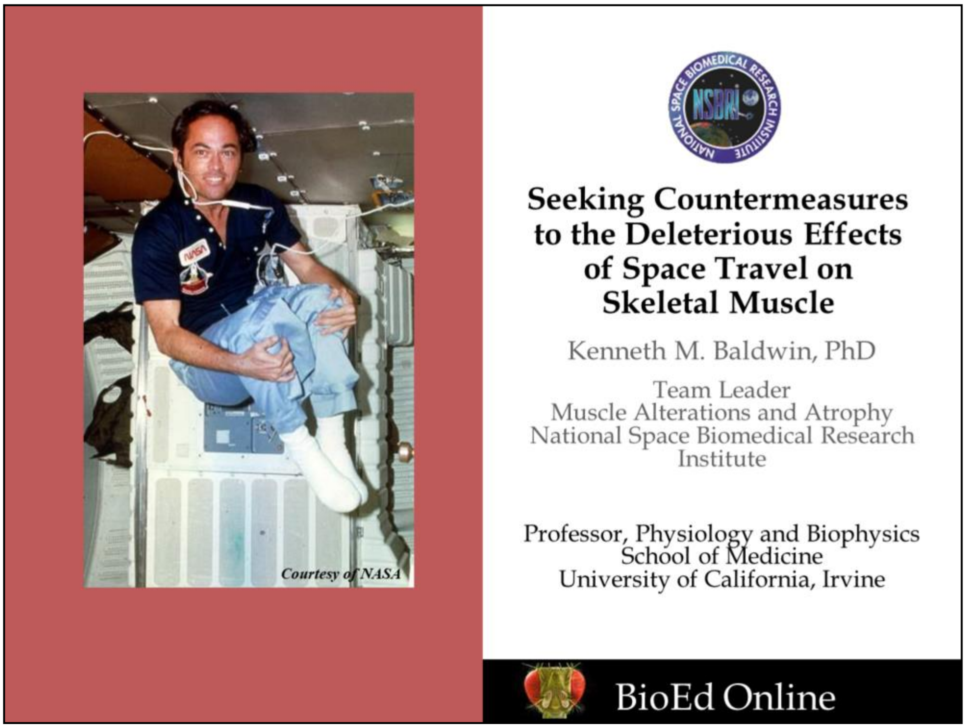


The goals of this presentation are to provide a brief synopsis of the key properties of the skeletal muscle system, and to examine the system's inherent dependence on the force of gravity. We will investigate what happens to the muscles when gravity is eliminated, as during prolonged exposure to space flight or under conditions of prolonged bed rest (an analogue of spaceflight). We also will formulate a strategy to maintain the integrity and functionality of skeletal muscle in the absence of gravity. Finally, we will apply some of the knowledge gained from the space program to enable individuals to live more productive lives on Earth.

ADDITIONAL NOTES FROM SPEAKER'S TRANSCRIPT (http://www.bioedonline.org/presentations/)

My name is Ken Baldwin. I am Professor of Physiology and Biophysics at the University of California-Irvine. I am also the team leader for the Skeletal Muscle and Authorizations Team of the National Space Biomedical Research Institute. Today, I am going to talk to you about the skeletal muscle system, the largest organ system in the body, and probably the body system most dependent upon gravity or mechanical stress for normal health. I also will talk about seeking countermeasures to the deleterious effects of space travel on this system.

Image Reference:

NASA. *Space Flight Images*. Retrieved 08-02-2007 from http://spaceflight.nasa.gov/gallery/index.html

Overview

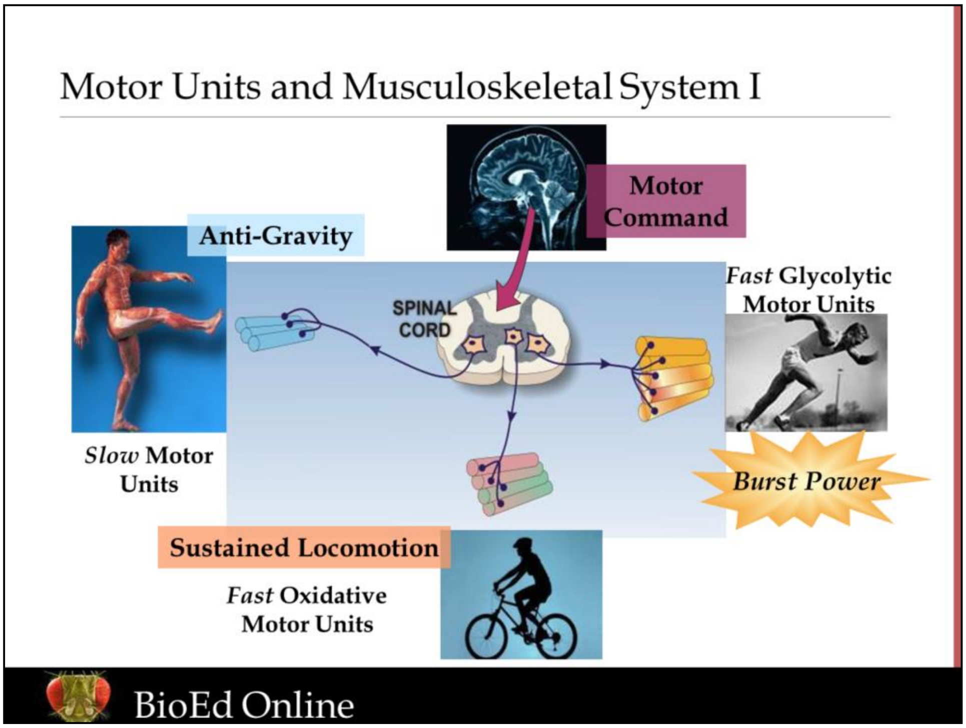
- Evolution of the Skeletal Muscle System to Meet the Body's Needs on Earth
- Key Structural Elements of Muscle Fiber Necessary for Function
- Skeletal Muscle Fiber Deterioration/Atrophy During Space Flight
- Functional Consequences of Skeletal Muscle Atrophy
- Strategies to Prevent Muscle Atrophy
- Current Evidence that Programs of High Loading are Successful in Counteracting Muscle Atrophy
- Implications for Living a More Productive Life on Earth

BioEd Online

Overview

First, we will provide fundamental information about how the musculoskeletal system evolved over millions of years to enable organisms to perform a wide variety of movement tasks. We will explore the key structural and functional capabilities of specific types of muscle fiber, as well as these fibers' unique sub-cellular structures that allow them to perform activities of different skill and intensity. Next, we will attempt to understand why gravity is so important to the muscle system's structural and functional integrity, and why muscle breaks down, or atrophies, when gravitational forces are eliminated. Then, we will examine the daunting task of designing a strategy to prevent such atrophy and discuss the progress that scientists and pragmatists have had in correcting the problem. Finally, we will try to translate some of what we have learned while working on the problem of muscle atrophy to the practical situation of enabling individuals to lead healthier and more productive lives on Earth.

Before we embark on this journey, ask yourself, "What is gravity? Is our health dependent on it?"



Motor Units and Musculoskeletal System

This slide shows three individuals, each performing a different task. The individual on the left is balancing on one leg in a static state; the individual in the center is riding a bicycle at a leisurely pace; the person on the right is in the process of "exploding" to run a sprint. This variety of performance is made possible by the diversity of specific groups of muscle fiber that comprise our muscle groups. These different groups of muscle fibers are connected to the higher centers of the brain that control all of our bodily movements by motor neurons.

A cluster of muscle fibers that is innervated by a single motor neuron is referred to as a **motor unit**. Three types of motor units (slow-oxidative, fast oxidative, and fast-glycolytic) have been identified in most animal species, including humans.

A slow oxidative motor unit possesses unique properties (details will follow later) that enable individuals to balance with stability and oppose gravity for relatively long durations without fatiguing. See how long you can stand and balance yourself on one leg.

Fibers of a fast oxidative motor unit contract somewhat faster than those comprising the slow unit and are able to sustain contractions for long durations. Fast oxidative motor units contain high levels of energy generating systems (called mitochondria), which use substrates, such as fats and carbohydrates, in the presence of oxygen to make energy available for muscle contraction. Think of the fats and carbohydrates that you eat as fuels to drive contraction (i.e., something similar to the gasoline that you put into your automobile to drive the pistons). When these units are recruited during activities of relatively moderate intensity (e.g., cycling, distance running, swimming, playing soccer etc.), such activities can be sustained for relatively long duration.

The final motor unit to consider is the fast-glycolytic motor unit. The fibers comprising this unit contract very quickly and a large number of them are linked to each neuron. Thus, these units are called upon to perform intense movements of high power output, as in sprinting or trying to "slam dunk" a basketball. The shortcoming to these units is that the fibers do not possess a high number of mitochondria. Thus, one cannot sustain the activity for long duration. Test yourself to see how long you can sprint when you run all out at full speed.

One final thought. Through evolution and via our recent ancestry, we all possess different levels of expression of these motor units. Most humans inherently express a mixture of the fast and slow units in nearly equal proportion. However, there are individuals, such as those who may excel in a marathon, who express as much as 80% slow fibers (probably due to both genetics and training); whereas, individuals who may excel in sprinting and power events express mainly the fast units.

Question: Can you predict the fiber-typing for either a lion or a cheetah? How about a sloth?

Suggested Reading:

Caiozzo, V. J. ,Haddad, F., Baker, M. J., Herrick, R. E., Prietto, N., & Baldwin K. M. (1996). Microgravity induced transformations of myosin isoforms and contractile properties of skeletal muscle. *J. Appl. Physiol. 81*: 123-132.

