#ExcemedMS

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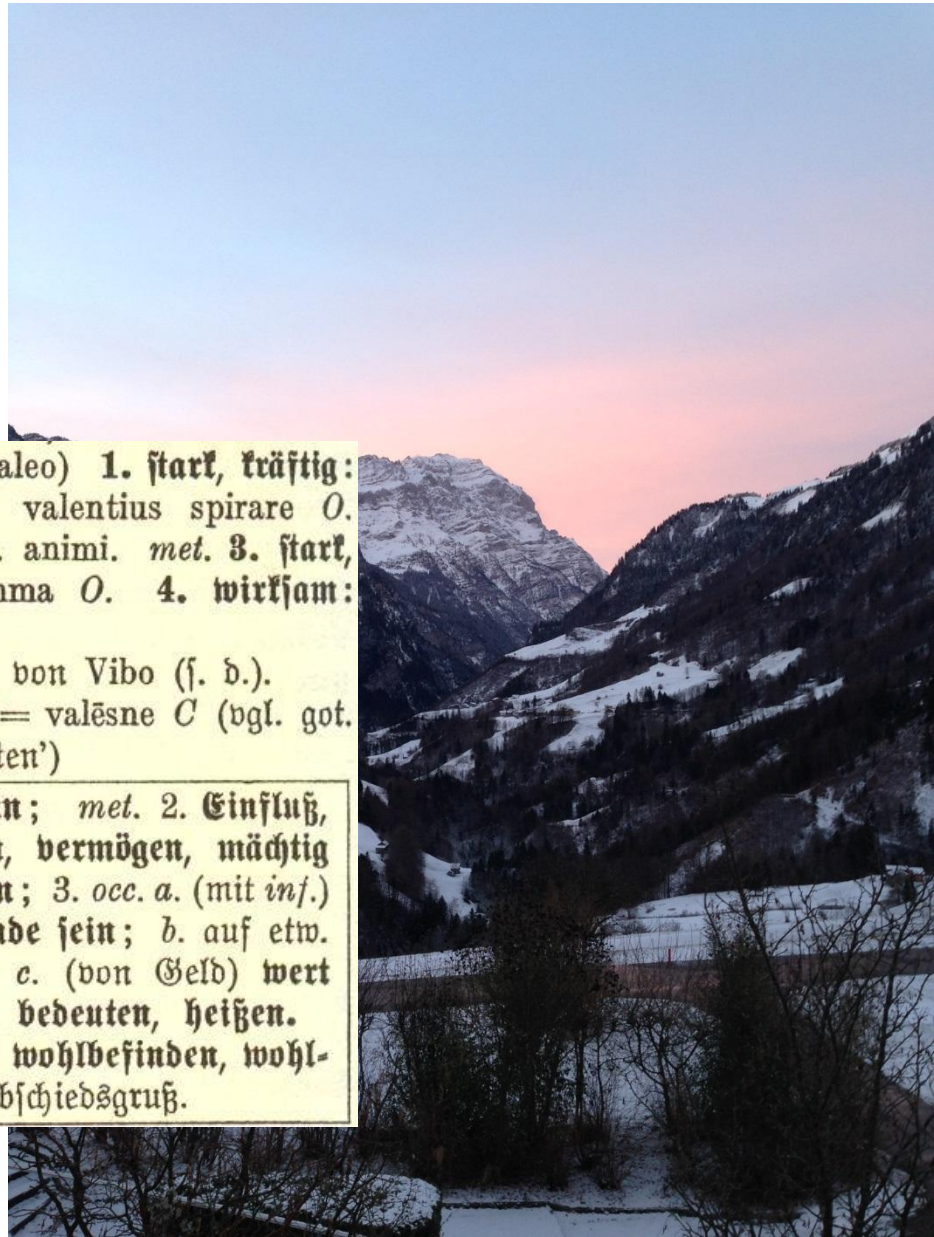
Declared receipt of honoraria or consultation fee from DMC Fingolimod studies. He declared to be member of a company advisor board, board of directors or other similar group: DMC Fingolimod studies

Neurorehabilitation – applied neuroplasticity

KLINIKEN VALENS



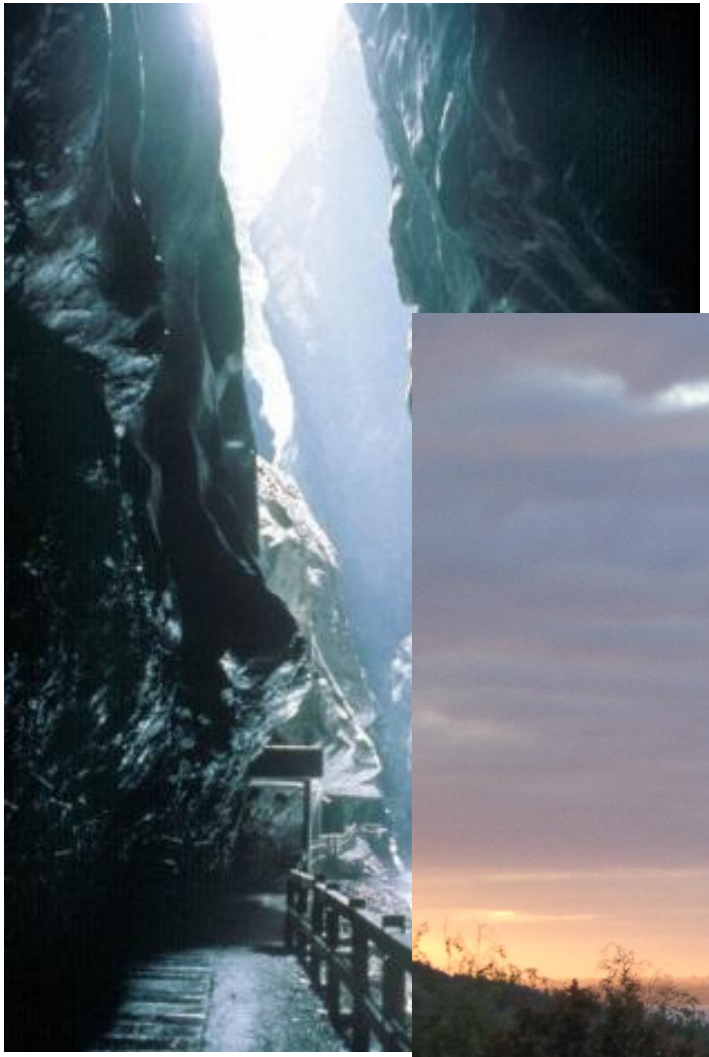
valēns, entis, *adv.* **enter** (valeo) **1. ſtark, kräftig:** bestia, iuvenis *O*; *met.* valentius spirare *O.* **2. geſund, wohlauf**; *met.* animi. *met.* **3. ſtark, mächtig**: opibus *N*, flamma *O.* **4. wirkſam:** causae *O*, carmina *H.*

Valentīnī, ōrum, *m.* Einw. von Vibo (ſ. d.).

valeō 2. uī, itūrus, valēn' = valēsne *C* (vgl. got. waldan, ahd. waltan 'walten')

I. 1. **ſtark, kräftig ſein**; *met.* 2. **Einfluß, Macht haben, ausrichten, vermögen, mächtig ſein, gelten, Geltung haben**; 3. *occ. a.* (mit *inf.*) **können, vermögen, imſtande ſein**; *b.* auf etw. **abzielen, ſich beziehen**; *c.* (von Geld) **wert ſein**; *d.* (von Wörtern) **bedeuten, heißen.**

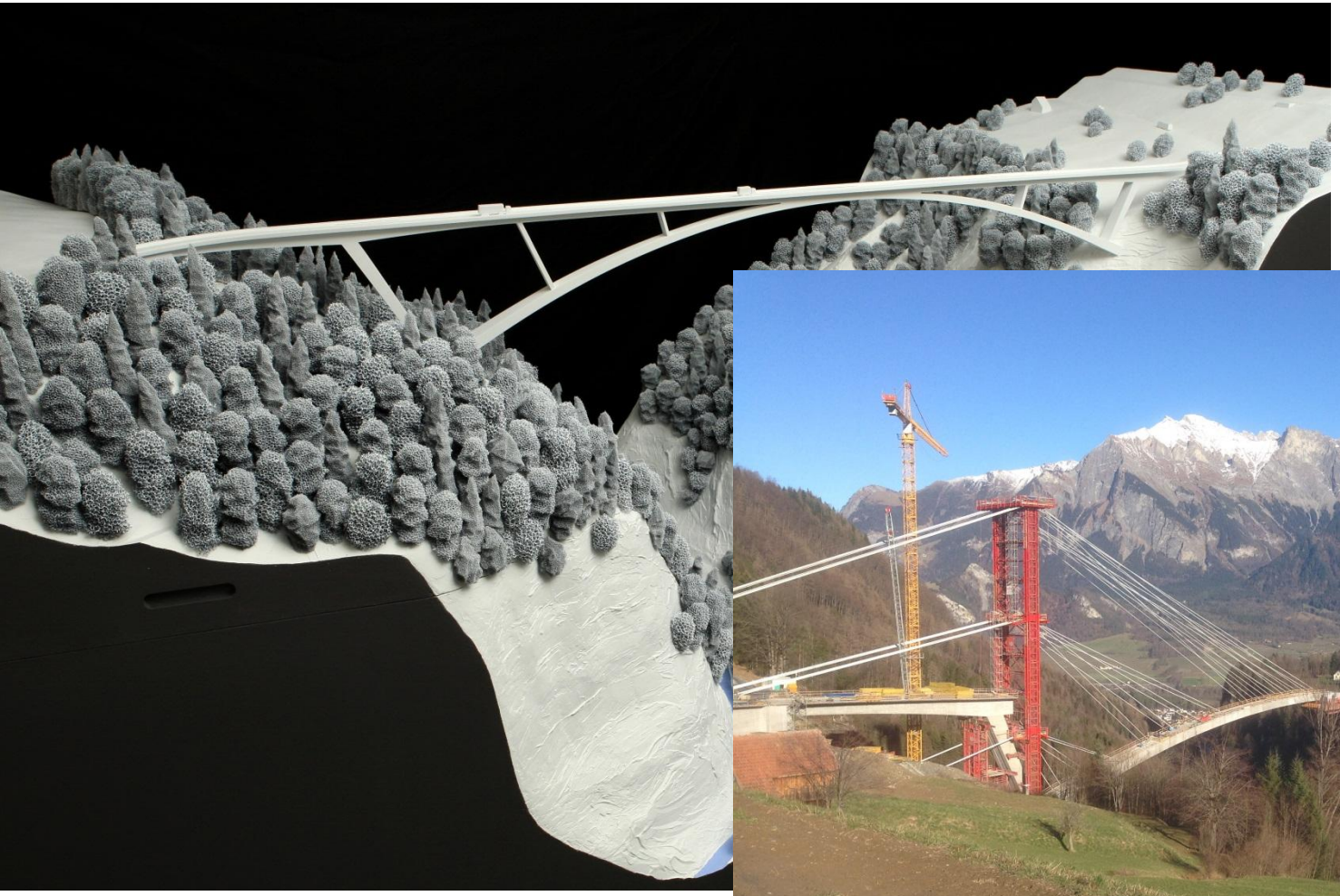
II. 1. **geſund ſein, ſich wohlbefinden, wohlauf ſein**; 2. **valē** als Abſchiedsgruß.



Quintessence of Happiness:
Not to live FROM but FOR something…
It‘s an attitude

No future can replace what has been missed in the present

Albert Schweitzer



Resilience

Dimensions of Resilience

- Fitness and stamina
- Nutrition for energy
- Rest and recovery

- Calming and focusing
- Impulse control
- Emotional regulation
- Positive emotion
- Realistic optimism

- Self-belief
- Outlook & perspective
- Thinking traps
- Sustained focus
- Causal analysis
- Control controllables

- Values and beliefs
- Empathy
- Reaching out

J Neurol (2000) 247 : 200–205

ORIGINAL COMMUNICATION

Jürg Kesselring

Constantin von Monakow's formative years in Pfäfers

Received: 25 May 1999
Received in revised form: 25 August 1999
Accepted: 16 November 1999

Dedicated to Prof. Konrad Akert,

Abstract Constantin von Monakow was the first professor of neurology in Switzerland and founder of the Swiss Neurological Society and of the *Swiss Archives of Neurology and Psychiatry*. He gained worldwide reputation as a neuroscientist mainly pathological comparisons during his early years, which he spent as assistant physician in the psychiatric clinic at St. Pirminsberg in Pfäfers, Canton St. Gallen, Switzerland from 1878 to 1885.

СТРАНИЦЫ ИСТОРИИ

Константин фон Монаков — русский основатель Швейцарского неврологического общества

Ю. КЕССЕЛЬРИНГ

Konstantin von Monakov — a Russian founder of the Switzerland Neurological Society

Y. KESSELRING

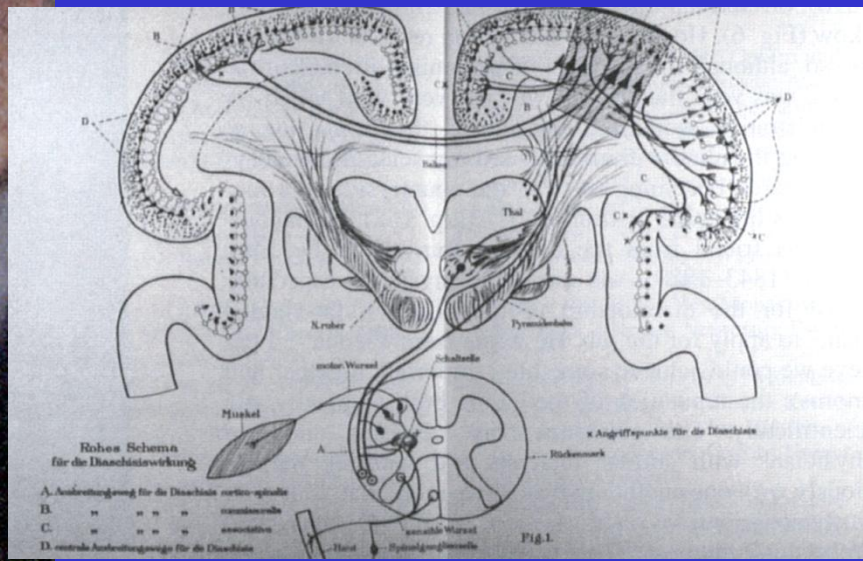
Отдел неврологии, центр реабилитации. Валенс, Швейцария

Известный швейцарский невролог Константин фон Монаков (Constantin von Monakow) родился 4 ноября 1853 г. в Вологде. Вместе с родителями он переехал в Швейцарию в 1866 г., где после окончания гимназии против воли отца занялся медициной. Уже во время обучения медицине он работал ассистентом в психиатрической клинике "Burgholzli", которой тогда руководил доктор Э. Хитциг (E. Hitzig, 1838—1907 гг.). Именно в этой клинике он стал проявлять интерес к строению мозга в норме и при патологии [2]. Однако его карьера не отличалась прямолинейностью. В связи с необходимостью укрепления своего материального положения он несколько лет работал корабельным врачом, сумев при этом не только расширить знания в области практической медицины, но и продолжить научную работу. В 1877 г. К. Монаков был приглашен участвовать в конкурсе на долж-

поведение двух кроликов, у которых в периоде новорожденности были удалены затылочные доли мозга. При последующем патологоанатомическом исследовании он обнаружил дегенеративные изменения в наружных коленчатых ядрах, тогда как остальные участки таламуса были интактны, что подтвердило его клинические наблюдения и данные хирургических операций [6, 7]. Эти исследования легли в основу его фундаментальных работ по изучению функциональных связей между корой и таламусом (следует иметь в виду, что наличие таких связей в то время отрицалось большинством исследователей). Описанные К. Монаковым в мозге кроликов связи затем были выявлены в мозге кошки и человека. К. Монакова можно считать основоположником современного представления о строении зрительных и мозжечковых путей.

