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論文審査委員	運動及び電気刺激誘発性筋収縮による体力要素向上と骨サイトカイン分泌 主査 田巻 弘之 副査 藤井 康成 副査 沼尾 成晴

論 文 概 要

Background

The global rise in aging populations, obesity, and chronic diseases highlights the critical need for exercise to improve cardiorespiratory fitness, reduce chronic disease incidence, and enhance overall quality of life. High-intensity interval training (HIIT) is an effective, time-efficient strategy that enhances cardiorespiratory fitness, body composition, and metabolic health, whereas probiotics have been shown to provide comparable benefits. However, the synergistic effects of combining HIIT with probiotics remain unclear.

Among the various benefits attributed to HIIT, the secretion of the bone-derived hormone undercarboxylated osteocalcin (ucOC) emerges as a critical underlying mechanism. During exercise, muscle contractions generate mechanical stress on bones, promoting ucOC secretion and providing multiple physiological benefits, including enhanced glucose metabolism in myofibers, improved insulin sensitivity, and increased fat metabolism. For individuals with physical limitations, electrical stimulation-induced muscle contraction (ESMC) offers a viable alternative to traditional exercise. However, the efficacy of ESMC in inducing ucOC secretion remains poorly understood.

To address these gaps, three interconnected studies were conducted: Study 1 examined the synergistic effects of HIIT and probiotics on physiological health; Study 2 investigated whether ESMC effectively stimulates ucOC secretion and explored the temporal effects of different ESMC conditions on ucOC secretion; and Study 3 assessed the long-term impact of ESMC on ucOC secretion. Collectively, these studies offer valuable insights into novel strategies for enhancing health in both active and physically limited individuals.

Study 1

To investigate the synergistic effects of HIIT and probiotics, forty-seven obese women without regular exercise habits were randomly assigned to one of four groups: control (n = 12), probiotics (n = 12), HIIT (n = 11), and HIIT combined with probiotics (n = 12). All participants consumed daily probiotic or placebo supplements, and those in the exercise groups performed HIIT sessions three times per week for eight weeks. Each HIIT session comprised seven cycles of 2-minute bouts at 85–90% $\dot{V}O_2\text{max}$, interspersed with 1-minute rest intervals. The results showed that HIIT improved cardiopulmonary fitness; however, it was associated with an adverse effect on waist circumference, which, as suggested by previous studies, may be mitigated by extending exercise duration. Notably, the combination of HIIT and probiotics enhanced cardiopulmonary fitness, reduced waist circumference, and further decreased hip circumference, indicating a synergistic effect.

Study 2

This study examined the effects of ESMC on the secretion of ucOC, a key mediator of exercise-induced physiological benefits. Young male Fischer 344 rats were randomly assigned to one of three groups: low-frequency ESMC at 10 Hz (LF, n = 8), high-frequency ESMC at 100 Hz (HF, n = 8), or control (CON, n = 6). Bone strain was measured under both LF and HF conditions. Blood samples were collected at multiple time points before and after a single 30-minute ESMC session to assess serum ucOC levels. Results demonstrated that bone strain can be synchronized with ESMC, with LF-ESMC inducing smaller, repetitive bone strains, while HF-ESMC generated larger,

singular strains. Serum ucOC levels significantly increased six hours after LF-ESMC, with effects persisting for up to 24 hours. Similarly, HF-ESMC induced a significant increase in ucOC levels, observed 24 hours post-stimulation. These findings highlight that, in addition to strain magnitude, the frequency of bone strain repetition is a critical factor in promoting ucOC secretion, with effects persisting for up to one day.

Study 3

Building on the findings from Study 2, a four-week intervention was conducted to investigate the long-term effects of both LF-ESMC and HF-ESMC on ucOC secretion. Twenty-two young male Fischer 344 rats were randomly assigned to one of three groups, as in Study 2: low-frequency ESMC at 10 Hz (LF, n = 8), high-frequency ESMC at 100 Hz (HF, n = 8), or control (CON, n = 6). The LF and HF groups underwent ESMC sessions twice weekly for four weeks, with ucOC and insulin levels measured at multiple time points. The results demonstrated significant increases in ucOC during the early phase of the intervention in both LF and HF groups. Although insulin levels did not change significantly throughout the intervention, a positive correlation between ucOC and insulin levels was observed. These findings confirm that ESMC effectively induces early increases in ucOC and underscore the positive relationship between ucOC and insulin levels.

Conclusion

These studies emphasize the potential of HIIT, probiotics, and ESMC as effective strategies for promoting systemic health, with ucOC identified as a key mediator. Importantly, the findings indicate that low-frequency ESMC at 10 Hz effectively stimulates ucOC secretion, providing a less painful and more tolerable alternative to the 100 Hz protocol. This finding highlights the potential of 10 Hz ESMC as a promising approach for rehabilitation and training. Collectively, these results provide valuable insights into the physiological mechanisms underlying exercise and its alternatives, offering innovative strategies for individuals unable to engage in conventional physical activity.

論文審査の要旨

本研究論文は、高強度短時間運動が身体機能や形態に及ぼす影響を検証するとともに、その背景として示唆される骨サイトカイン（ucOC）の分泌を促す骨への機械的刺激の影響を明らかにすることを目的としている。研究 1～3 を通して、運動生理学および組織細胞学的手法を用いて、特に電気刺激によって誘発された筋収縮（ESMC）を骨への機械的刺激として応用し、運動代替の可能性を検証した。前脛骨筋への ESMC において、刺激頻度の違いにより筋収縮力や脛骨のひずみの大きさ・パターンが異なることを確認し、いずれの条件でも 24 時間以内に ucOC 分泌を同様に促進することを示した。また、4 週間の介入においても ucOC 分泌の促進が認められ、さらに筋線維横断面積の増大や、ucOC と血中インスリンとの有意な相関関係が示唆された。総じて、研究の独創性、方法論、当該分野に対する包括的な理解、論文の構成などの観点から論文審査を行った結果、上記の知見を提示した本論文の内容は、博士（体育学）の学位論文として十分な学術的価値を有するものと判定した。