

ABSTRACT: Limitations associated with global measures of function in patients with amyotrophic lateral sclerosis (ALS) and the qualitative nature of needle electromyography have stimulated the development of alternate means of monitoring disease severity and progression in ALS. Thus, the objective of this study was to examine the ability of one these techniques, decomposition-based quantitative electromyography (DQEMG), to obtain electrophysiological data, including motor unit number estimates (MUNEs), from a group of patients with ALS. The first dorsal interosseous and biceps brachii muscles were studied in 10 healthy subjects and 9 patients with ALS. Following the acquisition of a maximum M wave, needle- and surface-detected EMGs were collected simultaneously during 30-second contractions performed at 10% of the maximum voluntary contraction force to obtain motor unit potential (MUP) trains. DQEMG was then used to extract the surface-detected MUP associated with each MUP train, the mean size of which was divided into the maximum M wave to obtain a MUNE. The results suggest that quantitative electrophysiological data obtained using DQEMG are representative of the pathophysiological changes in the lower motor system in ALS patients, supporting its use in studies documenting the natural history and progression of the disease.

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MOTOR UNIT NUMBER ESTIMATES AND QUANTITATIVE MOTOR UNIT ANALYSIS IN HEALTHY SUBJECTS AND PATIENTS WITH AMYOTROPHIC LATERAL SCLEROSIS

SHAUN G. BOE, PhD,¹ DANIEL W. STASHUK, PhD,² and TIMOTHY J. DOHERTY, MD, PhD^{1,3}

¹ School of Kinesiology, University of Western Ontario, London, Ontario, Canada

² Department of Systems Design Engineering, University of Waterloo, Waterloo, Ontario, Canada

³ Departments of Clinical Neurological Sciences and Rehabilitation Medicine, University of Western Ontario, University Hospital, London Health Sciences Centre, 339 Windermere Road, London, Ontario N6A 5A5, Canada

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Most studies that have examined the natural history of amyotrophic lateral sclerosis (ALS) or potential therapies for this disorder have attempted to quantify the combination of both upper and lower motor neuron (LMN) loss by means of global measures of function. Such studies have utilized a variety of methods, including measures of maximal isometric strength, activities of daily living scales, and a num-

ber of functional measures, most commonly pulmonary function.^{1–3,17,21,33} Although they have shown considerable success in documenting and predicting the course of disease,^{15,18,25,27,30,36} their ability to represent the underlying pathophysiology of ALS is limited as these measures of impairment or disability do not directly measure the changes occurring within the motor unit (MU) pool as a result of the disease.

Electrophysiological data pertaining to the organization of the lower motor system would be of considerable value, as they would provide insight into the extent of MU loss resulting from the disease. Needle electromyography (EMG) subjectively assesses the level of LMN involvement via analysis of the discharge frequency and size (amplitude and duration) of the first few detected motor unit potentials (MUPs).⁹ However, this type of analysis is limited both by the capacity of a needle electrode to represent MU size and the lack of information re-

Abbreviations: AAR, area-to-amplitude ratio; ALS, amyotrophic lateral sclerosis; ANOVA, analysis of variance; BB, biceps brachii; DQEMG, decomposition-based quantitative electromyography; EMG, electromyography; FDI, first dorsal interosseous; LMN, lower motor neuron; MU, motor unit; MUP, motor unit potential; MUNE, motor unit number estimate; MVC, maximal voluntary contraction; S-MUP, surface-detected motor unit potential

Key words: amyotrophic lateral sclerosis; isometric strength; motor unit; motor unit number estimation; quantitative electromyography

Correspondence to: S. Boe; e-mail: sboe@uwo.ca

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garding the numbers of MUs within the system.³⁴ Furthermore, the qualitative nature of the needle examination reduces its applicability in longitudinally tracking changes occurring at the level of the MU in ALS. In addition to needle EMG, the degree of LMN involvement in ALS may be quantified by the amplitude or area of the evoked maximum M wave, which represents the electrical contribution of all of the MUs within a given muscle group. However, maximum M-wave amplitude or area may remain within normal limits, despite changes in MU number, as a result of collateral reinnervation until a critical level of MU loss is reached, at which time M-wave size will decrease.^{13,29}

In an effort to address these limitations and provide additional information about the lower motor system in ALS, quantitative EMG techniques have been developed. One particular quantitative EMG technique, decomposition-based quantitative electromyography (DQEMG), is a valid and reliable method of obtaining electrophysiological data in healthy subjects, which can be used to assess MU complexity and firing rate and to estimate MU size and number.^{5-7,20,31,32}

The purpose of this study was to determine the applicability of DQEMG in obtaining the aforementioned electrophysiological data from both the first dorsal interosseous (FDI) and biceps brachii (BB) muscles in a group of ALS patients. Additionally, we sought to compare the data obtained from the ALS patient group with data from a group of healthy subjects in order to quantify the changes that had occurred as a result of the disease.