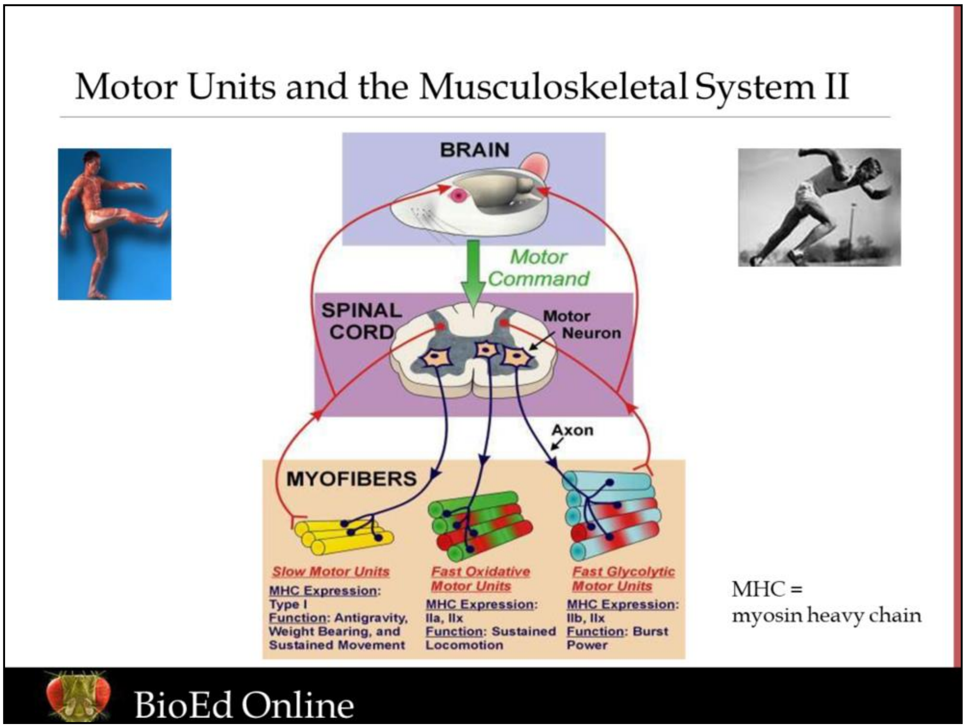
ADDITIONAL NOTES FROM SPEAKER'S TRANSCRIPT (http://www.bioedonline.org/presentations/)

What you see in this slide are three individuals. The one on the left is basically assuming an anti-gravity posture. That individual, while assuming that posture is using (through the nervous system) a series of fibers that we refer to as slow fibers. The slow fibers are innervated by common neurons that innervate each of these fibers. While the individual is standing in the balanced position, the motor units are being activated to enable this individual to assume that posture. If you think this is easy (and it looks like something easy to do), why don't you try that posture while looking at this slide presentation? You will see that this is no easy task. The individual in the middle is riding a bicycle. I am sure at some stage we have all ridden a bicycle, and it seems pretty easy to do, but if you are going to sustain that bicycle movement over time, it is generally more intense than the posture that the individual is assuming on the left part of the slide. The individual (on the bicycle) recruits fibers that are a little bit different than those slow fibers. These fibers are essential for sustaining our locomotion, whether it is running or, in this case, cycling, for fairly long durations, up to an hour or more. The person on the right is getting ready to perform bursts or power activities, such as sprinting or "exploding" away from the ground, as in jumping and so forth. In those types of movements, a different set of muscle fibers, activated again by motor neurons, are called into play. All the things that are being done here, are being carried out under the overall umbrella of gravity. Gravity is the constant force that is being imposed on the body, acting as a force to pull the legs and the body and more or less anchor the body to the ground.

I want you to think about what gravity means to you. Do you experience gravity in your daily activities? Are certain activities more strenuous than others?

Image Reference:

Baldwin, K. M. (2007). Seeking countermeasures to the deleterious effects of space travel on skeletal muscle. *BioEd Online (www.bioedonline.org).* Houston, Tx: Baylor College of Medicine.



Motor Units and the Musculoskeletal System II

Myofibers express a motor protein called myosin heavy chain (MHC). Focus on the bottom box in the center of the slide. MHC is the most abundant protein expressed in muscle. It is both a structural and regulatory protein that forms the backbone of the fiber (see next slide), and also drives the contraction process of the fiber. Slow motor units contain fibers that express what is termed a slow, type I MHC, which intrinsically causes the fiber, when activated electrically by the nerve, to contract slowly.

In contrast, the other two motor units express faster types of MHC, called **isoforms** (i.e., different forms of a nearly identical protein), and are designated as either IIa, IIx, or Iib, depending on the individual properties of the motor units. It is important to note that in the faster units, many of the fibers express two or more types of MHC. We don't know why this is the case, but it is postulated that this characteristic enables the fibers to change their contractile properties quickly (over a period of a few days), depending on the physiological conditions imposed on the muscle.

Can you think of a type of activity that may serve as a stimulus to induce expression of the slower myosin isoforms? What might induce faster isoforms?

Suggested Reading:

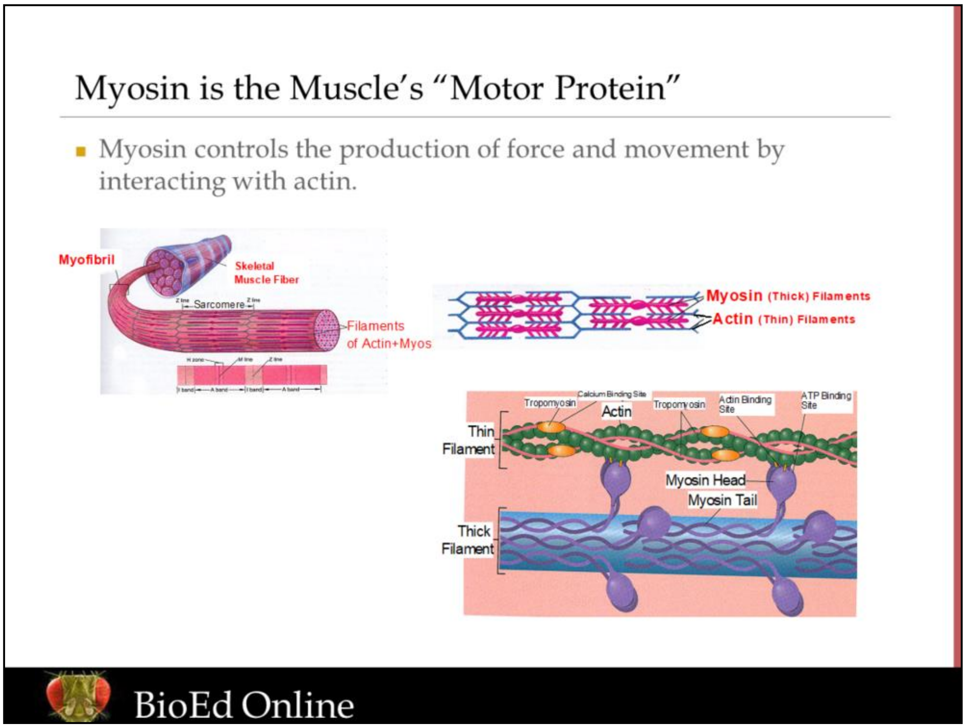
Caiozzo, V. J., Baker, M. J., Huang, K., Chou, H., Wu, Y. Z., & Baldwin, K.M. (2003). Single fiber myosin heavy chain polymorphism: How many patterns and what proportions? *Am J Physiol Regul Integr Comp Physiol.* 285: R570-R580.

ADDITIONAL NOTES FROM SPEAKER'S TRANSCRIPT (http://www.bioedonline.org/presentations/).

Look at the middle of the slide, and focus first of all on the fibers that are designated in yellow. These fibers express a certain motor protein that we call myosin heavy chain (MHC). Think of myosin heavy chain as the motor that drives the contraction process. The unique feature of these fibers is that they express only one kind of a motor protein, which we refer to as slow or type I myosin. The green and red fibers in the middle are the ones that the individual was using in the last slide, while cycling the bicycle. This motor unit, or this grouping of fibers, consists of two faster types of myosin (isoforms called IIa and IIx), one that is expressed as green, and another expressed as red. If we move to the right, we see another type of fiber that is really fast. These fibers express the fast myosin heavy chain and allow the muscle to shorten with a much more explosive capability, as illustrated on the right with the individual executing the burst power. Myosin heavy chains have evolved and been conserved over millions of years, and through many species. While I show these fibers to you in the human body, just about every animal system has the same types of myosin.

Image Reference:

Baldwin, K. M. (2007). Seeking countermeasures to the deleterious effects of space travel on skeletal muscle. *BioEd Online (www.bioedonline.org).* Houston, Tx: Baylor College of Medicine.



Myosin is the Muscle's "Motor Protein"

Skeletal muscle fibers are long and cylindrical in shape. The geometrical configuration is maintained in the subcelluar network, which is organized into bundles of filaments containing an array of proteins, the chief of which are two key proteins designated as myosin and actin. As depicted in the lower figure, the myosin molecule resembles a hockey stick consisting of the head and backbone (tail) units. When these myosin molecules are organized in the filament, they are called the thick filament.

In contrast, actin molecules are organized into another filament structure resembling a necklace of beads twisted around one another. When the myosin molecules are enabled to interact with the actin filament during the process of contraction, the myosin heads change configuration and slide the actin filaments along their structure. The process, long referred to as the sliding filament hypothesis, defines how muscle fibers shorten and allow our bodies to move our limbs and trunk. The dynamics of this process are illustrated on the next slide.

Do you think this molecular structure is well designed to enable muscles to create force and movement of the limbs?

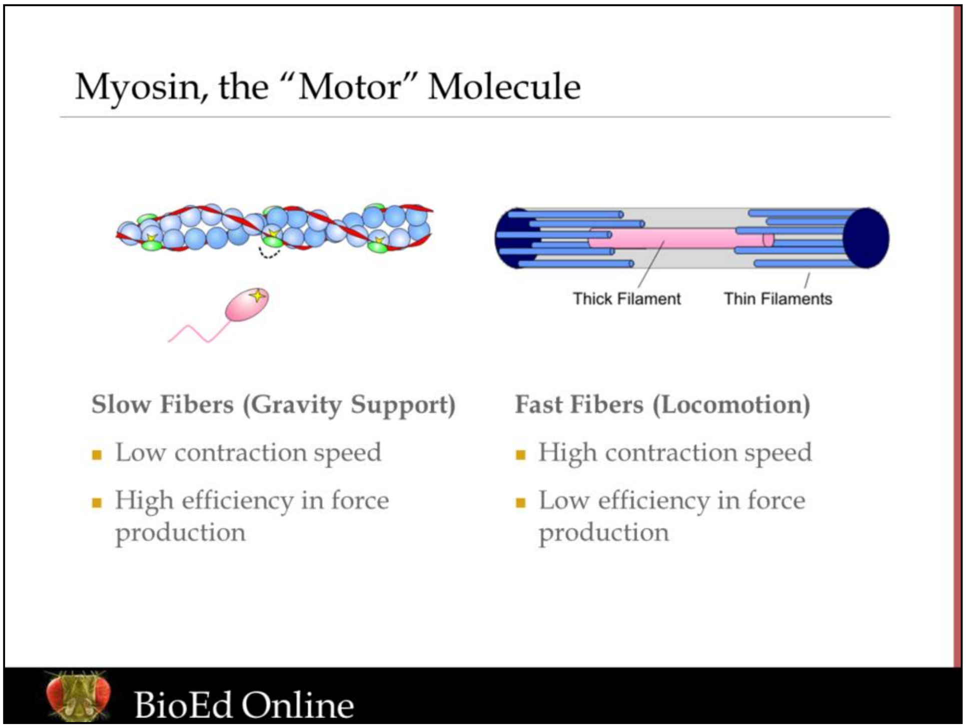
Suggested Reading:
Brooks, G. A., Fahey, T. D., White, T. D., & Baldwin, K. M. (2005). *Exercise Physiology 4th Edition: Human Bioenergetics and Its Applications.* McGraw Hill, New York, NY. pp. 363-395.

