"SPACEFLIGHT EFFECTS ON MAMMALIAN DEVELOPMENT"

SUMMARY OF RESEARCH

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Final Result Summary

Pregnant rats were flown as small payloads on the Space Shuttle and studied during the flight and for approximately a week after returning to Earth, when they were due to deliver their offspring. Studies of vestibular function in the rat pups were examined as part of the research program.

Daily videorecordings were made of the rats' behavior in the Animal Enclosure Modules (AEMs) and in identical compartments maintained in the Orbiter Environment Simulator at the Kennedy Space Center (referred to below as Synchronous Control groups). There was continuous postflight surveillance of the rat dams, including timelapse recordings of labor and delivery.

The videorecords provided by crewmembers constitute the best systematic views of spaceflown rats to date, despite the dramatic deterioration of visibility sustained after about the 4th day of flight. We were able to make both qualitative and quantitative observations. Rats were observed to engage in a varied repertoire of species-typical activities within the confines of the AEM. We devised a kinematic coding scheme by which we classified and quantified the movements made by dams in space and in the 1-g control condition. We found that movements involving pitch and yaw were about equivalent in Flight and Synchronous animals. In contrast, Flight dams displayed about *seven times* more rolling movements than did Control

NASA enabled early access to the AEMs after the Shuttle landed. Rats were intact and healthy. Body weight gain during the 9-11 day flights was equivalent to Controls. Post-flight observations, derived from 24hr/day videorecordings, showed that Flight rats ambulated less, reared fewer times and spent less time bipedal than did controls. Overall, their anti-gravitational responses appeared compromised.

Rat dams were next introduced into standardized nest chambers where they resided until parturition under continuous video surveillance. Readaptation to 1-g forces was apparent in the Flight dams. Flight dams exhibited about twice number of lordosis contractions during their labors than did Synchronous Controls. Nevertheless, the dams achieved uncomplicated, successful, vaginal deliveries. Number and size of litters was generally equivalent to that of controls. We had conducted preflight laparotomies on Day G7 and thus had noted number of implantation sites. It was thus possible to ascertain that that the difference between number of implantations and number of pups born was equivalent between groups.

The design of the missions was ideally suited to questions of vestibular development and function after early exposure to microgravity conditions. The rat dams were launched at the approximate midpoint of pregnancy and landed near term, thus providing spaceflight exposures during the establishment and early development of vestibular anatomy, physiology and function. We hypothesized that the absence of the constant stimulus of

system, thereby altering vestibular function.

In one of our postflight studies, we were able to examine vestibular function in the rat offspring almost immediately after re-entry to 1-g. Vestibular-mediated responses were evaluated in fetal rat using classic psychophysiological measures of sensory detection that relies on changes in heartrate (HR). This prenatal vestibular testing was conducted on offspring of four dams in each group (Flight, Synchronous, and Vivarium Controls). Briefly, we applied a precede whereby fetuses are externalized from the uterus while umbilical and placental connections to the dam are kept intact. A single fetus was released from the uterus and gently floated into a temperature controlled bath of buffered physiological saline and was positioned horizontally on one side in a tilt apparatus customized for this procedure. The fetus was fitted with subcutaneous electrodes for heartrate (HR) recording. EKG was monitored for one min, then each fetus was exposed to a vestibular perturbation consisting of a 10 s, 70 deg head-up tilt (considered to be a roll, due to the fetus' sidelying orientation in the apparatus). Signals were amplified, digitized, and computer-analyzed for beat-to-beat intervals (msec) and converted to HR.

Contrary to many predictions, we observed highly robust HR responses to tilt in Flight fetuses. In fact, responses by Flight fetuses were more dramatic than those of the Controls. One explanation is that the spaceflight conditions increased the responsivity of the Flight fetuses by affecting their activity-dependent stimulation during development. To address this hypothesis, we created a set of kinematic data of the dam's in-flight behavior. The enhanced rolling movements of the Flight dams indicated to us that Flight fetuses reside under remarkable conditions: The prenatal otolith is unloaded in conditions of orbital flight, whereas the prenatal labyrinths are seemingly *hyper*-stimulated, especially around the horizontal canals, via the altered behavior of the dam. Altered accelerations delivered to the fetuses by the weightless dam's behavior could account for the precocial and/or potentiated HR patterns observed in Flight fetuses.

Summarized briefly herein are results of the test battery of postnatal vestibular function. On Postnatal Day 0, we evaluated the ability of the pups to 'right' them. Each pup was placed in the supine position and filmed with an 8mm camcorder. We observed no differences in the latency or success rates of completion of the righting response, indicating that the flight pups' basic ability to orient themselves with respect to the gravity vector was intact.

In righting tests on a solid surface, tactile and proprioceptive cues are present that assist performance of the response. We conducted a different type of righting test that relies predominantly on vestibular function in which the pup is immersed in a tank of water. On Day P3, Synchronous control animals responded by rotating their bodies from supine to prone prior to reaching the bottom of the tank. In contrast, the performance of Flight pups was disrupted. They frequently failed to right themselves although, as evidenced from the results of the surface righting tests, they possessed the motoric control to perform the necessary movements. By P5, the water righting responses of the Flight

animals was indistinguishable from that of the controls, suggesting that developmental recovery or readaptation to 1-g has occurred.

We also examined responses to horizontal rotation, a kind of labyrinthine challenge. During horizontal rotation, the pup deflects its head in the direction opposite the rotation. When the rotation stops, the rat typically makes a compensatory movement in the direction it had been rotating. flight pups showed the same tendency as controls to perform the characteristic head adjustment during the rotary stimulus, but were much less likely than controls to perform the post-rotary component (Flight, 40%,; Synchronous, 89%; Vivarium, 76%). The responses patterns of Flight pups relative to controls to this labyrinthine challenge are suggestive of reduced vestibular sensitivity. Differences were absent in older pups, again suggesting recovery of function in the presence of Earth-normal gravitational cues.

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Spaceflight Effects on Mammalian Development

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