Published in final edited form as:

J Neural Eng. 2015 December ; 12(6): 066001. doi:10.1088/1741-2560/12/6/066001.

Assessing altered motor unit recruitment patterns in paretic muscles of stroke survivors using surface electromyography

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Abstract

Objective—The advancement of surface electromyogram (sEMG) recording and signal processing techniques has allowed us to characterize the recruitment properties of a substantial population of motor units (MUs) non-invasively. Here we seek to determine whether MU recruitment properties are modified in paretic muscles of hemispheric stroke survivors.

Approach—Using an advanced EMG sensor array, we recorded sEMG during isometric contractions of the first dorsal interosseous muscle over a range of contraction levels, from 20% to 60% of maximum, in both paretic and contralateral muscles of stroke survivors. Using MU decomposition techniques, MU action potential amplitudes and recruitment thresholds were derived for simultaneously activated MUs in each isometric contraction.

Main results—Our results show a significant disruption of recruitment organization in paretic muscles, in that the size principle describing recruitment rank order was materially distorted. MUs were recruited over a very narrow force range with increasing force output, generating a strong clustering effect, when referenced to recruitment force magnitude. Such disturbances in MU properties also correlated well with the impairment of voluntary force generation.

Significance—Our findings provide direct evidence regarding MU recruitment modifications in paretic muscles of stroke survivors, and suggest that these modifications may contribute to weakness for voluntary contractions.

Keywords

muscle weakness; chronic stroke; motor unit; recruitment threshold; surface electromyogram

Introduction

Hemispheric stroke is a major source of neurological disability, and it is increasing in prevalence worldwide. Many stroke survivors exhibit persistent impairments in voluntary muscle activation, resulting in long-term muscle weakness or paresis, even after extensive therapy [1, 2]. One potential mechanism underlying such impairment in muscle voluntary activation is the disorganization in the recruitment of the motor unit (MU) pool, in which larger and more fatigable MUs are potentially recruited prematurely [3]. Although altered MU firing rates may also contribute to paresis, the reported changes in rate patterns are not consistent [3–5] (also see discussion section for further details). Accordingly, in this study,

our objective was to focus on alterations in MU recruitment patterns in paretic muscles of stroke survivors, and to evaluate the contribution of this recruitment disruption towards the overall motor impairment.

Due to technical barriers, relatively few studies have attempted a complete investigation of disturbances of MU recruitment in paretic muscles of stroke survivors. Previous studies have shown that the MU recruitment threshold range is compressed in paretic muscles of some stroke survivors [3], but these data were collected piecemeal, not with simultaneous recordings of multiple units from the same contraction. Other studies have reported the apparent loss of larger, high-threshold MUs in some subjects through an analysis of the median amplitude of the action potentials recorded from macro-EMG [6]. These earlier studies used invasive intramuscular recordings, which are often limited to low force levels, and provide a relatively small yield of reportable MUs. Using such intramuscular methods, a systematic evaluation of global MU pool properties over a large force range is not feasible.

In light of these limitations, the objective of the current study was to perform a non-invasive examination of MU pool voluntary recruitment in stroke survivors, in order to identify potential disturbances in MU recruitment patterns in paretic muscles over a large force range. Specifically, we investigated whether there was disturbance in the rank order of recruitment by MU size [7], and in MU recruitment range as isometric force increased. Orderly recruitment patterns have been reported in neurologically intact individuals, and are crucial for effective muscle force generation [8, 9].

In the current study, these MU recruitment properties were examined in concurrently active MUs during a single isometric force task, using abduction forces generated by the first dorsal interosseous (FDI) muscles on both paretic and contralateral hands of stroke survivors. This information was obtained using an innovative surface electromyogram (sEMG) electrode array recording and decomposition method [10, 11] that provides the firing times of MUs and their corresponding action potential templates. This decomposition technique has been systematically validated using both computer simulations and experimental cross-validation with two-source intramuscular decomposition methods [12, 13]. The amplitude of the MU action potential (an estimate of the MU size) was then estimated, using a spike triggered averaging method [8, 14].

Compared with contralateral muscles, we found that the paretic muscle tended to show a weak relationship between recruitment order and MU size, in that the size of the recruited MUs in each contraction did not increase with increasing voluntary muscle contraction. In addition, the range (or spread) of recruitment force thresholds in the paretic muscle was clustered to lower values and also did not increase with voluntary muscle contraction levels, as compared with contralateral muscle. Our findings indicate that there is disorganization of MU pool recruitment properties in paretic muscle, and these changes can potentially contribute to muscular weakness after a stroke.

