

# Spierzwakte bij gehospitaliseerde geriatrische patiënten

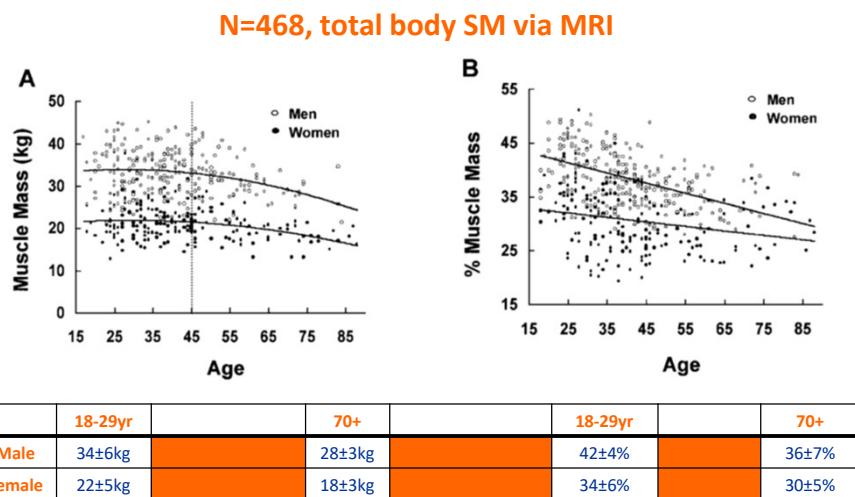
Ivan Bautmans

Frailty in Ageing research group  
[www.vub.ac.be/FRIA](http://www.vub.ac.be/FRIA)

## Disclosure Belangen Spreker

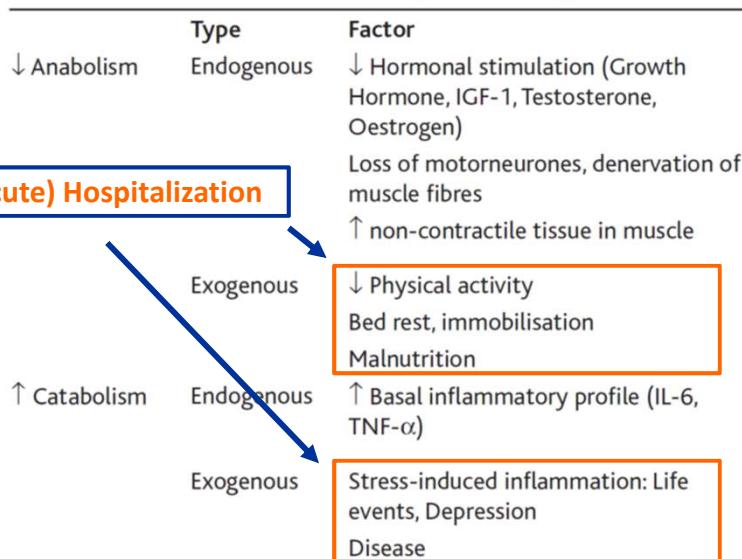
Geen (potentiële) belangenverstengeling

Voor bijeenkomst mogelijk relevante relaties:	<u>Bedrijfsnamen:</u>
Research grants: • Research Council (OZR), grant number OZR1444 • Scientific Fund Willy Gepts	• Vrije Universiteit Brussel • Universitair Ziekenhuis Brussel
Honorarium of andere (financiële ) vergoedingen	NIHIL
Aandeelhouder	NIHIL
Andere relatie, namelijk:	NIHIL



Janssen ea. *J Appl Physiol* 2000;89:81-8

**Table 2. Factors Contributing to Sarcopenia.**



**11 healthy subjects, aged 67±5 yrs, 10days bed rest**

Table 2. Lower Extremity Muscle Performance and Aerobic Capacity

Test	Pre-Bed Rest	Post-Bed Rest	% Change	p Value
Knee extension (N = 11)				
1-RM	—	—	-13.2 ± 3.5	.004
Isometric (N)	133.7 ± 15.1	117.6 ± 13.6	-11.2 ± 3.9	.017
Concentric 180° (N · m/s)	69.9 ± 8.1	60.1 ± 7.0	-13.5 ± 4.4	.011
Knee flexion (N = 11)				
Isometric (N)	76.8 ± 10.0	68.1 ± 10.5	-14.2 ± 3.6	.003
Concentric 60° (N · m/s)	80.3 ± 8.8	71.6 ± 9.4	-11.8 ± 4.6	.03
Concentric 180° (N · m/s)	51.8 ± 7.7	46.6 ± 8.2	-13.2 ± 4.3	.01
Stair ascent power (N · m/s) (N = 8)				
VO <sub>2max</sub> (mL/kg/min) (N = 9)	403 ± 67	337 ± 48	-14.0 ± 4.1	.01
	22.7 ± 2.0	19.72 ± 1.7	-12.2 ± 4.5	.04

Notes: All values are mean ± standard error of the mean.

1-RM = one repetition maximum; VO<sub>2max</sub> = maximal oxygen uptake.

