Space Physiology and Medicine in the Exploration Era

IAA Position Paper on future Strategies of Space physiology and medicine

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The general content of this Position Paper was discussed and agreed at the 19th IAA Humans in Space Symposium in Cologne, Germany on July 7 to 12 and endorsed by the 392 participants of the Symposium from 26 countries. This paper thus reflects the opinions of a significant proportion of the global space physiology and medicine community.

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From July 7 to 12, the 19th IAA Humans in Space Conference took place in Cologne, Germany. Nearly 400 scientists from 26 countries participated in this conference. A questionnaire was sent to all pre-registered participants before the conference asking about their priorities for future space life sciences research. About 100 scientists returned the questionnaire. These responses were then discussed during a dedicated plenary session at the beginning of the conference and again at the end of the conference. It was decided to prepare a consensus recommendation paper and present this to IAA as well as to the various space agencies. The executive summary of this paper is termed the "Cologne Resolution" and summarizes the recommendations given by the space physiology and medicine community. The current position paper gives the relevant background information and describes the recommended actions in detail.

Executive Summary

Our planet is in essence an amazing spaceship containing over 7 billion astronauts. Expanding our human presence beyond Earth and increasing the action radius of humans is a central vision of humankind. Therefore, further human exploration beyond Earth is a logical next step after orbital spaceflight. Life sciences research has the task of supporting such human exploration by keeping our voyaging astronauts healthy and able to perform complicated tasks well. For these reasons, and to enable safe, long-term human spaceflight (e.g., travel to Mars), further space and ground research focused on humans is not only necessary but mandatory. Voyaging astronauts require the development of physiological, psychological and radiation protective measures, as well as strategies for dealing with emergency situations, habitation issues and long-term self-sustaining life support.

Humans are the most complex known structure in the universe. Exploring and increasing knowledge about how humans function in health and disease is a major challenge today for basic and biomedical sciences and this will continue for the foreseeable future. We have learned in recent decades that studying humans under different gravitational situations, especially under microgravity, is a unique and novel way to better understand human physiology. Where we have had problems preventing functional systems of astronauts from degrading during spaceflight, the general main issue has been that we have not really understood the underlying physiology beforehand. Thus, studying humans in microgravity is an excellent tool to localize possible faults or lack in our understanding of human physiology, since microgravity offers a challenge for the human body at many different levels at the same time, i.e. bone loss, cardiovascular deconditioning, neurosensory disturbances etc. In addition, the search for countermeasures against the deleterious effects of microgravity is challenged by the fact that astronauts suffer these changes simultaneously at many physiological systems. This is in contrast to typical “Earth” medicine, where diseases usually affect only one system at the time. Pushing the limits of space science and technology to improve the wellbeing of astronauts at all these levels at the same time is inevitably of great use for “Earth” biomedical research, and thus are these efforts highly beneficial for both fields.

In view of future exploration goals, the IAA space physiology and medicine community strongly advocates increasing the available opportunities for life sciences research in space and on the ground, including research in medicine, physiology, biology, psychology and radiation effects and, at the same time, increasing efforts to better link the results of life sciences research on Earth and in space. Such a strengthening of the ties between Earth and space research will be beneficial for both parties by improving health care on Earth and supporting human exploration of space. It will also substantially increase the support for human spaceflight in the general population, as the results can be directly applied to normal ground-based medicine.

These goals can be achieved by the following actions:

- Strengthen the links between space and terrestrial life sciences
- Strengthen global collaboration in space life sciences
- Strengthen joint research on fundamental life sciences scientific questions
- Maintain the opportunities to study human physiology and molecular model systems in microgravity and the radiation environment in orbit by extending the lifetime of the International Space Station and through direct collaborations with governments and companies, thus providing additional opportunities for studying long term human adaptation to microgravity
- Perform human exploration step-by-step with sound scientific tasks for the astronauts

- Consider relevant scientific research beyond the scope of the International Space Station, in line with the goals set out under the ISECG (2013) Global Exploration Road Map, to undertake planetary exploration

