



Editorial

Muscle velocity recovery cycles: An evolving technique for assessing muscle fiber membrane properties



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Although conventional nerve conduction studies and electromyography are well-established methods for the diagnosis of neuromuscular disorders, these methods do not provide much information about the alterations in muscle fiber membrane properties that may underlie neuromuscular disorders. In the past, obtaining such information was only possible using intracellular electrodes in isolated muscles, or muscle biopsies. Ten years ago, however, Z'Graggen and Bostock developed a multi-fiber method of recording muscle velocity recovery cycles (MVRC) for the *in vivo* assessment of muscle membrane properties (Z'Graggen and Bostock, 2009). MVRC are measured by direct stimulation of the muscle and recording from the same bundle of muscle fibers. A sequence of paired-pulse electrical stimulations, with varying interstimulus intervals, is used to test how the velocity of a muscle action potential depends on the time interval after a preceding action potential. This enables determination of muscle relative refractory period (MRRP), and early- (ESN) and late supernormality (LSN). Following methodological studies (Z'Graggen et al., 2011a; Bostock et al., 2012), MVRC has been applied by the same research group to a limited number of neuromuscular disorders: myotonia (Tan et al., 2014, 2018), critical illness myopathy (Z'Graggen et al., 2011b) and chronic renal failure (Z'Graggen et al., 2010).

In the current issue of *Clinical Neurophysiology*, Lee and colleagues investigated for the first time patients with sporadic inclusion body myositis (sIBM) with MVRC, to explore pathophysiological mechanisms of this condition (Lee et al., 2019). Nicely demonstrating how MVRC can help in understanding the underlying mechanisms of neuromuscular disorders, the authors found depolarized resting sarcolemmal muscle membrane potential of sIBM muscle compared with normal controls, and they related this to intramuscular amyloid deposition in sIBM.

The authors aimed also to investigate the potential of MVRC as a biomarker for sIBM. Unfortunately, but not surprisingly, MVRC does not seem to be a specific test for sIBM, which has been appreciated by the authors. A similar MVRC pattern as in sIBM was seen in limb ischemia (Z'Graggen and Bostock, 2009), renal failure (Z'Graggen et al., 2010), critical illness myopathy (Z'Graggen et al., 2011) and in a recent study in neurogenic muscles (Witt et al., 2019). While the utility of MVRC has been shown in muscle channelopathies (Tan et al., 2012, 2014, 2018), further research is necessary to explore the potential of MVRC in sIBM and other

neuromuscular disorders, including non-inflammatory muscle disorders. Using a method similar to MVRC, Mihelin and colleagues showed that prolonged MRRP in neurogenic muscles could distinguish dystrophic muscles with shortened MRRP (Mihelin et al., 1991). They used single fiber recordings and supramaximal direct muscle stimulation, which may have been technically challenging, since their method has not been used later. The use of multi-fiber recordings and sub-maximal stimulation in MVRC makes the method simpler and more practical, and with the semi-automated protocol in the Qtrac software (written by Hugh Bostock, Institute of Neurology, London, UK) a recording takes less than 15 min.

MVRC has some methodological limitations. Recording is done in one site and only few muscle fibers, not necessarily representing the whole muscle, are examined. Lee and colleagues suggest that in this case the examined muscle fibers may be only the most excitable, intact muscle fibers from which a stable response can be measured. In a recent study, despite denervation activity in amyotrophic lateral sclerosis, MVRC did not differ between these patients and healthy controls (Kristensen et al., 2019), which supports this suggestion.

Overall MVRC, as applied by Lee and colleagues to explore the mechanisms of sIBM, is a method awaiting to have its potential as a biomarker explored. These types of electrophysiological tests are of particular interest in these days, when clinicians need to find more tools to help diagnose neuromuscular disorders, and search for the possibilities even with magnetic resonance imaging (Vaeggemose et al., 2017) and ultrasound (van Alfen et al., 2011). However, for widespread use and assessment of the potential clinical applications of MVRC, it is essential that the method be included in commercial EMG machines, which in principle is possible given its simple algorithm.

Declaration of Competing Interest

No conflict of interest.

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