Motor Unit Rate Coding is Severely Impaired during Forceful and Fast Muscular Contractions in Individuals Post Stroke

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Abstract

Information regarding how motor units are controlled to produce forces in individuals with stroke and the mechanisms behind muscle weakness and movement slowness can potentially inform rehabilitation strategies. The purpose of this study was to describe the rate coding mechanism in individuals post stroke during both constant (n=8) and rapid (n=4) force production tasks. Isometric ankle dorsiflexion force, motor unit action potentials, and surface electromyography were recorded from the paretic and non-paretic tibialis anterior. In the paretic limb, strength was 38% less and the rate of force development was 63% slower. Linear regression was used to describe and compare the relationships between motor unit and EMG measures and force. During constant force contractions up to 80 %MVC, rate coding was compressed and discharge rates were lower in the paretic limb. During rapid muscle contractions up to 90 %MVC, the first interspike interval was prolonged and the rate of EMG rise was less in the paretic limb. Future rehabilitation strategies for individuals with stroke could focus on regaining these specific aspects of motor unit rate coding and neuromuscular activation.

Keywords: motor control, CVA, muscle weakness and slowness
Introduction

Stroke is the number one cause of adult disability worldwide (Dobkin 2005). Stroke-induced damage to motor areas in the brain cause physical weakness and slowness, spasticity and impaired coordination (Chae et al. 2002; McCrea et al. 2003; Garland et al. 2009; Mottram et al. 2010). Weakness affects the ability to perform routine daily tasks such as grasping an object (Chae et al. 2002) or walking (Kim and Eng 2003; Gerrits et al. 2009). Impaired performance of rapid contractions in stroke is a less studied motor deficit (Canning et al. 1999; Clark et al. 2006). The inability to produce quick movements likely limits the ability to function independently by impairing the ability to react rapidly to alterations in postural stability. This may potentially lead to an increased risk of falls (Moroz et al. 2004; Salter et al. 2007). To date, limited research has investigated these impairments at the level of the motor unit.

During voluntary contractions, the recruitment of motor units and the modulation of their discharge rates (rate-coding) are the primary central nervous system mechanisms used to control muscular force (Person and Kudina 1972; Freund 1983). These motor unit control mechanisms are determined by descending commands from the brain, spinal level influences, and intrinsic motoneuron properties, each of which may be directly or indirectly affected by stroke. In addition to cortical neuron cell death, a cerebral vascular accident can cause secondary degeneration of the corticospinal tract (Kinoshita et al. 2002) and spinal motor unit loss can become evident as early as two weeks following an upper motor neuron lesion (Hara et al. 2004). Furthermore, the symptom of spasticity appears to be due to the abnormal occurrence of low-level synaptic input to spinal motoneurons (Mottram et al. 2010).

A decrease in the estimated number of motor units in upper extremity muscles of the paretic limb has been observed when compared to the nonparetic limb and to controls (Arasaki et al. 2006; Li et al. 2011). There is also evidence of increases in the motor unit’s electrophysiological size in the paretic limb, perhaps due to reinnervation (Li et al. 2011; Kallenberg and Hermens 2011), and with moderate correlations to the Fugl-Myer clinical test (Kallenberg and Hermens 2011). In the biceps brachii of the paretic limb, the modulation of motor unit firing rates is impaired and lower motor unit firing rates were observed in 3/6 subjects (Gemperline et al. 1995). In tibialis anterior, low-threshold paretic motor units produced firing rates within the lower end the normal range, and high-threshold units discharged below their normal range or were not recruited (Frontera et al. 1997). Surface-based motor unit recording methods in the first dorsal interosseous muscle also support compression of the rate coding mechanism in stroke (Suresh et al. 2011).