METHODS

Subjects. Nine patients (52 ± 12 years) with clinically probable or definite ALS, as defined by the revised El Escorial criteria,¹² and 10 healthy subjects (27 ± 4 years) volunteered to participate in the study. Two of the 9 ALS patients were unable to perform the FDI portion of the study due to severely atrophied muscles characterized by non-detectable M waves. All subjects gave informed consent and our institutional review board approved the study.

Force Measurement. The force measurement protocol used for both the FDI and BB muscles has been reported previously.⁷ For the FDI muscle, subjects were seated comfortably with their right arm pronated and placed in a custom-made force dynamometer during data collection. In order to isolate the action of the FDI muscle, the thumb was stabilized with a metal brace at 90° extension and the lateral

three digits separated from the second digit with a divider, and immobilized with a medium-density sponge placed over the digits and secured with a Velcro strap. Additional straps placed just distal and proximal to the wrist joint secured the forearm and hand position. The isometric abduction force exerted by the FDI was measured in Newtons (N) with a force transducer (Model FT-10; Grass-Telefactor, West Warwick, Rhode Island) that was anchored to the device and aligned with the proximal interphalangeal joint of the second digit. The output from the force transducer was amplified (Model CP 122 AC/DC Amplifier; Grass-Telefactor) and converted to digital format by a 12-bit converter (CED Model 1401 Plus; Cambridge Electronic Design, Cambridge, UK) at a sampling rate of 500 Hz and displayed on an analog storage oscilloscope (Model 5111A; Tektronix, Inc., Beaverton, Oregon) placed in front of the subject.

For the BB, subjects were supine on a padded table and the right arm placed in a custom-made force dynamometer. The legs were supported on a padded wooden box, with the hip and knee joints flexed to 90° and the right shoulder secured with a padded metal brace. The box and brace prevented the torso from sliding during contractions. The elbow joint was flexed 90° and placed in a padded cup with the forearm fully supinated. The wrist and fingers were prevented from flexing during contraction by a plastic splint that was strapped to the back of the wrist and hand. The ventral aspect of the wrist was secured with a strap to a padded curved bar (11 × 5.2 cm) that had a strain gauge attached (Model SST-700-100A; ASTechnology, Haliburton, Ontario, Canada). The output from the strain gauge was amplified (Neurolog Models NL 107 and NL 126; Digitimer, Welwyn Garden City, UK), and converted to digital format and displayed on an analog oscilloscope suspended above the subject as described for the FDI.

The force signals for both the FDI and BB were analyzed off-line using a commercially available software package (Spike 2, version 4.5; Cambridge Electronic Design, Cambridge, UK).

Electromyographic Data Collection. The DQEMG method and associated algorithms have been described in detail elsewhere.^{20,39} Electromyographic signals were acquired using DQEMG software on the Neuroscan Comperio (Neuroscan Medical Systems, El Paso, Texas). Intramuscular signals were recorded with a commercially available, disposable concentric needle electrode (Model N53153; Teca Corp., Hawthorne, New York) with a bandpass of 10 Hz to 10

kHz, while surface signals were recorded with a bandpass of 5 Hz to 5 kHz using self-adhering electrodes (Kendall-LTP, Chicopee, Massachusetts). For the FDI muscle, an electrode was cut in strips (1 cm × 3 cm) and the active electrode located over the motor point of the muscle with the reference electrode located over the first metacarpophalangeal joint. For the BB muscle, full-sized electrodes (2 cm × 3 cm) were used with the active electrode located over the motor point of the muscle and the reference electrode located over the distal tendon. A full-sized electrode served as a ground for both the FDI (dorsal aspect of the hand) and BB (forearm just distal to the elbow crease).

Experimental Protocol. The experimental protocol was similar for both the FDI and BB muscles. Prior to placement in the appropriate device, the maximum M wave was elicited with supramaximal stimulation of either the ulnar nerve at the wrist (FDI) or the musculocutaneous nerve at the axilla (BB). Markers indicating negative onset, negative peak, negative-peak duration, and positive peak were automatically positioned. Following a visual check of the markers (and manual adjustments if required), size-related parameters of the M wave, including negative-peak area, negative-peak amplitude, and peak-to-peak amplitude, were automatically calculated.

