Planning Strategies for Development of Effective Exercise and Nutrition Countermeasures for Long-Duration Space Flight

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Exercise and nutrition represent primary countermeasures used during space flight to maintain or restore maximal aerobic capacity, musculoskeletal structure, and orthostatic function. However, no single exercise, dietary regimen, or combination of prescriptions has proven entirely effective in maintaining or restoring cardiovascular and musculoskeletal functions to preflight levels after prolonged space flight. As human space flight exposures increase in duration, identification, assessment, and development of various effective exercise- and nutrition-based protective procedures will become paramount. The application of adequate dietary intake in combination with effective exercise prescription will be based on identification of basic physiologic stimuli that maintain normal function in terrestrial gravity, and understanding how specific combinations of exercise characteristics (e.g., duration, frequency, intensity, and mode) can be combined with minimal nutritional requirements that mimic the stimuli normally produced by living in Earth's gravity environment. This can be accomplished only with greater emphasis of research on ground-based experiments targeted at understanding the interactions between caloric intake and expenditure during space flight. Future strategies for application of nutrition and exercise countermeasures for long-duration space missions must be directed to minimizing crew time and the impact on life-support resources. *Nutrition* 2002;18:880–888. ©Elsevier Science Inc. 2002

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INTRODUCTION

Future space exploration and interplanetary travel will require humans to live and function in weightlessness for extended periods (i.e., months to years). The microgravity environment of space presents numerous biomedical challenges to the function and well-being of the human body that can potentially compromise the health, safety, and performance of astronauts. It is therefore critical that effective countermeasures be developed to ameliorate or eliminate physiologic alterations that may prove adverse to the function of astronauts during and after prolonged space missions.

Numerous investigations have provided evidence that specifically targeted physical exercise and/or nutrition on Earth, either independently or in combination, can maintain or increase physical working capacity (e.g., aerobic capacity, endurance, strength), improve blood pressure regulation during orthostatic challenges, promote muscle hypertrophy, and protect bone structure. However, less is known about the impact of the microgravity environment on the interaction of exercise and nutrition as possible countermeasures against the deleterious effects of space flight on these physiologic systems.

Perhaps the single most limiting factor to providing optimal nutritional requirements during long-duration space flight is the availability of food. As humans expand space exploration that takes them farther from a food supply, the ability to meet nutritional needs will depend solely on the food that can be stowed or grown on the spacecraft. Clearly, food availability will be restricted by space and weight limitations. It is therefore necessary that our design of countermeasures include careful planning to optimize dietary requirements with minimal food and fluid intake.

The use of physical exercise as a countermeasure against the deleterious physiologic effects of long-duration space flight presents at least two major challenges for meeting required nutritional intake during a condition of limited food availability. First, the energy expenditure required to perform exercise countermeasures can be significant. For instance, the average estimated metabolic cost of more than 1400 kcal for 2.5 h of daily exercise performed during prolonged missions on the Russian Mir space station represented as much as 35% to 50% of the total daily energy expenditure.[1] Second, mechanical efficiency is reduced in many of the physical activities performed by astronauts during space missions, thus requiring more energy expenditure for completion of the same task performed on Earth. Therefore, it is prudent that our research efforts be focused on the development of exercise countermeasures that use optimal mechanical efficiency and are designed to minimize the amount of physical activity and dietary intake required to maintain necessary physiologic function for safe return to Earth.

This article provides a review of some fundamental physiologic functions that have been altered by exposure to low-gravity environments and associated with the operational problems of reduced physical working capacity, development of orthostatic hypotension and intolerance, and compromised musculoskeletal integrity. I attempt to provide perspectives on our understanding about physiologic mechanisms associated with or underlying adverse effects of space flight on functional performance and health of astronauts. The specific purposes of this article are: 1) to present a physiologic basis for the integration and use of exercise and nutrition as countermeasures designed to minimize or eliminate adverse adaptations to space flight that may compromise the health, safety, and productivity of space travelers; 2) to review past

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and present exercise and nutrition regimens used during space flight and to evaluate the effectiveness and limitations of their application; 3) to outline special considerations for development of exercise and nutrition countermeasures for space flight; and 4) to provide new approaches, concepts, and future directions for development or implementation of effective exercise and nutrition countermeasures for future long-duration space travel.

OPERATIONAL BASIS FOR DEVELOPMENT OF COUNTERMEASURES

Reduced Physical Working Capacity

It is clear that, even in the presence of balanced nutritional intake, maximal oxygen uptake ($\dot{V}O_{2max}$) can be reduced by as much as 20% depending on the duration of exposure.[2] A 22% reduction in $\dot{V}O_{2max}$ was recently verified in astronauts after space missions of only 9 to 14 d.[3] One primary mechanism associated with lower $\dot{V}O_{2max}$ is a 10% to 20% reduction in circulating plasma volume that occurs during space flight.[2,4,5] Time course and magnitude of change in plasma volume are correlated with reduction in $\dot{V}O_{2max}$, with a rapid decrease within the initial days of exposure and a smaller gradual reduction from 1 to 4 wk.[2,4] Because circulating blood volume directly affects cardiac filling, it is not surprising that the reduction in $\dot{V}O_{2max}$ after exposure to simulated or actual lack of gravity can be explained by proportional decreases in stroke volume and cardiac output at maximal exercise.[2,3,6]