Materials and methods

Participants

Fourteen chronic hemiparetic stroke subjects were recruited from the outpatient clinics of the Rehabilitation Institute of Chicago. The demographic information of these subjects is shown in table 1. All participants gave informed consent via protocols approved by the Institutional Review Board at Northwestern University.

Inclusion criteria for the stroke subjects were: (1) hemispheric stroke with post-stroke duration >6 months; (2) unilateral movement impairment; (3) impairment of hand function (Chedoke-McMaster score ranged from 2 to 6); (4) ability to provide informed consent; (5) medically stable, with no concurrent severe medical illness; (6) no upper extremity pain, inflammation, or recent injury; (7) no medication that can impact neuromuscular function; (8) no severe cognitive impairment or aphasia sufficient to limit comprehension of the experimental task; (9) no prior recurrent vascular episodes.

Experimental setup

Participants were seated upright in a Biodex chair with their upper arm comfortably resting on a support. To standardize hand position and to minimize contributions of unrecorded muscles, the forearm was immobilized with a cast and placed in a ring mount interface attached to a forearm rest. This rest was securely mounted with magnetic stands to a steel table. The forearm was placed in full pronation and the wrist was held neutral with respect to flexion/extension. The little, ring and middle fingers were extended away from the index finger and strapped to a support surface. The thumb was secured at an approximately 60° angle to the index finger. The index finger was placed in line with the 2nd metacarpal and the long axis of the forearm creating a 0° or neutral metacarpophalangeal joint angle (figure 1(A)). The proximal phalanx of the index finger was casted and fixed to a ring-mount interface attached to a six degrees-of-freedom load cell (Gamma, ATI, Inc., Apex, NC). The recorded forces from the abduction-adduction direction were low-pass filtered (cutoff = 200 Hz) and digitized at a sampling frequency of 2 kHz. The subjects were instructed to voluntarily produce required abduction forces while minimizing the off-axis forces.

EMG recordings—The subject's skin was cleaned with alcohol pads to ensure proper electric contact and low baseline noise. sEMG was recorded from the FDI using a surface sensor array (Delsys, Inc., Natick, MA) as shown in figure 1(B) that consists of five cylindrical probes (0.5 mm diameter). The probes are located at the corners and at the center of a 5 × 5 mm square. Pairwise differentiation of the five electrodes yields four channels of sEMG signals (upper panels of figures 1(C) and (D)). The sEMG sensor and a reference electrode were connected to four channels of a Delsys Bagnoli sEMG system. The signals were sampled at 20 kHz and were amplified and filtered with a bandwidth of 20 Hz to 2 kHz.

Procedures

The stroke subjects performed two separate sessions (one for each side) of the same protocols, spaced less than a week apart. Prior to the main testing sessions, subjects were

asked to perform maximal voluntary contractions (MVCs) for 3 s. This maximum contraction was repeated 3 times in total, with 60 s rest between trials. The largest value of the three trials was designated as the MVC. To enable fair comparison between the two sides of stroke subjects, the MVC of the paretic side was used as the calibration level during the testing of the contralateral side, such that both sides produced the same absolute force. However, the MVC of both sides were also recorded to assess muscle weakness (see table 1). The rest of the session consisted of a series of isometric voluntary contractions during which the subject was asked to follow trapezoidal force trajectories displayed on a computer screen, each set at a different percentage of the MVC.

The force output in one exemplar trial from each side is shown in the bottom panels of figures 1(C) and (D). The trapezoid force trajectory contains five segments: a 5 s quiescent period for baseline noise calculation, an up-ramp increasing at a rate of 10% MVC/s, a constant force plateau at the prescribed % MVC for 12 s, a down-ramp decreasing at 10% MVC/s, and a 3 s quiescent period. To ensure that the subjects could follow the trapezoid trajectory closely, they practiced for a minimum of 5 trials of a 30% MVC constant force trapezoid before the main experiment.

For the main part of the experiment, the subjects performed five blocks of trials with five repetitions of each block. When the voluntary force output trajectory showed a large deviation from the target trajectory, such as a transient force change in the up-ramp and force plateau stages, the trial was terminated and repeated after the subject was given sufficient rest. Five constant force levels (20%, 30%, 40%, 50%, and 60% MVC) were tested, and each block contained one force level. The order of the force levels was randomized for each subject. A 60 s rest period between repetitions was provided to minimize fatigue, and additional resting was provided upon request.

Data analysis

Data processing—The sEMG and force trials were selected for further analysis based on the following criteria:

- a. there was no sudden change (i.e., larger than 20% MVC/s) in the up-ramp force,
- b. the force variability during the steady state hold was low (within ± 2 standard deviations of background force level), and
- c. the sEMG signal had a peak–peak (P–P) baseline noise $< 20 \mu\text{V}$, and signal to noise ratio > 5 . The signal to noise ratio was calculated based on the P–P amplitude of the baseline noise and P–P amplitude of the EMG signal at steady state contractions.