ADDITIONAL NOTES FROM SPEAKER'S TRANSCRIPT (http://www.bioedonline.org/presentations/)

The schematic at the top describes an individual muscle fiber. One unique feature of muscle *fiber is that it expresses a complex structure that we call the contractile component. In that contractile structure, there are two primary proteins. One is myosin, the motor protein, and the other is actin, which serves as a backbone for the myosin heavy chain (MHC). What you see at the bottom is a depiction of the myosin motor protein with a head region. That head region binds to the actin and creates a chemical reaction so that force can be generated. Actually, there can be movement occurring to slide the actin chain along the myosin, thus creating force as well as movement.*

Image Reference:

Baldwin, K. M. (2007). Seeking countermeasures to the deleterious effects of space travel on skeletal muscle. *BioEd Online (www.bioedonline.org).* Houston, Tx: Baylor College of Medicine.



Myosin, the "Motor" Molecule

This slide illustrates the contractile process. When the muscle is electrically activated by the nervous system, calcium molecules are released into the vicinity of the myofilaments. The calcium then binds to special sites on the actin filament so that the myosin head can attach to the actin. When these two proteins interact, energy molecules (called adenosine triphosphate) are broken down, as depicted by the "sparking action" in the animation. This energy transformation process enables the myosin to slide along the actin filament, thus producing force and movement in the muscle fiber, as depicted on the right side of the illustration. It is important to appreciate that every gravity-opposing action we carry out each day is mediated through the recruitment of the slow type motor units.

Can you predict what would happen if we lost expression of these slow units, in terms of how effectively we would be able to oppose the gravity field on Earth?

Suggested Reading:

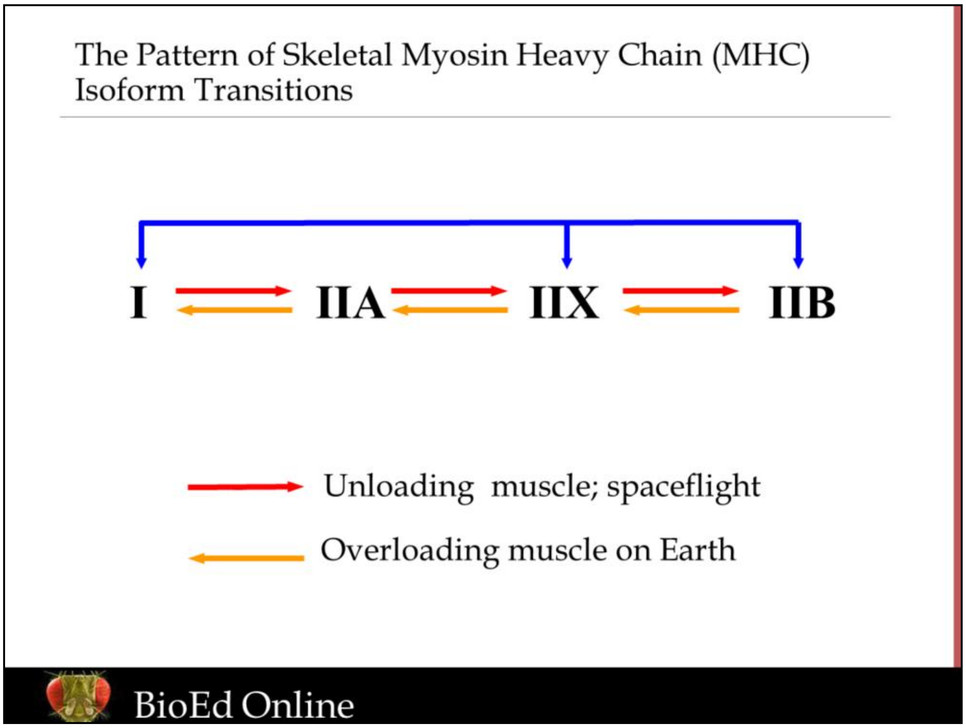
Brooks, G. A., Fahey, T. D., White, T. D., & Baldwin, K. M. (2005). *Exercise Physiology 4th Edition: Human Bioenergetics and Its Applications.* McGraw Hill, New York, NY. pp. 363-395.

ADDITIONAL NOTES FROM SPEAKER'S TRANSCRIPT (http://www.bioedonline.org/presentations/)

During a muscle contraction, calcium is released into the muscle fiber, which allows the myosin to interact with the actin. An explosion occurs and the myosin drives the actin along the chain. This creates the movement process. On the right side of the slide, we can see that dynamic of motion whereby the myosin, labeled in pink, is actually sliding those actin molecules along, and you can see the shortening action of that schematic representation. With a slow fiber, that whole dynamic action takes place much more slowly. It is not as explosive, but this type of movement is more economical, and the fibers that we recruit during postural adjustment allow the individual to sustain this anti-gravity capability in a more economical way. With a fast fiber, there is a much more dynamic action, which *favors types of activities involving a lot of movement, in which the muscle fibers have to contract with more speed and explosiveness. The type of myosin being expressed in these fibers really drives the essence of the diversity in the contraction process that can occur in our muscles. What kind of fibers would you predict exist in the leg muscles of the lion, which must chase down its prey? In contrast, what type of fibers would you expect to find in a sloth, which hangs onto trees for very long durations?*

Image Reference:

Baldwin, K. M. (2007). Seeking countermeasures to the deleterious effects of space travel on skeletal muscle. *BioEd Online (www.bioedonline.org).* Houston, Tx: Baylor College of Medicine.



The Pattern of Skeletal Myosin Heavy Chain (MHC) Isoform Transitions

Muscle fibers comprising our various muscle groups are very plastic, in that they can change their size and contractile properties depending on the chronic conditions imposed. Research involving both animals and humans suggests that if we reduce the force of gravity by sending animals and/or humans on either the space shuttle or the International Space station for several days or longer, we can change gene expression within the motor protein gene family. For example, under the conditions of spaceflight, the slow type I myosin heavy chain (MHC) gene becomes repressed and its encoded protein becomes degraded. In its place, the faster MHC genes become up-regulated (expression is increased). Thus, the muscle fibers become transformed into smaller and faster fibers. In contrast, if one is exposed to daily high levels of loading, as occurs during resistance exercise (lifting very heavy objects), the patterns of shift occur in the opposite direction: the muscle fibers get bigger and stronger, but somewhat slower.

When subjects return from space, can you predict any differences they will experience in performing tasks that are usually carried out to oppose the ongoing force of gravity?

Suggested Reading:

Baldwin, K. M. & Haddad, F. Skeletal muscle plasticity: cellular and molecular responses to altered physical activity paradigms. (2002). *Am. J. Physical Med. & Rehab. 81*: (Suppl) S40-S51.

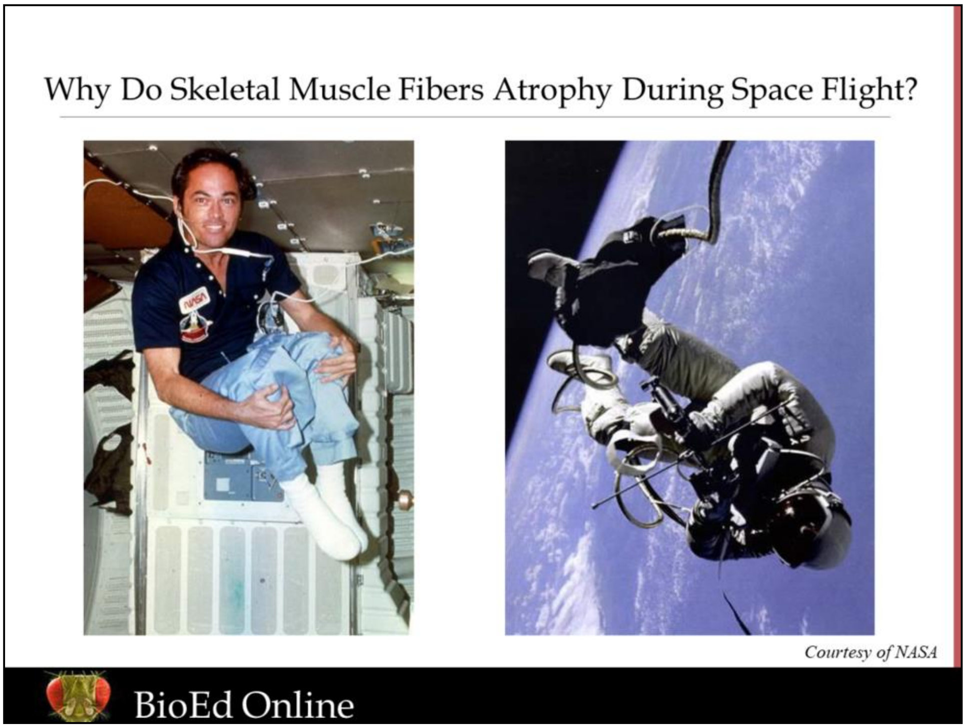
Caiozzo, V. J. ,Haddad, F., Baker, M.J., Herrick, R. E., Prietto, N., & Baldwin K.M. (1996). Microgravity induced transformations of myosin isoforms and contractile properties of skeletal muscle. *J. Appl. Physiol. 81*: 123-132.

ADDITIONAL NOTES FROM SPEAKER'S TRANSCRIPT (http://www.bioedonline.org/presentations/)

We know that the isoforms of myosin can be expressed in our individual fibers, and that this pattern of expression is not fixed. The various genes—and the protein products of these genes—can be manipulated. One gene can be turned on and another gene can be turned off, and now we have the ability to remodel muscle fibers, depending upon the physical conditions we are imposing onto our skeletal muscle system.

Image Reference:

Baldwin, K. M. (2007). Seeking countermeasures to the deleterious effects of space travel on skeletal muscle. *BioEd Online (www.bioedonline.org).* Houston, Tx: Baylor College of Medicine.



Why Do Skeletal Muscle Fibers Atrophy During Space Flight?

The photos in this slide provide some insight into the important question of why our muscles (and muscle fibers) atrophy during space flight. The photo on the left shows a typical posture of an astronaut in the space module. This individual is considered to be in a state of "free fall". That is, he is floating around and is essentially weightless. While he can move all of his muscle groups, he does not need to generate much force to float around. The flick of one finger against the wall or floor of the module is all that is needed to propel a person around in this space capsule. In essence, his key muscle groups, especially the lower leg calf muscles, the thigh muscles, and the back/neck muscles, are unloaded. That is, there is no need for these key muscle groups to generate any appreciable force to perform activities and, importantly, to oppose the strong force of gravity that is ever present on Earth.

The astronaut on the right is performing important construction duties outside the space module. This is referred to as extravehicular activity. To perform this task, the astronaut wears a very heavy and cumbersome space suit that would be difficult to wear on Earth because of its weight and restrictiveness on limb and hand movement. Yet the astronaut can tolerate wearing this device for many hours while performing various duties outside of the space capsule.

If astronauts experience this state of unloading, do you think the muscle systems are receiving appropriate stimuli to maintain their structural and functional integrity? What about the motor protein genes that evolved to provide movement diversity?

