Muscle Research and Human Space Exploration: Current Progress and Future Challenges

Daniel L. Feeback, Ph.D.
Muscle Research Laboratory, Johnson Space Center

Since the beginning of human space flight, there has been serious concern over the exposure of human crewmembers to the microgravity of space due to the systemic effects on terrestrially-evolved creatures that are adapted to Earth gravity. Humans in the microgravity environment of space, within our currently developed space vehicles, are exposed to various periods of skeletal muscle unloading (unweighting). Unloading of skeletal muscle both on Earth and during spaceflight results in remodeling of muscle (atrophic response) as an adaptation to the reduced loads placed upon it. As a result, there are decrements in skeletal muscle strength, fatigue resistance, motor performance, and connective tissue integrity. This normal adaptive response to the microgravity environment is for the most part of little consequence within the space vehicle *per se* but may become a liability resulting in an increased risk of crewmember physical failure during extravehicular activities or abrupt transitions to environments of increased gravity (such as return to Earth or landing on another planetary body).

In the U.S. Space Program the only countermeasure to skeletal muscle functional deficits that has been utilized is physical exercise by means of various modalities. In-flight exercise hardware and protocols have varied from mission to mission as have mission durations. Collective knowledge gained from these missions has aided in the evolution of exercise hardware and protocols to spaceflight-induced skeletal muscle atrophy. Long duration missions and missions with several transitions between gravitational environments present the greatest challenges to risk mitigation and to successful development of countermeasures of proven efficacy. Russian scientists have utilized a variety of exercise hardware and in-flight exercise protocols during long duration space flight (up to 1 year) aboard the Mir Space Station. Such protocols have included aerobic and resistive (both active and passive) exercise using a variety of exercise equipment. On the International Space Station (ISS), a combination of resistive and aerobic exercise has been employed. Outcomes have been acceptable based on current expectations for crewmember performance upon return to Earth. However, for a return to the moon mission, establishment of a lunar base, and interplanetary travel to Mars, the functional requirements for human performance during each specific phase of such missions needs to be well defined and countermeasures developed that meet those performance requirements.

NASA's current approach to identifying, soliciting and prioritizing facilitative research that is directed at mitigating risks to human crewmembers both within low earth orbit (ISS) and beyond is defined by the Bioastronautics Critical Path Roadmap (BCPR -- http://criticalpath.jsc.nasa.gov). Recently, the BCPR has been re-evaluated jointly by NASA scientists and external experts and changes made to reflect the current direction of efforts for a crewed return to the moon of longer duration than during the Apollo program and for human interplanetary travel to Mars. The BCPR includes a set of enabling questions to which answers will provide knowledge beneficial in mitigation of risks to crewmembers and to increasing the probability of successful missions.

Access to human crewmembers during both short and long duration missions for the study of skeletal muscle adaptation to microgravity and the efficacy of countermeasures is a limited resource thus requiring the use of ground-based models for conduct of both fundamental and applied skeletal muscle research. Various models for which sufficient data have been collected were reviewed recently (Adams GR, Caiozzo VJ, and Baldwin KM; J Appl Physiol 95:2185, 2003). Such models include horizontal or head-down bed rest, dry immersion bed rest, limb immobilization, and unilateral limb suspension. While none of these ground-based models provides a perfect simulation of human microgravity exposure during spaceflight, each is useful for study of certain aspects of muscle unloading and sensory/motor alterations. Future development, evaluation, and validation of novel countermeasures to skeletal muscle unloading will likely employ these same models. Prospective countermeasures may include pharmacologic interventions, innovative exercise hardware providing improved loading modalities, locomotor training devices, passive exercise devices, and artificial gravity either as an integral component of the spacecraft or as a discreet device contained within it. With respect to the latter, the hemodynamic and metabolic responses to increased loading provided by a human-powered centrifuge have been described quite recently (Caiozzo VJ, *et al.*, Aviat Space Environ Med, 75:101, 2004). Additionally, use of selected countermeasures during spaceflight will require monitoring of their effectiveness in meeting defined human performance requirements.

Development of truly novel approaches to countering the effects of microgravity on human physiology will require a more complete understanding of the processes that underlie them. Hypothesis driven research using mechanistic approaches will be required to advance the state of knowledge and to provide answers to many of the enabling questions contained within the BCPR. To this end, both animal studies using models of skeletal muscle unloading and cellular/molecular paradigms are fertile ground. Significant resources and efforts should be directed toward such studies; failure to fully exploit such investigations will impede both discovery and advancement of the state of the art.