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DETERMINANTS OF INTRA-INDIVIDUAL VARIATION IN  
ADAPTABILITY TO RESISTANCE TRAINING OF DIFFERENT  
VOLUMES WITH SPECIAL REFERENCE TO SKELETAL MUSCLE  
PHENOTYPES



# Determinants of intra-individual variation in adaptability to resis- tance training of different volumes with special reference to skeletal muscle phenotypes

Daniel Hammarström

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## THESIS FOR DOCTORAL DEGREE (Ph.D.)

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by

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Thesis for Philosophy of Doctoral Degree in Sport Sciences, at The Swedish School of Sport and Health Sciences (GIH), which, according to the decision of the dean, will be publicly defended on *DATE*. The thesis defense will be held at the auditorium at The Swedish School of Sport and Health Sciences (GIH), Stockholm.

### **Opponent**

Profesor . . . .

### **Principal supervisor**

Profesor . . .

### **Co-supervisor(s)**

-Professor . . .

-Professor . . .

-Professor . . .

### **Examination board**

-Associate professor . . .

-Professor . . .

-Professor . . .

# Abstract

The preface pretty much says it all.

Second paragraph of abstract starts here.





# List of scientific papers

- I. **Hammarström D**, Øfsteng S, Koll L, Hanestadhaugen M, Hollan I, Apró W, Blomstrand E, Rønnestad B, Ellefsen S Benefits of higher resistance-training volume are related to ribosome biogenesis. *The Journal of physiology*. 2020;598(3):543-65.
- II. Khan Y, **Hammarström D**, Rønnestad B, Ellefsen S, Ahmad R Increased biological relevance of transcriptome analyses in human skeletal muscle using a model-specific pipeline. *Submitted*.
- III. **Hammarström D**, Øfsteng S, Jacobsen N, Flobergseter K, Rønnestad B, Ellefsen S Ribosome accumulation during early phase resistance training. *Manuscript*



# Contents

<b>List of Tables</b> . . . . .	<b>xiii</b>
<b>List of Figures</b> . . . . .	<b>xv</b>
<b>1 thesisdown::thesis_gitbook: default</b> . . . . .	<b>1</b>
<b>2 Background</b> . . . . .	<b>3</b>
2.1 Exercise prescription . . . . .	3
2.2 Adaptations to resistance training . . . . .	3
2.2.1 Muscle hypertrophy and strength . . . . .	3
2.2.2 Muscle fiber-type transitions . . . . .	4
2.2.3 Mitochondrial function . . . . .	4
2.3 Effects of exercise prescription on muscle mass and strength . . . .	4
2.3.1 Effects of resistance exercise volume on muscle strength and mass . . . . .	4
2.4 Molecular determinants of training-induced muscle hypertrophy . .	6
2.4.1 Ribosomal biogenesis . . . . .	6
2.4.2 Transcriptional regulation of muscle mass . . . . .	7
<b>3 Aims</b> . . . . .	<b>9</b>
<b>4 Methods</b> . . . . .	<b>11</b>
4.1 Study participants, protocols and training interventions . . . . .	11
4.2 Resistance training interventions . . . . .	11
4.2.1 Ethical considerations . . . . .	11
4.3 Gene expression analysis . . . . .	11
4.4 Determination of protein abundance . . . . .	11
4.5 Statistics and data analysis . . . . .	11
4.6 Gene expression analysis . . . . .	11

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4.6.1	Normalization . . . . .	11
4.6.2	Literature search, inclusion criteria and coding of studies . . . . .	11
4.6.3	Calculations of effect sizes and statistical analysis . . . . .	11
<b>5</b>	<b>Results and Discussion . . . . .</b>	<b>13</b>
5.1	Effects of different training volume on changes in muscle size and function . . . . .	13
5.2	Acute effects of different training volume on determinants of muscle protein synthesis . . . . .	13
<b>6</b>	<b>General Discussion . . . . .</b>	<b>15</b>
	<b>Conclusion . . . . .</b>	<b>17</b>
	<b>References . . . . .</b>	<b>19</b>

## List of Tables



## List of Figures





1. thesishdown::thesis\_gitbook:  
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Placeholder



