

## Space-traveling flatworms help scientists enhance understanding of regenerative health

Experiments aboard International Space Station point to anatomical, behavioral and bacteriological impacts of space travel



An amputated flatworm fragment sent to space regenerated into a double-headed worm, a rare spontaneous occurrence of double-headedness. Credit: Junji Morokuma, Allen Discovery Center at Tufts University.

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MEDFORD/SOMERVILLE, Mass. (June 8, 2017) – Flatworms that spent five weeks aboard the International Space Station are helping researchers led by Tufts University scientists to study how an absence of normal gravity and geomagnetic fields can have anatomical, behavioral, and bacteriological consequences, according to a paper to be published June 13 in *Regeneration*. The research has implications for human and animal space travelers and for regenerative and bioengineering science.

Researchers led by the Allen Discovery Center at Tufts University sought to determine how microgravity and micro-geomagnetic fields would affect the growth and regeneration of planarian flatworms (*D. japonica*) and whether any changes would persist after the worms returned to earth. Planaria are frequently used for studies because of their remarkable ability to regenerate when parts of their bodies are amputated. Knowing what happens to them in space and upon their return to Earth could lead to a better understanding of how physical forces influence body shape and cellular decision-making.

“During regeneration, development, and c

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physical forces, such as electric fields, mag  
We want to learn more about how these forces affect anatomy, behavior and microbiology,” said the paper's corresponding author, Michael Levin, Ph.D., Vannevar Bush professor of biology and director of the Allen Discovery Center at Tufts and the Tufts Center for Regenerative and Developmental Biology.

“As humans transition toward becoming a space-faring species, it is important that we deduce the impact of space flight on regenerative health for the sake of medicine and the future of space laboratory research,” added Junji Morokuma, research associate in Levin’s lab and first author on the paper.

The researchers launched a set of flatworms into space via SpaceX Commercial Resupply Service Mission 5 on Jan. 10, 2015. The flatworms were either left whole or amputated and sealed in tubes filled half with water and half with air.

Meanwhile, researchers created two sets of control worms. One consisted of live worms sealed in spring water in the same manner as their space counterparts and kept in darkness at 20 degrees Celsius for the same amount of time. These worms were used as controls for all of the experiments except mass spectroscopic analysis. After the space-exposed worms returned to Earth, researchers prepared a second set of worms that were then exposed to the same changes in temperature as the space-exposed worms. These worms were used for the mass spectroscopic analysis.

After five weeks in space, the samples were evaluated immediately upon their return and over the course of 20 months. Through an array of behavioral, microbiological, and morphological tests, the researchers identified a number of differences between the space and terrestrial worms.

Most surprising, researchers discovered that one of the amputated fragments sent to space regenerated into a rare double-headed worm. In more than 18 person-years of maintaining a colony of *D. japonica* that involves more than 15,000 control worms in just the last five years alone, the Tufts researchers have never observed a spontaneous occurrence of double-headedness. Moreover, when the researchers amputated both heads from the space-exposed worm, the headless middle fragment regenerated into a double-headed worm, demonstrating that the body plan modification that occurred in the worm was permanent.

Additionally, whole worms sent into space underwent spontaneous fission -- division of the body into two or more identical individuals -- while their earth-bound counterparts did not. However, researchers noted that because of the variation in temperatures experienced by the space and terrestrial worms, the observed difference could be due to temperature differences.

Upon their return, worms from both the space-traveling and stay-at-home groups were transferred to petri dishes containing fresh spring water. While the stay-at-home worms exhibited normal behavior, the 10 whole worms that had spent time in space curled up and were partially paralyzed and immobile, returning to normal after two hours. The behavior suggests that the worms had altered their biological state to accommodate the environmental change of being in space, reacting strongly to a return to normal aqueous conditions.

Space-traveling and control group worms also differed in their reaction to light. Twenty months after returning to Earth, individuals from each group were placed in an arena, half of which was illuminated with red light, which cannot be seen by planaria, and half of which was illuminated with blue light. An automated behavior analysis device revealed that space worms spent 70.5 percent of their time in the dark while the Earth-based worms spent 95.5 percent of their time in the dark. While the difference in light preference means is not statistically significant because of small sample size, the difference in variance among the worms was notable and significant.

Researchers also analyzed the microbiome difference between the bacterial community analyzing the chemical composition of the water in which the animals lived during the duration of the experiment, the researchers determined that exposure to space induces distinct differences in metabolism and/or secretion.

Researchers cautioned that their experiments faced a number of unavoidable limitations. For the Earth-based control group, it was difficult to match the temperatures experienced by worms in space over the course of the entire mission. Future missions will use real-time data from space to fine-tune temperatures experienced by the controls on Earth. Additionally, the stress of liftoff and splashdown was not replicated, although future experiments will do so. Furthermore, the amputation of worms was done on Earth, a requirement of protocols on this mission. Ideally, this would be done on the space station, and researchers hope that an ISS astronaut will be willing to conduct these experiments aboard the space station in the future.

The researchers intend for their work to help establish protocols for performing planarian research in space by determining proper transfer logistics and conditions for future missions.

In addition to Tufts researchers, scientists from Kentucky Space LLC, NASA Kennedy Space Center, the Center for the Advancement of Science in Space, Exomedicine Institute, and Harvard University participated in the study.

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“Morokuma, J. et al, “Planarian regeneration in space: persistent anatomical, behavioral, and bacteriological changes induced by space travel,” *Regeneration*, June 13, 2017, DOI: 10.1002/reg2.79

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