Suggested Reading:

Edgerton, V. R. & Roy, R. R. (1996). Neuromuscular adaptation to actual and simulated spaceflight. In *Handbook of Physiology-Environmental Physiology. Vol 1. Part III. The Gravitational Environment* (721-763). Bethesda, MD: Am. Physiol Soc.

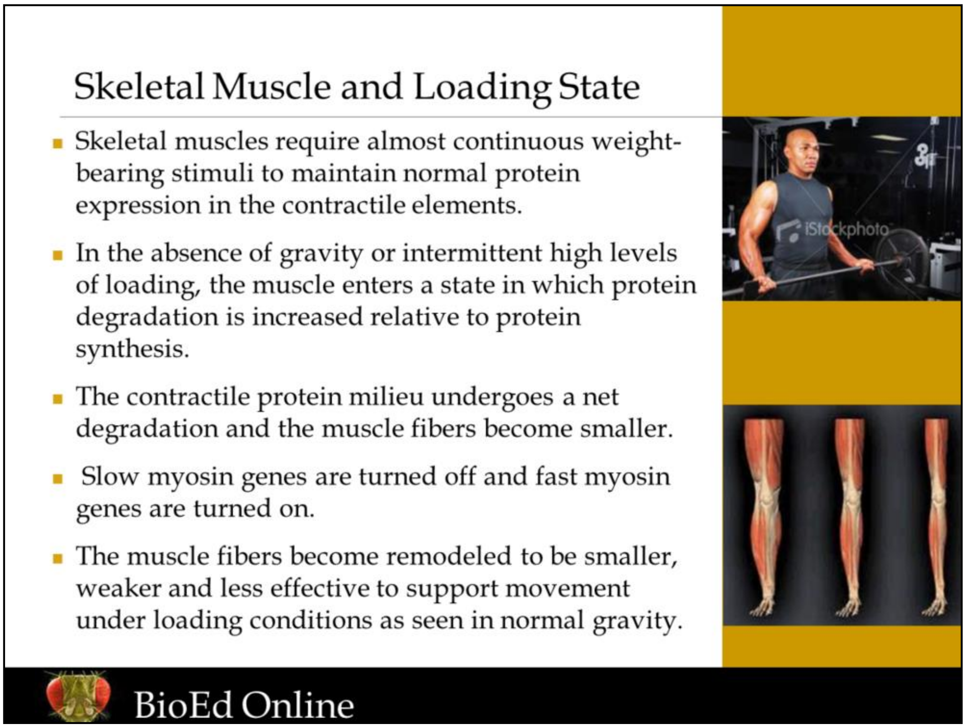
Baldwin, K. M., Edgerton, V. R., & Roy, R. R. Muscle Loss in space: physiological consequences. In H. Mark, M. Salkin, & A. Yousef (Eds.), *Encyclopedia of Space Sciences and Technology. Vol. 2* (pp. 149–166). Hoboken, NJ: John Wiley & Sons, Inc.

ADDITIONAL NOTES FROM SPEAKER'S TRANSCRIPT (http://www.bioedonline.org/presentations/)

When individuals enter the space environment, say on the space shuttle, they lose the Earth's force that would be pulling on the body. The individual you see on the left is in the space capsule, in a state of what we call suspension. He is free floating. That individual can sit there for hours and hours and hours without having the muscles or the hands actually pushing against any object. In this state of unloading, if an individual were to move to one side of the capsule by pushing one finger against the capsule wall, that would allow the individual to shoot across to the other side. Individuals can somersault. They can do all kinds of things because the body is essentially unloaded. If we look over to the right side, we see an individual outside the space capsule, wearing a spacesuit that is pressurized, much as if you were to wear scuba gear and dive below the surface in the ocean. But this spacesuit spacesuit weighs about 200 pounds, and that does not feel very heavy to this individual because in this environment, the spacesuit is actually weightless. But it is cumbersome. What you see up at the top of the screen is the umbilical system that attaches the individual to the space shuttle. This individual is performing some routine checks on the space capsule, which we do not see in this particular photo. The other thing I should point out is that that individual is traveling 17,500 miles an hour in this vacuum of weightlessness. So it looks like the astronaut is just sitting there, but in actuality they are moving at this very rapid speed through a vacuum.

Image Reference:

NASA. *Space Flight Images*. Retrieved 08-02-2007 from http://spaceflight.nasa.gov/gallery/index.html



Skeletal Muscle and Loading State

This slide helps to define what we know about the stimuli necessary to maintain homeostasis (normal structure and function) of the skeletal muscle system. If individuals do not receive daily exposure to weight bearing conditions (i.e., normal standing and movement), the muscles fibers will get smaller, weaker, and more easily fatigued. One does not have to travel in space to illustrate this problem. This phenomenon can be demonstrated by having individuals spend continuous time in the state of bed rest (the subject is not allowed to get out of bed), which has become a ground-based analogue to spaceflight.

Looking at these issues from a different perspective, if we put young individuals (i.e., pre-adolescent) in space, do you think their muscles would grow appropriately and achieve the normal myosin patterns that we have examined in the previous sections of the presentation?

Suggested Reading:

Gallagher, P., Trappe, S., Harger, M. , Creer, A. ,Mazzetti, S., Trappe, T., Alkner, B., & Tesch, P. (2005). Effects of 84-days of bed rest and resistance training on single muscle fiber myosin heavy chain distribution in human vastus lateralis and soleus muscles. *Acta. Physiol. Scand. 185*: 61-69.

ADDITIONAL NOTES FROM SPEAKER'S TRANSCRIPT (http://www.bioedonline.org/presentations/)

We have come to understand through a series of research studies that skeletal muscle is very sensitive to loading state. If we want to make the muscles bigger, we need to put high levels of mechanical stress on them. And so we say that the skeletal muscles require almost continuous weight bearing stimuli to maintain normal protein expression—the normal amounts of protein, myosin and actin in the *contractile element. If you eliminate the everlasting stress (that we call gravity) on the muscles, strange things happen to them. The muscle enters a state of protein imbalance in which the muscle proteins undergo degradation, the speed of which determined by the rate at which the muscle fibers are synthesizing protein. Keep in mind that every muscle fiber undergoes continuous buildup and degradation of protein. And if your muscles stay in a normal size, the degradation process is equaling the synthesis process. However, if the muscles are unloaded, this process changes and the degradation process exceeds the synthesis process. In the schematic on the lower side of the figure, you can see that over time, the nice bulky muscle gets smaller and weaker, and less effective to support movement under loading conditions, as seen during normal gravity. The slow myosin genes are turned off and the fast myosin genes are turned on.*

Image Reference:

iStock. *Weight lifting*, #3644853

Absolute and Relative Muscle Weight in Response to Muscle Unloading in Rodents

This slide presents data on the response of rodent skeletal muscle to conditions of unloading, such as during space flight. In space, the muscles lose their ability to generate force, because there is no gravity or load for the muscles to work against. This creates a signal to the muscles that there is no need for them to maintain their normal size. The laboratory rat is an ideal subject for this type of experiment, because, as can be seen in the figure, rat muscles will atrophy dramatically over a period of a few days (the magenta line color). That is, the muscle loses protein, and the muscle size and weight decrease. This change can be seen in the upper figure, depicting the weight of the soleus muscle, one of the key muscle components in our calf region (located in the posterior or rear position of the lower leg). Sometimes, scientists normalize the change in muscle weight by correcting it to the body weight. Generally, the greater the total body weight of the animal, the greater the individual muscle weight. As can be seen in the lower figure, when the muscle weight is normalized to body weight, the relative muscle weight of the rat is still smaller than in the normal control animals that remain on Earth. This information suggests that the muscle tissues are a key target for atrophy, relative to the other tissues, when they are not allowed to generate force, as during exposure to the lack of gravity. Additional research suggests that the same deterioration that affects rodent muscle also affects human muscle, although it take more time to observe the changes, because the metabolism of human muscle is slower than that of rodents. Ongoing studies suggest that there is an imbalance in the capacity of the muscle to synthesize the proteins that make up muscle, relative to the rate that the proteins are broken down (called protein degradation). As a result of this imbalance, muscle weight becomes reduced due to the loss in protein.

Can you think of any way that one could try to prevent this muscle loss from occurring?

Suggested Reading:

Caiozzo, V. J. ,Haddad, F., Baker, M. J., Herrick, R. E., Prietto, N., & Baldwin K. M. (1996). Microgravity induced transformations of myosin isoforms and contractile properties of skeletal muscle. *J. Appl. Physiol. 81*: 123-132.

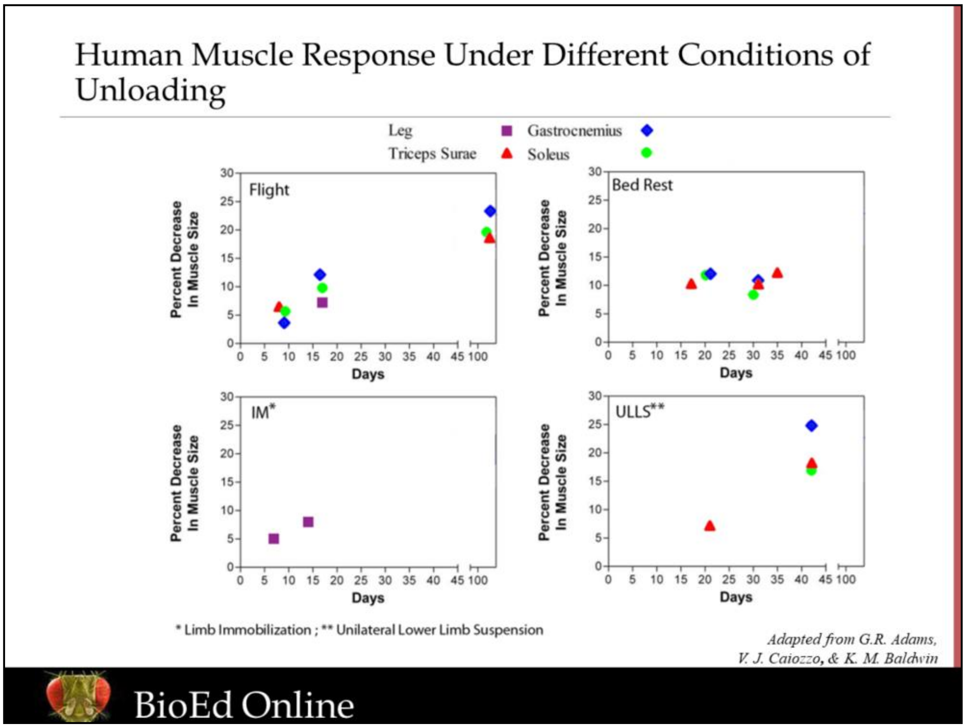
ADDITIONAL NOTES FROM SPEAKER'S TRANSCRIPT (http://www.bioedonline.org/presentations/)

Why would someone want to study a rat in space? First, it is important to realize that rats express the same type of muscle fibers as humans. Rats are under the influence of gravity just as humans are, so when we flew our rats in space, we were able to track a process by weighing the muscle. There was a rapid drop in the weight of the muscle over a period of 16 days. Contrast the magenta line in the upper graph with the blue line, which shows how ground bearing animals on Earth were maintaining their weight. Muscle is much more sensitive to the lack of gravity—the state of unloading—than are other organ systems that contribute to one's body weight.

