Toward better space health: Understanding the effects of microgravity on P-glycoprotein

September 13 2021

Credit: Pixabay/CC0 Public Domain

Deep space is most likely going to be humanity's final frontier, and space travel will undoubtedly become much more common in the future. However, space is a very hostile environment not only because of the technical difficulties that entail going there, but also because of the detrimental effects that constant microgravity has on the human body. Some examples of these are bone loss, muscle atrophy, and liver and kidney problems, as well as space motion sickness.

It should come as no surprise that astronauts resort to various drugs to ameliorate the symptoms caused by microgravity. Unfortunately for them, microgravity has been noted to have a significant impact on the pharmacokinetics of certain drugs, which could lead to altered efficacy and unexpected outcomes. In particular, delivering an accurate amount of a drug to the brain has become a key problem in space health.

In a recent effort to shed some light onto this issue, a team of scientists from Beijing Institute of Technology, China, studied the effects that microgravity has on P-glycoprotein (P-gp), an important efflux transporter. Their results are detailed in their paper published in *Space: Science and Technology*, on 17 Jun 2021.

P-glycoprotein is an ATP-dependent efflux pump that expels foreign substances out of cells. Presenting in the liver, kidneys, and intestines, this biomolecule can have a significant effect on drug metabolism, absorption, distribution, and excretion. Most importantly, P-gp is highly expressed in the capillary endothelial cells that create the blood–brain barrier and regulates the entry of many drugs into the brain. Thus, understanding how microgravity affects the expression and function of P-gp is important for future space missions.

The researchers employed a frequently adopted model to understand the effects of simulated microgravity (SMG) on P-gp in rats. In this model, the Morey–Holton model, microgravity is simulated by suspending rats by the tail so that their hind legs remain elevated, creating a head-down tilt that mimics many of the effects of real microgravity. Rats were divided into three groups: a control group and two other groups in which

SMG was maintained for 7 and 21 days (7d-SMG and 21d-SMG, respectively), through which the impacts of different microgravity durations are expected to be studied.

The team first performed experiments to determine the levels of P-gp expression and the efflux function of P-gp. They found P-gp expression and function to be significantly higher in the 21d-SMG group compared with 7d-SMG group and CON, highlighting the impacts of long-term microgravity exposure being different from the short-term ones. Afterwards, they looked for proteins that interact with P-gp and were expressed at significantly different levels between the three groups. Through a label-free proteomics strategy, they identified 26 proteins interacting with P-gp that were common to both SMG groups. Most of these differentially expressed proteins regulated ATP hydrolysis-coupled transmembrane transport, among other functions. Finally, interaction analyses hinted at many other potential proteins that P-gp might interact with, including heat shock proteins, sodium/potassium ATP enzymes, ATP synthase, microtubule-associated proteins, and vesicle fusion ATPase.

Considering that most astronauts have reported taking drugs that are substrates of P-gp, clarifying the roles of P-gp and the proteins it interacts with under a microgravity environment may be necessary to preserve their health in future missions. "As far as we know, this is the first report on P-gp function and its interacting proteins in the rat brain under simulated microgravity. Our findings might be helpful not only for further studies on nerve system stability, but also for the safe and effective use of P-gp substrate drugs during space travel," highlights Prof. Yuling Deng, who led the study.

Much remains to be clarified on how prolonged microgravity affects our body. Still, the results of this study pave the way to a more complete understanding of this issue. Let us hope further research will be conducted so that no adverse effects of being in space catch future astronauts off guard.

More information: Yujuan Li et al, Investigation on P-Glycoprotein Function and Its Interacting Proteins under Simulated Microgravity, *Space: Science & Technology* (2021). DOI: 10.34133/2021/9835728

Provided by Space: Science and Technology