Human space exploration, space physiology, and medicine

Human space exploration beyond earth orbit is a response to a deeply felt human need to explore and expand the reach of human beings. Robots or machines can assist in this endeavor, but cannot replace humans. Numerous roadmaps have been written about the necessities for physiology and medicine in order to decrease the risks for the respective crews and to keep the participating astronauts healthy and able to perform on a high level (e.g., Horneck et al, 2003; Horneck et al., 2006; Worms et al, 2009; Worms et al., 2012; Human Research Program, 2012; Human Research Roadmap, 2013; ISECG Global exploration roadmap, 2013). These studies have identified the scientific questions to be solved before sending humans on long-term exploratory missions and have suggested approaches to answering those questions (e.g., chapter 7 “Proposed European Strategy in life sciences and life support systems for human exploratory missions” of HUMEX). Therefore, the present position paper does not repeat nor enumerate such important operational tasks.

Space physiology and medicine as essential parts of human physiology and medicine

Operational problems arise during exploration, because we have not understood how the specific physiological functions involved in the problem are regulated and how mitigation strategies should be applied in order to maintain or retain optimal functions. Thus, the tasks that arise during exploration involve basic principles of physiology and medicine that are uncovered when the human body is in microgravity or in a “gravitationally neutral” position. Caring for astronauts during exploration pinpoints such problems of understanding humans, which are not evident under earth conditions. In other words, microgravity research is an excellent tool for basic science in physiology and medicine and this research can help to improve astronaut support during exploration and at the same time to increase understanding on how humans function in health or disease on earth. As astronauts need to be healthy and to perform well, medical care and space medical research are also model applications for the future needs of medicine to focus on prevention, on individualization and on telemedicine.

For example, recent results about the regulation of human sodium balance in space (Drummer et al. 2000, Heer et al, 2000) and in space analog studies (Titze et al. 2002) have triggered a completely new field in human physiology and medicine research on earth, whose terrestrial application potential is enormous. The results are currently revolutionizing our understanding of blood pressure regulation, of osteoporosis, of the immune system, of autoimmune diseases, of protein metabolism, of metabolic diseases and of ageing in general (e.g., Machnik et al, 2009; Kleinewietfeld et al., 2013; Kopp et al, 2013). Also, new diagnostic technologies such as sodium visualization by magnetic resonance imaging (MRI) are being developed. Without space research - in an approach dealing with basic questions and extending beyond solving operational problems – and without the strategy to see space and terrestrial life sciences research not as two separate topics, but as one, these new findings would not have been possible.

Currently, no other field of medicine besides space medicine examines healthy humans using long-term studies under highly standardized conditions. Until recently, it was assumed that we would know in principle how blood pressure is regulated and how it is interdependent with salt intake. The first study in which this was really tested under standardized conditions was done only very recently (in 2010 and 2011) during the MARS 500 simulation study at the Institute for Biomedical Problems in Moscow. The surprising results from this study uncovered many deficiencies about our knowledge of physiology of healthy humans (Rakova et al., 2013). Another example is bone metabolism: Recent data from space research show that miR-214 has a crucial role in suppressing bone formation, and that miR-214 inhibition in osteoblasts may be a potential anabolic strategy for ameliorating osteoporosis (Wang et al, 2013).

Up to now there is no culture in regular medicine of doing highly-defined, long-term studies involving healthy subjects, as regular medicine focusses on the sick human rather than on keeping healthy humans healthy. Linking general questions of physiology with these of space physiology in such studies will thus be very beneficial for both fields in the future. Studying healthy young and aged males and females under highly defined conditions has never been done systematically in the past, but the data obtained and the differences in the results should be the basis of much of our future physiological understanding. Space physiology has the infrastructure, the knowledge and the task to do those studies.

As for astronauts, central tasks for future medicine in our modern aging society are also to keep healthy people healthy and able to perform well as long as possible, to individualize personal support and to support individuals remotely if necessary, bringing the expertise to the bedside. For all these tasks it is imperative to collect the respective data first, before a data base with individual suggestions can be set up. Here, epidemiological studies, that are not the domain of space physiology, are very important in a first step. However, clean data on individual behavior of healthy persons can only be obtained from highly standardized studies in which the basis of individual differences can be determined. This is the classical asset of space physiology. A typical example would be to find out why some individuals react with huge decreases in bone density during a bed rest study or during long-term stays in microgravity, while others do not. Similar questions have to be asked in all fields of physiology as well as in radiation protection, where cells of individuals are exposed to radiation with the purpose of understanding the molecular and genetic reasons behind regulation of individual cellular protection mechanisms.