Because $\dot{V}O_{2max}$ is associated with endurance,[7] it is reasonable to assume that the reduced $\dot{V}O_{2max}$ resulting from adaptation to microgravity would lead to earlier onset of fatigue and lower physical working capacity in astronauts. In support of this notion, exposure to ground simulation of low gravity has demonstrated that increased fatigability during plantar flexion is associated with reduced peak calf vascular conductance, which in turn significantly correlates with the reduction in $\dot{V}O_{2max}$.[8] The notion that microgravity causes reduced oxygen delivery to (arterial blood flow) and/or oxygen consumption by skeletal muscle is supported by decreased capillary-to-fiber ratios and enzyme activities of aerobic metabolic pathways,[9] lower oxygen uptake with elevated expired carbon dioxide and respiratory exchange ratio, and higher recovery oxygen uptake with exercise in space flight.[10–12] Thus, development of exercise and nutrition countermeasures designed to maintain the function(s) of underlying mechanisms of aerobic capacity could be instrumental in ameliorating fatigue and limited physical working capacity during space missions.

Orthostatic Intolerance

Orthostatic intolerance has been a significant operational problem to astronauts for more than 35 y since a majority of crew members from US space shuttle flights demonstrated some degree of orthostatic compromise during postflight stand tests.[13,14] Reductions in circulating plasma volume of 10% to 20% are associated with reduced cardiac filling, stroke volume and cardiac output, and orthostatic intolerance after exposure to simulated or actual low gravity.[4,5,14,15] In addition, development of orthostatic hypotension after adaptation to low gravity is associated with several reflex mechanisms that include attenuated cardiac baroreflex sensitivity,[14,16] reduced peripheral vascular resistance,[14,15,17,18] and possible reduction in sympathetic responsiveness.[17,18] Therefore, development of exercise and nutrition countermeasures designed to maintain circulating vascular volume and baroreflex functions could prove instrumental in ameliorating the deleterious effects of microgravity on cardiovascular mechanisms associated with orthostatic compromise after space missions.

Muscle Structure and Function

The ability to develop and maintain forces with dynamic muscular contractions will affect work performance. Because skeletal muscles provide the force for moving the body and external objects against Earth's gravity, the absence of gravity removes a major stimulus to maintain normal strength and endurance in microgravity. Although this may not be detrimental to work and exercise performance in weightlessness, it seems to be a significant limiting factor on safe return and normal productivity in 1*g* after prolonged space flight.

Decrements of force development in various skeletal muscles have been documented in space crews during postflight testing. Ground and space flight experiments have demonstrated that as little as 3 to 4 wk of exposure to microgravity can result in average reductions of angle-specific peak torque across speeds for concentric and eccentric muscle actions by 20% for knee extensors and 10% for knee flexors.[1,2,19,20]

Studies from early space flight missions and ground-based experiments associated reduced force development of skeletal muscles of the lower limbs with decrements in the calculated volume of those limbs, suggesting the presence of significant muscle atrophy.[1,2,19,20] Despite normal or high dietary protein intake, extended space missions of 1 to 3 mo in duration increased urinary nitrogen and phosphorous excretion, resulting in negative nitrogen and phosphorous balance.[21] These excretory data were consistent with gross measurements of limb size that suggested skeletal muscle turnover and breakdown. With the emergence of more invasive techniques, collection and analysis of muscle biopsies from space flight and ground-experiments showed significant reduction in cross-sectional areas of all muscle fibers of the vastus lateralis,[9,19] with the relative reduction in muscle fiber cross-sectional area being greater in fast-twitch (23% to 36%) than in slow-twitch fibers (16%). Magnetic resonance imaging analyses after a 115-d space mission demonstrated 3% to 10% reductions in volumes of calf, thigh, and lower back muscles.[22] The average decline in maximum voluntary concentric force production in astronauts from whom biopsies were taken was approximately 15% for the knee extensor group, with a subsequent, approximately 20% average reduction in muscle fiber cross-sectional area.[9] The loss of structure and function in slow- and fast-twitch muscle fibers suggests that a combination of endurance and resistance exercises and appropriate dietary protein probably are required to effectively protect the integrity of skeletal muscle during prolonged space flight.

Bone Structure and Function

Despite normal dietary mineral intake, extended space missions of 1 to 3 mo in duration produced as much as two-fold increases in urinary calcium and phosphate excretion, resulting in negative calcium and phosphate balance.[21] Urinary hydroxyproline also increased by as much as 33%.[21] These excretory data provided indirect evidence from early space missions indicative of skeletal turnover and breakdown. Subsequent ground-based and space flight experiments provided further direct evidence that increased bone resorption and decreased bone formation contributed to loss of bone calcium and density at a rate of 0.4% to 1.0% a month,[23,24] with 7% to 12% mineral loss in trabecular bone and throughout the spine after 6 to 8 mo of space flight.[24–26] One consequence of reduced bone mass density caused by space flight is the potential increase in risk of bone fracture when physical activities such as running and jumping are performed in required mission operations on Earth or other planets with gravity forces. In addition, elevated urine calcium concentrations associated with bone resorption can increase the risk of renal stone formation during space flight.[27] The use of specific physical exercise designed to increase loading of the skeletal system in space in conjunction with dietary supplementation of minerals associated with skeletal growth and maintenance could provide an effective countermeasure against the deleterious effects of microgravity on bone and renal function.

