frontiers | Frontiers for Young Minds

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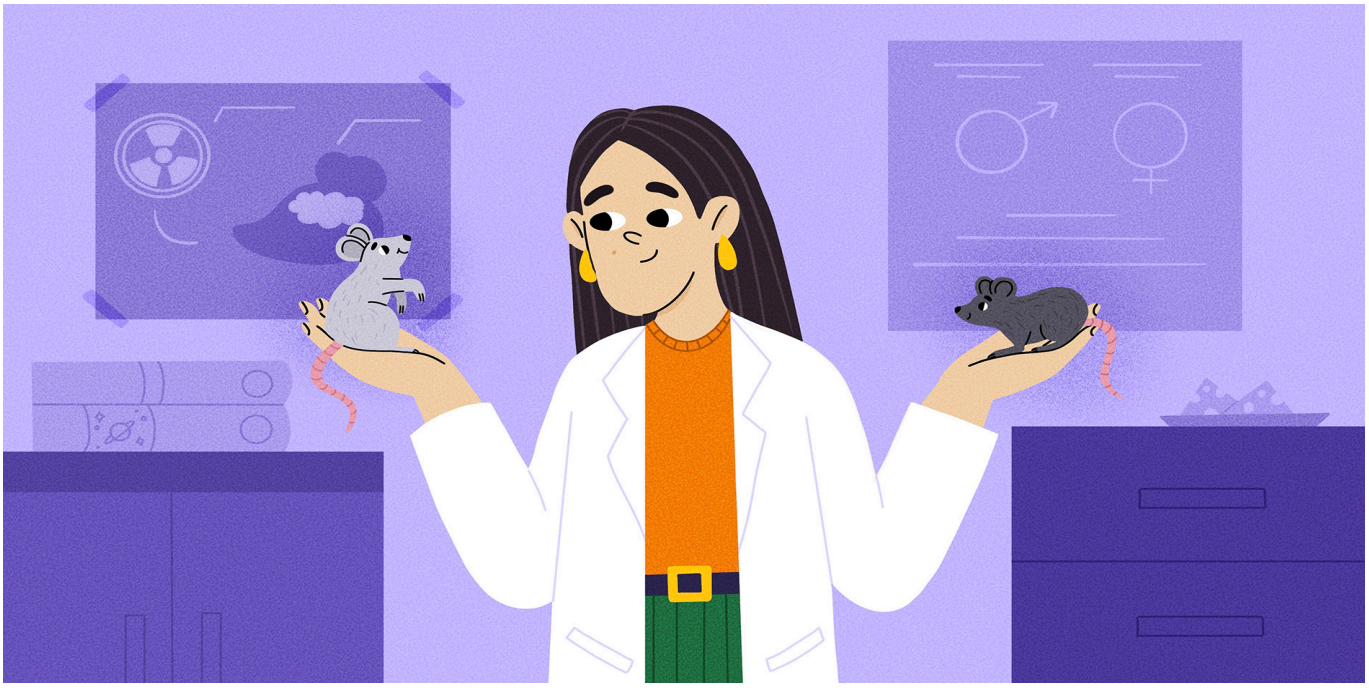

SPACE RADIATION MAY AFFECT MALE AND FEMALE BRAINS DIFFERENTLY

Robert G. Hinshaw* and Cynthia A. Lemere

Brigham & Women's Hospital and Harvard Medical School, Boston, MA, United States

YOUNG REVIEWERS:

ABYAN

AGE: 13

REAGAN

AGE: 10

Radiation in outer space can be dangerous for astronauts who leave the protection of Earth's magnetic field. On long space missions to the moon and Mars, even small amounts of radiation will add up... but how will this affect the brain? Alzheimer's disease is a common brain disease in older people that damages brain cells and affects memory. Because both Alzheimer's disease and radiation can change the brain, we want to know if astronauts are more likely to get Alzheimer's disease when they get older. That way, we can work to better protect astronauts traveling into deep space. In this article, we will tell you about one of the first long-term studies in mice, describing how radiation and Alzheimer's disease affect each other. What is interesting is that the effect seems different in male mice and female mice. While female mice had more Alzheimer's brain disease than male mice in general, the brains of male mice were hurt more by radiation!

WHAT IS SPACE RADIATION AND WHY DO WE STUDY IT?