Following placement in the appropriate dynamometer, subjects were instructed to perform two 4-s maximal voluntary contractions (MVC) that were separated by a 2-min rest period. The subjects were aided in these maximal contractions by visual feedback from the oscilloscope and strong verbal encouragement from the examiner. The peak of these MVCs was determined and a number corresponding to 10% of this value was marked on the oscilloscope. Subsequent contractions were performed within a range of this value to ensure that both groups were voluntarily contracting at a similar percentage of their MVC, as previous studies have shown the level of voluntary force to influence the results of DQEMG analysis (see results for force data).^{5,32}

The concentric needle electrode was then inserted into the muscle of interest just proximal or distal to the active surface electrode. Subjects were asked to minimally contract the muscle isometrically while the needle position was adjusted in order to minimize the rise-times of the MUPs of the first 2 or 3 recruited MUs. With the needle manually maintained in a stable position by the examiner, the subject was instructed to increase the contraction force to the desired percent of MVC. If the signal was of poor quality based on visual inspection, the nee-

dle was repositioned and the process repeated to ensure adequate signal quality. Each isometric contraction lasted for 30 s, with rest periods of 30–60 s provided between contractions. Subjects were instructed to maintain consistent contraction intensities throughout the contraction and were aided in doing so by the presence of a target line displayed on the oscilloscope. Contractions were performed until a minimum of 20 MUP trains were obtained. If more than three contractions were required, a second needle insertion at a different site was undertaken. Following needle-detected signal decomposition and analysis, the MUP trains and needle- and surface-detected MUPs (S-MUPs) were reviewed with regard to their acceptability based on criteria previously reported.⁵ Briefly, the variability of the instantaneous firing rate vs. time plot of each MUP train and the interdischarge interval histograms of each MUP train were examined visually. Those that were accepted displayed consistent firing rate plots and a physiological firing rate as quantified by an associated interdischarge interval histogram that displayed a Gaussian-shaped main peak and a coefficient of variation of the interdischarge interval of <0.3 .^{23,39} Each MUP train was required to include a minimum of 50 detected potentials that would serve as triggers for spike-triggered averaging. Needle- and surface-detected MUP waveforms were visually checked to ensure that the onset and peak markers were accurate (and repositioned manually if necessary). Last, the onset of the S-MUP waveform was required to occur within 10 ms of the needle-detected MUP waveform onset. MUP trains and needle- and surface-detected MUPs that failed to meet all the inclusion criteria were excluded from further analysis.

MUNE was automatically calculated by dividing a size-related parameter of the maximum M wave (negative-peak amplitude) by the corresponding size-related parameter of the mean S-MUP, determined by the datapoint-by-datapoint average of all acceptable S-MUPs aligned based on their onset.

Statistics. Mean values along with their standard deviations are presented throughout. Prior to analysis, all data were tested for normalcy and those data that were not normally distributed were analyzed using non-parametric statistics. Thus, differences between groups were determined using either a standard one-way analysis of variance (ANOVA) or a Kruskal–Wallis one-way ANOVA for non-parametric data (Graduate Student Package, version 14.0; SPSS, Chicago, Illinois) with an alpha level of $P < 0.05$ denoting significance.

Table 1. Maximal force and electrophysiological data for the FDI.

	MVC (N)	M wave (mV)	MUNE	S-MUP NpAmp (μ V)	Needle P-P Vol (μ V)	AAR	Needle duration (ms)	Firing rate (Hz)
ALS	17.8 \pm 10.7 (5.9–34.6)	8.7 \pm 3.7 (2.0–13.2)	65 \pm 39 (4–116)	197.3 \pm 110.2 (81.9–392.7)	669.2 \pm 183.7 (433.0–910.8)	2.0 \pm 0.4 (1.3–2.3)	12.9 \pm 2.1 (9.1–15.8)	12.8 \pm 2.2 (9.7–15.5)
Healthy Subjects	27.1 \pm 5.4 (17.4–36.0)	14.3 \pm 3.1 (10.5–18.8)	144 \pm 42 (78–213)	124.1 \pm 46.6 (66.0–229.0)	463.1 \pm 120.6 (325.6–726.6)	1.3 \pm 0.2 (1.0–1.6)	9.3 \pm 1.3 (7.6–11.8)	12.8 \pm 1.4 (10.4–15.5)

Values expressed as mean \pm SD. Data in parentheses indicate range. NpAmp, negative-peak amplitude; P-P Vol, peak-to-peak voltage. See text for other abbreviations.