**16 OM aged 55-65 yr & 16 YM aged 18–30 yr**

**14 days bed rest followed by 14 days rehabilitation**

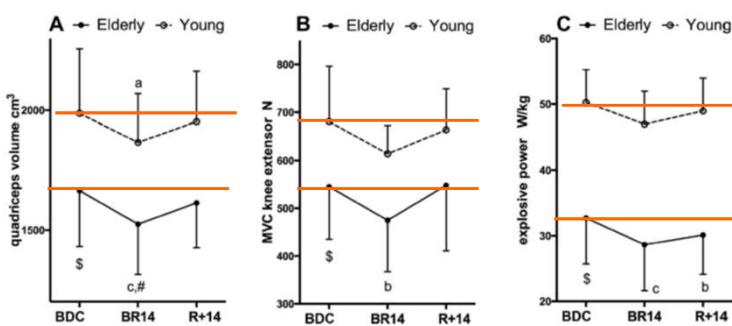


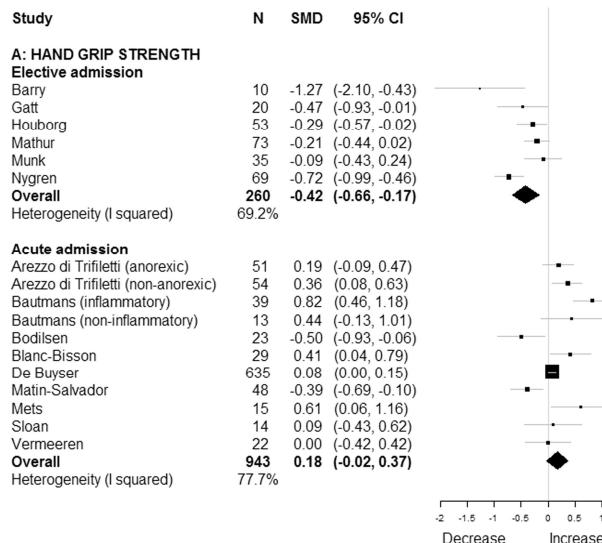
Fig. 1. Changes in muscle volume and contractile function in relation to bed rest (BR) and rehabilitation. Changes in quadriceps volume (QVOL), force in isometric maximal voluntary contraction (QF), and explosive power (QP) of leg extensor muscles during BR and rehabilitation are shown in A, B, and C, respectively. Baseline data collection (BDC) at the beginning of BR; BR14 values were determined after 14 days of BR; R+14 values were determined on day 14 of recovery. MVC, maximal voluntary contraction. Data are displayed as means ± standard deviation (SD). \$Denotes significant difference between groups at BDC with  $P < 0.05$ ; a, b, and c denote significant difference from BDC at BR14 or R+14 with  $P < 0.05$  (a),  $P < 0.01$  (b),  $P < 0.001$  (c); #denotes significant difference between groups at BR14 or R+14 after adjusting BDC differences with  $P < 0.05$ .

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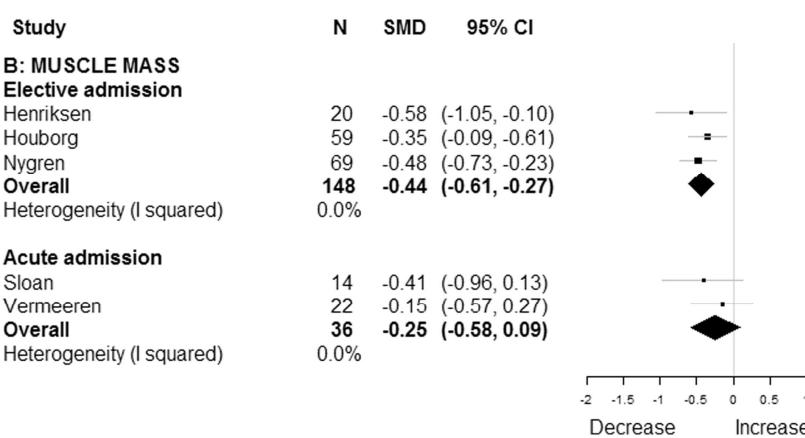
### Spierzwakte bij gehospitaliseerde geriatrische patiënten

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25 articles, 1789 patients, mean age 65-86 yrs, overall median LoS =15 days



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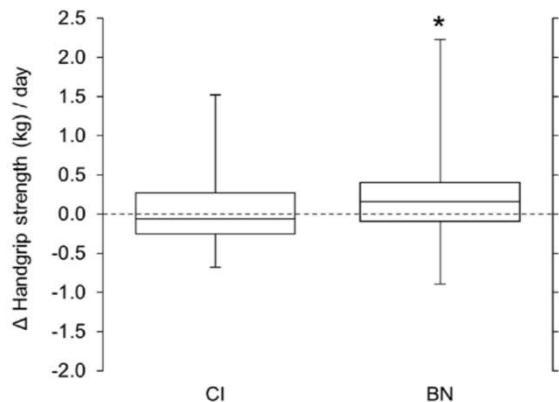
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N=214 hospitalized geriatric patients aged 81–91 yrs

CI: CRP remained ≥10 mg/L; BN: CRP decreased to <10 mg/L after one week of admission



**Fig. 1.** Box and whisker plots showing the change in handgrip strength (kg) per day (relative to days between tests) in the CI-group ( $n = 137$ ) and BN-group ( $n = 76$ ). CI = patients with continuous inflammation; BN = patients that became non-inflammatory. \*Significant difference between groups (Mann-Whitney  $U$  test,  $P < 0.05$ ). Displayed are medians, first and third quartile ranges, and max and min values.



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Norheim, Bautmans & Kjaer *Exp Gerontol.* 2017;99:115-9.



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*J Physiol* 590.23 (2012) pp 6187-6197

6187

## Impaired mitochondrial respiration and decreased fatigue resistance followed by severe muscle weakness in skeletal muscle of mitochondrial DNA mutator mice

Mouse model of premature ageing

Takashi Yamada<sup>1</sup>, Niklas Ivarsson<sup>1</sup>, Andrés Hernández<sup>1</sup>, Andreas Dahlström<sup>2</sup>, Arthur J. Cheng<sup>1</sup>, Shi-Jin Zhang<sup>1</sup>, Joseph D. Bruton<sup>1</sup>, Brun Ulfhake<sup>2</sup> and Håkan Westerblad<sup>1</sup>

<sup>1</sup>Department of Physiology and Pharmacology and <sup>2</sup>Department of Neuroscience, Karolinska Institutet, Stockholm, Sweden

### Early stage mtDNA mutator

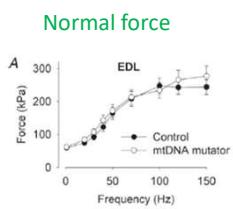


Figure 1. The force- and  $[Ca^{2+}]_i$ -frequency relationships did not differ between muscles from young mtDNA mutator and Control mice.

### Reduced fatigue resistance

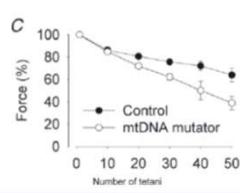


Figure 2. Muscles from young mtDNA mutator display reduced fatigue resistance. Representative mean data of relative tetanic force ( $[Ca^{2+}]_i$ ) from the 1st, 10th and 50th fast fatiguing contractions in a Control (A) and mtDNA mutator (B) FDB fibres. Mean ( $\pm$ SEM) relative tetanic force and  $[Ca^{2+}]_i$  during fatiguing stimulation are presented in C and D, respectively. Force and  $[Ca^{2+}]_i$  in the first tetanus was set to 100% in each fibre. Data from 10 Control and five mtDNA mutator mice.

