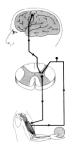
5th Congress of the Hellenic Society of Biochemistry and Physiology of Exercise
Athens · November 6-7th, 2015

Use of exercise training to reverse age-related changes in neuronal function and skeletal muscle morphology









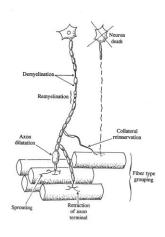


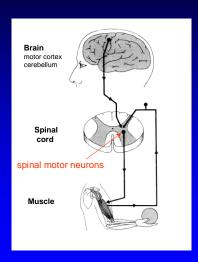
Per Aagaard

Muscle Physiology and Biomechanics Research Unit, Institute of Sports Science and Clinical Biomechanics, University of Southern Denmark / paagaard@health.sdu.dk



Age-induced changes in neuromuscular function: Loss of motor neurons, MU reorganization





Spinal motor neurons

reduced number of motor neurons in the spinal cord

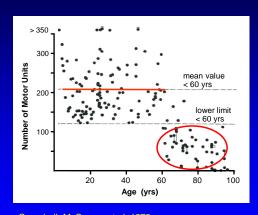
25% average loss of spinal motor neurons (lumbospinal segments L1-S3) from 20 yrs to 90 yrs of age

Tomlinson & Irving 1977

several subjects > 60 yrs showing ~ 50% less MN's compared to 20-40 yrs old

Tomlinson & Irving 1977

Ageing and neuromuscular function



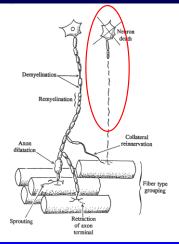
Campbell, McComas et al. 1973 Extensor digitorum brevis (n=207, age=3-96 yrs) AJ McComas: Skeletal muscle - form and function, 1996

Motor Units

reduced number of excitable (i.e. functioning) MU's observed at 60-70 yrs of age

Brown et al. 1988, Doherty et al. 1993, Campbell, McComas et al. 1973

Number of excitable MU's in aged subject (60-95 yrs) ~ 1/3 of that observed in younger subjects (1-60 yrs)



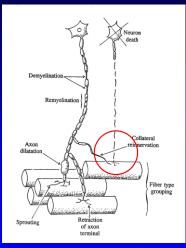
AJ McComas: Skeletal muscle form and function, 1996

↓ # motor neurons = ↓ # motor units at increasing age

ongoing process of denervation and reinnervation of skeletal muscle fibers late in life

Vandervoort 2002, McComas 1996

Ageing and neuromuscular function

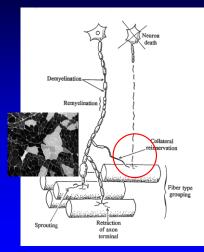


AJ McComas: Skeletal muscle - form and function, 1996

↓ # motor neurons = ↓ # motor units
at increasing age

ongoing process of denervation and reinnervation of skeletal muscle fibers late in life

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AJ McComas: Skeletal muscle - form and function, 1996

↓ # motor neurons = ↓ # motor units
at increasing age

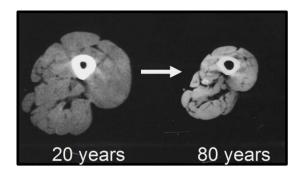
ongoing process of denervation and reinnervation of skeletal muscle fibers late in life

evidenced by

- histological findings of fiber type grouping
- elevated coexpression of MHC isoforms
- preferential atrophy of type II muscle fibers
- very large MUAPs, indicating ↑ innervation ratio

Vandervoort 2002, McComas 1996

Age-induced changes in neuromuscular function: Loss of muscle mass with aging: sarcopenia



Picture courtsey Paolo Caserotti Institute of Sports Science and Clinical Biomechanics University of Southern Denmark

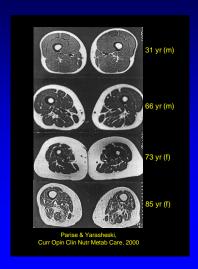
Loss of muscle mass with aging: sarcopenia

Reduced muscle cross-sectional area (↓ 40% between the age of 20 and 80 yrs)

The decline seems to start in early adulthood and accelerate after the age of 50 years

↑ content of non-contractile tissue such as intramuscular fat and connective tissue

> Vandervoort, Muscle & Nerve 25, 2002 McNeil et al, J Appl Physiol 102, 2007



Sarcopenia (loss of muscle mass)



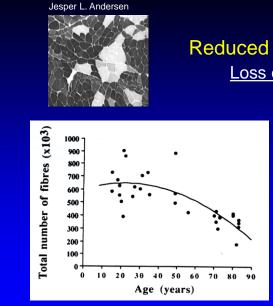
Photo courtsey Charlotte Suetta

Sarcopenia is significantly associated with a

- 3-4 times greater risk of physical disability
- 2-3 times greater risk of balance abnormality
- 2-3 times greater risk of falls

Baumgartner RN 1998, 1999

In frail elderly persons with advanced sarcopenia but without circulatory or pulmonary diseases, muscle weakness is typically more limiting for daily functioning than aerobic fitness.



