Fatigue has been defined as an overwhelming sense of tiredness, lack of energy, and feeling of exhaustion and is not the same as weakness. Fatigue is a common symptom in different neurological disorders such as multiple sclerosis, Parkinson’s disease, and stroke. In these patient populations it was found that the experience of severe fatigue can be a major determinant of disability and influences the quality of life. Surprisingly, fatigue in neuromuscular disorders has received little attention, though there have been studies in patients with particular neuromuscular disorders. Paul et al showed that 82% of a group of patients with myasthenia gravis reported fatigue as a regular symptom of their disease. A study by Berly et al showed that 68% of a group of post-polio myelitis patients reported daily fatigue. Half these fatigued patients noted that their fatigue had led to the need for assistance in daily life. In a group of patients with immune mediated polyneuropathies it was found that fatigue was a prominent and highly disabling symptom. Herlofson and Larsen showed that fatigued patients with Parkinson’s disease reported more problems in areas of functional limitation. Fisk et al found that fatigue had a significant effect on the general health status in patients with multiple sclerosis. The impact of fatigue in health related quality of life in patients with neuromuscular disorders has not been studied so far.

Clinical experience and preliminary findings of our research group indicated that many patients with a neuromuscular disorder also experience severe fatigue and consider it an important problem. Most psychological studies in neuromuscular disorders, however, have focused mainly on disability or loss of quality of life, and did not address the problem of experienced fatigue among different neuromuscular disorders.

Currently, no cross sectional study has compared the presence and severity of fatigue in various neuromuscular diseases using validated instruments.

This study concerned three genetically well defined, homogeneous, and large populations of patients with relatively common neuromuscular disorders, namely facioscapulohumeral muscular dystrophy (FSHD), adult onset myotonic dystrophy (MD), and hereditary motor and sensory neuropathy type I (HMSN-I).

Methods: 598 patients with a neuromuscular disease were studied (139 with facioscapulohumeral dystrophy, 322 with adult onset myotonic dystrophy, and 137 with hereditary motor and sensory neuropathy type I). Fatigue severity was assessed with Checklist Individual Strength (CIS-fatigue). Functional impairments in daily life were measured with the short form 36 item health questionnaire (SF-36).

Results: The three different neuromuscular patient groups were of similar age and sex. Severe experienced fatigue was reported by 61–74% of the patients. Severely fatigued patients had more problems with physical functioning, social functioning, mental health, bodily pain, and general health perception. There were some differences between the three disorders in the effects of fatigue.

Conclusions: Severe fatigue is reported by the majority of patients with relatively common types of neuromuscular disorders. Because experienced fatigue severity is associated with the severity of various functional impairments in daily life, it is a clinically and socially relevant problem in this group of patients.

Abbreviations: CIS, Checklist Individual Strength; FSHD, facioscapulohumeral muscular dystrophy; HMSN-I, hereditary motor and sensory neuropathy type I; MD, adult onset myotonic dystrophy; SF-36, 36 item short form general health questionnaire.
mental health, and bodily pain to fatigue severity in three different relatively common neuromuscular disorders.

METHODS

Patients

Adult patients aged 18 to 65 years with a definite diagnosis who could be classified into one of the three neuromuscular disease categories (FSHD, MD, HMSN-I) were asked to participate. Some of the patients were recruited from the Neuromuscular Centre, Radboud University Nijmegen Medical Centre in the Netherlands. The remainder were recruited from the Dutch Neuromuscular Diseases Association (Vereniging Spierziekten Nederland, VSN).

In all, 900 patients were informed by a letter and received a booklet with questionnaires (described below) at home. Subjects were asked what diagnosis had been made and if this was done by a neurologist or a clinical geneticist.

We used a cross sectional design to assess fatigue in patients with a neuromuscular disorder. Written information about the purpose of the study was provided to all the patients. The study was approved by the local ethics committee.

Fatigue severity

The Checklist Individual Strength (CIS) is a 20 item questionnaire and measures the following four separate aspects of fatigue during the previous two weeks: fatigue severity (eight items, score range 8 to 56), concentration problems (five items, score range 5 to 35), reduced motivation (four items, score range 4 to 28), and reduced activity (three items, score range 3 to 21). Each item was scored on a seven point Likert scale. High scores indicated high levels of fatigue, high levels of concentration problems, low motivation, and low levels of activity. A CIS-fatigue score of 35 or more was used to identify severe fatigue.

Functional impairment in daily life

The following subscales of the SF-36 were used to assess different areas of functional impairment in daily life: physical functioning, social functioning, role limitations caused by emotional problems, mental health, bodily pain, and general health perception. The transformed scores for all SF-36 scales ranged from 0 to 100. For each subscale a higher score indicated better functioning or less pain.