### End stage mtDNA mutator

#### Reduced force

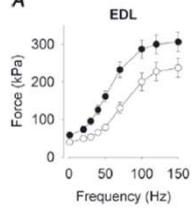


Figure 6. Tetanic force and  $[Ca^{2+}]_i$  are reduced in muscles of end-stage mtDNA mutator mice. A, mean data ( $\pm$ SEM) of the force-frequency relationship in isolated whole EDL muscles obtained from 11-month-mice (Control,  $n = 10$ ; mtDNA mutator,  $n = 12$ ). B,



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*Aging Clinical and Experimental Research*

**A fatigue resistance test for elderly persons based on grip strength: reliability and comparison with healthy young subjects**

Ivan Bautmans<sup>1,2</sup> and Tony Mets<sup>1,3</sup>  
<sup>1</sup>Gerontology, and <sup>2</sup>Rehabilitation Sciences, Free University of Brussels (VUB), <sup>3</sup>Geriatrics, Academic Hospital of the Free University of Brussels (AZ-VUB), Brussels, Belgium

**Fatigue resistance**

- Based on max. grip strength
- Time (seconds) until grip strength ↓ to 50%Max
- Reliability
  - Inter-observer ICC(3,1)= 0.77 – 0.91
  - Intra-observer ICC(3,1)= 0.82 – 0.94

**Grip Work**

- Integrating grip strength and fatigue resistance
- Reflecting muscle work during FR test



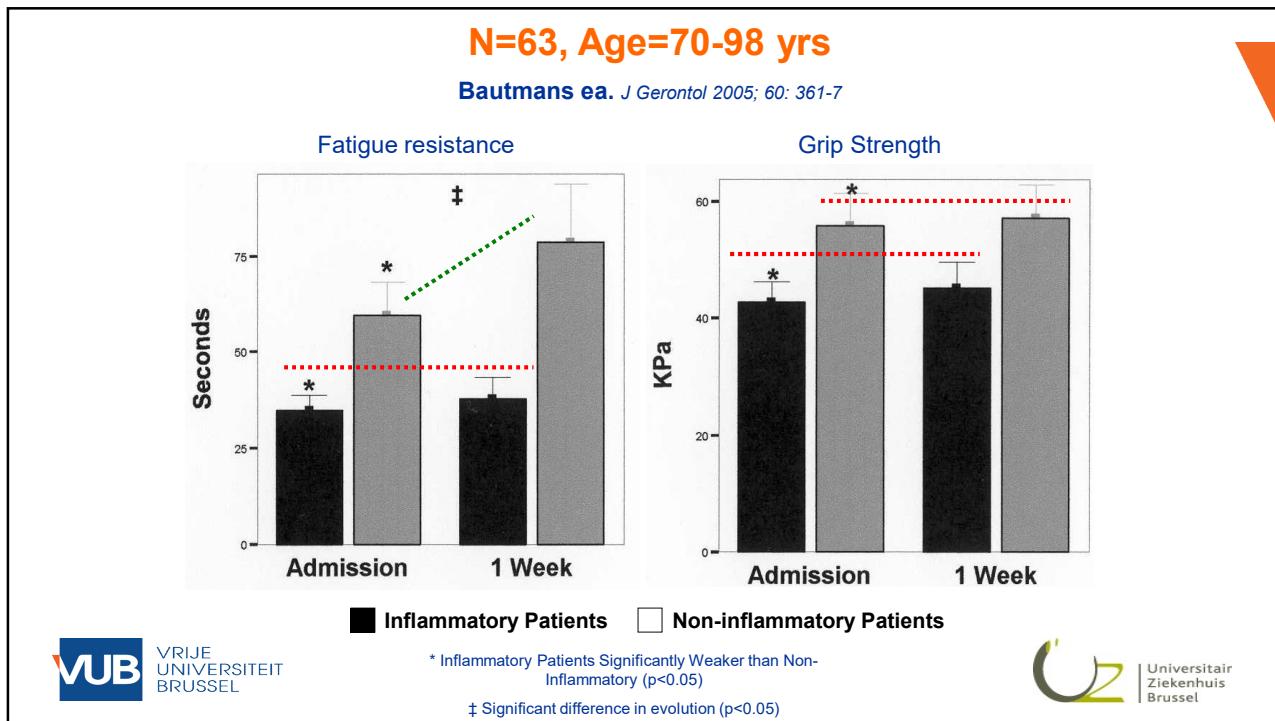



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Bautmans ea. Ageing Clin & Exp Res 2005; Mets ea. Am J Geriatr Pharmacother 2004; Bautmans ea. J Gerontol 2005; Bautmans ea. BMC Geriatrics 2007; Bautmans ea. J Am Geriatr Soc 2008; Bautmans ea. J Gerontol 2010; Bautmans ea. J Nutr Health & Ageing 2011; Beyer ea. Exp Gerontol 2011; Bautmans ea. Gait & Posture 2011; Beyer ea. BMC Musculoskeletal 2011; Arnold ea. Exp Gerontol. 2017; De Dobbelaer ea. Exp Gerontol. 2017;98:192-8.



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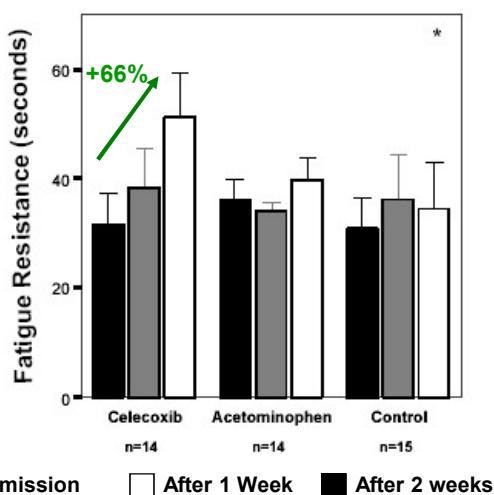


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Hospitalized geriatric patients with acute infection, N=43, aged 84 ± 6 years



Evolution FR significantly different between 3 groups ( $p=0.021$ ) and improvement celecoxib group significantly better than acetaminophen group ( $p<0.05$ ) control group ( $p<0.05$ )