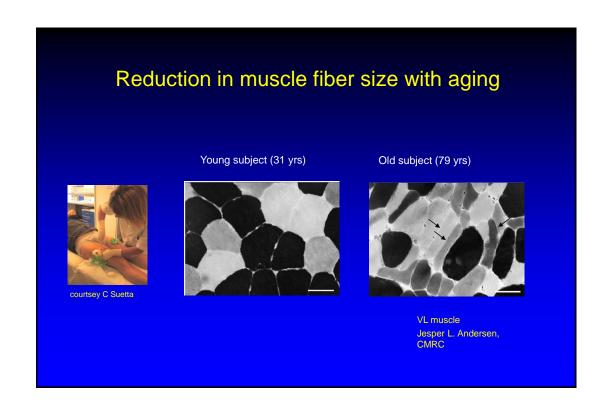
Reduced muscle mass with ageing Loss of skeletal muscle fibers

Elderly male subjects (70-75 yrs) show ~40% fewer muscle fibers than young subjects (19-30 yrs)

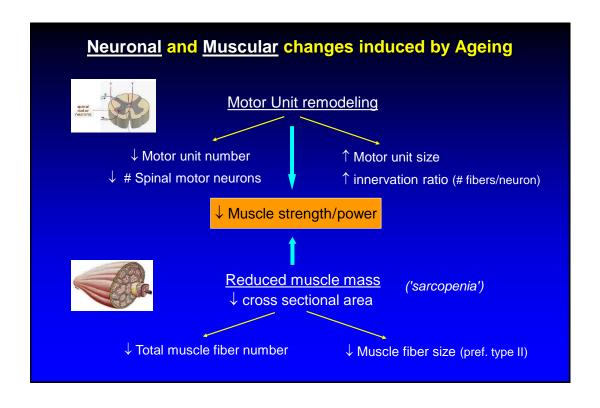
VL muscle, Lexell et al. 1983

Very old male subjects (>80 yrs) ~60% fewer fibers compared to young subjects

VL muscle, Lexell et al. 1988



Age-related reductions in skeletal muscle fiber size		Vandervoort, Muscle & Nerve 25, 2002			
			Percent reduction		
Study	Gender	Age (years)	Type I		Type II
Larsson et al., Acta Physiol. Scand. 103, 1978	M	22-65	1	<<	25
Essen-Gustavsson and Borges, Acta Physiol.	M	20-70	15	*	19
Scand. 126, 1986	F	20-70	25	<<	45
Lexell et al. J. Neurol. Sci. 84, 1988	M	15-83	1	<<	29
Hakkinen et al. J. Gerontol. 53B, 1998	M	29-61	+8	<<	10
Fiatarone Singh et al. Am. J. Physiol. 277, 1999	M, F	72-98	+7	<<	60
Hikida et al. J. Gerontol. 55, 2000	M	58-78	24	<<	40



Age-induced changes in neuromuscular function: Impairments in mechanical muscle function



Decreased Muscular Strength With Aging CROSS-SECTIONAL DATA 150 **Isometric muscle strength** 140 130 120 Is preserved to ~50-60 yrs of age 110 (cross sectional data) 100 90 Decreases at a rate of 1-1.5% 70 60 per year from 60-65th year 40 Substantial individual differences! 30 10 20 30 40 50 60 70 80 90 100 110 Age (years) Vandervoort & McComas 1986 Spirdoso 1995 Spirduso, Physical dimensions of aging, 1995

Decreased Muscular Strength and Power with Aging

Decreased maximal muscle force and contractile power from > 65 years

Loss of strength: 1.5% per year Loss of power: 3.5% per year

Young & Skelton, Int. J. Sports Med. 15, 1994



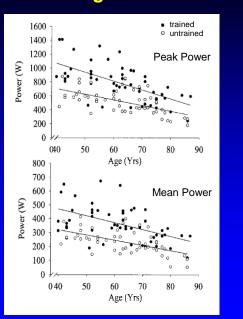
Muscle function in elite master weightlifters





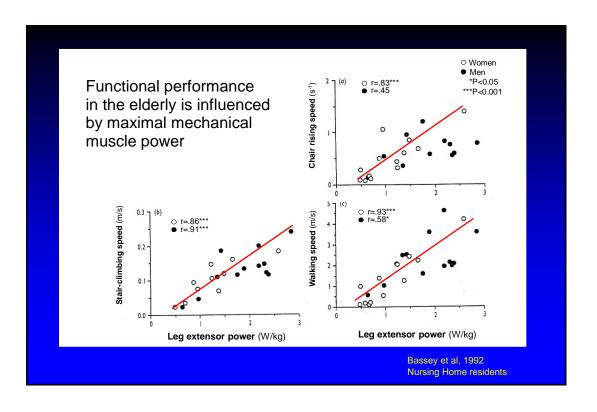
Trained (closed circles) and untrained (open circles) individuals demonstrated similar age-related decline rate in peak power (1.3% vs 1.2% per year, respectively)

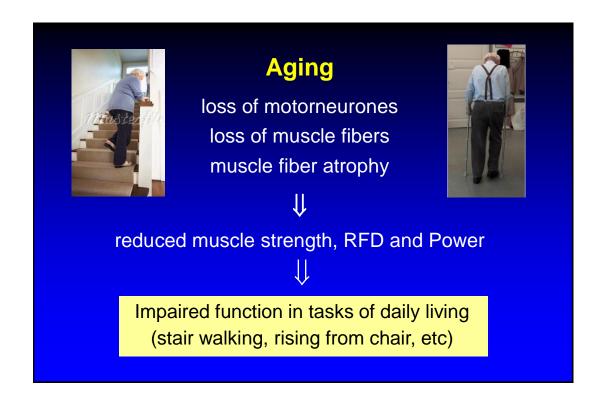
Pearson, Harridge et al; Med Sci Sports Exerc 2002

