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Spike sorting paradigm for classification of multi-channel recorded fasciculation potentials

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ABSTRACT

Background: Fasciculation potentials (FPs) are important in supporting the electrodiagnosis of Amyotrophic Lateral Sclerosis (ALS). If classified by shape, FPs can also be very informative for laboratory-based neurophysiological investigations of the motor units.
Methods: This study describes a Matlab program for classification of FPs recorded by multi-channel surface electromyogram (EMG) electrodes. The program applies Principal Component Analysis on a set of features recorded from all channels. Then, it registers unsupervised and supervised classification algorithms to sort the FP samples. Qualitative and quantitative evaluation of the results is provided for the operator to assess the outcome. The algorithm facilitates manual interactive modification of the results. Classification accuracy can be improved progressively until the user is satisfied. The program makes no assumptions regarding the occurrence times of the action potentials, in keeping with the rather sporadic and irregular nature of FP firings.
Results: Ten sets of experimental data recorded from subjects with ALS using a 20-channel surface electrode array were tested. A total of 11891 FPs were detected and classified into a total of 235 prototype template waveforms. Evaluation and correction of classification outcome of such a dataset with over 6000 FPs can be achieved within 1–2 days. Facilitated interactive evaluation and modification could expedite the process of gaining accurate final results.
Conclusion: The developed Matlab program is an efficient toolbox for classification of FPs.
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1. Introduction

Amyotrophic lateral sclerosis (ALS) is a progressive, degenerative disorder that affects both upper and lower motor neurons. There is currently no unique marker to diagnose ALS. The crucial factor in establishing the diagnosis of ALS is to observe the clinical progression of motor neuron loss, beginning from the region(s) of onset, and then as it spreads to muscles in other regions in the body [4]. Active denervation is reflected by abnormal spontaneous activity in the affected muscle, including fasciculation potentials (FPs), generated from single or multiple motor units (MUs). FPs are detectable by conventional clinical electromyography (EMG). While not necessarily an indicator of denervation, frequent occurrence of FPs in association with changes in motor unit potentials (reflecting MU reinnervation) has been recognized as important supportive evidence for the electrodiagnosis of ALS [4–5].

Needle electrodes are used to detect spontaneous muscle activity in routine clinical EMG studies. Conventional surface electrodes are historically limited by their non-selective measurement of the electrical activity of a muscle that may be attenuated by the large electrode size. In the last decade, High Density surface EMG (HDsEMG) electrode arrays have been developed [33]. This technique has attracted much attention in laboratory-based investigations including examination of FPs, [8,17,20,21]. A HDsEMG electrode contains an array of small recording surfaces spaced closely to one another. The muscle's electrical activity can then be simultaneously recorded by a number of channels. This multi-channel electrode array enhances temporal resolution and adds spatial information and selectivity that conventional surface

Abbreviations: ALS, amyotrophic lateral sclerosis; FP, fasciculation potentials; HDsEMG, high density surface electromyography; MU, motor unit; PCA, principal component analysis

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electrodes lack. A thorough review of surface electrode array EMG analysis and its advantages compared with concentric needle EMG has been described by Farina et al. [10]. Zhou et al. recently demonstrated that a HDsEMG array can be more sensitive than a needle electrode in capturing FPs from the superficial muscles in ALS patients [38].

Although different FPs, regardless of waveform or motor unit origin, would have the same clinical diagnostic significance, it would be helpful to further classify the FPs for laboratory-based investigations. Results of FP classification can be further analyzed to characterize the firing pattern and action potential waveforms of fasciculating MUs. Potential applications may include (but are not limited to) indirect discovery of their site of origin and distinguishing between FPs that are encountered in the normal population and those associated with pathological processes such as ALS [11,28]. These pieces of information can be obtained through classification of FPs into groups of similar waveform shapes. The task of FP classification is somewhat similar to the task of EMG decomposition, which is the process of breaking down an epoch of voluntary EMG signal to derive its constituent single MU potential firings. In the past several decades, much effort has been focused on EMG decomposition, but using traditional intramuscular needle electrodes. The concept and methods of decomposition in clinical EMG have been reviewed by Stashuk [32]. In recent years, there have been numerous studies on EMG decomposition using surface electrodes [2,3,7,12–16,22,24,26,27,29,37,39]. However, available EMG decomposition software, such as Spike2 (Cambridge Electronic Design Limited, Cambridge, England) or EMGLab [25] is not applicable to FP classification, due to different characteristics of spontaneously fired spikes compared with voluntarily firing MUs.

