two days before they were due to give birth. The timing of the missions coincided with the period when the vestibular system, which is an early-developing sensory system, was beginning to develop and function in the rats' fetuses.

Mother and nursing infant rats similar to those used in the flight experiment. Maternal care, including the onset of nursing, was comparable in flight and control rats.

Aboard the Shuttle, astronauts used video cameras to record the pregnant rats' movements during routine daily inspections. Back on the ground after the mission, continuous video surveillance documented the animals' labor and delivery. The researchers also performed a variety of tests on the newborn rats to learn how the absence of gravity had affected the developing vestibular system. They compared the data collected from the mother and infant rats flown on the Shuttle with data from two control groups of mother and infant rats on the ground.

Adaptability of Maternal-Fetal System

A surprising finding was that the flight rats all had uncomplicated, successful vaginal deliveries. Their litters were the same size on average as those of the control rats and the mothers lactated and cared for their young normally.

"Many investigators did not believe a rat could have a vaginal birth after being in microgravity for half of its pregnancy," says Alberts. "They thought labor contractions would be impossible because of the loss of muscle mass that's known to occur in space. In fact, the flight rats had more labor contractions than the controls. It may be that they had a larger number of less forceful contractions." The increase in labor contractions may be due in part to an observed decrease in the flight rats of a protein in the uterus called connexin 43, which is thought to play a role in synchronizing and coordinating labor contractions.

These experiments demonstrated that the latter half of the mother rats' pregnancy and the offspring's gestation could withstand the novel challenge of microgravity, says Ronca. "The maternal-fetal system is remarkably adaptable, and adjusted to conditions never before sustained during early development."

Balance Deficiencies Seen in Flight Offspring

The offspring of the flight rats responded differently than the control offspring to tests of the vestibular system's ability to regulate balance. One test involved turning the newborn rats onto their backs. "Newborn mammals know when they are upside down and reflexively turn over," explains Alberts.

When this test was performed on a flat surface, the flight offspring performed identically to the controls. However, when placed on their backs in a tank of water—a better test of vestibular function because the additional tactile and other sensory cues provided by the surface were not present—the flight offspring showed profound deficiencies in their ability to right themselves.

"Very few of them made any attempt to right themselves at first," says Ronca. "When we did the test again three days after birth, they still performed at a much lower level than the controls. But by day five they had recovered." These results suggest that development of the young flight rats' gravity sensors—the otoliths—was delayed, although the effect was transient. Anatomical studies showed that in young flight rats, gravity-sensing neurons had fewer or less mature synapses than were seen in ground controls. These observations are consistent with delayed development of the otoliths.

Effects of Weightlessness on Developing Semicircular Canals

In another test, performed within two hours of the Shuttle's landing, the investigators measured the heart rates of fetal rats in response to a rolling stimulus. The fetuses' heart rates slowed dramatically. "Their response was more mature than would have been expected," says Ronca. This suggests that development of the semicircular canals—the vestibular organs that detect angular changes—was more advanced than normal.

This observation may be explained by the pregnant rats' ability to roll in the weightlessness of space in ways impossible within the constraints of gravity. The mothers' increased rolling movements may have caused hyperstimulation of the semicircular canals, Alberts and Ronca suggest. In the absence of gravity, however, the fetuses' gravity sensors were not stimulated, resulting in delayed otolith development.

This research provides a foundation for understanding the forces that shape and maintain the vestibular system in humans and other mammals. Knowledge gained from further developmental studies involving altered gravity may also help point the way to more effective therapies for disabling vestibular disorders.

References

1. Ronca AE; Alberts JR. Effects of prenatal spaceflight on vestibular responses in neonatal rats. *Journal of Applied Physiology* 89(6):2318-24, 2000.
2. Ronca AE; Alberts JR. Physiology of a microgravity environment. Selected contribution: effects of spaceflight during pregnancy on labor and birth at 1 G. *Journal of Applied Physiology* 89(2):849-54; discussion 848, 2000.
3. Burden HW; Zary J; Alberts JR. Effects of space flight on the immunohistochemical demonstration of connexin 26 and connexin 43 in the postpartum uterus of rats. *Journal of Reproduction and Fertility* 116(2):229-34, 1999.
4. Plaut K; Maple R; Vyas C; Munaim S; Darling A; Casey T; Alberts JR. The effects of spaceflight on mammary metabolism in pregnant rats. *Proceedings of the Society for Experimental Biology and Medicine* 222(1):85-9, 1999.