Recovery mechanisms: diaschisis (von Monakow 1914)

A process in which neurons function abnormally because influences necessary to their normal functions have been removed by damage to neurons to which they have been connected



Neuroplasticity – the flexible brain

Unser Gehirn ist ein
plastisches System, d
sich zum Lerne
evolutioniert

Lernfähigke ns hohe
Alte

Use it or lose it !

Legal basis for neurorehabilitation in Switzerland

KVG Art. 32

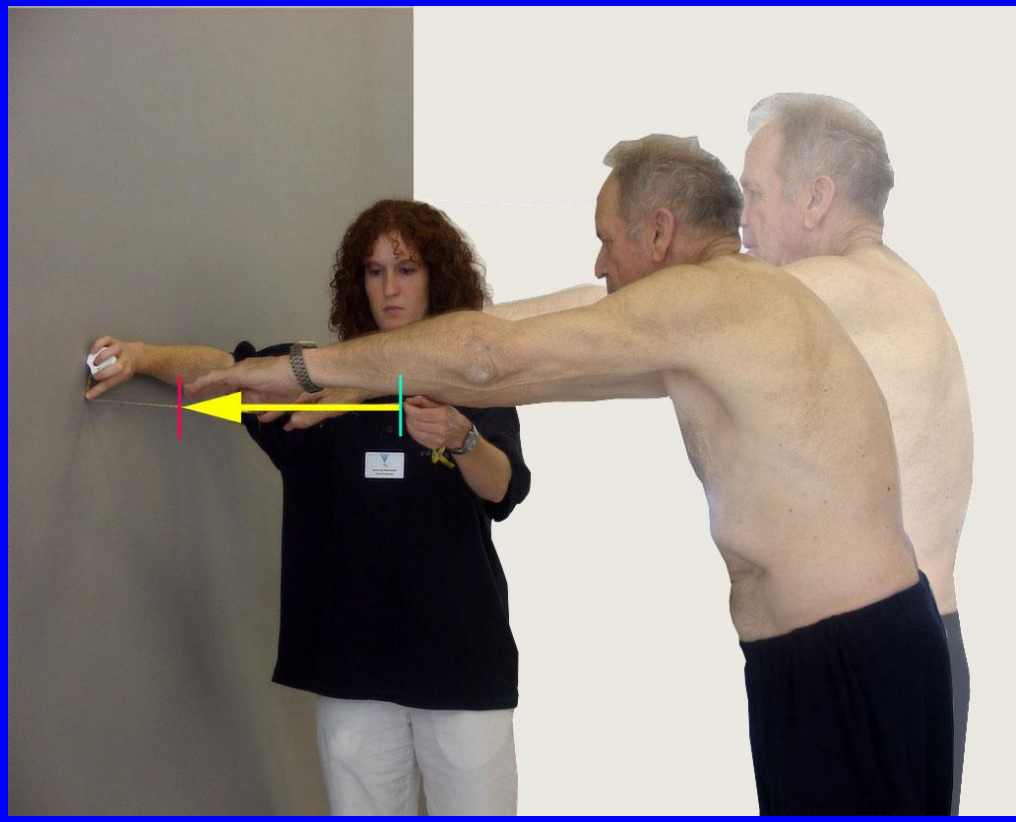
Medical applications must be

effective

appropriate

economic

effectiveness must be determined and proven by ***scientific methods***

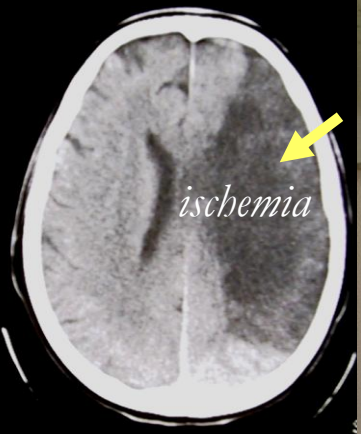


Neurorehabilitation Valens (2010 - 14)

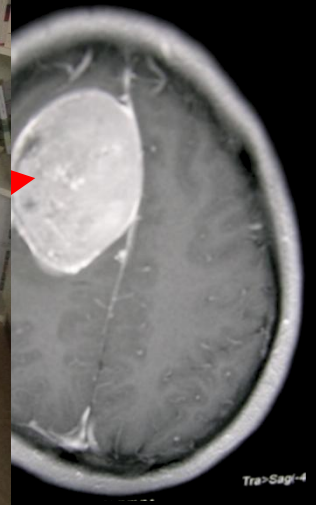
[N=2452 – 3113 (+15%); stationär (+36%), ambulant (+25%)]

stroke 519-595 (+15%))

Multiple Sclerosis 493-576 (+17%)

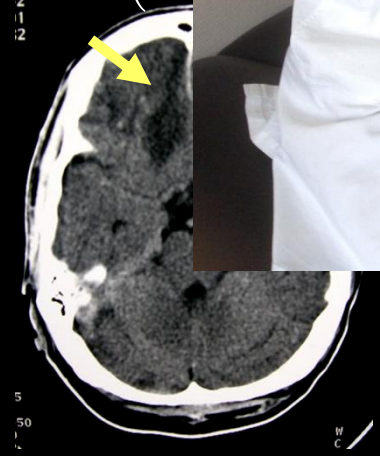


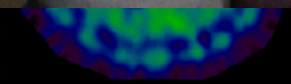
59-80 (+33%)



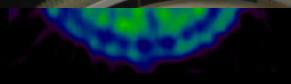
Trauma+ ot

197-309 (+5





Normal

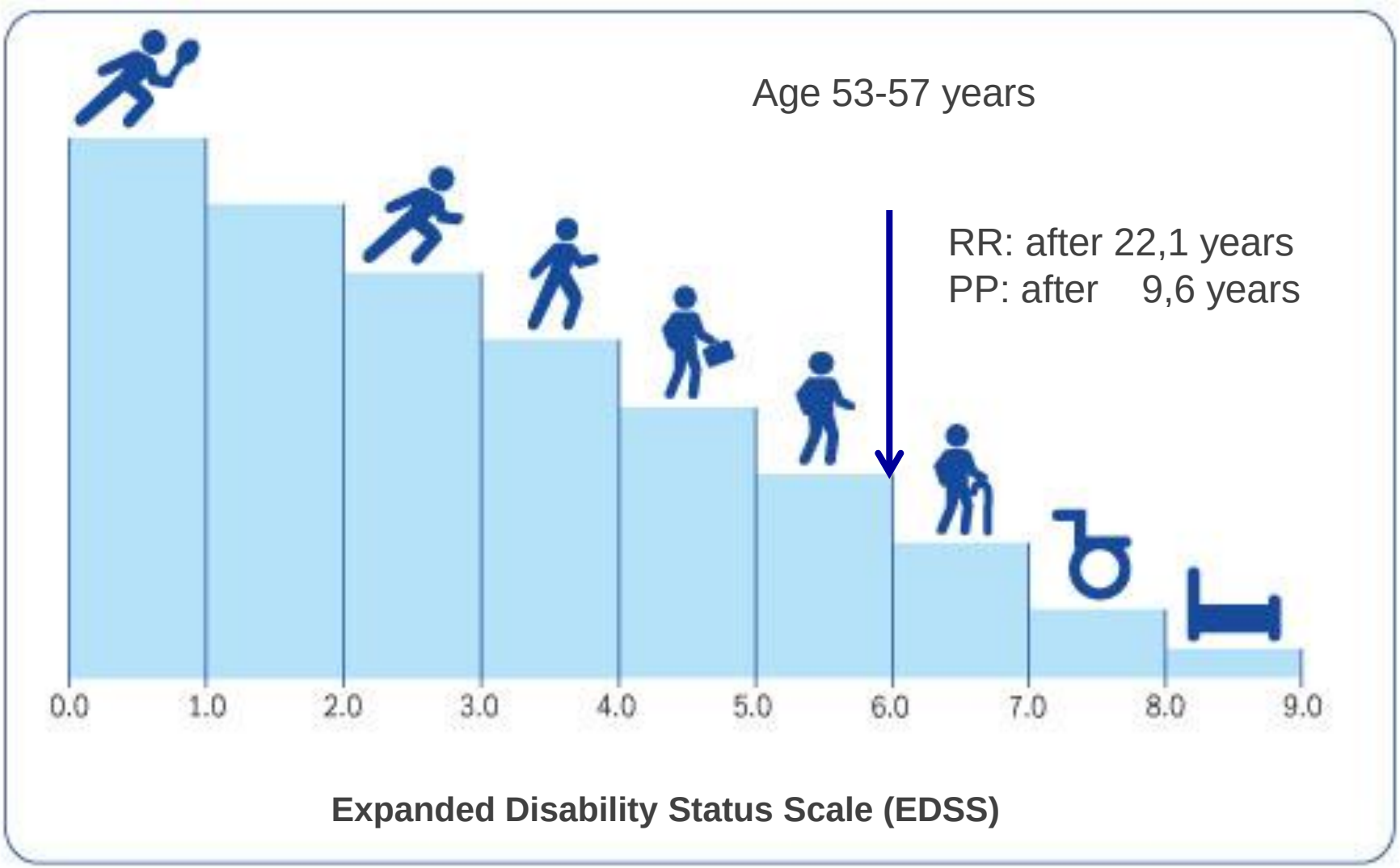


Parkinson's Disease

Epilepsy 83-112

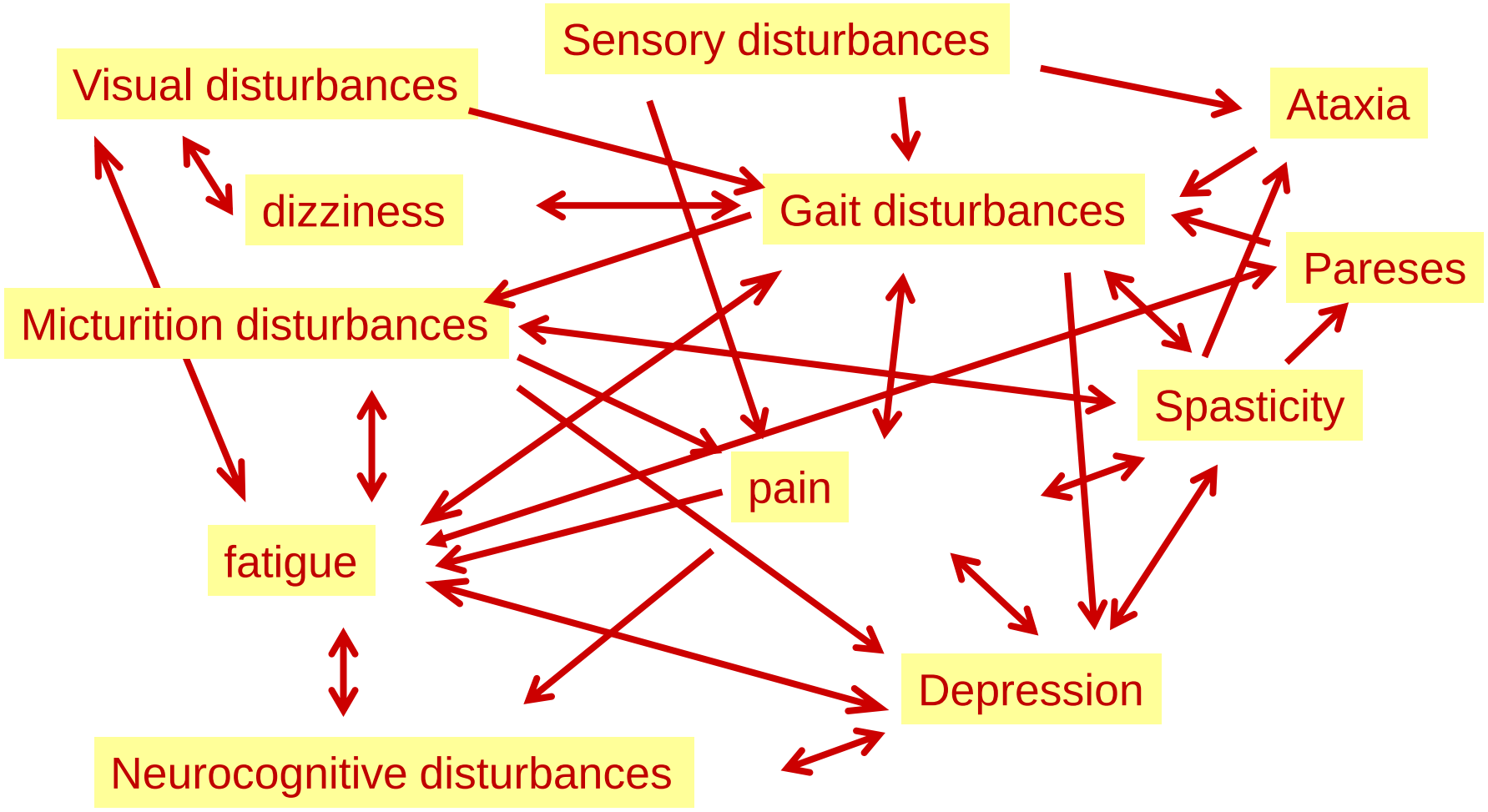
Peripheral 114-167

Multiple Sclerosis: longterm disease course



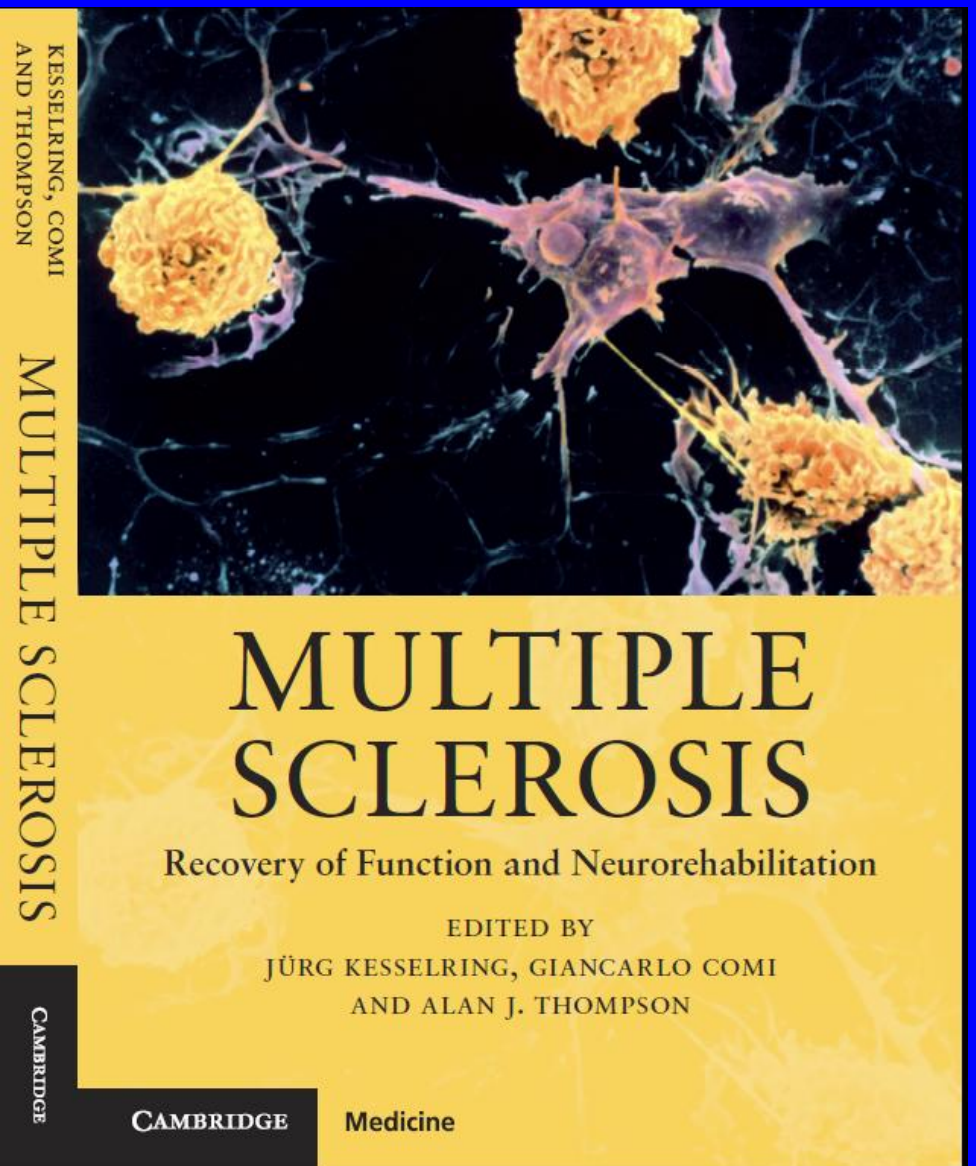
Harding & al, J Neurol Neurosurg Psych 2014