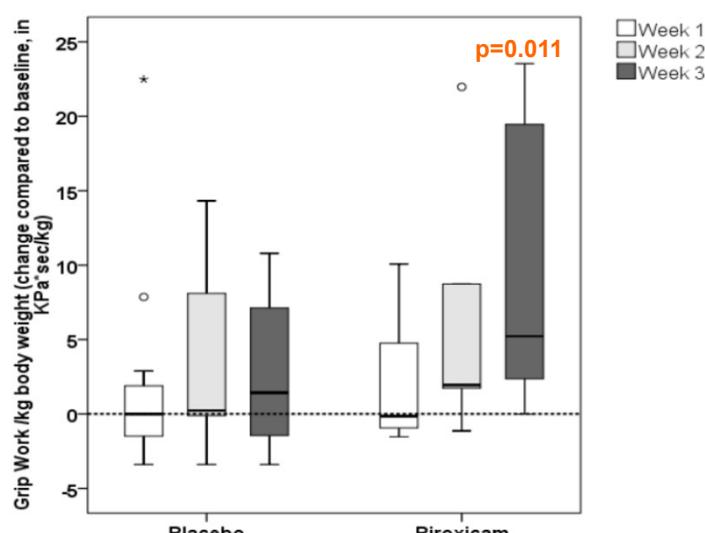
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Mets, Bautmans ea. Am J Geriatr Pharmacother 2004; 2: 230-8



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Hospitalized geriatric patients with acute infection, N=30, aged 70-94 years



Beyer, Bautmans ea. BMC Musculoskeletal 2012



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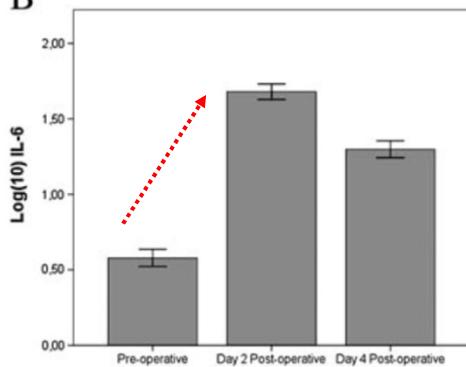
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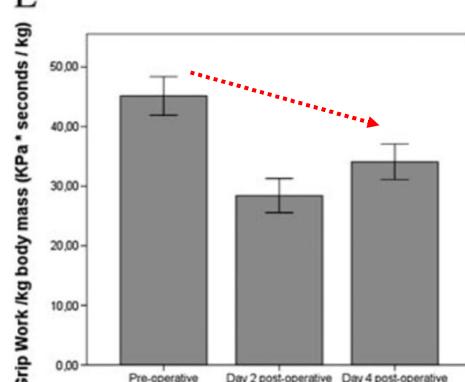
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N=66, age 24-91 yrs, elective abdominal surgery

B

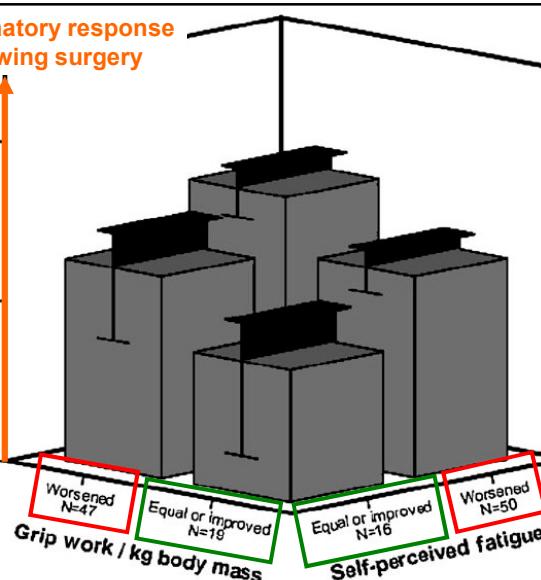


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Inflammatory response  
following surgery

Change IL-6 day4 post-surgery  
(log(10) transformed)



level as covariates). (B) Changes in levels of circulating IL-6 (log 10 transformed) were significantly different between groups ( $p = .02$ , ANOVA with age, postoperative medication use, occurrence of complications, and low preoperative albumin level as covariates). Bars represent  $M$  values  $\pm$  SE.

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Comparison of the effects of central or peripheral administration of cytokines with non-specific symptoms of sickness (Dantzer & Kelley, 1989)

CNS effects of cytokines	Non-specific symptoms of sickness
<ul style="list-style-type: none"> <li>General malaise</li> <li>Decreased activity</li> <li>Decreased social investigation</li> <li>Decreased food and water intake, weight loss</li> <li>Sleep changes</li> <li>Fever</li> </ul>	<ul style="list-style-type: none"> <li>Feeling sick</li> <li>Loss of energy or fatigue</li> <li>Loss of interest in usual activities</li> <li>Poor appetite and significant weight loss</li> <li>Sleep changes</li> <li>Fever</li> </ul>