PAST AND PRESENT USES OF EXERCISE AND NUTRITION IN SPACE FLIGHT

Interaction of Nutrition With Exercise During Space Flight

It is difficult to assess the interaction of diet and exercise during space flight because there are no systematic analyses of these factors together. For instance, nutritional composition was carefully quantified during the US Apollo space missions. Unfortunately, the application of physical exercise as a countermeasure was greatly limited by the confinement of astronauts to small space vehicles. The average nutritional composition of the typical Apollo diet was 18% protein (76 g), 17% fat (61 g), 61% carbohydrate (269 g), 1% fiber (5 g), and approximately 3% minerals, with an average energy intake of 1880 kcal/d.[28] When standardized for body size (weight), it became obvious that space flight alone inhibited hunger because calculations from eight astronauts on four different Apollo missions showed a significantly reduced average daily energy intake, from 37.0 kcal/kg on the ground to 26.5 kcal/kg in flight.[28] As a result, there was a significant average reduction of approximately 3.9 kg (~7%) in body weight. During missions of the Apollo space program, crew members failed to eat all the food available to them for reasons of decreased hunger, feeling of fullness in the abdomen, nausea, and preoccupation with critical mission tasks.

The US Skylab space missions were the first to incorporate regimented exercise programs as a countermeasure designed to minimize the deleterious effects of prolonged space flight on physical fitness ($\dot{V}O_{2max}$), orthostatic tolerance, and musculoskeletal structure and function. Nutritionally, the composition of the Skylab astronauts' diet was not altered significantly from that used in the Apollo program (i.e., 58% carbohydrate, 15.5% protein, and 26.5% fat), although caloric intakes increased to preflight levels at approximately 2830 kcal/d to accommodate the performance of extensive in-flight exercise countermeasures and extravehicular activities.[29] Interestingly, a reduction in average caloric intakes to approximately 2120 kcal/d in the Shuttle program probably reflects the significant decrease in in-flight exercise.

The increased volume (duration and frequency) and quality (modes) of exercise available to Skylab crew members were instrumental in maintaining caloric intake and body weight. For each successive mission, exercise duration was increased from 30 min/d on the 28-d Skylab 2 mission to 1 h/d on the 59-d Skylab 3 mission to 90 min/d on the 84-d Skylab 4 mission. On Skylab 2, only the cycle ergometer was used for in-flight exercise.[20,30] On Skylab 3, two devices called the MK-I and MK-II were developed and used with brake and spring mechanisms to provide some resistive exercise in addition to cycle ergometric exercise.[20,30] On the Skylab 4 mission, walking, jumping, and jogging on a "space" treadmill was added to cycling and resistive exercises.[20,30] Food availability was increased with each successive mission. With so many variables changing, it is difficult to interpret which factors affected physiologic adaptations and functions. However, some of the data may provide insight into the importance of increased exercise and food availability during space flight. Although one might expect that equal or greater weight loss would have occurred with increasing duration of flight and energy expenditure due to performance of more in-flight exercise, the opposite relation was observed. There was a positive correlation between total exercise time (i.e., minutes) and average dietary intake, with relative caloric intake (i.e., kcal/kg of body weight per day) increasing with each successive mission as the time of exercise was increased (Fig. 1, top). That is, with increased exercise volume as flight duration increased, astronauts were able to maintain their preflight caloric intakes during flight.[21,31] Consequently, there was a significant inverse correlation between average caloric intake during each mission and percentage of daily average body weight loss (Fig. 1, bottom). Therefore, increased exercise appeared to be responsible for maintenance of caloric intake and body weight. This association suggested that exercise is an important stimulus to hunger and/or nutrient absorption during exposure to microgravity and therefore may provide a critical method to optimize nutritional uptake and maintain body weight during long-duration space missions.