Multifocal: complex symptomatology



➔ **Complex interferences**

Rehabilitation: management of persons with chronic illness



- Recurrent planning process
- Problem assessment
- Goal setting
- Identification of appropriate treatment regimens

⇒ Fundamentally an education-training program designed to enable (empower) the person with impairments to maintain (and regain) life activities

Kesselring J, Beer S Symptomatic therapy and neurorehabilitation in Multiple Sclerosis The Lancet Neurology 2005; 4: 643 – 652

Beer S, Khan F, Kesselring J: J Neurol 2012

EXCEMED - Excellence in Medical Education <no-reply=excemed.org@mail97.suw15.mcsv.net>

Virtual courses from EXCEMED neurology

Advanced neurorehabilitation in MS

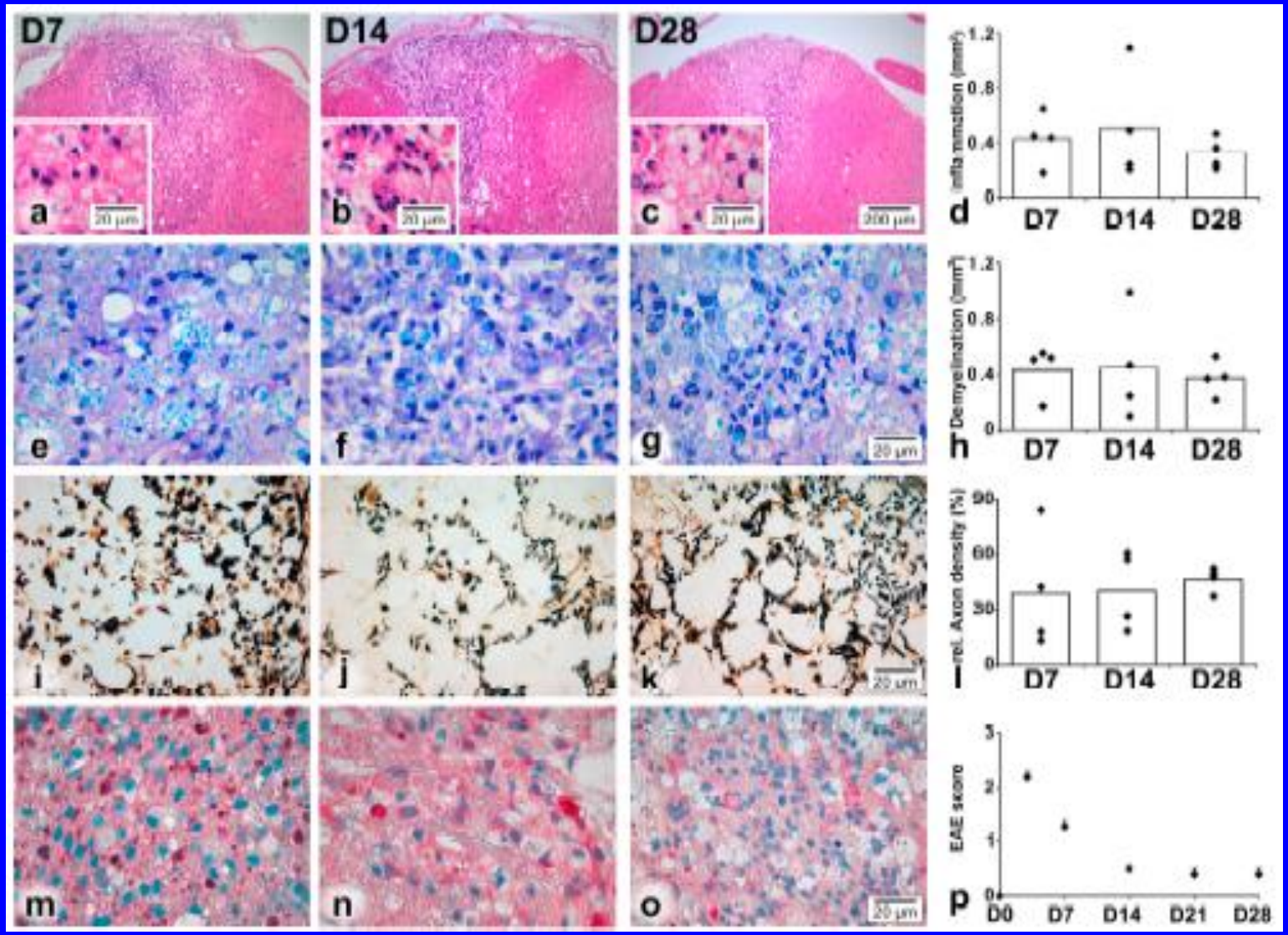
This Virtual Practice teaching course is designed for neurologists, physiotherapists and physiatrists willing to learn about the **most advanced neurorehabilitation techniques in multiple sclerosis**. Motor impairment, together with balance loss are the most frequent symptoms reported by patients, as well as the main causes of walking disability in MS. **This course focuses on the metrics for the assessment of motor and balance functioning, while also providing some practical clues on how to handle these issues through rehabilitation**. **Go there now.**

Neuroplasticity in MS: functional adaptations

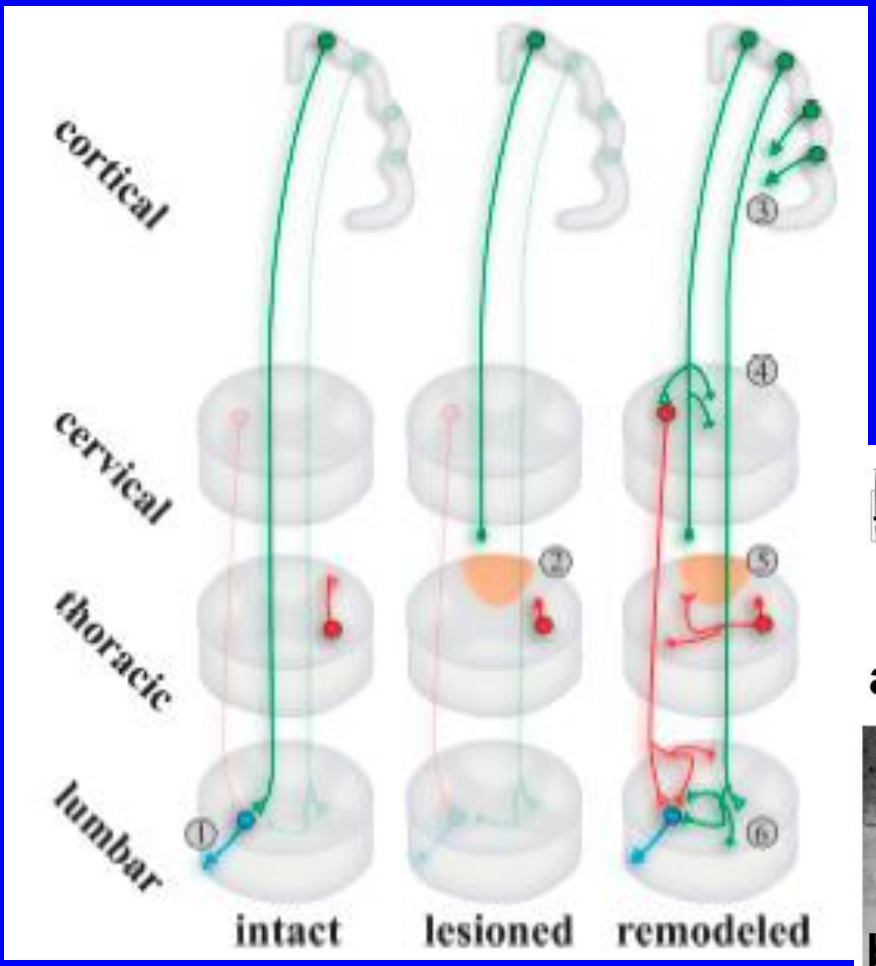
- Cellular level
  - Axonal sprouting (increased arborisation of neurones)
  - Changes of synaptic stability
  - Reorganisation of synapses
- Tissue level
  - Resorption of oedema
  - Re-arrangement of Na-channels on axons
  - Re-myelination
- System level: Takeover of functions via
  - contralateral homologous cortex
  - enlargement of representation zones
- Behaviour level
  - novel motor and cognitive strategies

Kesselring J: Neuroplastizität bei MS
In: Henze T (Hrsg): Symptomatische Therapie der Multiplen Sklerose
Georg Thieme Verlag Stuttgart, 2005, p. 163

Highly plastic response of motor system to single neuroinflammatory lesion

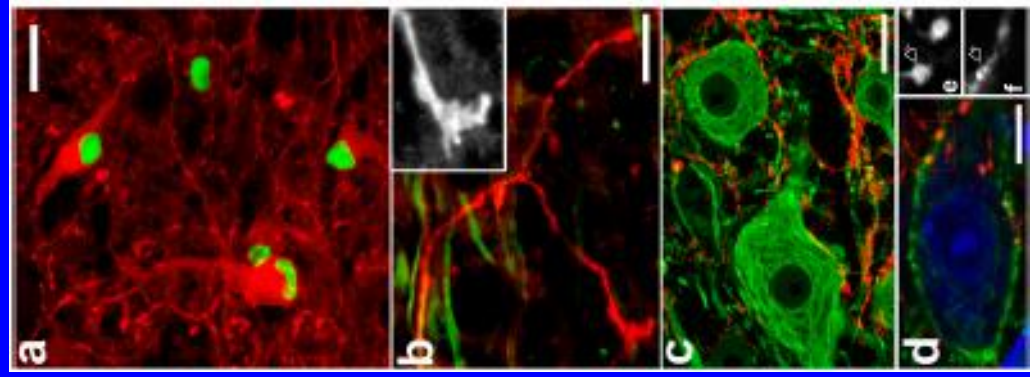


Kerschensteiner et al: Remodeling of axons contributes to recovery in an animal model of MS J Exp Med 2004; 200:1027

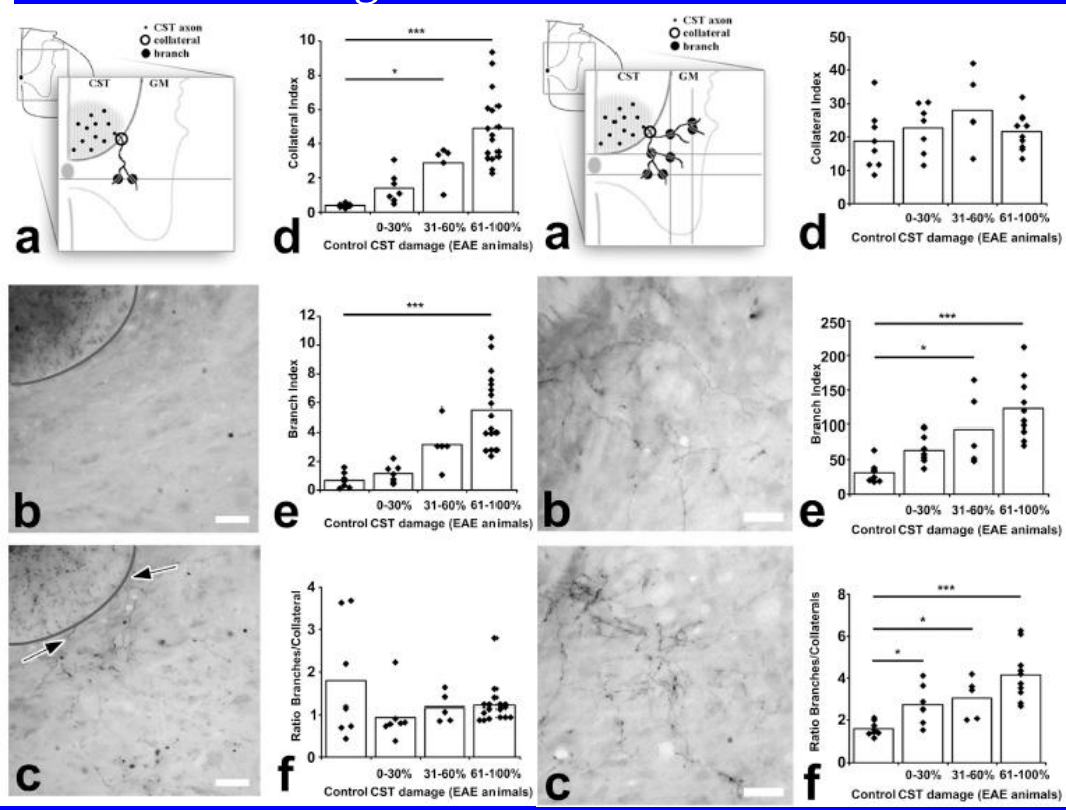


3) Remodeling of projection neurones in motor cortex

4) Behavioural tests show importance for recovery



1) Regenerative sprouting of interneurones surrounding lesion



2) „Detour circuit“ in descending corticospinal tr

above lesion below lesion

Evidence-based medicine:

Are figures really better than stories?