## 2. Background

### 2.1 Exercise prescription

Systematic physical exercise with the purpose to improve health or physical performance has been shown to be part of many early civilizations (**RN2640?**) Today's exercise-training prescription still bears traces of ideas from these eras, further developed during the renaissance and formalized in systems like Ling gymnastics during the nineteenth century (1) which in turn is referenced in twentieth century texts on exercise prescription (2). With the introduction of heavy-resistance exercises for the development of muscle strength and mass after injury, DeLorme outlined a system on which modern resistance-training (RT) exercise prescription is based (3). In contrast to previous recommendation (2), DeLorme specifically emphasized high-resistance, low-repetition exercise where progression was achieved with increased resistance as opposed to endurance-like exercise where progression was achieved through increased number of repetitions (2). The concept of repetition maximum (RM) as a way of prescribing and individual dosage and monitoring progress was introduced from case reports (3) and verified as a efficient way of improving muscular strength (4). DeLorme originally prescribed sessions of up to 100 repetitions performed in sets of 10 (3) but later revised this recommendation to three sets of 10 repetitions performed with increasing intensities (**RN2641?**, 5).

### 2.2 Adaptations to resistance training

#### 2.2.1 Muscle hypertrophy and strength

A well characterized response to systematic resistance training in humans is muscle growth. On the whole muscle level, resistance training can be expected to result in increases of 6-9%

(6)

On the muscle fiber level

### 2.2.2 Muscle fiber-type transitions

### 2.2.3 Mitochondrial function

Increased mitochondrial respiration after 12 weeks of RT in young men (7)

Fiber type distributions do not predict muscle mitochondrial density in endurance trained individuals (8)

PMID:158694 Reduced mitochondrial density per fiber area in response to RT

## 2.3 Effects of exercise prescription on muscle mass and strength

Precise exercise-training<sup>1</sup> prescription gives information on exercises, their sequential order, intensity and volume, rest periods between efforts or sessions and the frequency at which exercise sessions are to be performed (10). By manipulating these variables, resistance training programs can be tailored to better fit goals and starting points of any individual. The relative importance of exercise-training variables for training outcomes has been examined in numerous studies including (but not limited to) the overall organization of exercise sessions, (12, 14) training frequency (16), and intensity (18). It could be argued that training volume is of particular importance for muscle growth as when this variable is held constant, manipulation of other variables has little or no effect hypertrophy (20, 18). For development of strength, factors such as intensity and within session organization of exercises is of importance (22, 24), however, when other factors are held constant, increased training volume generally leads to increased strength (22,26, 28), similarly to effects of training volume on muscle growth (10,30).

### 2.3.1 Effects of resistance exercise volume on muscle strength and mass

Exercise volume can be prescribed as the within session number of sets performed per muscle group. This unit is practical as it comparable between individuals and muscle groups (32). Berger conducted an early study concerning effects of

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<sup>1</sup>Exercise is herein defined as an acute bout of physical activity designed to affect physical characteristics such as strength, speed or endurance. Training is defined as the systematic process of combining multiple exercise-sessions performed in sequence over time. Resistance-exercise is defined as an acute strength-promoting program requiring the neuromuscular system to exert force against resistance. Resistance training is defined as a long-term process of multiple resistance exercise-sessions performed over a defined period of time.

resistance exercise volume with the goal to determine what method most efficiently produced strength gains (in healthy young males) (34). Berger compared one, two and three sets performed with two, six or ten repetition maximum (RM) in the bench press, three times per week, over twelve weeks. As the combined effect of three sets per session was superior regardless of the number of repetitions performed Berger concluded in favor of three sets. This conclusion was later challenged on the basis of data interpretation (36, 38). Reviwing the study by Berger and others, Carpinelli and Otto arrived to the conclusion that there was “insufficient evidence to support the prevalent belief that a greater volume of exercise (through multiple sets) will elicit superior muscular strength or hypertrophy” (36). This stand has since been repeatedly put forward as a criticism of higher volume training programs (39,41) and sparked considerable scientific activity. The main argument against the recommendation of additional volume in strength training programs has been the lack of statistically significant results in single studies (38,39). Indeed, individual studies do not generally agree on dose-dependent effects of training volume on muscle mass and strength gains (43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65), including studies performed within participants, where different training volumes are allocated to either extremity (67, 69). For example, differences in strength are between volume conditions are found in older individuals (43, 45, 55) but not confirmed in another study (51)]. Studies shows that more volume does not lead to increased muscle gains in young individuals (61, 57, 47) a conclusion challenged by others (65, 49).