Kelley ea Brain, Behavior, and Immunity 2003; 17: S112–8

CYTOKINE-INDUCED SICKNESS BEHAVIOR

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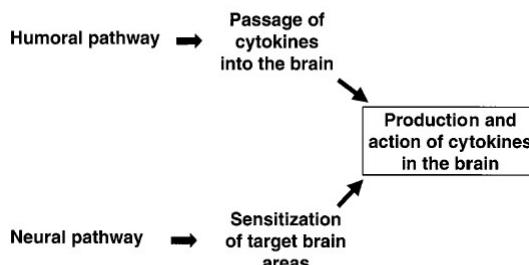
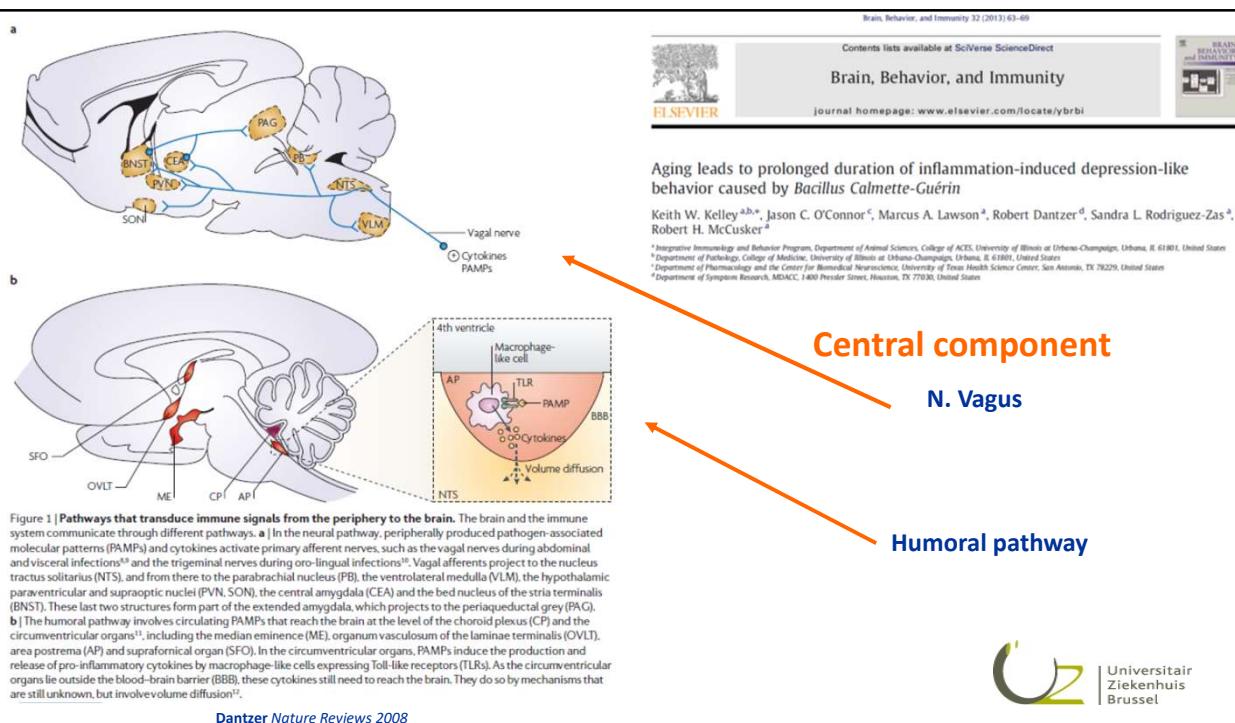


FIG. 5. Convergence of humoral and neural pathways in the transmission of the peripheral immune message to the brain. The possibility that neural pathways activated by peripheral immune stimuli sensitize target brain areas to the action of cytokines that propagate throughout the brain by volume diffusion remains to be tested.

Dantzer Brain, Behavior, and Immunity 2001; 15: 7–24



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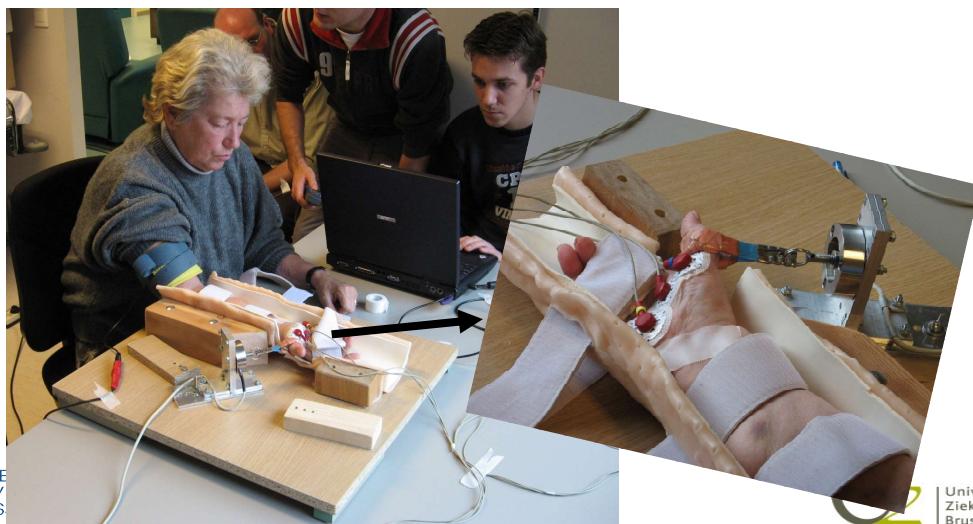
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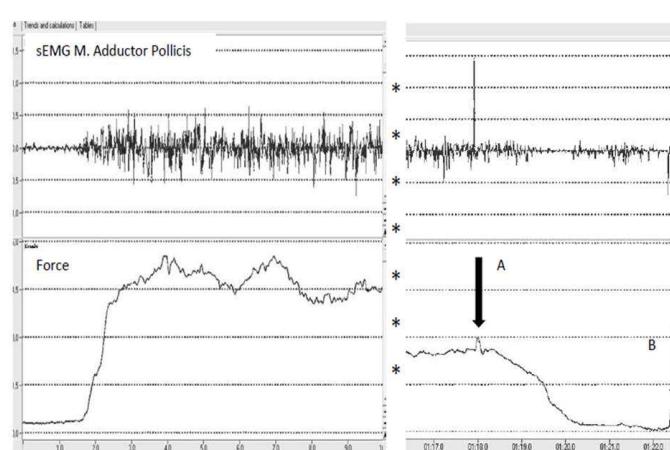
### Central or peripheral mechanism?

Age 66-91 yrs,  
18 healthy control,  
10 hospitalized with acute infection



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sEMG and voluntary force recordings of M. Adductor Pollicis at the start (left panel) and end of the fatigue protocol (right panel). Arrow A = superimposed force elicited by the interpolated twitch method when force declined to 50% of MVC; Arrow B = force elicited by the control twitch in relaxed muscle following the fatigue protocol.



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Arnold ea. *Exp Gerontol.* 2017;95:128-35.

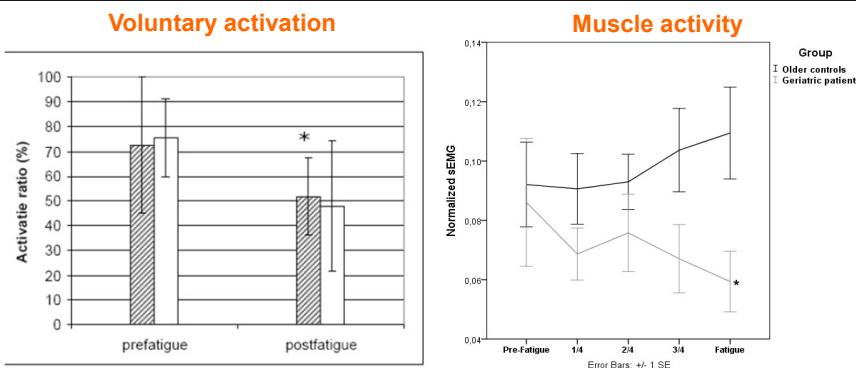
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Decreased activation ratio postfatigue \*p<0.05

▨ = Hospitalized Patients □ = Healthy Elderly

Muscle activity decreased significantly in the geriatric patients during the fatigue protocol (repeated measures ANOVA p<0.05). Significant time\*group interaction was observed when muscle activity at the end of the fatigue protocol was compared to pre-fatigue levels (repeated measures ANCOVA corrected for age p=0.014\*).

