The motor unit in muscular dystrophy, a single fibre EMG and scanning EMG study

PER HILTON-BROWN, ERIK STÅLBERG

From the Department of Clinical Neurophysiology, University Hospital, Uppsala, Sweden

SUMMARY Dystrophic muscle shows increase in fibre density, abnormally low jitter in some recordings and more often increased jitter. The cross section of the motor unit has normal length. There are no signs of abnormal volume conduction characteristics. The increased fibre density is believed to be due to localised increase in the number of muscle action potential generators. The findings are compatible with a remodelling of the motor unit due to fibre loss and a reparative process with fibre regeneration and reinnervation.

Muscular dystrophies are hereditary diseases in which diagnosis and classification are dependent upon the recognition of clinical syndromes.1,2 Frequently it is difficult to place the individual patient into one or the other of the typical dystrophies. The clinical classification may only partly reflect aetiological differences. For the diagnosis of muscular dystrophies electromyography (EMG) is an important complement to the clinical evaluation. The typical findings were first described by Kugelberg.3,4 The EMG changes in muscular dystrophies have commonly been attributed to loss of muscle fibres within the motor units5 although additional changes due to regenerative mechanisms have been suggested.6 Furthermore a neurogenic component has been suggested from findings of reduced number of motor units as seen by a neurophysiological technique for motor unit counting.7

The aim of this study is to further elucidate the microphysiology of the motor unit in different dystrophies. For these studies different electrophysiological techniques are used. By means of Single Fibre EMG (SFEMG) activity in individual muscle fibres and motor end-plates is studied and by Scanning EMG the total motor unit territory is determined.

Diagnosis

We chose to include patients with diagnosis of Duchenne, limb-girdle (LG), and facio-scapulo-humeral (FSH) dystrophies. For Duchenne, the diagnosis was made in accordance with the criteria suggested by Brooke et al.8 The diagnosis of LG and FSH were based on descriptions given by Walton and Gardener-Medwin.9,10 The following characteristics were required:

1) Clinical findings: (a) typical distribution of weakness and atrophy, (b) onset of the disease before 30 years of age and a history of steady progress, (c) normal sensation and preserved tendon reflexes (if muscles were not severely weak), (d) no findings indicating other reasons for weakness.

2) Laboratory findings: (a) essentially normal findings in routine laboratory tests (blood sedimentation rate, haemoglobin, white blood cell count. Serum sodium, potassium, chloride, calcium, albumin, glucose, creatinine, bilirubin, alkaline phosphatase, thyroxin, thyroxin binding globulin), (b) serum creatine kinase (CK) increased at some time during the disease.

3) Neurophysiology: findings in routine concentric needle EMG fulfilling conventional criteria for myopathy.8 Normal motor and sensory nerve conduction velocities.

4) Morphology, histochemistry: muscle biopsy findings in agreement with or at least not contradicting a primary myopathy.

Patients

Thirty-nine patients have been investigated. Fourteen had LG, 13 FSH and 12 Duchenne dystrophy (table 1). Five of the patients did not strictly fulfil the above mentioned requirements. One (no 23) was a 16-year-old boy who was subjectively well. He had slight proximal weakness, an abnormal EMG, biochemistry and biopsy findings and FSH in the family (mother, sister and brother) and was therefore included in the series. Two patients (nos 15 and 25) had clinically typical FSH but the CK had not been measured before the disease was very advanced at which stage it was within normal limits. Lacto-dehydrogenase electrophoresis had earlier shown a pattern as in...
myopathy. Two patients (nos 16 and 26) had a questionable biopsy suggestive either inflammatory or dystrophic myopathy. One of them had a history of steadily progressive proximal weakness for more than 15 years with early involvement also of facial muscles. There were no symptoms or signs of inflammatory disease. EMG showed short duration polyphasic action potentials and no signs of loss of motor units. The turn amplitude analysis indicated myopathic changes. The other patient who was younger had a disease duration of 5 years but otherwise similar findings. Both patients were diagnosed as having FSH dystrophy and were included in the study.

Three unrelated patients, (nos 15, 18, 23) with FSH had a history of subarachnoid haemorrhage, one of whom had a persisting slight unilateral paresis. The EMG investigations were made on the contralateral side. One patient (no 5) with LG had grand mal epilepsy and received phenytoin and carbamazepin. No neurological signs of drug induced neuropathy were present. Nerve conduction velocities and F-responses were all normal.

The adult patients were graded for
(a) over-all disability grading according to Walton¹⁰: grade 1 = preclinical disease, grade 10 = total disability, bedridden;
(b) degree of progression during the last two years,
grade 1 = no change
grade 2 = minimal progress
grade 3 = normal progress
grade 4 = rapid progress.
(c) Strength in EDC, biceps and tibial anterior muscles:
grade 0 = no visible contraction
grade 1 = visible contraction, minimal joint movement
grade 2 = can move the joint when gravity is eliminated
grade 3 = can move the joint against gravity, but not against more resistance
grade 4 = can move the joint against gravity and slight resistance
grade 5 = moderate loss of strength
grade 6 = barely detectable weakness
grade 7 = full strength

(d) Atrophy
grade 0 = no atrophy
grade 3 = severe atrophy (less than half expected volume)
grade −1 = hypertrophy.