RADIATION

Energy carried through space by particles like light and atoms

Radiation is a form of energy carried by particles through space. There are many kinds of radiation. The light you can see and the signals that make Wi-Fi work are both types of radiation. Different kinds of radiation have different energies, and types with very high energy can be dangerous because they can stop the cells of your body from working properly [1]. Outer space is filled with exotic kinds of very-high-energy radiation that we do not have here on Earth [2]. Astronauts very close to earth, like on the International Space Station, are protected from most of this radiation by the Earth's magnetic field. But on a long trip to the moon or to Mars, astronauts will be exposed to much more space radiation than anyone ever has experienced before. Space radiation is especially good at damaging cells, so we want to learn more about it to help keep astronauts safe.

WHAT IS ALZHEIMER'S DISEASE AND WHY DOES IT MATTER FOR ASTRONAUTS?

ALZHEIMER'S DISEASE

A brain disease that causes problems with memory

Alzheimer's disease is a brain disease that kills nerve cells in the brain and damages memory, and it is very common in older people (Figure 1). In fact, it is so common that it is likely some astronauts will develop it when they get older. We do not know if the radiation from space travel will make Alzheimer's worse, but we think it is possible. The kinds of damage that radiation does to cells can last for a long time, and similar damage can also be found in the brains of people with Alzheimer's disease. Because of this link, we suspect that space radiation might make brains more likely to develop Alzheimer's disease later in life [3]. It might also make the disease worse or make it develop faster. In our experiments, we studied a special type of mouse that gets Alzheimer's disease as it ages so that we could learn more about how the Alzheimer's disease process is affected by radiation.

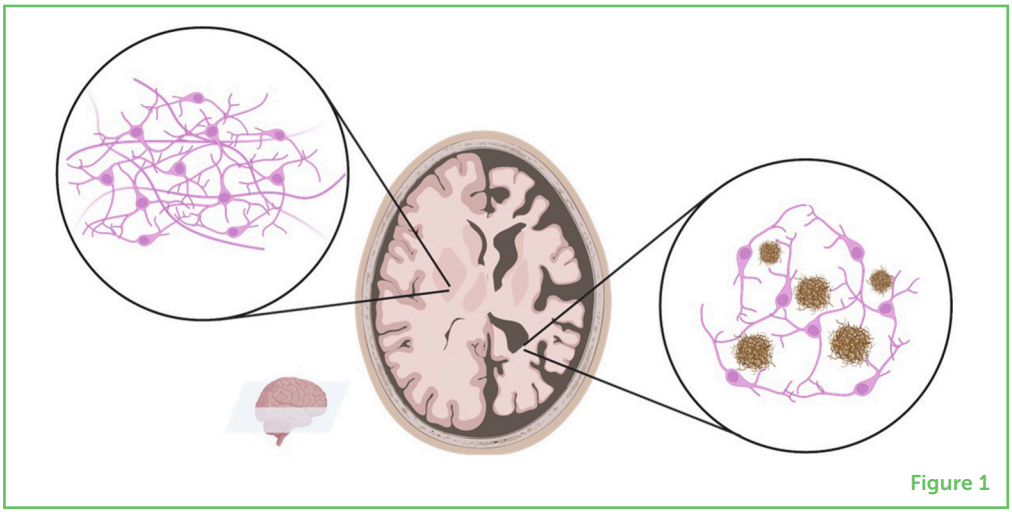

Figure 1

Figure 1

Here is an image of the brain, sliced as shown in the lower left. On the **left** side, you can see a healthy brain with no evidence of bad clumps of protein between the nerve cells. On the **right**, you can see a brain with Alzheimer's disease. Notice the Alzheimer's brain is smaller, with fewer nerve cells and bad clumps of protein between them (Created with Biorender.com).

HOW DID WE DO THIS EXPERIMENT?

To study the effects of radiation without putting people in danger, we tested male and female mice that were exposed to kinds of radiation similar to the radiation in space. This radiation is made in a **particle accelerator**, which is a large machine that pushes individual atoms with magnets until they are traveling at high speeds and have a large amount of energy. Remember that radiation is just energy carried by small particles like atoms. We exposed mice to this particle accelerator radiation to approximate the radiation exposure an astronaut would get over multiple years in outer space. We did this when the mice were young and then waited for them to get old. It only takes mice a little over a year to get very old, which makes studying aging easier in mice than in humans. Mice do not normally get Alzheimer's disease, so we used a special strain of mice **genetically engineered** to get the disease. When the mice were old, we studied their behavior with multiple tests, like solving mazes, and we also looked at their brains for signs of Alzheimer's disease. As a comparison, we also looked at the behavior and brains of mice that were *not* exposed to radiation. Figure 2 diagrams the structure of the experiment.

