短時間の温熱刺激が骨格筋糖輸送活性促進に及ぼすメカニズムの解明

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Effect of Acute Heat Stress on Muscle Glucose Metabolism

by

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ABSTRACT

Skeletal muscle is the major organ responsible for whole-body glucose metabolism and utilization. Heat stress（HS）has been implicated in the regulation of whole-body glucose homeostasis. Recently, we have demonstrated that short-term HS（for 10 and 30 min）in vitro activates insulin-independent glucose transport, at least in part by stimulating 5'-AMP-activated protein kinase（AMPK）via decreased energy status in rat skeletal muscle. However, there have been no reports about the effect of acute HS（< 30 min）on glycogen and protein metabolism in skeletal muscle. The purpose of this study was to investigate the effect of short-term HS on glycogen and protein

synthesis using rat skeletal muscle. Male Sprague-Dawley rats weighing 150 g were killed by cervical dislocation without anesthesia, and epitrochlearis muscles were isolated. Muscle was then incubated in the absence or presence of HS（42℃，30 min）in alpha minimum essential medium containing 50 μU/mL insulin. HS decreased glycogen content and activated glycogen synthesis with decreasing the phosphorylation of glycogen synthase kinase 3β, without affecting the phosphorylation of glycogen synthase. HS tended to decrease protein synthesis, and correspondingly, HS decreased the phosphorylation of p70 ribosomal protein S6 kinase and 4E-binding protein 1. On the other hand, HS did not affect the mRNA expression of muscle-specific ubiquitin ligases: muscle atrophy F-box/atrogin-1 and muscle ring finger 1, or protein expression of autophagy-related markers: microtubule-associated protein 1 light chain 3 and p62. In conclusion, short-term HS might be a physiologically relevant stimulus that promotes glucose transport/glycogen synthesis axis and inhibit protein synthesis in skeletal muscle. Although further study is warranted, HS has similar action to exercise by acutely activating glycogen synthesis and suppressing protein synthesis with a reduction of the glycogen content in skeletal muscle.

要　旨

我々はこれまでに短時間の温熱刺激が骨格筋糖輸送活性を亢進させることを報告したが，グリコーゲン代謝やタンパク質代謝への影響は不明であった．本研究では，温熱刺激がグリコーゲン合成とタンパク質合成に及ぼす影響を検討した．ラットから滑車上筋を単離して，緩衝液中にて熱刺激（42℃，30 分間）を与えた．温熱刺激はグリコーゲン含有量を減少させ，グリコーゲン合成速度を亢進させたが，GSK3β のリン酸化を抑制し，glycogen synthase のリン酸化に変化を与えなかった．一方，タンパク質合成速度は温熱刺激によって減少傾向を示し，p70S6K と 4E-BP1 のリン酸化も抑制された．温熱刺激はタンパク質分解制御因子とオートファジー制御因子には影響を与えなかった．以上より，骨格筋への短時間の温熱刺激は，分子機序は同一でないものの，急性運動と同様に，グリコーゲン合成を促進させタンパク質合成シグナルを抑制する生理的刺激であることが示唆された．