EMG-force relation in the first dorsal interosseous muscle of patients with amyotrophic lateral sclerosis

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Abstract

BACKGROUND AND PURPOSE: The relationship between surface electromyography (EMG) and muscle force is essential to assess muscle function and its deficits. However, few studies have explored the EMG-force relation in patients with amyotrophic lateral sclerosis (ALS). The purpose of this study was to examine the EMG-force relation in ALS subjects and its alteration in comparison with healthy control subjects.

METHODS: Surface EMG and force signals were recorded while 10 ALS and 10 age-matched healthy control subjects produced isometric voluntary contractions in the first dorsal interosseous (FDI) muscle over the full range of activation. A linear fit of the EMG-force relation was evaluated through the normalized root mean square error (RMSE) between the experimental and predicted EMG amplitudes. The EMG-force relation was compared between the ALS and the healthy control subjects.

RESULTS: With a linear fit, the normalized RMSE between the experimental and predicted EMG amplitudes was 9.6 ± 3.6% for the healthy control subjects and 12.3 ± 8.0% for the ALS subjects. The slope of the linear fit was 2.9 ± 2.2 mN/V −1 for the ALS subjects and was significantly shallower (p < 0.05) than the control subjects (5.1 ± 1.8 mN/V −1). However, after excluding the four ALS subjects who had very weak maximum force, the slope for the remaining ALS subjects was 3.5 ± 2.2 mN/V −1 and was not significantly different from the control subjects (p > 0.05).

CONCLUSIONS: A linear fit can be used to well describe the EMG-force relation for the FDI muscle of both ALS and healthy control subjects. A variety of processes may work together in ALS that can adversely affect the EMG-force relation.

Keywords: ALS, EMG-force relation, FDI, isometric contraction

1. Introduction

The relationship between surface electromyography (EMG) during muscle contraction and the resulting force has been extensively studied in the past (Perry & Bekey, 1981). A linear relation between force and EMG amplitude has been documented in small muscles with narrow motor unit recruitment force ranges, such as the first dorsal interosseous (FDI) muscle (Milner-Brown, Stein, & Yemm, 1973; Milner-Brown & Stein, 1975; Mortani & deVries, 1978; Woods & Bigland-Ritchie, 1983; Lawrence & De Luca, 1983; Zhou & Rymer, 2004), while nonlinear EMG-force relations have also been reported for larger muscles (e.g. proximal leg or arm muscles) with wide motor unit recruitment force ranges (Woods & Bigland-Ritchie, 1983; Lawrence

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The investigation of EMG-force relation has various clinical applications. For example, based on the established EMG-force relation, the EMG signal can be used to predict muscular force which may otherwise be difficult to measure directly. The EMG-force relation can be a useful marker of changes in motor unit or motor neuron pool activation during muscle force generation. For example, imposition of the spinal cord section in animal preparations may induce a significant increase in the regression slope of the EMG-force relation indicating an inefficient use of the muscle (Blaschak, Powers, & Rymer, 1988). Due to pathophysiological changes in motor neuron pool and intrinsic muscle properties in patients with neurological disorders, the EMG-force relation can also be profoundly affected. Namely, diverse changes in EMG-force slopes have been reported in paretic muscles of stroke patients compared with contralateral or neurologically intact muscles (Tang & Rymer, 1981; Gemperline, Allen, Walk, & Rymer, 1995; Zhou, Li, & Rymer, 2013).

In contrast to studies of EMG-force relation in neurological injuries such as stroke, it is presently unknown whether or how the EMG-force relations may be altered in patients with motor neuron diseases such as amyotrophic lateral sclerosis (ALS). ALS (also known as Lou Gehrig’s disease) is a progressive neurodegenerative disease that affects both upper and lower motor neurons. Intramuscular EMG examination has been routinely used for supporting the diagnosis of ALS (De Carvalho et al., 2008). Motor unit number estimation (that relies on electrical stimulation and surface EMG recording) and its various forms of modification or improvement can provide a useful tool for assessing spinal motor neuron degeneration and tracking disease progress (Shefner & Gooch, 2002; Liu et al., 2009; Nandedkar, Barkhaus, & Stålberg, 2010). The utility of interference surface EMG analysis has also been reported for supporting the diagnosis of the disease (Diószeghy, Egerházi, Molnár, & Mechler, 1996; Zhang, Barkhaus, Rymer, & Zhou, 2014).