PARTICLE ACCELERATOR

A very specialized machine that uses electricity and magnets to shoot small particles like atoms at very high speeds

GENETICALLY ENGINEERED

Artificial changes were made to the DNA

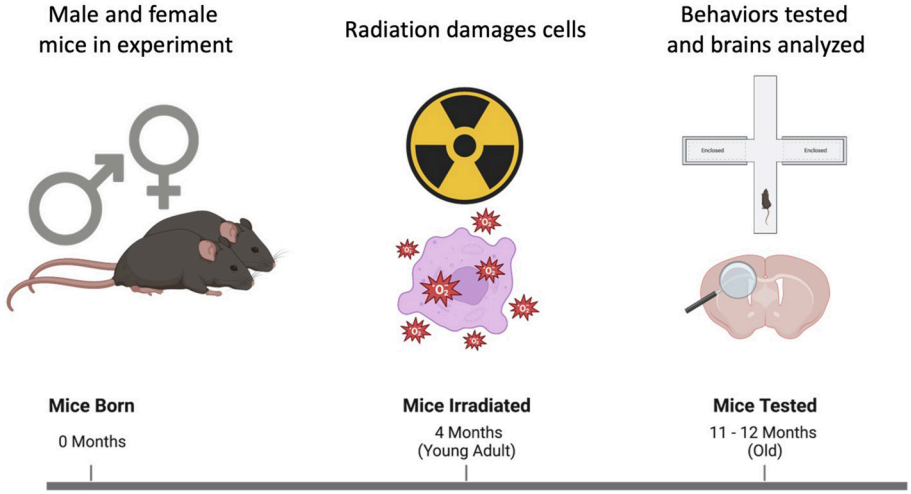

Figure 2

Experiment timeline. Male and female mice were exposed to radiation (irradiated) at 4 months old. This damaged their cells, including their brain cells. After the mice aged to 11–12 months old, we tested their behaviors and analyzed their brains for Alzheimer's disease. We compared these results to mice that were not exposed to radiation (Created with Biorender.com).

We measured the amount of Alzheimer's disease by looking at thin slices of the mouse brains under a microscope. The thin slices made it easier to detect the clumping of a particular kind of protein that builds up in Alzheimer's disease. Proteins, in addition to fats and sugars, are a very common type of molecule made by all cells. However, in Alzheimer's disease, very specific kinds of protein that brain cells make tend to clump together outside of the cells. This clumping can interrupt the normal function of cells and eventually cause them to die. Measuring the amount of bad clumps of protein can tell us how far the disease has progressed in the mice.

HOW DOES SPACE RADIATION AFFECT ALZHEIMER'S DISEASE?

When we looked at the brains of these mice with Alzheimer's disease, we noticed a couple different patterns. First, we observed that the female mice had worse Alzheimer's disease than the male mice, regardless of whether they were exposed to radiation. Second, we observed that the radiation *did* make Alzheimer's disease worse in some mice but not in others. It turns out that radiation made the disease worse in male mice but not in female mice (Figure 3). Even though the female mice had worse Alzheimer's disease, they did not appear to get worse with radiation like the male mice did. We do not know why this difference between males and females happens, but we are excited to keep doing our research to find out.

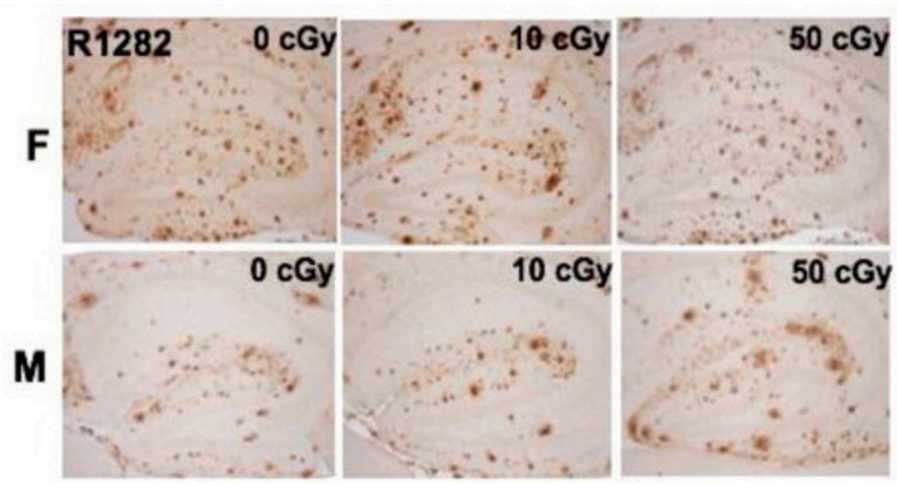

Figure 3

Figure 3

We examined thin sections of mouse brains and saw clumps of protein like those found in the brains of people with Alzheimer's disease. R1282 is the name of the molecule we used to detect these proteins. The top row of images are from female (F) mice, and the bottom images are from male (M) mice. The leftmost images are from mice that received no radiation (0 Centigray, cGy), and dose increases to the right. You can see that higher dose corresponded with more clumps in male but not female mice (Figure from original publication).