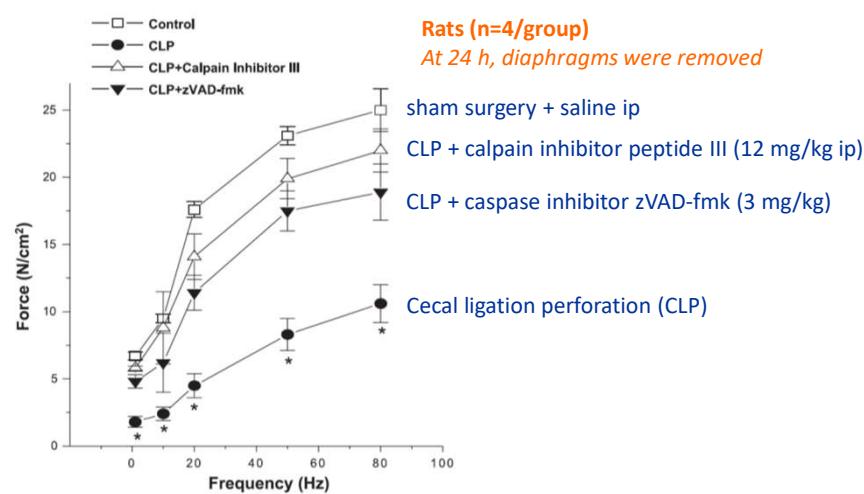


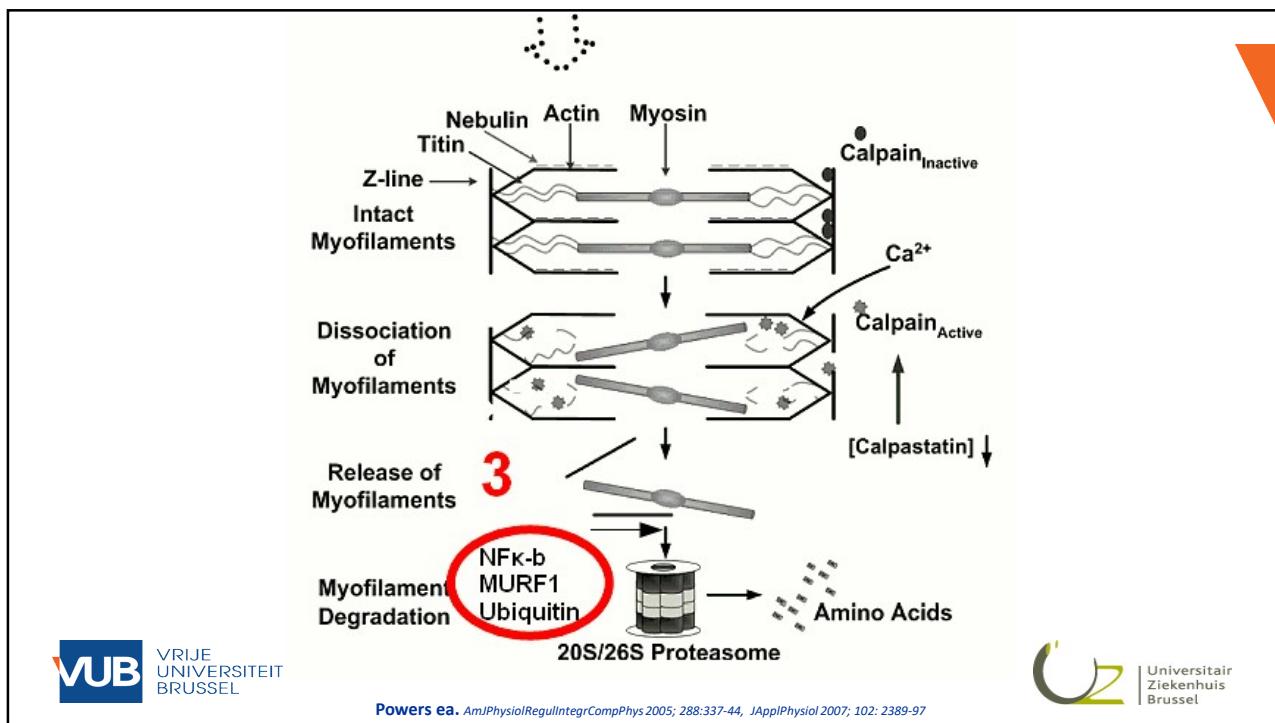
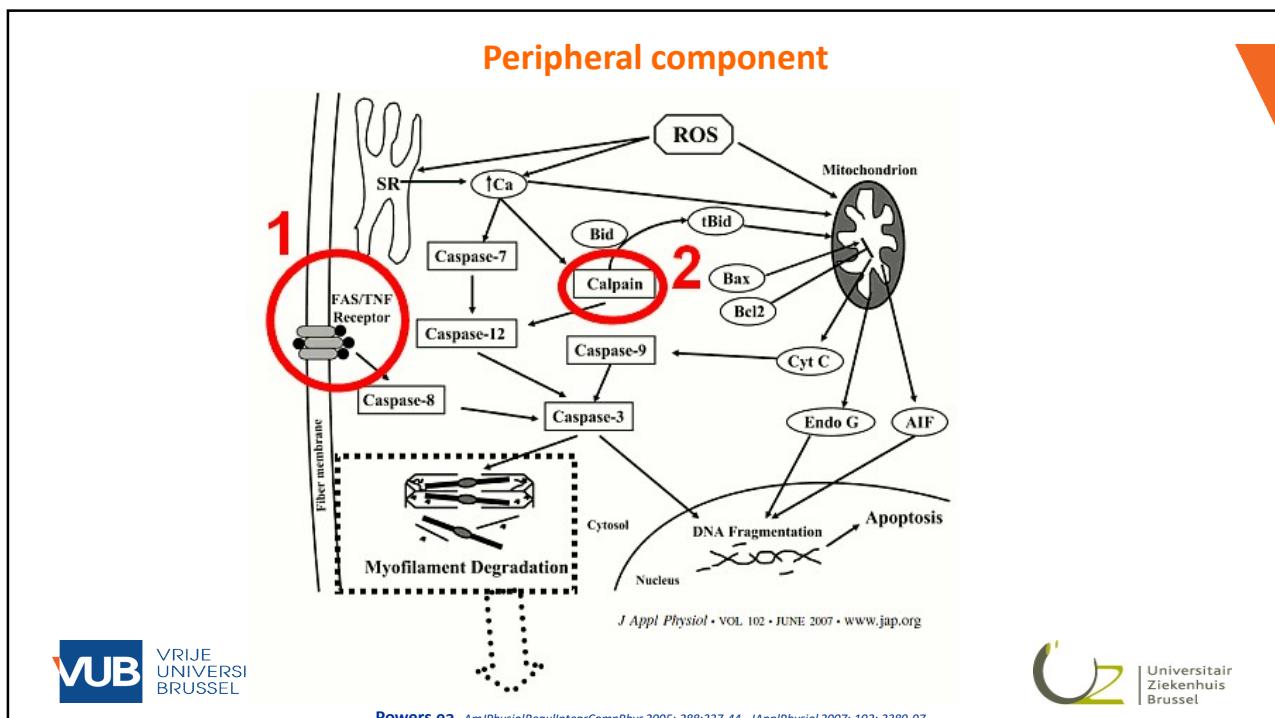
Fig. 3. Intact diaphragm force-frequency curves. Intact muscle force generation was significantly lower at stimulation frequencies from 1 to 80 Hz for diaphragms from CLP-treated animals (●) than for control animals (□) ( $P < 0.001$ ). Diaphragms from CLP animals given CI III (△) generated forces significantly higher than diaphragms from CLP animals for frequencies from 1 to 80 Hz ( $P < 0.01$ ). Force generation for muscles taken from CLP animals given zVAD-fmk (▼) was also greater than for CLP animals (frequencies 1–80 Hz,  $P < 0.01$ ). \*Significant statistical difference between CLP and the other groups.  $P < 0.05$ .

