Quantitative electromyography: carrier detection in Duchenne type muscular dystrophy using a new automatic technique

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SUMMARY An automated method of quantitating small electromyographic changes, based on the ratio of action potential duration to the number of phases per potential, was applied to carriers of X-linked Duchenne type muscular dystrophy. The ratio was found to be significantly raised in a proportion of these cases.

Detection of the carrier state in apparently normal female relatives of boys with X-linked Duchenne type muscular dystrophy has received considerable attention in recent years. Because the most widely used test, estimation of serum creatine phosphokinase (CPK) will identify only about 70% of known female carriers, further methods of investigation have been sought. Quantitative electromyography (EMG) was first advocated by Van den Bosch (1963) as a method of improving carrier detection, although some subsequent workers failed to reproduce his findings (Davey and Woolf, 1964; Willison, 1965). Gardner-Medwin (1968) found agreement with Van den Bosch, obtaining an increase of carrier detection from about 70% to 90% by using manual quantitative electromyograph assessment. This involved the measurement of motor unit action potential durations and number of phases per potential in order to calculate the ratio of these measurements. However, Gardner-Medwin found the method time consuming and the importance of obtaining control records and using blind assessment militated against routine use.

An automatic method of EMG analysis has been described (Rose and Willison, 1967) and using this method Willison (1968) found that five of eight definite carriers had abnormal values for the shortest 25% of the intervals between potential changes. A new automatic method of analysis was recently described from this centre (Brown, Whittaker, and Moosa, 1971; Moosa and Brown, 1971) and this method has now been applied to the detection of carriers.

METHODS

The subjects are listed in Table 1. The normal controls were all hospital staff members with no family history of neuromuscular disease. The carriers were all female relatives in the maternal line of proven cases of Duchenne muscular dystrophy. For the purpose of analysis they have been subdivided into three categories or genetic groups—namely, (1) definite carriers: women with an affected son and also an affected brother, maternal uncle or sister's son, or women with more than one affected son by different fathers; (2) probable carriers: women with more than one affected son; and (3) possible carriers:

<table>
<thead>
<tr>
<th>Subjects</th>
<th>Number</th>
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<tbody>
<tr>
<td>Normal controls</td>
<td>14</td>
</tr>
<tr>
<td>Definite carriers</td>
<td>6</td>
</tr>
<tr>
<td>Probable carriers</td>
<td>2</td>
</tr>
<tr>
<td>Possible carriers</td>
<td>33</td>
</tr>
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</table>
any woman being a female relative on the maternal side of a known case of Duchenne dystrophy.

The method of recording the signals and the two automatic methods of analysis have been fully described previously (Moosa and Brown, 1971; Brown et al., 1971). EMG signals were recorded, using concentric needle electrodes, from the biceps muscle, and samples were obtained from several points in each muscle. The EMG was recorded at maximum contraction but no fixed load was used. The two methods of analysis have been found to correlate very well and for the purpose of this paper only the results of the simpler and cheaper method of measurement have been used. This method attaches an index to each EMG signal and consists of a simple analogue system. This index $\psi$ max is increased in myopathy and has been found to be almost independent of the contraction strength of the muscle.

The known increase of duration of motor unit action potential with age has been allowed for, in a similar manner to that used by Gardner-Medwin (1968). While different methods of EMG analysis give different answers for action potential duration, it has been assumed that the percentage increase of duration with age will be similar for all methods. The durations obtained in the 14 control subjects have been compared with the values given by Buchthal (1957). The mean percentage deviation from Buchthal’s normal has been used to give a line with a similar gradient to that of Buchthal but representing the normal mean for this study. In Fig. 1 lines giving two standard deviations from the mean are shown and these were taken as the limits of normal.

In addition to the EMG measurements, estimates of serum CPK were made in all the patients under investigation. The method of Hughes (1962) was used (normal < 70 i.u. |l|).

RESULTS

The result of the EMG analysis in all 55 subjects is shown in Fig. 1. The control and definite, probable, and possible carrier groups are separated.

