Myosin heavy-chain isoform distribution, fibre type composition and fibre size in skeletal muscle: Response to exercise training and de-training

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Muscle fibres and Muscle fibre types

Muscle fibres

(diameter 20-100 um)

Myofibril

(diameter ca. 1 um)
**Muscle fiber types in human muscles**

- **Muscle**
  - **Muscle-fibre**
  - **Type I** (slow myosin)
  - **Type IIA** (fast myosin)
  - **Type IIX** (very fast myosin)

**Mitochondria**

**Capillary**

**Myosin**

Zacho og Andersen
Muscle fibre types

Muscle

- Type I: MHC I
- Type II A: MHC II A
- Type II X: MHC II X
MHC analysis

ATPase histochemistry
relative number

Type 1; 43%
Type 2; 57%

MHC II
MHC I

Type I; 29%
MHC II; 71%


Shortening velocity in single fibres (humane)

Type 1: Type IIA : Type IIX
1:3:8

MHC 1: MHC 2A: MHC 2X
1:4:10

Table 1
Unloaded shortening velocity (V₀) obtained with the slack test procedure and its ratio to maximum shortening velocity obtained from extrapolation of force-velocity curve in the three pure fibre types.

<table>
<thead>
<tr>
<th>Fibre Type</th>
<th>V₀</th>
<th>V₀/V₀max</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Slow fibers</td>
<td>0.29 ± 0.09</td>
<td>0.83</td>
<td>19</td>
</tr>
<tr>
<td>Fast 2A fibres</td>
<td>3.26 ± 0.35</td>
<td>1.81</td>
<td>10</td>
</tr>
<tr>
<td>Fast 2B fibres</td>
<td>3.07 ± 0.58</td>
<td>2.29</td>
<td>10</td>
</tr>
</tbody>
</table>

Harridge et al.

Bottinelli et al. J. Electromyogr. Kinesiol. 9, 1999

Figure; Per Aagaard
Contraction velocity in different muscles

Sol = soleus
VL = vastus lateralis
TB = triceps brachii
Differences between people

vastus lateralis

Fast fibres = 
Slow fibres =

deltiod

Variation in number of type 1 fibres in normal healthy subjects

Type 1 fibres in m. vastus lateralis

Subjects

21 young untrained male subjects
Theoretically muscle growth can occur in two different ways

1) By increase in the number of muscle fibres
   Hyperplasia

2) The individual fibres can increase in cross-sectional area
   Hypertrophy

Strength and Power in Sports, Chapt 8, MacDougall
Hyperplasia

Number of fibers in biceps brachii

Untrained controls: 172,000-381,000
Intermediate bodybuilders: 198,000-374,000
Elite bodybuilders: 204,000-419,000

MacDougall et al, 1984
Fig 14. The proportion of small-sized muscle fibres expressing developmentally-regulated proteins.
* Significantly different than U
# Significantly different than P

Kadi, 2000
Hypertrophy

D’Antona et al., 2005

Control

Body-builder
### Muscle fibre size

Data from Sjöström et al., 1988

- **Marathon runners**
- **Sprint runners**

<table>
<thead>
<tr>
<th>Type</th>
<th>Marathon Runners</th>
<th>Sprint Runners</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 1</td>
<td>5000</td>
<td>4000</td>
</tr>
<tr>
<td>Type 2A</td>
<td>6000</td>
<td>5000</td>
</tr>
<tr>
<td>Type 2B</td>
<td>7000</td>
<td>6000</td>
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</tbody>
</table>

### Body builder vs. normal, kvinder og mænd

Data from Alway, 1994

- **Type II areal**
- **Type I areal**

<table>
<thead>
<tr>
<th>Type</th>
<th>BBM</th>
<th>KM</th>
<th>BBF</th>
<th>KK</th>
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</thead>
<tbody>
<tr>
<td>Mænd</td>
<td>12000</td>
<td>8000</td>
<td>6000</td>
<td>4000</td>
</tr>
<tr>
<td>Kvinder</td>
<td>10000</td>
<td>6000</td>
<td>4000</td>
<td>2000</td>
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</tbody>
</table>
Fig 7. Light micrographs from the trapezius muscle in a subject in U (a), P (b) and PAS (c). Sections stained for myofibrillar ATPase pH 4.6, bar = 30 μm.

Fig 8. Mean fibre area in U, P and PAS.
* Significantly greater than U.
# Significantly greater than P.

Andersen, 2003
Can we change the fibre type composition of our muscles through training?

Not really!?

But that's not the whole story!
Strength-training followed by detraining.

Consequences for muscle fibre CSA and muscle fibre types

"Our model"
<table>
<thead>
<tr>
<th>Exercise session number</th>
<th>1-5</th>
<th>6-15</th>
<th>16-20</th>
<th>21-25</th>
<th>26-30</th>
<th>31-35</th>
<th>35-38</th>
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<tbody>
<tr>
<td>Hack squat</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of sets</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Number of reps</td>
<td>12,12,12</td>
<td>10,10,10,10</td>
<td>10,10,10,8,8</td>
<td>10,8,8,8,6</td>
<td>8,8,8,6,6</td>
<td>8,8,6,6,4</td>
<td>8,6,6,4</td>
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<tr>
<td>Incline leg press</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Number of sets</td>
<td>3</td>
<td>4</td>
<td>4</td>
<td>5</td>
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<tr>
<td>Number of reps</td>
<td>12,12,12</td>
<td>10,10,10,10</td>
<td>10,10,10,10</td>
<td>10,10,10,8</td>
<td>8,8,8,6,6</td>
<td>8,8,6,6,4</td>
<td>8,6,6,4</td>
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<tr>
<td>Knee extensions</td>
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</tr>
<tr>
<td>Number of sets</td>
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<td>5</td>
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<td>4</td>
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<tr>
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<td>10,10,10,10</td>
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<td>8,8,8,6,6</td>
<td>8,8,6,6,4</td>
<td>8,6,6,4</td>
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<tr>
<td>Hamstring curl</td>
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<td></td>
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</tr>
<tr>
<td>Number of sets</td>
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<td>4</td>
<td>4</td>
<td>4</td>
<td>5</td>
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</tbody>
</table>