Methods

Conventional EMG and nerve conduction studies
Motor and sensory nerve conduction studies including F response measurements were made according to standard procedures. Concentric needle EMG (CNEMG) was performed in all patients. Spontaneous activity, single motor unit potentials and interference pattern were analysed. Computerised turn amplitude analysis of the interference pattern was used as a diagnostic aid. This was performed in the brachial biceps and tibial anterior muscles. A study was considered abnormal when more than 1 out of 20 data points were above or below normal limits.

Single fibre electromyography
Fibre density: The local fibre density within motor units was studied with a SFEMG method. Fibre density (FD) is
the average number of muscle fibres belonging to the same motor unit in each of at least 20 different positions. The FD is also expressed as a relative fibre density (RFD) = obtained value/normal mean FD for age. When the recordings contained two or more spike components the duration from first to last component was measured. The proportion of complex potentials that is, containing more than two components was noted.

Jitter and blocking: The neuromuscular transmission was studied by means of Single Fibre EMG (SFEMG). The jitter is calculated as the Mean of Consecutive Interpotential Interval Differences (MCD). The interpotential interval (IPI) between components in a discharge is dependent on the interval to the previous discharge which adds an interdischarge interval (IDI) dependent jitter to the random jitter at irregular innervation rates. This is due to a variation in propagation velocity in the muscle fibres dependent on the preceding activity, the velocity recovery function, VRF. Therefore the jitter is analysed also in the following way. The material is arranged according to interdischarge intervals. In this sorted material the mean value of consecutive IPIs is calculated. The obtained value is the so called Mean of Interpotential Intervals in Sorted Data (MSD). If the index MCD/MSD exceeds 1-25, MSD is used to express the jitter, otherwise MCD is used. In the normal muscle the jitter is mainly due to a variability in the transmission time in the motor end-plate and is of the order of 10-55 μs. A small jitter, MCD less than 10 μs, is taken as evidence of recordings from branches of a split muscle fibre with a common motor end-plate. Ekestedt and Stålberg considered MCD below 5 μs to indicate split fibres when analysis was made on line. In the present study analysis was made off-line from potentials recorded on tape. The wow of the tape recorder adds a technical jitter of about 5 μs. In normal subjects the jitter is exceptionally below 10 μs in off-line analysis. This justifies the chosen limits. A study is considered abnormal if more than 10% of 20 recordings have MCD above given limits for the muscle. If less than 20 recordings are performed, at least two recordings must have MCD values that exceed upper normal limit to classify the study as abnormal. The study is also abnormal if the mean MCD exceeds a certain given limit for the muscle.

In the ischaemic test a blood-pressure cuff was loosely placed around the upper arm. A SFEMG recording was made from the voluntarily activated EDC muscle. After some minutes of continuous recording the cuff was insufflated to 200 mmHg. The potential was followed during ischaemia. It is normally unaffected during the first 2000 to 3000 discharges after which there is an increasing jitter and appearance of intermittent blockings.

In the local curarisation test a similar procedure as in the ischaemic test was followed. After the cuff insufflation 30 μg per kg bodyweight of d-tubocurarine in 20 ml saline was given intravenously distally in the arm. The cuff was released after 4 minutes. Recordings were made before, during and after the period during which the cuff was insufflated.

The effect of edrophonium (Tension) on the jitter was tested in recordings with increased jitter. 2 + 8 mg of the drug was injected intravenously at 1 minute interval. All the signals were recorded on tape, and were studied in detail off line.

Volume conduction
To estimate volume conduction a multi-electrode method was used. The electrode had 12 leading of surfaces with 25 μm diameters arranged in a row in a side-port of a steel cannula. The cannula was used as reference electrode. The row was parallel to the long axis of the cannula. From microphotos the exact positions of the 12 surfaces were known (455 μm between the most remote surfaces). The needle was introduced into the muscle perpendicularly to the fibre direction and kept in a position where the action potentials from a single fibre were recorded with maximal amplitude from an electrode surface at one end of the electrode row. This signal was used to trigger the oscilloscope. On another oscilloscope channel recordings were made from each electrode surface. The decay of the amplitude over distance was measured and expressed either as the distance where half the amplitude was lost or the distance where only 200 μV remained. In the latter measurement the signal obtained at the most remote electrodes was considered as cross-talk within the electrode and its amplitude was therefore subtracted from the signals recorded from the other electrode surfaces.

Scanning EMG
To get an estimate of the size of the motor unit so called Scanning EMG with a concentric needle electrode was performed according to the method described by Stålberg and Antoni. By using a separate SFEMG electrode for triggering the activity from one motor unit was obtained from a CNEMG needle which by a computer controlled step-motor was pulled through the muscle. For quantification, a profile of the peak-to-peak amplitude and area of the motor unit potential along the retraction path was plotted by the computer. The length over which the motor unit potential had an amplitude exceeding 50 μV was measured. A detailed description of the technique and analysis is given elsewhere.

Results
Results concerning routine EMG, turns/amplitude analysis, CK-values and muscle biopsy are summarised in table 2. All patients had a "myopathic EMG" and normal nerve conduction values. Serum CK levels were abnormal except in two patients in whom no test was performed. The muscle biopsy, performed in 21 of the patients was compatible with dystrophy in all cases. In FSH some biopsies showed round cell infiltration, in two patients to such an extent that inflammatory myopathy was considered.

