Single-fibre electromyography (SFEMG) at different firing rates in myasthenia with and without thymoma

Barbara Emeryk-Szajewska, Katarzyna Rowińska, Teresa Michalska and Halina Strugalska

Department of Neurology, Warsaw Medical School and Neuromuscular Unit, Medical Research Centre, Polish Academy of Sciences, 1a Banach St., 02-097 Warsaw, Poland

Abstract. The single fibre EMG differences during motor axonal stimulation at different firing rates were studied in myasthenic patients: 15 with, and 15 without thymoma. 10 healthy volunteers were also examined. Conventional repetitive stimulation EMG as well as SFEMG during weak voluntary contraction and on 10 and 20Hz stimulation was performed in every patient. The mean jitter in the control group was 30 µs on voluntary contraction and about 22 µs at 10 as well as at 20 Hz stimulation. In both groups of myasthenic patients under consideration SFEMG on voluntary contraction detected neuromuscular transmission disturbances of various degree. The results obtained at motor axonal stimulation (10 and 20 Hz) were unhomogeneous. In both groups jitter seemed to be slightly shorter at higher (20 HZ) frequency stimulation, probably due to facilitation but differences were insignificant.

Key words: single fibre EMG, axonal stimulation, neuromuscular transmission, myasthenia gravis, thymoma
INTRODUCTION

The present status of investigations on neuromuscular (n-m) transmission allows a relatively reliable and sensitive evaluation of the presence and severity of the neuromuscular block as well as its response to pharmacologic agents, compensation ability of the synapse, etc.

We are not considering here the scientific, experimental possibilities. We are interested, in this study, only in the applied clinical neurophysiology examining patients.

From the level of overall, summative evaluation of many simultaneously working synapses or even motor units (as in the classical supramaximal repetitive stimulation) these investigations attained, thanks to SFEMG, the level of evaluation of single, individual end-plates.

Despite all progress the differentiation still remains difficult and uncertain between the two types of the n-m block, that is between the postsynaptic one (with normal presynaptic ACh release but abnormal receptors and sensitivity of the postsynaptic membrane) and the presynaptic block (with a quite opposite situation).

Being difficult and doubtful it is of great clinical significance because that first type of postsynaptic block is typical of myasthenia (so important in clinical practice) and the other presynaptic block occurs in botulism, and in the Lambert-Eaton myasthenic syndrome, connected with bronchogenic lung carcinoma, perhaps also with other neoplasms and some immunological diseases.

There are, of course, some electrophysiologic features speaking for this or that character of block (Schwartz and Stålberg 1975a,b,c, O'Neil et al. 1988, Oh 1989). They are, unfortunately, unstable and not fully reliable. Recently contributions appear in the literature suggesting that the different response to the changes of the firing rate (on voluntary contraction or stimulation) may be the differentiating factor. In the presynaptic block, e.g. in the Lambert-Eaton syndrome the rise in the stimulation rate might temporarily decrease the n-m block, probably by transmitter mobilisation and facilitation. In the postsynaptic block, e.g. in myasthenia, n-m block might increase on faster stimulation due to the increasing functional insufficiency of the postsynaptic membrane receptors.

In the present study we have attempted to see whether that hypothesis may be correct. We have chosen two groups of patients: with myasthenia but without thymoma and with myasthenia due to infiltrating thymic neoplastic tumours. In the group I we had patients with postsynaptic block and in the group II the character of block was not clear.

METHODS

The study comprises two groups of myasthenic patients (with and without thymoma) and one group of 10 healthy volunteers.

The first group consisted of 15 patients (11 women and 4 men) aged 20 - 65 years (mean 38.2) with myasthenia. The disease duration was 1-13 years (mean 5.8). In 14 patients it was the generalized myasthenia, mild or severe (type 2A and 2B), in 1 patient the localised ocular myasthenia (1A).

Thymectomy was done in 12 patients. No thymoma was found but rudimentary persisting thymus, sometimes with follicular hyperplasia. In the remaining 3 patients thymoma was excluded by normal CT.