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# Exercise in acute settings to counter muscle weakness

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Brussel*J Nutr Health Aging*  
Volume 20, Number 7, 2016

## PHYSICAL ACTIVITY AND EARLY REHABILITATION IN HOSPITALIZED ELDERLY MEDICAL PATIENTS: SYSTEMATIC REVIEW OF RANDOMIZED CLINICAL TRIALS

N. MARTÍNEZ-VELILLA, E.L. CADORE, Á. CASAS-HERRERO,  
F. IDOATE-SARALEGUI, M. IZQUIERDO

Department of Health Sciences, Public University of Navarra (Navarra) Spain. Corresponding author: Mikel Izquierdo, PhD. Department of Health Sciences, Public University of Navarra (Navarra) Spain. Campus of Tudela, Av. de Tarazona s/n. 31500 Tudela (Navarra) Spain. Tel.: +34 948 417876. E-mail: mikel.izquierdo@gmail.com

- 17 articles included
- Positive effects on functionality
- No extra related costs but cost-effective
- Recommendations:
  - Start walking and encourage to increase the distance
  - Balance and gait retraining exercises
    - semi-tandem foot, standing, line walking, stepping practice, walking with small obstacles, proprioceptive exercises on unstable surfaces, and altering the base of support, and weight transfer from one leg to the other.
  - Exercises for executive and cognitive functions
    - stimuli for eating and dressing, space-time orientation, reasoning, memory, language, attention and perception
  - Resistance-training programs
    - include explosive mode
    - include exercises in which daily activities are simulated

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Kosse et al. BMC Geriatrics 2013, 13:107  
http://www.biomedcentral.com/1471-2318/13/107



**RESEARCH ARTICLE**

**Open Access**

## Effectiveness and feasibility of early physical rehabilitation programs for geriatric hospitalized patients: a systematic review

Nienke M Kosse<sup>1\*</sup>, Alisa L Dutmer<sup>1</sup>, Lena Dasenbrock<sup>2</sup>, Jürgen M Bauer<sup>3</sup> and Claudine JC Lamoth<sup>1</sup>

### 15 articles describing efficacy

- Functional benefits & safe

### 4 articles describing feasibility

- <50% of the geriatric hospitalized patients meet the inclusion criteria to start an exercise program
  - 3%-19% unwilling “*they felt unwell or did not feel like exercising*”  
= sickness behavior ~ inflammation



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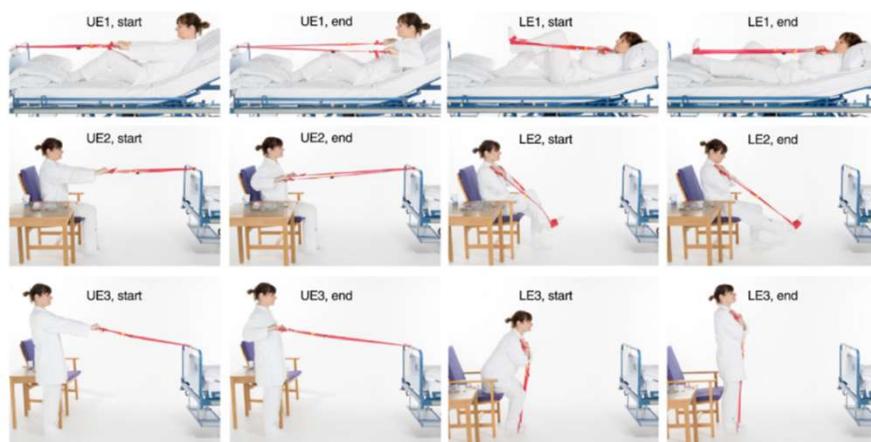


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N=15 hospitalized patients aged 71-94yrs

unsupervised elastic band exercises 1x/day 3x10 reps @10–12RM

Only 4/15 patients completed 33% of the recommended number of sets!



**Fig. 1** Elastic band exercises divided into three levels of progression. Elastic band exercises with start (start) and end position (end) shown for the three levels (1–3, 3 = highest level) of progression for the upper extremity (UE) and for the lower extremity (LE)



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Rathleff ea. Pilot and feasibility studies. 2017;3:56.