Andersen et al.,

Experimental design

Biopsies

resistance training

detraining

Days

0 30 60 90 120 150 180
Essentially, more protein is needed. Thus, the equilibrium between protein synthesis and protein degradation must be broken. If muscle has to grow, protein synthesis has to exceed protein degradation.

What happens while training and immediately after?

Most likely there is a negative net protein balance during the actual resistance training session seems probable. (Kumar et al., 2009)

But...

Change in protein synthesis and breakdown that happens during exercise are relatively small and occurs within a limited timeframe, and are therefore of less importance. (Kumar et al., 2009)
What happens in the hours and days after the training session.

In the initial post-exercise phase muscle protein synthesis is increased, but so is muscle protein breakdown (Dreyer et al, 2006, Fujita et al, 2009, Kumar et al, 2009, Phillips et al, 1997).

After strenuous resistance training exercise the protein synthesis is elevated for approximately 48 hours (maybe 72 hrs), whereas the protein breakdown is back to pre-training levels 24 hours after exercise (Kumar et al., 2009, Miller et al, 2005, Phillips et al, 1997).

Increased anatomical muscle CSA and volume in response to strength training:

Anatomical muscle CSA obtained by MRI or CT following prolonged exercise show an increase of 5-15%.

12 weeks of strength training followed by 12 weeks of detraining

![Graph showing muscle cross-sectional area changes](image)

Fig. 2. Resistance training induced muscle hypertrophy in the quadriceps muscle of 10%. After detraining, the muscle atrophied to pretraining levels. CSA, cross-sectional area. *Increase from pre- to posttraining (P < 0.001).

**Strength-training** followed by **detraining**.

Consequences for muscle fibre CSA

![Graph showing muscle fibre cross-sectional area changes](image)

Andersen et al., unpublished
Hypertrophy in Type I and Type II after strength training

Practical implications

MyHC isoform changes with resistance- and detraining

Fry et al., 2004
Andersen & Aagaard, 2000

Heavy resistance training followed by detraining

**MHC isoformer**

- MHC I
- MHC IIA
- MHC IIX

**Percent**

- Before resistance-training
- After resistance-training
- After detraining

Strength training → Tapering / detraining
⇒ boosting of MHC IIX

Figure by M. Zacho
Strength training followed by detraining (tapering)

- Type II fibres increases in fibre size
- IIX transformed to type IIA
- Type II fibre CSA decreased but to some extend above pre-training CSA.
- IIA fibres transformed to type IIX fibres, with possible overshoot …

Satellite cells
All is well, the muscles grow...

.. But only until a certain level, at some point the muscle fibres reach a level of hypertrophy at which further increase in size becomes difficult without an up-date of the machinery.

What other mechanisms are important in muscle hypertrophy?

Satellite Cells;
The muscle stem cells

*Myonuclei lack the ability to divide.*
Satellite cells function as the muscle stem cells providing new myonuclei to the adult muscle fibre during repair or hypertrophy

Picture from A. Mackey
**Number of Satellite Cells through strength and detraining**

No change in number of myonuclei at any point in time. Increase in Myoneuclear domain at T90 and D3.

**Muscle hypertrophy; responders vs. non-responders**

16 weeks of resistance training
- NON: Avg. 0% hypertrophy
- MOD: Avg. 28% hypertrophy
- XTR: Avg. 58% hypertrophy

Petrella et al., 2008
Muscle hypertrophy; responders vs. non-responders

Number of satellite cells for each 100 muscle fibres

Number of satellite cells relative to the number of myonuclei

Fig. 5. (A) (M+) satellite cells by response cluster before and after 16 wk of resistance training expressed per 100 fibers (A) and relative to total nuclei (B). Relative number of satellite cells = [number of NCAM+ cells]/(NCAM+ cells + myonuclei) × 100]. Values are means ± SE. *Significantly different from baseline within group, $P < 0.05$. Non, different from non-responders at the same time point, $P < 0.05$. Mod, different from modest responders at the same time point, $P < 0.05$.

Petrella et al., 2008

… leading to the idea of the myonuclear domain ceiling

(Kadi et al., 2004, Petrella et al., 2008)

The hypothesis is that at some point in the hypertrophic process new myonuclei have to be added for cellular hypertrophy to commence

This myonuclear domain ceiling has been suggested to arrive around a ~25% hypertrophy of CSA of the muscle fibres (Kadi et al., 2004)
How fast are changes in MHC isoform composition initiated?

EX = exercise bout
Before exercise

ATPase staining 4.6

Glycogen staining

After exercise

ATPase staining 4.6

Glycogen staining

In situ hybridisation

m. vastus lateralis

Andersen et al. unpublished
<table>
<thead>
<tr>
<th>Control leg</th>
<th>Work leg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td></td>
</tr>
<tr>
<td>24 hours</td>
<td></td>
</tr>
<tr>
<td>54 hours</td>
<td></td>
</tr>
<tr>
<td>96 hours</td>
<td></td>
</tr>
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</table>

Exercise-bout