We have received information that our patient (No 13) has later developed biopsy changes suggesting inflammatory myopathy.

SINGLE FIBRE EMG FINDINGS
The degree of abnormality, both concerning jitter and fibre density, varied considerably within the muscle, even with a change in needle position of
Table 2  Laboratory data in patients with LG (1–14) and FSH (15–27) dystrophy. EMG: myopathic pattern + = in proximal, ++ = in all investigated muscles. TA (quantitative analysis of interference EMG): ++ = myopathic in biceps and tibialis anterior muscles. Biopsy: Fibre degeneration +, ++ = frequency of necrosis and hyaline degeneration. Fibre regeneration (+) = central sarcoclemma nucleus, + = for example basophilic sarcoplasm. Inflammatory infiltrate (+) = sporadic lymphocytes, + = perivascular infiltrate. Interpretation O = normal, M = myopathic, D = dystrophic myopathy I = inflammatory myopathy E = end-stage, myopathic or neurogenic. The Duchenne patients showed “myopathic” EMG, and had increased CK. Biopsy was performed in 8 cases, all with characteristic changes.

<table>
<thead>
<tr>
<th>EMG</th>
<th>CK</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biopsy</td>
<td>Interpretaiton (No of SD above normal mean)</td>
</tr>
<tr>
<td>Myopathic pattern</td>
<td>Spontaneous activity</td>
</tr>
<tr>
<td>1</td>
<td>+</td>
</tr>
<tr>
<td>2</td>
<td>+</td>
</tr>
<tr>
<td>3</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td>++</td>
</tr>
<tr>
<td>5</td>
<td>++</td>
</tr>
<tr>
<td>6</td>
<td>++</td>
</tr>
<tr>
<td>7</td>
<td>++</td>
</tr>
<tr>
<td>8</td>
<td>++</td>
</tr>
<tr>
<td>9</td>
<td>++</td>
</tr>
<tr>
<td>10</td>
<td>+</td>
</tr>
<tr>
<td>11</td>
<td>+</td>
</tr>
<tr>
<td>12</td>
<td>+</td>
</tr>
<tr>
<td>13</td>
<td>+</td>
</tr>
<tr>
<td>14</td>
<td>+</td>
</tr>
<tr>
<td>15</td>
<td>+</td>
</tr>
<tr>
<td>16</td>
<td>+</td>
</tr>
<tr>
<td>17</td>
<td>+</td>
</tr>
<tr>
<td>18</td>
<td>+</td>
</tr>
<tr>
<td>19</td>
<td>+</td>
</tr>
<tr>
<td>20</td>
<td>+</td>
</tr>
<tr>
<td>21</td>
<td>+</td>
</tr>
<tr>
<td>22</td>
<td>+</td>
</tr>
<tr>
<td>23</td>
<td>+</td>
</tr>
<tr>
<td>24</td>
<td>+</td>
</tr>
<tr>
<td>25</td>
<td>+</td>
</tr>
</tbody>
</table>

only a few millimeters. Therefore care was taken not to make more than one recording in each site.

For fibre density data, see table 3 and fig 1. There was a considerable increase in recordings with multiple spike components. Often three to six but even more than 10 individual single fibre components belonging to the same motor unit were seen with a total duration from first to last component of up to 50 ms. On average 23% of the recordings in the EDC and biceps muscles had more than two spike components as compared to 2-3% in normal muscles.

There was no significant difference between RFD in EDC, biceps and tibialis anterior muscle within the same dystrophy group. This was the case also when muscles with the same strength-rating were compared.

For data concerning jitter see table 4. The jitter varied from normal to highly abnormal (fig 2). There was a tendency for higher jitter between late components than between early. An IDI dependent jitter was found relatively often, particularly in the late components. This jitter appears as parallel movements in all late components at irregular innervation rates (fig 3). In many recordings there were also short term trends in the IPIs, increasing slowly and returning abruptly to the initial value (fig 4). In some of these cases blockings occurred at the stage of maximal IPI. These potentials could have low jitter values. All potential pairs with abnormally low jitter were part of complex potentials. Another phenomenon seen occasionally was the recruitment of single or exceptionally complex potentials into the studied potential (fig 5). This was usually obtained when the innervation rate was voluntarily increased. When it was again reduced the recruited components disappeared with increasing IPI but without increase in jitter.
The motor unit in muscular dystrophy, a single fibre EMG and scanning EMG study