These criteria were based on the suggestions for robust MU discrimination using the dEMG decomposition system [10, 15]. For each subject, based on the preceding criteria, three trials were selected at each force level for further analysis. The dEMG decomposition algorithm was used to extract single MUs from the EMG signals.

For each identified MU, the output from this algorithm consisted of the firing times and four action potential templates from each of the four recorded sEMG channels (lower panels of

figures 1(C) and (D)). The decomposition accuracy has been validated using simulation approaches [12] and using a two-source cross-validation method where simultaneous intramuscular and surface EMG were recorded, and both signals were decomposed using separate decomposition algorithms [13]. An average accuracy of 95% was found in the surface decomposed units that were common to the intramuscular decomposition.

Action potential amplitude estimation—The sizes of the MUs were estimated from the action potential P–P amplitude using a spike triggered averaging technique [8]. This approach relies on the finding that MUs of different sizes in the FDI muscle are uniformly distributed throughout the muscle [16] and the duration (an estimation of MU fiber depth) of the action potential is independent of the recruitment threshold. The validity of the spike triggered averaging estimates has been assessed earlier using simulated sEMG signals [14]. Specifically, the spike triggered averaging was performed on each of the four channels of the sEMG signals resulting in 4 action potential estimates for each MU. The identified firing times for each MU were used as triggering events for the spike triggered averaging calculation. To ensure reliable estimate of action potential amplitude, we performed two separate tests to determine which MUs would be retained for further analysis [8]. The two tests were: (1) the correlation between the spike triggered averaging estimates and the decomposition templates, and (2) the waveform stability of the spike triggered averaging estimates. These tests were designed to assess the stability of the waveform over the trial duration and the degree of match with the decomposition estimated templates. For each retained MU, the P–P amplitude of the action potential calculated from the strongest EMG channel (with the largest root-mean-squared value) was used as the representative MU size estimate.

MU recruitment estimation—To estimate the recruitment threshold, the threshold force of the selected MU was calculated from the averaged isometric force data over an interval (–50 to 150 ms relative to the instance of the first firing event with an inter-spike interval smaller than 200 ms). An averaged force was calculated to reduce the influence of force fluctuations registered at the load cell. The window was asymmetric relative to the firing time because of the delay between the occurrence of an action potential and a registered force increment.

Statistical analysis

The interquartile range (IQR) of the MU size was estimated within each muscle contraction, and the changes of IQR with increasing muscle contraction levels were examined. The IQR was calculated because the MU size distribution in the FDI muscle has a greater representation at the lower end, or is skewed to the smaller values. The IQR was used to reduce the effect of outliers. If larger MUs were recruited as the muscle contraction level increased, the IQR of the MU size distribution would be expected to be larger at higher contraction levels. In order to quantify potential changes in the recruitment threshold, the median and range (IQR) of the threshold were calculated for each muscle contraction, and the median and IQR of the threshold values across different force levels were compared.

In order to assess the recruitment sequence (tracking the role of the size principle [7]), the MU size estimated from the P–P amplitude of the action potential was correlated with the recruitment threshold force of concurrently active MUs at individual force levels.

To further quantify the MU recruitment order, a least-squared linear regression of the P–P amplitude of the action potential as a function of threshold force was performed on concurrently active MUs at different force levels. To better capture the degree of recruitment order reversals, the MUs were sorted based on the threshold force in an ascending order. The order of the amplitude with increasing threshold force was calculated as $\text{sgn}(x_i - x_j)$, $i > j$. Here, $\text{sgn}(\cdot)$ represents the sign function, and x_i represents the action potential amplitude of MU i . Essentially, in each MU pair, if the later recruited MU is larger, the pair leads to 1, and if the later recruited MU is smaller, the pair leads to -1 . The order index was then calculated as:

$$\text{Order index} = \frac{\sum \text{sgn}(x_i - x_j)}{\sum \text{sgn}(x_i - x_j)}, \quad i > j, \quad i \in (1, n], \quad j \in [1, n). \quad (1)$$

In a given contraction, if the later recruited MU is always larger than the earlier recruited ones, the order index would be 1. If there is no ordering effect, the order index will be 0. If there are more MU recruitment reversals than sequences following the size principle, the order index would be negative.

To quantify the changes in MU properties between two sides of each subject, an asymmetry index was calculated from the relative difference between the two sides:

$$\text{Asymmetry index} = \frac{V_{\text{affect}} - V_{\text{contralateral}}}{(V_{\text{affect}} + V_{\text{contralateral}}) / 2}, \quad (2)$$

where V_{affect} is the estimated variable in the affected muscle and $V_{\text{contralateral}}$ is the estimated variable in the contralateral muscle.