The second group consisted also of 15 patients (10 women and 5 men) with myasthenia and surgically confirmed thymoma. The patients were older in this group: 38 - 73 years (mean 50.6). The disease duration was 3 months up to 13 years (mean 5.1). All had generalized myasthenia with different severity of clinical pattern (2A, 2B, 3). One patient, originally classified as having generalized severe myasthenia (2B) had a full clinical recovery following surgery and needed cholinergic drugs no more. Thymectomy was done in all of those patients after clinical and CT (or pneumomediastinographic) diagnosis of thymoma.

In 11 patients a tumour was found infiltrating the adjacent structures, invasive - so after surgery radiotherapy was performed in these patients. In 4 patients well encapsulated thymoma was found.
Moreover a group of 10 healthy volunteers (8 women and 2 men) aged 28 - 57 years (mean 38.4) was studied. Informed consent was obtained from all of them.

Routine examination of neuromuscular transmission, i.e. supramaximal repetitive stimulation were performed in all patients before surgery, in the course of clinical diagnosing. The latter served only to confirm the diagnosis and were not subject of this analysis.

In every subject the SFEMG was performed at slight voluntary contraction in extensor digitorum communis according to the classical method of Stålberg and coworkers. Jitter and blocking was evaluated (Stålberg and Trontelj 1979, Gilchrist 1992).

The Counterpoint (Dantec) equipment was used containing a programme for single fibre EMG with automatic measurements of jitter ($\mu$s) and % of blocking for every pair of potentials, that is for every end-plate investigated. For the high pass the 500 Hz filters and for the low pass the 16 kHz ones were used. Recording was made with the Medelec SF25 SFEMG electrode with a leading-off surface 25 microns in diameter in the side of a 0.6 mm steel cannula. The patient was asked to make a slight muscle contraction at a constant level: about 10 Hz at the frequency meter. Twenty potential pairs were recorded in every subject. The results were registered in form of histograms of potential pairs jitter, mean jitter with SD and % of blocking.

After voluntary SFEMG electrical microstimulation was performed of motor axons of the radial nerve with recording of evoked potentials of single muscle fibre acc. to the method of Trontelj and Stålberg (Trontelj et al. 1986, Trontelj et al. 1988, Trontelj and Stålberg 1992 (in press), Trontelj et al. 1992). The same SF25 electrode was used for the recording. The same Counterpoint machine was used for stimulation, recording and computation of the jitter. A pair of monofilier steel electrodes insulated to 1 mm from the tip (Medelec37) was used for stimulation. The rectangular stimulus, 50 microseconds duration, 15 - 20% suprathreshold was used. The stimulation rate was 10 Hz and 20 Hz. In every case 20 SF potentials were registered, so function of 20 end-plates was evaluated (Fig. I).

**RESULTS**

In the normal subjects the jitter during voluntary activity was 30.1±4.3 microseconds, on axonal stimulation 10 Hz it was 22.3±4.1 microseconds, the difference being statistically significant at $P<0.005$. Not only the mean for the whole group but also results in all 10 particular subjects were higher on voluntary activity than on stimulation, the differences
ranging 15-30%. Jitter on stimulation 20 Hz was 22.9±4.5 microseconds in this group. It did not differ from the results obtained on stimulation 10 Hz and was also 15-30% lower than on voluntary activity (Fig. 2.). Blocking during voluntary activity was found in 1% (2/200) of potential pairs only. On axonal stimulation it was never seen.

On the contrary to the control group the mean values are hardly applicable in myasthenia, since every patient presents a different degree of n-m transmission disturbances. It is different in different muscles of the same patient, even within the same muscle "healthy" end-plates exist and function along with the severely injured ones.

We have processed our results in two ways. First we calculated mean values for every patient. Then we evaluated the changes against the whole pool of individual end-plates (the pooled data). The individual patient's results and the pooled data results turned out to be very similar.

The Fig. 3 presents the results in the groups studied. Evidently, as well in the group of myasthenia without thymoma as in the group with thymic tumours jitter on voluntary activity was significantly higher than that measured on axonal stimulation, similar as in the control group. It was valid not only for the mean of the group but also for every patient analysed individually. In either group of patients the differences between jitter recorded during the voluntary activity and during axonal stimulation were irregularly different (sometimes small, sometimes very marked>50%), whereas in the control group the differences all fell between 15 and 30%.

