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学位論文名	Gravitational Load-dependent Regulation of Skeletal Muscles （重力負荷依存的な骨格筋の特性制御機構）
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論文内容の要旨

Removal of weight-bearing activity by hindlimb unloading or exposure to microgravity induces prominent atrophy and shift of fibers toward fast-twitch type, particularly in slow-twitch soleus muscle. As the causes for these phenomena, changes in neuromuscular activation and mechanical load are often reported. However, the effects of unloading condition on the characteristic changes of other skeletal muscles, such as adductor longus muscle and neck muscle are not clear. In addition, the effective countermeasure for skeletal muscle weakness is still unclear. Here I show that adductor longus muscle (slow-twitch muscle) of rats had region specific responses to hindlimb unloading and reloading in the part 1 experiments. Muscle activity patterns in the caudal region significantly changed in response to loading levels. Characteristic changes of muscle fibers in this region were greater than the rostral region. In part 2 experiment, I compared the response of neck and hindlimb muscle (soleus and extensor digitorum longus (EDL) muscle of mouse to prolonged spaceflight for 3 month. Spaceflight tended to cause fiber atrophy and shift of fiber type toward fast-twitch type in neck and soleus muscle. On the other hand, EDL muscle was not affected. In response to spaceflight, 18 genes in neck muscle were up-regulated and 13 genes were down-regulated vs. those in the ground-based laboratory control. Atrophy was associated with up-regulation of genes involved in protein break-down. Further, shift of fiber phenotype was related to down-regulation of genes, which are related to cellular metabolism, suggesting that oxidative muscular metabolism may be inhibited in microgravity environment. Finally, I studied the efficacy of exercise prescription, which has been imposed to astronauts during stay on the International Space Station in part 3 experiment. Soleus electromyogram activity during walking was increased depend on walking speed and degrees of uphill in rear-foot strikers. But in fore-foot striker, soleus muscle was most active during walking at a slower speed on a flat treadmill. It was suggested that neuromuscular activity and mechanical load are important for maintenance of skeletal muscle properties. It was also indicated that foot-strike patterns should be considered, when treadmill walking is prescribe for prevention of soleus atrophy. These results may be helpful for development of suitable countermeasures for prevention of muscle weakness and ataxia, which are also caused by lack of exercise and/or aging.

論文審査の結果の要旨

抗重力活動抑制に伴い、遅筋線維を多く含む長内転筋等の抗重力筋に顕著な萎縮や速筋化が誘発される。長内転筋では頭側部に比べて尾側の筋線維特性（筋線維サイズや速筋化、衛星細胞数の減少等）に顕著な抗重力活動抑制の影響が誘発され、同一筋でも部位特異的な制御がなされていることが明らかになった。現在、宇宙飛行士の抗重力筋衰弱防止策として国際宇宙ステーション内で、トレッドミル走を用いた運動等が行われているが、効果には個人差が見られる。そこで、ヒトにおける歩行運動中のヒラメ筋活動を推定するために筋電図を記録した結果、同一速度・上り勾配でも、かかと着地および足裏全体または前部着地歩行者では、運動負荷の増強に応じたヒラメ筋活動の増加が全く逆であった。目的とする筋に応じた運動処方には、各人の歩行様式などを考慮する必要があることが明らかとなった。これらの知見は、宇宙飛行士のみならず、高齢者のトレーニングやリハビリテーション等にも有用であるだけでなく、基礎的な筋の可塑機構にも大きな示唆を与えるものであり、学位に値するものと認める。