Table 3  Fibre density values

<table>
<thead>
<tr>
<th></th>
<th>No of patients pathol/total</th>
<th>No of invest pathol/total</th>
<th>RFD (mean±SD)</th>
<th>% complex potent /invest (mean±SD)</th>
<th>Mean potent. duration (msec) /invest (mean±SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Biceps brachii</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>0/59</td>
<td>0/59</td>
<td>1-00 ± 0-09</td>
<td>3-1 ± 4-1</td>
<td>less than in EDC</td>
</tr>
<tr>
<td>LG</td>
<td>9/10</td>
<td>15/17</td>
<td>1-46 ± 0-33*</td>
<td>17-5 ± 14-4*</td>
<td>2-70 ± 4-57</td>
</tr>
<tr>
<td>FSH</td>
<td>7/10</td>
<td>7/15</td>
<td>1-17 ± 0-22†</td>
<td>12-5 ± 9-5†</td>
<td>0-82 ± 0-77</td>
</tr>
<tr>
<td>FSH + LG</td>
<td>16/20</td>
<td>22/32</td>
<td>1-31 ± 0-31*</td>
<td>15-0 ± 11-5*</td>
<td>1-82 ± 3-45</td>
</tr>
<tr>
<td><strong>EDC</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>0/100</td>
<td>0/100</td>
<td>1-00 ± 0-11</td>
<td>2-3 ± 2-6</td>
<td>0-78 ± 0-63</td>
</tr>
<tr>
<td>LG</td>
<td>7/12</td>
<td>10/15</td>
<td>1-48 ± 0-52*</td>
<td>31-5 ± 20-0*</td>
<td>2-70 ± 3-60§</td>
</tr>
<tr>
<td>FSH</td>
<td>5/10</td>
<td>5/11</td>
<td>1-15 ± 0-23$</td>
<td>15-2 ± 14-0†</td>
<td>0-92 ± 1-22</td>
</tr>
<tr>
<td>FSH + LG</td>
<td>12/22</td>
<td>15/26</td>
<td>1-34 ± 0-45*</td>
<td>23-0 ± 18-5*</td>
<td>1-95 ± 2-90§</td>
</tr>
<tr>
<td>Duchenne</td>
<td>10/10</td>
<td>10/10</td>
<td>2-23 ± 0-26*</td>
<td>44-3 ± 32-8*</td>
<td>6-52 ± 6-15$</td>
</tr>
<tr>
<td><strong>Tibialis anterior</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>0/54</td>
<td>0/54</td>
<td>1-00 ± 0-12</td>
<td>7-5 ± 7-9</td>
<td></td>
</tr>
<tr>
<td>LG</td>
<td>5/8</td>
<td>6/9</td>
<td>1-43 ± 0-35†</td>
<td>35-0 ± 18-7*</td>
<td></td>
</tr>
<tr>
<td>FSH</td>
<td>5/11</td>
<td>7/13</td>
<td>1-26 ± 0-23*</td>
<td>18-9 ± 13-4</td>
<td></td>
</tr>
<tr>
<td>LG + FSH</td>
<td>10/19</td>
<td>13/22</td>
<td>1-33 ± 0-30*</td>
<td>25-2 ± 17-2*</td>
<td></td>
</tr>
</tbody>
</table>

* t, †, $ p <0-001 in t test when comparing to normals
If the n for the normals is set to the n of the patient group the p values are *<0-001 †<0-01 ‡<0-05, and $ non significant

The jitter value was higher in the biceps brachii than in the EDC muscle within the same dystrophy group (p < 0-030 in LG, <0-08 in FSH). When muscles with the same degree of weakness were compared, MCD was higher in EDC than in biceps muscle (p < 0-04). There was a positive correlation between RFD and MCD in biceps (r = 0-85, p < 0-002) and in EDC r = 0-50 p < 0-009).

SPECIAL TESTS
Ischaemia, which is supposed to affect the neuromuscular junction, was applied in complex recordings in order to differentiate between branched fibres and reinnervation as a cause for the complexity. In the former case, many spike components should disappear together, in the latter individually. Experiments with local ischaemia were performed in three patients. Four recordings, with a total of 24 spike components were studied. During the ischaemia most spike components showed increasing jitter. This was true also for pairs with abnormally low jitter between the spike components. In two cases jitter below 10 μs increased to normal jitter values (from 4-2 to 15 and from 8 to 20 μs respectively). In five spike components the jitter gradually increased and intermittent blockings began to appear with gradually increased IPI. These phenomena occurred after 5–10 minutes of ischaemia and were similar to what is seen in normals. Another type of behaviour, not present in normal muscles was seen in five other spike components. Here blockings occurred abruptly, with only slight increase in jitter, but with increase in IPI (fig 6). In two of these recordings the blocking spike component had an initial jitter of less than 10 μs.

Fig 1  Fibre density in muscular dystrophy. The values are given in RFD. Hatched areas indicate normal values (mean ± 2 SD).

When blocking was seen, this usually affected individual components with increased jitter. Exceptionally paired blockings occurred. In these situations the concomitantly blocking components showed normal or abnormally low jitter between each other, but usually increased jitter relative to the main part of the complex (fig 2).
Table 4  Jitter values

