HUMAN FLIGHT TO MARS – CHALLENGES FOR INTEGRATIVE HUMAN PHYSIOLOGY

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ABSTRACT

The necessity to focus research activities on the multifaceted task of bringing humans safely to Mars and back can be seen as a challenge to concentrate on major developments for the future of Medicine. These challenges will shift medicine from the present organ and disease focussed statistical approach to individualized medicine, in which as much individual information on properties/features of single subjects as possible is used as a prerequisite for individualized solutions during a specific problem. For astronauts this happens during their flight to Mars, while for the general population this will be wherever they need this help. Two key developments for this change of paradigms, which will shift medicine from expertise-centered statistical approaches to patient-centered individualized approaches, will be to focus on integrative physiology and on the development of modelling systems that contain up-to-date medical knowledge as well as individualized knowledge on individual subjects. Such solutions are still decades away, but the task for medicine to keep astronauts healthy on their flight to and from Mars can be used as a visible task to develop such a system. Thus, flights to Mars could also be used as test grounds for the flights into the future of medicine.

MEDICAL CHALLENGES FOR HUMAN FLIGHTS TO MARS

Human flights to Mars may still be decades ahead. However, the tasks for medicine in order to keep the crews physically and mentally healthy during these flights are not yet resolved. Five major areas of challenges for medicine that need to be resolved for human flights to Mars can be identified.

Weightlessness. Presently, crews on the International Space Station are supposed to do a daily physical training of more than two hours per day using a variety of training equipment in order to avoid major degradations of the body systems in weightlessness, such as the musculoskeletal or the cardiovascular systems. However, in reality, individual training duration and intensity vary largely between individual astronauts (Bogomolov et al., 2007). As a consequence, negative health effects of spaceflights differ as well. Several countermeasures are currently in use, including treadmill as the most important countermeasure, ergometry, resistive exercise training and several others. In addition, new methods such as vibration platforms are currently being tested.

The most promising novel approach – that had already been tested in the 1970s (e.g., Young, 1977; Kotovskaya et al., 1980) – is the use of artificial gravity. Various space agencies and institutions around the globe have currently started or are planning research campaigns on the use of short arm centrifuges for countermeasures during long term spaceflight. Potential major benefits are that (1) a gravity vector pushes body fluid towards the lower body and thus induces a hyper-g situation at the feet, while the head is only exposed to moderate *g* loads, (2) during centrifugation this can be combined with physical exercise countermeasures, so that the combination of countermeasures will consume less time than presently required, and (3) countermeasure effectiveness would increase even in little motivated astronauts since centrifugation per se is a passive process. Hopefully, a combination of artificial gravity with other countermeasures will largely decrease the need for daily physical exercise and at the same time will have superior effects on current procedures.

All these novel developments will require extensive testing on earth before their usefulness in weightlessness can be tested. The major challenge for this will be to start an internationally harmonized approach. Presently, most investigator groups worldwide use the model of -6^o head down tilt bed rest as the analogue of weightlessness. These studies often involve up to several months of bed rest including several groups of scientists. However, up to now, study protocols are usually done without international standardization approaches and results are therefore usually difficult to compare. An international standardization approach, as has been recommended previously (Gerzer and Ruyters, 2000), would be very appropriate. At present, such an approach to standardize international large bed rest study campaigns has jointly been started by NASA, the Institute for Biomedical Problems in Russia and the German Aerospace Center in Germany. In addition, ESA has recently also started such an approach.

Radiation. Radiation is a major hazard for the crews flying to Mars. When leaving the protective magnetic belts outside the earth, the radiation exposure for the crews will increase and there will be little protection in case of solar particle events (Horneck et al., 2003). One can assume that the annual dose during a flight to Mars will amount to around 1 Sievert – one fifth of the lethal dose during acute radiation exposure (Hellweg and Baumstark-Khan, 2007). Presently, a major experiment is being conducted on the International Space Station to assess radiation exposure inside the human body in order to find out e.g., at what level radiation exposure is critical for organs and how exposure changes inside the human body (Reitz and Berger, 2006). Over 16 groups worldwide participate in this concerted approach that will

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also lay ground for the better prediction of radiation exposures during a flight to Mars.

While this approach is improving space radiation dosimetry, radiation protection for Mars crews requires further steps. There are two possibilities, either to protect from the outside – developing novel and better shielding material and shielding strategies - or to protect the body from the inside on a molecular basis. One possibility is to include a genetic assessment of potential Mars astronauts and exclude those with an increased risk of developing cancer; the other possibility is to learn more about the molecular mechanisms that protect humans from developing cancer, e.g., by studying the role of the nuclear factor kappaB in cancer protection (Baumstark-Khan et al., 2005), and finding ways to upregulate protecting mechanisms during a flight to Mars and especially during high radiation exposure phases.

