HHS Public Access

Author manuscript

J Electromyogr Kinesiol. Author manuscript; available in PMC 2022 February 01.

Published in final edited form as:

J Electromyogr Kinesiol. 2021 February ; 56: 102475. doi:10.1016/j.jelekin.2020.102475.

Longer electromechanical delay in paretic triceps surae muscles during voluntary isometric plantarflexion torque generation in chronic hemispheric stroke survivors

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Abstract

Electromechanical delay (EMD) is the time delay between the onset of muscle activity and the onset of force/joint torque. This delay appears to be linked to muscular contraction efficiency. However, to our knowledge, limited evidence is available regarding the magnitude of the EMD in stroke-impaired muscles. Accordingly, this study aims to quantify the EMD in both paretic and non-paretic triceps surae muscles of chronic hemispheric stroke survivors, and to investigate whether the EMD is related to voluntary force-generating capacity in this muscle group. Nine male chronic stroke survivors were asked to perform isometric plantarflexion contractions at different force levels and at five different ankle joint angles, ranging from maximum plantarflexion to maximum dorsiflexion. The surface electromyograms were recorded from triceps surae muscles. The longest EMD among triceps surae muscles was chosen as the EMD for each side. Our results revealed that the EMD in the paretic muscles was consistently longer than in non-paretic muscles. Moreover, both paretic and non-paretic muscles showed a negative correlation between the EMD and maximum torque-generating capacity. Separately, there was a strong positive relationship between increasing EMD and the shear wave speed in paretic muscles as well as a negative relationship between increasing EMD and the passive range of motion for the ankle. These findings imply that the EMD may be a useful biomarker, in part, associated with contractile and material properties in stroke-impaired muscles.

Keywords

Stroke; Electromyogram; Muscle weakness; Muscular contraction efficiency; Muscle material properties

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Conflicts of interest

None of the authors has any conflict of interest to disclose.

Introduction

The electromechanical delay (EMD) is the time delay between the onset of active state in skeletal muscle, estimated from the onset of the surface electromyogram (sEMG), and the onset of voluntary force/torque development (Cavanagh and Komi, 1979). This delay appears to be associated with muscular contraction type (Cavanagh and Komi, 1979), muscular strength (Hannah et al., 2014) as well as aging and fatigue (Yavuz et al., 2010). A longer EMD was also found in patients with Duchenne muscular dystrophy compared to neurologically intact individuals (Lacourpaille et al., 2014). However, limited evidence is available regarding chronic hemispheric stroke survivors who often suffer from major motor impairments such as voluntary muscle weakness. Accordingly, this study aims to quantify the EMD in paretic and non-paretic triceps surae muscles of chronic stroke survivors, and to investigate whether the EMD is linked to voluntary force-generating capacity.

The dominant factors contributing to the EMD may include electrochemical processes in the excitation-contraction coupling mechanism, and mechanical processes required to transmit forces produced by the contractile elements through the series elastic component (SEC) (Cavanagh and Komi, 1979, Hill, 1950). The delay attributed to electrochemical processes has been estimated to be relatively short compared to mechanical processes (Cavanagh and Komi, 1979), but estimating the relative contributions of each process to the EMD has been limited by technical barriers. Recently, this delay has been examined more precisely, owing to the emerging use of ultrafast ultrasound imaging technique (Hug et al., 2011a, Lacourpaille, Hug, 2014, Lacourpaille et al., 2013, Nordez et al., 2009) or combined approaches of sEMG, mechanomyogram and force measurements (Cè et al., 2017, Esposito et al., 2016, Esposito et al., 2017, Esposito et al., 2011, Longo et al., 2017, Smith et al., 2017). Collectively, it now appears that the relative contribution attributed to electrochemical processes is approximately 50% of the total EMD, depending on the muscle and its structure. This indicates that the delay attributed to electrochemical processes could be significant when disease or physiological processes induce altered electrophysiological properties of neuromuscular junctions or membranes.

The delay attributed to mechanical processes arises because time elapse is necessary to stretch the SEC within the muscle and tendon, taking up the slack of the surrounding tissue (Cavanagh and Komi, 1979). Indeed, earlier findings have suggested that the greater the slack of a muscle-tendon unit, the longer the EMD (Chan et al., 2001, Longo, Cè, 2017, Muraoka et al., 2004). Moreover, the EMD is influenced by the type of muscle contraction, by muscle architecture as well as by muscle fiber type composition (Cavanagh and Komi, 1979, Norman and Komi, 1979). Interestingly, an earlier study reported that an inter-subject variability of muscle force transmission velocity along aponeuroses and tendon tissues could be linked to the variability in mechanical properties of these structures (Nordez, Gallot, 2009), suggesting that the material properties of muscle and tendon tissues may also contribute to the EMD.