In light of these limitations, the objective of this study is to design a spike sorting program specific to the unique features of FPs. Some routines derived originally from EMG decomposition are adopted for FP classification. However, our classification strategy does not rely on MU firing rate information because of the sporadic character of FPs. In this program, robust unsupervised and supervised classification techniques are combined with facilitated interactive decision making modules. Throughout this process, automatically classified FPs are evaluated in several steps. Erroneous assignments are corrected interactively. Consistency of waveforms in each class is visually examined. In addition to qualitative evaluation, quantitative within-class distance and between-class distances are also examined for the sake of class accuracy estimation. Moreover, performance of the classification is examined using the concept of "two-source" method by applying independently to two non-overlapping sets of channels derived from an array recording. The classification program is tested with FP data sets of ALS patients. Both advantages and limitations of the program are discussed.

2. Materials and methods

2.1. Experiments

FPs recorded from subjects with Definite ALS or Probable ALS with Laboratory Support based on El Escorial criteria [1] were used to test the classification program. Data recording was performed at the second author's institution and had the approval of the local Human Studies Committee. All subjects gave written informed consent prior to their participation. Subjects were seated comfortably in a regular chair or in their wheelchair, with their elbow partially flexed and forearm semi-pronated. Subjects were asked to completely relax.

A linear array of 20-channel HDsEMG electrodes, designed and fabricated in our laboratory, is used for the recording of FPs in the biceps brachii muscle. The electrode is oriented along the long axis of the muscle fibers such that the center of the electrode array is close to the center of the muscle belly, with the proximal edge oriented toward the muscle's origin and the distal edge oriented toward the muscle's tendinous insertion. Each bar of electrode is 1 mm in width and 10 mm in length. The inter electrode distance is 5 mm. The signals are amplified by the Refa128 EMG Recording System (TMS International BV, the Netherlands). The reference electrode is placed on the ipsilateral elbow. Sampling rate is 2 kHz per channel. Band pass filter is set for 20–500 Hz, which can slightly smooth out waveform shapes, but does not affect classification performance. Hardware-based common feedback (average of all available channels) is subtracted from each channel.

In this study, 10 data sets of FPs recorded from the biceps brachii muscles of five ALS subjects (56 ± 10 years; 4 males, 1 female) are presented. The duration of recording ranges from 300 to 2500 s, with an average of approximately 1000 s.

2.2. FP classification program description

The FP classification program includes the following steps or modules. Prolonged recordings of spontaneous muscle activity are broken down into 100-s epoch. Spike detection algorithm [18] is applied to the EMG signal. Extracted FPs are stored in a database along with information of their firing times. Below, we describe the feature extraction, spike sorting, evaluation and interactive modification processes. All programs are coded in Matlab version 7.12 (R2011), the MathWorks Inc.

2.2.1. Database of detected FPs

Prior to classification, FPs are detected using a modification of previously described algorithm [18]. This algorithm starts by transforming the HDsEMG multi-dimensional signal into a one-dimensional signal. Amplitude thresholding is then applied to the one-dimensional signal to determine the timings of individual spikes. To construct the one-dimensional signal, the difference between maximum and minimum voltage values across all the channels is used to make a new data point at each time sample. In this study, we use the standard deviation of the EMG data at each sample time across all channels. Although it is a common practice to apply spatial filtering on multichannel EMG data in order to improve the quality of the signal [27], we deliberately chose not to do so, since it has been shown that sensitivity of FP detection is dramatically reduced after spatial filtering [19]. Fig. 1 illustrates the procedure for FP extraction, starting from raw EMG (recorded at rest) at left. At the right panel, a sample database of FPs recorded by the 20-channel electrode array is shown. Firing times and maximum peak-to-peak amplitude across all channels are also reported.

2.2.2. Feature extraction

A matrix ($[]_{n\mathrm{Ch}\times \mathrm{w}}$) is used to represent a spike, where 'nCh' is the number of channels and 'w' is the duration of the waveform (in this work: $[]_{20\times 55}$), and this is done regardless of electrode configuration. Two features from each channel are measured:

(1) Peak to peak amplitude (polarity considered). Amplitude 'polarity' is considered positive when the negative peak of the waveform occurs prior to the positive peak;
(2) Area under the curve (sum of absolute values).

An FP is 'nf'-dimensional vector, where $nf = n\mathrm{Ch} \times 2$. To increase the efficiency of the feature domain, Principal Component Analysis (PCA) is applied. By selecting only a limited number of principal components, we can reduce the dimensionality of the feature