Maintenance of physical fitness and high performance levels requires high motivation both for the individual and the group. How such motivation can be maintained, especially during rather boring missions – such as flights to or from Mars – is of great operational importance for future human space flight, and at the same time for our modern society, that needs active members of an aging work force that currently suffers from increasing problems of burn-out and depression. This also includes the huge field of performance in general. Discoveries from space performance research can be beneficial for helping people on Earth cope with extreme/high-risk conditions, such as victims and responders to natural disasters, management of safety in 24-hour industries, survival in extreme environments, etc.

Altogether, caring for astronauts means asking the same questions as caring for healthy humans and means tackling central tasks of the medicine of the future, i.e., personalization. Thus, astronauts could serve as role models for these future tasks.

The next Kondratieff Cycle: Specific challenges for space life sciences

According to a popular hypothesis, economic developments go in cycles (Kondratieff). The next such cycle, the 6th, will probably be the cycle of healthcare, nano/biotechnology and green technology (e.g., Allianz Global Investors). Strategically linking the needs of future human exploration with these challenges is based on two pillars. First, the direct link of space research to economic development uses the need to care for astronauts as models of healthcare for humans in general and focusses on certain areas where space research opportunities provide advantages over other possibilities on Earth. Second, when questions are answered jointly, that are relevant both for Earth and space applications, the process of discovery will be speeded up, leading to better treatments on Earth and in space. In space, the treatments (countermeasures) will have a much higher maturity and will thus enable better and quicker human exploration. This aspect of exploration has been completely neglected in the past.

From what aspects of space medicine will the next Kondratieff cycle profit?

Enormous investments are currently being made worldwide in healthcare research and technology development. Considering the fact that space life sciences research receives only a very small fraction of these funds, it is unreasonable to expect major breakthroughs and new technology developments from space life sciences research on the short term. Yet, government officials seem to expect an almost immediate return from space research and this expectation strongly affects their decisions about research priorities. It is time to change this short-term reward attitude, because the big successes await those who are in the business for the long term.

On Earth, nano- and biotechnology research, including molecular, genetic and “omics” R&D, are all developing rapidly, fueled by massive investments. This is not the area where space life sciences research will have strong impact. It is better to use these developed technologies in space than to try to develop them in space.

However, another area that is a driver for the next Kondratieff cycle is associated with green technology (solar energy, water management and recycling, etc.). This is an area where space research must develop an “ideal” model of remote life support that is critically dependent on the development of a plethora of “green” technologies. Only in this way the problems of life support on Mars or other bodies or even on the next generation of space stations will be solved. Such bioregenerative life support systems that provide energy, air, clean water and food, have been around the space world for a long time and are prerequisites to keep high-performing astronauts healthy and able to perform their demanding tasks. This is a research area where Earth research will produce the breakthroughs but space research will have the ultimate driving requirement to construct an optimum life support system. This will be no small task and is an example of the dual synergy of Earth and space life sciences research.

Healthcare is another field drawing huge investments on Earth, and this is the field in which space research has much to offer. Space physiology and medicine possess three special assets that complement ongoing strategies in Earth medicine. First, only space flight allows studying healthy humans without the perturbation of Earth’s gravity. Removing humans, tissues, or cells from the action of gravity allows the study of normal regulatory systems and functions in a novel way not possible on Earth. While general medical research on Earth focusses on disease mechanisms, understanding the healthy human of both sexes and at different ages has been and is being neglected. It is equally important to be able to control gravity while specific effects are being tested. Indeed, once fundamental mechanisms have been understood, one can make testable predictions about their functioning in gound-based analogues in an Earth laboratory, such as during bed rest studies. Because of the world-wide infrastructure and expertise that space physiology and space medicine provides, breakthroughs are beginning to appear, as described earlier. This infrastructure should be applied strategically in joint campaigns involving both space and terrestrial research questions.

