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INTRODUCTION

Muscle fiber conduction velocity (MFCV) is the speed of the depolarization wave along the muscle fiber membrane, or sarcolemma. The depolarization of the sarcolemma is one of the steps in the cascade that ultimately causes the muscle fiber to contract. The assessment of these action potentials forms the basis of electromyography (EMG). Important clinical applications of electromyography are the measurement of the surface EMG signal (muscular or M-wave) in nerve conduction studies, and the investigation of the invasive EMG signal, for example the motor unit action potential (MUAP), as measured with concentric needle electrodes. Although the speed of depolarization or MFCV has important influences on the aspect of the M-wave as well as on the shape of the MUAP, direct measurement of the MFCV is not a standard technique in clinical EMG, and is only sparsely used for research purposes.

However, it is likely that there are some fields of EMG where estimation of MFCV could clarify phenomena which are not yet completely understood. For example, a fundamental problem in concentric needle EMG diagnostics is that changes in the shape of the MUAP are determined by neural as well as by muscular factors. The most important neural factors are alterations in the (terminal) innervation pattern, usually due to reinnervation. Important muscular factors are variations in fiber diameter and changes in muscle membrane properties. Neurogenic lesions, myogenic lesions and end-plate disturbances can all result in a combination of changes in these elements. This probably explains the common finding that visual inspection of the MUAP alone is not always sufficient for an adequate interpretation of the nature of the underlying dysfunction. Measurement of the MFCV may permit a view on this specific aspect of muscle function, without any interference due to changes in the (terminal) innervation pattern or the end-plate function.

A major distinction can be made between invasive and non-invasive (surface) MFCV determination techniques. Both methods are based essentially on the extracellular measurement of the volume conducted single fiber action potential, which is a direct reflection of important properties of the muscle fiber membrane. An outline of each technique is given below.

Invasive MFCV determination

Invasive MFCV determination can be performed during either voluntary muscle activation or electrical stimulation of the muscle at rest. The techniques used during voluntary contraction have some drawbacks, depending on the method chosen. Most methods can be used only with low-force contractions. Since the motor units (MUs) are recruited according to their size (Henneman, 1957), this results in a bias toward the smallest muscle fibers, which have the smallest diameters and lowest MFCVs (Andreassen and Arendt-Nielsen, 1987). Reliable MFCV measurements at higher force levels are generally not possible due to the interference pattern. Additionally, the individual fibers of voluntarily recruited, healthy MUs are scattered throughout
the muscle. This makes the finding of a large number of single fiber potentials during voluntary contraction, necessary for a reliable MFCV estimation, very time-consuming (Stålberg, 1966). Moreover, variations in the depolarization rate and muscle fiber length, which are not known, cause MFCV changes (Buchthal et al. 1955; Nishizono et al. 1989; Trontelj, 1993).

An alternative technique is based on MFCV estimation in resting muscle by means of direct muscle stimulation by needle electrodes. Early experiments performed by Buchthal et al. (1955a), were very time-consuming. An easier and much faster method has been suggested by Troni et al. (1983). A resting muscle (for example biceps brachii) is stimulated directly by needle electrodes. Guided by the twitch, an uptake electrode is inserted at some distance. The MFCV is calculated from the distance and the spike latencies. This approach forms the basis of the invasive MFCV determination method, as used in the present study.

The main problem encountered in MFCV determination by means of direct muscle fiber stimulation is that of avoiding nerve or end-plate stimulation. For example, in case of stimulating a nerve branch, erroneously short latencies will result. This is because motor nerves have much higher conduction velocities (30-60 m.s\(^{-1}\)) than muscle fibers (3-5 m.s\(^{-1}\)). The degree of latency shortening depends on the relative contribution of the nerve and muscle fiber conduction and the neuromuscular transmission time to the overall conduction time. Obviously nerve or end-plate stimulation can only be avoided in muscles with a clearly defined end-plate zone (Christensen, 1959; Masuda et al. 1983; Aquilonius et al. 1984). Important advantages of direct muscle fiber stimulation are complete control of the depolarization rate and depolarization of the muscle fibers, irrespective of the state of innervation (Buchthal et al. 1955b, Zwarts, 1989).