RESULTS

FDI Force, M Wave, and MUNE. Maximal voluntary contraction values differed between healthy subjects and ALS patients ($P < 0.05$; Table 1 and Fig. 1). Similar to the MVC values, the ALS patients demonstrated significantly lower maximum M-wave values and MUNE (Table 1 and Fig. 1). The intensity of the voluntary contractions at which the needle- and surface-detected EMG signals were sampled was similar between the healthy subjects ($11.0 \pm 3.4\%$ of MVC) and ALS patients ($12.3 \pm 4.4\%$ of MVC).

FDI Needle-Detected MUPs and Firing Rate. An average of 33 ± 5 MUP trains were sampled per healthy subject from an average of 7 ± 2 contractions with slightly lower values observed for the ALS group, with an average of 19 ± 8 MUP trains from 5 ± 2 contractions. Mean MUP identification rates were similar between groups, with rates of $56.8 \pm 5.4\%$ and $60.9 \pm 9.0\%$ for healthy subjects and ALS patients, respectively. The amplitude of the needle-detected MUPs (peak–peak voltage) was larger ($P < 0.05$) for the ALS patients than for healthy subjects

(Table 1 and Fig. 1). Similarly, needle-detected MUP duration was longer in the ALS patients than the healthy subjects ($P < 0.05$, Table 1). Despite these differences, the mean MU firing rates were similar between groups (Table 1) as was the complexity of the needle-detected MUPs with an equal number of phases (3 ± 3) and turns (3 ± 1). Finally, the area-to-amplitude ratio (AAR) or “thickness” of the needle-detected MUPs differed between healthy subjects and ALS patients ($P < 0.05$, Table 1).

FDI Surface-Detected MUPs. Despite a considerable difference in the magnitude of the mean negative-peak amplitude values for healthy subjects and ALS patients, a statistical difference was not present (Table 1 and Fig. 1). Lastly, the duration of the S-MUPs sampled from both groups was similar, with values of 24.0 ± 3.2 ms and 25.5 ± 5.7 ms for the healthy subjects and ALS patients, respectively.

BB force, M Wave, and MUNE. Maximal voluntary contraction values differed between groups, with considerably higher values observed for the healthy

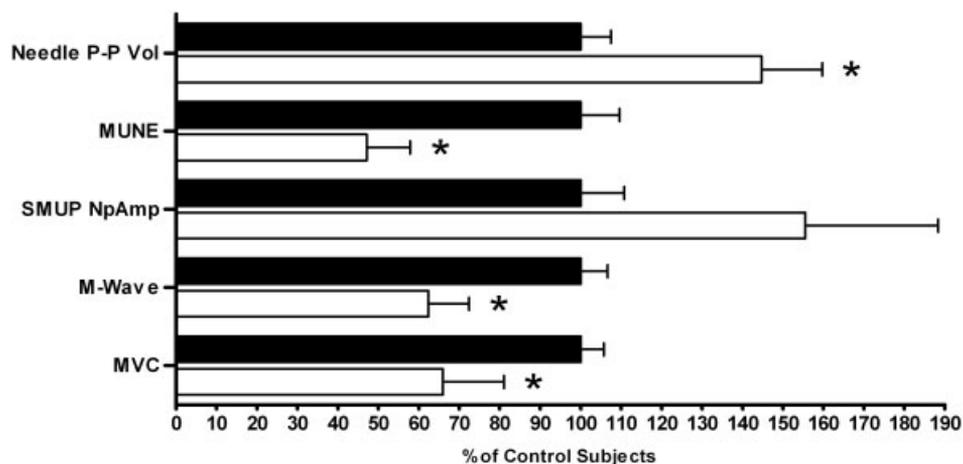


FIGURE 1. Maximal force and electrophysiological data for the FDI. The ALS patients' values (open bars) are expressed as a percentage of values obtained for the control subjects (solid bars) \pm standard error. Asterisk indicates a significant difference ($P < 0.05$). NpAmp, negative-peak amplitude; P-P Vol, peak-to-peak voltage.

Table 2. Maximal force and electrophysiological data for the BB.