To date, the EMG-force relation has not been systematically examined in ALS except for one study that was performed toward an estimation of muscle contraction levels using EMG amplitude in patients with neuromuscular disorders including ALS (Boe, Rice, & Doherty, 2008). In addition to force estimation, a systematic analysis of the EMG-force relation in individuals diagnosed with ALS can provide valuable information to assist in the assessment of neural and muscular pathological changes. The objective of this study was then to examine EMG amplitude and force levels of the FDI muscle during voluntary isometric contractions tested in both neurologically intact and ALS subjects. First, we investigated whether a linear regression, as previously reported for the FDI muscle in healthy subjects, can be used to characterize the EMG-force relation for the ALS subjects. Second, the EMG-force relation observed from the ALS subjects was compared with the healthy control subjects to assess whether there was a systematic alteration in the relation.

2. Methods

2.1. Subjects

Ten subjects with confirmed ALS (7 male and 3 female; 53 ± 12 years, range: 31–67 years; years from symptom onset: 1–6 years; years from diagnosis: <1–4 years) and 10 neurologically intact subjects (5 male and 5 female, 52 ± 15 years, range: 25–80 years) participated in this study. The first dorsal interosseous (FDI) muscle of the stronger hand was tested in 9 ALS subjects, and for one ALS subject the test was performed bilaterally. Therefore, 11 datasets were available in total for the ALS group. For the control subjects, the test was performed on the dominant side. All subjects signed informed consent via protocols approved by the Institutional Review Board under the Office for the Protective of Human Subjects at Northwestern University (Chicago, USA).

2.2. Experimental design

Subjects were seated in a Biodex chair in a standardized posture with the forearm resting on an arm base. As shown in Fig. 1, the wrist and forearm were placed in an arm brace and secured to the supporting surface to avoid movement when the subject performed index finger isometric abduction. Extra foam was placed around the arm brace for further securing purpose to avoid force contamination on the FDI muscle. The thumb angle relative to the index finger was held at 45 degrees. The three medial fingers were secured on specifically designed surfaces. Isometric force of the FDI muscle was measured at the 2nd metacarpophalangeal (MCP) joint (Fig. 1).
F. Jahanmiri-Nezhad et al. / EMG-force relation of the FDI muscle in ALS

Fig. 1. Experimental setup for surface EMG and contraction force recordings from the FDI muscle.

A flexible surface electrode array with 64 channels (8 rows and 8 columns, each recording probe 1.2 mm in diameter, inter-probe distance 4 mm for both directions) was used to measure electrical activity of the FDI muscle through a 128-channel EMG system (Refa model, TMS International BV, Netherlands), with the reference electrode positioned over the elbow. For each channel there was a built-in feedback subtraction of the average of all the recording channels. The system has adjustable filter settings and real time display, providing visual feedback to the examiner to assess signal quality. The EMG signal was sampled at 2000 Hz per channel with a bandpass filter setting at 5–500 Hz. The auxiliary channels of the system were used to record muscle force. The force signal was sampled at 2000 Hz with a low pass filter at 20 Hz. The EMG and force recordings were synchronized for the experiment. All the data were stored in ASCII format for offline analysis.

The experimental protocol started by measuring the isometric maximum voluntary contraction (MVC) force of the FDI muscle during index finger abduction. Once the MVC was determined, the subject was asked to perform isometric contractions at 10%, 20%, 30%, 40%, 50%, 60% and 70% of the MVC in different trials. For each trial, one level of muscle contraction was performed. The subject was instructed to reach the target force and hold it for approximately 10 seconds. The order of contraction levels was randomized and each contraction level was repeated at least twice. Sufficient resting periods between trials were provided to the subject to minimize mental and muscle fatigue.

In order to guide the subject to perform a desired level of contraction, a home-designed Graphical User Interface (GUI) Matlab program was used to provide visual feedback. This GUI program showed a two dimensional Cartesian coordinate plane, where x-axis represents force on the horizontal direction (Fx, index finger abduction/adduction) and y-axis represents force on the vertical direction (Fy, index finger flexion/extension). A cursor in the shape of a triangle was used to indicate the current position of muscle contraction force in the x-y plane, which was at the origin during rest. To perform each level of contraction, an open circle and a filled circle were used to represent the Target position and the Guide position, respectively. The filled circle can change colors from yellow to orange and then to green in order to indicate to the subject that a trial was about to start. The subject was asked to generate force by abducting the index finger to move the cursor to the Target, stay at the Target position for 10 s and then relax slowly until the cursor was back at the starting point.