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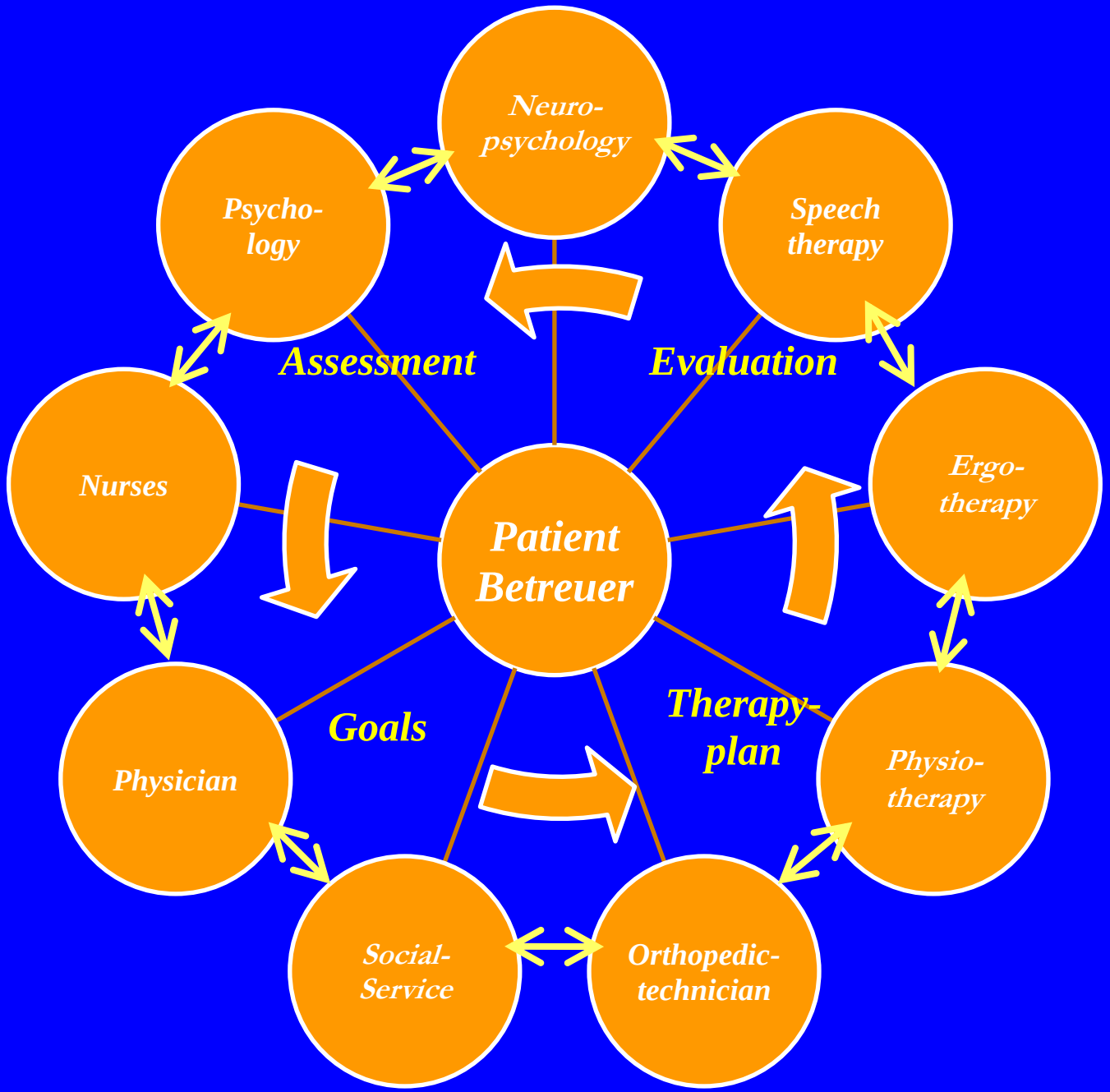
05.2003	22.06.2003	22.07.2003	22.08.2003	22.09.2003
05.2003	23.06.2003	23.07.2003	23.08.2003	23.09.2003
05.2003	24.06.2003	24.07.2003	24.08.2003	24.09.2003

Without effort you won’t get even a little fish out of the pond

Multidisciplinary Team

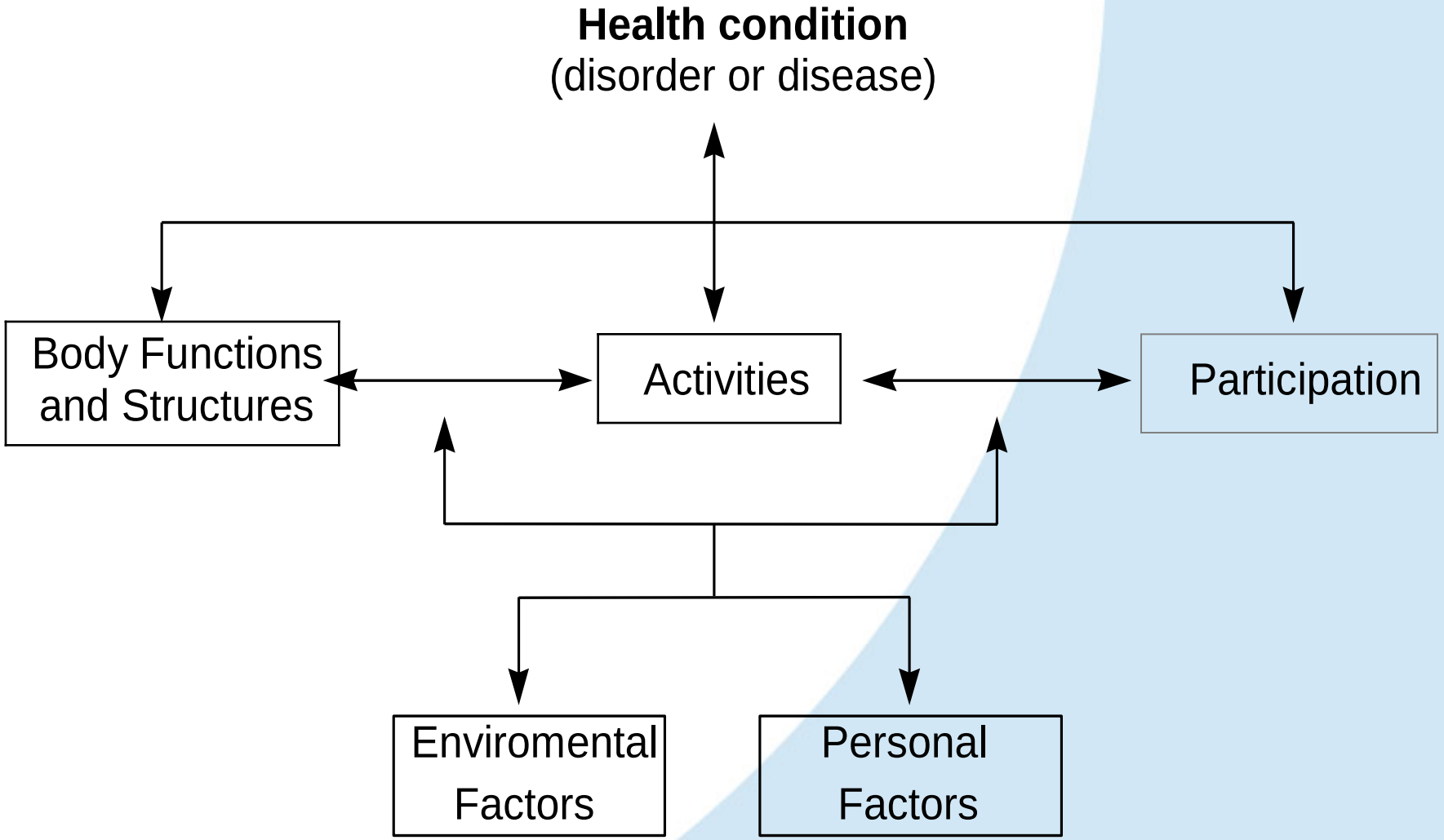
- Person with Multiple Sclerosis
- Caregiver
- Neurologist with special interest in disability, trained in rehabilitation medicine
- Nurse specialist in Neurorehabilitation
- Occupational Therapist
- Physiotherapist
- Speech Therapist (incl. swallowing)
- Neuropsychologist (incl. Driving)
- Social Worker
- Continence Advisor
- Behavioural Therapist

Neurorehabilitation



Integrated clinical care pathway

- Patients‘ descriptions of needs and goals
- Assessement: therapsists‘ functional description of problems (mobility, self-care ADL, communication, daily occupations, social interactions)
- Interdisciplinary setting of common goals
  - clear and meaningful
  - realistically achievable
  - measurable
- Assessement of goal achievements (timed)



The current framework of functioning and disability –
the WHO International Classification of Functioning, Disability and Health (ICF)

ICF Consensus Conference on Core Sets for MS 02.05.2008 – 04.05.2008

KLINIK VALENS
REHABILITATIONSZENTRUM

ICF International Classification of Functioning, Disability and Health

Core sets

b1
b130
b134
b152
b180
b1801
•
•
•
s299
s710
s720
s730
s73001
s73011
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1454

Kesselring J, Coenen M, Cieza A, Thompson A, Kostanjsek N, Stucki G: Developing the ICF Core Sets for multiple sclerosis to specify functioning.Mult Scler. 2008;14:252-4

Holper L, Coenen M, Weise A, Stucki G, Cieza A, Kesselring J:Characterizing functioning in MS using the ICF J Neurol 2010; 257: 103-113

Therapeutic strategies

Sensori-motor

active motor training
sensory stimulation
functional electrostimulation
„Constraint-induced training“ (CIT)
Tonusregulation
Strength-training/aerobic training

Gait

conventional, treadmill, Lokomat

Cognition

Memory- /Attentional training
Perception: neglect-training,
visual compensation (Nova-Vision)

Speech

Speech therapy

Eating/swallowing

Swallowing assessement and therapy

Bladder & bowel function

Pelvic floor training

Activities of daily living (ADLs)

Self care
Orientation training (AOT)

Technical aids

Instruction of patients/careres

Social service/reintegration

Evaluating Neurorehabilitation: Problems

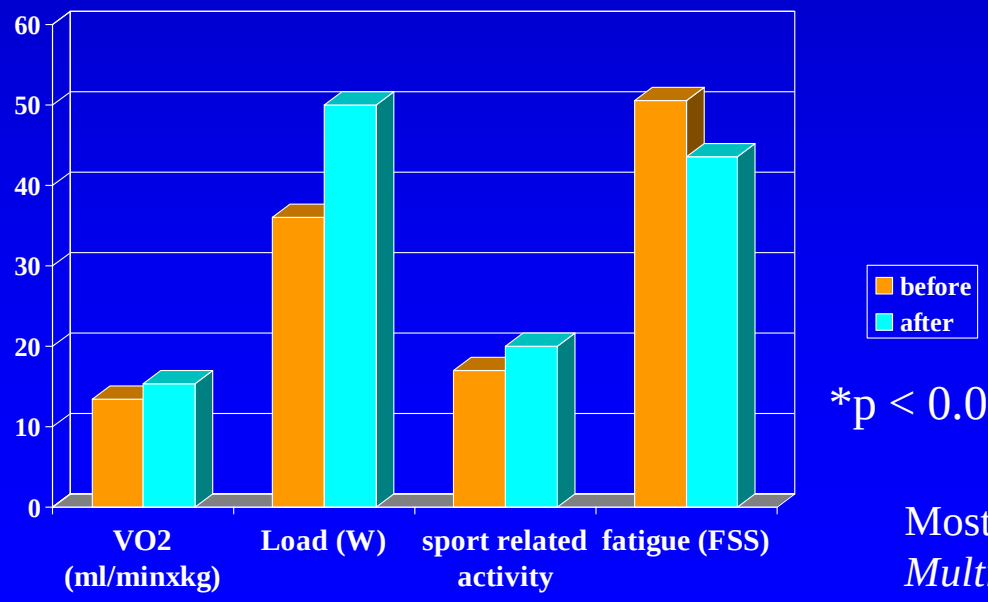
- Standardization of input
  e.g. location/duration/intensity
- Reluctance to use control group
- Difficulty with blinding
- Lack of consensus on outcome (Impairment, Disability and handicap, Quality of life, Goal achievement, Coping skills, Self efficacy
- Variable choice of goals and measures (Clinically useful; Scientifically sound [reliable, valid and responsive], Acceptable [appropriate to sample])

Kesselring J: Neurorehabilitation in multiple sclerosis – what is the evidence-base? J Neurol 2004 ; 251, Suppl 4: iv25 - iv29 ;

Beer S, Khan F, Kesselring J J Neurol 2012, Textbook of Neurorehabilitation, 2nd edition, Cambridge University Press 2014

Effects of a short term exercise training program on aerobic fitness, fatigue, health perception and activity level of subjects with multiple sclerosis.

- 37 MS patients, 5*30 min sessions per week of bicycle exercise with individualised intensity. Graded maximal exercise test with measurement of gas exchange and a lung function test before and after 4 weeks of aerobic exercise training,



*p < 0.05

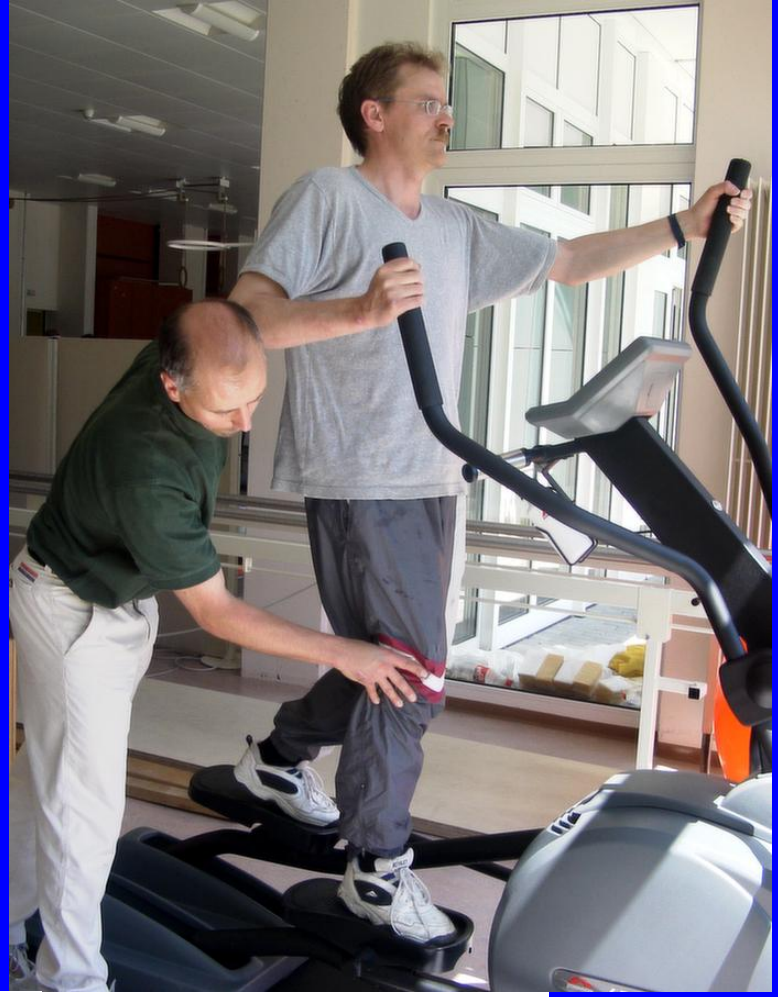
- Results:
  - significant rightward placement of the aerobic threshold (VO_2 +13%; work rate +11%)
  - improvement of health perception (vitality +46%; social interaction +36%)
  - increase of activity level (+17%)
  - tendency to less fatigue.