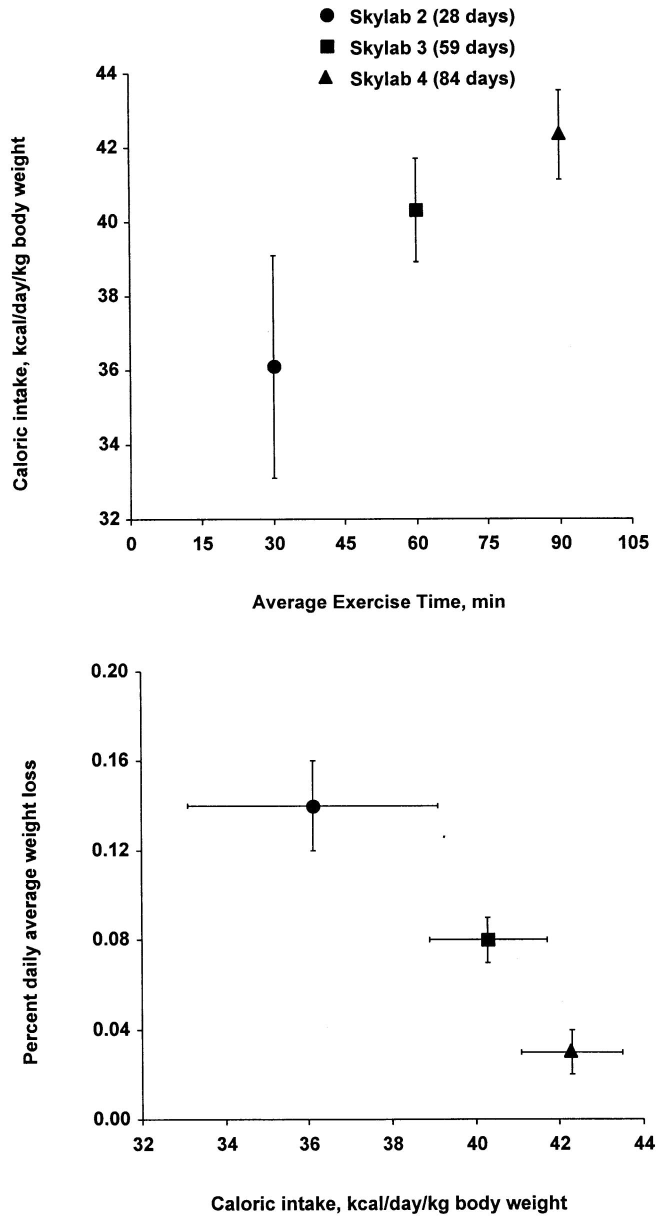

FIG. 1. Mean (standard error) data from the three Skylab missions show the relations between average exercise time and average energy intake (top) and between average energy intake and average daily reduction in body weight (bottom). n = 3 for each space mission. Data modified from Lane and Schulz.[76]

Effects on Physical Working Capacity

Historically, exercise designed for aerobic metabolism has been performed by astronauts as the primary countermeasure to prevent physical deconditioning during space flight. Exercise regimens used during long-duration space missions usually consist of one to two daily exercise sessions. Based on exercise heart rates and oxygen uptakes, each exercise session may be 30 to 75 min in duration, with exercise intensities between 50% to 75% of $\dot{V}O_{2max}$; the average amount of exercise usually increases during the second half of the flight.[1] The importance of regular, prescribed physical activity during space flight was demonstrated during a Russian 96-d mission when exercise training was interrupted for the initial 25 d, resulting in diminished exercise endurance.[1] Resumption of regular training improved hemodynamic responses, and exercise endurance increased to preflight levels by day 70 of the mission and was maintained thereafter.

The measurement of $\dot{V}O_{2max}$ during maximal exercise in weightlessness has been reported in the three Skylab 4 astronauts who were in space for 84 d.[11] Despite the volume of data demonstrating the consistent reduction of $\dot{V}O_{2max}$ after exposure to simulated and actual microgravity in the absence of exercise countermeasures,[2,3] average $\dot{V}O_{2max}$ of the three astronauts increased by approximately 8% after nearly 3 mo of exposure to microgravity.[1] Ground-based experiments also substantiated that daily aerobic exercise can maintain $\dot{V}O_{2max}$.[32] It is clear that, through an intense aerobic exercise program during flight, crews can maintain their aerobic and physical working capacities. However, some degree of diminished cardiovascular reserve to exercise upon return to terrestrial gravity after flight indicates a need for further refinement of exercise regimens to conduct longer space missions safely. In addition, current aerobic exercise programs used during space missions are costly with regard to energy requirement, and there have been no systematic assessments of nutritional strategies in an effort to optimize aerobic exercise training effects during space flight on physical work capacity and minimize the requirement of food intake.

Effects on Orthostatic Intolerance

Data from various space programs suggest that average daily fluid (>2000 mL) and sodium (>3500 mg) intakes are at or above recommended requirements.[29] Despite meeting these nutritional needs, negative body fluid and sodium balances occur during space flight[2,5,21] and are associated with reduced circulating blood volume (hypovolemia) and development of postflight orthostatic intolerance.[13,33] A dietary supplementation of approximately 1 L of an isotonic saline drink (saline loading) consumed approximately 2 h before return to Earth has been tested as a "nutrition" countermeasure.[13] Although there are no direct measurements of blood volume after oral saline loading in astronauts, ground experiments suggested that plasma volume can be completely restored using this technique.[34] Although a protective effect of saline loading was demonstrated after short-duration space flights (<4 d) of the Shuttle program,[13] these effects disappeared when the mission exceeded 8 to 10 d.[35] There is no evidence to suggest that fluid loading alone is effective in protecting against development of orthostatic hypotension and intolerance after long-duration space flight.

Aerobic exercise training similar to that used in space flight can increase blood volume[36] and orthostatic tolerance.[37,38] However, despite the extensive in-flight daily cycle ergometric exercise program during the 3-mo Skylab 4 mission,[1] astronauts experienced 16% plasma volume reduction that was associated with orthostatic instability postflight.[1,39] The Skylab results were verified by a subsequent ground experiment in which neither daily endurance exercise nor resistive exercise could ameliorate the reduction in orthostatic intolerance after 30 d of exposure to head-down tilt.[40] Results from space flight and ground-based studies suggest that repeated endurance or resistance exercise by themselves do not provide all the appropriate stimuli that could restore mechanisms that underlie orthostatic instability.

Microgravity leads to substantial and progressive development of baroreflex attenuation[41–44] that is independent of hypovolemia[41–43] and significantly related to the occurrence of hypotension and syncope during standing.[43] Unfortunately, dynamic and resistive training regimens in the Earth gravity environment employing repeated daily work sessions similar to those applied during space flight have failed to produce chronic changes in cardiac baroreflex function.[38] Therefore, development of effective exercise and nutrition countermeasures for orthostatic hypotension might have to include techniques that can specifically increase baroreflex responses before re-entry.