	MVC (N)	M wave (mV)	MUNE	S-MUP NpAmp (μ V)	Needle P-P Vol (μ V)	AAR	Needle duration (ms)	Firing rate (Hz)
ALS	132.6 \pm 78.8 (16.9–252.7)	4.6 \pm 2.1 (1.2–8.0)	101 \pm 126 (2–419)	238.2 \pm 451.4 (26.2–1415)	494.7 \pm 132.4 (360.3–730.7)	1.9 \pm 0.5 (1.3–2.8)	12.9 \pm 2.1 (9.3–16.0)	13.1 \pm 2.9 (9.9–19.1)
Healthy Subjects	349.3 \pm 56.2 (245–441.7)	12.2 \pm 2.2 (7.3–15.5)	271 \pm 125 (159–547)	58.0 \pm 20.7 (32.4–91.3)	398.9–124.5 (230.7–562.3)	1.4 \pm 0.3 (1.0–1.8)	9.8 \pm 2.1 (6.6–13.2)	12.1 \pm 1.3 (9.9–14.1)

Values expressed as mean \pm SD. Data in parentheses indicate range. NpAmp, negative-peak amplitude; P-P Vol, peak-to-peak voltage. See text for other abbreviations.

subjects than for ALS patients ($P < 0.05$; Table 2 and Fig. 2). Analogous to this finding was the observation of significantly lower maximum M-wave and MUNE values in the ALS patients than healthy subjects (Table 2 and Fig. 2). Lastly, during sampling of the needle- and surface-detected EMG signals, the healthy subjects and ALS patients were voluntarily contracting at a similar intensity ($11.1 \pm 2.2\%$ and $13.9 \pm 5.3\%$ of MVC, respectively).

BB Needle-Detected MUPs and Firing Rate. An average of 34 ± 5 MUP trains were sampled per healthy subject from an average of 7 ± 1 contractions with slightly lower values observed for the ALS group, with an average of 19 ± 9 MUP trains from 5 ± 2 contractions. Mean MUP identification rates were similar between groups, with rates of $63.6 \pm 7.1\%$ (healthy subjects) and $63.3 \pm 15.1\%$ (ALS). Needle-detected MUP amplitude (peak-peak voltage) differed between groups, with lower amplitude MUPs sampled for the healthy subjects compared to the ALS patients ($P <$

0.05 ; Table 2 and Fig. 2). Similarly, needle-detected MUP duration was shorter in the healthy subjects than patients with ALS ($P < 0.05$, Table 2). Despite these differences, mean MU firing rates were similar between groups (Table 2). Needle-detected MUP complexity was also comparable between groups, with a similar number of phases (healthy subjects, 2 ± 0 ; ALS, 3 ± 0) and an equal number of turns (3 ± 1). Lastly, needle-detected MUP AAR was different between groups, with larger values observed for the ALS patients than healthy subjects ($P < 0.05$, Table 2).

BB Surface-Detected MUPs. Similar to the results observed for the FDI muscle, the difference in the mean S-MUP amplitude (negative peak) observed between healthy subjects and ALS patients was not significantly different (Table 2 and Fig. 2). The mean duration of the S-MUPs did not differ, with mean values of 25.9 ± 4.4 ms (healthy subjects) and 27.0 ± 6.4 ms (ALS). NpAmp, negative-peak amplitude; P-P Vol, peak-to-peak voltage.

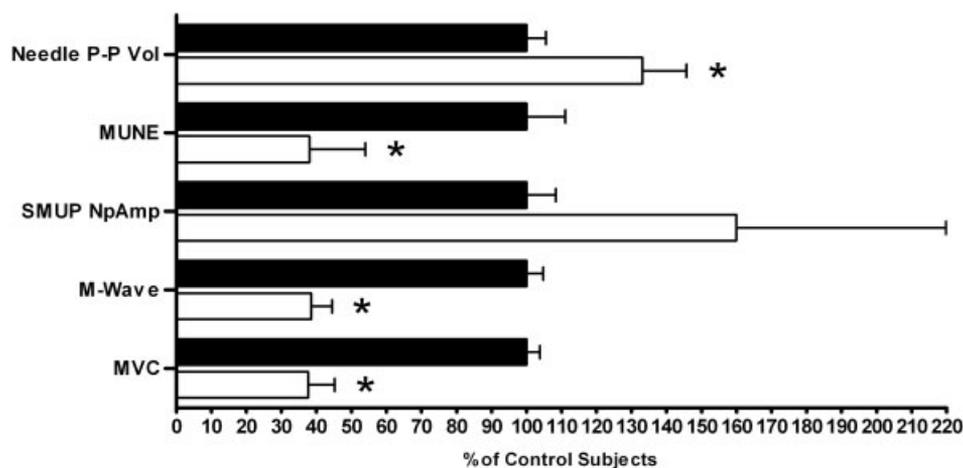


FIGURE 2. Maximal force and electrophysiological data for the BB. The ALS patients' values (open bars) are expressed as a percentage of values obtained for the control subjects (solid bars) \pm standard error. For illustrative purposes, one patient's mean S-MUP value (1415 μ V) was not included (see Table 2 for complete data). Asterisk indicates a significant difference ($P < 0.05$). NpAmp, negative-peak amplitude; P-P Vol, peak-to-peak voltage.

