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Modified motor unit number index: A simulation study of the first dorsal interosseous muscle

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ABSTRACT

The motor unit number index (MUNIX) technique has provided a quick and convenient approach to estimating motor unit population changes in a muscle. Reduction in motor unit action potential (MUAP) amplitude can lead to underestimation of motor unit numbers using the standard MUNIX technique. This study aims to overcome this limitation by developing a modified MUNIX (mMUNIX) technique. The mMUNIX uses a variable that is associated with the area of compound muscle action potential (CMAP) rather than an arbitrary fixed value (20 mV ms) as used in the standard MUNIX to define the output. The performance of the mMUNIX was evaluated using motoneuron pool and surface electromyography (EMG) models. With a fixed motor unit number, the mMUNIX output remained relatively constant with varying degrees of MUAP amplitude changes, while the standard MUNIX substantially underestimated the motor unit number in such cases. However, when MUAP amplitude remained unchanged, the mMUNIX showed less sensitivity than the standard MUNIX in tracking motor unit loss. The current simulation study demonstrated both the advantages and limitations of the standard and modified MUNIX techniques, which can help guide appropriate application and interpretation of MUNIX measurements.

1. Introduction

The recent advent of the motor unit number index (MUNIX) technique has provided a quick and convenient approach to estimating the number of functioning motor units in a muscle [1,2]. It uses compound muscle action potential (CMAP) and surface electromyography (EMG) signals (or interference patterns) at different contraction levels to produce an index that is proportional to the number of motor units in the muscle. Compared with the conventional motor unit number estimation (MUNE) techniques using laborious incremental stimulations or EMG decomposition based spike triggered averaging (for estimating the average motor unit size) [3–5], the MUNIX technique is quick and easy to implement and can minimize discomfort caused by electrical stimuli. Thus, there have been an increasing number of applications of MUNIX measurements on assessing motor unit loss or tracking disease progress in amyotrophic lateral sclerosis (ALS) [1,6–10], as well as in aging [11–14] and neurological injury studies [15–17].

To evaluate the MUNIX technique and its applications in different circumstances, multiple studies have been conducted to examine the reproducibility, validity and sensitivity of the MUNIX estimate [6,7,9,18–20]. For example, the reproducibility of MUNIX was assessed in the thenar and hypothenar muscles by independent operators for both ALS patients and control subjects [6,9]. Comparison of MUNIX with MUNE methods was also made and a positive correlation was found in ALS patients [7,8]. In our previous study [18], we employed motoneuron pool and surface EMG models to explore the sensitivity of MUNIX technique to changes of motoneuron and muscle properties. The findings indicated that MUNIX estimates are not sensitive to changes in motor unit control property including motor unit rate coding strategies, and modulations of motor unit recruitment and firing rate ranges [18]. However, reduction in motor unit action potential (MUAP) amplitude can have a substantial impact on MUNIX calculations, leading to an underestimation of the MUNIX. This suggests that there are potential limitations when the MUNIX method is applied in atrophied muscles, where the atrophy is dominantly accompanied by loss of muscle fiber size (decrease of muscle fiber cross-sectional area) or/and reduced number of innervated muscle fibers.

A modified MUNIX (mMUNIX) method is presented in the current study to provide a more appropriate approach (than the standard

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MUNIX) to estimating an index of motor unit population in atrophied muscles with concurrent MUAP amplitude reduction. This modified method uses a variable that is associated with each muscle's CMAP area rather than an arbitrary constant value (for example, 20 mV ms was used in the standard MUNIX) to define the mMUNIX. To understand the difference between standard MUNIX and mMUNIX estimates, a simulation approach using established models of motoneuron pool and surface EMG was implemented. Based on the simulation outputs, the applicable situations as well as the limitations for standard and modified MUNIX techniques were discussed.

2. Methods

2.1. Model description

Surface EMG signals were simulated based on the established motoneuron pool model developed by Fuglevand et al. [21]. Similar to our previous study, a single MUAP recorded at the skin surface was simplified as the first order derivative of the Hermite-Rodriguez function [18,22–25]. It was assumed that MUAP amplitude changed linearly with twitch force, which was proportional to the number of muscle fibers. All muscle fibers were assigned the same cross-sectional area [21]. Different motor units were assumed to be widely distributed within the muscle, and resultant MUAPs were simulated to have the same duration (∼12 ms). The amplitude of MUAPs was simulated to be exponentially distributed over a wide range:

$$Amp_i = \exp\left(\frac{\ln(Amp_{range})}{n} i\right) \quad (1)$$

where Amp_{range} is the amplitude range of MUAPs which was set to be 100, n is the number of motor units in a muscle which was set to be 120, and i is motor unit index. Similarly, the motor unit recruitment threshold (RTE) was also exponentially distributed:

$$RTE_i = \exp\left(\frac{\ln(RTE_{range})}{n} i\right) \quad (2)$$

where RTE_{range} is the range of motor unit recruitment threshold. Two RTE_{range} settings (40% excitation and 80% excitation) were implemented in the current study. A motor unit remained inactive if the excitation was lower than the recruitment threshold. As the excitation exceeded the recruitment threshold, it became active and discharged in a rate linearly proportional to the excitation drive above the recruitment threshold. The inter-firing interval of each motor unit was modeled as a Gaussian distribution. All the motor units were set to have the same minimum firing rate of 8 pulses per second (pps). The lower and upper limits of the motor unit peak firing rate were set to be 23 pps and 52 pps, respectively. Two rate coding patterns (the 'onion-skin' pattern and the reverse 'onion-skin' pattern) were also implemented [21,25]. The surface EMG signal, or surface EMG interference pattern, was composed of the superposition of multiple MUAP trains from all active motor units. We simulated 15 steady-state surface interference pattern signals for MUNIX calculation with excitation ranging from 5% to 50% excitation at 5% increments and from 50% to 100% excitation at 10% increments (examples shown in Fig. 1). The duration of a typical steady state surface EMG signal (or interference pattern) corresponding to each excitation level lasted for 3 s.

The CMAP represents the electrical equivalent of the recruitment of all the motor units in a muscle. It was simulated as a linear summation of all the MUAPs in a synchronous mode [24]:

$$CMAP = \sum_{i=1}^{n} x_i(t_i) \quad (3)$$

where x_i is the ith MUAP, n is the total number of motor units, and t_i indicates the time instance when the ith MUAP reaches the recording electrode. The time variation of all the different motor units reaching the electrode was limited within a 2 ms period. An example of CMAP simulation is shown in Fig. 1.

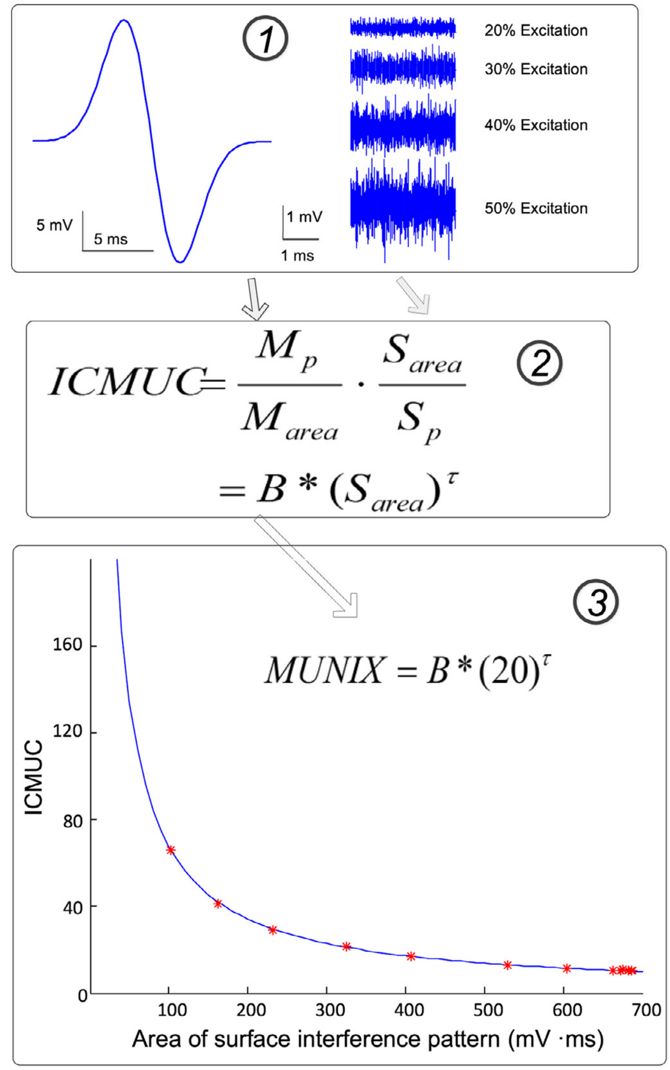

Fig. 1. Three steps for standard MUNIX calculation. (1) Left: simulated CMAP waveform; right: simulated surface EMG (or interference pattern) at different excitation levels. (2) Calculation of the "ideal case motor unit count (ICMUC)". (3) Nonlinear curve fitting for estimation of the standard MUNIX.

2.2. Calculation of standard MUNIX

Estimation of standard MUNIX involves three steps (Fig. 1). The first step was to calculate the area and power of the individual surface EMG interference pattern as well as the area and power of the CMAP. The surface interference patterns were rectified prior to computation of their area and power. The parameters were calculated over the 3 s steady state period and normalized to 1 s epoch. The parameters of CMAP, including peak-to-baseline amplitude, area and power, were obtained from the first negative phase of the waveform. Next, the surface EMG interference pattern and CMAP parameters were used to calculate the "ideal case motor unit count (ICMUC)" [1,2]:

$$ICMUC = \frac{M_p S_{area}}{M_{area} S_p} \quad (4)$$

where M_p and M_{area} represent the power and area of the CMAP, S_p and S_{area} represent the power and area of the surface EMG interference pattern, respectively. A typical trial contains 15 simulated surface interference patterns, which produce 15 corresponding ICMUC