In this context, it is relevant to note that the EMD may become longer in stroke-impaired muscles compared to intact muscles. This is because there are measurable changes in muscle architecture and in material properties of muscle and tendon tissues (Jakubowski et al., 2017,

Son et al., 2020, Svantesson et al., 2000, Zhao et al., 2015, Zhao et al., 2009), potentially contributing to additional deficits in muscular contraction efficiency of the paretic muscles, reflected as the slope of EMG-force relations (Son and Rymer, 2020, Tang and Rymer, 1981).

Accordingly, our first objective of this study is to test our primary hypothesis that the EMD in the paretic muscles is longer than in the non-paretic muscles, by quantifying the EMD in both the paretic and non-paretic triceps surae muscles of chronic stroke survivors. Our second objective is to investigate the association between the EMD and maximum joint torque-generating capacity and between the EMD and shear wave speed (SWS) as an indirect surrogate of muscle stiffness (Bercoff et al., 2004, Deffieux et al., 2009). Our hypothesis is that the longer the EMD, the smaller the maximum joint torque-generating capacity and the faster the SWS.

Methods

Subjects

Nine male chronic stroke survivors participated in this study (age: 56.9 ± 7.8 yrs.; height: 174.8 ± 7.3 cm; weight: 81.1 ± 8.9 kg; years after stroke: 8.1 ± 4.1 yrs.). Our inclusion criteria were: (1) age 18 to 70 years old; (2) more than 6 months after stroke (chronic); (3) a single hemispheric stroke (unilateral movement impairment); (4) medically stable; (5) no lower extremity pain, inflammation, or recent injury; (6) no severe cognitive impairment to limit comprehension of the experimental task; (7) no history of multiple recurrent vascular episodes; and (8) no botulinum toxin treatments within the past six months. All participants were ambulatory and were not currently receiving physical therapy. Written informed consent was obtained from all participants before testing and Northwestern University's Institutional Review Board approved all procedures.

Experimental setup

Participants were seated upright in a chair with the trunk and thigh firmly strapped to the chair (Figure 1). The foot was secured to the footplate with a 6-axis force-measuring sensor (Omega160, ATI Industrial Automation, Apex, NC, USA) to determine the onset of the voluntary plantarflexion torque development. The ankle center of rotation was aligned with the rotation axis of the dynamometer. A slight adjustment in the subject's posture was then allowed to make sure the subject was comfortable (in most cases, the knee was flexed ~10°).

To estimate the activation onset of triceps surae muscles, single differential sEMG electrodes (GRASS, Asto-Med, Inc., West Warwick, Rhode, Island) were placed over the muscle belly of the MG, the lateral gastrocnemius, and the soleus. The tibialis anterior was also monitored to evaluate potential muscle co-contraction. A ground electrode was attached to the patella, and the area for the electrodes was cleaned with alcohol pads before electrode placement.

A shear wave elastography ultrasound system (Aixplorer Supersonic Imagine, Aix-en-Provence, France) with a linear transducer array (4–15 MHz, SuperLinear SL15-4, Vermon, Tours, France) (Bercoff, Tanter, 2004, Deffieux, Montaldo, 2009) was used to record SWS

of the MG muscle. The transducer was positioned at the mid-belly region of the MG muscle and secured to the shank, avoiding interference between the transducer and the sEMG electrode. A custom holder was used to secure the transducer, to minimize translation and pressure induced by the transducer.

During the experiment, voluntary isometric plantarflexion torque and EMG signals were recorded at a sampling rate of 2 kHz and synchronized through a data acquisition system (NI USB-6259 BNC, National Instrument, Austin, TX, USA).

Procedures

As the EMD may be affected by muscle-tendon unit length (Chan, Lee, 2001), five different ankle angles were chosen: maximum plantarflexion (PF), maximum dorsiflexion (DF), neutral anatomical position (i.e., 90 deg), and two intermediate angles. First, the RoM was determined by measuring the maximum PF and DF positions while the ankle joint was passively moved by the experimenter. Two intermediate angles were then set as angles between the maximum DF and the neutral or between the maximum PF and the neutral.