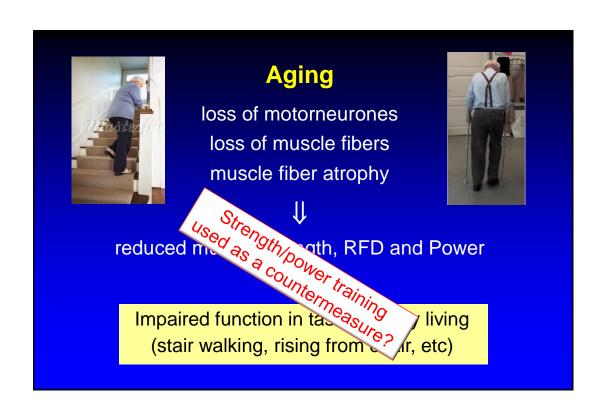


Muscle function in elite master weightlifters traineduntrained 1600 1400 1200 Peak Power Power (W) 1000 800 600 400 200 040 Age (Yrs) 800 Trained (closed circles) and 700 untrained (open circles) 600 Mean Power individuals demonstrated 500 400 similar age-related decline 300 rate in peak power (1.3% 200 vs 1.2% per year, respectively) 100 Pearson, Harridge et al; 040 60 Med Sci Sports Exerc 2002 Age (Yrs)





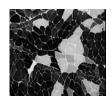




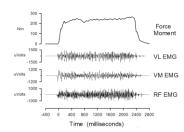




Age-induced changes in neuromuscular function: Adaptive alterations in neuromuscular function with strength/power training







Percentage increases in Muscle Size (CSA) and Maximal Muscle Strength (MVC) with Strength Training in old vs young adults

Population	Training Duration (weeks)	ΔMVC (%)	ΔMVC /day (%)	ΔCSA (%)	ΔCSA/day (%)	Reference
Young adults	24	26.8	0.16	6.8	0.04	Häkkinen 1985
Young adults	12	15.0	0.18	5.7	0.06	Jones & Rutherford 1987
Young adults	24	29.6	0.18	19.0	0.11	Narici 1996



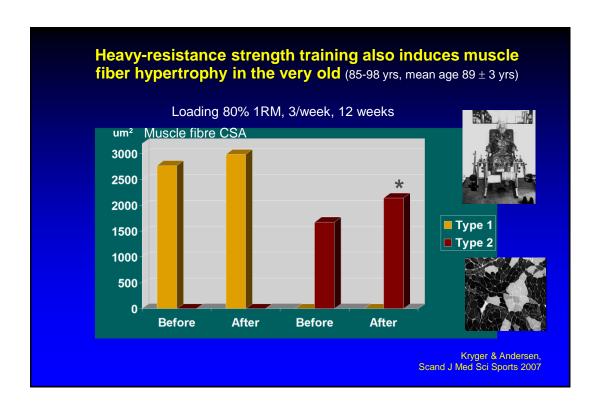
Aagaard et al,

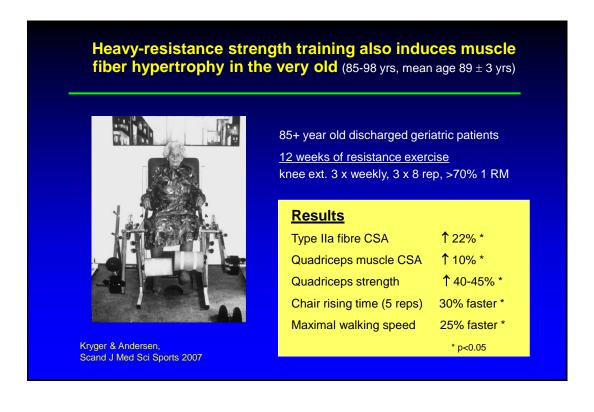
Narici et al, J Musculoskel Neron Interact 2004

Percentage increases in Muscle Size (CSA) and Maximal Muscle Strength (MVC) with Strength Training in old vs young adults

Population	Training Duration	AMVC	ΔMVC /day	ΔCSA	ΔCSA/day	Reference
ropulation	(weeks)	(%)			(%)	Reference
	(weeks)	(%)	(%)	(%)	(%)	
Young adults	24	26.8	0.16	6.8	0.04	Häkkinen 1985
Young adults	12	15.0	0.18	5.7	0.06	Jones & Rutherford 1987
Young adults	24	29.6	0.18	19.0	0.11	Narici 1996
Elderly (65-81 vrs)	16	19.0	0.17	7.4	0.07	Ferri 2003
Elderly						
(60-72 yrs)	12	16.7	0.20	9.3	0.11	Frontera 1988
Elderly						Häkkinen
(61 yrs)	10	17.0	0.25	9	0.12	1998
Elderly						Harridge
(85-97 yrs)	12	37	0.44	10	0.11	1999

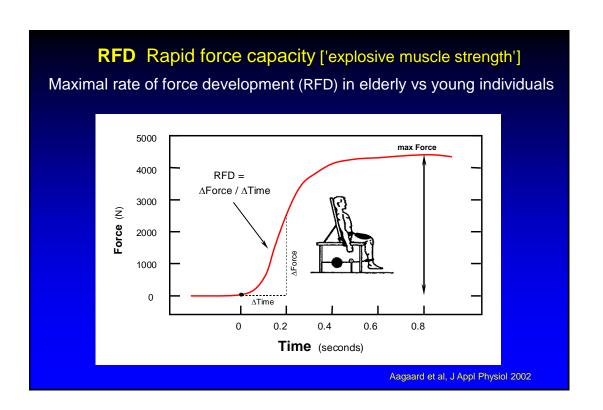
Narici et al, J Musculoskel Neron Interact 2004

