Del 2: Does baseline myonuclear density in type-1 and type-2 muscle fibers predict the hypertrophy response following a 6-week RT-protocol in trained, young men?

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Table of contents

1 Abstract

Background:

Methods:

Results:

Conclusion:

2 Introduction

Resistance training (RT) is an effective method to induce skeletal muscle hypertrophy [1]. However, the individual responses to the same RT-protocol can vary greatly. Research has shown a wide array of responses when it comes to improvements in skeletal muscle hypertrophy, maximal strength and metabolic markers of health [2,3]. There have been several proposed mechanisms as to why this inter-individual response exists, and includes but is not limited to genetics, epigenetics and environmental factors (sleep, stress and dietary patterns) [4].

Within genetics, the myonuclei are thought to play a major role in the process of skeletal muscle hypertrophy [5]. Skeletal myofibres are multinucleated cells, which contain hundreds to thousands of myonuclei. Each one of these myonuclei govern a finite amount of cytoplasm and serve an important function for enhancing both gene transcription and protein synthesis [5]. In the early stages of hypertrophy, myonuclei can expand their domains to accommodate the initial rate of growth, also known as myonuclear expansion [6]. Beyond a certain threshold, it has been hypothesized that quiescent satellite cells (SC) must proliferate and differentiate into new myonuclei to facilitate further skeletal muscle hypertrophy. This concept is also known as myonuclear accretion. However, this concept remains controversial, and the research is equivocal as to whether this threshold exists [7].

There has been extensive research on the roles of myonuclei accretion and expansion for skeletal muscle hypertrophy. Petrella and colleagues in 2008 found that the differences in hypertrophy between high and low responders to RT can be explained by the degree of myonuclear accretion [6]. However, Haun and colleagues found no group differences in pre- to post-measurements in myonuclear density following a 6-week RT-protocol, despite significant differences in measured hypertrophy [8]. There is also other literature challenging the notion that myonuclear accretion is associated with skeletal muscle hypertrophy [9].

On the topic of myonuclear expansion, Petrella and their group has suggested that there exists a maximum ceiling for how much the domains of individual myonuclei can expand to [6]. This consequently led to the suggestion that a fibre size increase of more than ~26-27% must be accompanied by myonuclear accretion [10]. The research here is also diverging, as another group of researchers found significant myonuclear accretion without myonuclear expansion, despite the type-II fibres of the participants growing with more than 40% from pre- to post-measurements [5].

The question of whether baseline myonuclear density in type-I and type-II myofibres predict the magnitude of the hypertrophic response following RT remains unclear. Previous research has found association between baseline myonuclear *number* in type-I and type-II and the hypertrophic response following a 12-week RT protocol in young, untrained men [9]. Another study found a moderate correlation between satellite cell count and myofibre growth [6]. This brings us to the study performed by Haun's research group from 2019 on young, trained males, with their data suggesting that pre- and W3 values of type-I myonuclear number was a significant predictor of hypertrophy. While the researchers performed baseline testing of the participants myonuclear density of type-I and type-II fibres, it was not used in the final analysis. Since there is divergent research on whether myonuclear accretion occurs in the presence of significant hypertrophy, an unexplored baseline predictor to examine is *myonuclear density* – the amount of myonuclei per cross-sectional area. A logical assumption would be that a increased baseline myonuclear density would reflect a greater transcriptional machinery, thus allowing for a superior hypertrophic response to RT.

The aim of this study was to analyse the data from the experimental study performed by Haun and colleagues [8] and perform an observational study to determine whether baseline myonuclear density in type-I and type-II fibres is predictive of the hypertrophic response following a 6-week resistance-training protocol in young, trained men. We hypothesize a positive correlation between myonuclear density in both type-I and type-II fibres and hypertrophy in the vastus lateralis, as a higher density is reflective on increased transcriptional rate and protein synthesis.