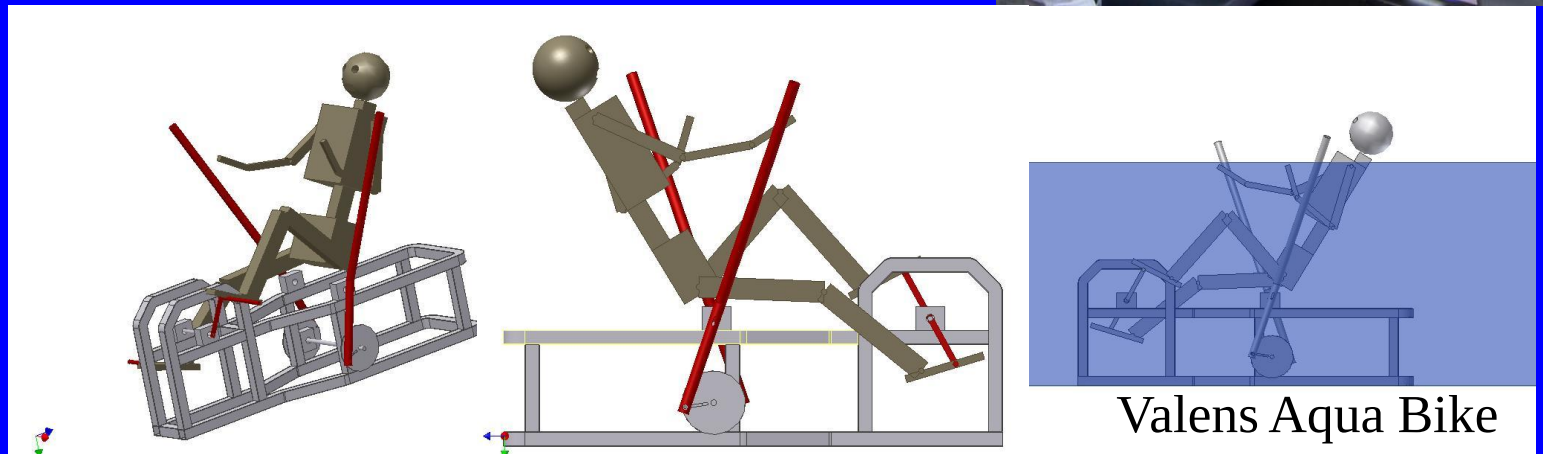
Mostert S, Kesselring J
Multiple Sclerosis 2002;8:163-170

Arguments for physical activity in MS

- positive effects of aerobic training (Morbidity of CHD↓, Mortality↓, Anxiety↓, Cholesterol↓, Blood pressure↓, Blood sugar↓ Mood↑, Wellbeing↑, Mental performance↑, Bone mineralisation↑)

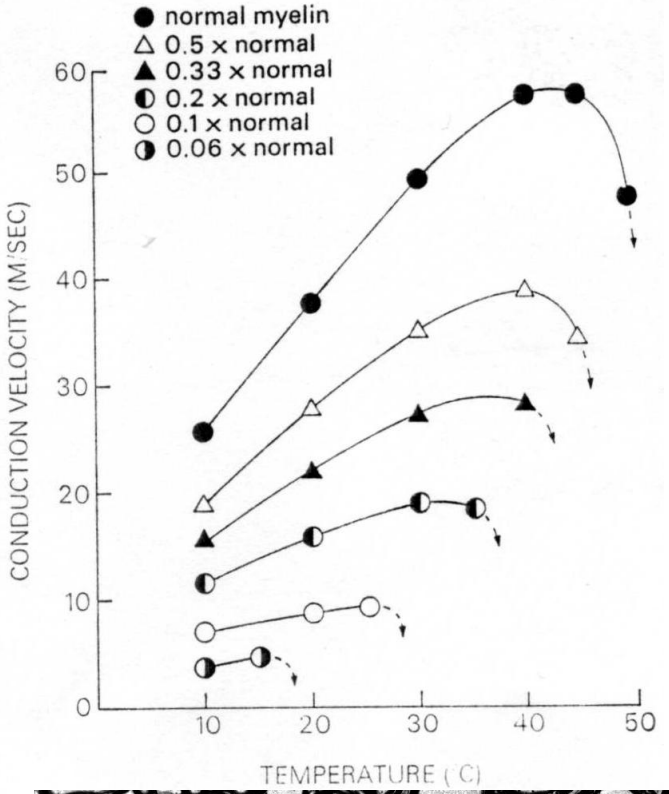
- Good functional reserves required in a chronic progressive disorder leading potentially to relapsing functional impairments
- Clinical findings often compatible with chronic deconditioning
- Training is possible without danger

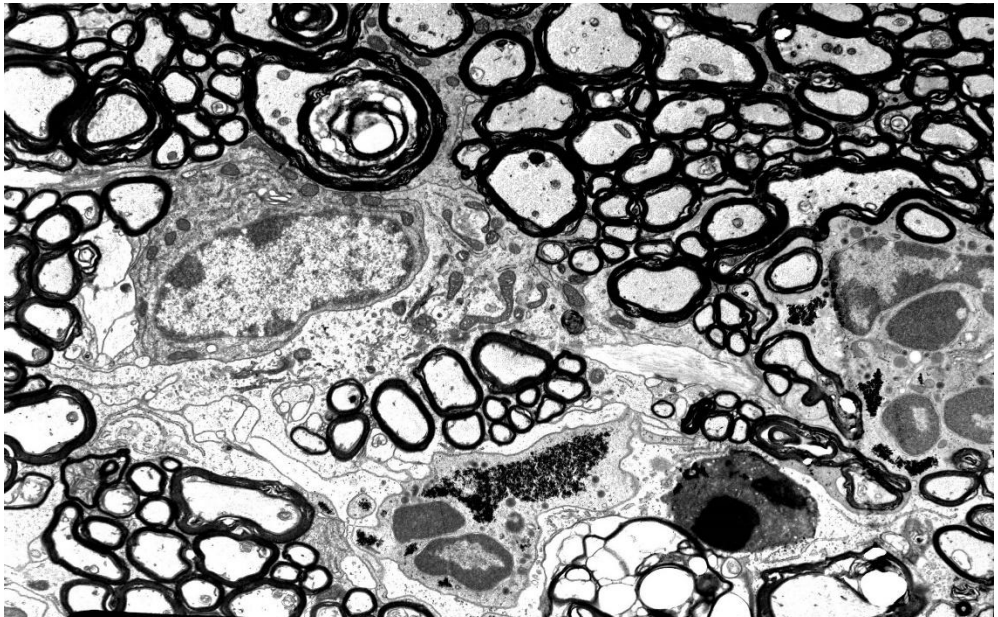




Valens Aqua Bike

Cooling





A.M.Humm, S.Beer, J.Kool, M.R.Magistris, C.W.Hess, J.Kesselring, K.M.Rösler
Altered central motor conduction caused by changing body temperature: A quanitfication of the Uhthoff phenomenon in multiple sclerosis. Clin Neurophysiol 2004;115:2493-501

Wilhelm Uhthoff – A Phenomenon 1853–1927

P Stützer, J Kesselring
Departement of Neurology and Neurorehabilitation

Summary

The name of Wilhelm Uhthoff is associated with several aspects of progress in neurology in the 19th and 20th Century but is best known for his contribution to the pathophysiology of transient visual disturbance . Uhthoff was born on 31 July 1853 in Klein Warin, Germany and

Int MS J 2008; 15: 90 - 93

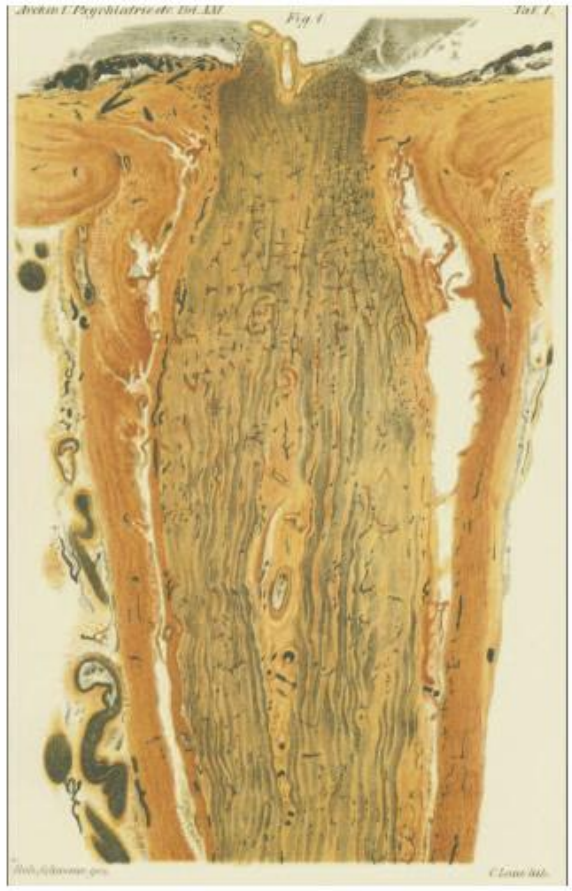
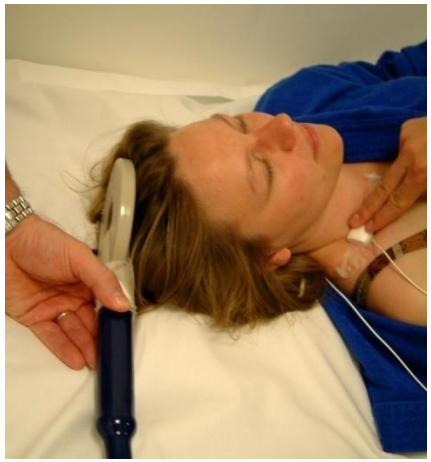
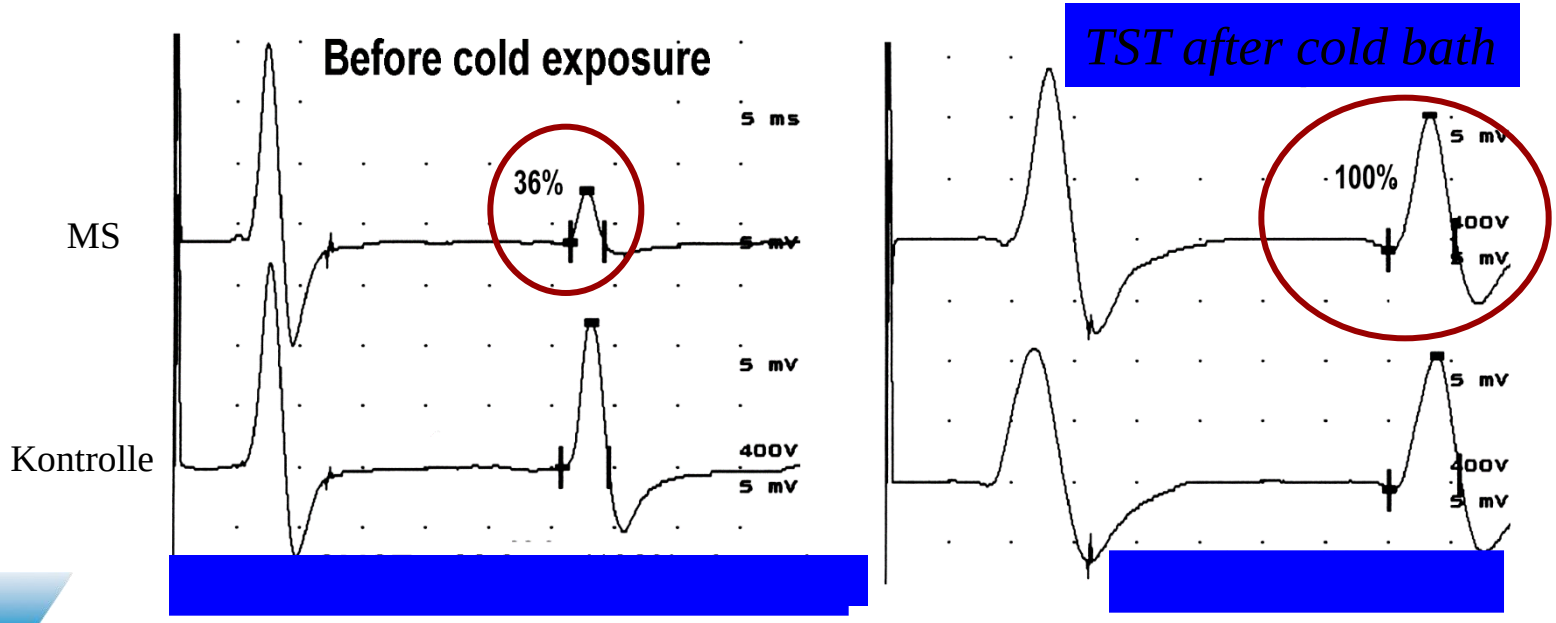


Figure 2. Sclerosis multiplex cerebri: longitudinal section across the right papilla and a ten millimetres long retrobulbar piece of optic nerve of case II (Uhthoff W.) Wigert coloration. Patchy disseminated changes. Marked shrinking of anterior parts immediately behind lamina cribrosa with marked proliferation of vessels in temporal half. Ophthalmoscopically: discrete pallor of the entire papilla.

Improvement of central motor conduction time and function after cold exposure in MS-patients



Cold bath
(15°C, 15 min)



Humm A, Beer S, Kool J, Magistris MR, Kesselring J, Rösler KM, A quantification of the Uhthoff phenomenon in multiple sclerosis Clinical Neurophysiology 2004; 115: 2493-501

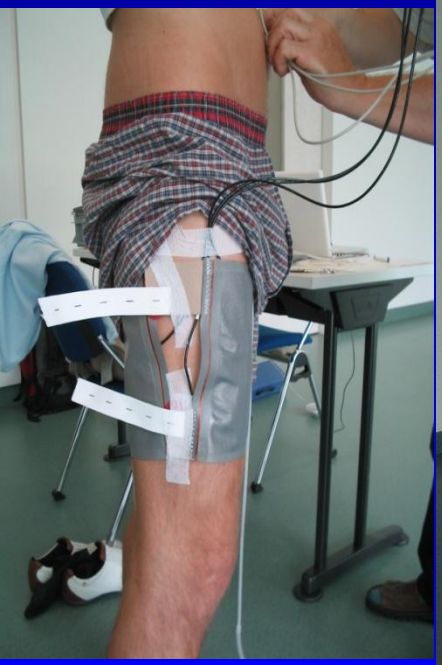
A. Meyer-Heim[1], M. Rothmaier[2], M. Weder[2], J. Kool[1], J. Kesselring[1]

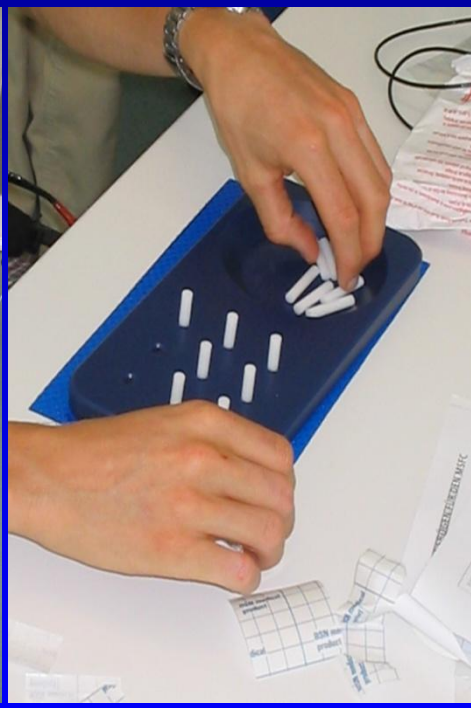
Advanced cooling - garment technology: functional improvements in thermosensitive patients with multiple sclerosis