Percentage deviations from the normal, as shown in Fig. 1, were calculated for all subjects and the results are shown in Table 2. The definite carriers are significantly different from the control group ($P < 0.001$). The possible

<table>
<thead>
<tr>
<th>Group</th>
<th>No.</th>
<th>Age (yr)</th>
<th>% Deviation from normal ($n = 14$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definite carriers</td>
<td>6</td>
<td>37.2 (27-48)</td>
<td>34.1 ± 8.6 (1 SEM)</td>
</tr>
<tr>
<td>Probable carriers</td>
<td>2</td>
<td>28 and 36</td>
<td>21.5</td>
</tr>
<tr>
<td>Possible carriers</td>
<td>33</td>
<td>28-6 (12-52)</td>
<td>14.5 ± 4.6 (1 SEM)</td>
</tr>
</tbody>
</table>

**TABLE 2**

RESULTS OF ACTION POTENTIAL MEASUREMENTS IN 55 SUBJECTS

**FIG. 1.** The electromyographic index $\psi$ max plotted against age for all the subjects studied. The 'normal' and 2 SD curves were derived from our normal controls and Buchthal's results, as explained in the text.
carriers show a difference at a much reduced level of significance ($P=0.07$). The two probable carriers cannot be treated statistically, although one gave an EMG result well outside the 2 SD level for the controls. Taking individual results, three of the six definite carriers gave results outside the 2 SD limit and 10 of the 33 possible carriers.

Figure 2 plots the % deviations of the EMG indices from the controls against CPK levels. It can be seen that the subjects giving abnormal values for CPK are not necessarily those giving abnormal EMG indices, and vice versa. A detection ratio based upon both CPK and EMG will be greater than one based upon either method in isolation. Of the six definite carriers three gave abnormal EMG results and two gave abnormal CPK estimates. Only one of the six escaped detection by either measurement. These results and comparative figures for the possible carriers are given in Table 3.

**TABLE 3**

<table>
<thead>
<tr>
<th>Group</th>
<th>No.</th>
<th>Detection by EMG (No. %)</th>
<th>Detection by CPK (No. %)</th>
<th>Detection by EMG and/or CPK (No. %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definite carriers</td>
<td>6</td>
<td>3/6 50</td>
<td>2/6 33</td>
<td>5/6 83</td>
</tr>
<tr>
<td>Probable carriers</td>
<td>2</td>
<td>1/2 50</td>
<td>1/2 50</td>
<td>1/2 50</td>
</tr>
<tr>
<td>Possible carriers</td>
<td>33</td>
<td>10/33 30</td>
<td>9/33 27</td>
<td>15/33 45</td>
</tr>
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</table>

**DISCUSSION**

Van den Bosch (1963) first suggested electromyography as a method of carrier detection, as myopathic motor unit action potentials are known to have short durations and increased numbers of phases. From photographic records of the signals Van den Bosch measured action potentials in order to derive an index $\phi$ phases/second. He found good discrimination of the carriers and control subjects. His work was criticized by a number of workers (Davey and Woolf, 1964; Willison, 1965) who failed to reproduce his findings. However, Gardner-Medwin (1968) determined an index $\phi$, defined similarly to Van den Bosch, but made allowance for some of the points criticized in the work of Van den Bosch. He did not preselect action potentials of more than three phases, used multiple observers to reduce subjective bias, and corrected results for the age of the subjects. His results confirmed those of Van den Bosch, giving a useful discrimination of carriers. However, his method was too time-consuming for routine use.

Automatic methods of analysis would appear to eliminate the subjective element in analysis.
and we have sought an automatic method which gives an index similar to that of Van den Bosch and Gardner-Medwin. Our method of analysis (Brown et al., 1971; Moosa and Brown, 1972) is automatic and derives an index which increases with either decreasing duration of motor unit action potential or increasing numbers of phases. The method is relatively cheap and can be carried out during the recording of the EMG.

The number of definite carriers available to us does not enable an accurate assessment of detection rate to be made when using either CPK or EMG assessment as the criterion. However, the results of the quantitative EMG measurements leave no doubt that a significant percentage of carriers can be detected by this method and that these are not necessarily those detected by CPK. A detection percentage greater than 80% appears to be possible when using both CPK and EMG assessment. The addition of biopsy should give a further increase in detection. Of our six definite carriers, three were detectable by EMG, two by CPK, and the remaining one had unequivocally abnormal histological changes on biopsy.

Some coordination of results of CPK, EMG, and biopsy results seems called for if the best information is to be made available for the purposes of genetic counselling. Certainly a combination of the results can give a detection rate greater than 80% and systematic study to determine the best combination of available results should enable this to be further increased.

This work has been supported in part by grants from the Muscular Dystrophy Group of Great Britain. We wish to thank Mr. D. W. Graham for his technical assistance and the Regional Medical Physics Department for the use of its facilities.

REFERENCES