At each designated ankle angle, and in a randomized order, ultrasound images from the MG muscle were captured while the muscle was relaxed. The region of interest (RoI) for SWS measurements was manually located over the muscle belly. Subjects were then asked to perform maximum voluntary isometric contractions (MVICs) in ankle plantarflexion for 5 s each, with a one-minute break between each MVIC trial. The average value of three maximum MG muscle activations for each MVIC trial was used to calculate the level of the MG muscle contraction intensity for visual feedback. The subject was then asked to follow trapezoidal trajectories displayed on a computer screen, each at a different percentage of the MVIC, by performing voluntary isometric plantarflexions. The trapezoid trajectory contained 5 segments: an initial 5 s quiescent period for baseline noise calculation, an up-ramp increasing at a rate of 100%MVIC/s, a constant MG muscle activity at a prescribed %MVIC for 5 s, then a down-ramp decreasing at 100%MVIC/s, and a final 5 s quiescent period. Three isometric plantarflexion contractions were collected at each designated contraction level in a randomized manner (20, 40, and 60%MVIC). A 30 s rest period between repetitions was provided to minimize fatigue effect. Two sessions were conducted separately for paretic and non-paretic sides.

Data analysis

All EMG signals were processed by applying a zero-phase fourth-order bandpass Butterworth filter (bandwidth: 20–450 Hz), followed by a full-wave rectification. A zero-phase fourth-order low pass Butterworth filter with a cut-off frequency of 50 Hz was then applied to all processed EMG signals and to torque signals (Go et al., 2018). The onset of the processed EMG and torque signals was then defined as a time event when the amplitude of the signals was greater than 3 standard deviations from the mean baseline noise observed for each signal (Smith, Housh, 2017). The EMD of each trial was determined as the longest time among triceps surae muscles. When the signal-to-noise ratio of each torque signal was too low to detect the torque onset, due to the small magnitude of voluntary torque generated by the paretic muscles, the trial was rejected.

To quantify the isometric plantarflexion torque level at each contraction intensity, raw torque signals were processed separately by applying a zero-phase fourth-order low pass Butterworth filter with a cut-off frequency of 6 Hz, followed by 1-s moving average filter. The peak values of the moving averaged signals were then used to represent the torque level of contraction intensities for each trial. The maximum value across all joint angles was defined as the maximum torque-generating capacity of each individual.

The SWS values were calculated from the ultrasound images. All RGB values in the RoI of each ultrasound image were converted into the corresponding SWS values, and the average value of the SWS values over the largest muscular region was then calculated for each image (Lacourpaille, Hug, 2013).

All data processing was performed, using custom-written software in MATLAB (Mathworks, Natick, USA).

Statistical analysis

A linear mixed-effects model was used to test whether the EMD during voluntary isometric plantarflexion at different contraction intensities and at different ankle joint angles is different between the paretic and non-paretic triceps surae muscles of chronic stroke survivors. The EMD was considered as a dependent factor. Fixed effects were intercept, side (i.e., paretic vs. non-paretic), ankle joint angle (i.e., five different angles), ankle joint torque (i.e., isometric plantarflexion torque levels at each contraction intensity), interaction between side and angle, interaction between side and torque, and interaction between angle and torque. In all analyses, subjects were treated as a random effect.

The Kolmogorov-Smirnov test was performed to assess the normality of biomechanical data (i.e., the maximum torque-generating capacity, SWS, DF, PF, and RoM). Since all the biomechanical variables did not satisfy the assumption ($p < 0.05$), the Wilcoxon signed-rank test was performed to evaluate the paired difference in the variables between the paretic and non-paretic sides.

The Spearman ranked correlation coefficient was calculated to determine the relationship between the EMD and other clinically relevant variables (i.e., the maximum torque-generating capacity, SWS, RoM, age, and years after stroke) from data of each side, and from pooled data from both sides. We also calculated the Spearman ranked correlation coefficient to evaluate the relationship between the side-to-side difference in the EMD (i.e., paretic – non-paretic) and the relative (i.e., paretic / non-paretic) maximum plantarflexion torque and the relative SWS. The greater the side-to-side difference in the EMD, the longer the EMD on the paretic side compared to the non-paretic side. If the relative maximum plantarflexion torque or SWS is smaller than 1, the corresponding parameter on the paretic side is smaller than on the non-paretic side. To consider potential correlations between the clinically relevant variables or between the relative variables, the *p*-value for each correlation analysis was adjusted via false discovery rate using the Benjamini–Hochberg method (Benjamini and Hochberg, 1995).