3 Methods

3.1 Baseline characteristics of participants

3.2 Resistance-training protocol

3.3 Myonuclear number determination

3.4 Statistical analysis

Modellen først. Normalfordeling, residualplot –> avvik fra residualene er normalfordelt Shapiro wilk??

datasett$resid resid()

plot it

3.5 Model assumptions (residualplot, shapiro-wilk)

3.5.1 Rationale for use of model

ANCOVA - Controlling for baseline differences in CSA.

Why did you not choose x or y instead?

4 Results

5 Discussion

5.1 Limitations

Outcome variable

Limited ecological validity

Inability to establish causality with an observational design.

6 Conclusion

Bibliography

[1] Roberts MD, McCarthy JJ, Hornberger TA, Phillips SM, Mackey AL, Nader GA, et al. Mechanisms of mechanical overload-induced skeletal muscle hypertrophy: Current understanding and future directions. Physiological Reviews 2023;103:2679–757. https://doi.org/10.1152/physrev.00039.2022.

[2] Erskine RM, Jones DA, Williams AG, Stewart CE, Degens H. Inter-individual variability in the adaptation of human muscle specific tension to progressive resistance training. European Journal of Applied Physiology 2010;110:1117–25. https://doi.org/10.1007/s00421-010-1601-9.

[3] Ahtiainen JP, Sallinen J, Häkkinen K, Sillanpää E. Inter-individual variation in response to resistance training in cardiometabolic health indicators. Scandinavian Journal of Medicine & Science in Sports 2020;30:1040–53. https://doi.org/10.1111/sms.13650.

[4] Ross R, Goodpaster BH, Koch LG, Sarzynski MA, Kohrt WM, Johannsen NM, et al. Precision exercise medicine: Understanding exercise response variability. British Journal of Sports Medicine 2019;53:1141–53. https://doi.org/10.1136/bjsports-2018-100328.

[5] Snijders T, Smeets JSJ, van Kranenburg J, Kies AK, van Loon LJC, Verdijk LB. Changes in myonuclear domain size do not precede muscle hypertrophy during prolonged resistance-type exercise training. Acta Physiologica 2016;216:231–9. https://doi.org/10.1111/apha.12609.

[6] Petrella JK, Kim J, Mayhew DL, Cross JM, Bamman MM. Potent myofiber hypertrophy during resistance training in humans is associated with satellite cell-mediated myonuclear addition: A cluster analysis. Journal of Applied Physiology 2008;104:1736–42. https://doi.org/10.1152/japplphysiol.01215.2007.

[7] Murach KA, Englund DA, Dupont-Versteegden EE, McCarthy JJ, Peterson CA. Myonuclear Domain Flexibility Challenges Rigid Assumptions on Satellite Cell Contribution to Skeletal Muscle Fiber Hypertrophy. Frontiers in Physiology 2018;9. https://doi.org/10.3389/fphys.2018.00635.

[8] Haun CT, Vann CG, Mobley CB, Osburn SC, Mumford PW, Roberson PA, et al. Pre-training Skeletal Muscle Fiber Size and Predominant Fiber Type Best Predict Hypertrophic Responses to 6 Weeks of Resistance Training in Previously Trained Young Men. Frontiers in Physiology 2019;10. https://doi.org/10.3389/fphys.2019.00297.

[9] Mobley CB, Haun CT, Roberson PA, Mumford PW, Kephart WC, Romero MA, et al. Biomarkers associated with low, moderate, and high vastus lateralis muscle hypertrophy following 12 weeks of resistance training. PLOS ONE 2018;13:e0195203. https://doi.org/10.1371/journal.pone.0195203.

[10] Petrella JK, Kim J, Cross JM, Kosek DJ, Bamman MM. Efficacy of myonuclear addition may explain differential myofiber growth among resistance-trained young and older men and women. American Journal of Physiology-Endocrinology and Metabolism 2006;291:E937–46. https://doi.org/10.1152/ajpendo.00190.2006.