2.3. Data analysis

The segments of EMG signal during which the force was held constant were used for later analysis. To facilitate signal segmentation, a simple interface program was designed for the user to choose the most constant part of the force profile. Based on the timing of force signal segmentation, EMG signals were segmented as well. The average rectified value (ARV) of each channel’s EMG was measured. Due to the fact that the electrode array is larger than the FDI muscle and the EMG channels on the edge of the array were off the muscle, the ARV values from the 16 centered channels of the electrode array were averaged to represent the EMG amplitude of the FDI muscle.

A linear function in the form of \( y = ax + b \) was derived based on a 1st order polynomial least-square fit, where \( x \) represents force measurement, \( y \) represents EMG amplitude, \( a \) is the slope of the EMG-force relation, and \( b \) is the intercept. To evaluate the linear fit of the EMG-force relation, we calculated the normalized root mean square error (\( R_{\text{norm}} \)) between the experimental EMG amplitudes and those predicted by the linear fit from the force measurement.

The analysis was performed on all the ALS and healthy control subjects. Two-sample t-tests were used to examine the difference between the slopes of the EMG-force relation of ALS and healthy control subjects. Statistical significance was defined as \( p < 0.05 \).
3. Results

3.1. MVC force and EMG measurement

The MVC force in abduction was recorded for the FDI muscle of both ALS and healthy control subjects. As we expected, the MVC force of the ALS was systematically lower than that of the healthy control subjects. Across healthy control subjects, the average MVC force was $32 \pm 12 \text{ N}$ (range: 17–55 N), which was significantly larger than the ALS subjects with an average MVC force of $15 \pm 13 \text{ N}$ (range: 1.5–32 N) ($p < 0.05$). It was also observed that the average EMG amplitude at the MVC was $146 \pm 34 \mu\text{V}$ (range: 98–201 \mu\text{V}) for the healthy control subjects, which was significantly higher ($p < 0.05$) than the maximum EMG amplitude for the ALS subjects [$47 \pm 41 \mu\text{V}$ (range: 3–132 \mu\text{V})].

3.2. EMG-force relation

Figure 2 shows the sample recordings of the EMG and force signals at two different muscle contraction levels from a healthy control subject. For each level, the force in directions of index finger abduction and flexion was measured. Among 64 channels of the electrode array, only 6 channels (channels 26 to 31) of data are shown to avoid complexity in the figure. Figures 3 and 4 present the experimental EMG and force relation for all healthy control and ALS subjects, respectively. The line drawn in each panel is the result of a 1st order polynomial least-square fit for the recorded sets of data points. It was evident that a linear fitting can be used to well describe the EMG-force relation for the FDI muscle of both ALS and healthy control subjects. For four ALS subjects (ALS 1, ALS 2, ALS 3, and ALS 7), the maximum force of the FDI muscle was very weak. Among this group, three subjects (ALS 1, ALS 3, and ALS 7) showed a more scattered sets of data points, with a linear trend still visible between the recorded EMG and force signals. Fitting a linear function into the experimental data, the normalized root mean square error (RMSE) value was $9.6 \pm 3.6\%$ for the healthy control subjects and $7.5\% \pm 3.5\%$ for the ALS subjects, after excluding the three subjects (ALS 1, 2, 3).
ALS3, and ALS 7) with scattered data points. No significant difference was found between the two groups \((p>0.05)\), whereas including these three subjects, the normalized RMSE value was 12.3 \pm 8.0\% for the ALS subjects, which was significantly higher than that of the healthy control subjects \((p<0.05)\).

### 3.3. EMG-force slope comparison

The slope of the 1st order polynomial curve fit of the EMG-force relation was calculated and compared between the two groups. The slope was 5.1 \pm 1.8 \mu V^{-1} N^{-1} for the healthy control subjects and was significantly steeper than the ALS subjects \((2.9 \pm 2.2 \mu V^{-1} N^{-1}) (p<0.05)\). It is noted that the slope for the ALS subjects with weak maximum contraction force \(i.e.,\) ALS 3 and ALS 7, Fig. 4) was very small. After excluding the four subjects who had very weak force or scattered EMG-force data points \(ALS 1, ALS 2, ALS 3, and ALS 7)\), the slope for the remaining ALS subjects was 3.5 \pm 2.2 \mu V^{-1} N^{-1}. A trend of slope reduction can still be observed when compared with healthy control subjects, but no statistical difference was found between the two groups \((p>0.05)\).

