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Project Title:	An Integrated Low-Volume Nutritional Countermeasure to Maintain Muscle Mass and Function During Space Exploration		
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Task Description:

Our long-term goal is to identify, prevent and remedy defects in the metabolic pathway that contribute to the loss of muscle mass and function during exposure to microgravity. Demographic data indicate that the average age of shuttle crew members has increased from 40.7 yrs in 1995 to 46.7 yrs in 2007 with an increasing number of astronauts over 50 yrs of age. We contend that the loss of muscle mass and function during spaceflight is facilitated by an age-associated, progressive impairment in the ability to mount an anabolic response to standard mixed nutrient meals. We propose that enriching daily meals with a low-volume leucine supplement will reduce the deleterious effects of microgravity on skeletal muscle and facilitate recovery during rehabilitation.
We will employ our established 14 day bed rest protocol to model the skeletal muscle unloading that occurs during microgravity. We will also examine recovery of muscle mass and functional capacity during a 7 day rehabilitation period. We will study 2 groups: CON (Bedrest/Recovery + Placebo; n=15), LEU (Bedrest/Recovery + Leucine; n=15). We will assess a) markers of translation initiation, b) muscle protein synthesis, c) muscle mass and body composition and d) strength and aerobic capacity.

We will test the following hypotheses:

1. Bedrest will blunt the anabolic response to a mixed nutrient meal, facilitating a loss of muscle mass and functional capacity that is only partially restored during rehabilitation.

2. Enriching daily meals with leucine will promote protein synthesis and maintain the anabolic response to mixed nutrient meal ingestion. This will preserve lean muscle mass and function during bedrest and facilitate the recovery of functional and metabolic capacity during rehabilitation.

This project builds on our recent series of bed rest studies and seeks to provide a refined and practical countermeasure that is supported by comprehensive mechanistic evidence. Research plans for 2011-2012 include continued subject recruitment and data analysis.

Rationale for HRP Directed Research:

Research Impact/Earth Benefits:

Our long-term goal is to identify, prevent and remedy defects in the metabolic pathway that contribute to the loss of muscle mass and function during exposure to microgravity. Protein catabolism and muscle loss occurs in many circumstances. The regulatory mechanisms controlling protein turnover are particularly sensitive to a reduction in the neuromuscular stimulus that occurs during physical inactivity or exposure to microgravity and it is clear that muscle loss is greatly exaggerated with increasing age.
Demographic data indicate that the average age of shuttle crew members has increased from 40.7 yrs in 1995 to 46.7 yrs in 2007 with an increasing number of astronauts over 50 yrs of age. We contend that the loss of muscle mass and function during spaceflight is facilitated by an age-associated, progressive impairment in the ability to mount an anabolic response to standard mixed nutrient meals. Protein supplementation is routinely employed to combat inactivity and age-related muscle loss. However, aggressive supplementation regimens are often impractical or ineffective due to issues including increased satiety, poor palatability, cost and compliance.

We propose that enriching daily meals with a low-volume leucine supplement will reduce the deleterious effects of microgravity on skeletal muscle and facilitate recovery during rehabilitation. This supplement has the potential to also benefit individuals whose ability to perform physical activity is compromised (e.g., hospitalized patients, frail elders).

Task Progress:

Leucine Attenuates Bed Rest-Induced Muscle Loss and Enhances Recovery in Middle-Aged Adults: Preliminary Results
BACKGROUND

Mechanical unloading, an inherent characteristic of spaceflight, results in a loss of muscle mass and muscle strength. These losses threaten the integrity of space missions and crew health upon return to Earth's gravity. Nutrition-based countermeasures represent one of the few viable intervention strategies available during long-duration spaceflight. Previous work has demonstrated that an essential amino acid supplement rich in leucine maintains leg lean mass in young adults during bed rest inactivity. Fourteen days of leucine supplementation has also been shown to increase basal and post-prandial muscle protein synthesis in healthy, ambulatory older adults.

METHODS

We added leucine (0.06 g - kg lean mass - meal-1; LEU) to the regular meals served 3 - d-1 to middle-aged adults (45-60 y, representative of long-duration crew members) during 14 d of horizontal bed rest (BR) and 7 d of rehabilitation. Changes in muscle mass were assessed by DEXA; strength was evaluated with standard isokinetic dynamometry. Stable isotope tracer methodology was used to quantify muscle protein synthesis pre-BR, post-BR, and post-rehabilitation.

RESULTS

Preliminary data indicate that during BR, LEU lost 1172 ± 525 g of whole body lean mass compared to 2704 ± 347 g for control (CON). After 1 wk of rehabilitation, LEU regained nearly all lean mass (-108 ± 765 g) while CON remained below pre-BR values (-1448 ± 78 g). After BR, isometric knee extensor strength was decreased 17.4% in CON and only 2.9% in LEU and was partially restored during rehabilitation. Early results also indicate that muscle protein synthesis in response to feeding was preserved in the LEU group.

CONCLUSION

These preliminary data indicate that, in the absence of exercise countermeasures, low-volume leucine supplementation may partially attenuate losses in muscle mass and strength during bed rest and facilitate recovery upon resumption of activity in middle-aged adults.

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