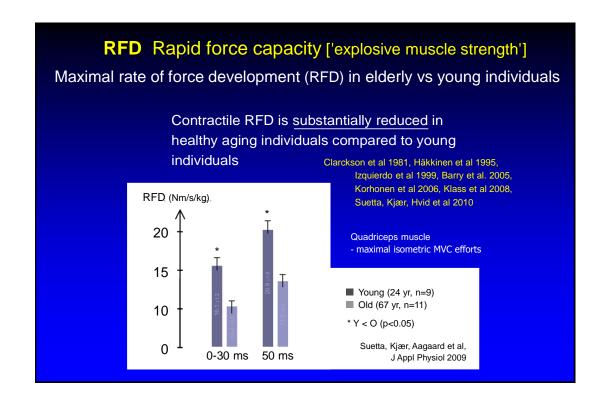




Increases in muscle fibre size in older individuals following high-intensity dynamic leg strength training. Based on biopsy samples obtained from vastus lateralis	Muscle fibe		ervoort, Muscle & Nerve 25, 2002
Study	Type I		Type II
Frontera et al., J. Appl. Physiol. 64, 1988	34	æ	26
Charette et al., J. Appl. Physiol. 70, 1991	7	<	20
Grimby et al., J. Appl. Physiol. 73, 1992	8	*	5
Häkkinen et al. J. Gerontol. 53B, 1998	23	*	27
Fiatarone-Singh et al. Am. J. Physiol. 277, 1999	5	>	-12
Hunter et al., J. Appl. Physiol. 86, 1999	14	<	23
Hikida et al. J. Gerontol. 55, 2000	46	*	43

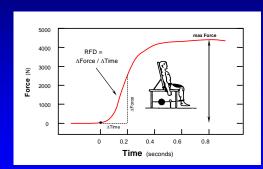
Changes in explosive muscle strength (rate of force development, RFD) induced by strength training in the elderly





RFD Rapid force capacity

Effects of resistance training on RFD in the elderly?







Scand J Med Sci Sports 2008: 18: 773–782 Printed in Singapore . All rights reserved DOI: 10.1111/j.1600-0838.2007.00732.x

sounal complation of 2007 Blackwell Munksgaard S C A N D I N A V I A N J O U R N A L O F M E D I C I N E & S C I E N C E I N S P O R T S

Explosive heavy-resistance training in old and very old adults: changes in rapid muscle force, strength and power

P. Caserotti^{1,2}, P. Aagaard^{1,2}, J. Buttrup Larsen³, L. Puggaard^{1,2}

¹Centre of Applied and Clinical Exercise Sciences (ACES), University of Southern Denmark, Odense, Denmark, ²Institute of Sports Science and Clinical Biomechanics, University of Southern Denmark, Odense, Denmark, ²Medical Office of Health, County of Fineen, Odense, Denmark, The Addical Office of Health, County of Fineen, Corresponding author: Paolo Caserotti, PhD, Centre of Applied and Clinical Exercise Sciences, University of Southern Denmark, Campiusey (55, 523 Odense, M, Denmark, E-mail: peaserotti@health.sda.dk

Accepted for publication 13 July 2007

Age-related decline in muscle power predicts falls, motor impairments and disability. Recent guidelines suggested that training programs should be tailored to maximize muscle power. This study investigated the effects of 12 weeks of explosive-type heavy-resistance training (75-80% of 1 repetition maximum) in old (60-65 years, TG60) and very old (80-89 years, TG80) community-dwelling women. Training was performed with maximal interational acceleration of the training load during the concentric movement phase. Maximal isometric voluntary muscle strength (MVC), rapid force capacity, assessed as rate of force development (RFD), and impulse, maximal muscle power during a countermovement jump (CMJ) and during

unilateral leg extension task (LEP) were evaluated. RFD, impulse and MVC increased by \$15%, 42% and 28% in TG80, and by 21%, 18% and 18% in TG60, respectively, CMJ jump height increased by 18% and 10% in TG80 and TG60, respectively, while jump peak power increased in TG60(5%), Finally, LEP increased 28% in TG80 and 12% in TG80 in TG80, in TG80 and 12% in TG80 and 12% in TG80 respectively, while jump peak power increased in TG60(5%), Finally, LEP increased 28% in TG80 and 12% in TG60. These findings demonstrate that explosive-type heavy-resistance training seems to be safe and well tolerated in healthy women even in the eighth decade of life and elicits adaptive neuromuscular changes in selected physiological variables that are commonly associated with the risk of falls and disability in aged individuals.

Muscle power, which is the product of contractile force and movement velocity, is a stronger predictor of functional motor performance, incidence of falling and self-reported functional status than maximal muscle strength in community-dwelling old adults (Foldvari et al., 2000; Skelton et al., 2002). Furthermore, lower limb muscle power declines at a faster

related to the number of active sarcomeres in series (Edgerton et al., 1986; Kraemer & Newton, 2000). Thus, maximal muscle power depends on the muscle morphology (e.g. physiological muscle cross-sec-tional area, muscle fiber pennation angle, muscle fiber length, fiber-type composition) and neuromus-cular activation properties (discussed below), and it

Explosive-type strength/power training in the old (60 yrs) and the very old (80 yrs)

Subjects

Mean age 62.7 (SD 2.2) and 81.8 (SD 2.7) yrs n = 20 + 20 con n = 12 + 13 con

> Caserotti, Aagaard et al, 2008

Explosive-type strength/power training in the old (60 yrs) and the very old (80 yrs)

Subjects

Mean age 62.7 (SD 2.2) and 81.8 (SD 2.7) yrs

Duration, frequency of training

12 weeks, twice a week

Familiarisation period

2 wks with lower training loads (50% 1RM), and reduced movement velocity

Progressive load adjustment:

Every two weeks with a new estimated 1RM (5-RM test)

Exercises (bilateral)

Horizontal leg press, knee extension, calf rise, incline leg press, leg curl - slow ECC, rapid (max acc) CON actions

