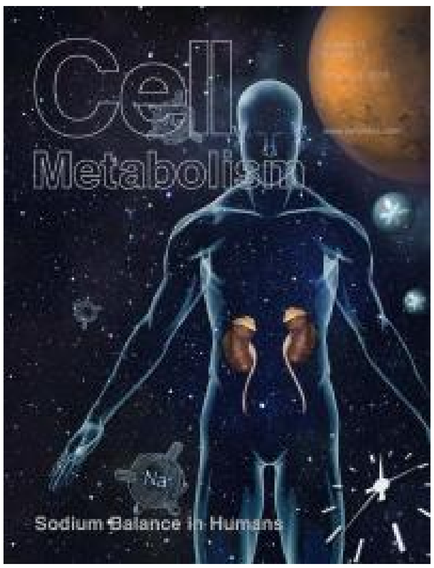
Simulated Mars mission reveals body's sodium rhythms

January 8 2013



High salt intake and hypertension are thought to be linked. The steady-state concept of sodium balance implies that Na+ accumulation leads to water retention while salt intake correlates with rapid urinary excretion. Rakova et al. studied cosmonauts in Mars space flight simulations over 105 and 205 days and found that Na+ excretion and retention exhibit hormone-dependent rhythmic patterns unrelated to blood pressure, body water, or salt intake. The cover image highlights the importance of the kidneys in sodium balance, which is under clock control. Mars, sodium ions, and atomic models are represented in the background. Credit: *Cell Metabolism*, Rakova et al. Artwork by Dominic Doyle.

Clinical pharmacologist Jens Titze, M.D., knew he had a one-of-a-kind scientific opportunity: the Russians were going to simulate a flight to

Mars, and he was invited to study the participating cosmonauts.

Titze, now an associate professor of Medicine at Vanderbilt University, wanted to explore long-term sodium balance in humans. He didn't believe the textbook view – that the salt we eat is rapidly excreted in urine to maintain relatively constant body sodium levels. The "Mars500" simulation gave him the chance to keep salt intake constant and monitor urine sodium levels in humans over a long period of time.

Now, in the Jan. 8 issue of Cell Metabolism, Titze and his colleagues report that – in contrast to the prevailing dogma – sodium levels fluctuate rhythmically with 7-day and monthly cycles. The findings, which demonstrate that sodium is stored in the body, have implications for blood pressure control, hypertension and salt-associated cardiovascular risk.

Titze's interest in sodium balance was sparked by human space flight simulation studies he conducted in the 1990s that showed rhythmic variations in sodium urine excretion.

"It was so clear to me that sodium must be stored in the body, but no one wanted to hear about that because it was so different from the textbook view," he said.

He and his team persisted with animal studies and demonstrated that the skin stores sodium and that the immune system regulates sodium release from the skin.

In 2005, planning began for Mars500 – a collaboration between Russia, the European Union and China to prepare for manned spaceflight to Mars. Mars500 was conducted at a research facility in Moscow between 2007 and 2011 in three phases: a 15-day phase to test the equipment, a 105-day phase, and a 520-day phase to simulate a full-length manned mission. Crews of healthy male cosmonauts volunteered to live and work in an enclosed habitat of sealed interconnecting modules, as if they were on an international space station.

Titze and his colleagues organized the food for the mission and secured commitments from the participants to consume all of the food and to collect all urine each day. They studied twelve men: six for the full 105-day phase of the program, and six for the first 205 days of the 520-day phase.

"It was the participants' stamina to precisely adhere to the daily menu plans and to accurately collect their urine for months that allowed scientific discovery," Titze said.

The researchers found that nearly all (95 percent) of the ingested salt was excreted in the urine, but not on a daily basis. Instead, at constant salt intake, sodium excretion fluctuated with a weekly rhythm, resulting in sodium storage. The levels of the hormones aldosterone (a regulator of sodium excretion) and cortisol (no known major role in sodium balance) also fluctuated weekly.

Changes in total body sodium levels fluctuated on monthly and longer cycles, Titze said. Sodium storage on this longer cycle was independent of salt intake and did not include weight gain, supporting the idea that sodium is stored without accompanying increases in water.

The findings suggest that current medical practice and studies that rely on 24-hour urine samples to determine salt intake are not accurate, he said.

"We understand now that there are 7-day and monthly sodium clocks that are ticking, so a one-day snapshot shouldn't be used to determine salt intake."

Using newly developed magnetic resonance imaging (MRI) technologies to view sodium, Titze and his colleagues have found that humans store sodium in skin (as they found in their animal studies) and in muscle.

The investigators suspect that genes related to the circadian "clock" genes, which regulate daily rhythms, may be involved in sodium storage and release.

"We find these long rhythms of sodium storage in the body particularly intriguing," Titze said. "The observations open up entirely new avenues for research."

More information: Rakova et al.: "Long-term space-flight simulation reveals infradian rhythmicity in human Na+ balance." dx.doi.org/10.1016/j.cmet.2012.11.013

Provided by Vanderbilt University Medical Center