HUMAN AND RODENT GROUND-BASED MODELS OF SPACE FLIGHT ENVIRONMENTS
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INTRODUCTION

Today, as we stand on the brink of the 21st century, access to space is still limited and flight costs are still high. Flight opportunities of any kind are rare, but at the same time it is clear that a new era is dawning. The completion of the International Space Station (ISS) will provide mankind, for the first time, with an international, permanently manned outpost for research in space. Looking ahead further, practically every national or international space agency is studying approaches for a return to the moon or an initial manned mission to our “sister planet” Mars. All these circumstances clearly indicate that human presence in space will be a continuing and growing event well into the new century. When we look back at the 40-year history since the first man travelled through space, many questions regarding the effects of space flight on human beings have been examined and answered. Yet our knowledge is still far from complete. More questions remain to be asked and answered, and as usual in science, for every question we answer a host of new questions arise. To answer those new-born questions there is great need for more research opportunities to be undertaken in both the traditional arena of space flight operations, and the often over looked ground-based models that simulate microgravity.

ANIMAL MODELS ARE NEEDED

One option that provides more opportunities for research is the use of animal models. Although not always well understood by the public, this approach has proven highly successful, especially in the medical and pharmacological fields (Ballard et al. 1992; Grindeland at al. 1992). For example, most of the work awarded the Nobel Prize in Medicine has been done on experimental animals. Since 1998 the European Space Agency (ESA) has supported space research using rodents as test organisms. These rodents are used according to strict ethical guidelines, and used only if no other alternative can be found to answer the scientific questions.

While the main thrust in space life-science research will continue to explore the effect of microgravity on humans (West, 2000) the exclusive use of humans for this research would severely limit the range of possible experiments. The scope of research with animal models is significantly greater than with humans, and a wide variety of techniques is available for use on rodents. Indeed, many investigations can only be performed on these animals due to the clinical issues involved.

Specifically, it will be possible to take advantage of the many advanced molecular biological techniques developed during the last decade, such as the use of transgenic (genetically modified) mice and rats. Furthermore, on the ISS, 1-g in-flight controls and g- threshold studies are only possible with animal subjects and not with humans. Other areas of interest that might benefit from animal research in the microgravity environment are early post-natal development and multi-generation studies.

There is no lack of scientifically valuable experiments requiring rodent subjects. With regard to the US and European experiment proposals written for the Life Science Research Announcement (LSRA) from 1998, about 1/3 of the recommended experimental work in the fields of medicine and physiology required the use of rodent test subjects

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Table 1. Number of recommended experiments in LSRA ‘98

It should not be forgotten, however, that careful testing methods and supporting studies should always be performed extensively first on the ground in order to ensure only our very best focused experimental work in space.

THE GROUND-BASED ANIMAL MODELS

To simulate some effects of microgravity on the ground, whole body suspension models as well as hindlimb, or tail suspension models have been developed (Morey et al., 1979). As the name implies, rodent test subjects are suspended by their tails, or fitted into a harness resulting in fluid shift and unloading from the hindlimbs. This model has been so successful that its use is no longer exclusive to the areas of space-related research. A simple search in the medical literature database “Medline” yields hundreds of publications where the hindlimb suspension model is used (e.g. in neurophysiology research, drug testing, developmental research).

The use of hypergravity, either for short or extended durations, is also of growing interest, especially in the field of bone and developmental neuroscience. Since a centrifuge will be available on board the biology module of the ISS to serve as either a control environment or a tool for research on thresholds, it makes sense to give researchers the

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opportunity to perform ground experiments using hypergravity.

**HUMAN ANALOGS**

While the benefits of animal research are remarkable, some research questions remain that can only be answered by using human beings as test subjects. With regard to space flight, two ground-based models for research on humans are relevant: bed-rest and confinement experiments.

**Bed rest**

Since the time of the classical physician, Hippocrates, we have known that prolonged immobilization results in physiological and functional deterioration. Scientific studies with bed-rested patients and normal healthy subjects began as early as 1855 (Fortney et al. 1996), but the American and Russian space programs of the 1960s certainly gave new impetus to this type of research. In bed-rest studies numerous phenomena can be observed that are similar to effects of microgravity (i.e. the loss of bone and muscle mass, fluid redistribution, hormonal changes, enhanced calcium excretion, etc.) (Fortney et al. 1996). Apart from gaining insight into the mechanisms of these bodily changes, experiments can also be conducted regarding effects of diet and evaluation of countermeasures. Although the completion of bed-rest protocols is complex and requires special facilities, the scientific benefit is enormous. For example, in one 42-day, bed-rest study done in Toulouse, France, 15 research teams conducted experiments which led to more than 30 publications in peer-reviewed journals (Pavy-Le Traon, 1997). Similar studies will be conducted in the future. ESA, in cooperation with the French and Japanese national space agencies are organizing a new long-term, bed-rest study that will be implemented over the period of 2001-2002. Three groups of 9-10 subjects will stay in strict anti-orthostatic (-6 degrees) bed-rest for 90 days. One control group, one group using an anti-osteoporosis drug and one group using resistive exercise training will be tested. The main fields of research considered will be bone and muscle physiology and countermeasures, neuroscience, and cardiovascular physiology, including hormonal and metabolic regulations. Similar coordinated investigations will be initiated in the US. These studies make even more sense now that we are in a fortunate situation in which enough data exist in fundamental space physiology to aid us in finding countermeasures that will have additional relevance to future clinical applications.

**Confinement and isolation**

Confinement experiments are intended to model the setting of the ISS mission environment or future Mars missions. Long-term isolation and confinement of small groups of people is one of the major characteristics of missions like these. Similar to microgravity, the closed environment is something physically and psychologically new for a human being. Confinement under these conditions is complicated by deficient and imposed social contacts, monotony and limited locomotion. In addition to these factors the international character of the ISS and future Mars missions adds national and cultural project aim at identifying possible sources of problems. For this set of simulations seven different groups spent periods from 28 to 240 days in isolation with various overlapping periods of stay. A total of 80 investigations were included in the overall project, covering the following areas of research:

1. Intergroup and group behavior
2. Individual and operator psychology
3. Clinical/physiological investigations
4. Biochemical and immunological assays
5. Sanitary/hygienic and microbial survey
6. Biological studies
7. Functional and operational engineering tests and data base verification.

Together with data gathered from similar isolated environments (e.g. submarines, Antarctic bases or oil drilling platforms and previous dedicated isolation studies), these experiments will help avoid pitfalls that await man’s future presence in space.

**CONCLUSION**

Animal models for space flight research are now well established and are leading to discoveries beyond the borders of space-related research. Such studies, especially those requiring large facilities like centrifuges, should be carefully planned by the space agencies to encourage research under hypergravity, which will in turn prove beneficial to a much larger research community. These ground-based initiatives should start immediately since animal research capabilities on the ISS are delayed until after 2006.

Confinement and isolation experiments devoted to operational and psychological studies have been supported by our Russian colleagues. ESA has a good historical record in this field as well, and no doubt will continue studies in this direction. In the US such analogs are used mainly for the testing of life-support technology. In the future years, in view of our eventual manned Mars missions, it is essential that all agencies involved recognize the importance of the psychological and intercultural issues on such a long-duration flight. Such issues, underestimated until now, have the potential to jeopardize extended space travel and solutions will emerge only from both a global and intercultural approach.
REFERENCES