Exercise intensity and reps

75-80% 1RM loads, 8-10 reps, 4 sets each exercise

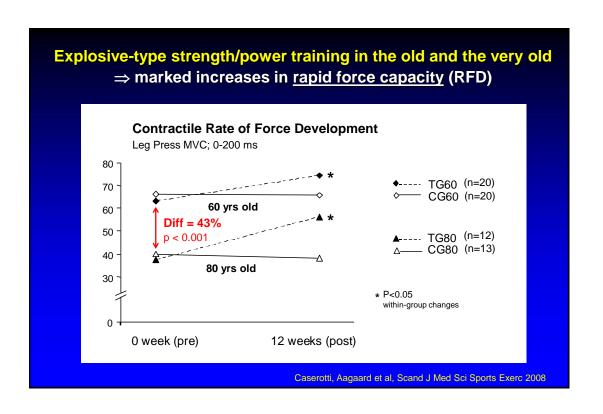


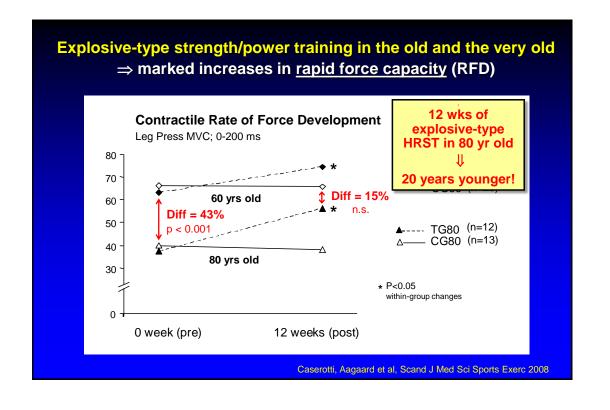


Caserotti, Aagaard et al, 2008

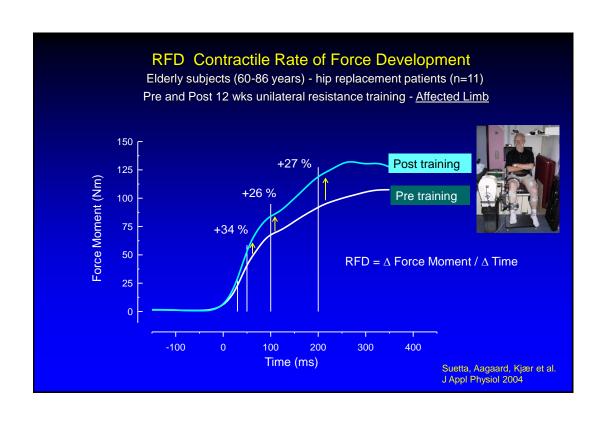








Explosive-type streng ⇒ marked i	th/power training in t ncreases in MVC, RFI		
		TG 60	TG80
	MVC (maximal strength)	+22%*	+28%*
	RFD (rapid force capacity)	+18%*	+51%*
	SSC muscle power (CMJ force plate)	+5%*	+6%*
	1-leg muscle power (Power rig)	+12%*	+28%*
		* pre vs po	ost (p<0.05)
	Caserotti, Aagaard e	t al, Scand J Med	d Sci Sports Exerc 2008



Training induced changes in explosive muscle strength (RFD)

Adaptive responses in aged individuals

Heavy-resistance strength training



Concurrent increases in <u>maximal RFD</u> and <u>neuromuscular activity</u> (iEMG) in elderly individuals



Häkkinen & Häkkinen 1995 (age 50, 70 yrs, gender F, M) Häkkinen et al. 1998 (age 40, 60 yrs, gender F, M) Häkkinen et al. 2001 (age 63 yrs, gender F) Suetta et al. 2004 (post hip replacement surgery, 60-86 yrs) Barry et al. 2005 (age 60-79 yrs, gender F, M)

Training induced changes in explosive muscle strength (RFD)

Adaptive responses in aged individuals

Heavy-resistance strength training



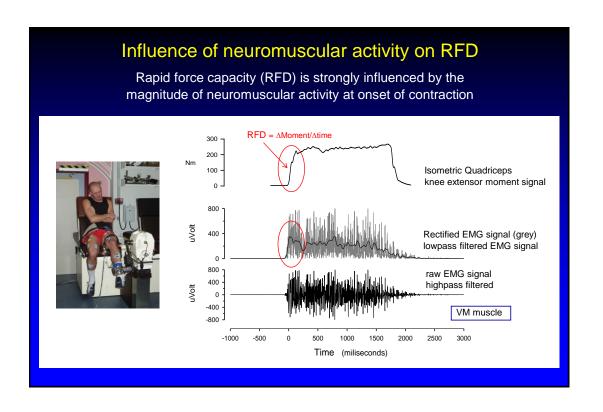
Concurrent increases in <u>maximal RFD</u> and <u>neuromuscular activity</u> (iEMG) in elderly individuals