Multiple Sclerosis 2007; 13: 1 – 6

[1]Rehabilitation Centre, Valens, Switzerland

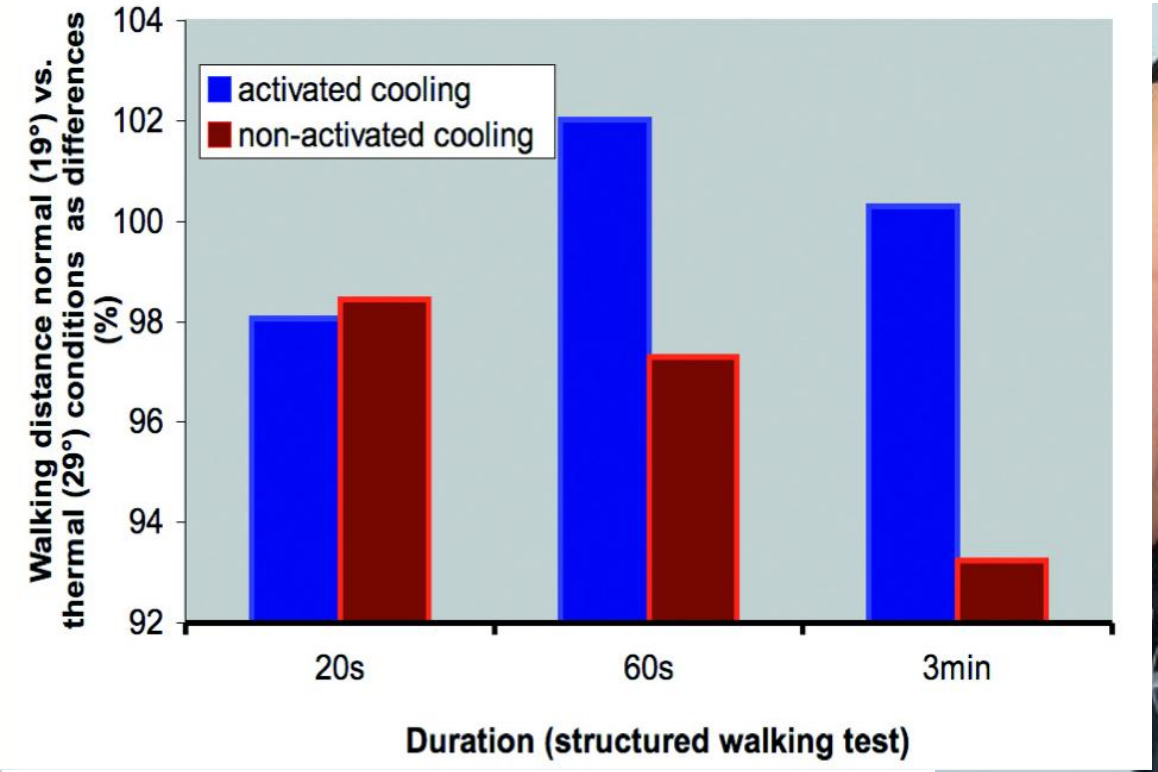
[2]EMPA (Swiss Federal Laboratories for Materials Testing and Research)

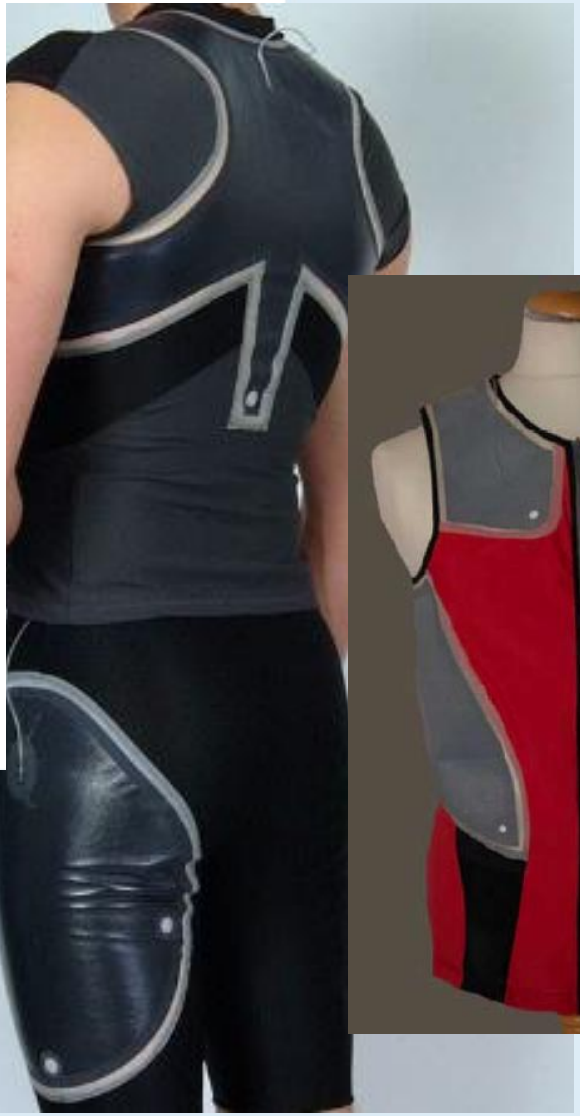


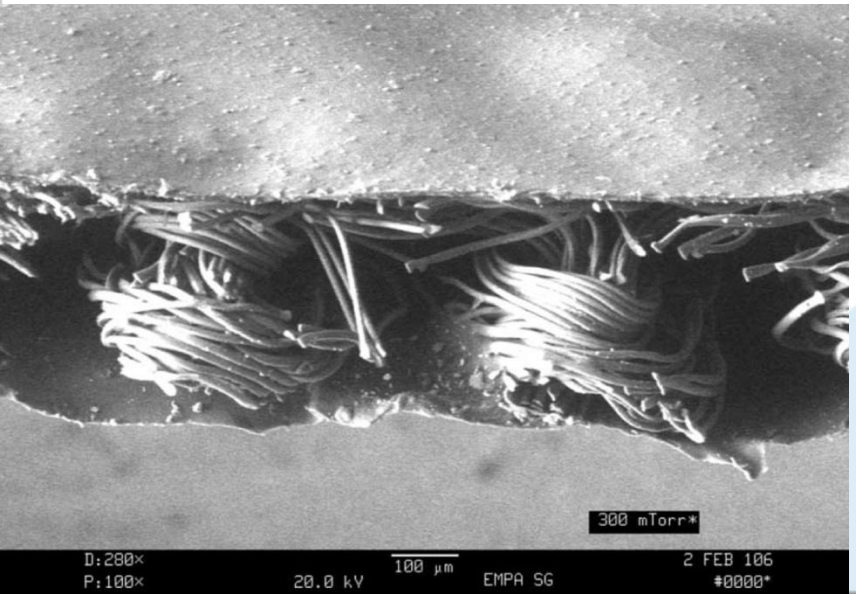


ETH/McKinsey
Innovation prize 2008

Queckenstedt Preis DMSG
17.1.2009







Cooling garment (Unico Swiss Tex) consists of a vest and shorts leading to a large cooling area. Cooling is attained by filling the membranes with water.

Robot-assisted Treadmill training (*Lokomat®*)

Beer S, Manoglou D, Kesselring J: Robot-assisted gait training in MS – a randomised controlled trial

ROBOT-ASSISTED GAIT TRAINING (RAGT) IN MS
PILOT TRIAL IN PATIENTS WITH HIGHER DISABILITIES (EDSS 6.0-7.5)

Assessment	Robot-assisted gait training (RAGT) N=14			Conventional walking training (CWT) N=15		
	baseline	3 w	p	baseline	3 w	p
20m walking velocity, m/s (mean, SD)	0.21 (0.14)	0.35 (0.29)	**0.002**	0.27 (0.16)	0.33 (0.22)	**0.021**
3 min walking distance, m (mean, SD)	77 (66)	103 (92)	**0.010**	97 (56)	109 (70)	n.s.
Strength knee extensor right (N) (mean, SD)	31 (14)	36 (17)	n.s.	33 (12)	37 (10)	n.s.
Strength knee extensor right (N) (mean, SD)	15.9 (7.5)	19.4 (7.5)	**0.006**	13.9 (7.5)	13.0 (6.0)	n.s.
Strength knee extensor left (N) (mean, SD)	13.6 (6.3)	16.9 (6.4)	**0.004**	13.6 (9.4)	14.2 (8.7)	n.s.

Higher benefit by

- reduction / adaptation of physical load
  - *preventing motor fatigue/exhaustion*
- physiological movement pattern
- more efficient training of leg muscles
- postural stability during gait training
  - *single task, reduction of fear of falling*
- enhancement of central adaptive processes?

Beer & al, Multiple Sclerosis (2008)

GAITRite® Analysis System

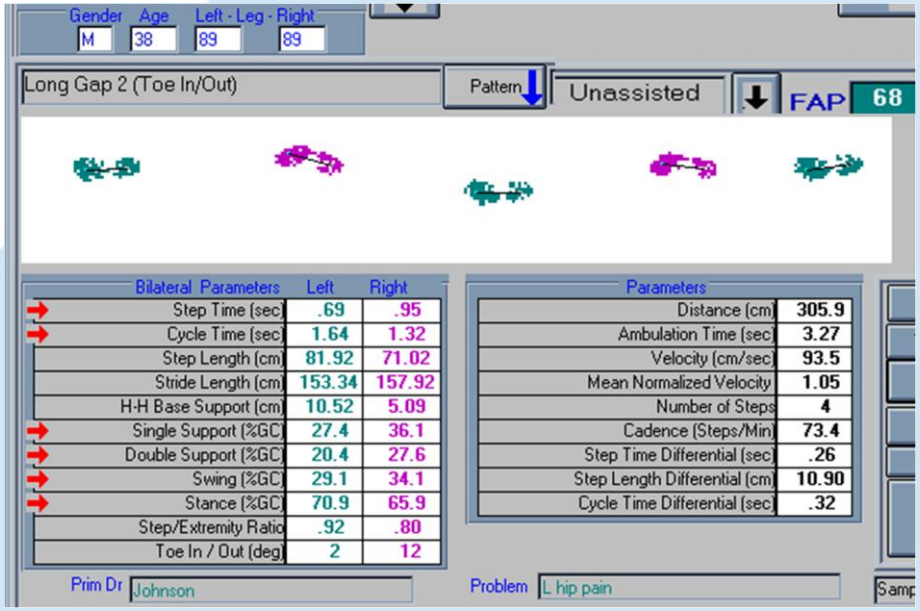
High reliability and validity compared with video-based motion analysis
(Bilney & al 2003)

Electronic walkway (10x0.9m)

- mat (active area 7.6x0.6m) with 16’128 pressure sensors
- continuous registration of temporal and spatial parameters (data sampling 80Hz, time resolution 11ms)

Data collection and processing (GAITRite Gold, Version 3.9)

•Recording and data analysis of different qualitative gait parameters

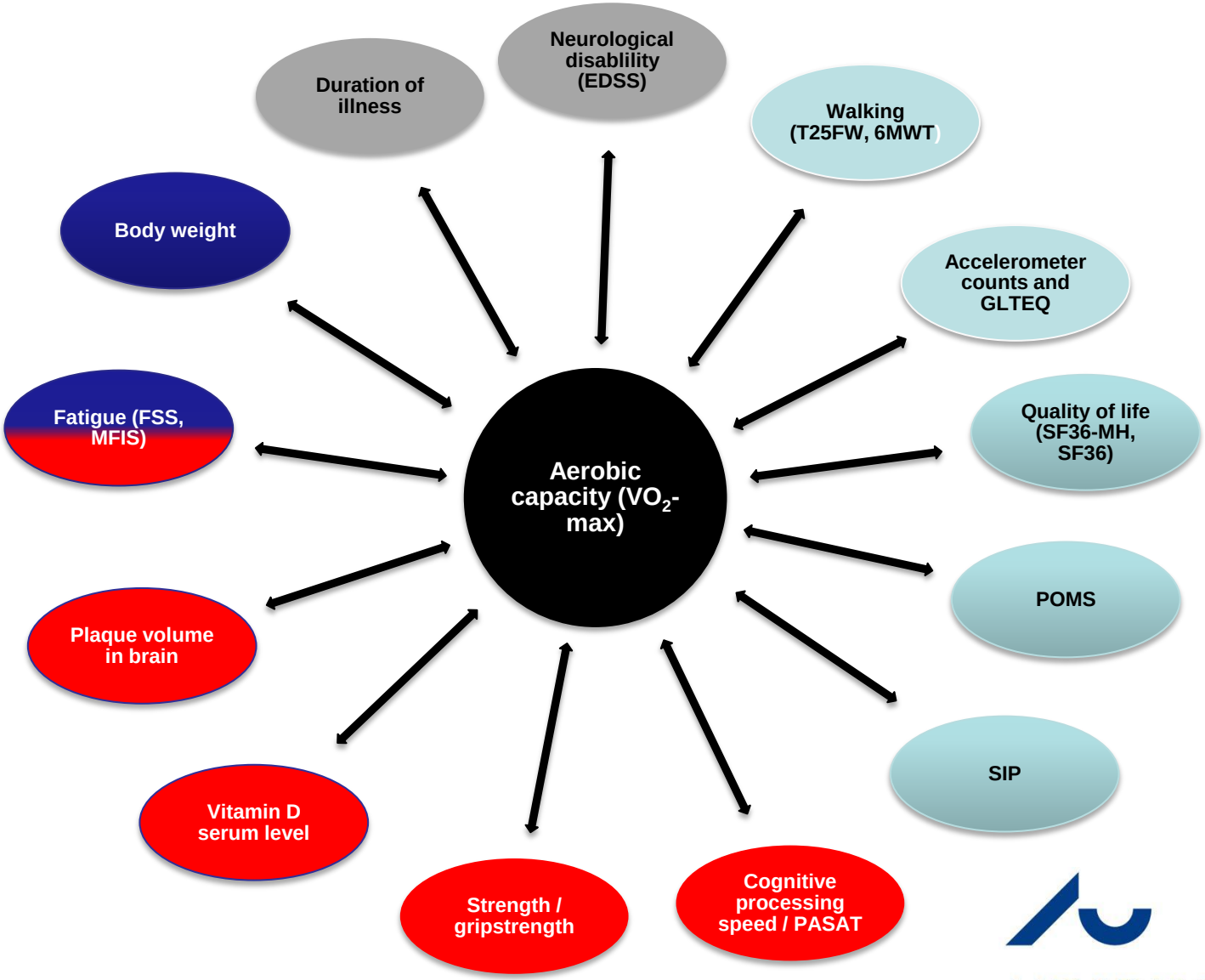


PHYSICAL TRAINING IN MS
RECOMMENDATIONS

- Endurance training / aerobic training
  - *running, rowing in patients with no or minimal disabilies*
  - *ergometric training, water training, treadmill training*
  - *starting intensitiy 50-70% VO2-Max (60-80% max. heart rate)*
  - *2-3 sessions p. week*
- Resistance training
  - *supervised by a therapist*
  - *max. 8-15x repetitions*
  - *2-4 min resting periods between exercises*
  - *focussing on leg muscles*
- Combined training
  - *alternating 1-2 sessions endurance and resistance training p. week*
  - *resistance training before endurance training*

Dalgas & al, Multiple Sclerosis (2008)