Image Reference:

Baldwin, K. M. (2007). Seeking countermeasures to the deleterious effects of space travel on skeletal muscle. *BioEd Online (www.bioedonline.org).* Houston, Tx:

Baylor College of Medicine.



Human Muscle Response Under Different Conditions of Unloading

This figure illustrates what happens in human muscle under different conditions of unloading, or a state of non-weight bearing, especially during space flight. It summarizes information that has been gathered from human astronauts living in space, as well as human subjects exposed to unique conditions on Earth that stimulate protein breakdown, as discussed in the previous slide. These studies involve: 1) Bed Rest; 2) Limb Immobilization (IM), in which the lower limb is placed in a cast and the individual is not allow to ambulate (this is a common practice when one breaks a bone in the leg); and 3) Unilateral Lower Limb Suspension (ULLS), in which the individual wears a shoe with a very thick sole so that the opposing leg cannot make contact with the ground (the opposing leg is placed in a sling and the subjects can move about only by using crutches). This latter paradigm demonstrates that when we can no longer perform normal weight bearing activity, as in standing and walking etc., the muscle undergoes an atrophy response. The data focus on different components of one’s calf muscles—a bulky group of muscle in the back of the lower leg.

In the graph above, the vertical axis presents the decrease in the size, or girth, of the muscle, while the horizontal axis depicts the length of time that the muscle is unloaded. The findings clearly suggest that 1) all types of unloading paradigms result in similar degrees of loss in muscle fiber size; and 2) the longer the duration of exposure, the greater the loss in muscle fiber size. Note that all the different points on the graph are clustered together. This tells us that muscle atrophy is not necessarily linked to space flight. Any condition that creates a state where the muscles cannot perform their primary function of generating force and creating movements under loading conditions will cause muscles to atrophy.

What do you think the effects will be on muscle strength if one lives a lifestyle described as a “couch potato?”

Suggested Reading:

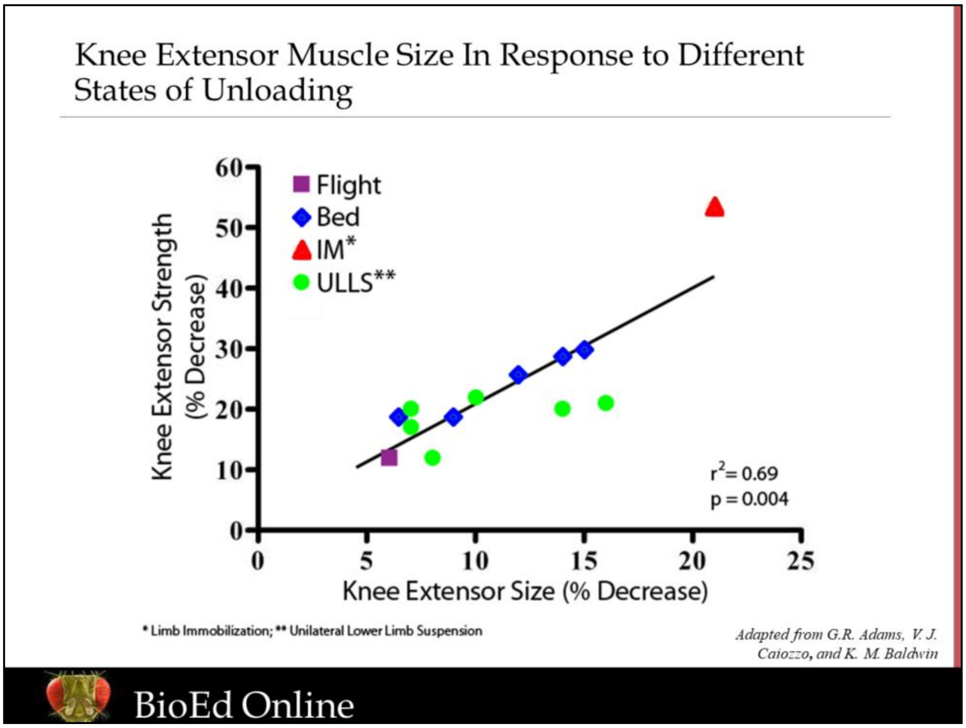
Adams, G. R, Caiozzo, V. J., & Baldwin, K. M. (2003). Skeletal muscle unweighting: spaceflight and ground based models. *J. Appl. Physiol. (Invited Review) 95:* 2185-2201.

ADDITIONAL NOTES FROM SPEAKER'S TRANSCRIPT (http://www.bioedonline.org/presentations/)

What we have here are data plots for leg muscles under a variety of conditions. You see ground-based analogs that we call bed rest. All one needs to do is put individuals in bed and not let them get out for many days. We have kept individuals in a bed rest state for as much as 90 days. While we all like to sleep and take things nice and easy, it is not easy for the subjects to participate in this type of an experiment. We can also illustrate some interesting phenomena by immobilizing limbs. If you have ever broken your leg, and the leg is placed in a cast, the muscle is basically immobilized. Usually, the muscle is not allowed to bear weight. Just by not letting the limb come in contact with the ground, we can see that these muscles are affected. Another type of a situation illustrated in the red figures is called ULLS, or Unilateral Limb Suspension. This does not involve any kind of injury to the muscle. All we do is have the subject wear a large shoe that has a lot of padding to it so that the opposite leg cannot come in contact with the ground. The individual walks around on crutches, and the opposing limb is put into a sling to help the individual support the leg without it coming in contact to the ground. This is a unique experiment in that it also shows that there is a tremendous impact on the muscle by not being able to make contact with the ground, or to assume any ground reaction forces. The longer we prevent the limb from weight bearing or being able to bear force and so forth, the greater the decease in muscle size. Whether an individual is in space, in bed rest, or incapacitated in some way, the end result is a similar response. The muscles will wither away.

Image Reference:

Adams, G. R, Caiozzo, V. J., & Baldwin, K. M. (2003). Skeletal muscle unweighting: spaceflight and ground based models (Adapted from). *J. Appl. Physiol. (Invited Review) 95:* 2185-2201



Knee Extensor Muscle Size in Response to Different States of Unloading

This slide helps to answer the question raised at the end of the last slide: "What do you think the effects will be on muscle strength if one lives a lifestyle described as a couch potato?" The graph illustrates the relationship between knee extensor muscle size decrements (i.e., the extent that the muscle gets smaller due to the different unloading conditions, and the resulting change in strength- or force-generating capacity, such as needed for lifting a weight). Note the loss in strength as a function of the decrease in muscle size (e.g., muscle atrophy). This important relationship highlights the need to maintain muscle mass, which is critical in assessing the physical fitness of an astronaut to perform a variety of tasks while exposed to varying gravity states.

Do you think performance would be compromised further when living in the space suits, as shown in the figure above? If so, how could the loss of muscle mass and strength be minimized?

Suggested Reading:

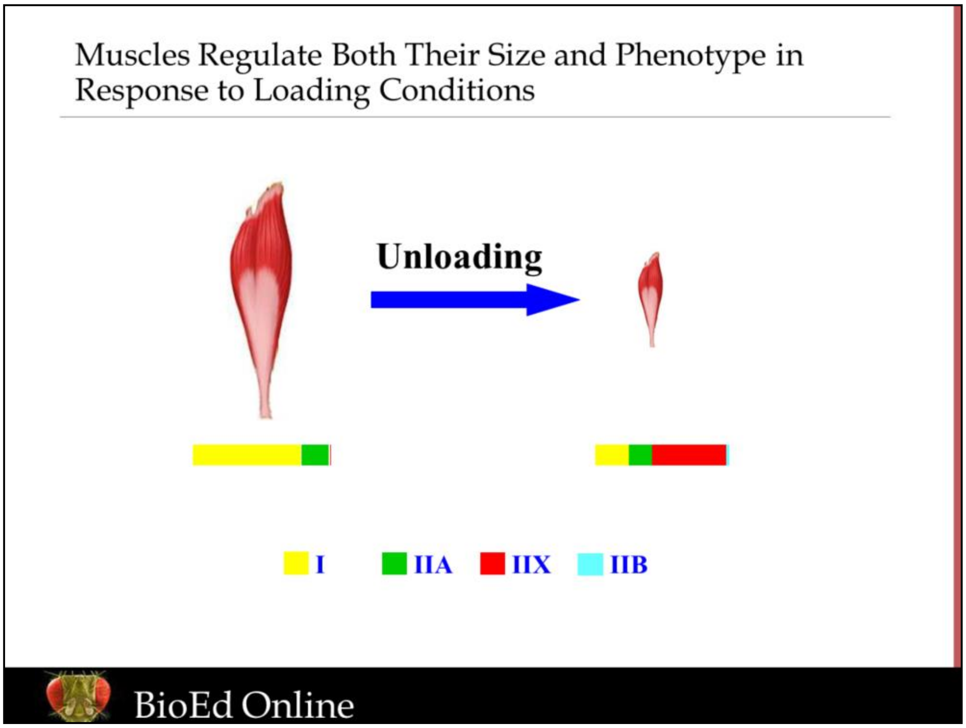
Adams, G.R, Caiozzo, V.J., & Baldwin, K.M. (2003). Skeletal muscle unweighting: spaceflight and ground based models. *J. Appl. Physiol. (Invited Review) 95*: 2185-2201.

ADDITIONAL NOTES FROM SPEAKER'S TRANSCRIPT (http://www.bioedonline.org/presentations/)

Our muscles get smaller under the conditions of unloading. And what are the consequence of this lost muscle size? The graph shows a decreasing size of the knee extensor (thigh) muscles. As those thigh muscles decrease in size, note that the strength of these muscles, as depicted on the Y axis, is now decreasing, as well. So there is a direct relationship: the smaller the muscle, the less strength it can generate. Conversely, bigger individuals with bigger muscles generally are stronger than smaller individuals with smaller muscles. That is why athletes, for example, or football players, do a lot of strength training in their legs and in their arms to build up strength, so that they can be more effective.

Image Reference:

Adams, G. R, Caiozzo, V. J., & Baldwin, K. M. (2003). Skeletal muscle unweighting: spaceflight and ground based models (Adapted from). *J. Appl. Physiol. (Invited Review) 95*: 2185-2201



Muscles Regulate Both Their Size and Phenotype in Response to Loading Conditions

In addition to muscle size, the contractile phenotype (type of myosin expressed) can change under different conditions of loading and unloading. In the normal muscle on the left, the fibers express primarily the slow type I MHC isoform and some of the fast IIa isoform. Following prolonged exposure to microgravity models, the muscle becomes atrophied and at the same time, expresses predominantly fast MHC isoforms, especially the type IIx, which imparts faster contractile properties on the muscle. Thus, in this state the muscle would be compromised by the combined loss in size, strength and ability to perform activities that are heavily dependent on continually overcoming the force of gravity.