The slope asymmetry of the regression analysis between MU size and recruitment force, the asymmetry of the computed median threshold, and the asymmetry of threshold IQR were calculated using equation (2).

The changes of IQR of MU size, median threshold, and IQR of recruitment threshold as a function of muscle contraction level were quantified using a least-squared linear regression for each side of individual subject. The regression slopes were compared between the paretic and the contralateral sides using a paired t -test. A one-sample t -test was also performed on the asymmetry indices across different repetitions of individual subjects to evaluate the changes in MU properties in the paretic muscle. $P < 0.05$ was taken as statistical significance.

Results

Our results include on average yield of 13 MUs per single isometric contraction of the FDI muscle, and 38 MUs per force level (based on three trials at each force level) for the paretic side; 16 MUs per trial and 47 MUs per force level respectively for the contralateral side. Through the analysis of these simultaneously active MUs in our tested stroke survivors, we routinely observed disorganized MU pool recruitment properties in the paretic FDI muscle. This disorganization was manifested as a disturbance in the recruitment order of the MUs based on unit size in the affected muscle, and a change in the threshold of MU recruitment, which was sharply compressed in a majority of our cohort of stroke survivors.

Size principle

The IQR of MU sizes (P–P amplitude of action potentials) at different levels of muscle contractions for all 14 stroke survivors is illustrated in figure 2. Each color represents an individual subject. With increasing force output, the amplitude IQR in the affected muscle (figure 2(A)) did not show a progressive increment as was evident in the contralateral muscle (figure 2(B)). The regression slope between the amplitude IQR and force output (figure 2(C)) revealed a significantly weaker increment of amplitude IQR with force level in the affected muscle ($p < 0.05$). Among the 14 subjects, 9 subjects revealed weaker increment in the affected muscle compared with the contralateral muscle. The results indicated that the range of MU size did not increase with higher muscle contraction levels in the affected muscle, when compared to the contralateral limb.

In order to further quantify MU recruitment rank order during each muscle contraction, the correlation between the MU size and the recruitment threshold force was assessed in stroke survivors. The results for a representative subject are shown in figure 3. The MU size increased progressively at higher threshold force on the contralateral side (figure 3(B)), indicating an orderly recruitment based on unit size, whereas there was not a strong recruitment order on the affected side (figure 3(A)). Three trials are plotted at each force level. Note that the % MVC value on the contralateral side refers to the value obtained on the affected side. In other words, the x -axis represents the same absolute force for the same subject. The recruitment rank order, as estimated from the P–P amplitude of the action potential was discernibly weaker on the affected side (figure 3(A)) than on the contralateral side (figure 3(B)) across multiple force levels.

The symmetry of the regression slope between P–P amplitude and threshold force was examined on each side for individual subjects (figure 4(A)). A negative asymmetry value signifies a shallower slope on the affected side compared with the contralateral side, and a positive value signifies a steeper slope on the affected side. Among the 14 subjects, ten subjects revealed more shallow slopes on the affected side ($p < 0.05$), and two subjects showed steeper slopes on the affected side ($p < 0.05$). Specifically, the slope asymmetry index was 1.42 ± 0.04 for subject 7 and was 0.88 ± 0.07 for subject 8. The remaining 2 subjects showed no significant difference between two sides (asymmetry index not significantly different from zero ($p > 0.05$)).

The computed order index (figure 4(B)) quantifies the degree of order reversals (i.e., whether larger units were recruited before smaller units). This second index was computed because a more shallow regression slope between amplitude and recruitment threshold could have arisen solely from reduced MU size, while recruitment order can still be preserved. Eleven subjects revealed a larger degree of recruitment reversals (i.e., a smaller order index number) on the affected muscle compared with the contralateral muscle ($p < 0.05$). Three subjects did not show a significant difference in recruitment order reversals between two sides ($p > 0.05$).

Recruitment threshold

In order to quantify the recruitment threshold compression in the affected muscle, the median threshold force and the IQR of the threshold forces were examined at different muscle contraction levels (figure 5). The median threshold did not show a consistent increase with the force level in the affected muscle (figure 5(A)), as much as it did in the contralateral muscle (figure 5(B)). The regression slope between the median threshold and the force level (figure 5(C)) revealed that the increase of median threshold with force level on the affected side was not as well-defined as on the contralateral side ($p < 0.05$). Eleven out of 14 subjects revealed weaker increment of median threshold in the affected muscle compared with the contralateral muscle. Similarly, the threshold IQR in the affected muscle tended to be limited to a low level across different muscle contraction levels (figure 5(D)), whereas the threshold IQR in the contralateral muscle scales up with force levels (figure 5(E)). The regression slope between the threshold IQR and the force level (figure 5(F)) also revealed that the increase of IQR threshold with force level in the affected muscle was not as evident as in the contralateral muscle ($p < 0.05$). Ten out of 14 subjects revealed weaker increment in the affected muscle compared with the contralateral muscle. The results showed that both the median threshold force and the IQR of the threshold force were compressed on the affected side in comparison with the contralateral side.