### 4. Discussion

This study examined the alteration of the relation between EMG amplitude of the FDI muscle and the corresponding isometric force during index finger abduction in individuals diagnosed with ALS. The observed relation was further compared with that of the healthy control subjects to assess neuromuscular deficits in ALS. A linear fit between the surface EMG amplitude and the muscle contraction force was confirmed to be valid for the FDI muscle of the healthy controls and the ALS subjects. A trend of decreased
The linear fit of the EMG-force relation was observed in the ALS subjects compared with healthy control subjects. However, no significant difference was found between the two groups when the reduction of MVC was taken into account.

The findings of this study may be a result of various types of interactive processes in ALS patients that can impact the EMG-force relation in different ways. These may include spinal motor neuron degeneration, muscle fiber reinnervation following the degeneration process, impairment of motor unit control properties, and muscle fiber atrophy, etc. The influence of these processes on EMG-force relation has been investigated using a simulation of motor neuron pool activity (muscle force and surface EMG) (Zhou, Suresh, & Rymer, 2007). The decreased slope of EMG-force relation can arise from several factors such as a selective degeneration of high threshold motor units, increased motor unit firing rates, atrophy of muscle fibers, and muscle contractile property changes, which have been reported in ALS patients. For example, a weaker correlation was found between motor unit action potential and twitch force in the FDI muscle for rapidly progressing ALS subjects, compared with healthy controls or subjects with slowly progressive motor neuron degeneration such as spinal muscular atrophy (Vogt & Nix, 1997; Dengler et al., 1990). This suggested degeneration of high threshold motor units, resulting in prevalence of relatively a large number of slow motor units in the muscle. For ALS patients with dominant lower motor neuron dysfunction, elevated motor unit firing rates were also observed, possibly due to compensatory mechanisms to cope with the loss of motor units (Kasi et al., 2009). With all these changes, surface EMG of the affected muscle involves summation of a larger number of motor unit action potentials with smaller amplitudes in order to reach a desired force. Due to increased degree of action potential cancellation, the surface EMG amplitude in such
a case would be lower. This effect would be more evident at higher force levels, resulting in a slope reduction in the EMG-force relation (Zhou, Suresh, & Rymer, 2007).

On the other hand, factors increasing the slope of the EMG-force relation were also reported in ALS subjects, such as muscle fiber reinnervation following motor neuron degeneration. Decreased motor unit firing rate was also observed in patients with dominant upper motor neuron dysfunction possibly due to decreased central drive or intrinsic motor neuron property changes (Kasi et al., 2009). It is noted that for motor neuron diseases such as ALS, a variety of processes may work together (for example, denervation and reinnervation of muscle fibers) at different stages of the disease, which in turn may affect the disease progress. Thus experimentally observed EMG-force slope variations in affected muscles of ALS subjects could be the overall effects of many different factors.

In this study, a non-invasive electrode array was used for EMG data recording. The advantage of high density surface EMG has been reported by Staudenmann, Kingma, Daffertshofer, and Stegeman (2006) and Staudemann et al. (2007) for improving estimation or tracking of muscle force using principal component analysis and independent component analysis. In this study, the objective was to examine the EMG-force relation. We found that the EMG amplitude varied significantly on different channels even for a specific level of contraction. As force increases, the pattern of amplitude variation versus force might be different from channel to channel. Thus we averaged the EMG amplitude of all the selected channels to have a more robust and comprehensive measurement of the EMG-force relation.

Finally, given recent advances in surface EMG decomposition using high density surface EMG (Holobar & Zazzula, 2007; Holobar, Farina, Gazzoni, Merletti, & Zazzula, 2009), it is feasible to decompose the EMG signals collected in this study, thus providing more definite information about motor unit alteration than that obtained from the EMG-force relation analysis. Indeed, this was the primary motivation of using high density surface EMG recordings in this study. As an overall effect of many different factors, EMG-force relation analysis can provide a general estimation of motor unit changes in an affected muscle. To obtain more definite information, our future work will focus on decomposition based motor unit analysis (e.g., motor unit control property, quantitative motor unit action potential analysis, etc.) in ALS subjects.

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