Table 1  Demographic characteristics of patient groups

<table>
<thead>
<tr>
<th>Age (years) (mean (SD))</th>
<th>FSHD (n = 139)</th>
<th>MD (n = 322)</th>
<th>HMSN-I (n = 137)</th>
</tr>
</thead>
<tbody>
<tr>
<td>43.7 (10.1)</td>
<td>43.1 (10)</td>
<td>42.5 (10.7)</td>
<td></td>
</tr>
<tr>
<td>Age range (years)</td>
<td>22 to 61</td>
<td>18 to 63</td>
<td>19 to 63</td>
</tr>
<tr>
<td>Sex (M/F) (%)</td>
<td>49/51</td>
<td>47/53</td>
<td>41/59</td>
</tr>
<tr>
<td>Marital status</td>
<td>Married/living together 74%</td>
<td>70%</td>
<td>69%</td>
</tr>
<tr>
<td>Single 25%</td>
<td>30%</td>
<td>31%</td>
<td></td>
</tr>
<tr>
<td>Missing information 1%</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Education level* Lower 32%</td>
<td>34%</td>
<td>28%</td>
<td></td>
</tr>
<tr>
<td>Intermediate 34%</td>
<td>28%</td>
<td>27%</td>
<td></td>
</tr>
<tr>
<td>Upper 34%</td>
<td>19%</td>
<td>29%</td>
<td></td>
</tr>
<tr>
<td>Missing information 1%</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
</tbody>
</table>

Table 2  Comparison of functional impairments in FSHD, MD, and HMSN

<table>
<thead>
<tr>
<th>Area of functional impairment</th>
<th>FSHD</th>
<th>MD</th>
<th>HMSN-I</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical functioning</td>
<td>37.4 (12.2)</td>
<td>40.4 (11.8)</td>
<td>37.4 (12.5)</td>
</tr>
<tr>
<td>Social functioning</td>
<td>37.4 (12.2)</td>
<td>40.4 (11.8)</td>
<td>37.4 (12.5)</td>
</tr>
<tr>
<td>Role limitations (physical)</td>
<td>37.4 (12.2)</td>
<td>40.4 (11.8)</td>
<td>37.4 (12.5)</td>
</tr>
<tr>
<td>Role limitations (emotional)</td>
<td>37.4 (12.2)</td>
<td>40.4 (11.8)</td>
<td>37.4 (12.5)</td>
</tr>
<tr>
<td>Mental health</td>
<td>37.4 (12.2)</td>
<td>40.4 (11.8)</td>
<td>37.4 (12.5)</td>
</tr>
<tr>
<td>Bodily pain</td>
<td>37.4 (12.2)</td>
<td>40.4 (11.8)</td>
<td>37.4 (12.5)</td>
</tr>
<tr>
<td>General health perception</td>
<td>37.4 (12.2)</td>
<td>40.4 (11.8)</td>
<td>37.4 (12.5)</td>
</tr>
</tbody>
</table>

Regression analyses were carried out to examine the contribution of different dimensions in relation to fatigue severity (table 3). Separate analyses were done for each domain. Significant differences were found in age, sex, or marital status between the three groups.

RESULTS

From the 647 adult patients (72%) who returned the questionnaires, 49 were excluded for the following reasons: no diagnosis of FSHD, MD, or HMSN-I (n = 30); incomplete booklets (n = 19). In all, 598 patients fitted the inclusion criteria and completed the questionnaires (66%). This group consisted of 139 patients with FSHD, 322 with MD, and 137 with HMSN-I. Diagnoses in a quarter of these patients were made at our hospital according to established criteria.

Results from this subgroup did not differ from the results of the group as a whole. Demographic characteristics of the three groups are listed in table 1. No significant differences were found in age, sex, or marital status between the three groups. The MD group had a significantly lower level of education than the two other groups.

Fatigue and functional impairment in FSHD, MD, and HMSN

All patient groups experienced high levels of fatigue. The mean (SD) CIS-fatigue score in the FSHD group was 36.5 (12.5), in the MD group 40.4 (11.8), and in the HMSN group 37.4 (12.2). In the FSHD group 61% were severely fatigued, in the MD group 74%, and in the HMSN group 64%.

Table 2 shows a comparison of functional impairments in daily life between the three patient groups. The MD group reported having significantly more concentration problems, higher levels of reduced motivation, and reduced levels of activity. The MD group perceived lower general health but experienced less bodily pain than the FSHD and HMSN patients.

Age related problems

In the FSHD and MD groups, age correlated significantly with fatigue severity (FSHD: \( r = 0.19, p = 0.002 \); MD: \( r = 0.17, p = 0.002 \)). In all three patient groups, higher age was associated with more impairment in physical functioning and more bodily pain. Among the MD patients, age correlated significantly with all subscales of the SF-36 and with reduced motivation and reduced activity on the CIS.

