NASA’s Twins Study: A great control, but a sample size of one

Enlarge / Scott Kelly returned from space with a lot of blood and stool samples. They’ve now told the tale of the changes he underwent during his time on the International Space Station.

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The US has big plans for putting humans in space. In doing so, it will be building on our experience at the International Space Station, which is approaching the 20th anniversary of the arrival of its first occupants. Some of that experience comes in the form of knowledge of habitation and operations in low gravity. But a large chunk of it is in the form of understanding what time in space does to the human body.

Today, NASA is releasing detailed results of its most audacious experiment yet: sending one half of a pair of identical twin astronauts into space and carefully monitoring both of them for a year. Three years after astronaut Scott Kelly returned to Earth, and a year after some horrifically speculative press coverage, a paper in today’s issue of Science provides excruciating detail on the changes Kelly’s body experienced over a year in orbit. While many of the problems highlighted in the new paper had been identified previously, the results aren’t exactly good news for the US’ long-term exploration plan.

Changes

Over the course of many long-term stays in space, the US and Russia have identified a number of health issues caused by extended stays in minimal gravity. Some of them are pretty simple to correct. Without gravity's constant pull, bones and muscles don't experience the resistance that helps keep them robust. A careful exercise plan, however, can minimize these issues. Less easy to minimize is the fact that the body's internal water content shifts upwards—about two liters of fluid move to the upper body over the short term. Among the consequences are eye problems that can persist after the astronaut returns to Earth.

The other big issue is radiation exposure. The interplanetary environment is filled with energetic light and particles that are mostly shielded out by our atmosphere and magnetic field. The International Space Station gives up the atmosphere's protection; journeys to the Moon and beyond will be without both. The particles and photons can do a variety of damage to our cells, but the big worry is that they'll alter the DNA, placing astronauts at elevated risk of cancers.

We've known about all of these previously, but the Twins Study has provided an opportunity to examine them in exquisite detail, including at the level of changes in DNA and the genes it contains. In addition, by monitoring a huge range of human biology through things like blood and stool samples, it has provided us with the chance to identify any not-as-obvious surprises. The existence of an identical twin offers a good control for genetic changes, although, as the paper itself says, "It is important to note that with a single test subject in the spaceflight environment for this particular set of measures, it is impossible to attribute causality to spaceflight versus a coincidental event."

Not everything worked out. For example, some cell samples

ended up at room temperature for the 40-hour trip from the International Space Station to NASA (via Kazakhstan), which killed the activity of an enzyme researchers had hoped to measure. But enough did work that the Kellys may now be the most exhaustively documented human subjects on the planet.

What's new?

The human genome contains roughly 20,000 genes, and the study looked at the activity of these before, during, and after Scott's time in space. The exact number of genes with altered activity varied depending on the cells examined (mostly types of white blood cells, in this case) but were typically in the area of 500. The number of genes with changed activity also went up over time—there were more changes after a year than after six months. And roughly a quarter of the genes that showed changes in activity in space did not return to their pre-space state after Kelly was back on Earth.

A similar study of hundreds of molecules normally found in the blood provided a glimpse into Kelly's metabolism. In total, 39 of these showed significant changes while he was in space. Among these are metabolites that indicate problems with DNA damage and inflammation.

Looking at the DNA itself, it was clear that the metabolites were accurate. The space-based twin showed extensive signs of radiation-induced DNA damage, including pieces of DNA that were lost, moved to a different chromosome, or had their orientation flipped. This DNA damage was cumulative over the time in space, and it continued to increase after Kelly's return to Earth, suggesting that there is additional damage to stem cells that takes a while to make its presence felt.

One striking change was found in the telomeres, the ends of chromosomes that serve as a protective cap. Telomeres tend to shrink as a cell ages, limiting the number of times it can divide. But Kelly's expanded by about 15 percent while in

space, a phenomenon that has been seen in other astronauts and even in experimental animals sent to space. Strikingly, it only took 48 hours for the telomeres to return to their pre-flight length once Kelly was back on Earth. The significance of these changes is unclear.

More changes

The other thing suggested by the metabolites was inflammation, a sign of altered immune activity. Lots of genes involved in the immune system showed altered activity consistent with that. In addition, the researchers looked at 62 different immune signaling molecules called cytokines, finding that almost all of them (50 of the 62) showed changes during the pre-flight/in-orbit/post-return timeline.

All of that could be a potential sign of immune dysfunction. Yet NASA had Kelly take a flu vaccine shot while he was on the Space Station and found that his immune system responded appropriately. Thus, it’s not clear what these immune changes are indicating.

The immune system interacts extensively with all the bacteria that live on or inside us, collectively called the microbiome. Kelly’s microbiome was largely stable. Although the relative amounts of certain species changed while he was in orbit, the total species richness remained stable.

While many of these molecular tests provide a unique window into Kelly’s response to space, NASA also looked for issues that had been identified previously. Kelly had the eye problems that typify extensive time in space, as well as the cardiac changes (increased heart output and expanded blood vessels). Over the course of the flight, he lost seven percent of his body mass. Part of this was eating less and part was an injury that limited his in-flight exercising, causing bone and muscle loss.

There had been previous indications that time in space led to a small mental decline. Kelly didn't experience this while he was in space—in fact, his tests in flight showed an enhanced cognitive speed relative to preflight testing. The problems came when he returned to Earth. Cognitive speed decreased on most tests, as did his accuracy. This effect persisted for at least six months, at which point the testing stopped.

The road ahead

Overall, this is not great news for our future plans for long-term stays on or near the Moon or a journey to Mars. DNA damage was, as expected, significant, and both of those initiatives would involve time spent outside the shielding of Earth's magnetic field. Some ideas for a Mars mission include three total years before a return to the Earth, with time spent on Mars only providing limited protection due to its thin atmosphere and lack of a significant magnetic field.

The cognitive decline is also worrisome, though knowing why it occurs would help clarify what the risks are. It is possible that it is triggered by a return to gravity; alternately, it may be the mission-driven focus provided by being in space staves off a decline that would otherwise have started earlier. If the latter is the case, then astronauts might expect to be in top form throughout an extended mission to Mars. But if the former is true, then problems might set in right after astronauts land on Mars—about the least ideal situation possible and one that has the authors of the Twins Study paper pondering the prospects of heavy automation limiting the need for astronauts' mental acuity.

Overall, the study seems to have been a mixed effort. It confirms some of the problems we've seen before, although it indicates that many of these don't get much worse with time. The study does identify a few new potential problems, however. And in some cases, it raises nearly as many questions as it

answers. Those questions can only be answered by doing more studies like this—with more than just a single pair of twins.

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