Towards a definition of fatigability profile in myotonic dystrophy type 1 (DM1)

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Introduction

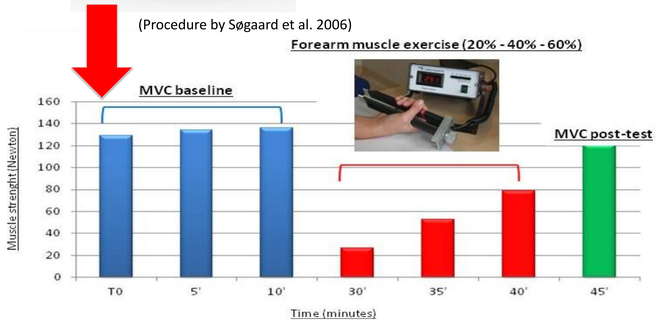
Myotonic dystrophy type 1(DM1) is characterized by high fatigability (Kalkman et al. 2005). Oxidative stress has been proposed to be one of the pathogenic factors (Angelini and Tasca, 2012); Bray et al. (2012) suggested that the decrease in maximal force production (MVC) observed during muscular effort can be caused also by central mechanisms.

Our aim was to investigate the fatigability profile in DM1 patients looking specifically at the relationship between self-reported fatigue, objective measures of peripheral fatigue, cognitive performance and gross brain structure.

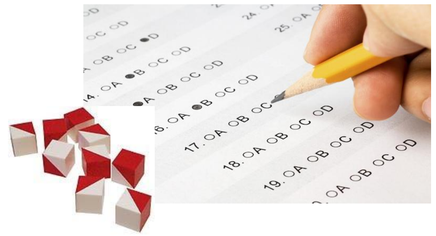
Materials and methods

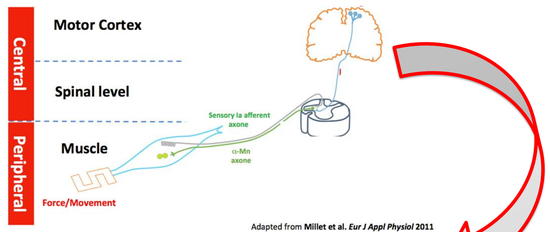
N = 26
17 M, 9 F
mean age 41.6 ±12.7

(Procedure by Søgaard et al. 2006)



- **Fatigue Severity Scale (FSS)**
- **Cognitive testing**
- **3T MRI**





Adapted from Millet et al. *Eur J Appl Physiol* 2011

Results

✓ Patients exhibit various alterations of subjective dimensions of fatigue (Fig. 1)

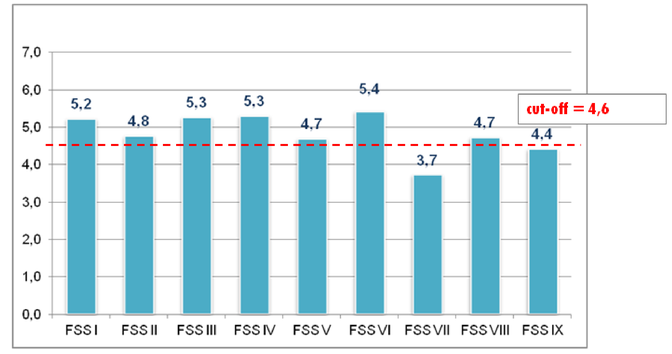


Figure 1. Subjective fatigue in DM1 patients assessed by Fatigue Severity Scale (FSS)

✓ Out of the six measures of cognitive performance administered, **40% (8/20) of DM1 patients had impairment in two or more cognitive scores related to attention processes** compared to that of 15% (3/20) in the healthy control group (not shown)..

