

Skeletal Muscle Discipline Report on Countermeasures

I. Nature of the Problem

Accumulated evidence, based on information gathered on space flight missions and ground based models involving both humans and animals, clearly suggests that exposure to states of unloading (microgravity conditions) for varying duration (days to weeks to months) induces a variety of adaptations in the intrinsic structural and functional properties of skeletal muscle. These alterations or deficits include the following structural, biochemical/molecular, physiological, and biomechanical properties.

- 1) Atrophy of both slow-twitch and fast-twitch muscles (fibers) comprising the lower extremity and trunk musculature.
- 2) A change in contractile protein isoform expression in a select population of slow-type fibers reflecting a faster phenotype for controlling both cross bridge and calcium cycling processes, i.e., the primary pathways for energy consumption in performing mechanical activity.
- 3) Corresponding changes in the functional properties of the muscle manifesting a speeding in the shortening and relaxing properties of the muscle.
- 4) A reduction in both the absolute and relative force and power generating properties of fiber-types comprising antigravity and locomotor skeletal muscle.
- 5) A shift in the intrinsic activation patterns of antigravity muscles whereby a greater frequency of neural activation is required to generate submaximal force output of the muscle. These alterations are likely impacted further by alterations in the metabolic and functional properties of dorsal root ganglia cells in small motoneurons, which could impact the intricate function of both sensory and motoneurons linked to the skeletal muscle system.
- 6) A shift in the intrinsic substrate utilization profiles of the muscle whereby the capacity to metabolize fat as a primary fuel is reduced relative to that of carbohydrate. Such a shift in profile could potentially compromise the intrinsic endurance properties of the muscle.

Collectively, the above listed alterations provide the underlying factors contributing to the well documented profile whereby individuals following prolonged space flight (and/or ground based states of unloading) have reduced strength, power, and musculoskeletal endurance as well as a reduced capability of performing routine motor activities requiring both stability and fine motor skills. Presently, it is uncertain as to

what extent these functional deficits a) impair one's ability to perform strenuous extravehicular activity, particularly after more prolonged exposure to microgravity, and b) deleteriously affect one's ability to perform high intensity egress activities in the event of an emergency upon landing. Further, in the absence of adequate control data (i.e., information obtained on individuals in the absence of countermeasures) on human subjects exposed to microgravity, it is presently unknown as to what extent these deficits can be ultimately manifest.

II. Countermeasures to the Problem

The successful performance of any movement activity of varying intensity relies upon three important properties of neuromotor function:

- 1) the ability to coordinate contractile activity across the muscle groups involved in that task (the property of motor unit recruitment and coordination);
- 2) the ability to generate adequate force (and power) to accomplish the movement and/or work requirements (the property of strength);
- 3) the ability to sustain the activity over a period of time (the property of endurance).

Based on the available evidence, it appears that the countermeasure strategies used to date for maintaining the skeletal muscle system in microgravity have been biased to maintaining muscular endurance (chiefly as an outgrowth of maintaining cardiovascular fitness) with relatively less attention focused on maintaining muscle strength and motor control. This conclusion is based on the types of exercise equipment and exercise paradigms that have been used during space flight, i.e., the use of treadmills, rowing devices, and cycle ergometers. While these activities are largely suitable for providing adequate stimuli to the cardiovascular system, it is uncertain as to how effective they have been in maintaining muscle performance. The concern is that routine activities of running, cycling and rowing are manifest as "high frequency and low force" activities, which theoretically should enhance the endurance of the muscle. However, in order to prevent muscle atrophy and minimize the loss of strength and power of the musculature (which are influenced by both muscle mass and neural factors), activities which require maximal or near maximal force output of the muscle (i.e., high forces and low frequencies) are required. The activities presently used are likely imposing force requirements on the muscle groups in the range of only 25-35% of what is thought to be required.