Emergency. After leaving Earth or Moon orbit towards Mars, there will be no way back before arriving in Mars orbit. Thus, crews will be on their way for at least 500 days if they use the currently available propulsion systems. Since there will be a considerable time delay in communication, crews will need their own emergency system and cannot rely on telemedical assistance. Therefore, Mars expeditions will require at least two doctors experienced in emergency medicine. In addition, diagnostics and treatment facilities onboard must be as minimally invasive as possible. It would be of enormous help if a system was available that could instantly make suggestions to the astronauts for optimal individual help for their colleague, in case of an accident or the outbreak of a disease. This “digital friend” or “digital astronaut” (White and McPhee, 2007) would “know” the individual features of each astronaut and link them to up to date medical knowledge, which is also available in the digital friend system. Such a system is currently not available nor in sight, but considering the rapid progress made in medical knowledge on the one hand and the progress in information technology on the other, it might be available in at least a rudimentary stage when human missions to Mars become reality.

Isolation. Astronauts on a mission to Mars will be isolated with no way to return for at least 500 days and will be locked up together in a “tiny tin can”. Therefore, the psychological care for crews is an enormously important aspect of flights to Mars. Crew selection, crew composition, crew training and care for the crew during and also after the flight are important steps for successful missions. Probably the most important work will have to be done before the mission starts since any mistake in selection and training of the crew will not be reversible inflight. As known from previous experience (e.g., Gushin, 2002; Kanas, 2002), it is not uncommon to observe psychological problems among crewmembers or during the interaction of crews with ground subjects. If mixed crews will fly, then there should be at least two persons of the same sex to avoid isolation situations and all flying astronauts should have stable relationships on the ground. A digital friend approach that will not only contain medical information, but will also be able to suggest personal behavioural strategies for stressful situations based on individual properties/features of the respective astronaut would be extremely helpful. However, such an approach appears even more complex and difficult than a digital friend approach solely for physiology.

Life Support. Habitation and life support are integral parts of crew care for missions to Mars. Presently, the monitoring of cabin environment is already a task of space surgeons on the ground, who are responsible for the medical care of the astronauts. The habitat will not only protect the crews from the hostile space environment, but will also be required to provide an internal environment that includes basic properties like pressure, oxygen content, air quality, temperature and the absence of any toxic agents as well as sufficient food and water supply. The habitat will also influence the mental well-being and the motivation of the astronauts. This has been proven true when astronauts report that even astronauts that had never thought about gardening before are positively emotionalized when they grow plants in space. Thus, support for astronauts with the concept of a “digital friend” will also need to include habitation questions.

CHALLENGES FOR INTEGRATIVE PHYSIOLOGY

All the above-mentioned challenges require a joint integrated approach. This integrated physiology approach not only involves the horizontal approach of mutual influences of various organ and tissue systems, but will also have to involve a vertical approach that takes into account genetic properties and molecular regulatory mechanisms. In addition, it will have to integrate further dimensions expanding into individual personality properties and environmental influences.

A first step to achieve these goals is to set standards for conducting studies with harmonized study protocols connecting leading research institutions worldwide. Approaches for this are presently done at the European Space Agency, at NASA, at the Institute for Biomedical Problems in Russia and at the German Aerospace Center. This has to be linked with personal mental properties of individual subjects. Such psychological evaluations can start with “simple” methods to assess individual stress reactions to given stressors (Johannes et al., 2007), and will require extensive testing of individual reactions to predefined situations and predefined environments.

The final and most important step is to interconnect molecular studies with systems interaction approaches to allow and link observatory results with molecular signal cascades and their regulatory mechanisms. Unfortunately, during the last decades molecular and systems physiology have become separate entities. The molecular world studied tiny details in order to start to understand observations that had been made on the systems level, while the systems world was not interested in the molecular world since myriads of details alone cannot explain how a system operates. It will be a very fascinating task for integrative physiology to recombine these worlds of research strategies in order to be able to explain observations to the very detail level. This step is still at its beginning; it will take decades and will allow individualization of results and most importantly of predictions for the future. All of these tasks can only be united into one model if a major systems development in the direction of a "digital friend" approach is made.

THE DIGITAL FRIEND VISION

Ever since the pioneering work of Arthur C. Guyton (e.g., Guyton et al., 1972), there exists the vision of being able to eventually modulate human physiology, pathophysiology and behaviour (e.g., White and Mc Phee, 2007). This – linked to current best practice medical knowledge - would make it possible to simulate all the abovementioned aspects and would decrease the need for human research since reactions could be predicted as e.g. during the design of a complex aircraft. It could be used as a guide for individuals to prevent disease and to assist in case of diseases and emergency situations. It would also allow us to shift from statistical to individual medicine. However, it is unclear when and whether such a system can be developed since every human being including primarily genetically identical twins is unique, reacts uniquely and is by far more complex than the most complicated technical system we can dream of. Still, approaches like training models for intensive care medicine with virtual patients, like the Physiome project, the visible human project or the digital soldier project of DARPA show that it is now time to develop first approaches for a digital friend concept (for overview see White and McPhee, 2007).

Human flights to Mars can be used as a chance to bring this vision closer to reality. The system would certainly not be designed for the astronauts primarily, but the globally visible task to keep astronauts healthy and motivated and the chance to have several highly trained professionals in a defined environment for over 500 days is a huge chance to test and improve such a system with astronauts. The flight to and from Mars could also be used to give the crew the task to improve the digital friend system by testing and improving the predictive power by daily inputs and feedback. Thus, the mission to Mars could have a dual task: It would not only be the mission to expand the borders of human presence, but would also be the mission into the future of Medicine.

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