Second, space physiology and medicine offer the continually developing capability to deal effectively with small numbers of subjects and to draw conclusions from limited data. Large epidemiological studies are the primary domain of terrestrial medicine and will always be so, but the challenge of dealing with individuals requires the kind of capability that space medicine has already built. Thus, highly defined studies on small numbers of humans are the domain of space medicine, and should be strategically employed for application in terrestrial medicine. These studies will also provide the typical scenarios to test modeling solutions that are central to the needs for future intelligent support systems for healthy persons that want more automated personal mobile support for their individual well-being.

Third, astronaut care in general should be used as a highly visible and effective model for future preventive and individualized care for humans in the mobile society. Thus, individual, preventive care for astronauts should become the best-care role model for other elements of society. Such care involves individual genetic screening, individual assessment of properties, application of advanced data management systems including modeling applications and individualized lifestyle suggestions for risk mitigation strategies and a lifelong surveillance mechanism. Such models could then also be applied to other selected groups like pilots and select managers and, in the long run, to the general population. The visibility of astronauts within society should then be used in an outreach strategy to motivate the general population to do personal healthcare “like an astronaut.”

Human spaceflight and society

Currently, support for human spaceflight in many nations is dwindling. One major reason is that human spaceflight projects are often seen as expensive prestige projects without proper scientific reasoning and with goals that can never be achieved. Justifying human spaceflight by “spin-offs” has not proven effective in the world of today. Such a justification can only come from an approach that embeds space medicine in the vastly larger field of terrestrial medicine. Then one can appreciate why it is urgent to optimize the scientific return from human space programs such as the International Space Station (ISS) rather than to terminate scientific research on the ISS after expenditure of billions of dollars to enable that research. The space life sciences community urges support and implementation of the recommendations summarized in this paper as one means of stabilizing and increasing support of human spaceflight in the general population. One sometimes reaches a goal quicker, when one proceeds slower, but at the same time keeps the support lines intact. Currently, the support lines are not intact and need repair. The subsequent recommendations give suggestions how to correct this situation.

Finally, as human spaceflight especially motivates the young generation to lead an active live and go beyond frontiers, human spaceflight should be used as model application to inspire the young generation to get an excellent education as a basis to be able to tackle the challenges of the future of humankind in general.

Recommendations: What should be done in the next decade?

Funding

- Space Agencies should intensify joint research strategies with “terrestrial” scientific funding organizations like NIH (US), ESF (EU), EU (EU), NSFC (China) etc. and focus on using microgravity for answering scientific as well as operational questions.
  Specific Recommendation:
  - *Space Agencies should solicit specific joint announcements of research opportunities with “terrestrial” funding agencies that focus on scientific questions with both “terrestrial” and “space” aspects*

Collaboration

- Global collaboration in space life sciences should be intensified
- Opportunities for research under microgravity, including those available from commercial providers, should be used intensively, involving any country that supports space life sciences research
  Specific Recommendations:
  - *A coordinated international list of providers of spaceflight opportunities should be established and global access to these research opportunitiesshould be enabled*
  - *Special emphasis should be put on enabling emerging countries to participate in space life sciences research*

Infrastructure

- Facilities and research opportunities to study scientific questions on healthy subjects, such as the facility :envihab at the German Space Center DLR, the facility L.U.N.A.R. Palace at Beihang University in Beijing, the MARS 500 Facility at IBMP in Moscow or similar unique facilities that focus on answering scientific questions, should be strongly supported.
  Specific Recommendations:
  - *An International Human Spaceflight virtual Institute should be established.*
  - *The core element of this Institute should be major Installations such as the DLR :envihab in Cologne, the IMBP MARS 500 Facility in Moscow or the L.U.N.A.R. Palace Facility at Beihang University in Beijing*

Prioritization of human spaceflight projects

- Utilize ISS intensively and extend its life time as long as possible, at least beyond 2025
- Provide continuous access to LEO Space Stations as a long-term strategy to solve future human exploration problems and to answer basic scientific questions
- Develop and prepare for flights beyond LEO and utilize such preparation to address both basic scientific and operational questions

Specific Recommendation:
  - *Long term LEO human research capabilities should be maintained continuously far beyond 2025*
  - *Additional exploration projects beyond LEO should be done in parallel and not instead*

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