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EDITORIAL

Evolution of single fiber potential (SFP) criteria towards improving jitter measurement

Single fiber electromyography (SFEMG) was introduced by Stålberg and Ekstedt in the 1960s to study abnormalities in neuromuscular transmission. It was found that when motor action potentials are recorded from two single muscle fibers innervated by the same axon, there is always slight variability in the time interval between the two potentials, perceived as a pair of potentials [1]. The original definition of the single fiber potential (SFP) recorded with SFEMG electrode was a sharp spike with a rise time of the order of 100—200 μs and a constant shape of the consecutive discharge [1]. One of the two paired potentials belonging to the same motor unit is used as a reference potential. In healthy muscle, physiological variability in the time between the first and the second potential is due to physiological difference in transmission by two neuromuscular junctions in two different muscle fibers, but it falls within specified, normal limits. The mean of the absolute values of consecutive time of interval differences (MCD), that is, the time between two spikes, is calculated as jitter.

Because of improved understanding of mechanisms underlying the SFP generation and progression of jitter measurement techniques, the SFP criteria had to be modified. Since for SFEMG jitter measurement it is crucial to record potentials generated by separate fibers, the following specific criteria were established: amplitude range 200 μV—20 mV, rise time $\leq$ 0.3 ms, filters from 500 Hz to 10 kHz (to eliminate the effect of other, distant fibers) and regular shape of potential without phases and turns [6].

Stalberg et al. [7] described possible errors in acquisition of the pair of potentials due to complexity of generation. One pitfall is recording a positive triangular wave that follows an apparent single fiber action potential, which most often has raised jitter and frequent blocking, and is probably a component of the preceding spike [6]. Another error in voluntary jitter occurs with a very short inter-discharge interval, in which the fiber is refractory to the second discharge. Since in such a case the interval increases, there is a phase of increased velocity that will increase the calculated jitter if the firing rate is very irregular.

With the introduction of concentric needle electrodes (CNE) for jitter measurement the appropriate criteria had to be reconsidered. Contribution of potentials from other fibers because of the larger CNE recording area may affect measured jitter mostly by its reduction [6]. To avoid errors when using CNE, modified criteria were proposed: only including those spike components of the motor unit potential (MUP) that have a fast rising slope to a well-defined negative peak with a constant shape in consecutive discharges, with the time between potentials exceeding 150 ms. A jitter value less than 9 μs should not be accepted (as it may be due to split muscle fibers or to summation of components of single fiber potentials in each of the spikes that have been used in the analysis) [5]. To this end, it is recommended to use the smallest CNE (facial electrode) possible, with filter settings at 1 kHz—10 kHz. Other high-pass settings have been suggested, but 1 kHz has been recommended in order to balance the effect of removing slow wave components while still preserving a good signal-to-noise ratio [5]. Stalberg et al. concluded that SFEMG is the most sensitive technique to measure jitter, and that it may uniquely detect subtle abnormality [5]. CNE studies may be acceptable for clinical use when SFEMG electrodes cannot be used.

When using CNE, attention should also be paid to possible technical errors, termed pitfalls by Stalberg et al. [7], in both voluntary and stimulation jitter. ''Riding potentials'' (when the second spike begins during the falling phase of the first) and positive triangular artifacts belonging to the immediately preceding spike should not be used for jitter

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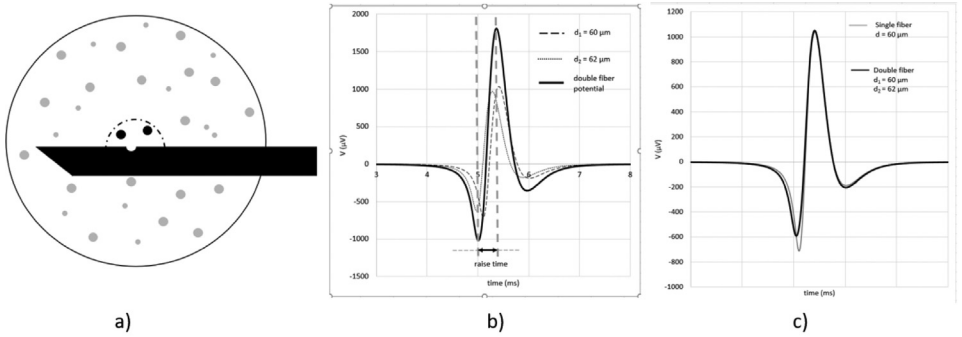

Figure 1 a: recording of single fiber potential (SFP) using single fiber electro (SFE) contaminated by a second fiber located in an uptake area; b: contaminated SFP shows a shift of the negative peak; c: superimposed contaminated and single fiber potentials indicate differences in the shape of the first positive peak.

analysis [7]. Also, very low jitter makes summation of individual spikes difficult to detect, particularly where several fibers contribute to the signal [7].