All statistical analyses were done using MATLAB (Mathworks, Natick, USA), and the significance level (α) of 0.05 was used.

Results

The EMD was significantly affected by side (non-paretic vs. paretic: $F_{(1,924)} = 4.950$, $p = 0.026$), but there was no significant effect of either ankle angle ($F_{(1,924)} = 0.453$, $p = 0.501$) or ankle torque ($F_{(1,924)} = 0.063$, $p = 0.801$). Moreover, no significant interaction was found either between side and angle ($F_{(1,924)} = 1.402$, $p = 0.237$) or between side and torque ($F_{(1,924)} = 0.422$, $p = 0.516$). Thus, a median value of pooled data from each side of each individual was used as a representative EMD, since the Kolmogorov-Smirnov test revealed that the EMD data did not conform with a normal distribution ($p < 0.05$). The EMD was 62% longer on the paretic side (102.8 ms; interquartile range (IQR) = 87.4–144.8 ms) than on the non-paretic side (63.5 ms; IQR = 51.7–70.9 ms) ($p = 0.020$; Figure 2).

The maximum torque-generating capacity on the paretic side (32.1 N m; IQR = 25.7–57.6) was significantly reduced by approximately 50% compared to the non-paretic side (79.4 N m; IQR = 56.7–87.3) ($p = 0.012$). Moreover, the ankle joint RoM on the paretic side (32°; IQR = 30–40) was significantly smaller by approximately 25% than on the non-paretic side (42°; IQR = 37–45) ($p = 0.031$), although there was no significant side-to-side difference in the maximum DF ($p = 0.063$) or in the maximum PF ($p = 0.156$).

A strong negative relationship was found between the EMD and the maximum isometric plantarflexion torque when considering the paretic side only ($r = -0.817$, $p = 0.027$; Figure 3B) and pooled data ($r = -0.822$, $p < 0.001$; Figure 3C). However, the relationship was not significant on the non-paretic side only ($r = -0.733$, $p = 0.156$; Figure 3A).

Moreover, a strong positive relationship was found between the EMD and the SWS measured at the neutral ankle angle when considering the paretic side only ($r = 0.917$, $p = 0.007$; Figure 4B) and pooled data ($r = 0.496$, $p = 0.036$; Figure 4C), but no significant relationship was found on the non-paretic side ($r = -0.150$, $p = 0.752$; Figure 4A).

The pooled RoM data was negatively correlated with the pooled EMD data ($r = -0.503$, $p = 0.036$; Figure 5C), but the RoM data did not show a significant correlation with the EMD data on either the non-paretic ($r = -0.230$, $p = 0.752$; Figure 5A) or paretic side ($r = -0.094$, $p = 0.816$; Figure 5B). Our data showed that the EMD was not correlated with either age or years after stroke ($p > 0.05$).

As the difference in the EMD between the paretic and non-paretic sides increased, the relative torque-generating capacity decreased ($r = -0.833$, $p = 0.014$; Figure 6A) but the relative SWS increased ($r = 0.800$, $p = 0.014$; Figure 6B).

Discussion

This study showed that the EMD in the paretic triceps surae muscles is longer than in the non-paretic muscles of chronic stroke survivors, suggesting that the longer EMD on the paretic side may be associated with the reduced torque-generating capacity after stroke.

Moreover, there was a strong positive relationship between the EMD and the SWS in the paretic MG muscles, indicating that the EMD may potentially be linked to the modified material properties of muscle tissues. Although there is limited evidence for mechanisms underlying these longer EMD in stroke-impaired muscles, we can evaluate several potential factors.

Potential factors in electrochemical processes associated with the longer EMD after stroke

Defects in ion channels at the neuromuscular junction can adversely affect neuromuscular function in patients with neuromuscular disorders (Goodman, 2008). This is because altered ion conductances may lead to changes in resting membrane potential in neurons and, ultimately, to changes in the excitability of nerves and skeletal muscles constituting the neuromuscular junction. According to earlier findings (Cè, Rampichini, 2017, Esposito, Cè, 2016), the delay attributable to synaptic transmission at the neuromuscular junction level is approximately 1.5 ms in neurologically intact subjects (approximately 5% of the total EMD). However, this amount is not significant when compared to our EMD values (102.8 ms and 63.5 ms on the paretic and non-paretic sides, respectively) and thus, any added delay at the neuromuscular junction level might not contribute measurably to the measured and longer EMD after stroke.