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N=16, 85±2 yrs, acute hospitalized geriatric patients  
7d/wk unilateral leg extension 3-6 sets of 10-12 reps @12RM

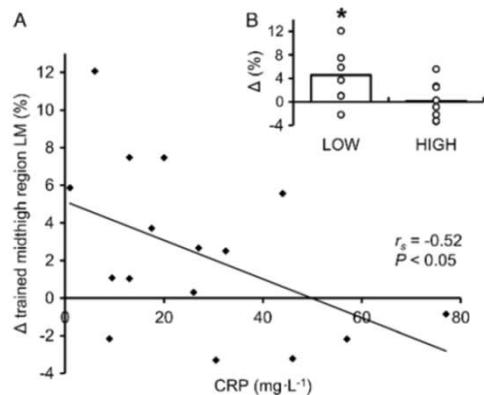


FIGURE 2—A, Correlation between CRP levels during the intervention period and the relative changes in midthigh region lean mass (LM) of the trained leg. B, Relative changes in midthigh region LM of the trained leg for the eight patients with the lowest levels of CRP (LOW) versus the eight patients with the highest levels (HIGH). Histograms are mean values with individual values displayed as open circles. \*Significant difference between LOW and HIGH ( $P < 0.05$ ).



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Norheim ea. *Med Sci Sports Exerc.* 2017;49(6):1079-85.



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## Hip Fracture

### High prevalence of (pre-fracture)

- Sarcopenia (47% based on muscle mass)
- Frailty (69% intermediate to high frailty)
- Malnutrition (84-91% MNA<24, 71% Vit D deficiency)

### Return to pre-fracture state = inappropriate goal!

### Rehab targets

- Recovery from fracture / surgery
- Countering weakness, malnutrition & frailty  
= long term!

Krishnan ea *Age & Ageing* 2014; Hida ea *Geriatr & Gerontol Int* 2013; Fiatorone Singh *Curr Opin Nutr Metab Care* 2014;  
Shyu ea *J Gerontol* 2013; Bryson ea *Acta Orthop Belg* 2013;



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**N=40, age 79±8 yrs, hip fracture surgery**

### Strength training fractured limb

- start Day1 postsurgery
- Knee extension
- Seated on the bed, weight-cuff around ankle
- 3x 10rep @ 10RM (until fatigue), 5d/wk
- Throughout hospitalization, 4±2 sessions

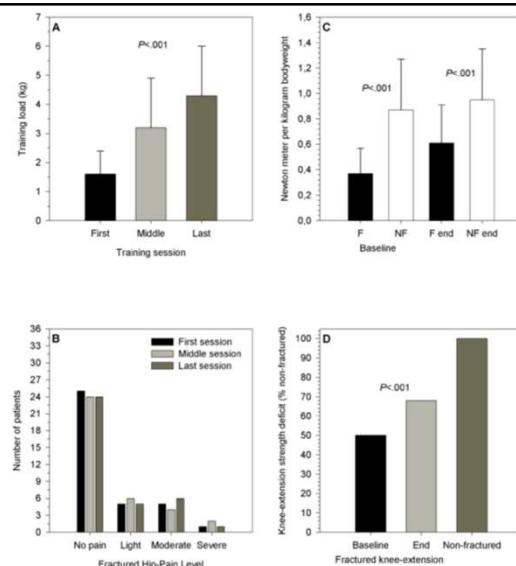
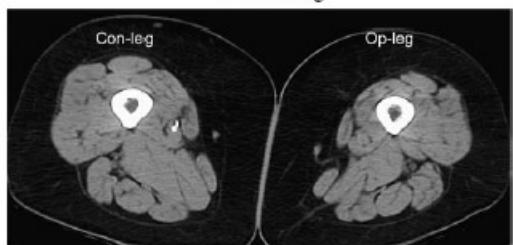


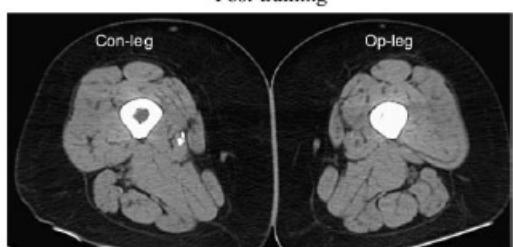
Figure 2. Outcomes on training load, hip-pain and knee-extension strength. A) Progression of training loads (kg) during the first, middle and last strength training session. B) Hip fracture-related pain during the first, middle and last strength training session. C) Knee-extension strength (Nm/kg). fractured (F) and non-fractured (NF) limb at baseline and discharge (end). D) Fractured limb knee-extension strength (% non-fractured) before and after training.  
doi:10.1371/journal.pone.0093332.g002

## Elective Hip Replacement n=36 aged 60–86yrs

Pre-training



Post-training



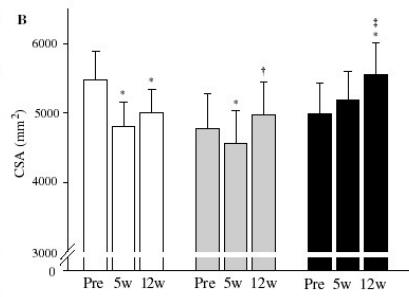
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Rehab initiated 1–2 days post surgery

RT: 3-5 reps @ 8–12 RM, 3x/wk

ES: electrical stimulation of  
the quadriceps muscle (1 h/day)

SR: functional exercises and isometric  
muscle contractions without external  
loads



Suetta et al. J Appl Physiol 2004; 97: 1954-62; Suetta et al. JAGS 2004; 2016-22

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## Exercise during inflammation

### Chronic inflammation (CF, DM-1, COPD, asthma, MS, CHF, Mc Ardle)

- ↑↑ acute IL-6 + ↑TNF-α, longer elevated in CF COPD
- other studies found no significant differences
- bias by NSAIDs or corticosteroids

### Acute inflammation

- Geriatric hospitalized patients
  - Functional benefits & safe
  - <50% included to start exercise
    - 3%-19% unwilling "they felt unwell or did not feel like exercising"
    - = sickness behavior ~ inflammation
- Post-surgery
  - Strength training: feasible, no ↑pain, strength gain
- No data on immune response!



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## PRESENTATION

### Spierzwakte bij gehospitaliseerde geriatrische patiënten

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## Take home messages

Muscle ageing = sarcopenia

- Hospitalization at higher age
  - Acute & inflammatory patients are weaker
  - Inflammation delays recovery
- Exercise interventions
  - Safe and beneficial in acute setting
    - Implementation remains challenging
    - Supervision & coaching by PT's
    - Dose-response relationships



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## Thank you

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