3D Modeling Characterization of Regional Mechanical Stimuli of Mouse Dorsiflexor Muscles During Resistance Exercise

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Summary

Our goal is to characterize tissue-level mechanics of muscles during a mouse resistance exercise model of hypertrophy response. We used a finite element model representing mouse dorsiflexor structure to simulate exercise conditions, predict tissue mechanics, and quantify loading across muscle regions.

Introduction

Skeletal muscle mass is inversely related to mortality, aging, and disease [1], driving research interest in resistance exercise to elicit hypertrophy, or increase muscle mass. While methods to explore molecular mechanisms of hypertrophy in response to overload have grown increasingly sophisticated [1], studies remain limited in quantifying muscle loads during prescribed resistance training. Loading of muscle tissue during a resistance exercise depends on both the body's biomechanics and muscle's structural architecture. Biomechanical studies, particularly those utilizing simulations, have related external loads to joint kinetics and muscle forces during motion and have linked variability in muscle structure to mechanical function required for those motions [2,3], but have not yet been used to characterize muscle loads during exercise to determine mechanical stimuli eliciting hypertrophy responses.

Mice are used extensively in hypertrophy mechanism studies utilizing advanced molecular-based approaches; however, we have limited information on mouse muscles mechanics in the overload conditions of these studies. Dynamic imaging of muscle contractions reveals regional variations in mechanics [3], yet molecular studies do not account for load variability within a muscle of interest. *We hypothesize that the tissue-loads will vary spatially in mouse dorsiflexor muscles during fixed-end contractions in resistance exercise.* We aim to predict regional differences in exercise mechanical stimuli by quantifying stresses and strains in three regions of the tibialis anterior (TA) and extensor digitorum longus (EDL) muscle.

Methods

All experiments were performed with the approval of the Animal Care and Use Committee at the University of Florida. Twelve Jackson C57Bl/6 mice (6F/6M, 29±7wks, 30±5g) performed an *in vivo* resistance exercise protocol of high force electrically stimulated tetanic dorsiflexor muscle contractions (Aurora Scientific). Force-frequency tests were performed to establish stimulation frequency to generate 80% max force that was used for the exercise protocol where mice completed 10 sets of 8 repeated 1s contractions (rest: 6s/rep, 120s/set). An hour post-exercise, mice were anesthetized, and TA and EDL muscles were dissected and measured before freezing for RNA sequencing. Dorsiflexor muscle were also measured in 12 control mice (6F/6M, 26±4wks, 32±6g) and 6 additional mice (3F/3M, 12wks, 25±5g) used for more detailed structural analysis. These 6 mice were perfusion fixed for microCT imaging and dissection to measure TA and EDL architecture.

A 3D finite element model (FEM) of mouse dorsiflexors was created to represent experimental muscle measurements. The FEM was meshed as tetrahedral elements with assigned fiber directions in FEBio [3]. Fixed-end contraction simulations were performed by increasing muscle activation to predict musculotendon deformation and force production. Fiber strain and first principal stress were averaged for elements in the distal, middle, and proximal third of the TA and in the EDL.

Results and Discussion

The mice produced varied mean peak forces during exercise, so FEM simulations were performed at the average of 53% maximum force. The FEM predicted strains decreased in magnitude (negative strains for muscle shortening) from the proximal to distal TA while stress was similar across regions but increased in variability from proximal to distal (Figure 1).

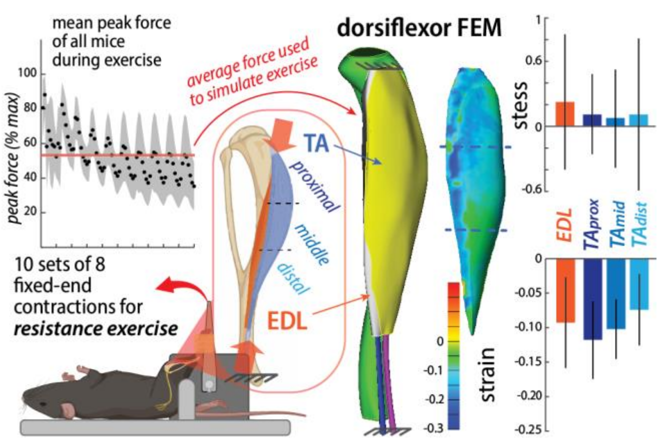

Figure 1: *FEM predicted stress and strain in exercise experiment*

Conclusions

Resistance exercise improves human health through effects on muscle mass stimulated by mechanical loading. Prescribing exercise to elicit these benefits requires identifying a "dose". Results of this study quantifying tissue mechanics in exercise conditions equips us for better mechanistic exercise dosing.

Acknowledgments

Work is supported by Wu Tsai Human Performance Alliance.

References

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