For stimulation jitter measurements, the time between the stimulus and the evoked spikes (latency) is measured. The CNE signal may be complex not only because of motor unit topography, but also because of superimposition of signals from different motor units. In stimulation jitter, superimposition of spikes from many fibers is caused not only by the summation of activity from fibers in one motor unit but also by the simultaneous activation of different motor units [7]. Stimulation jitter analysis is thus more difficult using CNE except for recordings from the facial muscles, where the anatomy makes it possible to readily identify individual spikes [7].

In voluntary SFEMG, errors such as poor signal quality, inappropriate time reference points on the signal, irregular firing rate and signals with dual latencies should be avoided [7].

Similar to CNE recordings, potentials recorded using SFEMG electrode can also be affected by distant fiber potentials as shown by Zalewska and Gawel [8], while still being accepted as SFP using standard SFP criteria. Contamination by distant fibers generally tends to decrease the jitter [8].

This suggested the need to verify the effectiveness of single fiber potential (SFP) criteria in cases when recorded SFP is contaminated by distant fibers. To this aim, morphological counterparts of SFP were studied using computer simulations and a model of linear source of a muscle fiber potential [9]. We found that SFP criteria do not prevent classification of a potential as SFP even though it may be formed by two or more fibers. SFP contaminated by fibers of diameters to within a few percent can fulfill criteria but a negative peak may be shifted in time and therefore impact jitter measurements as explained in Fig. 1 using simulated potentials. Fig. 1 illustrates potentials recorded from two fibers of similar diameters located in an SFE uptake area (a). This potential fulfills the SFP criteria, but its peak is shifted as compared to single fiber potentials (b). Comparison of shape of superimposed potentials indicates that a difference is evident in part of the first positive peak (c). As result of analysis, a new approach to the identification of SFP was presented to enable maximum sensitivity to potential contamination by the effect of a second fiber [9].

Evolution of single fiber potential (SFP) criteria towards improving jitter measurement is of great importance for clinical practice. SFEMG is of particular importance in the diagnosis of myasthenia gravis (MG) and other diseases with fluctuating and fatigable weakness, such as Lambert—Eaton myasthenic syndrome or congenital myasthenic syndrome.

MG is an autoimmune disease with different antibodies such as acetylcholine receptor antibodies (anti-AchR) (70—80%) or muscle specific kinase antibodies (anti-MuSK) (1—10%). Anti-AchR is routinely tested for, while anti-MUSK is more rarely analyzed. Sensitivity of AchR antibodies in diagnosis of ocular MG has been shown to be 44% and in generalized MG, 80—90% [2]. The specificity of AchR positivity for the diagnosis of MG is extremely good (98—99%), but in some cases these antibodies are not found. In this subgroup of seronegative MG, SFEMG result is diagnostically extremely important, and it is the diagnostic test with highest sensitivity (being abnormal in 99% of patients with generalized MG and in 97% of patients with ocular MG) [2]. Moreover, in Sirin et al.'s study [4], abnormal CNE jitter was present in 93% of newly diagnosed MG patients, being more prevalent than antibody positivity (73.3%), which confirms very high diagnostic usefulness of jitter [4].

Especially in mild cases, and those without characteristic fluctuating weakness and/or borderline jitter, the conclusive SFEMG result is crucial. In clinical practice, positive SFEMG results indicating synaptopathy means 2 pairs of potentials with jitter above the upper limit of normal and/or mean value over the normal level; in some cases even subtle shifts in these values may change the diagnostic result from negative to positive. Therefore, contamination by the effect of a second fiber for the jitter result should be avoided.

In conclusion, currently used criteria, although somewhat modified according to CNE application, are not sufficient for elimination from jitter measurement potentials contaminated by other fibers. We have suggested improving criteria of SFP recorded using SFEMG electrode to avoid potential influence of other fibers on jitter measurement, by introducing an index describing variability of the first positive peak (shown in Fig. 1b) [7].

Evolution of SFP criteria must continue, because of the importance of jitter accuracy in cases of mild symptoms of abnormal neuromuscular transmission and in cases of borderline jitter due to possible underestimation of the result.

In this perspective, since the jitter results are influenced by distant fibers, for further studies on the jitter criteria it would also seem to be worth considering a ''thickness'' index (amplitude/area) [3]. This index is related to potential duration and normalization with amplitude reduces the influence of amplitude. Therefore, it provides indirect information about the number of fibers in the field of the recording electrode.

Disclosure of interest

The authors declare that they have no competing interest.

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