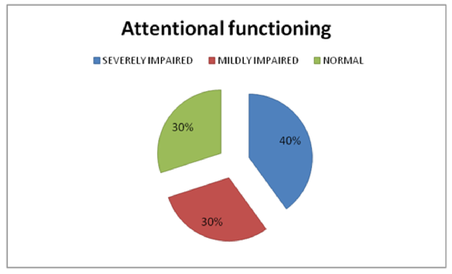


Figure 2. Prevalence of attentional dysfunctions in the sample

✓**FSS score was significantly correlated to maximum voluntary contraction (MVC) before and after the effort**, (r_before = -0.583, p < 0.01, r_post= -0.534, p < 0.05), and **to motor disability measured by MRC** (r = -0.496, p < 0.05); moreover we found a strong tendency towards significance in the association to **lactate baseline** (r = 0.378, p = 0.057).

✓MR imaging investigations revealed that patients with DM1 had **reduced gray-matter volume in the bilateral prefrontal cortex**, consistently with previous studies reporting this area to play an important role in the neural regulation of fatigue.

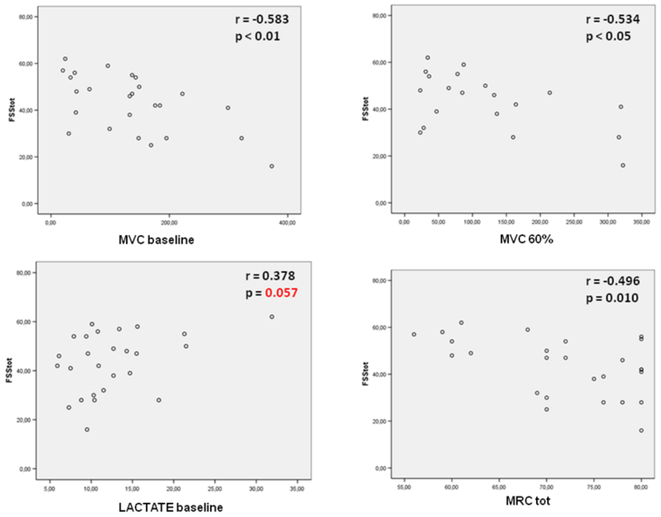


Figure 3. Correlations between central (FSS) and peripheral (MVC, Lactate, MRC) measures of fatigue in DM1 patients.

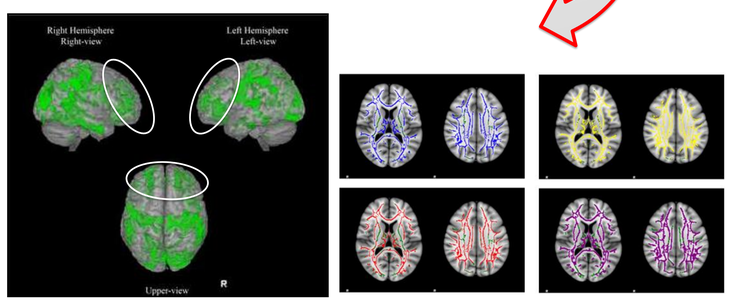


Figure 4. VBM revealed several clusters of reduced cortical GM in DM1 patients compared to healthy controls (TFCE p<0.001 corrected for multiple comparisons).
- BPF value in DM1 subjects was 0.760 ± 0.035.
- Atrophy was diffuse in both cerebral hemispheres and in particular in perirolandic, orbitofrontal, dorsolateral frontal, insular, temporo occipital, parietomesial, anterior and posterior cingulated areas.
Figure 5. White matter (WM) tract lesions assessed by tract-bases spatial statistics (TBSS). DM1 patients have reduced white matter and white matter abnormalities, with bilateral distribution.
- Fatigue severity (FSS) was not related to the total extent of cerebral abnormalities, or to MRI-based atrophy measures (p<.05).

Conclusions

- The tools used in this study may be used as an effective means to define fatigability profile in DM1 patients.
- DM1 patients exhibit clinical signs of both, central and peripheral (#EP1161) fatigue.
- As in other neurological disorders (multiple sclerosis, chronic fatigue syndrome) fatigue in DM1 may be a multifaceted entity, also **related to the disruption of fatigue-related processes in the brain**, particularly in the frontal premotor areas.
- These regions are also related to neuropsychological functioning of attentional abilities.

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