<table>
<thead>
<tr>
<th></th>
<th>No of patients pathol/total</th>
<th>No of invest pathol/total</th>
<th>No of potential MCD (mean ± SD)</th>
<th>% pot with block/invest</th>
<th>% pot with increased jitter/invest</th>
<th>% pot with MCD &lt;10 μs/invest</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Biceps brachii</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>0/7</td>
<td>0/7</td>
<td>125</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>LG</td>
<td>6/7</td>
<td>9/11</td>
<td>155</td>
<td>50.1 ± 67.5*</td>
<td>9.0</td>
<td>20.6</td>
</tr>
<tr>
<td>FSH</td>
<td>6/7</td>
<td>6/7</td>
<td>75</td>
<td>31.2 ± 21.3*</td>
<td>6.6</td>
<td>17.0</td>
</tr>
<tr>
<td>LG + FSH</td>
<td>12/14</td>
<td>15/18</td>
<td>230</td>
<td>43.9 ± 57.3*</td>
<td>8.1</td>
<td>19.2</td>
</tr>
<tr>
<td><strong>EDC</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>0/38</td>
<td>0/38</td>
<td>759</td>
<td>24.6 ± 10.6</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>LG</td>
<td>8/13</td>
<td>12/20</td>
<td>411</td>
<td>40.1 ± 35.7*</td>
<td>2.6</td>
<td>17.4</td>
</tr>
<tr>
<td>FSH</td>
<td>5/10</td>
<td>6/11</td>
<td>288</td>
<td>36.6 ± 27.8*</td>
<td>7.1</td>
<td>11.7</td>
</tr>
<tr>
<td>Duchenne</td>
<td>8/9</td>
<td>8/9</td>
<td>135</td>
<td>51.2 ± 57.2*</td>
<td>10.0</td>
<td>40.0</td>
</tr>
<tr>
<td>LG + FSH</td>
<td>13/23</td>
<td>18/31</td>
<td>699</td>
<td>38.7 ± 32.7*</td>
<td>4.2</td>
<td>15.4</td>
</tr>
</tbody>
</table>

* p values in two tailed t test <0.001 when comparing to normals

Fig 2  Examples of SFEMG recordings in muscular dystrophy. A. Normal jitter. B. Increased jitter. C. Potential complex with 4 components. The two last components are probably obtained from a branched fibre. D. Complex recording with largest jitter for late components (both MCD and MSD are increased). A–D show superimposed traces. E. Multispike recording with a total duration of 50 ms. With an innervation rate exceeding 20 Hz (interdischarge intervals less than 50 ms) a confusing pattern is obtained since the first components reoccur before the end of the complex, third trace. Arrow indicates the first spike component. F. Complex recording with blocking in the last part consisting of three spikes. There is no jitter between the blocking spikes indicating recording from a branched fibre. G. Concomitant blocking of spike component showing a jitter relative to each other. This block probably takes place in the nerve.
The motor unit in muscular dystrophy, a single fibre EMG and scanning EMG study

The latency changes are related to the discharge rate. Lower part shows superimposed traces giving the impression of a jitter. This is due to the velocity recovery function. Jitter between individual spikes is in all cases less than 10 μs.

Fig 3 Complex SFEMG recording from a patient with Duchenne dystrophy. Note the common change in latencies in all components, most in the late; the so called "accordeon phenomenon". The latency changes are related to the discharge rate. Lower part shows superimposed traces giving the impression of a jitter. This is due to the velocity recovery function. Jitter between individual spikes is in all cases less than 10 μs.

Fig 4 Jitter recording in a patient with LG. The plot shows sequential histogram of interpotential intervals (upper part) and interdischarge intervals (lower part). Note the rhythmic changes in mean interpotential intervals, probably due to pronounced VRF since there is a slight but parallel change in the innervation rate. There are individual blockings at the largest IPIs.

Fig 5 Complex recording showing the recruitment of individual components at increasing rate and blocking of these components when the rate is again reduced. The two recruited components have a relative jitter of 2 μs and a normal jitter to the triggering spike but with trends in the interpotential interval particularly in the phase of recruitment and blocking.

relative to another component which did not block (fig 7). Concomitant blockings occurred three times and contained 2, 3 and 3 components respectively. These components had abnormally low jitter with each other.

Fibres were suddenly recruited into the studied potential during the ischaemia in two recordings. The recruited fibres had immediately a normal jitter in one case and an abnormally low in the other.

Since ischaemia also may evoke jitter and blocking in individual components in recordings assumed to indicate branched fibres, the test could underestimate the number of branched fibres. Therefore curare experiments were performed, assuming the effect to be localised purely to the motor end-plate.

Three experiments with local curarisation were performed in one patient. Sixteen spike components
VOLUME CONDUCTION
The amplitude decline over distance was studied for 16 fibres in the brachial biceps in three patients, two with LG and one with FSH. These muscles were weak and had increased RFD. The single fibre action potential amplitude was 9.4±3.5 mV (mean, SD; range 4.8±18.4 mV), (range in normals 2±16 mV). The mean distance along the multielectrode between the electrodes recording maximal amplitude and 200 μV was 256±45 μm. These values are not significantly different from that seen in normals (273±33 μm n = 62) (p = 0.24). Distance from maximal to half amplitude was 94±24 μm which is not significantly different from normals (13) (81±19 μm n = 5) (p = 0.28) (fig 8).

SCANNING EMG
Scanning EMG was performed in five patients with LG and in two with FSH dystrophy. The investigation was performed in the tibial anterior and brachial biceps muscles, which in all the patients were moderately to severely weak. Scanning was also performed in four healthy controls (fig 9).

The intramuscular distance between the extreme electrode positions where motor unit activity was obtained (corresponding to the cord of the motor unit territory) did not differ significantly in the dystrophic muscle (in biceps 7.8±2.3 mm, n = 5; in tibialis anterior 7.5±2.3 mm, n = 33) compared with controls (in biceps 6.0±3.9 mm, n = 13; in tibialis anterior 7.9±1.3 mm, n = 11) (p > 0.3). The maximal recorded length was about 15 mm in both muscles studied in the patients. This is similar to findings in normals.

