Space Life Sciences Research Highlights

Space-Based Research Yields New Understanding of Muscle Development

Can space-based research on muscle development teach scientists how to prevent the muscle wasting that seems an inevitable part of normal aging? Kenneth Baldwin thinks so. In his research on muscle development in rats, he has identified molecular and genetic changes that accompany muscle wasting. Such insights may one day yield new treatments to help people avoid the debilitating effects of muscle atrophy in space and on Earth and allow people to maintain muscle mass, strength and coordination into old age.

Human skeletal muscles come in two varieties: slow-twitch muscles that enable us to stand upright and walk, and fast-twitch muscles that provide the power for such movements as pushing, pulling, lifting and throwing. These muscles share a common building block: the protein myosin, which forms the bulk of the contractile apparatus within muscle fiber and controls how powerfully a muscle contracts.

One component of myosin, called myosin heavy chain, plays a central role in differentiating muscle types. Myosin heavy chain can appear in any of four forms (called isoforms) in adult animals and two forms in developing animals. Each isoform is the product of a different gene, and the proportion of isoforms expressed in a given muscle determines how fast or how slowly it contracts.

In adult animals and humans, muscle tissue has the ability to remodel, or change the proportion of myosin heavy chain isoforms, when subjected to changing conditions. This remodeling process, researchers believe, plays an important role in muscle wasting. Muscle overuse or decreased use initiates remodeling, as does a change in the amount of thyroid hormone present in the bloodstream. Thyroid hormone is a key regulator of myosin heavy chain production.

Kenneth Baldwin and his colleagues at the University of California, Irvine, have been studying this remodeling process since 1978. Their work has shown that when the force of gravity is eliminated from skeletal muscles, either by suspending an animal's hind limbs or by placing it in the microgravity of space flight, the proportion of myosin heavy chain isoforms changes. In particular, the large predominantly slow-twitch muscles that support body posture and locomotion under normal gravity remodel to express more of the myosin heavy chain isoforms associated with fast-twitch muscles.

These experiments also showed that levels of thyroid hormone in the blood can affect the degree of remodeling that takes place when muscles are overloaded or unloaded. Too little thyroid hormone impedes the remodeling of muscle from slow-twitch to fast-twitch, while an excess of thyroid hormone can hasten that same process.

To better understand the basic biology of remodeling, Baldwin conducted an experiment on the April 1998 Neurolab space shuttle mission (STS-90) using newborn rats. The study's goal was to see whether infantile forms of myosin heavy chain in the young rats' skeletal muscles would undergo similar changes when their muscles were unloaded to those seen in adult animals. Baldwin found that a large antigravity muscle in the rats' legs, the soleus muscle, developed less of the myosin heavy chain isoform associated with slow-twitch muscles than did the soleus muscles of newborn rats raised in Earth's gravity. He also found less of the RNA that codes for the slow-twitch isoform, indicating that the change was at the genetic level. The remodeling was less pronounced among Neurolab-raised newborn rats with thyroid deficiencies, suggesting that adjusting thyroid hormone levels may be a way to regulate the remodeling process when gravity is absent.

Baldwin's Neurolab experiments were among the first to study the effects of muscle unloading on newborn animals, because such experiments cannot be conducted in Earth's gravity. "In Earth-based experiments, you can't completely eliminate gravitational effects, because the newborn rats can't feed in the hindlimb suspension position," Baldwin said.

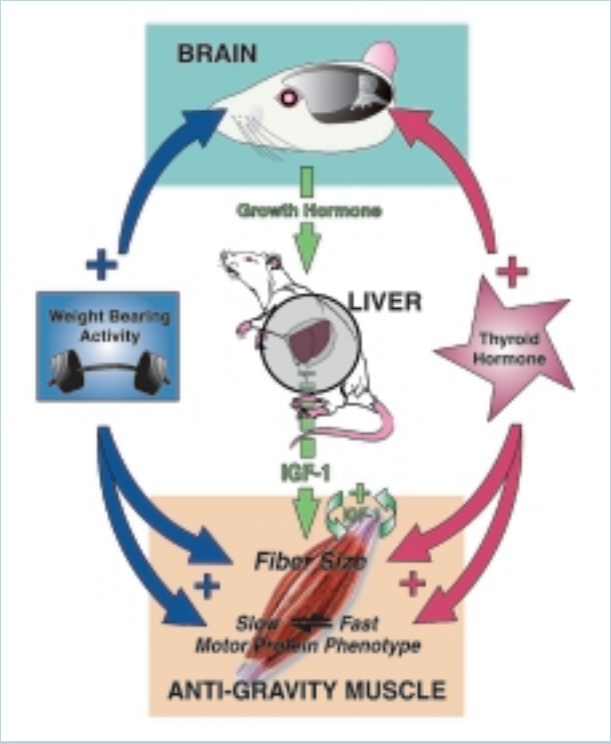
Remodeling is only one of the processes involved in muscle wasting. The next step, Baldwin says, is for researchers to gain a better understanding of the complex processes that control protein synthesis and protein breakdown in muscle tissues. "We think that muscle may atrophy when there aren't appropriate stimuli to keep the muscle producing insulin-like growth factor 1," he says. "This growth factor is manufactured in the liver under stimulation from the pituitary gland, but there is evidence to suggest that the muscle cell itself also produces it." Baldwin hopes to learn more about protein balance through experiments on a future shuttle mission.

With a better understanding of how muscle tissue develops and remodels, Baldwin says, researchers can one day offer an exercise prescription to prevent muscle atrophy during long space flights and during the later decades of life. "We know that pumping iron ameliorates the atrophy process, but we don't have a good feel for what the ideal contraction process might be," Baldwin says. "We need more specifics about the numbers and frequency of each exercise."

Will there ever be a hormonal treatment or pill to prevent muscle wasting? "Some people would like a pill, but I don't think there will be one that will completely replace the blood, sweat and tears of exercise," Baldwin says. "However, down the road we may be able to use drugs or genetic engineering to augment the effects of an exercise prescription."

Baldwin feels there is an urgent need to continue research into muscle wasting. "Muscle mass is in a negative slope after age 40 for all individuals," he says. "We're all in the same sinking boat, although some sink faster than others based on activity level, lifestyle and disease states. By understanding the basic mechanisms of muscle remodeling and protein balance, we may be able to prevent some of the debility, injury and premature death associated with muscle wasting in age. More than half of those over 70 years old who experience a major bone fracture will never recover—they die of complications. Many of these bone fractures could be prevented by preserving muscle strength and coordination."

This research will also be crucial to the health of astronauts who will live and work on the space station for months or even years at a time. "We need to understand the basic science of what happens when you chronically unload the major muscles," he says. "That knowledge will help us protect the health of astronauts in the microgravity of space and during their transition back to Earth's gravity."



Factors involved in regulating muscle growth and the expression of the muscle protein myosin during development. Two factors—weight bearing activity (as in opposing gravity) and thyroid hormone—interact to influence these processes. Both weight bearing activity and thyroid hormone are thought to exert their influence on muscle growth through the growth hormone, insulin-like growth factor 1 (IGF-1). However, these two factors oppose one another in regulating the type of myosin that is expressed. Increased weight bearing activity increases the relative amount of slow motor myosin and vice versa, whereas thyroid hormone causes the opposite responses.

References

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