順天堂大学大学院スポーツ健康科学研究科 和文抄録
2023年度修士論文

加齢および性差が骨格筋リボソーム生合成に及ぼす影響

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【目的】
骨格筋は筋線維の集合体であり、筋線維はその収縮特性から速筋線維（typeⅡ）と遅筋線維（type Ⅰ）に大別される。加齢に伴う筋萎縮は、遅筋線維よりも速筋線維の方が萎縮が認められるのが特徴である。筋萎縮の発生機序は、筋線維内の収縮および構造タンパク質の合成と分解の変化による筋タンパク質の減少が、筋線維の萎縮を引き起こしていることが知られている。しかし、筋萎縮の要因となっている筋タンパク質の減少がタンパク質合成器官であるリボソームに着目した研究はされていない。
タンパク質合成速度はリボソーム生合成に依存する。そこで本研究は、加齢および性差が骨格筋リボソーム生合成に及ぼす影響を明らかにすることを目的とした。

【方法】
6・12・18・24・30ヶ月齢の雄性および雌性F344ラットから足底筋を採取した。採取した足底筋からTotal RNA、筋タンパク質、タンパク質合成シグナル経路およびリボソーム生合成関連因子を分析した。

【結果】
雄および雌ラットでは、加齢による骨格筋量および体重あたりの骨格筋量の減少が認められた。しかし、リボソーム生合成の指標である骨格筋1mgあたりのTotal RNA量および28S＋18S rRNA量、RPL10タンパク質量の増加が認められた。Akt S473リン酸化量およびp85S6K Thr412リン酸化率、p70S6Kタンパク質量、p70S6K Thr389リン酸化率、4E-BP1 Thr37/46リン酸化量、4E-BP1タンパク質量で加齢による影響に性差が認められた。

【結論】
雄および雌ラットの足底筋において加齢に伴うタンパク質合成経路（Akt/mTORシグナル経路）とリボソーム生合成の変化には性差が生じることが示唆された。

Juntendo University, Graduate School of Health and Sports Science 英文抄録（Abstract）
2023 Master's Thesis

Effects of aging and sex on ribosome biogenesis in skeletal muscle

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[Purpose]
Skeletal muscle, the largest organ in the human body, plays crucial roles in physical activity, metabolism, and endocrine function. Consequently, maintaining and enhancing skeletal muscle mass is considered essential for a healthy lifestyle. However, given that skeletal muscle undergoes atrophy and a decline in strength with age (sarcopenia), developing coping strategies and treatments to prevent or at least minimize sarcopenia is important. Skeletal muscle is an aggregate tissue of muscle fibers that can be broadly classified into fast (type II) and slow (type I) muscle fibers based on their contractile characteristics. Age-related muscle atrophy is characterized by a deterioration of the fast rather than slow muscle fibers, the underlying mechanism of which is a reduction in muscle protein attributable to changes in the contraction, synthesis, and degradation of structural proteins within muscle fibers. To date, however, no studies have focused on the ribosomes (protein-synthesizing complexes) associated with muscle atrophy. Given that the rate of protein synthesis is dependent on ribosome biogenesis, in this study, we sought to clarify the effects of aging and sex on ribosome biogenesis in skeletal muscle.

[Methods]
Plantaris muscles were collected from 6-, 12-, 18-, 24-, and 30-month-old male and female F344 rats, in which we analyzed total RNA, muscle proteins, protein synthesis signaling pathways, and ribosome biogenesis-related factors.

[Results]
In both male and female rats, we observed age-related reductions in skeletal muscle mass and skeletal muscle mass per body weight. Conversely, increases were observed in total RNA and 28S+18S rRNA per milligram of skeletal muscle and RPL10 protein levels, indicative of ribosomal biosynthesis.
Results: We also detected differences between the sexes with respect to Akt S473 phosphorylation, p85S6K Thr412 phosphorylation, p70S6K protein content, p70S6K Thr389 phosphorylation, 4E-BP1 Thr37/46 phosphorylation, and 4E-BP1 protein content. Levels of Akt S473 phosphorylation increased with aging in male rates although declined in female rats; whereas, the rate of p85S6K Thr412 phosphorylation declined in male rats and increased in female rats with aging. Furthermore, reductions in p70S6K protein levels were detected in male rats, whereas levels remained unchanged in female rats. Additionally, aging-related increases were detected in p70S6K Thr389 phosphorylation rate and 4E-BP1 Thr37/46 phosphorylation and 4E-BP1 protein levels in male rats, although no significant changes were detected in female rats.

[Conclusion]
Our findings in this study revealed aging-related increases in the amounts of 28S and 18S rRNA in rat plantaris muscle, alongside reductions in muscle protein levels. In the case of male rats, we speculate that the mechanism associated with this decline is a reduction in the efficiency of protein translation; however, this decline appears to be attributable to a different mechanism in females.