HOW DOES SPACE RADIATION CHANGE MOUSE BEHAVIOR?

The clumping of protein is one part of Alzheimer's disease, but what we really care about is whether the memory and other behaviors of the mice got worse after radiation. We tested the mice on 10 different behaviors, including various kinds of memory. We saw changes in mice exposed to radiation. In general, the behaviors of male mice were more likely to be affected by radiation exposure than those of female mice. In particular, radiation appeared to make the male mice move around less and do worse in tests of their memory. This matches with the observation that the radiation made Alzheimer's disease worse in the male mice brains but not in the female mice brains. The good news is that these changes were small, and in many tests, we did not see any difference between radiation-exposed mice and normal mice.

SUMMARY

Space radiation can threaten the health of astronauts traveling in outer space. We want to understand if this radiation could worsen Alzheimer's disease later in life. To test this, we exposed mice to radiation when they were young and looked at their behavior and brains much later, when they were old. The long-term changes caused by radiation were small but still observable. To begin with, female mice had worse Alzheimer's disease than male mice regardless of radiation. We saw that radiation worsened Alzheimer's disease in the brains of only the male mice and not in the female mice. We also saw that the radiation changed the behaviors of the male mice more than it did to the female mice. We still do not know how space radiation will affect humans, but this experiment with mice can give us clues. We can now guess that space radiation could worsen Alzheimer's disease as astronauts get older. We also suspect that these changes might vary greatly from person to person, depending on things like whether they are male or female. As astronauts return to the moon and then venture out toward Mars, scientists and doctors will have to watch their health carefully, even after they get back to Earth. Space is a dangerous place! In addition to radiation, altered gravity levels, confined spaces, high carbon dioxide levels, and poor sleep all add stress to the brain during spaceflight. But by studying and understanding the risks of traveling in space, we can help make it safer for people to explore.

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ORIGINAL SOURCE ARTICLE

Schroeder, M. K., Liu, B., Hinshaw, R. G., Park, M., Wang, S., Dubey, S., et al. 2021. Long-term sex- and genotype-specific effects of ^{56}Fe irradiation on wild-type and APPswe/PS1dE9 transgenic mice. *Int. J. Mol. Sci.* 22:13305. doi: 10.3390/IJMS222413305

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CONFLICT OF INTEREST: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

YOUNG REVIEWERS

ABYAN, AGE: 13
Hi, I am Abyan! I like Science, specifically space related Science, and Physics! I also like Mathematics and English. I would say that I am an independent person who loves new challenges. An example would be that I just recently started playing competitive tennis. I have a pet cat named Astro and I love spending time with him! In my free time, I play and interact with my friends and read about new space discoveries.

REAGAN, AGE: 10
I love science, astronomy, volleyball, swimming, and taekwondo. I am learning to play the violin. This past summer, I had fun at space camp learning a computer program to send the Mars Rover to the moon. I want to be an officer in the U.S. Space Force and be an astronaut when I grow up.

AUTHORS

ROBERT G. HINSHAW

Dr. Robert Hinshaw, Ph.D., is 30 years old and a scientist at NASA Ames Research Center in California, working to improve biology research in space. Before that, he trained as a graduate student under Professor Cynthia Lemere at the Brigham & Women's hospital in Boston, Massachusetts, where together they studied the effects of radiation on Alzheimer's disease. He graduated with his Ph.D. from the Massachusetts Institute of Technology in September 2022. Robert likes to spend his free time hiking and rock climbing with his friends as well as playing games online and reading science fiction. *rghinshaw@gmail.com

CYNTHIA A. LEMERE

Dr. Cynthia Lemere, Ph.D., is 65 years old and a professor of neurology at Brigham and Women's Hospital and Harvard Medical School in Boston, MA, where she has worked for 33 years—mostly to understand what causes Alzheimer's disease and how to prevent or treat it. She also works on a NASA-funded project to determine if astronauts on long-term missions to deep space will be more likely to get Alzheimer's disease later in life. She had the pleasure of mentoring Rob for his Ph.D. on this project. Cindy likes to spend her free time at the beach, kayaking, and traveling the world.