DIFFERENCE BETWEEN DYSTROPHIES
There were a few differences between the dystrophy groups which reached significant levels. The fibre density values in the EDC muscle were higher in Duchenne dystrophy than in LG (p < 0.001). In biceps the RFD was higher in LG than in FSH (p = 0.004), but there was no significant difference between LG and FSH for RFD in EDC (p = 0.06) or in tibialis anterior muscles (p = 0.08).

Duration of potential complexes with two or more spike components was highly increased in Duchenne, less but significantly in LG, and not in FSH in comparison with normals. Some potential complexes with long duration (up to 30 ms) were seen also in FSH.

The jitter was significantly higher in Duchenne dystrophy than in LG (p = 0.008) in the EDC muscle. LG patients had a higher jitter than the FSH patients (p = 0.018) in the biceps muscle. (This muscle was too weak to be studied in Duchenne dystrophy.)

were studied. Three recordings with abnormally low jitter with 3, 3 and 4 components respectively showed concomitant blocking, 4 components with normal jitter showed individual blocking.

In four recordings with increased jitter Tensilon was injected. The jitter decreased slightly but significantly in one of the experiments.

Four complex potentials, two containing fibres with decreased jitter and two with increased jitter were studied during 10 minutes of continuous activity. No significant long-term change in jitter was noted during the test.

Fig 6 Jitter recording in patient with LG during ischaemia. Before ischaemia there is a normal jitter between spike all components but between components 2, 3 and 4 where the jitter is below 10 μs. During ischaemia the fourth component shows rhythmic changes in interpotential interval and blocking. At a later stage the jitter in the fifth component is increasing until block. The blocking in the fourth component is considered to take place in the muscle fibre, in the fifth component in the neuromuscular junction.
The motor unit in muscular dystrophy, a single fibre EMG and scanning EMG study

In the volume conduction and scanning EMG studies no difference between the LG and FSH cases was noted.

RELATIONSHIP BETWEEN CLINICAL AND NEUROPHYSIOLOGICAL FINDINGS

Multiple stepwise linear regression analysis was performed with age, duration of the disease, disability score, progression, strength, atrophy and CK as independent variables and MCD and RFD as dependent. The total linear correlation was usually high but different first step variables were found for the different analyses (table 5). A decreasing strength was significantly correlated with increasing abnormality of RFD in EDC and to MCD in EDC and biceps muscles respectively. The degree of impulse blocking showed a weak but significant (p < 0.05) correlation to strength in the studied muscles. In some severely affected muscle no impulse blockings were recorded.

In muscles with normal strength there were only exceptionally abnormal MCD or RFD findings. In weak muscles it was unusual to record normal SFEMG findings (fig 10). Exceptions to this were seen in patients with FSH. In three of them (nos 15, 20, 27) the RFD was normal in comparatively severely and quickly deteriorating biceps muscles. Their EDC was comparatively less involved, but RFD was increased in two of them. The patient with “preclinical” FSH (no 23) had significantly increased RFD in his normally strong biceps and tibial anterior muscles, but not in EDC.
Fig 9 Examples of Scanning EMG in the tibialis anterior muscle. Recordings from normal control, FSH and LG dystrophy. Arrows indicate measured motor unit length.

Table 5 Multiple stepwise linear regression analyses of age, disease duration, disability score, progression score, strength score, atrophy score, CK level on RFD or MCD as dependent variable

<table>
<thead>
<tr>
<th>Dependent variable</th>
<th>RFD in EDC</th>
<th>RFD in biceps</th>
<th>RFD in tib. anterior</th>
<th>MCD in EDC</th>
<th>MCD in bic</th>
</tr>
</thead>
<tbody>
<tr>
<td>First step variable</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>score</td>
<td>0·77</td>
<td>0·40</td>
<td>0·83</td>
<td>0·70</td>
<td>0·73</td>
</tr>
<tr>
<td>progression score</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>correlation</td>
<td>0·77</td>
<td>0·58</td>
<td>0·70</td>
<td>0·73</td>
<td>0·74</td>
</tr>
<tr>
<td>Total correlation</td>
<td>0·77</td>
<td>0·14</td>
<td>0·02</td>
<td>0·70</td>
<td>0·50</td>
</tr>
<tr>
<td>Correlation to strength score</td>
<td>0·77</td>
<td>-0·02</td>
<td>0·70</td>
<td>-0·50</td>
<td></td>
</tr>
</tbody>
</table>

Discussion

The SFEMG results show abnormal fibre density and jitter, confirming an earlier investigation.20 The results reflect a changed muscle fibre distribution within the motor unit and abnormal impulse transmission. The Scanning EMG findings add information about the spatial (and temporal) organisation of the motor unit.

The increase in fibre density seems to be in contradiction to earlier interpretations of the electrophysiological findings in muscular dystrophies. This needs to be discussed. A number of factors may influence the fibre density parameter, the most important of which are volume conduction properties of the muscle tissue and the size and distribution of the electrical generators, the muscle fibres.

An increased volume conduction in dystrophic muscle would give an increase in FD because of a larger effective pick up area of the electrode. Our measurements did not show any difference between normal and dystrophic muscles as judged from the shape of the amplitude/distance curve over the distance of 455 μm. Other factors therefore seem more important for the change in FD values.