DISCUSSION

Our primary goal was to determine the effectiveness of DQEMG in obtaining electrophysiological data that are representative of the pathophysiology affecting the LMN. Our observation of significantly decreased MUNE in patients with ALS coupled with significantly larger-amplitude and longer-duration needle-detected MUPs, despite statistically similar mean surface-detected MUP amplitudes, suggest that these results are reflective of the expected changes occurring at the MU level in ALS. Additionally, the similarity between our healthy subjects and ALS patients in the number of MUP trains sampled per contraction and MUP identification rates between groups and in comparison to previous studies⁵⁻⁷ are evidence that DQEMG is applicable in this particular patient population.

Needle-Detected MUP Size, Complexity, and Firing Rate. In addition to abnormal spontaneous activity, electrodiagnostic evidence of a neuropathic process includes the presence of large-amplitude, long-duration, and complex MUPs representative of enlarged MUs resulting from collateral reinnervation.^{9,16,22} Although our study demonstrated a significant difference in needle-detected MUP amplitudes between groups and across muscles (Figs. 1 and 2), the mean amplitude value of the ALS group does not fall outside of the typical range observed for these muscles.^{4,24,35} For example, mean BB needle-detected MUP amplitude of the ALS group in the current study ($494.7 \pm 132.4 \mu\text{V}$) was similar to that reported for the BB of healthy subjects using a different quantitative EMG technique at a comparable percentage of MVC ($463 \pm 139 \mu\text{V}$).²⁴ Similarly, values for the FDI using multi-MUP analysis in healthy subjects ($752 \pm 247 \mu\text{V}$) were similar to those of our ALS patients ($669.2 \pm 183.7 \mu\text{V}$).⁴ Lastly, a comparison of the MUP amplitude distributions (Fig. 3) reveals that, despite a rightward shift in the ALS group, the relative magnitude of these differences was small. Together, these results support the notion that needle-detected MUP amplitude may not accurately represent MU size.

Our results offer no evidence that the needle-detected MUPs recorded from either muscle in our ALS patients were more complex than those of healthy subjects. This result may be related to the time at which the sample of MUPs was obtained and its relationship with the time since disease onset.²² Support for the concept that MUP complexity may vary with the degree of disease progression was provided by a previous study of 51 ALS patients with a disease duration of 6 months to 5 years, wherein

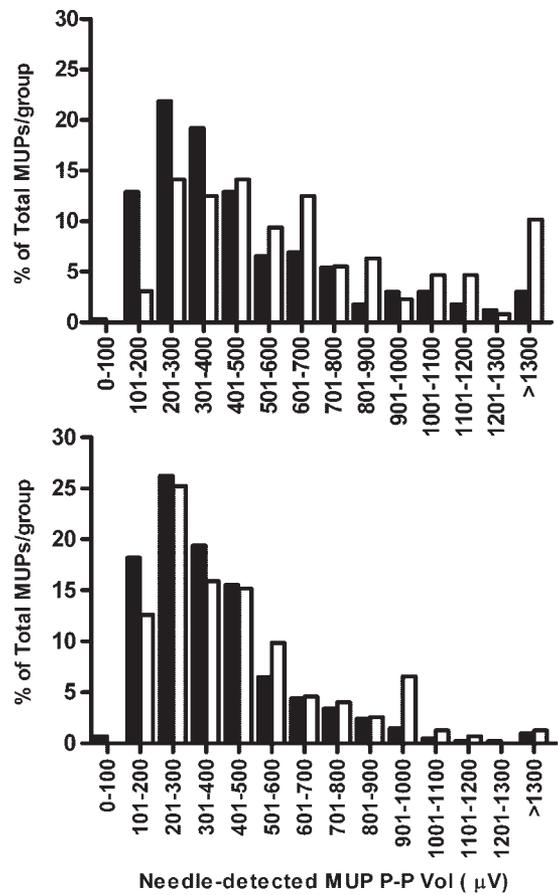


FIGURE 3. Distribution of FDI (upper graph) and BB (lower graph) needle-detected MUPs based on amplitude for both controls subjects (solid bars) and ALS patients (open bars). The y-axis represents the percentage of the total number of needle-detected MUPs per group.