To better capture the recruitment threshold changes in the affected muscle, the threshold asymmetry and the threshold IQR asymmetry between two sides were calculated across individual subjects. A negative asymmetry value represents a reduced recruitment threshold and a reduced IQR of threshold in the affected muscle. As shown in figure 6(A), the recruitment threshold was compressed in the affected muscles in 11 out of 14 subjects ($p < 0.05$). Similar to threshold reduction, the spread (IQR) of recruitment threshold was also reduced ($p < 0.05$) in the affected muscle in 11 out of 14 subjects (figure 6(B)).

Clinical correlations

When a linear correlation analysis was performed between the different MU pool properties, we found significant correlations between IQR of the MU size and the IQR of recruitment threshold on the affected side ($r = 0.609$), between median threshold and IQR of threshold on the affected side ($r = 0.539$), as well as between median threshold and IQR of the MU size on the affected side ($r = 0.326$). These correlations suggest that stroke survivors, who failed to recruit larger MUs with increasing force level, also tended to show a compression of the recruitment threshold (both median and IQR).

When MU pool properties were correlated with the motor impairments (muscle strength reduction, Chedoke scale and Fugl-Meyer scale), we found that the MVC asymmetry showed a weak but significant correlation with the asymmetry values of the IQR of the MU size ($r = 0.281$), the median threshold ($r = 0.322$), and the IQR of the recruitment threshold ($r = 0.217$). However, no significant correlations were found between clinical assessment scales (Chedoke and Fugl-Meyer) and the different MU pool properties.

Discussion

The purpose of this study was to assess altered MU pool recruitment properties in paretic FDI muscles of hemispheric stroke survivors. Using a novel sEMG decomposition system, we evaluated changes of MU pool control properties in a substantial sample of concurrently active MUs. In a majority of our subject cohort, the normal orderly recruitment based on MU size in the affected muscle was disturbed; namely the recruitment of larger MUs at higher muscle contraction levels was less evident in the affected muscle, compared with the contralateral muscle. In addition, the threshold force range for MU recruitment was compressed to a lower level on the affected side, and this recruitment range also scaled to a lesser degree with increasing force in the affected muscle. We also found a significant (though weak) correlation between recruitment properties and FDI muscle strength reduction. The overall results revealed systematic disturbances of MU pool activation in the affected hand muscle of stroke survivors, which could potentially contribute to stroke-induced motor impairment.

Orderly recruitment

Orderly recruitment of MUs as a function of their size is a critical feature of normal MU pool organization. In muscles of intact subjects, smaller MUs generate a smaller and longer duration twitch force; hence early recruitment of the small MUs can generate a sustained and fine-tuned force output readily, even with a low level of excitation drive. With an increase in excitatory drive, newly recruited and larger MUs can then increase the total force progressively. Subsequent recruitment of larger and more fatigable MUs also avoids/ delays muscle fatigue, and facilitates a sustained force output.

In our tested stroke survivors, we found that the MU recruitment order was weaker (as quantified by more shallow slopes of the relation between MU size and threshold force) and there were more recruitment reversals on the affected side in most subjects (as quantified by lower order indices). The disordered recruitment, particularly the earlier recruitment of the larger and more fatigable MUs, could potentially promote early onset of muscle fatigue, and ultimately contribute to muscle weakness.

Such a disorganization of recruitment order may arise from different mechanisms. First, a differential change in MU size at the peripheral level across the MU pool can lead to recruitment reversals; namely, an increase of the size of low threshold MUs as well as a reduced size of the large MUs [6] can disrupt the order effect. Such enlargement of low threshold MUs can arise from muscle fiber reinnervation due to motoneuron loss or degeneration, whereas a MU size reduction can be induced by a reduction of muscle fiber diameter, and/or by the loss of muscle fibers, arising from disuse atrophy. Muscle fiber loss

can also be mediated by motor axon loss, and can preferentially impact estimates of fast twitch type II fibers, as reported from biopsy studies [17, 18].