Is the fibre density measure changed due to abnormal fibre diameters? The action potential amplitude is normally thought to be correlated with the fibre diameter and the recording distance to the fibre. The histological picture of muscular dystrophies is characterised by increased variability in muscle fibre diameter.21 There is a small proportion of hypertrophic fibres that may generate high action potentials. In the volume conduction studies the
The motor unit in muscular dystrophy, a single fibre EMG and scanning EMG study

Fig 10 Summary of jitter and FD measurements in the patient material in relation to strength. Note that patients with normal strength have in general normal recordings whereas the SFEMG parameters are abnormal in weak muscles. An exception is found for FD in FSH patients. N = normal findings. P = increased FD or increased jitter.

High action potentials were recorded over a slightly longer distance than the average but within the range found in normal muscles. Large fibres were typically not seen in groups in the biopsy and their contribution to the increased FD is therefore considered to be of minor importance.

Atrophic fibres, on the other hand, produce low action potential amplitudes and are recorded over a shorter distance. This should lead to a reduced, not increased FD value. The atrophy could however lead to shrinkage of the muscle with a more closely packed motor unit which should increase the FD. The net result of the two opposing effects of atrophy on FD, lowering because of weak electrical generators, increasing because of packing, is difficult to predict.

In normal children with small muscles but presumably with the same number of fibres and motor units as in adults, the FD is only slightly higher than in adults. In cases with inactivity atrophy due to leg fractures the FD is unchanged. (unpublished observations) Therefore it is unlikely that a generalised fibre atrophy with corresponding motor unit shrinkage would account for the high FD values.

It, however, a heterogeneous atrophy took place, abnormal FD could be seen. In case all fibres in some motor units became atrophic while other motor units were preserved, the latter would become more densely packed but with normally sized fibres. This change in motor unit topography is not supported by the results of the Scanning EMG indicating that the motor unit territory is unchanged compared with findings in normal muscles.

The increased fibre density seems most likely to be due to abnormal fibre distribution. Fibre density increase is most often seen in neurogenic lesions where it is interpreted as a sign of reinnervation giving increased number of fibres in the motor unit. A local increase of number of fibres could also be the explanation for the increase in fibre density in the dystrophies (fig 11).

The increase could be due to myogenic mechanisms by which a muscle fibre is "branched". Splitting of fibres, which is described as a common phenomenon in myopathies, is seen as incomplete septa passing into an otherwise complete muscle fibre or by the formation of separate muscle fibre branches arising from one muscle fibre, seen in transverse sections. Splitting often takes place in large regenerating fibres formed by satellite cells within the endomysial sheath which remains after a degenerated fibre segment. When the branches are functionally connected by a common synapse or by ephaptic transmission, they are assumed to have a
low jitter (below 10 μs in this study).\textsuperscript{15} Decreased jitter was found more frequently in this study than in normal muscles, but it was not a prominent finding. The evidence that the low jitter indicated branched fibres in dystrophic muscles was the occurrence of concomitant blocking of the spike components with low jitter during ischaemia or curare. This is different from the blocking in recordings with normal jitter in such tests in which the spikes block independently after preceding increase in jitter.\textsuperscript{16} Exceptionally spikes with low jitter blocked independently in muscular dystrophies, but they had a neglectable increase in jitter, suggesting a myogenic block in an abnormal muscle fibre branch.

No quantitative estimation of the branched fibres is made in this study. The number of branched fibres can be underestimated for the following reasons. Firstly a low jitter may be superimposed with interdischarge interval dependent jitter, particularly prominent in dystrophic muscles.\textsuperscript{20} This effect is mainly neutralised mathematically by expressing the jitter as MSD. Secondly it is difficult to detect all individual components with low jitter since they are disturbed by neighbouring jittering spikes in the complex recordings. Thirdly it cannot be excluded that some branched fibres may have a jitter due to randomly varying impulse transmission along the muscle fibre. Such a jitter was seen to develop during ischaemia in recordings suggesting branched fibres. The number of branched fibres can be overestimated since their cardinal sign, low jitter is also seen in cases of ephaptic transmission between separate muscle fibres.\textsuperscript{29}

\textit{Ephaptic transmission} is another mechanism through which increased number of muscle fibres may be recorded. If an active muscle fibre triggers an action potential in a neighbouring hyperexcitable fibre, an increased FD should be obtained. This mechanism, seen as recruitment has been shown to take place in denervated muscles\textsuperscript{29} and the phenomenon was also seen several times in muscular dystrophies. Usually the locking of a fibre is obtained with increasing innervation rate, and unlocking when the rate is again decreased. Since the ephaptic transmission could occur between different fibre types, this may lead to a discrepancy between morphological fibre type grouping and FD. The quantitative importance of this phenomenon for increased FD is not settled.

In muscular dystrophies double discharges were sometimes encountered. These are easy to recognise and the phenomenon is therefore not causing an erroneous FD value.

Can all the increase in FD be explained by
myogenic mechanisms that is, branched fibres and ephaptic transmission? This is not likely since signs of abnormal innervation, primary or secondary, are present.