Alterations in the excitation-contraction coupling mechanism can appear in fatigue (Fitts, 2007), in aging (Boncompagni et al., 2006), and in neuromuscular disorders such as myopathies (Marty and Fauré, 2016), muscular dystrophy (Allen et al., 2010), and myocardial ischemia (Zucchi and Ronca-Testoni, 1997). Such alterations are related to the splicing of key proteins involved in Ca^{2+} homeostasis or to the partial disarrangement and/or the spatial reorganization of Ca^{2+} release units, which may interfere with efficient delivery of Ca^{2+} ions to the contractile proteins. Indeed, a delay attributable mainly to electrochemical processes was prolonged by >25% in fatigued TA muscles of neurologically intact subjects and by >45% in the TA muscles of patients with myotonic dystrophy type 1 (Esposito, Cé, 2016, Esposito, Cé, 2017). Although the relative elongation of the delay seems considerable, the absolute delay of the previous studies remains considerably shorter (i.e., on the order of 10 ms) when compared to our findings. It allows us to speculate that the efficiency in the excitation-contraction coupling mechanism likely has a minor impact on the elongated EMD that we observed.

The propagation of motor unit action potentials (MUAPs) may be disturbed in muscle fatigue (Balog et al., 1994, Edwards et al., 2012) and in patients with neuromuscular diseases and disorders (Blijham et al., 2006, Conrad et al., 2017, Drost, 2001). Considering that the muscle fiber conduction velocity is proportional to the muscle fiber diameter, the muscle fiber conduction velocity may become slower with muscle atrophy which is typically observed in patients with as myopathies and neurogenic disorders (Blijham, ter Laak, 2006) and in chronic stroke survivors (Conrad, Qiu, 2017). Moreover, the peak-to-peak amplitude of the MUAPs was significantly smaller in the generalized myotonia patients than in the normal subjects, indicating the efficiency of the MUAP propagation is lower in the neurological disorders (Drost, 2001). Collectively, the alterations of MUAPs propagation properties may affect the efficiency of the MUAP propagation as well as effective muscle

contraction, potentially resulting in the elongated EMD. However, given that the impact of the MUAP conduction velocity on the EMD is not considerable (Schmid et al., 2019), the alterations of MUAPs propagation properties are also likely to have a minor impact on the elongated EMD.

Potential factors in mechanical processes associated with the longer EMD after stroke

The elongation of the EMD is likely attributable to the prolonged transmission of forces produced by the contractile elements through the SEC in the muscle (Cavanagh and Komi, 1979, Hill, 1950). These elements are impacted by muscle fiber type composition, by material properties of muscle and tendon tissues, and by initial tension or length (Schmid, Klotz, 2019).

The longer EMD on the paretic side in this study may potentially be associated with fast-to-slow shifts in muscle fiber type composition, which have been observed on the paretic side in some chronic stroke survivors (Dattola et al., 1993, Hachisuka et al., 1997, Lukács et al., 2008, Scelsi et al., 1984). Different types of muscle fibers have different rates of Ca^{2+} release from the sarcoplasmic reticulum to initiate the cross-bridge formation, showing that fast-type muscle fibers release Ca^{2+} ions at a faster rate when compared to slow-type muscle fibers (Harigaya and Schwartz, 1969). Moreover, the rate of sarcotubular Ca^{2+} uptake tends to be linked to the rate of Ca^{2+} release from the sarcotubules, and its rate is thus related to the tension development rise time of the isometric twitch contraction (Brody, 1976). Considering that the rate of cross-bridge cycling is much lower in slow-type muscle fibers (Lännergren, 1978), it is conceivable that a muscle with more slow-type muscle fibers may require a longer time to develop the force, for a given muscle activity, as also supported by an earlier simulation study showing that a muscle consisting purely of slow-twitch muscle fibers increases the EMD by up to 20.3 ms (approximately 60% increase of the baseline) (Schmid, Klotz, 2019).