increased polyphasic MUPs were found in only 10 of 51 muscles studied.⁴⁰

Much evidence suggests that MUP duration and AAR may also be representative of MU size.³⁴ In our study, MUP duration and AAR for both the FDI and BB muscles of the ALS group were significantly different from those of healthy subjects, as was MUP amplitude. Unlike amplitude, however, MUP duration and AAR of both muscles in the ALS group exhibited differences that were similar in magnitude to those of healthy subjects in previous studies,^{4,35} suggesting that these parameters provide information pertaining to MU size in ALS that complements MUP amplitude. These measures, as obtained with DQEMG, also appeared sensitive to the changes occurring at the MU level in ALS, thus providing an indication of the degree of LMN involvement.

The mean firing rates of the needle-detected MUPs did not differ significantly between healthy subjects and ALS patients for either of the muscles

studied (Tables 1 and 2), a finding that may be attributed to physiological, pathophysiological, or technical factors. Physiologically, the process of collateral reinnervation produces larger MUs with greater twitch tensions, resulting in an increased force-generating capacity per MU.¹⁹ Thus, for a given level of contraction, fewer MUs discharging at a normal physiological rate can produce the required force output. The degree to which this occurs in ALS is uncertain, as the extent to which collateral reinnervation can compensate for MU loss is not precisely known. It has been speculated that as little as 30% or as much as 80% of the MU population in a given muscle is lost before clinical symptoms manifest,^{13,29,41,42} at which time MU firing rates should increase as the twitch tensions of the surviving MUs decrease.¹⁹

Pathophysiologically, it has been shown that patients with ALS are unable to provide adequate excitatory input to the LMN pool because of upper motor neuron involvement.²⁶ Reduction in descending drive may limit the force-generating capacity of the muscle despite an adequate population of LMNs. Lastly, there is the possibility of technical limitations in the firing pattern analysis used in DQEMG.³⁹ With the current algorithms for DQEMG analysis, there is no attempt to resolve superpositions that reflect the overlap of MUPs. Gaps in the interdischarge intervals caused by missed or erroneous firings may therefore lead to inaccurate firing-rate information. However, this is unlikely as interdischarge interval values falling outside a particular range of the mean interdischarge interval are removed from subsequent analyses.³⁹

The need to control the level of voluntary force in the current study resulted in the assessment of firing rates at relatively low levels of MVC (~10%–15%), in contrast to routine clinical EMG, where the level of voluntary contraction may be increased in patients with a reduced interference pattern to allow for assessment of a “fuller” interference pattern. At this higher level of contraction, increases in MU firing rates can be more readily observed, albeit at a considerably higher percentage of MVC.

Surface-Detected MUP Size. Although MUP duration, AAR, and to a lesser extent amplitude offer insight into the size of the MUs, they are influenced by the limitations of the needle electrode used to detect them.³⁴ Estimating MU size in surface EMG recordings is thought to be a more accurate representation as there is a higher probability of a greater number of muscle fibers per MU contributing to the EMG signal.^{37,38}

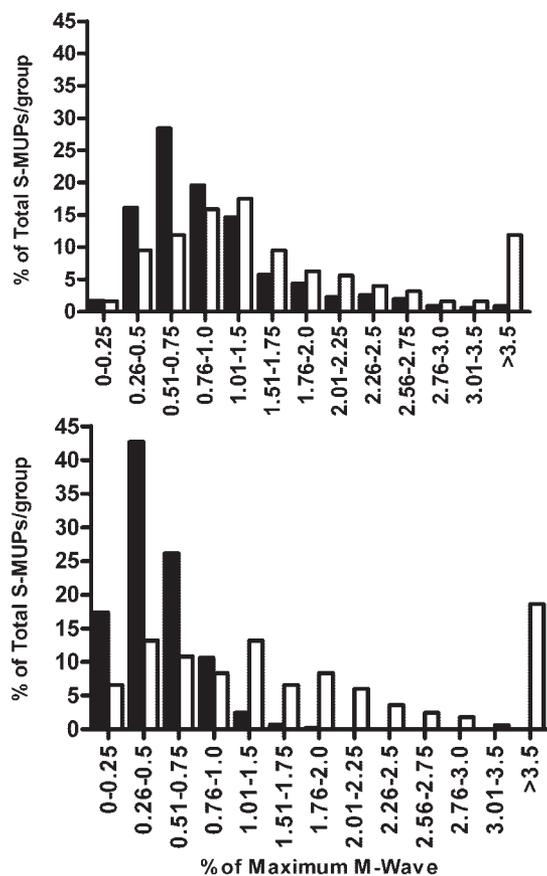


FIGURE 4. Distribution of FDI (upper graph) and BB (lower graph) surface-detected MUPs expressed as a percentage of the maximum M wave for both control subjects (solid bars) and ALS patients (open bars). The y-axis represents the percentage of the total number of S-MUPs per group.

