Fatica centrale e periferica nella malattie neurologiche

Machiel J Zwarts

Kempenhaeghe epilepsiecentrum/ UMCN

Paesi Bassi
Different kinds of fatigue!
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

The different dimensions of fatigue and assessment tools

<table>
<thead>
<tr>
<th>Type of fatigue</th>
<th>Methodology</th>
</tr>
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<tbody>
<tr>
<td><em>Physiological</em></td>
<td></td>
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<tr>
<td>Central fatigue</td>
<td>- Twitch interpolation</td>
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<tr>
<td></td>
<td>- Motor cortex stimulation</td>
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<tr>
<td>Peripheral fatigue</td>
<td>- Readiness potential</td>
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<tr>
<td></td>
<td>- Force measurement (ergometer)</td>
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<tr>
<td></td>
<td>- Surface EMG</td>
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<td></td>
<td>- Direct muscle stimulation</td>
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Clinical neurophysiology of fatigue

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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).

**Fatigue in neurological disorders**

Figure 4: General sites of pathology in muscle fatigability and neuromuscular fatigue (peripheral fatigue)
Multidisciplinary research

Three neuromuscular disorders:

Muscle – FSHD

Nerve – HMSN I

Multisystem - MD
Experienced fatigue

Questionnaires

Physiological fatigue

Elektrophysiological changes over time
Method

Stimulator

Stimulation-electrodes

Force transducer
Elektrophysiological measurement: twitch interpolation

2 min. maximal voluntary contraction

Diagram: Force over time with markers indicating different stages of contraction, including $F_0$, $F_t$, $F_s$, $F_s'$, and $F_f$. Timing notes: 300 ms, SE = 1240 ms, 40 ms.
Method

Peripheral fatigue

2 min. maximal voluntary contraction
Central fatigue = increase of central activation failure during 2 min.

Average central activation failure indicates amount of central drive
## Participants

<table>
<thead>
<tr>
<th>Group</th>
<th>Age Mean (SD)</th>
<th>Male: Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>65 FSHD</td>
<td>43.1 (10.3)</td>
<td>27:38</td>
</tr>
<tr>
<td>79 MD</td>
<td>41.0 (9.8)</td>
<td>35:44</td>
</tr>
<tr>
<td>73 HMSN</td>
<td>42.4 (9.8)</td>
<td>43:30</td>
</tr>
<tr>
<td>24 controls</td>
<td>42.1 (13.5)</td>
<td>12:12</td>
</tr>
</tbody>
</table>
result 1:

More than 60% of all patients experience extreme fatigue!

Abbreviated Fatigue Score (AFQ): scores range from 4-28
result 2:

Peripheral fatigue

![Graph showing peripheral fatigue in different conditions: FSHD, MD, HMSN, and controls. The controls show the highest fatigue level, while FSHD, MD, and HMSN have lower levels.](image-url)
result 3:  

Central fatigue

![Bar chart showing central fatigue (%)](chart.png)
result 4:

Central drive

![Bar chart showing mean central activation failure for FSHD, MD, HMSN, and controls.](chart.png)
Neuromuscular 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)?
Experienced fatigue and central activation failure

FSHD

\[ y = 0.9918x + 19.021 \]

\[ R^2 = 0.0929 \]

MD

\[ y = 0.9226x + 23.505 \]

\[ R^2 = 0.0776 \]

HMSN

gesond

controls
Fatigue in neurological disorders

Figure 5: General sites of pathology in central fatigue
RAS=reticular activating system.
Figure 3: Assessment of muscle fatigability and fatigue
Table 3
Neurological disorders associated with central fatigue

<table>
<thead>
<tr>
<th>Disorder</th>
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<tbody>
<tr>
<td>Cerebral vasculitis and cerebrovascular diseases</td>
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<tr>
<td>Channelopathies</td>
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<tr>
<td>Developmental disorders (cerebral palsy, Chiari malformations)</td>
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<tr>
<td>Encephalitis lethargica</td>
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<tr>
<td>Hypothalamic and pituitary diseases</td>
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<tr>
<td>Intracranial infections (meningitis and encephalitis)</td>
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<tr>
<td>Metabolic encephalopathy and mitochondrial diseases</td>
</tr>
<tr>
<td>Migraine</td>
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<tr>
<td>Motor neuron disease</td>
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<tr>
<td>Multiple sclerosis</td>
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<tr>
<td>Multiple system atrophy</td>
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<tr>
<td>Narcolepsy and related sleep disorders</td>
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<tr>
<td>Paraneoplastic (limbic encephalitis, opsoclonus-myoclonus)</td>
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<tr>
<td>Parkinson’s disease and other parkinsonian disorders</td>
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<tr>
<td>Posterior head injury</td>
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<tr>
<td>Post-infective fatigue states (poliomyelitis, Lyme disease, Q fever, and</td>
</tr>
<tr>
<td>viral fatigue)</td>
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<tr>
<td>Post-operative (posterior fossa and cardiopulmonary bypass surgery)</td>
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</tbody>
</table>

(Adapted from Chaudhuri and Behan, 2004)
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 Curi,* Paolo Rossi,† Vittorio Martinelli,† and Giancarlo Comi*†

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.
Reduced central activation during maximal voluntary contraction in chronic fatigue syndrome

M.L. Schillings, J.S. Kalkman, S.P. van der Werf, B.G.M. van Engelen, G. Bleijenberg, M.J. Zwarts