Our results showed that in the paretic MG muscles, a longer EMD is also associated with a higher SWS (Figure 3B and 6B). This finding indicates that a stiffer muscle may potentially lead to a longer EMD, in agreement with a previous simulation study (Schmid, Klotz, 2019). The increased passive muscle stiffness is presumably a result of fibrosis that is often associated with an abnormal accumulation of materials in the extracellular matrix (ECM) (Alnaqeeb et al., 1984, Booth et al., 2001, Jakubowski, Terman, 2017, Lieber and Ward, 2013, Mathewson and Lieber, 2015, Meyer and Lieber, 2011). Although the contribution of the increased ECM to muscle mechanical properties is yet unclear, it is plausible that the orientation of collagen fibers in the ECM can change muscle mechanical properties. For example, as muscle actively shortens, the distribution of collagen angles within the ECM appears biased toward more circumferential orientations (Purslow and Trotter, 1994, Trotter and Purslow, 1992) and thus, the increased ECM content such as collagen likely contributes to greater transverse tensile stiffness against radial expansion and fascicle shortening (Azizi et al., 2017, Gindre et al., 2013, Hodgson et al., 2012, Wheatley et al., 2018). A computational model also suggested that at a given muscle activation level, an increase in the amount of intramuscular fat (i.e., increase in overall muscle stiffness) leads to a decrease in muscle force (Rahemi et al., 2015). Collectively, a greater muscle activation may be

needed for a stiffer paretic muscle to deform muscle shape and in turn, to shorten fascicles enough to generate a comparable force by a non-paretic muscle. The time required for such processes may be reflected in the elongated EMD.

Altered mechanical properties of aponeurosis and tendon tissues may also lead to the longer EMD after stroke. Indeed, it is likely that the greatest relative contribution to the EMD is attributed to the process required to transmit forces produced by the contractile elements through the SEC to a joint (approximately 50% of the total EMD) (Cè, Rampichini, 2017, Esposito, Cè, 2016, Esposito, Cè, 2017, Esposito, Limonta, 2011, Hug, Gallot, 2011a, Nordez, Gallot, 2009) and that a longer time is required when a tendon is more slack (Lacourpaille, Hug, 2013, Longo, Cè, 2017, Muraoka, Muramatsu, 2004, Sasaki et al., 2011). Considering that the Achilles tendon on the paretic side is routinely more compliant than on the non-paretic side of chronic stroke survivors (Svantesson, Takahashi, 2000, Zhao, Ren, 2015, Zhao, Ren, 2009), it is plausible that the longer EMD in this study may be attributed to the more compliant tendon on the paretic side.

Potential implication of longer EMD after stroke

The EMD may be a useful biomarker associated with muscular contraction efficiency. It has been reported that the greater the muscle strength, the shorter the EMD (Cavanagh and Komi, 1979, Hannah, Minshull, 2014), as also supported by our findings (Figure 2). Given that muscular contraction efficiency may become lower after stroke (Son and Rymer, 2020, Tang and Rymer, 1981), the reduction in maximum torque-generating capacity on the paretic side might be reflected as the elongation of the EMD on the paretic side. Indeed, we observed a strong negative relationship between the difference in the EMD and the relative (paretic / non-paretic) torque (Figure 6A), suggesting that the relative deficit of maximum torque-generating capacity may be greater as the EMD on the paretic side is longer than on the non-paretic side.

Moreover, the elongated EMD may reflect altered material properties of muscle tissues after stroke, based on our finding of a strong positive relationship between the difference in the EMD and the relative (paretic / non-paretic) SWS (Figure 6B). There is evidence showing that the amount of non-contractile tissues increases after stroke (Ramsay et al., 2011, Ryan et al., 2002) and that such increased ECM may be a primary source of the increased passive muscle stiffness (Alnaqeeb, Al Zaid, 1984, Booth, Cortina-Borja, 2001, Jakubowski, Terman, 2017, Lieber and Ward, 2013, Mathewson and Lieber, 2015, Meyer and Lieber, 2011). Considering that the SWS could be a surrogate of passive muscle stiffness, it is suggested that the EMD might be helpful to invasively estimate passive muscle stiffness.

Limitation

Although the EMD may be a useful parameter to understand muscular contraction efficiency, there are several related issues to consider. First, we did not take account for altered neural factors after stroke. A loss of descending excitatory drive is thought to be a primary factor contributing to voluntary muscle weakness, and there are alterations in motor unit behaviors such as the reduced motor unit firing rates, the disorganization in the rank order of recruitment, and the recruitment compression (Gemperline et al., 1995, Hu et al.,

2015, Mottram et al., 2014). In addition to fast-to-slow shifts in muscle fiber type composition (Dattola, Girlanda, 1993, Hachisuka, Umezu, 1997, Lukács, Vécsei, 2008, Scelsi, Lotta, 1984), altered motor unit behaviors might elongate the EMD after stroke.