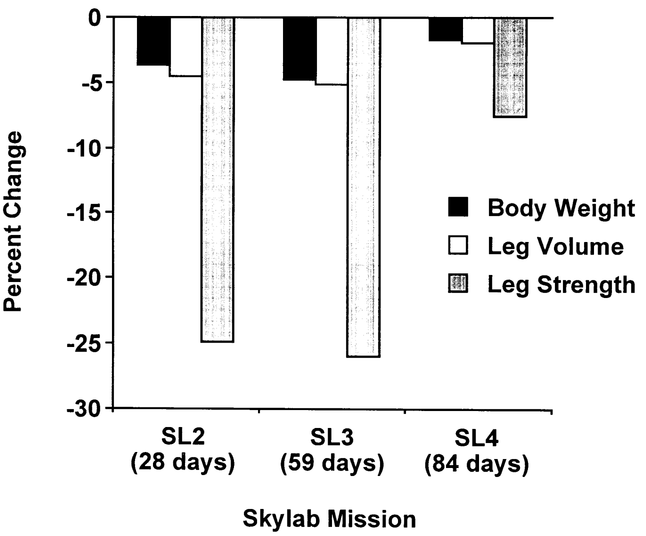

FIG. 2. Average reductions in body weight, leg volume, and leg strength during the three Skylab missions. $n = 3$ for each space mission. Data modified from Thornton and Rummel.[20] SL2 to 4, Skylab missions 2 to 4.

Effects on Muscle Structure and Function

Several observations reported from space and ground experiments support the notion that resistive exercise can be instrumental in preserving muscle structure during space flight. For instance, the preservation of leg muscle circumference and strength in two cosmonauts during a 16-d Russian orbital mission was associated with in-flight use of a resistance pulling device and the wearing of spring-loaded suits 8 to 12 h/d that provided consistent axial-load resistance of up to 50% of body mass to the musculoskeletal system of arms, legs, and torso during waking hours.[45]

After the initial 28-d flight of Skylab 2, which produced 15% to 20% reductions in arm and leg size and strength,[20] a concentric resistive isokinetic exercise device was added to the subsequent 59-d Skylab 3 mission that preserved arm strength.[20,30] However, despite the significant increase in volume and mode of exercise during the 59-d mission, postflight losses of leg size and strength were similar to those of the 28-d mission.[10,20] On the subsequent 84-d Skylab 4 mission, a Teflon-coated plate "treadmill" was added to the exercise arsenal and total daily exercise time was increased.[20,30] The tethering harness of the treadmill device was used especially for jumping and toe rises.[11] After the Skylab 4 mission, the reductions of body weight, leg volume, and leg strength were not eliminated but were less than half those of the previous two missions (Fig. 2). In addition to greater exercise volume, smaller reductions in volume and function of the leg muscles on Skylab 4 were associated with increased energy intake and less nitrogen loss.[22] Despite small sample sizes and variable flight conditions, investigators argued that, together with adequate nutrition, force loading with the treadmill provided resistive characteristics that were effective in preventing muscle atrophy and loss of muscle strength. Ground-based experiments support the qualitative observations from space flight that resistance exercise training preserves skeletal muscle function of unloaded muscles.[2,32,46] However, effects of specific protein, amino acid, and other dietary supplements with and without resistive exercise on muscle structure and function during space flight or other unloading models are not known.

Effects on Bone Structure and Function

Although exercise on Earth has improved calcium retention,[47] extensive use of the cycle ergometer and treadmill exercise in flight failed to eliminate postflight bone density losses.[21] Although phosphorous intakes were at or above daily requirements, inadequate dietary calcium intake may have contributed to in-flight bone loss because nutritional data suggested that average dietary calcium intake of approximately 900 mg/d was below the recommended dietary allowance of 1000 to 1200 mg/d.[29] However, bone resorption appears to be the primary mechanism of in-flight bone loss because in-flight urinary calcium and phosphate were elevated even though calcium intake was minimal.[21] As a result of reduced time of musculoskeletal loading during space flight, bone and calcium losses during space flight support the notion that bone calcium retention may require greater magnitude and/or duration of loading forces than those generated with cycle or treadmill exercise regimens applied in space. For instance, data indicated that approximately 1 h/d of isokinetic resistance leg exercise reduces calcium excretion in subjects who undergo 30 d of exposure to a ground simulation of microgravity when compared with other subjects who undergo cycle or no exercise.[30] However, there are no known data addressing the effects of mineral dietary supplements with and without various loading exercise profiles during space flight or other unloading models on bone integrity.

NEED FOR ADEQUATE DIETARY INTAKE IN SPACE

Although there is no systematic quantification that energy requirements are greater in microgravity, there is evidence that the average daily caloric intake required to maintain normal health and physiologic function on Earth may be insufficient to sustain astronauts during prolonged space missions. The average daily baseline energy expenditure during space flight has been reported to be approximately 2500 kcal/d or an average oxygen uptake of 320 mL/min.[1] Average daily energy expenditure is higher than this because of the performance of daily physical exercise and infrequent extravehicular activities. Despite average daily dietary intakes as high as 3000 kcal during long space missions,[1] a negative caloric balance was demonstrated by consistent reductions of body weight during space flight.[48] Higher daily baseline energy costs observed during space flight compared with those on Earth may be surprising because lower metabolism might be expected due to less muscular force requirements to function in the absence of gravity. The observation that cosmonauts and astronauts required greater muscular effort during movement in the spacecraft cabin and a longer time to perform certain physical operations argues for the notion that there is a reduction in mechanical efficiency in the microgravity environment.[1]