While recent reports concerning the exercise programs designed more specifically for the Extended Duration Orbiter Program are beginning to address the importance of incorporating heavy resistance paradigms as part of the countermeasure strategic plan, this is a strategy that only recently has received any attention, but one that needs to be brought to the forefront. This conclusion is based on the fact that in spite of the large

volume of exercise that has been routinely performed by individuals on extended orbit in both the American and Russian Space Programs the overwhelming evidence indicates that the exercise paradigms and other countermeasure strategies have been marginally successful, at most, in preventing deficits in muscle structure and function. Furthermore, in ground based models involving animals, it is most apparent that exercise programs of the endurance type are markedly inefficient compared to heavy resistance paradigms in preventing the marked degree of muscle atrophy and loss of strength that occurs in response to muscle unloading.

III. Concerns

While it is recognized that endurance exercise continues to be an important constituent in the overall health maintenance for prolonged space flight, NASA must re-examine the almost exclusive dependence on aerobic exercise countermeasures and establish a new set of priorities in its countermeasures program. These priorities need to be better aimed at targeting a broader scope of the physiological systems of the body, including a greater focus on the skeletal muscle system.

At the present time there is little data indicating which muscles will be needed in work performed during extra vehicular activity (i.e., arms, shoulders, upper chest) nor is there assurance that appropriate countermeasures are in place that sufficiently maintain skeletal muscle structural and functional properties necessary to support the work capacity for extravehicular activity necessary for the construction of space station. This activity will require exercise tasks highly dependent on sustained work capacity under loading conditions confounded by the cumbersome space suits that are necessary for extravehicular activity.

Further, there is little information available that defines the minimal (essential) level of strength, power, agility/motor skill, and endurance necessary for assuring astronaut capability of successfully performing either work necessary to begin exploration of a distant planet, nor emergency egress activity during the landing phase of a mission following prolonged astronaut exposure to microgravity. Hence, it is uncertain whether individuals have the performance capability to handle such events.

IV. Recommendations

1) Heavy resistance training paradigms, aimed at eliciting maximal force production of key muscle groups supporting posture and locomotion, need to be initiated as soon as possible as an integral strategy for maintaining the skeletal muscle system. As an initial approach, strategies similar to those currently used on earth to optimize strength and enhance muscle enlargement should be used at the outset of such a program.

2) NASA Life Sciences and Operational Medical Programs should explore the utilization of currently available equipment that is capable of meeting the needs of such an exercise program rather than looking to build new equipment devices.

3) Exercise of high frequency-low force, i.e., the endurance type, should be continued as part of the conditioning regimen. Further, activities which impact on neuromotor skills to support posture, balance vestibular-oculomotor activities also need to be incorporated as part of the training program.

4) NASA needs to assess the level of physical skills (strength, power, endurance, motor control etc.) necessary to perform the type of work used in EVA, distant planetary landing, and emergency egress activity likely encountered by astronauts. These levels of skill should serve as the guideline(s) for establishing the level of fitness to be maintained by the exercise programs used in the countermeasures program. It seems reasonable to expect that all training programs will not maintain individuals at their respective pre-flight physical capacity; and thus more reasonable performance standards need to be sought.

5) Long term goals of NASA, in conjunction with the Countermeasures Program, need to establish basic and applied research that identifies the mechanisms of muscle wasting and to seek more effective countermeasures for preserving skeletal muscle homeostasis. Research in this area should focus on strategies to increase the effectiveness of physical activity via studies on the interaction of physical activity, pharmacological, and hormonal/growth factor approaches to understanding muscle plasticity.

V. Overarching Issues

This discipline endorses recommendations of the other disciplines covered in this report which support a greater focus on including research on 1) establishing better nutritional requirements and standards for astronauts; and 2) the establishment of an exercise countermeasure strategy that integrates activities supporting cardiovascular, vestibular and neuromotor, and musculoskeletal objectives. Since it is unlikely that there is an all encompassing type of exercise capable of counteracting microgravity-induced deficiencies in these systems, studies should be undertaken to take advantage of the technologies currently being developed to produce forms of artificial gravity via the use of exercise-cycling and other exercise devices that have the potential to transiently generate g-forces known to positively impact on the cardiovascular, vestibular, muscle and bone systems while simultaneously providing an exercise stimulus mimicking that currently seen with most conventional devices. Since technology to support this type of activity is rapidly emerging with design configurations that are feasible for incorporation into the space station modules, appropriate research to verify that intermittent use will protect without causing additional physiologic problems is needed.