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Review

Pitfalls and errors in measuring jitter

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HIGHLIGHTS

- Quality requirements for jitter analysis with concentric needle electrodes.
- Jitter recordings with voluntary activation; how to detect and handle artefacts.
- Jitter recordings with electrical stimulation; how to detect and handle artefacts.

ABSTRACT

The safety factor of neuromuscular transmission can be assessed by measuring the neuromuscular jitter, which reflects the time variability of processes in the motor end-plate. Jitter is increased in any condition with disturbed end-plate function, such as myasthenic conditions and ongoing reinnervation. Jitter is increasingly being measured with concentric needle (CN) electrodes, which are more prone to artefacts than single fiber EMG recordings.

The objective of this review is to identify and demonstrate pitfalls that can be seen with CN jitter measurements, made with both voluntary activation and electrical stimulation.

With voluntary activation, errors are caused by poor signal quality; inappropriate time reference points on the signal; an irregular firing rate; and signals with dual latencies, i.e., "flip-flop." With electrical stimulation, additional errors result from insufficient stimulation intensity; from abrupt change in firing rate; and from axon reflexes.

Many pitfalls cannot be avoided during recording and can only be detected during post-processing.

It is critical to be aware of these artefacts when measuring jitter with CN electrodes.

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1. Introduction

The jitter parameter, measured from recordings with a single fiber EMG (SFEMG) electrode or a small concentric needle (CN) electrode, is the most sensitive electrophysiological test for neuromuscular transmission.

Jitter results from variability in the time when a depolarizing nerve signal arrives at the neuromuscular junction until a muscle fiber action potential is initiated, and is due to variability in the processes of acetylcholine release, ion channel opening and achieving the muscle depolarization threshold. This can be seen in intracellular recordings (Elmqvist et al., 1964) as variation in the time from nerve stimulation to the generation of a muscle fiber action potential (Fig. 1). This variation is increased when any of the above-mentioned steps are impaired, leading to miniature end-plate potentials that are reduced in size and/or number, and to an abnormal end-plate potential.

For jitter analysis, individual muscle fibers can be activated either by voluntary contraction or by electrical stimulation of their motor axon (Trontelj et al., 1986, 1992; Trontelj and Stålberg, 1996). The time variability is measured in different ways for the two activation methods. For voluntary activation, one of a pair of synchronously firing spikes from the same motor unit is used as the time reference point. The time between the two paired signals is then measured and the summated variability in the two end-plates is seen on the display screen. The inter-spike interval duration was initially measured between points on the steep rising phase of the signals, and this is still used in some equipment. In other equipment, the mathematically-estimated signal peaks are used to assess inter-spike time – this is the method used in all figures in this report unless otherwise indicated. This method has the advantage that all accepted intervals are calculated immediately, without any reanalysis. For stimulation jitter measurements, the time between the stimulus and the evoked spikes (latency) is measured.

In both activation methods, the jitter is calculated as the mean of the absolute values of consecutive time interval differences (MCD): for voluntary activation, this is the time between two spikes; for stimulation activation, this is the time between the stimulus and individual spikes. This calculation method is used to minimize the effect of slow trends in the intervals during the 100 discharges commonly analyzed (Ekstedt et al., 1974; Baslo, 2003). It should be noted that the jitter is less (by approximately $\sqrt{2}$) for stimulation jitter since the values obtained with voluntary activation contain contributions from 2 end-plates, while only 1 end-plate produces the stimulation jitter.

Reference values have been obtained in multicenter studies for SFEMG (Gilchrist et al., 1992; Bromberg and Scott, 1994) and for jitter studies with CN electrodes (CNE) (Kokubun et al., 2012; Stålberg et al., 2015). Other CN jitter reference value studies from single laboratories have also been published (Ertas et al., 2000; Kouyoumdjian and Stålberg, 2008, 2011, 2012, 2013). CN jitter has, as for SFEMG, been assessed in myasthenia gravis (Benatar et al., 2006; Sarrigiannis et al., 2006; Farrugia et al., 2009; Kouyoumdjian et al., 2011; Orhan et al., 2013) and in other conditions (Liu, 2015).

The normality of a voluntary jitter study is assessed by the mean of the paired MCD values. To reduce the effect of occasional extreme values on the calculated mean, individual values more than 4 SD from the mean were excluded from the overall mean calculations in the SFEMG reference value study (Gilchrist et al., 1992). This was necessary in only 6 of 592 recordings in the extensor digitorum and a large unspecified number in other muscles in that study. In the CNE reference study, individual jitter values above 150 μsec were truncated to 150 μsec, and this was necessary in only 3 of more than 11,000 recordings in that study (Stålberg et al., 2015). In voluntary activation studies, the 18th paired MCD value in a tested muscle can also be used to assess normality, i.e. 2 of 20 paired MCD values can be higher than this value. In the CNE reference value study, the normal limit for the 18th value

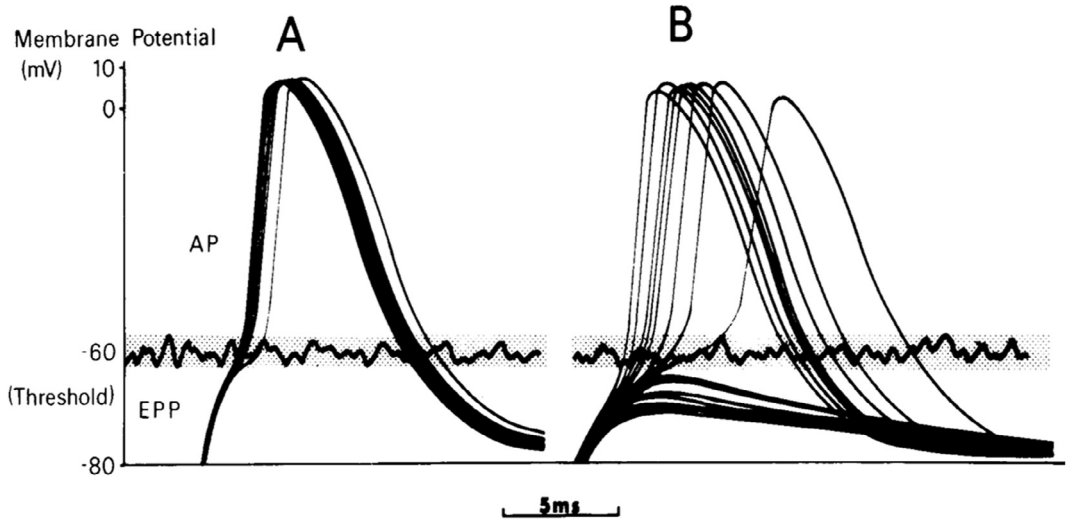

Fig. 1. Schematic drawing illustrating the origin of neuromuscular jitter, based on an intracellular recording from human intercostal muscle fibers (Elmqvist et al., 1964).