CONSIDERATIONS FOR DEVELOPMENT OF FUTURE EXERCISE AND NUTRITION COUNTERMEASURES

Mechanical Efficiency of Exercise in Space

Average daily workloads and energy expenditures recorded during cycle exercise showed that mechanical efficiency (~20%) of performing exercise in a stabilized device such as a cycle ergometer is unaltered by weightlessness.[1,11] However, the energy cost of locomotion during walking or running on a treadmill in weightlessness is much higher. During exercise on the space treadmill, a system of bungee cords provides a pull to the long axis of the body. Biomechanical analysis of treadmill exercise during exposure to simulated microgravity also supports the notion that there is a reduced mechanical efficiency, i.e., maximum ground reaction forces generated during microgravity running were lower than those obtained during over-ground running, even when speeds of locomotion were 66% greater than those in 1*g*.[49] Running, i.e., both feet leaving the ground at the same time, is nearly impossible because of the spring-loaded harness pulling the astronaut toward the treadmill surface. Further, the motion of walking and running is performed on tiptoe during treadmill in space in contrast to heel to toe in 1*g*.[1] Based on average running speeds and energy expenditures, the mechanical efficiency of treadmill walking and running has been calculated to be as low as 11% in weightlessness compared with the predicted 20% in 1*g*.[1] Thus, the mechanical advantage of using gravity during exercise can be reduced by using specific devices in a weightless environment.

The issue of mechanical efficiency during exercise in weightlessness presents several relevant implications for development of nutritional requirements for long-duration space missions. From the viewpoint of mission operations, exercise performed on equipment that reduces mechanical efficiency will require more energy (i.e., food and fluid) to support a given amount of required exercise. For instance, if the space treadmill is selected as the mode of exercise for providing the muscular forces and impact to bone that are absent in the microgravity environment, as much as a 50% reduction in mechanical efficiency during running exercise in space would require twice as much dietary intake to support maintenance of musculoskeletal integrity during long-duration missions. Clearly, new methods for providing exercise with mechanical loading of the musculoskeletal system in weightlessness must be investigated if we are to provide our astronauts with forces and nutrition to muscles and bones of the lower extremities in a similar fashion to that in terrestrial gravity.

Metabolic Cost of Exercise in Space

The requirement for greater volume of exercise during space flight is the product of intensity, duration, and frequency. Work rates and metabolic costs of in-flight exercise indicate that an emphasis has been placed on aerobic conditioning with longer duration (>2 h) and moderate to high intensity (>70% $\dot{V}O_{2max}$). Unfortunately, the resulting time and intensity of daily exercise are extremely costly to the operational work day and in caloric expenditure. For instance, the average daily metabolic cost of 1450 kcal for 2.5 h of exercise performed during missions on the Mir space station represents about half of the total 3150-kcal intake on these missions.[1] If the combination of exercise intensity, duration, and frequency could be optimized to halve the total exercise volume, this could save approximately 225 000 kcal over a 6-mo mission, or enough to feed one astronaut for an additional 75 d. An approach to reduce the total energy requirement to sustain exercise countermeasures has significant logistical implications. For instance, even if foods were 90% dehydrated and water were totally recycled, an astronaut with a daily energy requirement of 3150 kcal would require a 310-kg food locker to provide a 1-y food supply.[31] Because the cost to launch 0.45 kg (1 lb) of water has been estimated at $10 000,[5] each additional amount of water consumed to replace sweat loss during exercise could add significant cost to the mission. Clearly, underestimates of energy and fluid requirements could lead to serious dehydration and shortage of food, and overestimates could have significant effects on the cost to launch large masses into space. Productive working time and life support (oxygen, water, and food) are at a premium the farther we extend our exploration away from Earth, so the ability to use research for identification of exercise and dietary regimens that can reduce energy requirement while maintaining physiologic function will prove critical to the planning and successful execution of long-duration space missions.

Identification of Effective Modalities of Exercise

In addition to identifying effective dietary regimes, the direction of research for development of exercise and nutrition countermeasures must focus on identification of specific modalities of exercise that most effectively provide the stimuli for maintenance of aerobic capacity, orthostatic tolerance, muscle, and bone. The equipment currently available for exercise on the International Space Station include a treadmill, cycle ergometer, and a device designed to provide resistance exercise to the leg muscles (squat exercise). These devices are intended to provide both components of aerobic and resistive exercise but may not provide adequate combinations of high force and impact required for maintenance of musculoskeletal structure and function.[29] New state-of-the-art exercise devices that employ intermittent hypergravity equivalents have the potential of achieving all the exercise targets of high aerobic metabolism, cardiovascular stimulation, and high musculoskeletal impact loading.[30,50,51] The test and development of exercise and nutrition countermeasures in combination with artificial gravity should be considered seriously in future research for the possibility of enhancing physiologic functions associated with physical work capacity, orthostatic performance, and musculoskeletal integrity.

Exercise and Nutrition for Restoration of Aerobic Capacity in Space

There is evidence to suggest that the use of graded maximal exercise can acutely restore some of the cardiovascular and metabolic capacities associated with the physical deconditioning of space flight. Performance of one bout of maximal exercise at the end of 10 d of exposure to simulated microgravity (head-down tilt bedrest) restored $\dot{V}O_{2max}$, heart rate, blood pressures, rate pressure product, oxygen pulse, and endurance time on a treadmill to pre-exposure levels within 2 h of ambulation.[52] Experiments have demonstrated that a single bout of graded exercise designed to elicit maximal effort can expand plasma volume as much as 10% in ambulatory subjects[53] and restore 15% plasma volume decrements in subjects exposed to simulated microgravity.[54] Because the decrement in $\dot{V}O_{2max}$ during space flight can be explained by the effect of lower circulating blood volume on reduced stroke volume and cardiac output,[3,6] acute restoration of plasma volume with maximal exercise should provide a mechanism to restore maximal cardiac filling and output. The primary mechanism for the acute hypervolemia induced by maximal exercise is an increase in renal retention of fluid and sodium without dietary water or salt supplementation.[55,56] Thus, without nutritional supplementation other than normal dietary intake, the periodic use of a single bout of maximal aerobic exercise (every 1 to 2 wk) represents a novel approach to the maintenance of aerobic and work capacity and the concurrent reduction of the current requirement for hours of weekly exercise and life-support resources.