Despite the absence of a significant difference between groups, our results suggest that S-MUP amplitude reflects the ongoing reinnervation process in ALS. This finding is particularly evident in Figure 4, which shows a greater number of larger-amplitude S-MUPs in ALS patients than healthy subjects. In comparing the two groups, S-MUP amplitude was found to be 55.5% (FDI) and 59.9% (BB) greater in ALS patients than healthy subjects, values considerably larger than the increases of only 44.7% (FDI) and 33.1% (BB) for needle-detected MUP amplitude (Figs. 1 and 2).

There were instances in which S-MUPs sampled from individual ALS patients had amplitudes similar to or, in some cases, less than the mean for healthy subjects. For example, in the BB of one patient, the mean S-MUP amplitude was determined to be 26.2 μ V, a value that represents ~11% of the mean S-MUP amplitude calculated for the entire ALS group (Table 2). Similar findings have been reported pre-

viously, with the smaller S-MUPs believed to represent the remaining muscle fibers of normal-sized or enlarged MUs at some stage of terminal denervation.¹⁴ Alternatively, depending on the degree of disease progression, these smaller S-MUPs may represent the muscle fibers of MUs in the early stages of reinnervation.

Motor Unit Number Estimates. Perhaps the best assessment of the degree of LMN involvement in ALS is provided by MUNE, as this is the only available measure that attempts to quantify the number of MUs within the system. A previous study revealed weak correlations between MUNE and other measures of impairment in the motor system (i.e., isometric MVC and maximum M wave) used in studies of ALS, suggesting that MUNE is more sensitive to the effects of collateral reinnervation.^{10,11} Examination of the mean MUNE, MVC, and maximum M-wave amplitude values in our study (Figs. 1 and 2) suggests that MUNE provided a better indication of LMN loss in the FDI than BB, based on the magnitude of the difference between mean MUNE values and the mean MVC and M-wave values of the ALS patients (~16% for the FDI, negligible for the BB; Figs. 1 and 2). Furthermore, for the FDI, with the exception of one patient, all MUNE values in the ALS group were reduced to a greater extent compared to the mean for healthy subjects than either maximal M wave or MVC. For the BB muscle, variable results were observed; for instance, one patient had a greater reduction in MUNE (~95%) than either maximal M wave (68%) or MVC (74%), but several patients displayed similar reductions in both their MUNE and maximal M-wave values, suggesting both measures provide similar information pertaining to the extent of MU loss. Nevertheless, our observations show that MUNE does provide information pertaining to the degree of MU loss that is not necessarily reflected in a reduction in the amplitude of the maximal M wave or the magnitude of the MVC.

The differences in the relationships between maximal M-wave, MVC, and MUNE values observed between the two muscles and across individual patients may be due to several factors, including the rate of disease progression and the time-point at which a study is performed, as well as differences across individual patients in terms of body region and spinal segments in which LMN loss has occurred or is most severe.

Methodological differences and the variability associated with disease progression limit the ability to compare our results with those of previous MUNE

studies in ALS. However, comparing the percentage difference of MUNE values between ALS patients and healthy subjects observed across studies allows for an appropriate comparison to be made. Expressed in this manner, the relative MU losses observed in the ALS group were 52.9% (FDI, Fig. 1) and 61.5% (BB, Fig. 2). These values approximate the relative decreases in MUNE observed in intrinsic hand muscles of 65.7% (abductor pollicis brevis) and 54.2% (abductor digiti minimi),²⁸ and are slightly lower than those observed in a study of the BB (73.1%),⁸ providing evidence that DQEMG is a suitable means of deriving MUNE in patients with ALS.

Overall, the results of this study demonstrate the applicability of DQEMG in obtaining electrophysiological data that are representative of the pathophysiology of the LMN component of ALS. These results support the use of DQEMG in future studies of ALS as an efficient means to longitudinally document the natural history and progression of the disease.

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