Second, a change of recruitment threshold can also lead to a weaker recruitment rank order. In a spinal hemi-sectioned cat model, for example, a non-uniform change of recruitment threshold has been described, in that the low threshold MUs showed an increment in recruitment threshold and the high threshold MUs showed a reduction of threshold [19]. This non-uniform change in recruitment rank order exemplifies a disruption of orderly recruitment.

In addition, the recruitment of larger MUs with increasing muscle force was not as evident in the affected muscle as in the contralateral muscle, in that the recorded MU size range was relatively similar across all tested contraction levels on the affected side. This would suggest that the increased force levels were attained with a greater number of MUs at a given force and/or with firing rate modulation. Our results are consistent with reports of a larger number of active MUs at a given force in the biceps [20] and FDI muscle [21]. The lack of increase in MU size with increasing force levels could also be a sampling issue of the surface recording electrodes. Namely, between the FDI muscle boundary and the electrode on the skin surface, there may be a thicker layer of non-contractile tissue on the affected side that may limit effective EMG recording and decomposition (i.e., low-pass filtering blurs the ability to identify distinct action potential shapes). This sampling issue may result in an overall limit in the EMG amplitude, thereby compressing the amplitude range. Further studies are required to characterize tissue composition of the affected limbs and to quantify the influence of tissue properties on skin surface EMG recordings.

Compression of recruitment threshold

The MUs in the affected muscle also tended to be recruited at a smaller absolute force compared with the contralateral muscle. Such an alteration is manifested by a reduction in both the median and the range (IQR) of recruitment within a force ramp-up. There are several mechanisms that could induce such a compression of recruitment threshold.

The threshold reduction could be a direct consequence of muscle atrophy and/or inefficient activation of MUs. With peripheral muscle atrophy, expressed through a reduction of fiber diameter or even a loss of fibers, the amplitude of individual twitch force is reduced, and summed MU force for a given number of active MU is also reduced. This possibility is supported by the significant association between the range (IQR) of MU size and the range of recruitment thresholds. Namely, the stroke survivor that exhibits a reduced IQR of MU size with increasing force, also tends to exhibit a consistently compressed recruitment range at different force levels.

In addition, low firing rates potentially due to low excitatory descending drive, as reported in stroke literature [3, 4] could potentially contribute to inefficient force generation because these rates may not result in proper fusion of MU twitches, and widely spaced twitches contribute minimally to muscle force output. As a result, to achieve the designated force output, additional MUs would need to be recruited early, leading to a compressed recruitment threshold. The earlier recruitment of the fatigable MUs can, thus, lead to early

fatigue and a failure of sustained force generation. However, a reduction in firing rate is not a consistent finding in stroke survivors [3], and a majority of stroke survivors show a recruitment compression. Therefore, the causal relation between these two altered MU properties (rate versus recruitment) is not strong. Nevertheless, further studies that can estimate the MU twitch properties are necessary to quantify the amplitude and duration of the force twitch to identify possible muscle atrophy and establish the required unit fusion frequencies.

With increasing muscle contraction level, the range of MU recruitment threshold increases as additional units are recruited at higher force levels, both in normal controls and in the contralateral muscle of stroke survivors. However, this increment in force recruitment range is weaker in the affected muscle of stroke survivors. This weaker increment of recruitment range could be due to MU loss in the affected muscles. In particular, using different MU counting techniques, earlier studies have shown that the numbers of MUs are reduced in the affected muscles [22, 23]. A preferential loss of large, high threshold units in the pool has also been reported [6]. Such alterations of MU number can potentially limit the possibility of recording high threshold MUs with an increment of muscle force.

The issue remains as to where the needed force is generated, if no new units are being recruited at higher forces. There are several potential sources of force generation at the MU pool level. Recruitment of new MUs can contribute to force output. Although there is no visible MU recruitment at higher force levels, a larger number of units can be recruited earlier at lower force levels in the affected muscle, and this would lead to a larger number of active units at low forces, whose firing rate can be increased readily. Unfortunately, the number of active units cannot be quantified using our current MU recording techniques, because the surface sensor array only captures a sample of the active MU pool; however, our results are consistent with reports of increased EMG-force slopes in stroke affected muscles [20, 21].

Contributions of altered MU recruitment to clinical impairment

The MU recruitment patterns are clearly different in the paretic FDI muscle, but we are currently unable to make a strong case that these factors are a major source of motor impairment. Instead, it appears that many of these changes may be a by-product of both central and peripheral changes in the spinal cord and muscle, including altered motoneuron properties, MU structural changes, and synaptic reorganization following a hemispheric stroke. To quantify such a role more precisely, we will need to undertake detailed simulations of the motoneuron pool properties, including measures of recruitment and firing properties, coupled with acquisition of data about potential changes in MU twitch profiles.

