

## Fatica centrale e periferica nella malatti neurologiche

## **Machiel J Zwarts**

## Kempenhaeghe epilepsiecentrum/ UMCN

## Paesi Bassi







#### The different dimensions of fatigue and assessment tools

Type of fatigue

*Psychological* Concentration

Restrictions in daily functioning

Physical activity Attributions about fatigue (e.g. attitude, self-efficacy) Social support Social functioning Psychological well-being Sleep disturbances

#### Methodology

Subscale Checklist Individual Strength (CIS) Abbreviated Fatigue Questionnaire (AFQ)

#### Clinical neurophysiology of fatigue

M.J. Zwarts , G. Bleijenberg , B.G.M. van Engelen

Clinical Neurophysiology 119 (2008) 2-10



#### The different dimensions of fatigue and assessment tools

Type of fatigue

*Physiological* Central fatigue

Peripheral fatigue

Methodology Twitch interpolation Motor cortex stimulation Readiness potential Force measurement (ergometer) Surface EMG Direct muscle stimulation

#### Clinical neurophysiology of fatigue

M.J. Zwarts , G. Bleijenberg , B.G.M. van Engelen

Clinical Neurophysiology 119 (2008) 2-10

Fatigue has been defined as a time-related phenomenon of decline in the maximal force-generation capacity.

Usually, this is expressed by a deterioration in maximal voluntary contraction (MVC).











#### Review

#### Fatigue in neurological disorders

Abhijit Chaudhuri, Peter O Behan Lancet 2004; **363:** 978–88

UMC St Radboud Introduction

Multidisciplinair research

Three neuromuscular disorders:

Muscle – FSHD

Nerve - HMSN I

Multisystem - MD







UMC 🛞 St Radboud

Method

## Experienced fatigue



# Elektrophysiological changes over time

## Questionaires

# Physiological fatigue







### Stimulator

### Stimulation-electrodes



#### Force transducer-



#### Method

#### Elektrophysiological measurement: twitch interpolation





### Method







#### Method



UMC 🕀 St Radboud

## Methode





## Participants

65 FSHD	age 43.1 (10.3)	🕴 : 27, 🕴 : 38
---------	-----------------	----------------

79 MD age 41.0 (9.8) \$\frac{1}{2}:35, \$\frac{1}{2}:44

73 HMSN age 42.4 (9.8) \$\frac{1}{2}: 43, \$\frac{1}{2}: 30

24 controls age 42.1 (13.5) ‡ : 12, ‡ : 12

UMC 🗘 St Radboud

Results

#### result 1:

# More than 60% of all patients experience extreme fatigue!

Abbreviated Fatigue Score (AFQ): scores range from 4-28



#### Results



#### result 2:

## Peripheral fatigue



#### Results



#### result 3:

# Central fatigue



result 4:

# Central drive



Results

UMC 🛞 St Radboud



Neuromusculair patients:

Large experienced fatigue
Small peripheral fatigue
Normal central fatigue
Strongly diminished central drive

Which physiological measure is related to the large experienced fatigue (if any)?

FSHD MD 100 100 y = 0.9226x + 23.505y = 0,9918x + 19,021 $R^2 = 0,0929$  $R^2 = 0.0776$ 

UMC 🛞 St Radboud

Results

#### Experienced fatigue and central activation failure













Review

#### Fatigue in neurological disorders

Figure 5: General sites of pathology in central fatigue RAS=reticular activating system.

Abhijit Chaudhuri, Peter O Behan

Lancet 2004; 363: 978-88



Objective motor weakness, abnormal neurological signs, or both?



Figure 3: Assessment of muscle fatigability and fatigue

Table 3 Neurological disorders associated with central fatigue Cerebral vasculitis and cerebrovascular diseases Channelopathies Developmental disorders (cerebral palsy, Chiari malformations) Encephalitis lethargica Hypothalamic and pituitary diseases Intracranial infections (meningitis and encephalitis) Metabolic encephalopathy and mitochondrial diseases Migraine Motor neuron disease Multiple sclerosis Multiple system atrophy Narcolepsy and related sleep disorders Paraneoplastic (limbic encephalitis, opsoclonus-myoclonus) Parkinson's disease and other parkinsonian disorders Posterior head injury Post-infective fatigue states (poliomyelitis, Lyme disease, Q fever, and viral fatigue) Post-operative (posterior fossa and cardiopulmonary bypass surgery) (Adapted from Chaudhuri and Behan, 2004)



NeuroImage 13, 1186–1192 (2001) doi:10.1006/nimg.2001.0759, available online at http://www.idealibrary.com on IDE L®

### Fatigue in Multiple Sclerosis Is Associated with Abnormal Cortical Activation to Voluntary Movement—EEG Evidence

Letizia Leocani,\* Bruno Colombo,† Giuseppe Magnani,† Filippo Martinelli-Boneschi,† Marco Cursi,\* Paolo Rossi,† Vittorio Martinelli,† and Giancarlo Comi\*<sup>,†</sup>

These findings are consistent with a central origin of fatigue in MS and indicate cortical dysfunction even during a simple motor task, resulting in hyperactivity during movement execution and failure of the inhibitory mechanisms intervening after movement termination. © 2001 Academic Press



In sum, fatigue seems to be a more or less universal symptom in central disorders.

In the disorders in which the symptom has been extensively studied it was found to correlate with specific brain dysfunctions and thus to have a specific pathophysiology in the different diseases,

Examples of which are its relationship with impairments of the inhibitory circuits in the primary motor cortex in MS, its reversal by levodopa in PD



*In conclusion*, fatigue in neurological disorders is a complex problem that merits a multilevel approach to disentangle the diverse mechanisms involved in this devastating symptom.





M.L. Schillings<sup>a</sup>, J.S. Kalkman<sup>b,c</sup>, S.P. van der Werf<sup>c</sup>, B.G.M. van Engelen<sup>d</sup>, G. Bleijenberg<sup>b</sup>, M.J. Zwarts<sup>a,d,\*</sup>

Clinical Neurophysiology 115 (2004) 2518-2524









Eur J Appl Physiol (2006) DOI 10.1007/s00421-006-0211-z

#### ORIGINAL ARTICLE

 $M.~L.~Schillings \cdot J.~S.~Kalkman \cdot S.~P. van der Werf G. Bleijenberg <math display="inline">\cdot$  B. G. M. van Engelen  $\cdot$  M. J. Zwarts

## Central adaptations during repetitive contractions assessed by the readiness potential