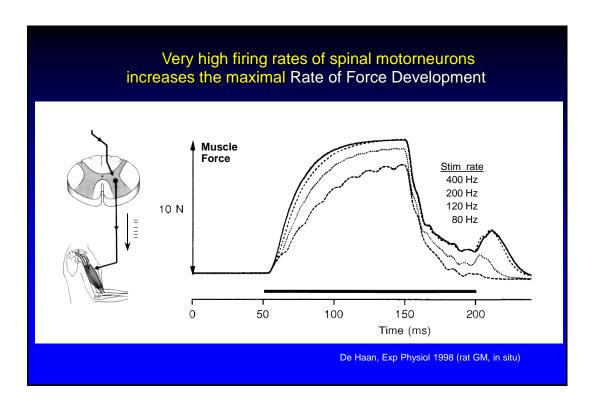


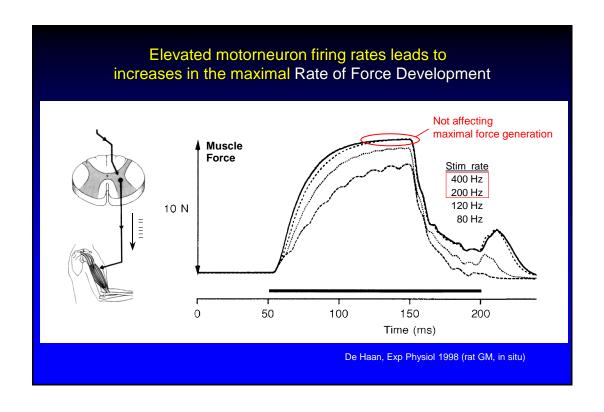
Functional consequences

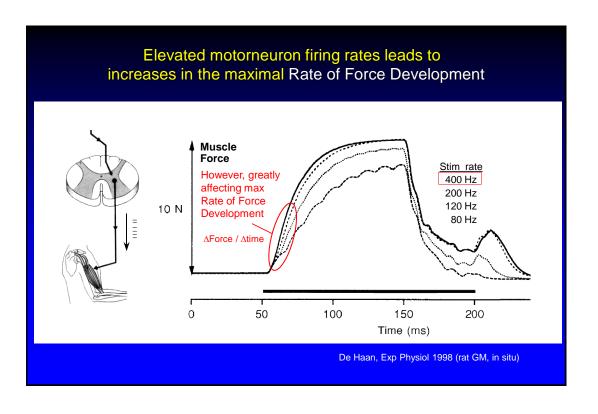
- enhanced acceleration
- elevated maximal movement velocity
- elevated muscle force & power during rapid movements
- reduced risk of falls







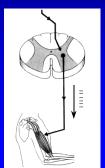




Motorneuron firing frequency

What is the effect of strength/power training on maximal MN firing frequency in old adults?





Ageing and neuromuscular function

Motorneuron firing frequency

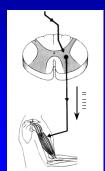
What is the effect of strength/power training on maximal MN firing frequency in old adults?

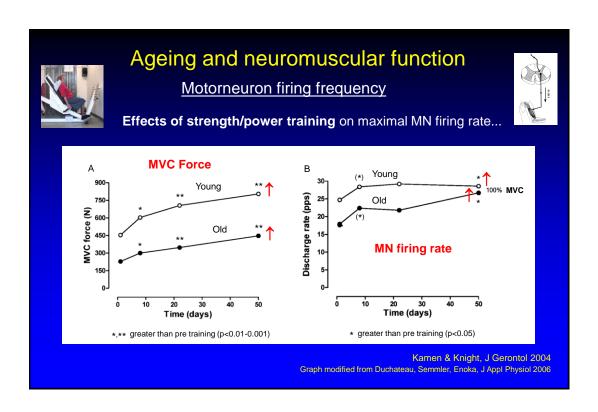


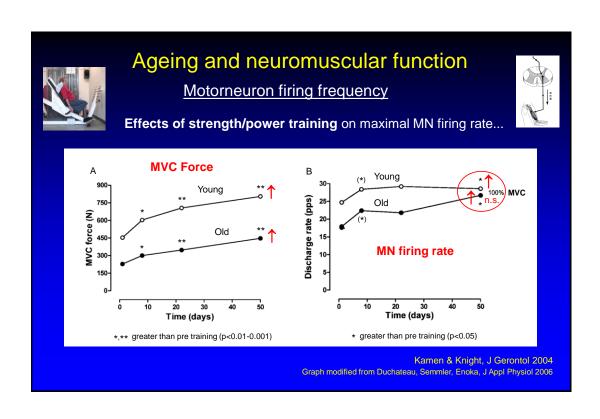
UNTRAINED STATE:

Maximal motorneuron firing frequency recorded during MVC is <u>reduced in elderly</u> vs young subjects

Patten et al. 1999, 2001, Connelly et al. 1999, Kamen & Knight 2004, Klass Duchateau et al. 2008, Christie & Kamen 2010





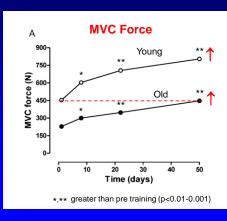


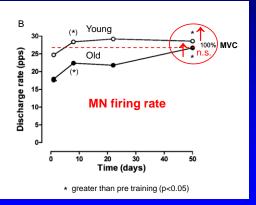


Motorneuron firing frequency



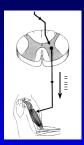






Kamen & Knight, J Gerontol 2004 au, Semmler, Enoka, J Appl Physiol 2006

Strength training induce changes in maximal motorneuron firing frequency in young and old individuals



Strength/power training

↑ motorneuron firing rate (at 100% MVC) in both young and old subjects



Patten et al. 1999 (old, young), 2001 (young) Van Cutsem et al. 1998 (young), Kamen & Knight 2004 (old, young) Christie & Kamen 2010 (old, young)

Furthermore, after strength training maximal motorneuron firing rate did not differ between old and young subjects

Patten et al. 1999, Kamen & Knight 2004, Christie & Kamen 2010

Effects of strength training in frail elderly patients

Well, does the need exist?





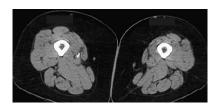
Effects of strength training in frail elderly patients

Well, does the need exist? YES!



Often, severe muscle atrophy is observed in elderly patients...

Strength training is the only exercise modality known to effectively increase muscle mass





Effects of strength training in frail elderly patients

Does it lead to improved functional capacity?



pre

post training?

