INTRODUCTION

Dr Donald B. Sanders, when introducing Erik Stålberg who invented single fibre electromyography (EMG), at a meeting in Uppsala in 2001, told a true story about a lady with puzzling symptoms, suspected of having myasthenia gravis. Finally after the diagnosis of myasthenia was made on the basis of single fibre EMG, the lady said to Dr Sanders, ‘Doctor, I just thank the Lord he made someone smart enough to figure all this out, so you doctors could help me!’ Single fibre EMG practitioners are used to hearing words like this because the technique can be the only test to show an abnormal result when repetitive nerve stimulation, the tension test and acetylcholine receptor antibodies are negative in myasthenia gravis. Although the major clinical role of single fibre EMG is in the diagnosis of myasthenia gravis, it is helpful in some other conditions, such as the congenital myasthenias, Lambert–Eaton myasthenic syndrome (LEMS) and botulism.

Single fibre EMG is abnormal in almost every patient with generalized myasthenia gravis, and in 90% with ocular myasthenia if one muscle is examined, and in 99% if two muscles are examined (Sanders 2002). However, although it is the most sensitive test, it is not as specific as the older tests such as acetylcholine receptor antibodies, repetitive nerve stimulation and the tension test.

THE PARAMETERS OF SINGLE FIBRE EMG

To detect abnormal neuromuscular transmission, two parameters are analysed: ‘jitter’ as an indicator of irregularity of neuromuscular transmission, and ‘blocking’ as an indicator of failure of transmission (Stålberg and Trontelj 1994). Each lower motor neurone arising from an anterior horn of the spinal cord connects with a number of muscle fibres via the terminal branches of its axon. With discharge of the motor neurone, all the connected muscle fibres fire more or less simultaneously. Conduction of the discharge along the axon is fast but neuromuscular transmission from axon terminal to the muscle fibre at the motor end plate is slower. And the transmission time across the motor end plate varies from one end plate to another. Even in the same motor end plate, it can differ from one firing to another. This variation is what is meant by jitter (Fig. 1a). While the variation in transmission time is least during regular firing of a muscle fibre, it increases with irregular firing, and is most pronounced when the motor end plate is defective, as in myasthenia gravis.
(i.e. there is increased jitter, Fig. 1b). Sometimes the transmission may be too slow to fire the muscle fibre at all, so blocking neuromuscular transmission (Fig. 1c).

Another parameter of single fibre EMG, unrelated to neuromuscular transmission, is fibre density, which indicates the number of muscle fibres belonging to the same motor unit within the recording area of a single fibre electrode (Stålberg 1990). This number increases with collateral reinnervation (the electrophysiological equivalent of typespecific grouping in a muscle biopsy from a patient with a neuropathy), and with muscle fibre atrophy in myopathies.

TECHNIQUE

Single fibre EMG is performed with a special single fibre needle electrode. The recording pole on the side of the electrode is small enough to record the action potential of a single muscle fibre – the single fibre action potential. The EMG machine has to be set up to record these potentials by using a suitable filter. The low cut filter, at 5 Hz to allow recording of motor unit potentials in conventional concentric needle EMG, has to be increased to 500 Hz to filter out any slow potentials coming from sources other than a single muscle fibre. The criteria (AAEM

![Figure 1](http://pn.bmj.com/)

Consecutive discharges of the same motor unit, recorded from extensor digitorum communis by a single fibre needle electrode during voluntary contraction. (a) Traces from a normal subject. Calculated jitter: 24 µs. (b) Traces from a myasthenic patient. Calculated jitter: 56 µs. (c) Traces from a myasthenic patient. Impulse blockade in second trace. Calculated jitter: 91 µs IPI: interpotential interval

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Quality Assurance Committee 2001) for accepting a single fibre action potential are:
- a stable shape;
- a rise time of less than 0.3 ms;
- an amplitude of more than 200 µV (Fig. 1a).
Although the recording can be taken from any muscle, the most diagnostically helpful muscles in myasthenia gravis are extensor digitorum communis, orbicularis oculi and frontalis. There are two techniques for activation of muscle: by the patient's voluntary contraction, and by electrical stimulation of the motor axon branches within the muscle using a stimulating needle electrode (Trontelj and Stålberg 1992).

**Voluntary contraction single fibre EMG**
Recordings are taken during slight voluntary contraction of the examined muscle, maintained in a steady state. After inserting the needle into the muscle, the first step at each recording site is to find at least two separate single fibre action potentials, satisfying the single fibre potential criteria above, and firing simultaneously. Because simultaneously firing potentials have to belong to the same motor unit except in some extreme conditions such as tremor, and epheptic transmission as in demyelinating conditions, the variation in time – jitter – between the two potentials reflects changes in transmission at the two motor end plates. Within the first few seconds of the contraction, the firing patterns of the motor units are unstable and so jitter may be high. Therefore, jitter analysis is done during stable firing of the motor unit, usually a few seconds after the start of firing.