To our knowledge, no previous studies have investigated deficiencies in the rate coding mechanism during rapid muscle contractions of the lower extremity in patients with stroke. In these types of contractions, motor units in healthy young and older adults typically discharge at
greater rates than during ramp contractions to maximal force (van Cutsem et al. 1998; Klass et al. 2008). For example, in tibialis anterior, the median initial discharge rates in tibialis anterior were 72 and 59 pps for young and elderly adults, respectively (Klass et al. 2008). It has also been reported that during contractions in tibialis anterior, approximately three times more motor units are recruited to produce a quick force pulse compared to a slow ramp contraction with the same amplitude (Desmedt and Godaux 1977).

Considering the variety of possible stroke-related changes that affect input to the spinal motor neuron pool as well as those that affect the output from motor neuron to the muscle fibers, the aim of the present study was to describe the motor unit rate coding mechanism in patients with stroke during both forceful and fast isometric muscular contractions. In addition to motor unit recordings, surface electromyograms provide gross measures of muscle activation. It was hypothesized that 1) motor unit discharge rates would be lower and the range of motor unit discharge modulation would be less in stroke, and 2) surface electromyograms would demonstrate reduced neural activation of muscle. A more complete understanding of impaired motor unit rate coding in stroke could elucidate the motor consequences of stroke and inform rehabilitation strategies intended to improve strength and speed of movement.

**Methods**

**Subjects.** Nine hemiplegic stroke survivors (1 female; 62 years old (SD 10.8); 3.9 years post stroke (SD 3.3)) participated in this study. The inclusion criteria were: chronic stroke involving cerebral cortical regions, > 6 months post stroke, ability to produce ankle dorsiflexion on the paretic side, and no history of other neurological disorders. The exclusion criteria were: diabetes, dementia (Mini-Mental State exam < 22), and an inability to understand instructions or communicate with investigators. The subjects signed informed consent documents, which were approved by the University of Delaware Human Subjects Review Board.

**Clinical Testing** was conducted during a separate test session. Self-selected gait speed was determined by a 6 meter walk test (Evans et al. 1997) and the average of three trials was taken. Timed-Up-and-Go (TUG) tests (Flansbjer et al. 2005) were also performed and the average of three trials taken. All clinical testing was performed by a licensed physical therapist.

**Experimental setup.** Subjects were seated comfortably on a chair with the knee flexed at 90 degrees and hip flexed at 110 degrees. Seat belts and hook-and-loop fasteners were used to stabilize the subject's trunk and thigh. The foot and ankle were stabilized at neutral position on a custom force measuring device that included a strain gauge force transducer (SM-100, Interface Inc., Scottsdale, AZ, USA). Dorsiflexion forces, electromyograms and motor unit action potentials were digitized at 51.2 kHz (PowerDAQ II, United Electronic Industries, Inc., Canton,
MA, USA). Data acquisition and biofeedback were controlled using DasyLab Software (Measurement Computing, Norton, MA, USA).

Maximal voluntary contraction (MVC) forces in ankle dorsiflexion were determined as the greatest force from three maximal effort trials. Subjects were instructed to increase force from rest to their maximum over a 3-second period and received verbal encouragement and real-time visual feedback of their force on a computer monitor. After the MVC force was determined, biofeedback of force amplitude was then prescribed as a percentage of maximal force (%MVC) from within the same limb. Force was displayed to the subject as a vertical bar graph. All subsequent analyses of force were normalized to the ipsilateral MVC.

Surface electromyograms were recorded from the tibialis anterior muscle using disposable Ag-AgCl pre-gelled electrodes (1-cm diameter, 5-cm spacing, Vermed A10033, Bellows Falls, VT USA). The recording sites were shaved and cleansed with ethyl alcohol. Electromyograms were band-pass filtered from 30Hz-3kHz and gains were adjusted to optimize resolution within a 10 volt range.