There are morphological findings of longitudinal displacement of motor end-plates and presence of numerous unemployeds, freely ending axons in Duchenne dystrophy. In LG and FSH the terminal nerve endings were frequently expanded and increased Terminal Innervation Ratio (TIR) was observed in some cases. There was no increase in TIR in Duchenne. The discrepancy between FD and TIR in Duchenne may indicate either myogenic mechanisms for FD or that the nerve branching is proximal to the observation area used in determinations of TIR, which therefore is underestimated. Engel and co workers found no morphological abnormality in intramuscular nerves, or nerve terminals in Duchenne muscles but there was focal atrophy of the postsynaptic regions. In contrast to the situation in myasthenia gravis the acetylcholine receptors were preserved.

Also the SFEMG findings indicate abnormal innervation. Increased jitter and blocking is a common finding and is compatible with the transmission disturbance in motor end-plates or nerve twigs after reinnervation. The concomitant blocking sometimes seen in components with increased jitter is assumed to indicate transmission failure in the common nerve branch. The jitter does not respond to edrophonium as it does in for example, myasthenia gravis and is therefore probably not due to loss of receptors.

A reinnervation process indicated by these morphological and electrophysiological findings may be initiated by several mechanisms. One mechanism may be segmental necrosis, often seen in dystrophies. The sequestered fibre fragment would become denervated, show fibrillation potentials and may later receive innervation by collateral sprouting. Another possibility is generation of new fibres from satellite cells or by complete fibre splitting as supposed to occur in muscular dystrophies which will be innervated to become functional. Possibly there is also a neurogenic component of the disease, with denervation and reinnervation, primary or secondary. McComas et al have suggested that there is an actual loss of motor units due to sick motor neurons but this has so far not been confirmed. Reduced motor nerve conduction velocity and increased distal latencies are reported in muscular dystrophies.

In a preliminary (in preparation) study with intramuscular nerve stimulation the jitter is found to be increased in about 25% of the spike components of the recordings, contrasting with the findings of low or normal jitter values at direct muscle stimulation. This seems to be strong evidence that the jitter often is generated in the distal nerve twigs or in the motor end-plates supporting the idea of ongoing innervation.

In muscles with increased FD the total duration of the multispike complex is prolonged, even more than that observed in neurogenic disorders with an equivalent increase in FD. The increase could be due to a large variation in the propagation velocity of the muscle fibres which has also been confirmed by direct measurements. Neurogenic factors may also contribute to the total duration such as abnormal end-plate position or slow conduction velocity in the nerve terminal.

In summary we find increased FD in the motor unit. This finding independent of causative mechanism, does not seem to fit the general concept of loss of active fibres in muscular dystrophies. One explanation for the apparent contradiction would be degenerative-regenerative phenomena. These result in heterogeneous distribution of muscle fibres in the motor unit, with groups of fibres locally, recorded by the SFEMG, separated by “silent areas” within the motor unit, not detected by the SFEMG.

Scanning EMG was used to highlight the problem of fibre topography within the motor unit. Since we have no way of finding the centre of the motor unit the exact diameter could not be determined, but a cord of the motor unit cross section was studied. This was found to be the same in the LG and FSH patient material and in normals. This is in agreement to what is reported in multielectrode studies. The mean length obtained in this study is longer for both patients and normal subjects than in the multielectrode studies. In another study in the same patient material “silent areas” within the motor unit territory were seen, supporting the idea of rearrangement of muscle fibres within the motor unit with local fibre grouping mixed with silent areas.

The increase in FD and jitter and the other SFEMG abnormalities were usually seen when the studied muscle was clinically involved, but not if the muscle was clinically preserved. This was also confirmed by multiple regression analysis. Exceptions to this were present. In two FSH cases RFD was normal in biceps in spite of a comparatively rapid and severe deterioration in muscle strength. This might be a sign of reparative failure. Increased RFD on the other hand seen in the “preclinical” FSH patient might be a sign of complete compensation of the degeneration by regenerative mechanisms. Since the clinical parameters reflect the summed effect of degeneration and repair and FD mostly regenerative phenomena, the absence of correlation between the two in individual cases is not
surprising.

There is a slight correlation between the amount of blockings and muscle strength but not to the same degree as for myasthenia gravis. This indicates that blocking contributes only to a minor degree to the weakness. Many clinically weak muscles with increased FD and without gross atrophy showed no blocking. This is either due to defect contractile properties in muscular dystrophies or otherwise impaired mechanical output in regenerating structures.

The findings were of the same nature in Duchenne, LG and FSH dystrophies but most pronounced in Duchenne and least in FSH.

Supported by the Swedish Medical Research Council, Grant 135. We thank Mrs A Alsterlind, K Daniellson, J Eriksson and A Larsson for technical and secretarial help and Eng L Antoni for the computer work.

References
The motor unit in muscular dystrophy, a single fibre EMG and scanning EMG study

The motor unit in muscular dystrophy, a single fibre EMG and scanning EMG study.
P Hilton-Brown and E Stålberg

*J Neurol Neurosurg Psychiatry* 1983 46: 981-995
doi: 10.1136/jnnp.46.11.981

Updated information and services can be found at: http://jnnp.bmj.com/content/46/11/981

**Email alerting service**

*These include:*

Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

**Notes**

To request permissions go to: http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to: http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to: http://group.bmj.com/subscribe/