Effects of strength training in frail elderly patients

Does it lead to improved functional capacity?

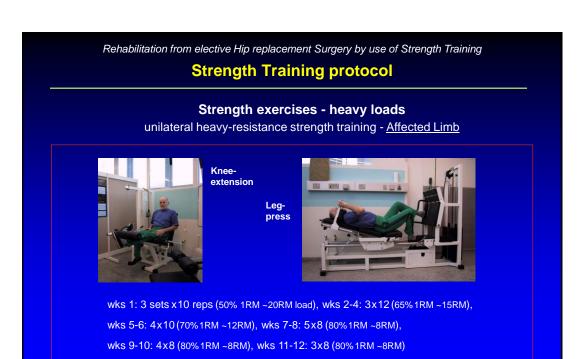


pre

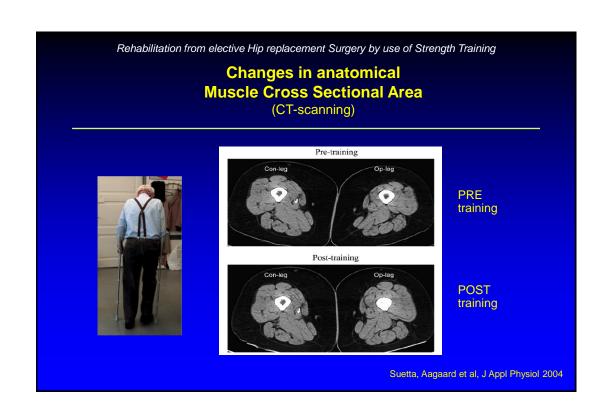


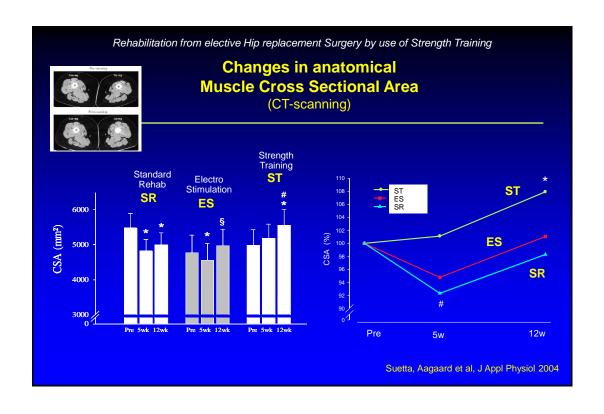
post training

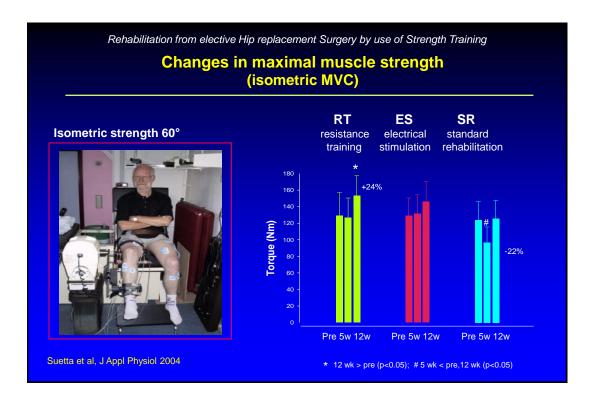
YES!

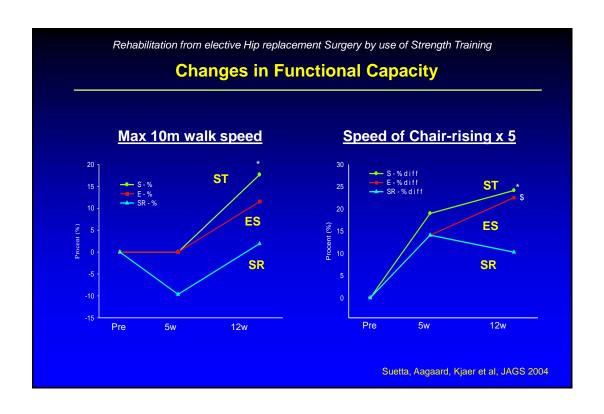


Suetta, Aagaard et al, JAGS 2004, J Appl Physiol 2004

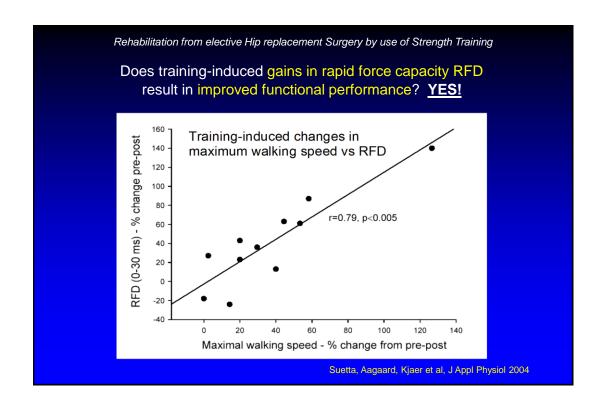


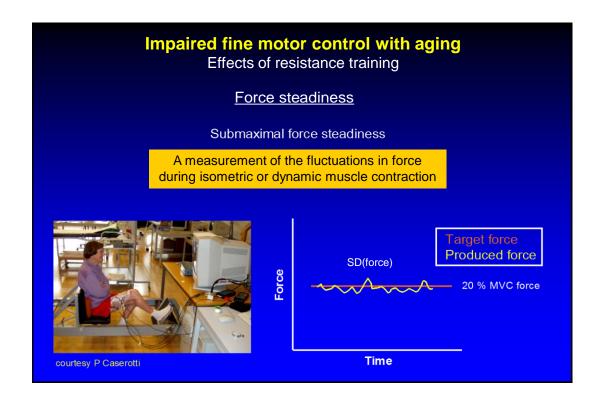












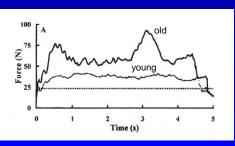
Impaired fine motor control with aging

Effects of resistance training

Force steadiness

Greater force error, less steady muscle forces (↑SD) during submaximal constant-force motor tasks in elderly compared to young subjects