Motor unit action potentials were recorded from the tibialis anterior using a custom stainless steel needle electrode containing four 50 µm stainless steel wires epoxied in a 200 µm square array at a side port 3 mm from the tip of the cannula. Differential amplification of three pairs of wires provided three channels of motor unit recordings (Fig 1). To facilitate spike sorting, each channel presented the same motor unit action potential with different shape and amplitude characteristics due to the orientation of the bipolar recording surfaces relative to the source of the electrical potential. The motor unit signals were amplified (2k-10k X) and filtered (750 Hz– 6 kHz, Model 15-LT, Grass-Telefactor, Warwick, RI; with a custom high pass filter). Together with a multichannel template-matching algorithm, this technique can successfully identify individual motor units even at maximal contraction intensities (Leong et al. 1999).

With the aid of visual and audio feedback of motor unit signals, the needle electrode was manipulated within the muscle to find recording sites containing motor unit action potentials with high signal to noise ratios. When a suitable site was found, recordings were taken during constant force and rapid isometric force pulse conditions. Recordings were one minute in duration. The duration of contractions and the number of pulses performed were specified based on the force level being produced in a manner to minimize fatigue. Subjects were given at least one minute of rest between recordings. Between recordings, subjects were typically asked to perform brief contractions to 5-10 %MVC so the investigator could assess the current recording site and manipulate the electrode as needed.

Constant force conditions. Subjects were asked to gradually increase their ankle dorsiflexion force in stepwise ramp-and-hold contractions to force levels ranging from 10 to 100% MVC (Fig
Multiple recordings were obtained with the intent of obtaining good motor unit representation across the full range of force levels. At each recording site the constant force conditions were performed before the rapid force pulses.

Rapid isometric force pulses. Subjects were instructed to produce force pulses as quickly as possible to approximate amplitudes of 20, 40, 60, 80 and 100 %MVC, with immediate relaxation thereafter (Freund and Budingen 1978; Bellumori et al. 2011). Subjects were told that accuracy was not important. The resulting variability resulted in representative data across the force continuum (Fig 5). There was approximately 3-5 seconds of rest between rapid force pulses and each recording of this condition contained between 15 and 20 contractions (Fig 2). At least one minute of rest followed each recording. Based on subjective assessment of the recordings in real time, the investigator sought data from representative force levels while keeping the total number of contractions minimal. After multiple recordings were obtained at a recording site, the electrode was repositioned to sample from other locations.

Rate of force development scaling factor. From the rapid contractions, a rate of force development curve was computed as the derivative of the force-time curve over overlapping 0.1 s segments (Fig 2). Using numerous pulses within each limb, the relationship between the peak rate of force development and peak force was then analyzed with linear regression (Fig 4). The slope of this relationship, the rate of force development scaling factor, describes the ability of the subjects to scale their rates of force development with the amplitude of force pulses across the continuum of submaximal to maximal force levels (Freund and Budingen 1978). Note that the rate of force development scaling factor is only a measure of the scaling of quickness with the size of a contraction and not a measure of quickness alone. The rate of force development scaling factor is known to have good day-day reliability (Bellumori et al. 2011) and is determined partly by initial motor unit discharge rates (van Cutsem et al. 1998; Klass et al. 2008).

Neuromuscular Activation. Analysis of surface electromyograms (EMG) was performed using Spike2 software (v 5.21, CED, Cambridge, ENGLAND). For the constant force conditions, the dependent measure of interest was the root-mean-square amplitude of EMG (rmsEMG) at each force level of interest. rmsEMG was measured at segments of the electromyogram corresponding to stable force production and where corresponding observations of motor unit discharge rates were available. For the rapid isometric contractions, the dependent measure of interest was the rate of rise in the electromyogram. Rate of EMG rise was computed as the peak slope (0.1s window) of the rectified and smoothed (0.05s moving average window) EMG burst.

Motor unit analysis. The original motor unit recording contains motor unit action potentials (spikes) from one or more motor units within the recording volume of the needle. Spikes were sorted into series belonging to individual motor units using custom automatic and manual
template-matching algorithms that use amplitude, shape and probability criteria (Figs 1 and 2). For each identified MU, time histories of discharge were then used to compute measures of discharge behavior. At each force level in the constant force condition, mean discharge rates were calculated from five consecutive action potentials. For rapid isometric pulses, the first interspike interval (ISI1) was selected as the dependent measure of interest.