How would you predict the muscle performance capacity/capability of an individual returning to Earth from long-term space flight with these defined muscle properties?

Suggested Reading:

Baldwin, K.M. & Haddad, F. (2002). Skeletal muscle plasticity: cellular and molecular responses to altered physical activity paradigms. *Am. J. Physical Med. & Rehab. 81*: (Suppl) S40-S51.

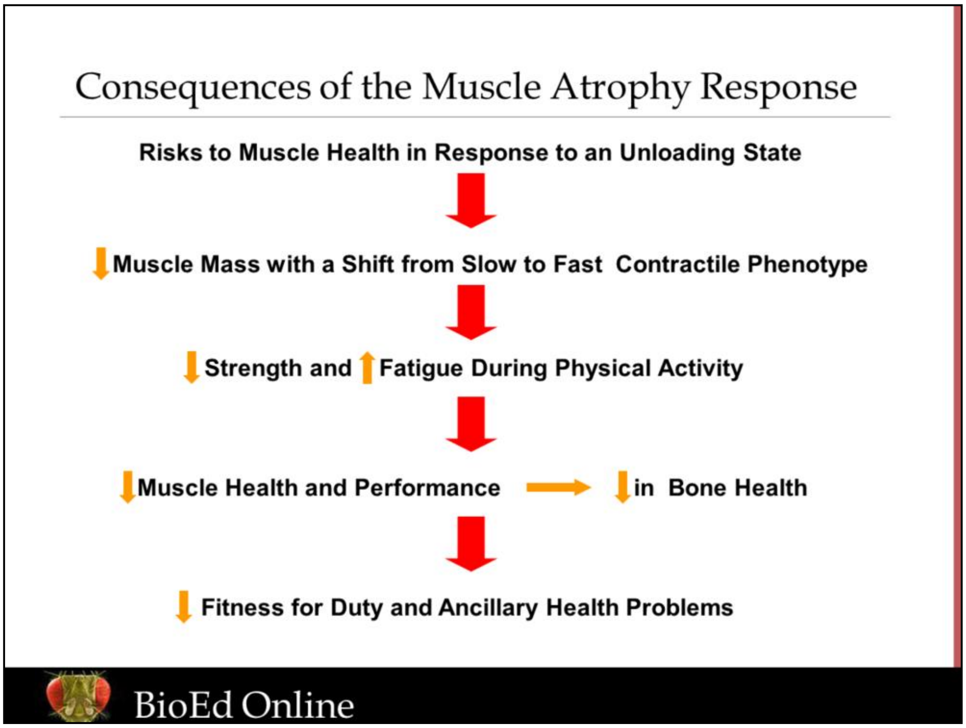
Caiozzo, V.J., Baker, M.J., Huang, K., Chou, H., Wu, Y.Z., & Baldwin, K. M. (2003). Single fiber myosin heavy chain polymorphism: How many patterns and what proportions? *Am J Physiol Regul Integr Comp Physiol. 285*: R570-R580.

ADDITIONAL NOTES FROM SPEAKER'S TRANSCRIPT (http://www.bioedonline.org/presentations/)

When we unload the muscles under the conditions described, the muscle fibers get smaller. If we look at the type of myosin expressed in this particular muscle, it expresses mostly type I myosin heavy chain. Over time, as the muscle gets smaller, it also changes its phenotype, and it expresses 2-X and 2-B types *of fibers that are fast, creating a normal-sized muscle that atrophies, and the phenotype is switched to a faster type. What do you think would be the consequence of shifting this muscle to a smaller, faster size? Do you think muscles under these conditions would be very effective in supporting gravity?*

Image Reference:

Baldwin, K. M. (2007). Seeking countermeasures to the deleterious effects of space travel on skeletal muscle. *BioEd Online (www.bioedonline.org).* Houston, Tx: Baylor College of Medicine.



Consequences of the Muscle Atrophy Response

This illustration defines the cascade that one would expect to occur if some form of high loading activity is not routinely imposed on the space traveler exposed to the microgravity environment over long periods of time (months). Based on the scenario laid out in this figure, one would predict a low level of fitness in such an individual. Most individuals should perform various types of exercise on a routine basis on Earth, but the question is, what can be done to maintain the fitness and general health of anyone likely to be exposed to microgravity (or bed rest, for that matter) for long periods of time?

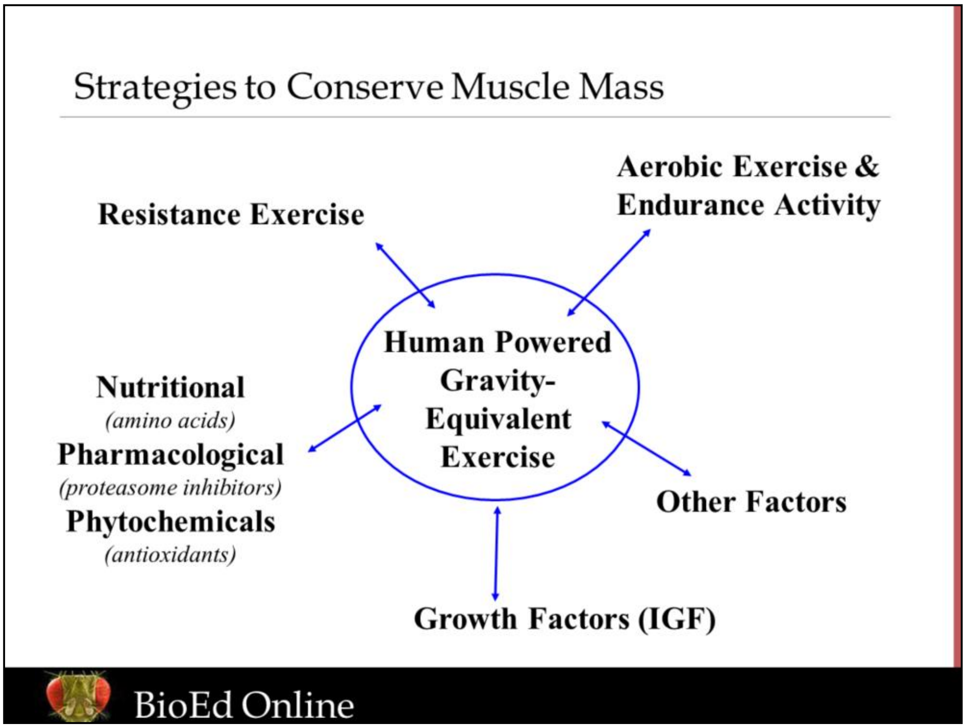
What types of activities would you recommend to ensure muscle homeostasis? Would you need special devices to bring this about?

Suggested Reading:

Baldwin, K. M., White, T. P., Arnaud, S. B., Edgerton, V. R., Kraemer, W. J., Kram, R., Raab-Cullen, D., & Snow, C. M. (1996). Musculoskeletal adaptations to weightlessness and development of effective countermeasures. *Medicine and Science in Sports and Exercise*. 28: 1247-1253.

ADDITIONAL NOTES FROM SPEAKER'S TRANSCRIPT (http://www.bioedonline.org/presentations/)

The atrophy process creates what I refer to as "risk to muscle health" in response to the unloading state, whether we are talking about someone in space flight, or someone in a prolonged state of bed rest. There is a decrease in muscle mass, and a shift of the myosin phenotype from slow to fast contractile capabilities. In addition, the muscle becomes more fatigable when an individual engages in physical activity. So it is weaker, and it has less stamina. There is a general saying that, as the muscle goes, the bone goes. So when we start to atrophy muscle, the muscles are no longer putting stress on *bone, and there is a loss in bone health. For an astronaut, and for an individual who is bed ridden, fitness falls dramatically. This person cannot do routine, normal things. Further, this condition creates ancillary health problems, one of the biggest being Type II diabetes.*



Strategies to Conserve Muscle Mass

This schematic depicts some of the current activities proposed to maintain the homeostasis of the musculoskeletal system. In an ideal world, one could create a gravitational field on the International Space Station (ISS) or in the spacecraft used for long-term transportation. This strategy would go a long way toward maintaining the physiological status and health of humans while in space. However, for now, this strategy appears too costly. Nevertheless, artificial gravity, especially when generated by the astronaut, is a definite possibility that has been proposed by many individuals for a long time. The current NSBRI muscle team contingent has made this approach a high priority, in fact, it is the epicenter of the strategies to conserve muscle mass and enhance human performance. There also is strong advocacy for including two types of exercise regimens. The first pertains to resistance exercise, in which the astronaut would use sophisticated machines that do not require free weights for loading the muscles (use of free weights are currently considered the “gold standard” for resistance exercise on Earth). The second regimen involves some form of aerobic exercise, designed to challenge both the cardiovascular and skeletal muscle systems and enhance endurance properties in the muscle. This could involve running on treadmills or cycling bicycle-type ergometers. In addition to physical exercise strategies, many scientists believe that the homeostasis of various organ systems, including skeletal muscle and bone, can be attained through some form of nutritional supplements and/or specific pharmacological agents that can enhance (or interfere with) biological processes involved in building up (or breaking down) muscle protein content. Many individuals, in essence are looking for a “magic pill,” which may include known growth factors, to solve the problems of body wasting in space.

Whether such a pill can be designed remains a big question. What do you think of efforts by scientists to design a “magic pill” to prevent muscle wasting?