Clinical implications

In our study, we found that the MU pool recruitment properties were disturbed in the paretic muscle of stroke survivors, and that the recruitment properties correlated significantly with FDI muscle weakness. These altered recruitment properties can originate from both central and peripheral changes. The non-invasive and efficient sampling nature of the sEMG methods used in this study can potentially facilitate the development of new diagnostic tools

assessing impairment of MU control. The additional understanding of altered MU pool activation acquired through these methods can also help us assess neuromuscular changes in the control of muscle force during therapy. The outcomes can potentially provide theoretical foundations for clinical decision-making that involves prescription of interventions (e.g., cortical or peripheral stimulations and pharmacological therapies including neurotrophic factors) with the potential to maximize functional recovery of stroke survivors.

References

1. Adams RW, Gandevia SC, Skuse NF. The distribution of muscle weakness in upper motoneuron lesions affecting the lower limb. *Brain*. 1990; 113:1459–76. [PubMed: 2245306]
2. Burke D. Spasticity as an adaptation to pyramidal tract injury. *Adv Neurology*. 1988; 47:401–23.
3. Gemperline JJ, Allen S, Walk D, Rymer WZ. Characteristics of motor unit discharge in subjects with hemiparesis. *Muscle Nerve*. 1995; 18:1101–14. [PubMed: 7659104]
4. Hu, X., Suresh, AK., Li, X., Rymer, WZ., Suresh, NL. Impaired motor unit control in paretic muscle post stroke assessed using surface electromyography: a preliminary report. 2012 Annual Int. Conf. of the IEEE Proceedings Engineering in Medicine and Biology Society (EMBC); San Diego, CA: IEEE; 2012. p. 4116–9.
5. Chou LW, Palmer JA, Binder-Macleod S, Knight CA. Motor unit rate coding is severely impaired during forceful and fast muscular contractions in individuals post stroke. *J Neurophysiol*. 2013; 109:2947–54. [PubMed: 23554434]
6. Lukacs M, Vecsei L, Beniczky S. Large motor units are selectively affected following a stroke. *Clin Neurophysiol*. 2008; 119:2555–8. [PubMed: 18809353]
7. Henneman E. Relation between size of neurons and their susceptibility to discharge. *Science*. 1957; 126:1345–7. [PubMed: 13495469]
8. Hu X, Rymer WZ, Suresh NL. Motor unit pool organization examined via spike triggered averaging of the surface electromyogram. *J Neurophysiol*. 2013; 110:1205–20. [PubMed: 23699053]
9. De Luca CJ, Contessa P. Hierarchical control of motor units in voluntary contractions. *J Neurophysiol*. 2012; 107:178–95. [PubMed: 21975447]
10. Nawab SH, Chang SS, De Luca CJ. High-yield decomposition of surface EMG signals. *Clin Neurophysiol*. 2010; 121:1602–15. [PubMed: 20430694]
11. De Luca CJ, Hostage EC. Relationship between firing rate and recruitment threshold of motoneurons in voluntary isometric contractions. *J Neurophysiol*. 2010; 104:1034–46. [PubMed: 20554838]
12. Hu X, Rymer WZ, Suresh NL. Assessment of validity of a high-yield surface electromyogram decomposition. *J Neuroeng Rehabil*. 2013; 10:99. [PubMed: 24059856]
13. Hu X, Rymer WZ, Suresh NL. Accuracy assessment of a surface electromyogram decomposition system in human first dorsal interosseus muscle. *J Neural Eng*. 2014; 11:026007. [PubMed: 24556614]
14. Hu X, Rymer WZ, Suresh NL. Reliability of spike triggered averaging of the surface electromyogram for motor unit action potential estimation. *Muscle Nerve*. 2013; 48:557–70. [PubMed: 23424086]
15. De Luca CJ, Adam A, Wotiz R, Gilmore LD, Nawab SH. Decomposition of surface EMG signals. *J Neurophysiol*. 2006; 96:1646–57. [PubMed: 16899649]
16. Milner-Brown HS, Stein RB. The relation between the surface electromyogram and muscular force. *J Physiol*. 1975; 246:549–69. [PubMed: 1133787]
17. Brooke MH, Engel WK. The histographic analysis of human muscle biopsies with regard to fiber type: 1. Adult male and female. *Neurology*. 1969; 19:221–33. [PubMed: 5812978]
18. Chokroverty S, Reyes MG, Rubino FA, Barron KD. Hemiplegic amyotrophy muscle and motor point biopsy study. *Arch Neurology*. 1976; 33:104–10.