Statistical analysis. The relationships between EMG or motor unit firing behavior and force level were compared between limbs though comparisons of linear regression equations (Fig 5). Before applying statistical tests to regression models from aggregated data, individual data were visually inspected to ensure that similar force levels were represented in both limbs. Cases were excluded from analysis as necessary to promote balance. In addition to the comparisons of linear regression equations from aggregate data, regression equations were computed for each limb within individuals (Tables 2 and 3). The intent was to characterize the main effects of stroke and also present individual variability. The threshold for statistical significance is \( \alpha = .05 \).

Results

Among nine subjects, one experienced spasms in the lower extremity and testing was terminated before quick force pulses could be recorded. Motor unit data were obtained from both limbs in eight subjects in the constant force condition and four subjects in the rapid force pulses condition. Approximately 16 recordings were obtained from each subject, distributed across two limbs and two conditions as follows. There were 8.4 (SD 1.7) recordings from the nonparetic limb, with an average of 2.3 (SD 0.5) recordings from the rapid force pulse condition. There were 8.1 (SD 3.3) recordings from the paretic limb, with an average of 2.5 (SD 0.6) recordings in the rapid force pulse condition. In the rapid force pulse condition, each subject performed between 37 and 50 isometric force pulses per limb. Maximal effort dorsiflexion contractions were 38% weaker (MVC: paretic=117 N (SD 69), nonparetic =197 N (SD 45); t=4.2, p =.004) and 63% slower (rate of force development: paretic=279 N/s (SD 149), nonparetic= 662 N/s (SD 199); t=6.35, p= 0.001) in the paretic limb.

Motor unit sample. In either condition, it was not possible to confirm the uniqueness of motor units across different recordings or different needle locations. Between 1 and 9 unique motor units were identified in each recording with a median of 4 unique motor units per recording (e.g. 2 unique units in Fig 1, 5 in Fig 2). In the rapid force pulse condition, there was less electrode stability and motor units could not always be reliably tracked across force pulses. Between 1 and 5 unique motor units were identified in each force pulse with a median of 2 unique motor units (e.g. 1 motor unit in Fig 2, 2 motor units in Fig 2).

Constant Force Condition. The slope of the relationship between rmsEMG and force was significantly greater than zero in both limbs (Fig 5A, nonparetic: \( t=7.8 \ p<.001 \); paretic: \( t=5.6, \)
The slope of this relationship was less in the paretic limb (t=3.7, p<.001) with the
greatest differences at higher force levels. The slope of the relationship between motor unit
discharge rate and force was significantly greater than zero in both limbs (Fig 5C, nonparetic:
t=14.9 p<.001; paretic: t=12.5, p<.001). Similar to the results of rmsEMG, the slope of this
relationship was significantly less in the paretic limb (t=5.6, p<.001), with the greatest difference
in firing rates at the higher force levels. The predicted firing rate at 80 %MVC was 34% less in
the paretic limb (11.8 pps) than in the nonparetic limb (17.8 pps). Table 2 shows that there were
few exceptions to the overall regression results.

Rapid force pulses. The positive scaling of rate of force development with peak force was
markedly less in paretic than in non-paretic limbs (Fig 4). Rate of force development scaling
factors computed for individual limbs were significantly lower in the paretic limb (paretic: 2.35
s⁻¹ (SD 1.60), nonparetic: 3.47 s⁻¹ (SD 1.69), t=9.8, p<.001). There was a significant positive
relationships between the rate of EMG rise and peak force in both limbs (Fig 5B, nonparetic:
t=4.74 p<.001; paretic: t=3.94, p<.001). The slope of this relationship was less in the paretic
limb (t=2.22, p=.028). Although the difference between y-intercepts (t=4.30, p<.001) is
influenced by the different slopes, the larger t-statistic, compared to that for slope, supports the
observation that rate of EMG rise was much greater in the non-paretic limb at all force levels.