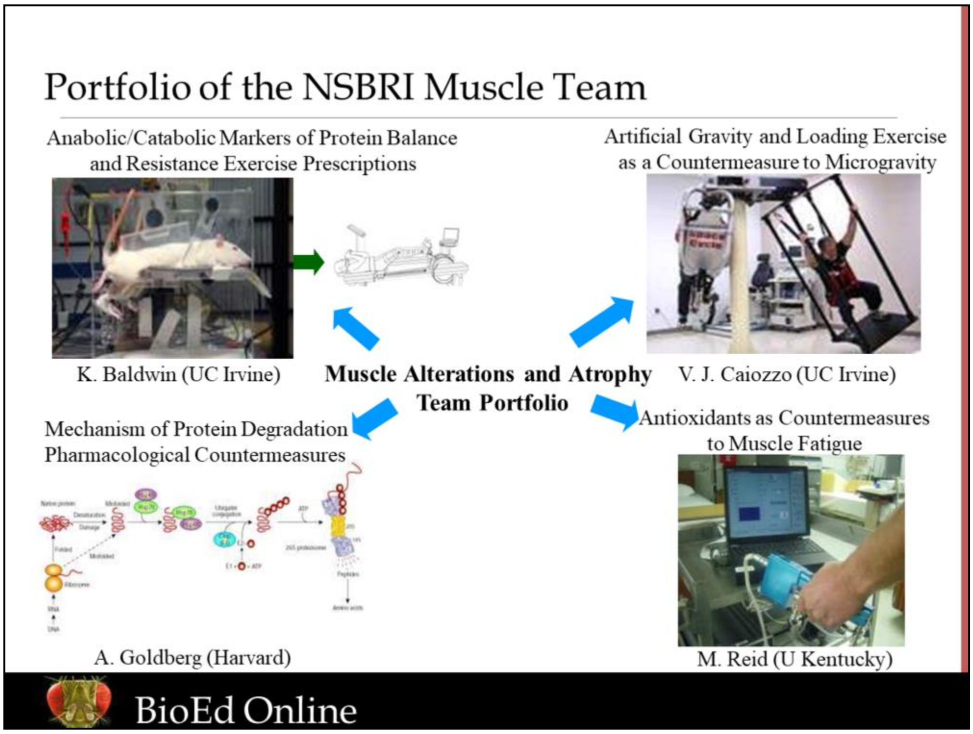
Suggested Reading:

Shackelford, L. C., LeBlanc, A. D., Driscoll, T. B., et al. (2004). Resistance exercise as a countermeasure to disuse-induced bone loss. *J. Appl. Physiol. 97*: 119-129.

Caiozzo V. J., Rose-Gottron, C., Baldwin, K. M., Cooper, D., Adams, G., Hicks, J., & Kreitenberg, A. (2004). Hemodynamic and metabolic responses to hypergravity on a human-powered centrifuge. *Aviat Space Environ. Med. 75*: 101-108.

ADDITIONAL NOTES FROM SPEAKER'S TRANSCRIPT (http://www.bioedonline.org/presentations/)

So what are we going to do about this problem (of maintaining muscle mass and strength) among astronauts in prolonged space travel? Within the National Space Biomedical Research Institute, we have developed a strategy with several components. One component is the idea that if we could reconfigure or capture gravity, or develop a gravity stimulus while individuals are in space, we probably could solve a lot of our problems, because this is really a gravity problem. If we could recapitulate gravity, we might be able to maintain normal muscle health, normal bone health, etc. Another component is weight lifting, shown in the upper left corner, of the slide. We call this resistance exercise. The big challenge for space travelers is to find a device that can load the muscles and subject them to an exercise routine, just like many of you are probably doing when you go to the gym. Obviously, we need to enable individuals to have muscle endurance, which is primarily a factor of having the individual contract the muscles at a very high frequency. This is usually done by having individuals cycle. The challenge is: can we design a cycle or a treadmill for use in space? We know that astronauts really enjoy having some form of physical activity. The treadmill or cycle might be their primary choice, but there are other strategies that people are trying to develop, including some involving growth factors. Can we give individuals a hormone, referred to as an insulin-like growth factor, that inherently induces a growth related process in the muscle? Other strategies involve better nutrition, pharmacological strategies to try to block the degradation process, and phytochemicals (referred to an anti-oxidants) in the normal diet, to decrease oxidative stress on the muscle. Some people think what is really needed is a "magic pill." But the question is, could we design a pill that could take the place of gravity? That is a big item of debate. I think it is better to have individuals exercise.



Portfolio of the NSBRI Muscle Team

This diagram presents some of the key skeletal muscle projects currently being conducted by the NSBRI research program. One project, by Dr. Ken Baldwin at UC Irvine, is designed to ascertain specific molecular markers in the muscle cell that can be used to predict whether the muscle cell is in a net anabolic (building up muscle) or a net catabolic (wasting) state. This research uses resistance exercise involving animals (the same type of exercise used with humans) that are undergoing hind limb suspension (a well accepted ground-based analogue that mimics the muscle wasting of rodents seen during space flight). Baldwin’s findings have identified several markers in conjunction with a resistance exercise prescription that are effective in preventing muscle atrophy. The current goal is to extend this research to studies involving humans.

Another project focusing on animal subjects is that of Dr. Fred Goldberg at Harvard University. Goldberg’s project seeks to identify a safe and effective pharmacological agent that successfully inhibits the primary pathway in which skeletal muscle proteins (especially actin and myosin) are normally degraded. If this could be accomplished, it would provide a way to preserve skeletal muscle and thus reduce the amount of time astronauts have to spend carrying out specific exercise regimens.

A third NSBRI project is being directed by Dr. Vince Caiozzo, also at UC Irvine. Dr. Caiozzo and his colleagues have designed and built a unique type of bicycle device that, when pedaled at different speeds, creates a “merry-go-round” type of spinning that produces an acceleration field that translates into gravity equivalents actually much greater than normal gravity (i.e., 2x, 3x Earth gravity). The idea is to create hyper G stimuli for different durations in order to impose brief episodes of gravity, in the hope that intermittent stimuli will provide sufficient stress on the body to maintain muscle mass and strength as occurs in the normal state of gravity stress on Earth. Under the conditions of hyper-gravity, one goal is to have subjects perform exercises that would be equivalent to those seen in heavy resistance exercise paradigms on Earth.

The fourth project involves a unique approach to administering high levels of antioxidant substances (common in the normal diet) to see if they can prevent the fatigue common in the hands and forearm muscles when performing long duration activities linked to the building of the ISS. These endurance exercise experiments specifically target the forearm muscles using hand grip dynamometers.

All of these projects are critical to improving the health and performance of astronauts. Can you think of any other experiments that the NSBRI should be doing to benefit the functional properties of the skeletal muscle system?

Suggested Reading:

Garma, T., Kobayashi, C., Haddad, F., Adams, G. R., Bodell, P. W., & Baldwin, K. M. (2007). Similar acute molecular responses to equivalent volumes of isometric, lengthening or shortening modes of resistance exercise. *J. Appl. Physiol. 102*: 135-143.

Goldberg, A. L. (2007). Functions of the proteasome: from protein degradation and immune surveillance to cancer therapy. *Biochem Soc Trans.;35(Pt 1)*: 12-7.

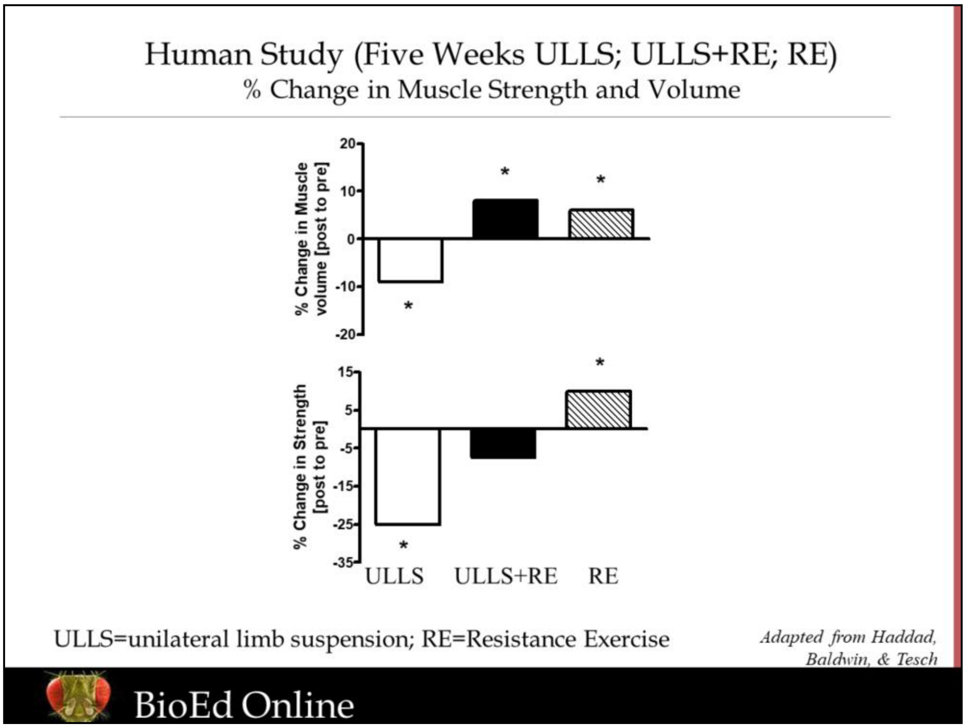
Reid, M. (2007). Highlighted Topic: Oxidant Activity in Skeletal Muscle. *J Appl Physiol. [Epub ahead of print] PMID*: 17204571 [PubMed - as supplied by publisher]

Yang, Y., Kaplan, A., Pierre, M., Adams, G., Cavanagh, P., Takahashi, C., Kreitenberg, A., Hicks, J., Keyak, J., & Caiozzo, V. (2007). Space Cycle: A Human Powered Centrifuge That Can Be Used for Hypergravity Resistance training. *Aviation Space Environmental Medicine*.

ADDITIONAL NOTES FROM SPEAKER'S TRANSCRIPT (http://www.bioedonline.org/presentations/)

At the University of California, Dr. Vince Caiozzo has designed a space cycle, a very unique device. An individual, or two individuals, will sit on the space cycle. One of them will ride just like you would pedal a bike, and this will sort of make it like a gondola, or a merry-go-round. Another individual can be standing on this platform and doing resistance exercises, because you can spin this at a sufficient speed for the individual actually to be spun at one G, two Gs, and three Gs. And so these individuals, when they are riding on the platform and doing these squat exercises, actually get to a point where they have to lift three times their bodyweight. This is a tremendous stress on the muscle, and it illustrates one of the strategies being considered for counteracting the loss of muscle mass. My project involves both animal and human subjects. We can design a heavy resistance training program, that will put stress on the muscles. This would be complementary to the artificial gravity program. In the lower right hand corner of the slide is a project being conducted by Dr. Michael Reed at the University of Kentucky. You see here is an individual gripping a hand ergometer, which allows one to improve the strength of the forearm and fingers. These muscles are used extensively when an individual performs EVA, extra vehicle activity, mentioned a number of slides ago. Dr. Reed is trying to provide anti-oxidants that are normal in the diet, along with resistance exercise, to induce a stronger and more fatigue-resistant forearm muscle, so that the astronauts are more effective in performing their duties outside the spacecraft. Finally, this slide tries to illustrate the unique protein degradation pathways that get activated when an individual's muscles become unloaded. It breaks the proteins down into individual amino acids. If one could design a pharmacological drug or agent that blocks this pathway, or slows it down, it would play a significant role in trying to reduce the atrophy process.

Can you think of something that one could do that might play a role in reducing this atrophy process?



Human Study

This slide presents results obtained from a study published in collaboration with Dr. Per Tesch, Department of Physiology and Pharmacology at the Karolinska Research Institute in Stockholm, Sweden. Subjects were randomly divided into three groups. One group was subjected to the unilateral lower limb suspension (ULLS) model. Recall that this manipulation is designed to unload the leg so that it cannot perform any weight-bearing activity. A second group also was subjected to ULLS, but this group received resistance exercise every three days to provide heavy loading stimuli to the thigh muscles. A third group did not receive the ULLS treatment, but received the same resistance exercise loading treatment as the second group. The findings clearly indicate the following.