**Stimulation single fibre EMG**
The motor axons of the muscle, either at a point outside the muscle (extramuscular axonal stimulation) or within the muscle (intramuscular axonal stimulation) are stimulated by small electrical pulses (a few milliamper pulse intensity and a 0.05 ms or less pulse duration) delivered regularly (usually five pulses per second) by Teflon coated needle electrodes. The active stimulation needle electrode (cathode) has to be at least 2 cm away from the recording electrode. As it may not be possible to stimulate only one axon alone, more than one single fibre action potential may appear on the screen. These simultaneously appearing potentials may or may not belong to the same motor unit. Because the firing patterns of these potentials are artificially elicited, and the machine delivers the electrical pulses regularly, when the stimulation time point is used as the trigger any flicker (jitter) of any potential on the screen reflects its own neuromuscular transmission change from stimulus to stimulus (Fig. 2). A pitfall in this technique is to deliver the electric shocks at only threshold levels for evoking single fibre action potentials. In this situation the jitter value is artificially high. To avoid this artifact, the stimulus strength must be increased by 10–15% above threshold.

**Analysis**
Twenty different potential pairs (in voluntary contraction single fibre EMG) or potentials (in stimulation single fibre EMG) from different recording points of the same muscle are recorded and 20 jitter values are calculated. For each jitter analysis, 50–100 consecutive traces containing single fibre action potentials are recorded. Most EMG machines are capable of automatic jitter analysis. In voluntary contraction single fibre EMG, the time interval between each potential pair is called the interpotential interval (Fig. 1a) and the mean value of consecutive differences in the interpotential intervals is called the mean consecutive difference (the jitter value) calculated by the formula:

\[
MCD = \left(\frac{|IPI_1 - IPI_2| + |IPI_2 - IPI_3| + \cdots + |IPI_{n-1} - IPI_n|}{n-1}\right)
\]

where MCD is the mean consecutive difference and IPI is the interpotential interval.

In stimulation single fibre EMG, the interpotential interval used in the jitter calculations is...
the time interval between the beginning of the stimulus artifact and the evoked single fibre action potential.

Another important parameter is the mean jitter value, which is the mean of the mean consecutive differences (i.e. of the individual jitter values). Because a split muscle fibre (in voluntary contraction single fibre EMG) or direct electrical stimulation of a muscle fibre (in stimulation single fibre EMG) may give rise to no or small jitter, up to 5 µs due to bypassing of the neuromuscular junction, individual jitter values have to be more than 5 µs to be accepted.

To label jitter in voluntary contraction single fibre EMG as abnormally high, the upper limit generally used in daily practice is 55 µs for an individual jitter value and 36 µs for a mean jitter value. However, the most detailed reference upper limits for different muscles at different ages have been defined by a collaborative multicentre study, and these values are more acceptable (Bromberg and Scott 1994).

In stimulation single fibre EMG, the normal limit for individual jitter is 40 µs for extensor digitorum communis and 30 µs for orbicularis oculi, and the normal limit for mean jitter values is 25 µs and 20 µs, respectively.

**INTERPRETATION**

Single fibre EMG is the most sensitive test for abnormalities in neuromuscular transmission, but its specificity is low. Although it may be abnormal in all of the myasthenic conditions as well as botulism, motor neurone diseases and motor neuropathies, the test is mostly used for the diagnosis of myasthenia gravis, especially the ocular form. But great care should be taken, both during the test itself and in interpretation (Padua et al. 2000) for technical errors and artifacts, or misinterpretation, may result in labelling a person mistakenly as having myasthenia gravis. This is especially the case in suspected ocular myasthenia gravis and when the other tests are normal (acetylcholine receptor antibodies, etc.). The orbicularis oculi and/or frontalis muscles should be examined even if extensor digitorum communis is normal.

Voluntary contraction single fibre EMG is a little more sensitive than stimulation single fibre EMG (Murga et al. 1998) but requires good patient co-operation for maintaining stable muscle contraction. With poor patient co-operation, in infants and young children, and in patients with so much weakness that they cannot maintain a stable contraction, stimulation single fibre EMG is preferable. Stimulation single fibre EMG is also quicker because there is no need to look for a single fibre action potential pair. Stimulation single fibre EMG is superior to voluntary contraction single fibre EMG in the Lambert–Eaton myasthenic syndrome and other presynaptic myasthenic conditions because it may be possible to demonstrate improvement in abnormally high jitters by increasing the stimulation frequency up to 10 Hz or more.

In any muscle, with either single fibre voluntary contraction or electrical stimulation, 20 jitter analyses are performed. According to generally accepted guidelines, a study should be considered abnormal if more than 10% of the single fibre action potential pairs (i.e. more than 2 in 20) exceed the normal upper limit for jitter, or have impulse blockade, and/or mean jitter exceeds normal limits. However, in manifest neuromuscular transmission abnormality, if more than two abnormal individual jitter values have been obtained, there may be no need to analyse further, even if the number of pairs is less than 20. Because anticholinesterase drugs may improve the jitters in neuromuscular transmission abnormalities, these kinds of drug should be withdrawn at least 3 days before the neuromuscular jitter analysis. However, in serious conditions, in which it may be dangerous to withdraw the drugs, single fibre EMG may be performed during their use. But, if the single fibre EMG is normal, it should be repeated after the medication has been stopped.

**REFERENCES**