The slope of the relationship between ISI1 and force was significantly different from zero in both
limbs (Fig 5D) with a positive slope in the nonparetic limb (t=2.28, p=.023) and a negative slope
in the paretic limb (t=2.81, p=.006). The difference between slopes was significant (t=4.37,
p<.001). Again, although the y-intercepts are influenced by differences in slope, the greater y-
intercept in the paretic limb (t=9.63, p<.001) agrees with the observation that ISI1 is quite
limited during attempts at fast contractions to low force levels.

On average, there were more action potentials per isometric force pulse in the paretic limb
(nonparetic: 2.6 (SD 1.46), paretic: 5.4 (SD 2.98), F=49, p=.002). In the paretic limb, the
number of action potentials within a pulse ranged from 2 to 14 with the majority (78%) of the
motor unit observations distributed between 2 to 7 spikes. In the nonparetic limb, 53% of the
motor unit observations had only 2 spikes within a force pulse.

Discussion

Despite the challenges of obtaining motor unit data at numerous force levels from both limbs and
in two conditions, only one person withdrew due to discomfort. The effects of stroke were large,
based on a 38% reduction in strength and a 63% reduction in rate of force development in the
paretic dorsiflexors. In the constant force condition, differences in firing rates became more
pronounced as force levels increased (Fig 5C). In the rapid force pulse condition, the rates of
force development scaled with pulse amplitude, albeit with less gain (Fig 4). The first interspike
interval was substantially prolonged (Fig 5D) in the paretic limb and both surface EMG measures (Figs 5A and B) demonstrated differences between limbs that agree with the motor unit results.

While the results offer a logical extension of the current knowledge of motor unit discharge behavior in stroke, there are important limitations to consider. Even though the sample was small and highly variable based on subject characteristics and function (Table 1), the individual results in Tables 1-3 demonstrate that the overall regression models were indeed representative of the majority. For all subjects and in both conditions, the mean firing rates were lower and mean ISI1s were all prolonged in the paretic limb. Another limitation was the inability to track motor units across force levels due to electrode movement at higher forces and in rapid contractions. This limits the interpretation of the results to a description of observed firing rates at different force levels rather than a description of the modulation of firing rates within motor units. Also, despite an efficient experimental design, the test sessions lasted between 60 and 90 minutes and the performance of several contractions in both limbs could have caused fatigue.

The main differences between limbs summarized by the regression models were large enough to achieve statistical significance. Nevertheless, interesting variability in the regression plots warrants further consideration. Some individuals presented data indicating high rmsEMG (Fig. 5A) and brief ISI1s (Fig 5D) in the paretic limb. This is evidence that some aspects of neuromuscular activation can operate within normal ranges despite pronounced functional limitations. One subject (613) had similar dorsiflexion strength in both limbs. Although this could be interpreted as the absence of impairment, this strength ratio is paired with similar firing rates in both limbs and these particular rates were among the lower values observed in the paretic limbs of the entire sample. Thus, this subject’s stroke may have either affected neuromuscular activation in both of his limbs and/or his post-stroke reductions in physical activity may have resulted in bilateral maladaptation. In the rapid force pulse condition, there were several ISIs that were less than 20 ms in duration. The majority (10/12) of these ISIs were from subject 616 but this individual also provided 15 prolonged ISI1s (> 50 ms) that were representative of the paretic limb.

Constant Force

In the paretic limb during the constant force condition, motor unit discharge rates were lower and increased less with increases in volitional drive. This is consistent with what others have described as a compressed motor unit rate coding mechanism (Barry et al. 2007). Using our regression equations, the predicted discharge rates at 80 %MVC were 17.8 and 11.8 pps in the non-paretic and paretic limbs, respectively (a 34% difference). This represents a substantial slowing when one considers that healthy young and older adults produce firing rates of 14 pps during 40-50 %MVC dorsiflexion contractions (Patten and Kamen 2000; Connelly et al. 1999).
In both limbs, the range of MU discharge rates was lower than that reported for healthy elderly (Barry et al. 2007; Connelly et al. 1999; Christie and Kamen 2006; Kamen et al. 1995; Kamen and Knight 2004; Klass et al. 2008).