**MFCV determination by surface EMG**

Surface EMG has gained much interest in the recent past. A clear advantage of the use of the surface signal is its non-invasive character. This makes it particularly well-suited to applications in kinesiology and fatigue research, where longer lasting or repeated measurement is often required. The most-studied characteristics of the surface EMG signal during voluntary contraction, are (1) the energy content, mainly by means of the rectified or integrated EMG (IEMG), or related statistical variables (Perry and Bekey, 1981), (2) the power density spectrum of the signal, determined especially by the mean or median frequency, and (3) the muscle fiber conduction velocity (MFCV). It is possible to calculate the MFCV by means of several techniques (Arendt-Nielsen and Zwarts, 1989; Yaar and Niles, 1992). In the present investigation the so-called "cross-correlation" method is used (Lynn, 1979; Sollie et al. 1985; Naeije and Zorn, 1983). This method is applicable in muscles that meet certain criteria, concerning the localization of the end-plate zone, the muscle fiber length, the fiber direction, the size of the muscle and the localization of the muscle with respect to the skin.
In kinesiology, the parameters most often used are related to the energy content of the surface EMG, since this is supposed to be linearly related to the exerted force (Hof and van den Berg, 1977). In fatigue studies, the median frequency (Fmed) of the power density spectrum is regarded as a useful parameter (Hermens et al. 1984). During fatiguing contractions the Fmed shifts to lower frequencies (Stulen and DeLuca, 1978). It is supposed that the changes of the Fmed during fatigue are caused by a combination of central factors (variations in motor neuron firing patterns) and peripheral factors (variations in the muscle fiber itself, especially the MFCV) (Naeije and Zorn, 1982; Zwarts et al. 1987). However, the relative contribution of the central and peripheral changes to the observed changes of the Fmed is not known. Little is known about the surface EMG and MFCV during recovery. Under aerobic conditions some authors reported an "overshoot" of the Fmed some minutes after fatiguing contractions (Hara, 1980; Zwarts et al. 1987). Additionally, the IEMG shows values that are increased for a longer period of time (hours) after fatiguing contractions at moderate force levels (Miller et al. 1987). This suggests a decrease in muscular efficiency. It is likely that direct estimation of the MFCV in combination with other surface EMG parameters can clarify some aspects of the changes in electrical properties of the muscle during fatigue and recovery.

Recently, surface MFCV determination has been used in the study of certain neuromuscular diseases, such as hypokalemic periodic paralysis (HOPP) (Zwarts et al. 1988), myotonic congenita (Zwarts and van Weerden, 1989) and myophosphorylase deficiency (Linssen et al. 1990). It appeared that the surface EMG signal can provide valuable information about the muscle membrane function. This information has been used in research on pathogenic mechanisms, but also as a diagnostic tool and in therapeutic management. In this perspective, a logical step would be research in other neuromuscular diseases.

Theoretical studies on surface EMG predict the relation between the source of electrical activity in the muscle, the intracellular action potential, and the surface EMG signal by means of a series of filtering operations (Lateva, 1988; Stegeman and Linssen, 1992). However, it is difficult to get experimental evidence for these hypotheses. Studies in pathological situations will probably help to explain the theoretical basis of the surface EMG signal.

**Aim of the study**

The combination of the invasive and the surface MFCV determination method makes it possible to study different aspects of the function of the muscle, and to compare the results of the invasive and the surface determination techniques. After some preliminary investigations, two promising fields of research were chosen: (1) The study of fatigue and recovery, and (2) the measurement of MFCV and surface EMG parameters in neuromuscular disorders. In both fields the emphasis is on the nature of the variations or disturbances of the MFCV. Possible explanations and suggestions for the underlying pathogenic mechanisms are discussed.
The following questions emerged:

1. Which factors determine the changes of MFCV and surface EMG parameters during fatigue and recovery, and how are these changes related to muscle force and simultaneous biochemical changes?

2. What are the changes in MFCV and surface EMG parameters in neuromuscular diseases? By which factors are these changes determined? What is the value of determination of these parameters in clinical neurophysiological diagnosis?
Outline of the study

(1) Normal values in healthy individuals are given acquired by means of the invasive and surface determination techniques. The differences and similarities between the two methods are discussed (chapter 2).

(2) Emphasis is placed on the physiological changes in MFCV and surface EMG parameters, during muscle fatigue and recovery, and during exercise (chapter 3 and 4).

(3) The changes in MFCV and surface EMG parameters are studied in neurogenic and myogenic disturbances. The changes in MFCV are studied in patients after complete traumatic brachial plexus lesions and during recovery, as a model of acute peripheral neurogenic lesion, as well as the changes in MFCV in amyotrophic lateral sclerosis (chapter 5). In hypokalemic periodic paralysis (HOPP), the diagnostic values of the invasive and surface MFCV-determination techniques are compared. During an attack of HOPP and thyreotoxic periodic paralysis MFCV, IEMG and force are studied as well (chapter 6 to 8). The effect of short-term methylprednisolone therapy on the MFCV is discussed (chapter 9), the changes in MFCV during chronic myositis are studied and related to the therapy, and the diagnostic value is discussed (chapter 10).

(4) The changes in MFCV and EMG parameters are compared with current findings in magnetic resonance spectroscopy. The benefits and limitations of the invasive and surface method are described. The dynamics of the MFCV changes are placed in the perspective of pathological or adaptive changes of the muscle cell membrane (chapter 11).

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Chapter 1

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Introduction