Absolute EMD values are also not comparable with previous studies. These differences are most likely due to the different approaches to determine the EMD (Hug et al., 2011b, Yavuz, Şendemir-Ürkmez, 2010). For example, the use of electrical stimulation that activates all motor fibers in a well-synchronized manner resulted in a shorter EMD (Cè, Rampichini, 2017, Esposito, Cè, 2016, Esposito, Cè, 2017, Esposito, Limonta, 2011, Hug, Gallot, 2011a, Nordez, Gallot, 2009). Moreover, during voluntary contraction, the EMD can be affected by the sEMG electrode location with respect to the first recruited muscle fibers (Hug, Lacourpaille, 2011b, Yavuz, Şendemir-Ürkmez, 2010), potentially leading to high variability in the onset times depending on the electrode location up to 20 ms mainly due to a limited muscle fiber conduction velocity (Hug, Lacourpaille, 2011b). We believe that such an artifact may be a minor factor in the longer EMD on the paretic side in this study because the median difference in the EMD of our results was considerably greater than the variability previously reported (i.e., 102.8 ms on the paretic side vs. 63.5 ms on the non-paretic side).

Fatigue may potentially be induced by a number of contractions especially for the paretic muscles, although a 30-s break was provided between each submaximal contraction. Since our findings showed a measurable difference in the EMD between sides, it is unlikely that the longer EMD on the paretic side may result from fatigue. It would be interesting to investigate how the EMD is differently affected by fatigue in stroke-impaired muscles compared to contralateral or intact muscles.

Lastly, our findings are potentially limited by small sample size and by only male participants. Thus, special care should be taken to generalize our findings mainly due to potential gender differences in muscle architecture (Chow et al., 2000) and in tissue properties (Chino and Takahashi, 2016, Otsuka et al., 2018). Future studies are required to examine gender differences in the EMD after stroke.

Conclusion

This study found that not only the EMD in the paretic triceps surae muscles is longer than in the non-paretic muscles of chronic hemispheric stroke survivors but also the longer the EMD, the smaller the maximum torque-generating capacity. There was also a strong positive relationship between the EMD and the SWS in the paretic MG muscles. These findings imply that the EMD may be a useful biomarker, in part, associated with altered contractile and material properties in stroke-impaired muscles.

Acknowledgment

We thank all participants in this study. We also thank Andres Cardona for technical preparation. This study was supported by grants from the National Institute on Disability, Independent Living, and Rehabilitation Research (90SFGE0005), the Davee Foundation Stroke Research Seed Grant initiative and the Northwestern University Department of Neurology, Division of Stroke and Neurocritical Care, and the National Institutes of Health (R01HD089952).

Biography

Jongsang Son obtained a Ph.D. in neuromuscular biomechanics and rehabilitation engineering from Yonsei University, Wonju, South Korea. He is currently a Research Scientist at Shirley Ryan AbilityLab and a Research Assistant Professor in the Department of Physical Medicine and Rehabilitation at Northwestern University, Chicago, IL, United States. His research priorities are to understand the underlying neuromuscular mechanisms of motor impairments in various clinical populations and to investigate neuromuscular adaptations to potential rehabilitation interventions. Ultimately, he hopes to translate his discoveries into practical interventions that can prevent the development of motor impairments and help people with chronic disease improve motor functions.

William Zev Rymer, MD, PhD is Director of the Single Motor Unit Laboratory at the Shirley Ryan AbilityLab (formerly the Rehabilitation Institute of Chicago, or RIC). He served as the former Vice President for Research and the John G. Searle Chair of Rehabilitation Research at the RIC. Dr. Rymer has appointments as Professor of PM&R, Physiology, and Biomedical Engineering at Northwestern University. He received his medical training from the University of Melbourne, graduating with honors, and his PhD in Neuroscience from Monash University. His research concerns the neural control and biomechanics of movement in human and animal models, and the disturbances of voluntary movement and their origins in people with neurological disabilities, particularly those with stroke and spinal cord injury. He currently holds grants from the NIH, NIDILRR, and several foundations. He has published more than 300 papers, with more than 150 in the fields of biomechanics and control of movement. Dr. Rymer has conducted large and successful pre- and post-doctoral training programs in bioengineering and physiology for many years. He is currently Project Director of a NIDILRR-funded multicenter clinical trial to evaluate the effectiveness of intermittent hypoxia therapy in individuals with spinal cord injury.