The present results are consistent with the small body of literature that describes the reduced rate coding capacity of patients with stroke. Gemperline and colleagues (1995) compared motor unit discharge behavior in the paretic and contralateral biceps brachii and found that all six subjects demonstrated impaired discharge rate modulation of MUs in the paretic muscle. In addition, three out of their six subjects showed significant reduction in mean motor unit discharge rates in the paretic muscle compared to the contralateral side. In the present results (Fig 5C, Table 2), the majority of subjects demonstrated this firing rate reduction. Similarly, Frontera and colleagues (1997) found that low-threshold paretic MUs discharged within the lower end of their normal range, and high-threshold units discharged below their normal range or were not recruited.

Rapid Isometric Force

During the performance of rapid isometric force pulses, the paretic limb exhibited less of an increase in rates of force development as pulse amplitude increased (RFD-SF, Fig 4). This reduced scaling is in the same direction as that observed in older adults (Klass et al. 2008) and opposite in direction to the effects of power training (van Cutsem et al. 1998). A favorable scaling of rate of force development with peak force is associated with brief interspike intervals at the onset of contraction and a greater rate of EMG rise (van Cutsem et al. 1998). In the present sample, ISI1 was severely prolonged in the paretic limb. Predicted ISI1s for 50%MVC pulses were 27 ms in the nonparetic limb and 89 ms in the paretic limb, a 2.3 fold difference. Also in tibialis anterior, Klass and colleagues (2008) found that ISI1s were 13.9 ms and 17.1 ms for young and older adults, respectively. Therefore, not only is ISI1 prolonged in the nonparetic limb compared to normal aging but the magnitude of the difference between limbs in stroke survivors is immense compared to the difference attributed to the aging process.

Although one could suggest that an increase in initial discharge rate in the nonparetic side might occur due to greater dependence on this limb in activities of daily living, the non-paretic limb cannot be assumed to be unaffected by stroke and there is also a potential disuse effect due to general reductions in physical activity after stroke. Given the advantage of high motor unit discharge rates on augmenting the rate of force development (Binder-Macleod and Barrish 1992; Garland and Griffin 1999; Christie and Kamen 2006), the inability to discharge closely spaced action potentials at the beginning of quick force pulse is a major factor causing slowed force production and movement. In the absence of high initial discharge rates, motor units delivered more action potentials to the muscle fibers in order to reach the intended pulse amplitude.
Though one must consider contributions from motor unit recruitment to the amplitude of the surface electromyogram, it is not surprising that the EMG to force relationships were generally consistent with those between firing rate and force. The present findings add to the existing support for clinical applications of surface electromyography where neuromuscular activation is deficient. However, the data also indicate that sensitivity to between-limb differences during constant contractions might be lost at lower force levels (Fig 5A).

Compared to the effect size (approximated by t-statistics) of the rmsEMG measure in constant force conditions, the difference between limbs in the rate of EMG rise was considerable. Even with the relatively large dispersion in the data from the nonparetic limb (Fig 5B), there was very little overlap with the rate of EMG rise of the paretic limb. Others have shown that while the rate of EMG rise measure may not differentiate between middle aged and older healthy adults, it is quite capable of differentiating between older adults with and without mobility limitations (Clark et al. 2011). The present findings provide further support for the utility of the rate of EMG rise measure in rehabilitation. Furthermore, the corresponding deficiencies in ISI1 and rate of EMG rise in the paretic limb further strengthen the link between motor unit behavior and this more accessible, surface-based measure (van Cutsem et al. 1998). Other potential contributors to the reduced rates of force development include loss of large motor units (Lukacs et al. 2008), altered motor unit recruitment (Suresh et al. 2011), and greater muscle cocontraction (Chae et al. 2002). Interestingly, the mechanical slowing occurs despite a shift towards fast myosin heavy chain isoforms in the paretic limb of stroke survivors (De Deyne et al. 2004).