Exercise and Nutrition for Restoration of Orthostatic Tolerance After Space Flight

In addition to its potential benefits for restoring aerobic work capacity, maximal exercise may act as a possible in-flight countermeasure against orthostatic intolerance. Extensive aerobic exercise of moderate intensity and long duration performed during US and Soviet space missions failed to provide complete protection against postflight orthostatic hypotension.[1] Two primary mechanisms associated with the development of postflight orthostatic hypotension appear to be reduced blood volume[13,14,33,54] and impaired baroreflex activity.[14,16,41,43] In addition to the acute expansion of blood volume induced by maximal exercise,[53,54] a single bout of maximal exercise increased the responsiveness of the arterial baroreflexes[55,56] and reversed fainting episodes after acute exposure to simulated microgravity.[56] More than a decade ago, specific attention was given to a single exposure of graded exercise designed to elicit maximal effort performed within 24 h before re-entry from a space mission as a potential countermeasure against postflight orthostatic intolerance. The impressive characteristics of this protective effect on orthostatic tolerance was that it occurred within 24 h after the maximal exercise countermeasure was applied and specifically targeted primary mechanisms associated with changes in blood pressure regulation after space flight.

Subsequent to ground-based experiments, the use of a single bout of maximal-effort cycle ergometric exercise performed by astronauts within 18 to 24 h before landing was tested during space flight missions as a possible means to ameliorate orthostatic hypotension and intolerance after space flight.[14,57] Unexpectedly, heart rate and arterial blood pressure responses during postflight standing were similar in astronauts who performed exercise and those who did not. However, because all astronauts who participated in the evaluation of the maximal exercise countermeasure (i.e., exercisers and controls) completed the stand test before and after space flight, orthostatic tolerance could not be assessed. Interestingly, echocardiographic measurements demonstrated that stroke volume and cardiac output was restored to preflight levels in the exercise group during standing after space flight, but fell in the control group in a similar fashion as that reported in the ground-based investigation.[14,56] Taken together, ground and in-flight experiments provide compelling evidence that orthostatic tolerance after space flight could be protected with application of acute maximal exercise performed within 24 h before re-entry to Earth. This approach is also operationally attractive because it could be performed within 24 h before the end of a mission and would require minimal time of the astronauts (one bout of less than 20 min).

Exercise and Nutrition for Protection of Muscle Structure and Function in Space

Because amino acids and proteins provide the fundamental building blocks of muscle, it is clear that appropriate dietary protein will prove essential as part of an exercise and nutrition countermeasure against atrophy and loss of strength in skeletal muscle during space flight. Nutritional data collected from space missions suggest that dietary protein intake has been well above the recommended daily allowance.[22] These and plasma amino acid distribution patterns in blood samples taken in flight support the notion that amino acid supplementation is not required during space flight as long as energy intake is adequate and the diet is balanced.[22] However, the volume of resistive exercise (intensity, frequency, and repetitions) required to protect against muscle atrophy and loss of strength during space flight can be large. Despite greater intake of food and protein, Skylab crews had greater negative nitrogen balance than did crews of subsequent space missions who performed little exercise.[22] It is important that dietary regimens developed for use with exercise countermeasures be designed to meet the energy costs superimposed by required exercise activities. There are several nutritional strategies that could be considered for the enhancement of protein synthesis and muscle maintenance during space flight. Timing of dietary protein intake should be considered because muscle protein synthesis is increased when postexercise amino acid supplementation is provided immediately after a resistance exercise training session compared with 2 h after exercise.[58] Another nutritional challenge for maintenance of muscle structure during space flight is that of maintaining energy balance on missions with heavy exercise requirements.[22] It has been demonstrated that protein synthesis is reduced during space flight in proportion to the magnitude of energy deficit.[59] This important relation raises a concern that perhaps energy balance cannot be well maintained with a high volume of exercise during space flight, i.e., large amounts of exercise may exacerbate the problem of protein and muscle loss during space flight. Therefore, identification and development of the most effective exercise and nutrition countermeasures for maintenance of muscle structure and function may require a reduction in total exercise volume in an effort to avoid negative energy balance.