Reduced VO_2-max



Langeskov-Christensen et al. Sports Med 2015 Jun;45(6):905-23

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Reduced VO_2-max

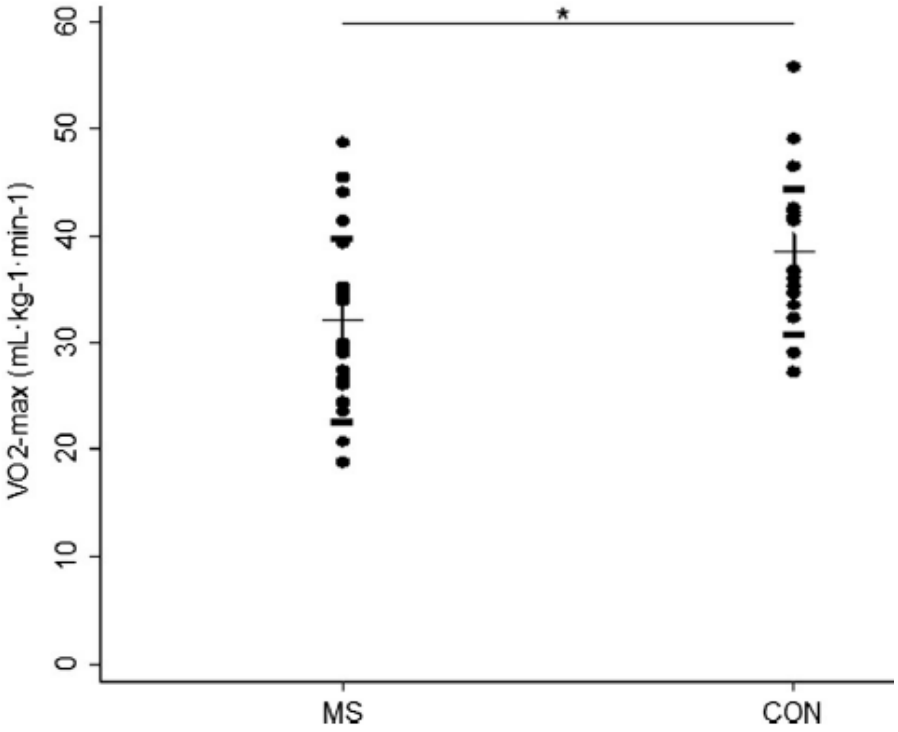
Contents lists available at ScienceDirect

Journal of the Neurological Sciences

journal homepage: www.elsevier.com/locate/jns

Validity and reliability of VO_2-max measurements in persons with multiple sclerosis

Martin Langeskov-Christensen [a,*,1], Daniel Langeskov-Christensen [a,2], Kristian Overgaard [a,3], Andreas Buch Møller [b,4], Ulrik Dalgas [a,5]



VO_2-max is an important health and performance marker

~20% lowering of VO_2-max

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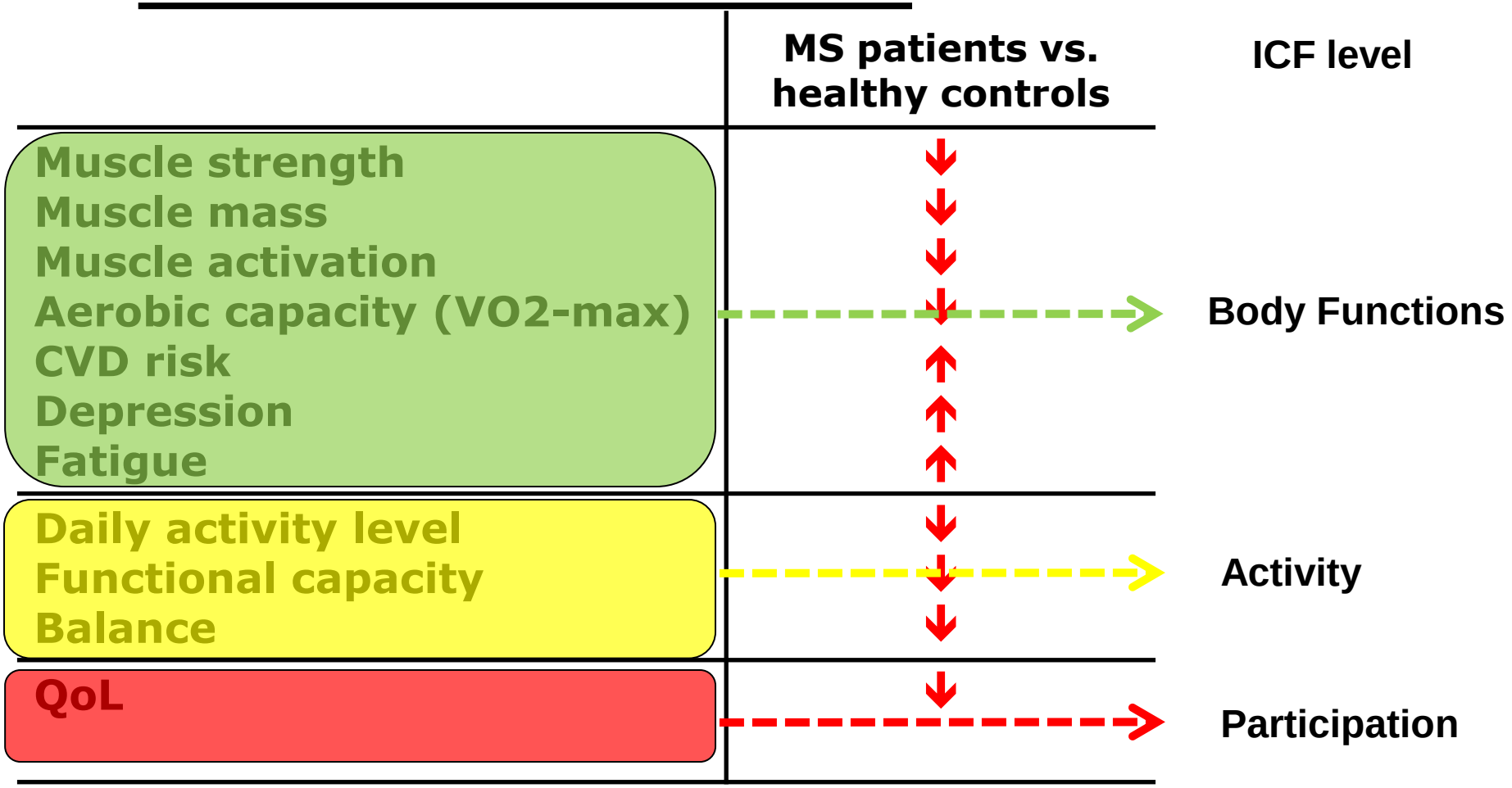
MS patients vs. healthy controls



Red arrow = Impaired in MS patients

Motl & Pillutti, Nat Rev Neurol; Sep;8(9):487-97.*2012*

Dalgas et al. Mult. Scler.14(35);35-53:2008

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MS- secondary aspects

- Reduced cardio-respiratory capacity (1,2)
- Reduced activity level (3)
- Inactivity negative for health status (4)
- Increased incidence of cardio-vascular diseases (5)

1 Mostert and Kesselring *Mult Scler 2002*;8(2):161-168.
2 NG Kent Braun *J Appl Physiol* 1997;83(2):1998-2004.
3 Motl et al. Mult Scler 2011;17(9):1034-1040.
4 Miller and Dishon *Qual Life Res 2002;15:259-271.*
5 Wens et al. *Mult Scler* 2013;19(12):1556-1564.

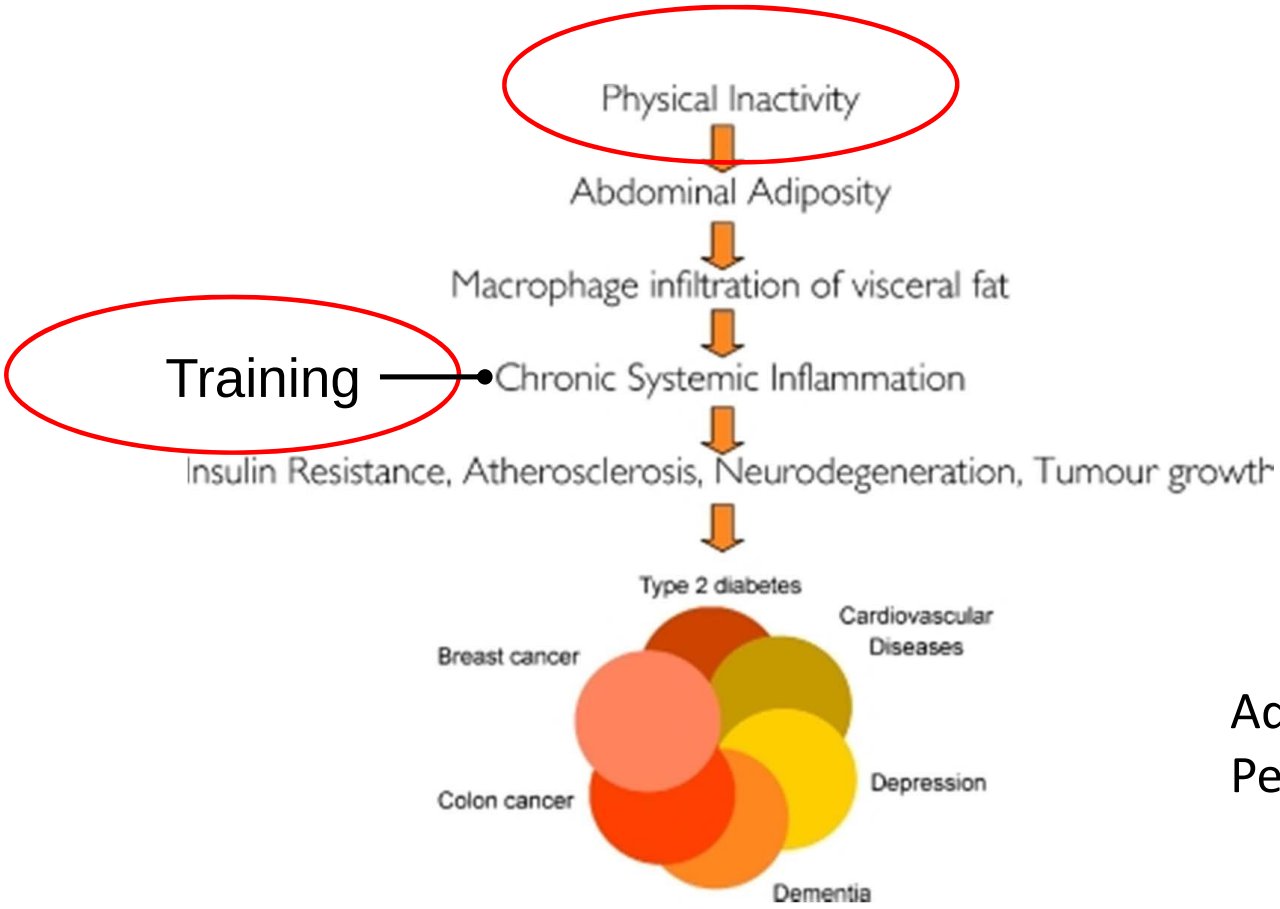
Different health profiles

Table 1 Summary of differences between MS patients and healthy subjects

	MS patients versus healthy subjects
Daily activity level	Decreased
VO_2-max	Decreased
Blood pressure (rest)	
Systolic	No difference
Diastolic	No difference or increased
Resting heart rate	No difference or increased
Muscle strength	
Isokinetic strength	Decreased
Isometric strength	Decreased
Rate of force development	No difference or decreased
Muscle mass (% FFM)	No difference or decreased
Musclefibre area	No difference or decreased
Muscle activation	Decreased
Function (ADL)	Decreased
CVD risk	Increased
Bone mineral density (BMD)	Decreased
Depression risk	Increased
Fatigue	Increased
HRQOL	Decreased

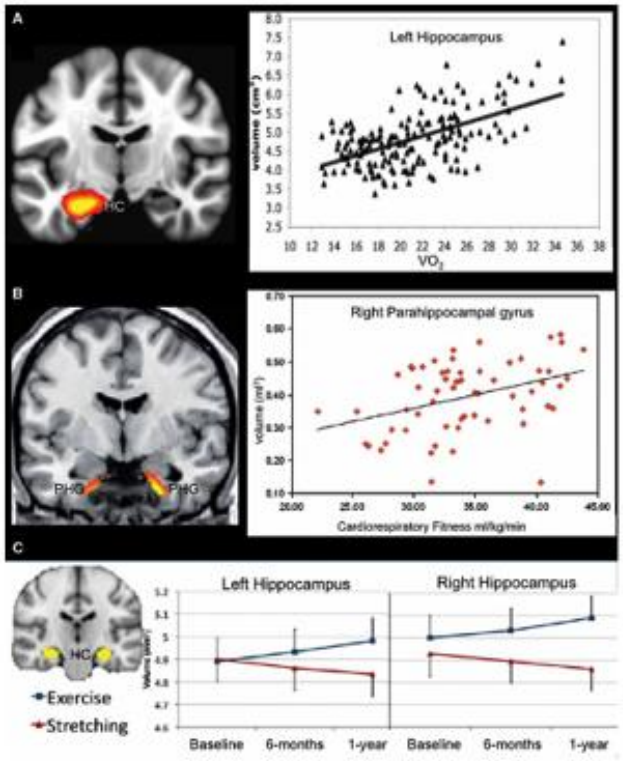
Dalgas et al. *Mult Scler* 2008;14(35):35-53

Inactivity = risk factor



Adapted from Pedersen 2009

Training enhances neuroplasticity



Erickson et al. (2009),

Honea et al.(2009)

Erickson et al. (2011),

BRAIN RESEARCH 1121 (2006) 59–65

available at www.sciencedirect.com

ScienceDirect

www.elsevier.com/locate/brainres

ELSEVIER

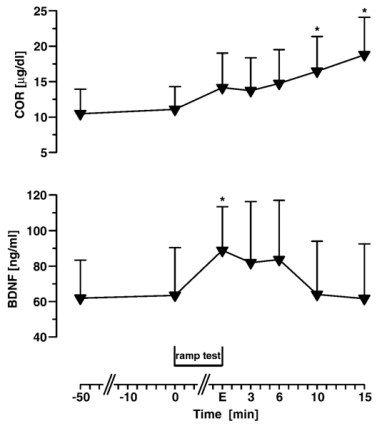
BRAIN RESEARCH

Research Report

Acute BDNF and cortisol response to low intensity exercise and following ramp incremental exercise to exhaustion in humans

Sandra Rojas Vega[a,*], Heiko K. Strüder[a], Bertha Vera Wahrmann[b], Annette Schmidt[c], Wilhelm Bloch[c], Wildor Hollmann[c]

[a]Institute of Motor Control and Movement Technique, German Sport University Cologne, Carl-Diem-Weg 6, 50933 Cologne, Germany
[b]Department of Anesthesiology, San Antonius Hospital, Cologne, Germany
[c]Institute of Cardiology and Sports Medicine, German Sport University Cologne, Carl-Diem-Weg 6, 50933 Cologne, Germany