**Mechanisms**

The deficient motor unit rate coding mechanism has possible explanations including decreased descending excitation to the lower motor neuron pool (McComas et al. 1971) and changes in the dynamic sensitivity with which spinal motor neurons enhance neural activation of muscle (Baldissera et al. 1998). It is also possible that commands to motor units from the affected hemisphere are interrupted before reaching the final common pathway, possibly by excessive inhibition from the unaffected hemisphere (Murase et al. 2004; Takeuchi et al. 2005). Larger, higher threshold, motor units are more severely affected following stroke (Lukacs et al. 2008) and such units are usually associated with higher firing rates (Kudina and Churikova 1990) and greater dynamic sensitivity (Baldissera et al. 1998). Thus, with increasing time since stroke and reduced levels of physical activity, the motor neuron pool can undergo biased loss of the neurons that contribute most to rapid movement. One must also consider the potential role of muscle atrophy in this particular model. Based on measures from magnetic resonance imaging post
stroke, there is relatively little atrophy in the tibialis anterior muscle (4%) compared to that seen in the medial gastrocnemius (38%) (Ramsay et al. 2011).

**Conclusion**

Together with existing literature, the current results make it clear that substantial reductions in motor unit firing rates accompany the pronounced reductions in physical strength and quickness of the paretic lower extremity of patients with stroke. Although the sample size for the rapid contractions is small, the results show relatively large differences in neural factors that ultimately contribute to speed of movement. While the current data do not explain the extent to which the reduced discharge rates are caused by deficiencies in descending drive or motor neuron function, rehabilitation researchers should strongly consider the gains that may be possible though strategies to improve neural substrates for quickness. Fortunately, it already known that maximal motor unit firing rates (Kamen and Knight 2004) and initial interspike intervals (van Cutsem et al. 1998) are both adaptable with standard resistance training practices. The effect of such training on motor unit behavior in patients with stroke remains unknown.

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Table 1. Subject characteristics, functional tests and mean firing rate and interspike interval results. ND = no data. Ratios of maximal voluntary strength (MVC) and rate for force development (RFD) express the paretic limb relative to the nonparetic limb (P/NP).

<table>
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<tr>
<th>Subject</th>
<th>Age (years)</th>
<th>Months since stroke</th>
<th>Ratio of MVC (P/NP)</th>
<th>Ratio of RFD (P/NP)</th>
<th>6-meter walk (m/s)</th>
<th>Timed up and go (s)</th>
<th>Firing Rate: NP, P (pps)</th>
<th>ISI1: NP, P (ms)</th>
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<td>59</td>
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<td>0.68</td>
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<td>10</td>
<td>0.33</td>
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<td>0.39</td>
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Table 2. Individual linear regression results for the constant force condition.

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Table 3. Individual linear regression results for the rapid isometric force pulse condition.

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Average slopes and Y-intercepts for nonparetic and paretic subjects under the rapid isometric force pulse condition.


30. **Klass M, Baudry S and Duchateau J.** Age-related decline in rate of torque development is accompanied by lower maximal motor unit discharge frequency during fast contractions. *J Appl Physiol* 104: 739-746, 2008.


34. **Lukacs M, Vecsei L and Beniczky S.** Large motor units are selectively affected following a stroke. *Clin Neurophysiol* 119: 2555-2558, 2008.