1) ULLS treatment induces muscle atrophy (indicated by the decreased muscle volume) as well as a reduction in strength.
2) This atrophy response was significantly meliorated by the resistance exercise program.
3) Resistance exercise induces muscle hypertrophy and increases in strength among individuals undergoing normal weight bearing activity.

This experiment demonstrates that periodic high levels of muscle loading have a profound effect on skeletal muscle, especially in individuals who undergo states of non-weight bearing activity. This suggests that with appropriate training programs, muscle mass and strength can be preserved in astronauts experiencing long term space travel. However, the prescription may need to be altered because some missions will be longer than the five-week duration of the present study.

Do you think exercises, such as walking and jogging, would be successful in preventing muscle atrophy and loss of strength?

Suggested Reading:

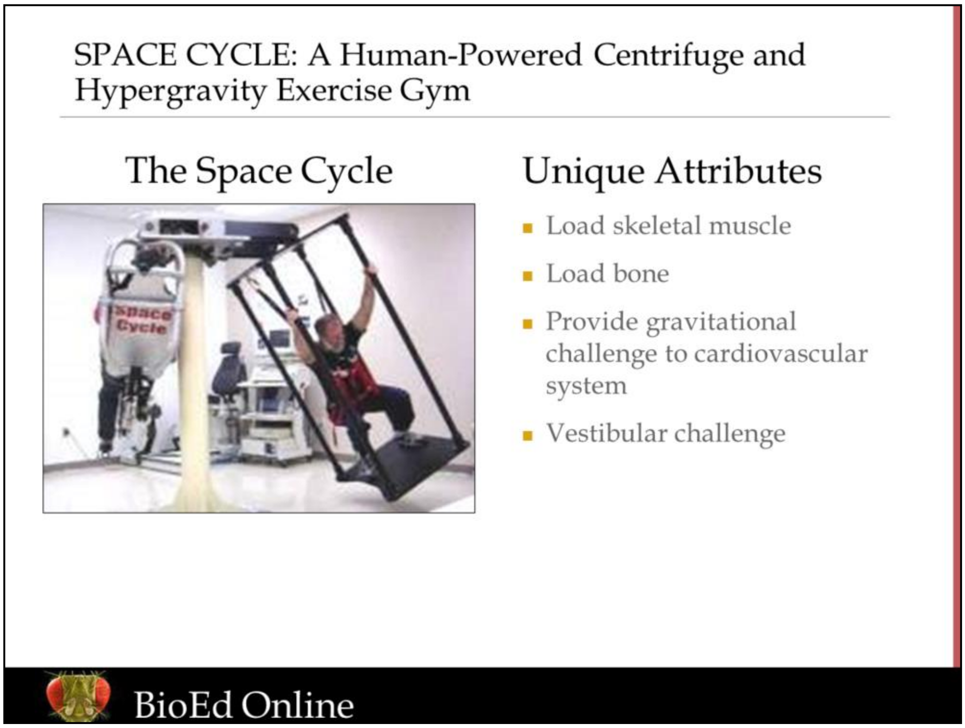
Haddad, F., Baldwin, K. M., & Tesch, P. A. (2005). Pretranslational markers of contractile protein expression in human skeletal muscle: effects of limb unloading plus resistance exercise. *J. Appl. Physiol. 98*: 46-52.

ADDITIONAL NOTES FROM SPEAKER'S TRANSCRIPT (http://www.bioedonline.org/presentations/)

This slide illustrates what happens to the change in muscle size, and the change in muscle strength when individuals undergo an unloading stimulus (unilateral limb suspension model). Note that the muscles indeed get smaller and weaker, as shown by the bar graph going down into the negative range, relative to normal. You can blunt that atrophy response and create a positive effect, in terms of muscle size and strength, by providing brief bouts of resistance exercise to individuals undergoing the limb suspension stimulus. In fact, this approach is almost as effective as if you gave resistance exercise to an individual going through normal weight bearing activity. These outcomes give us hope that we can enable our astronauts to try to keep themselves healthy by these various exercise prescriptions.

Image Reference:

Haddad, F., Baldwin, K. M., & Tesch, P. A. (2005). Pretranslational markers of contractile protein expression in human skeletal muscle: effects of limb unloading plus resistance exercise (Adapted from). *J. Appl. Physiol. 98*: 46-52.



Space Cycle

A bike-like centrifuge that creates artificial gravity may help astronauts combat several physiological problems encountered by individuals spending time space. This research program still is in its infant stages, and while some early findings appear to be promising in terms of maintaining human health and fitness, a lot of additional research needs to be accomplished. As shown in this picture, one feature of artificial gravity is that it provides a form of physical stress in that it can load skeletal muscle. Also, it provides significant challenges to the cardiovascular system because it puts a stress on the heart and blood vessels for delivering blood to the various organ systems. An additional feature of the gravity stimulus is that it imposes a challenge on the sensory motor system, which is critical in establishing fidelity of movement. Therefore, since gravity controls a major component of the various organ components that intimately influence function of the entire organism, it is proposed that this form of exercise, that specifically imposes gravity stimulus of varying magnitude, may hold the key to counteracting all the key imbalances to performance of the various organ systems during long-term spaceflight.

Do you think that the space cycle can be an effective device for improving the fitness of a person based on what has been described above? Do you think that this device can play a role for helping individuals to be healthier and fitter on Earth?

Suggested Reading:

Yang, Y, Kaplan, A., Pierre, M., Adams, G., Cavanagh, P., Takahashi, C., Kreitenberg, A., Hicks, J., Keyak, J., & Caiozzo, V. (2007)Space Cycle: A Human Powered Centrifuge That Can Be Used for Hypergravity Resistance training. *Aviation Space Environmental Medicine*

78: pp. 2-9.

ADDITIONAL NOTES FROM SPEAKER'S TRANSCRIPT (http://www.bioedonline.org/presentations/)

I want to say a few words about the space cycle, because we think that this is an item or a modality that speaks to the issue of hitting several birds with one shot. What you see is that by using this artificial gravity stimulus, we can load the muscle and bone. And we can provide a gravitational challenge to the total body, because the total body is impacted. Just about all the organ systems are affected by the lack of gravity. In particular, the case where we are putting stress on the cardiovascular system through this hypergravity stimulus highlights one of the biggest problems that astronauts experience when they go into space. That is when they return from space travel, they are in what we call a hypo-tensive state, where they cannot maintain a normal blood pressure and they are very sensitive to changes in posture. In fact, one astronaut who returned recently from space, when giving an interview, actually passed out twice while on the podium trying to say what a great experience it was to go into space. But it is not a great experience coming back, because you have to recondition the system. But what about conditions on earth? Does the science that we are using to make headway in studying problems in space have an impact in some way on Earth? The answer is definitely yes.

Practical Applications: Muscles and Exercise

Finally, it is important to note that while the NSBRI program in space life sciences is targeted at solving problems of human health and performance during space flight, there also are important problems to be addressed in the daily setting on Earth. Shown on the left side of the slide are two individuals with spinal cord injuries. Both subjects have marked atrophy of the lower legs because the lesions were encountered in the spinal cord between the waist and the shoulders. The individual in the top left figure uses the upper extremities only for getting from one place to another, whereas the individual in the lower left figure is an avid endurance exercise athlete. By performing a high volume of exercise, this individual not only has developed large muscles in the arms and shoulders, but bone scans show that this individual has bones with a high mineral density and size. This suggests that increased physical activity involving a high level of muscular involvement is essential to maintain bone mass and mineral density.

The idea that increased physical activity is of benefit also holds true for the individuals in the middle figures. People who live a very active life are able to maintain their muscle mass and youthful body structure, as opposed to those who maintain a sedentary lifestyle that eventually leads to frailty. While we think of physical activity as essential for athletes, it is important to remember that one’s quality of life depends upon how much effort we put into taking care of our bodies. Thus, as new findings are demonstrating, sound bodies and sound minds are dependent on an active lifestyle. The question is, how do you presently take care of yourself? Do you think you are doing the right things to keep you fit? Research evolving from the space program should provide a prescription for keeping yourself active. Are you up to the challenge?

Suggested Reading:

Rittweger, J., Frost, H. M., Schiessl, H., et al. (2004). Muscle atrophy and bone loss after 90 day bedrest and the effects of flywheel resistive exercise and pamidromate: results from the LTBR study. *J. Bone 11*: 014-033.

Clasey, J. L., Janowiak, A. L., Gater, D.R. (2004). Relationship between regional bone density measurements and the time since injury in adults with spinal cord injuries. *Arch Phys Med Rehab 85*: 59-64.

Shackelford, L. C., LeBlanc, A. D., Driscoll, T. B, et al. (2004). Resistance exercise as a countermeasure to disuse-induced bone loss. *J. Appl. Physiol. 97*: *119-129*.

ADDITIONAL NOTES FROM SPEAKER'S TRANSCRIPT (http://www.bioedonline.org/presentations/)
The individual on the upper left of the slide has had a spinal injury. This individual has to be maintained in a wheelchair for locomotion. If you looked at his leg muscles, they would be small. And his bone would be relatively small and demineralized. The individual on the bottom left of the slide competes in wheelchair marathons. And while the muscles below the lesion (somewhere between the waist and shoulders) are small, and the bone in his legs has been demineralized, you see in the upper torso, by this individual putting a lot of stress on his arms by wheeling, the arms and chest have become extremely well developed. The bone mass is greater, and if you looked at the bone mass in this person's spinal column, it also would be greater than in the individual at the top left. So we know that by exerting muscle and putting more muscle stress on bone, and keeping our muscles very active, we can impact bone health. This is important as individuals get older, especially women who experience osteoporosis, which is very common. If we look at the center part of the slide, the individual in the top image is experiencing the number one disease in the world. Every human being is faced with this disease, Sarcopenia, or atrophy and wasting of the muscle fibers. The individual on the bottom has led a very active life, and has used a heavy resistance weight training program. While these two individuals are the same age, the body structure speaks for itself. Which individual would you like to emulate in this aging process? Finally, the resistance training paradigms paradigms we are designing for astronauts can help athletes to be much fitter and more competitive. So the science we are conducting for the space program has obvious spin-offs that can impact a broad range of people in the general population. And as I close, I ask, how do you want to age? Do you want to age with a lot of pizzazz, or do you want to become a couch potato?

Image References:

iStockphoto. *Atrophy of legs # 177380*

iStockphoto. *Back of wheelchair # 2514311*

iStockphoto. *Man lifting weights # 3644853*

iStockphoto. *Spinning for Fitness at 50 plus # 2275868*

Axelson, P. *Racing wheelchairs.* US Department of Transportation, Federal Highway Administration. Retrieved 08-06-2007 from www.tfhrc.gov/safety/pubs/04103/03.htm