Severely fatigued patients

Severely fatigued patients (CIS-fatigue \( \geq 35 \)) were compared with less fatigued patients (CIS-fatigue <35) within the three neuromuscular disorders. Severely fatigued FSHD patients, MD patients, and HMSN patients had more concentration problems, higher scores on reduced motivation, and reduced levels of physical activity. Severely fatigued patients also had significantly lower scores at all subscales of the SF-36.

Contribution of different dimensions to fatigue severity

Regression analyses were carried out to examine the contribution of different dimensions in relation to fatigue severity (table 3). Separate analyses were done for each domain.
group, with CIS-fatigue as the dependent variable. In none of the groups did age contribute to fatigue severity. In the FSHD group, physical functioning, social functioning, and bodily pain contributed significantly to fatigue severity; in the MD group, physical functioning and social functioning contributed significantly; in the HMSN group, none of the independent variables contributed significantly. The correlations between CIS-fatigue and the SF-36 subscales were weaker in the HMSN group than in the FSHD or MD group.

**DISCUSSION**

As far as we know this is the first cross sectional study in which fatigue has been investigated in three large homogeneous groups of neuromuscular disorders with validated measurements. Our study shows that 61–74% of the subjects in the investigated groups were severely fatigued. This means that the experience of severe fatigue is a major complaint in most patients with these neuromuscular diseases. In all three groups, being severely fatigued was associated with greater levels of functional impairment in daily life.

The results also showed that patients with myotonic dystrophy had significantly higher scores of severe fatigue, reported more problems with concentration (CIS-concentration), and had more difficulty in initiating and planning (CIS-reduced motivation) than the other two groups. Daytime sleepiness is an established clinical manifestation of myotonic dystrophy.\(^1\) It is possible that patients with this disease confuse the experience of fatigue with daytime sleepiness, which may have affected the CIS-fatigue scores of this disease.\(^2\)

**Table 3** Linear regression analysis to predict fatigue severity

<table>
<thead>
<tr>
<th>Independent variable</th>
<th>FSHD, (p) value</th>
<th>MD, (p) value</th>
<th>HMSN-I, (p) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical functioning</td>
<td>-0.228</td>
<td>-0.398</td>
<td>-0.188</td>
</tr>
<tr>
<td>Social functioning</td>
<td>-0.219</td>
<td>-0.157</td>
<td>-0.107</td>
</tr>
<tr>
<td>Mental health</td>
<td>-0.031</td>
<td>-0.112</td>
<td>-0.166</td>
</tr>
<tr>
<td>Bodily pain</td>
<td>-0.195</td>
<td>-0.062</td>
<td>-0.146</td>
</tr>
<tr>
<td>Age</td>
<td>0.022</td>
<td>-0.087</td>
<td>-0.148</td>
</tr>
<tr>
<td>Total (R^2) (adjusted)</td>
<td>0.238</td>
<td>0.270</td>
<td>0.143</td>
</tr>
</tbody>
</table>

*FSHD, facioscapulohumeral muscular dystrophy; HMSN-I, hereditary motor and sensory neuropathy type I; MD, adult onset myotonic dystrophy.*

In addition, we found that MD patients had a lower education level than the FSHD and HMSN patients. These differences may be explained by disease specific problems associated with a multisystem disorder such as myotonic dystrophy. Mental dysfunction—such as reduced intelligence and lower levels of concentration and initiation—has been recognised in myotonic dystrophy, in contrast to the lack of such defects in other disabling neuromuscular disorders.\(^1\) Patients with FSHD and HMSN turned out to have higher scores of bodily pain than the MD patients. These results are consistent with reports of presence of pain in other studies in FSHD and HMSN.\(^1\) Pain, particularly back pain, is often cited as a problem but has been poorly studied in MD patients.\(^2\)

Age and fatigue severity did not seem to be related in any of the groups, as no contribution of these variables was found in the regression analyses. Karlsen showed that fatigue severity is not regarded as part of the normal aging process.\(^3\)

The significant correlations between age and functional impairment in daily life suggest that greater age is associated with increasing impairment in physical functioning and bodily pain in all three patient groups. This is in accordance with the progressive nature of these disorders. An increase in physical limitation with age in these conditions is well known.\(^1\) In myotonic dystrophy, age is also correlated with all the other functional impairments. These results are in line with the known differences between these three neuromuscular disorders.\(^1\)
Fatigue in muscular dystrophy

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Competing interests: none declared

REFERENCES

Experienced fatigue in facioscapulohumeral dystrophy, myotonic dystrophy, and HMSN-I

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

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