A New Framework to Study Muscle Fatigue with an Integrative Neuro-Mechano-Energetic Approach

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Summary

Muscle fatigue can be subdivided into central factors (i.e., adaptations in motor control) and peripheral factors (i.e., muscle behavior). Current modalities typically consider either central or peripheral aspects of muscle fatigue. This work presents an integrative experimental approach combining magnetic resonance spectroscopy and electromyography to investigate central and peripheral fatigue simultaneously. Further, we bridge the gap between measurements and the cellular behavior of muscle fibers and motor neurons using computer simulations.

Introduction

Skeletal muscle contractions power human physical performance. However, task failure during high-intensity or prolonged physical work is common and known as muscle fatigue. Yet, despite almost a century of scholarly investigations that identified peripheral and central origins of muscle fatigue, none of the phenomenon's basic mechanisms have been firmly established. A particular obstacle to progress has been the lack of experimental or theoretical methodologies to study excitation-contraction coupling and energetics across multiple scales ranging from individual myofibers to working muscles in living humans.

Methods

We developed a novel experimental platform that combines (i) phosphorus magnetic resonance spectroscopy (P-MRS) [1] and (ii) high-density electromyography (EMG). P-MRS measures the dynamics of metabolites in different muscle fiber types and is the quantitative benchmark for studying peripheral fatigue in living humans. The decomposition of EMG into the spike trains of individual motor units [2] allows us to track central adaptations in motor control. The combined measurement of P-MRS and high-density EMG required the development of specialized non-magnetic EMG electrodes.

Further, we have established a modeling framework [3] to relate the observed data and the biophysical function of individual muscle fibers [4] and motor neurons [5]. The computer models are parameterized using in-vitro data from the literature.

Results and Discussion

We show proof-of-concept data, illustrating the feasibility of combined P-MRS and high-density EMG recordings using novel non-magnetic EMG arrays. This includes validating the EMG arrays and artifact characterization, as well as the correlation between central fatigue parameters (motor neuron discharge statistics) and quantitative markers of muscle energetics (phosphocreatine dynamics and intramuscular pH). Further, we showcase the potential of simulation-based data augmentation to understand cellular adaptations during fatiguing exercise.

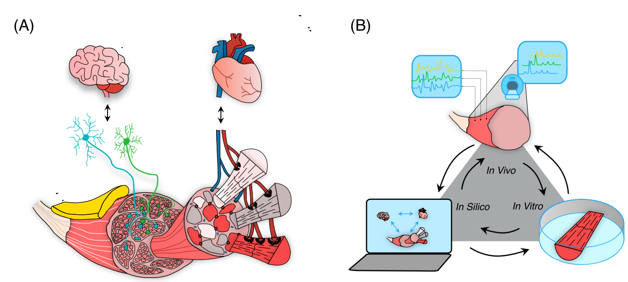

Figure 1: Schematic showing (A) the factors involved in muscle fatigue and (B) the combined in-vivo and in-silico framework to integrative study central and peripheral aspects of muscle fatigue.

Conclusions

We propose a new tool for the integrative study of central and peripheral muscle fatigue. This combined in-vivo and in-silico framework will enhance our understanding of abnormal fatiguability in patients and guide the development of subject-specific therapies.

Acknowledgments

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