As previously noted, combining the above results and additional studies, meta-analyses concluded that training volume dose-dependency exists for the development of muscle mass and strength [(22); (26); (28); (10,30)]. As a second argument against additional volume in resistance training recommendation has been the cost/benefit relationship of adding training volume without meaningful or substantial additional gains (38, 39), a subsequent question is, whom would benefit from greater volumes and whom would not? Schoenfeld *et al.* combined data from published studies to explore if participant characteristics of the above mentioned studies interacted with training volume in explaining study outcomes. Neither sex, muscle groups nor age interacted with volume prescription indicating that no such factor would be able refine training prescription guidelines (30). As the number of studies used to synthesis the meta-analysis was relatively low ( $n = 15$ ) and the studies were heterogeneous in terms of e.g. outcome measurements, it may have lacked in power to detect any meaningful interactions. Additionally, included studies may not have been reporting relevant characteristics for such analysis.

Collectively, the available evidence suggest that there is overlap between training outcomes in studies where different volume has been utilized. The overlap cannot, with available data, be explained by general population characteristics such as age or sex. Studying the effect of different training volumes within participants could potentially help to define determinants of training outcomes in response to different volume conditions. Two within-participant studies have investigated the effects of training volume on strength and hypertrophy outcomes. Sooneste *et al.* compared strength outcomes in response to three- and one-set elbow flexor training for 12 weeks in young males using a within-participant protocol (arms allocated to either volume condition). The results showed general benefit of three- over one-set training for muscle hypertrophy and tended to do so also for strength gains (69). No attempts were made to relate baseline characteristics to the magnitude of differences between volume conditions, presumably due to the small sample size ( $n = 8$ ). Mitchell *et al.* compared muscle hypertrophy and strength gains in response to three- and one-set of knee-extension exercise performed three times per week for ten weeks. The study contained an additional training condition (low intensity, 30% of 1RM performed with three sets) with participants legs assigned to either of the three conditions in a random fashion. No significant differences were reported between volume conditions for muscle mass or strength gains (67). However, the analyses were performed without taking the correlation between individuals into account due to the mixed design (67). No attempts were made to relate any measured characteristic to differences in responses.

## 2.4 Molecular determinants of training-induced muscle hypertrophy

Muscle mass change as a consequence of muscle protein synthesis and breakdown. When a net positive balance is achieved the muscle increase in mass. Resistance exercise leads to acute blunting of muscle protein synthesis followed by an increase over resting levels in the post exercise period . .

### 2.4.1 Ribosomal biogenesis

(71) (72)

(73)

### 2.4.2 Transcriptional regulation of muscle mass

(74)

(75)

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### 3. Aims

The primary aim of this thesis was to relate the adaptive response to resistance training with low- and moderate-volume to skeletal-muscle characteristics in previously untrained individuals. The key question was whether manipulation of exercise-volume will have diverse effects in different individuals related to muscular intrinsic characteristics. A further aim was to characterize exercise-volume dependence in muscle molecular characteristics and determine a time course profile of markers of ribosomal biogenesis in response to resistance training. Based on these aims, the objectives of the present thesis were;

- to relate skeletal muscle and systemic characteristics to benefit of moderate-compared to low-volume resistance training;
- To determine volume-dependence in molecular networks related to muscle growth and remodeling in response to resistance training
- To determine a time course of markers related to ribosome biogenesis in the early phase of resistance training.



## 4. Methods

Placeholder

4.1 Study participants, protocols and training interventions

4.2 Resistance training interventions

4.2.1 Ethical considerations

4.3 Gene expression analysis

4.4 Determination of protein abundance

4.5 Statistics and data analysis

4.6 Gene expression analysis

4.6.1 Normalization

4.6.2 Literature search, inclusion criteria and coding of studies

4.6.3 Calculations of effect sizes and statistical analysis



## 5. Results and Discussion

Placeholder

- 5.1 Effects of different training volume on changes in muscle size and function
- 5.2 Acute effects of different training volume on determinants of muscle protein synthesis



## 6. General Discussion





# Conclusion

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