Especially essential for the aim of this study was to compare jitter values and % of blocking, reflecting the degree of n-m disturbances, on stimulation at different firing rates, 10 and 20 Hz. It turned out that jitter was only slightly lower on stimulation 20 Hz in either group of myasthenia, without and with the tumour, the differences being statistically insignificant. There were no differences in blocking as well (Table II).

Suspecting that mean values of the whole group might obscure the individual results, the results of
Fig. 2. The results of jitter expressed as MCD (mean consecutive differences) measured during voluntary activity (VA) and axonal stimulation (AS) in the control group.

Fig. 3. The jitter results in groups investigated.
TABLE II

<table>
<thead>
<tr>
<th>Groups</th>
<th>VA</th>
<th>10 Hz</th>
<th>AS</th>
<th>20 Hz</th>
<th>AS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>1.03%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td></td>
</tr>
<tr>
<td>Myasthenia</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>without thymoma</td>
<td>55.79%</td>
<td>47.37%</td>
<td>44.98%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>with thymoma</td>
<td>37.69%</td>
<td>30.00%</td>
<td>29.41%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

VA, voluntary activity; AS, axonal stimulation

the individual patients were analysed separately. Jitter and blocking in patients without tumour were sometimes enhanced by faster stimulation but in some cases stimulation 20 Hz caused blocking less frequent and jitter shorter. Such differences may occur even in the same patient, in the same muscle in different single fibre potentials.

Similar phenomenon was seen in patients with thymic neoplasms.

DISCUSSION

In the course of the study it turned out that the method was very reliable and useful in the diagnostics of n-m transmission disturbances, not inferior to jitter measurement on voluntary activity. Its advantage is that the cooperation of the examined person is not needed therefore it is easy applicable in children with suspected children myasthenia, congenital myasthenia, in the patients with severe myasthenia unable to perform prolonged voluntary contraction. This method allows also to examine patients poisoned with agents causing n-m block, often unconscious and unable to perform voluntary contraction. The method is also applicable in experimental animals.

Duration of jitter in stimulated measurements shorter than on voluntary activity, seen in all our subjects, needs explanation. Several years ago similar differences were observed by Trontelj et al. 1986. It may be explained by the technical differences. In the stimulation SFEMG the stimulus artifact triggers the sweep and the differences in latency are measured between this artifact and the action potentials. It represents the variability (jitter) of one end-plate. In the voluntary study a potential pair is needed. The sweep is triggered by one potential while jitter is measured in another. In this situation the interpotential interval includes the variability of two endplates (Jabre et al. 1989). Second difference between voluntary and stimulation SFEMG is that different populations of motor units are activated in these two methods. In the voluntary study, during mild contraction, the smaller size, low-threshold motor units are sampled. In the intramuscular stimulation study nerve terminals of the large and the small unit are stimulated, then both types of units are sampled. It can also influence the final result (Jabre et al. 1989).

The next problem concerns the changing jitter and blocking at different firing rates, 10 and 20 Hz. Our studies, as well as studies of Sanders (1986 and 1992), Trontelj and Stålberg (1990), Trontelj et al. (1992), have shown that in myasthenia the individual motor end-plates behave in different way on changing stimulation rate. Although Trontelj found some regularities in the mean values, the differences were small. He observed a slight elongation of jitter and increased blocking at stimulation rates from 0.5 up to 1 - 2 - 5 Hz and some small decrease (improved transmission) at 20 Hz. In one case, of the Lambert-Eaton syndrome an improvement of transmission (decrease of jitter and blocking) was seen in all single muscle fibre potentials with the increase of the stimulation rate (Trontelj 1990, Trontelj and Stålberg 1990). In 1992 a letter of Sanders to the Editor of the "Muscle and Nerve" was published relating different, often opposite, responses of individual end-plates to the changing of stimulation rate in a patient with a typical Lambert-Eaton syndrome.

The things are then more complicated than it has been expected. The response to the increase of the firing rate may, perhaps, depend not only on the type of the n-m block but also on the ability of mobilising the transmitter, on facilitation, and on the sensitivity of the postsynaptic membrane at the time of investigation. Perhaps all those factors play a role.
We must conclude that, the way in which jitter and blocking change at different stimulation rates is different in individual patients with myasthenia, probably even in different endplates of the same patient. It concerns the myasthenic patients without and with thymoma. Further investigations are certainly needed.

ACKNOWLEDGEMENT

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