Fig 1. Top panel: Example recording of a stepwise constant force isometric contraction in which the subject maintained forces approximating 20, 40 and 60 %MVC in the paretic limb. From top to bottom are isometric force, the surface electromyogram and three channels of motor unit recordings. Fluctuations in force were more common in the paretic limb due to impaired control. For analysis of firing rate and rmsEMG, data were selected from the most stable regions at each force level. The consequence of electrode instability and the strength of the multi-channel approach are evident as the amplitude of the motor unit action potentials change over time. Although difficult to see among the originally recruited motor unit (due to the greater spike density), a new motor unit is recruited as force increased from 40 to 60 %MVC near 22s. Bottom panel: Higher resolution excerpt of the same recording near 28s. In the bottom three plots (MU channels 1-3), 2 different motor units are identified. Differences in shape and amplitude characteristics across the three channels facilitate accurate spike sorting.

Fig 2. Sample results from the paretic limb in both conditions after the spike sorting process. Top: Instantaneous discharge rate data (dots) are available for 5 motor units including a newly recruited unit above 90% MVC. The stability of the recording of the first four motor units supports the identity of mu6 as a newly recruited unit rather than electrode movement towards an already active unit. Also note the de-recruitment and re-recruitment of motor mu2 as force decreased near 3-5 seconds. Within each row of discharge rate data (0-15 pps scale), firing rates remained low (~8-10 pps) despite large increases in force. Bottom: In the rapid isometric force pulse condition discharge rates of two motor units (also within 0-15 pps scale) were surprisingly low and there was no evidence of upward modulation with increases in pulse amplitude. The new recruitment of mu3 for the >60 %MVC pulses demonstrates one means to increase neuromuscular drive in the absence of initial motor unit discharge rates.

Fig 3. Example recording of a rapid isometric force pulse from the paretic limb. From top to bottom are the rate of force development, the isometric force pulse, the rectified surface electromyogram and three channels of motor unit action potentials. Stars mark four action potentials from the same motor unit and the waveforms from all three channels are overlaid as they would be during manual spike sorting procedures.

Fig 4. Rate of force development as a function of the peak force level of rapid isometric dorsiflexion contractions. The slope of the regression line is the rate of force development scaling factor. With slow initial firing rates (Fig 5D) and less neuromuscular activation overall (Fig5B), there is less scaling of RFD with the amplitude of the rapid contractions. While the greatest differences are at the highest levels, the lower rates of force development at low force levels have significant implications in activities of daily living.
Fig 5. Linear regression plots and equations for surface electromyogram (top) and motor unit (bottom) measures in relation to the amplitude of constant force (A and C) or rapid force pulses (B and D). Data are from 8 and 4 subjects in the constant force and rapid force pulse conditions, respectively.
The graph shows the relationship between force development and force (%MVC) for non-paretic and paretic sides.

- Non Paretic: $Y_{np} = 3.2x + 67$, $R^2 = 0.76$
- Paretic: $Y_p = 1.7x + 51$, $R^2 = 0.60$
**Figure 1**

(A) Mean surface EMG (mV) as a function of relative force output. The line represents the linear regression for each group. The equation and R² value are provided for each group:

- Non-paretic: \( Y_{np} = 1.38x - 1.74, R^2 = 0.43 \)
- Paretic: \( Y_p = 0.55x + 16.65, R^2 = 0.29 \)

(B) Rate of EMG rise (units/msec) as a function of relative force output. The equation and R² value are provided for each group:

- Non-paretic: \( Y_{np} = 5.38x + 439, R^2 = 0.19 \)
- Paretic: \( Y_p = 2.03x + 92, R^2 = 0.20 \)

(C) Mean firing rate (pps) as a function of relative force output. The equation and R² value are provided for each group:

- Non-paretic: \( Y_{np} = 0.15x + 5.52, R^2 = 0.44 \)
- Paretic: \( Y_p = 0.08x + 5.16, R^2 = 0.40 \)

(D) First Inter-Spike Interval (ms) as a function of relative force output. The equation and R² value are provided for each group:

- Non-paretic: \( Y_{np} = -0.71x + 126, R^2 = 0.06 \)
- Paretic: \( Y_p = 0.13x + 21, R^2 = 0.02 \)