Efficient use of resistive exercise regimens for protecting size and strength of skeletal muscle during extended space missions will depend heavily on appropriate identification and application of fundamental exercise characteristics such as muscle actions, muscle loading, rest periods between repetitions, velocity of movements, and frequency of training.[60] It is also reasonable to suggest that preservation of muscle structure and function during exposure to microgravity would include replacing muscle actions and forces that occur in the normal 1*g* environment. The consistent reduction in strength of the lower extremities after space flight,[1,19,20] despite the use of extensive dynamic exercise, suggests that greater resistances are required to preserve muscle function. An equally important factor may be the absence of eccentric movements in the weightless environment. Nearly all muscle actions in microgravity require fiber shortening (concentric actions), whereas fiber lengthening (eccentric actions) is virtually absent.[19] Because eccentric muscle actions are a regular part of our daily ambulatory activities on Earth, it seems that an efficient exercise program during space flight would include eccentric in addition to concentric actions. There are several important advantages of using eccentric muscle exercise in a microgravity environment. Eccentric exercise can provide greater "overload" to a muscle because forces generated by eccentric muscle actions are greater than those produced by maximum isometric or concentric contractions.[19,61,62] As a result, resistive exercise training that involves a combination of eccentric and concentric muscle actions induces approximately twice the increase in strength as training with only concentric actions.[61,63] Further, eccentric muscle actions occur with relatively low metabolic cost and less muscle fatigue compared with the equal force developed by concentric muscle actions.[19,60–62,64] Therefore, eccentric muscle exercise provides "a bigger bang for the buck" because it generates high mechanical muscle tensions at low metabolic costs. The relevance of this improved mechanical efficiency with eccentric exercise training can translate to high force development required for protection of muscle structure and function at significantly reduced oxygen (i.e., energy) requirement, a relation that can reduce the risk of developing energy and protein deficits. Ground-based and space flight investigations designed to test eccentric resistance exercise training and energy balance as a protective countermeasure against in-flight and postflight muscle atrophy and dysfunction should be pursued.

Exercise and Nutrition for Protection of Bone in Space

Because available calcium is a major determinant of maintaining bone mineral density, adequate dietary calcium intakes or supplementation will prove critical as part of the strategy for ameliorating or eliminating loss of bone during space flight. In addition, increased content of certain vitamins and minerals in the diet such as vitamin D may be required to ensure better absorption of dietary calcium, particularly if there is insufficient lighting in the spacecraft. Pharmacologic countermeasures such as the use of bisphosphonate alendronate have been proposed for bone maintenance during space flight. However, it should be appreciated that it is unlikely that supplementations with dietary calcium or bisphosphonates will be effective in preventing bone mineral losses without an adequate stimulus to the mechanisms underlying bone synthesis. It is likely that loading exercise can provide such a stimulus. As with strategies for developing exercise countermeasures for physical working capacity, orthostatic tolerance, and muscle atrophy, the primary emphasis on development of countermeasures for in-flight bone loss must focus on the ability to identify a physical exercise that requires minimal energy use with optimal loading strategies.

The observation that muscle loss precedes bone loss[65] supported the hypothesis that loads to which bone adapts are generated from skeletal muscle contractions during normal physical activity.[66] This relation between muscle forces and bone loading presents the possibility that an exercise and nutrition countermeasure designed to effectively defend against in-flight muscle atrophy could likewise protect bone loss during space flight. Therefore, future research should focus on experiments designed to determine whether bone loss during exposure to models of unloading can be eliminated with efficient use of the same resistive exercise regimens that involve significant amounts of eccentric muscle actions that generate high muscle forces and are effective in ameliorating muscle atrophy.

In addition to investigation of traditional exercise, future research should focus on the development and use of mechanical loading profiles specific to stimulating increases in bone mass density. It is clear that using high-impact exercise (e.g., running and jumping) is more effective than low-impact exercise (e.g., cycling and swimming) in development or maintenance of bone mass density.[67–69] Recent experiments have demonstrated that mechanical loading of bone increase bone mineral density.[70,71] Perhaps more relevant to efficient application of force loading on bone during space flight is the observation that increases in bone mineral density caused by mechanical loading sessions were greater when the mechanical loading regimens were divided into shorter, more frequent sessions.[72,73] Therefore, improved efficiency of force loading on bone by eliciting similar increases in bone density with less total force loading can translate to more efficient exercise and nutrition countermeasure effects at significantly reducing energy requirement, a relation that can reduce the risk of developing energy and mineral deficits. Future ground-based and space flight investigations should focus on investigations designed to test combinations of eccentric resistance exercise training regimens, specifically targeted mechanical loading profiles, dietary calcium supplementation, and other substances (e.g., bisphosphonates) in an effort to identify the most effective and efficient protective countermeasure against in-flight and postflight bone loss.

SUMMARY AND CONCLUSIONS

It is clear from data collected from numerous space missions that nutrition is a key component in the maintenance of astronaut well-being and performance. Although it is unlikely that diet alone can provide an effective countermeasure against the deleterious effects on physiologic function associated with adaptation to microgravity, consumption of adequate nutrients in combination with specific exercise countermeasures will be critical to astronaut health during long-duration space missions. Future research should focus on the use of less frequent and optimally timed exercise in the presence of nutritional supplementations during space flight to identify the most effective countermeasures for restoration of aerobic work capacity, orthostatic tolerance, and musculoskeletal structure and function. Such an exercise prescription would be maximally cost effective by enhancing crew health maintenance and postflight recovery and minimizing in-flight use of work time, food, water and oxygen for exercise activities.

Various professional dietetic and exercise associations have recognized the importance of appropriate selection of food and fluids, timing of intake, and supplement choices in combination with exercise in promoting health and fitness.[74] Unfortunately, optimal exercise and dietary combinations targeted at enhancing specific physiologic systems have not been identified. The direction for future research proposed in the present review on development of exercise and nutritional strategies for maintenance of physical working capacity, orthostatic stability, and musculoskeletal integrity during long-duration space missions can be applied on Earth to various patient populations. For instance, acute maximal exercise has been used to eliminate orthostatic hypotension in paraplegics who have been constrained to wheelchairs for at least 5 y.[75] Optimal dietary amino acid and calcium intakes taken at optimal times before or after exercise can be developed for combating osteoporosis in postmenopausal women and elderly persons in general. It is clear that research designed to provide new insights into management of deleterious physiologic effects of space flight will also be instrumental to the treatment of various clinical conditions on Earth.

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