19. Powers RK, Rymer WZ. Effects of acute dorsal spinal hemisection on motoneuron discharge in the medial gastrocnemius of the decerebrate cat. *J Neurophysiol.* 1988; 59:1540–56. [PubMed: 3385472]
20. Tang A, Rymer WZ. Abnormal force–EMG relations in paretic limbs of hemiparetic human subjects. *J Neurol Neurosurg Psychiatry.* 1981; 44:690–8. [PubMed: 7299407]
21. Suresh NL, Concepcion NS, Madoff J, Rymer WZ. Anomalous EMG-force relations during low-force isometric tasks in hemiparetic stroke survivors. *Exp Brain Res.* 2015; 233:15–25. [PubMed: 25224701]
22. Li X, Wang YC, Suresh NL, Rymer WZ, Zhou P. Motor unit number reductions in paretic muscles of stroke survivors. *IEEE Trans Inf Technol Biomed.* 2011; 15:505–12. [PubMed: 21478079]
23. McComas AJ, Sica RE, Upton AR, Aguilera N. Functional changes in motoneurons of hemiparetic patients. *J Neurology Neurosurg Psychiatry.* 1973; 36:183–93.

Figure 1.

Experimental setup, EMG signals and motor unit decomposition. (A) Experimental setup with surface EMG and force signal recordings. (B) The 5-pin surface EMG sensor array. (C) Four channels of surface EMG signals from the affected muscle, and decomposition results (motor unit discharge timings of motor unit 2, 4, ..., 18, and corresponding action potential templates from the EMG channel with the largest root-mean-squared value). The force output in black line is superimposed on top of the firing spikes. The up-ramp and the initial steady state force are shown to highlight the motor unit recruitment properties. (D) Surface EMG signals from the contralateral muscle, and motor unit discharge timings of motor unit 2, 4, ..., 20, and action potential templates.

Figure 2.

Interquartile range (IQR) of the P-P amplitude of action potentials as a function of muscle contraction levels. (A) Amplitude IQR of the affected side at different muscle contraction levels in all the subjects. One color represents an individual subject. (B) Amplitude IQR of the contralateral side at different muscle contraction levels in all the subjects. (C) Regression slope of the amplitude IQR versus force level. Error bars represent standard error across subjects.

Figure 3.

Size principle of an exemplar subject. (A) Peak to peak (P-P) amplitude of action potential as a function of the recruitment threshold of the affected muscle. Individual lines represent individual linear regressions at different force levels. (B) Size principle of the contralateral muscle.

Figure 4. Orderly recruitment asymmetry between two sides. (A) Regression slope asymmetry of the orderly recruitment in individual subjects. A negative value represents a shallower slope in the affected side. Error bars represent standard errors. 'x' sign represents non-significant difference from zero. (B) Order index. 'x' sign represents non-significant difference between two sides. A positive value represents an orderly recruitment based on motor unit size.

Figure 5. Median and IQR of the recruitment threshold as a function of muscle contraction levels. (A) Median threshold of the affected side at different muscle contraction levels in all the subjects. One color represents an individual subject. (B) Median threshold of the contralateral side. (C) Regression slope of median threshold versus force level. (D) Threshold IQR of the affected side. (E) Threshold IQR of the contralateral side. (F) Regression slope of the threshold IQR versus force level.

Figure 6. Recruitment threshold asymmetry between two sides. (A) Threshold force asymmetry of individual subjects. 'x' sign represents non-significant difference from zero. A negative value represents a compressed recruitment in the affected side. (B) Asymmetry of Threshold force IQR of individual subjects.

Table 1

Subject demographic information.

Subject ID	Gender	Age	Years since stroke	Paretic side	MVC contralateral (N)	MVC paretic (N)	Chedoke	Fugl-Meyer
1	M	61	4	R	39.0	30.0	6	63
2	F	62	15	L	31.0	13.2	2	17
3	F	59	23	R	37.0	8.3	2	22
4	M	66	9	L	22.0	6.7	4	16
5	F	53	3	R	65.0	26.0	6	63
6	F	58	5	R	16.5	6.8	4	38
7	F	71	7	R	33.0	13.6	6	66
8	M	60	11	R	31.0	17.7	5	52
9	M	61	7	R	33.6	22.0	4	3
10	F	69	15	L	27.2	23.0	4	30
11	M	58	4	R	51.5	40.0	5	45
12	F	59	1	L	52.0	25.0	3	20
13	F	62	9	R	24.0	13.0	6	53
14	M	48	7	L	66.0	51.0	5	60

Note: Age: year of age; Chedoke: Chedoke-McMaster Stroke Assessment ranging from 1 to 7 with 1 being the most severe impairment; Fugl-Meyer: Fugl-Meyer Assessment ranging from 1 to 66 with 1 being the most severe impairment. M: Male; F: Female; R: Right; and L: Left.