KLINIKEN VALENS

Research Paper

MULTIPLE SCLEROSIS JOURNAL | MSJ

Multiple Sclerosis Journal
0(0) 1–9
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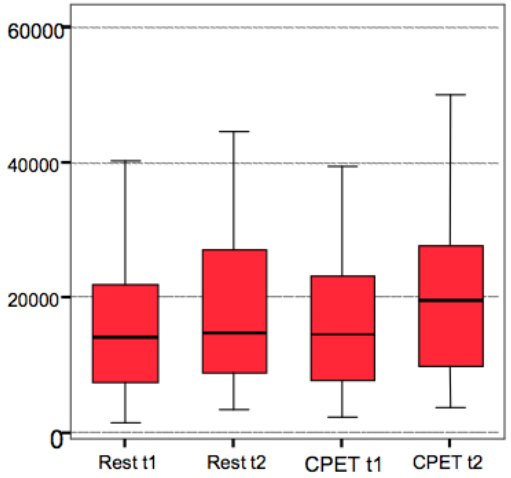
DOI: 10.1177/1352458512458605
msj.sagepub.com
SAGE

Training in MS: influence of two different endurance training protocols (aquatic *versus* overland) on cytokine and neurotrophin concentrations during three week randomized controlled trial

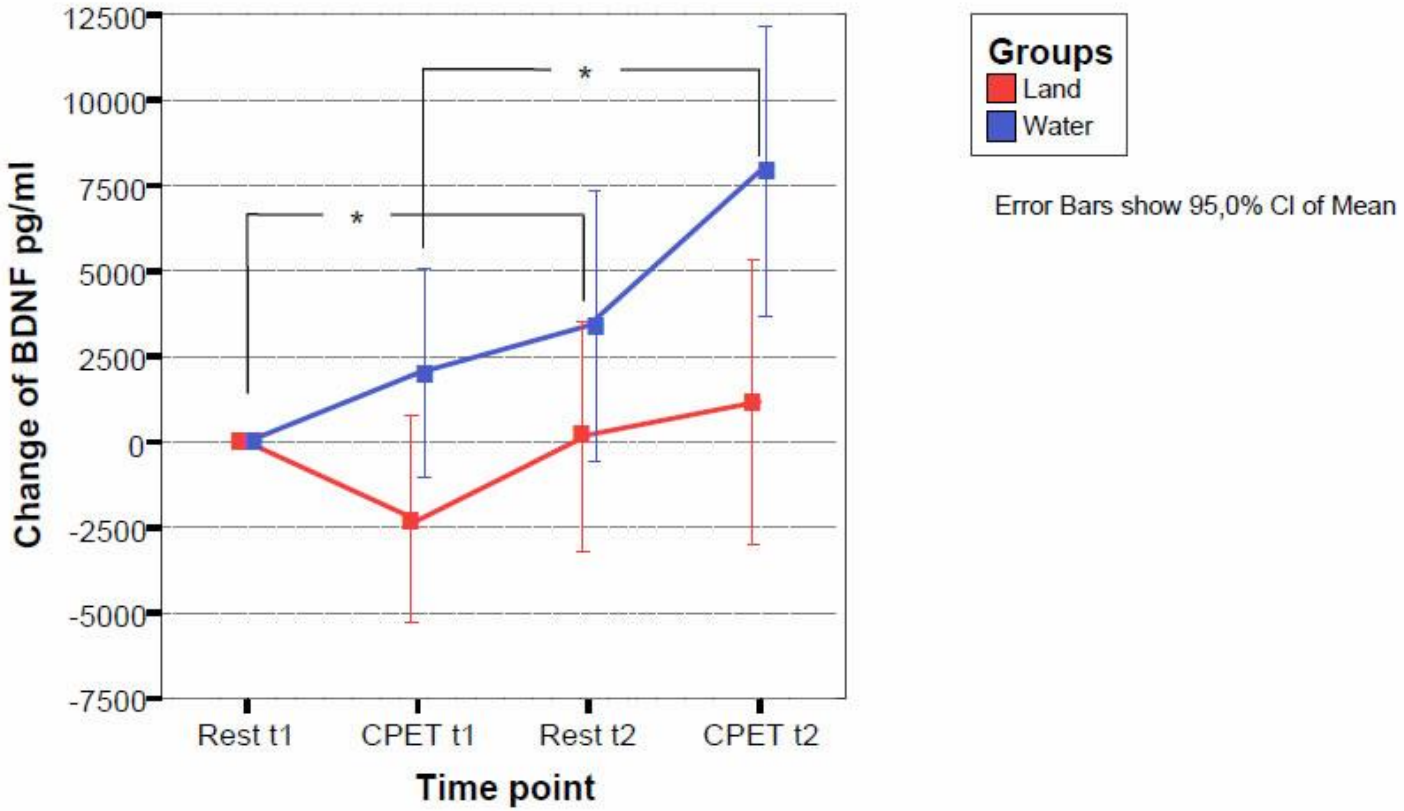
J Bansi[1], W Bloch[2], U Gamper[1] and J Kesselring[1]

Increased BDNF expression under immersion

Significant BDNF increase by 3387 pg/ml (95% CI -593.4-7367.6; ***p*=0.046**) within the water group



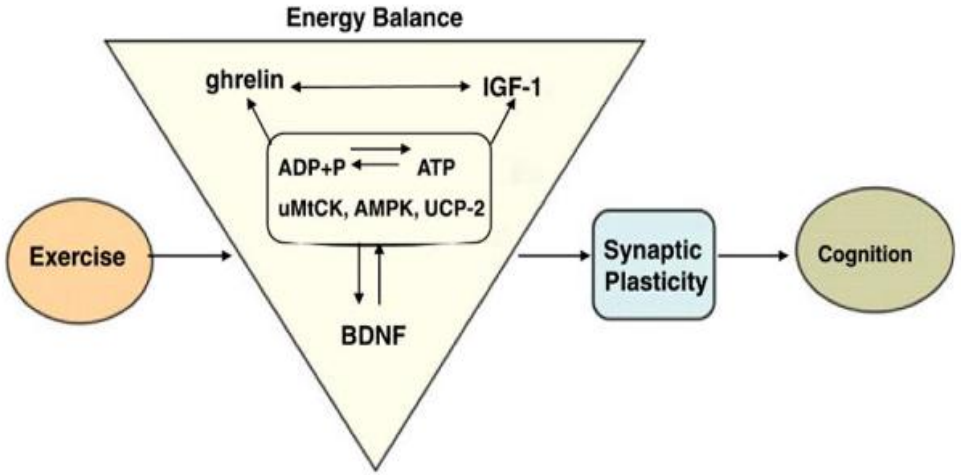
Results study 1 / Primary outcomes - Long-term effects



BDNF regulates energy supply of the brain

Neurotrophic factors

Enriched Environment



Gomez-Pinilla et al. 2009

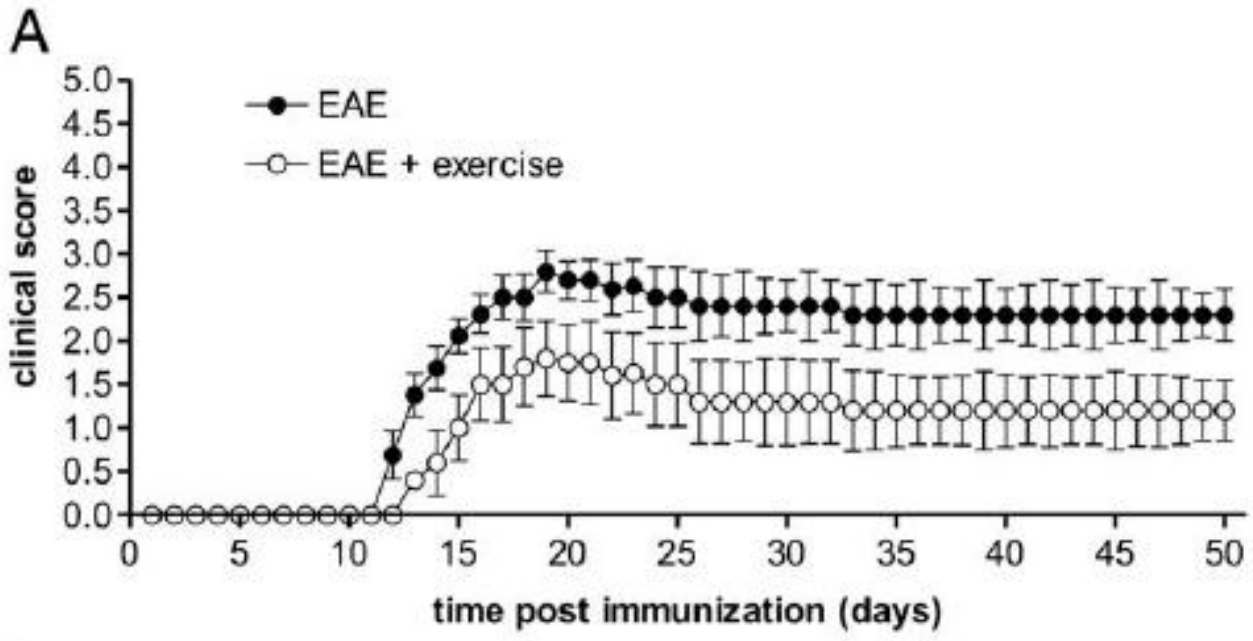
Contents lists available at ScienceDirect

Neurobiology of Disease

journal homepage: www.elsevier.com/locate/ynbdi

Exercise attenuates the clinical, synaptic and dendritic abnormalities of experimental autoimmune encephalomyelitis

Silvia Rossi [a,b,1], Roberto Furlan [c,1], Valentina De Chiara [a,b], Alessandra Musella [a,b], Temistocle Lo Giudice [a,b], Giorgia Mataluni [a,b], Francesca Cavasinni [c,2], Cristina Cantarella [a,b], Giorgio Bernardi [a,b], Luca Muzio [c], Alessandro Martorana [a,b], Gianvito Martino [c,3], Diego Centonze [a,b,3,*]



Journal of the Neurological Sciences xxx (2014) xxx–xxx

Contents lists available at ScienceDirect

Journal of the Neurological Sciences

journal homepage: www.elsevier.com/locate/jns

Review article

The safety of exercise training in multiple sclerosis: A systematic review

Lara A. Pilutti [a,*], Matthew E. Platta [a], Robert W. Motl [a], Amy E. Latimer-Cheung [b]

	Rate of relapse	Relative risk of relapse (vs. Control)
Control	6.3%	
Exercise	4.6%	0.73

→ Exercise may protect against relapses in persons with MS.

What is exercise therapy?

Resistance training

Body building
Basketball
Soccer
Swimming
Rowing
Running
Cycling

Endurance training

- Endurance training: Continous contractions against low loads *(”Aerobic metabolism”)*
- Resistance training: Few contractions against heavy loads *(”Anaerobic metabolism”)*

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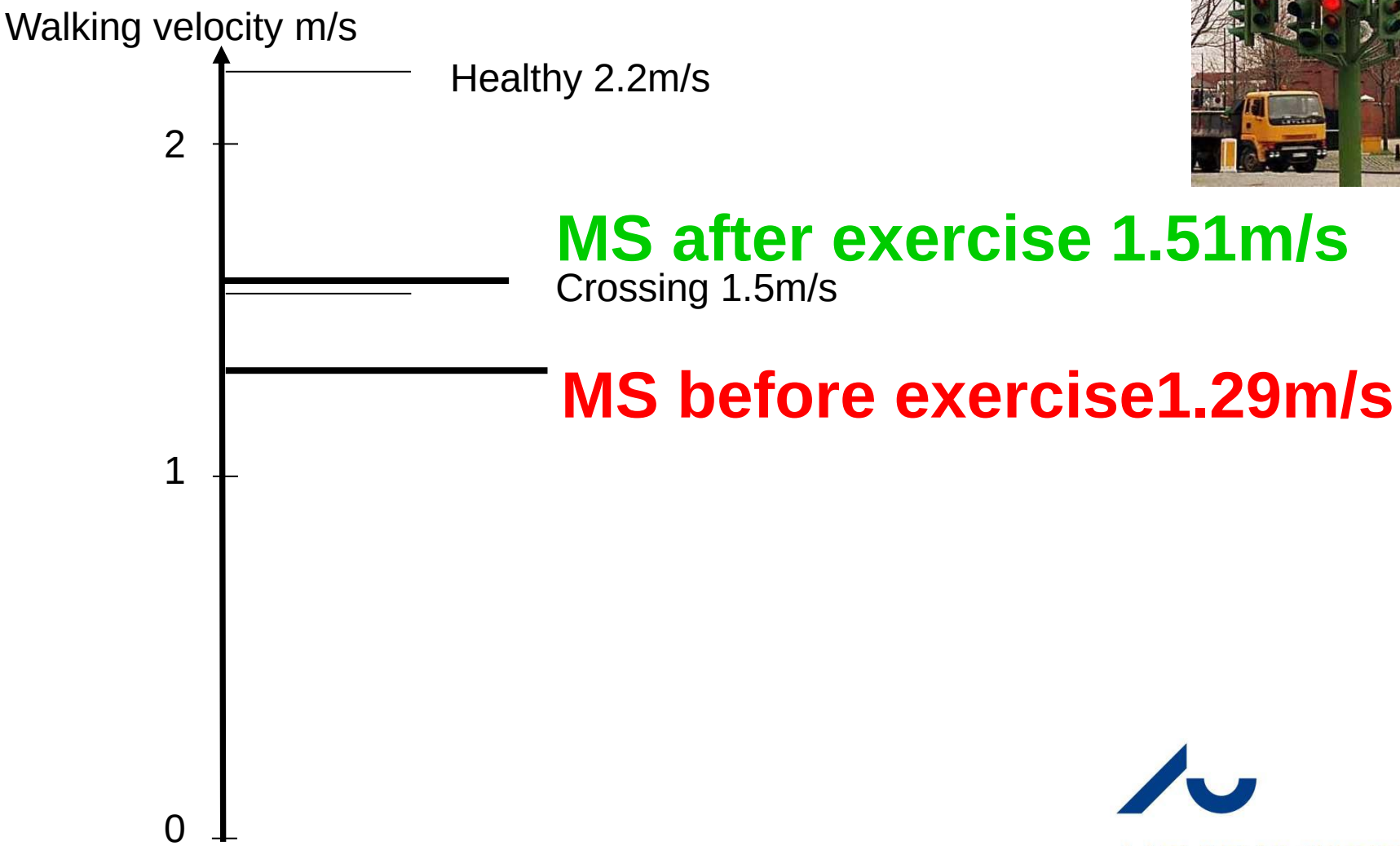
Results



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Summary

- Benefit of rehabilitation measures in MS
  - improvement of disability/handicap/QoL/wellbeing by multidisciplinary inpatient rehabilitation
  - benefit of physiotherapy (inpatient/outpatient) on disability
  - benefit of other specific components
- Long-term effects
  - benefits outlasting treatment period after inpatient rehabilitation, cognitive training (?)
  - short-term effect of outpatient physiotherapy
  - no influence on disease activity/progression

Take home message: 3 basic rules in neurorehabilitation

- Neurorehabilitation is applied neuroplasticity: forming of new synaptic networks and consolidation of existing ones according to requirements from the environment

- Neuroplasticity is the basis of learning. induced, exploited and enhanced must be resilience: all forces which act against and counterbalance the forces of gravity (in the physical, mental, emotional, and spiritual domains)

- Learning is always an activity. It does not happen just on its own or by chance. It is most effective in an appropriate environment under adequate guidance by good teachers and therapists

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Head of the Department of Neurology and Neurorehabilitation
Rehabilitation Centre Valens
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www.kliniken-valens.ch

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