Tracy & Enoka 2002, Hortobagyi et al. 2001



tracking of 25-N target force during 5-sec slow-speed eccentric quadriceps contraction (15%s) post 10 familiarization trials

Hortobagyi et al. 2001

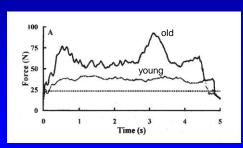
Impaired fine motor control with aging

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Force steadiness

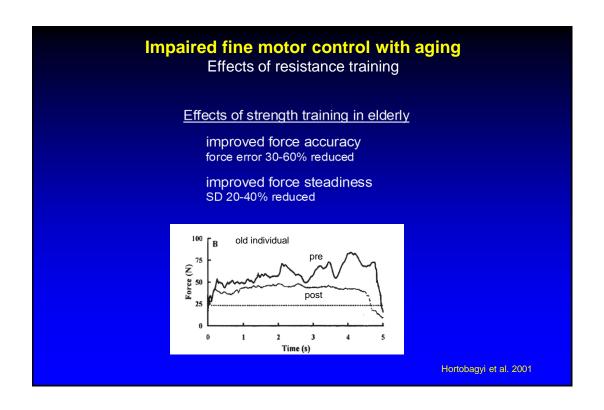
Potential mechanisms: age related changes in

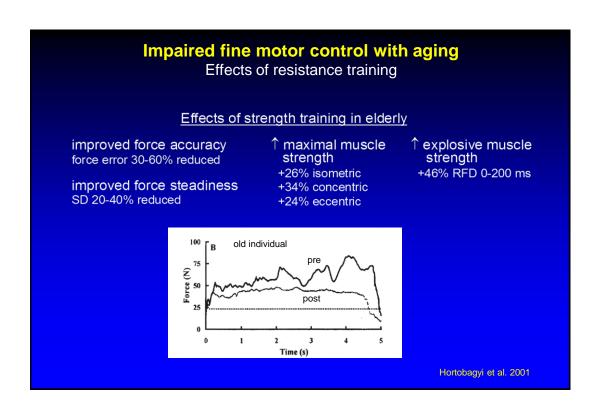
- MU size and firing rate variability Tracy & Enoka 2002, Barry & Enoka 2007
- MU synchronization Patten & Kamen 1996
- Antagonist coactivation Enoka 1997



tracking of 25-N target force during 5-sec slow-speed eccentric quadriceps contraction (15°/s) post 10 familiarization trials

Hortobagyi et al. 2001



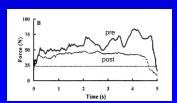


Impaired fine motor control with aging

Effects of resistance training

Effects of resistance training in elderly

- ▼ Improved force steadiness reduced SD(force)
- Improved force accuracy
- = Improved fine motor control



Hortobagyi et al, J Gerontol 56A 2001 Tracy, Enoka et al, JAP 96, 2004 Tracy & Enoka, MSSE 38, 2006

SUMMARY Effects of strength/power training on neuromuscular function and muscle size in the elderly



SUMMARY Effects of strength/power training on neuromuscular function and muscle size in the elderly ↑ dynamic muscle strength, ↑ isometric muscle strength Frontera 1988, Fiatarone 1990, Häkkinen 1998, Harridge 1999, Suetta 2004, Beyer 2007 Strength and Power ↑ muscle power Beyer 2007, De Vos 2005, Caserotti 2008 properties ↑ rapid force capacity (rate of force development: RFD) Häkkinen 1995 1998 2001, Hortobagyi 2001, Suetta 2004, Barry 2005, Caserotti 2008 ↑ EMG amplitude and rate of EMG rise Häkkinen 1995 1998 2001, Suetta 2004, Barry 2005 **Neural** ↑ maximal motor neuron firing frequency factors Patten 1999, Kamen & Knight 2004, Christie & Kamen 2010 improved force steadiness, enhanced fine motor control Hortobagyi 2001, Tracy 2004, Tracy & Enoka 2006 ↑ single muscle fiber CSA, ↑ whole muscle CSA Frontera 1988, Häkkinen 1998, Harridge 1999, Esmarck 2003, Kryger & Andersen 2007, Suetta 2004 2008 Muscular myogenic satellite cell activation factors MacKey 2007, Petrella 2008

Effects of aging on muscle and neural function - influence of training

↑ muscle fiber pennation angle, ↑ tendon stiffness Reeves 2003, Reeves 2006, Suetta 2008

OVERALL CONLUSION

The age-related loss in muscle mass and the concurrent decrease in maximal muscle strength, rapid force capacity (RFD) and power can be slowed or reversed by training (strength training!)

Likewise, the age-related impairment in neural function can be effectively compensated by training (strength training)







!! ALSO the case in frail elderly patients !!

OVERALL EFFECT OF STRENGTH/POWER TRAINING IN THE ELDERLY?



Strength/Power TRAINING



Adaptive changes in muscle size and neuromuscular function



improved function in ADL

(activities of daily living)

Aagaard, Suetta, Caserotti, et al, Scand J Med Sci Sports 2010

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Institute of Sports Science and Clinical Biomechanics, University of Southern Denmark;

Institute of Sports Medicine Copenhagen, University of Copenhagen