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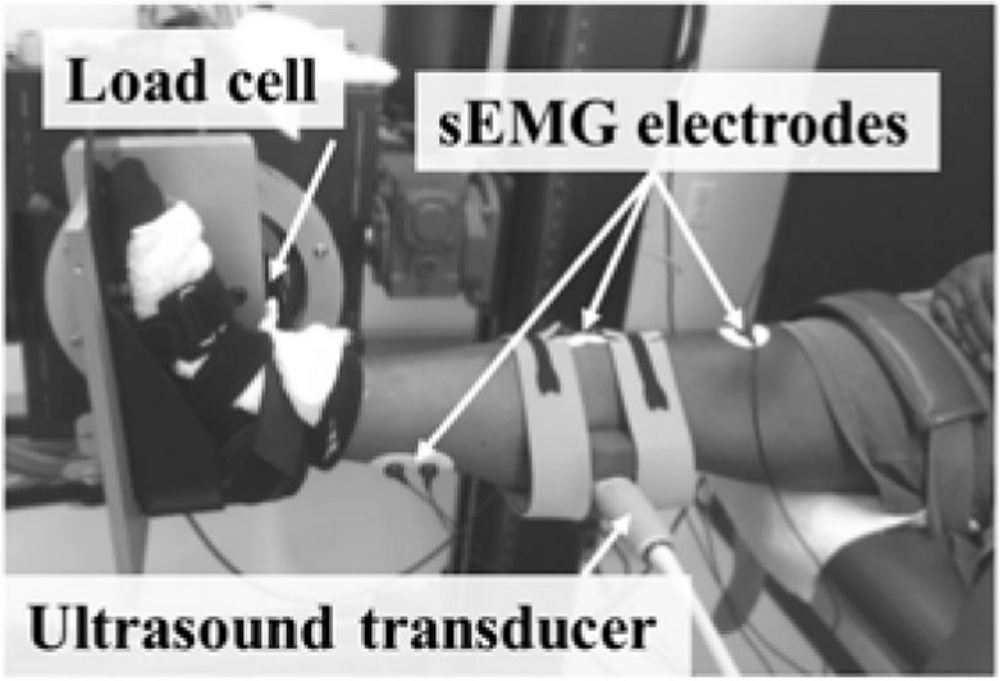

Figure 1.
Experimental set-up.

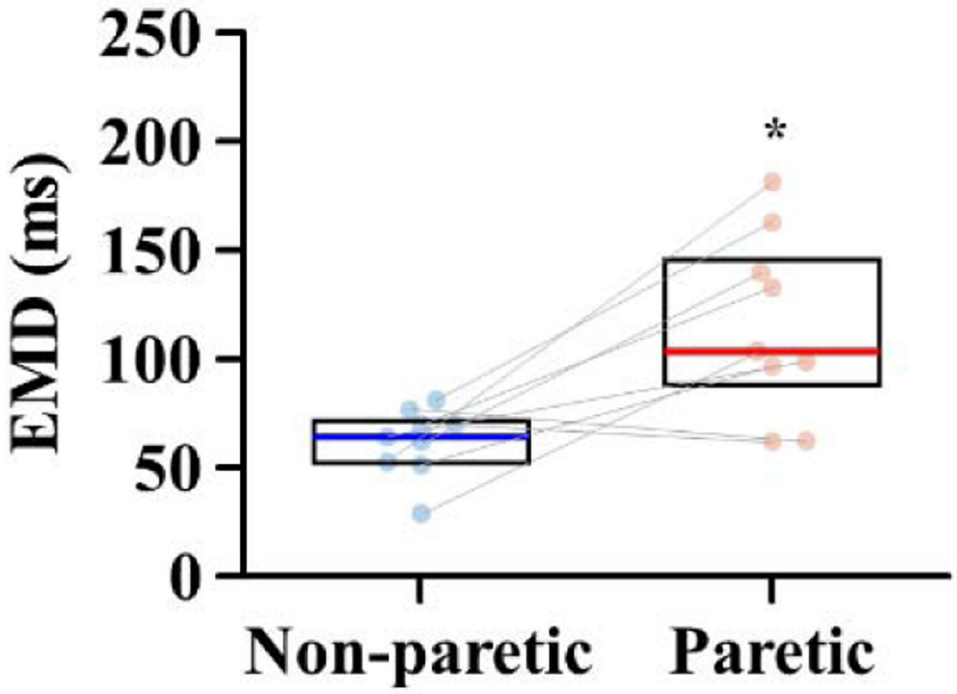

Figure 2.

Comparison of the electromechanical delay (EMD) between the non-paretic and paretic sides. Each marker indicates an individual and gray lines indicate paired data. Asterisk (*) indicates a significant difference in the EMD between sides ($p < 0.05$).

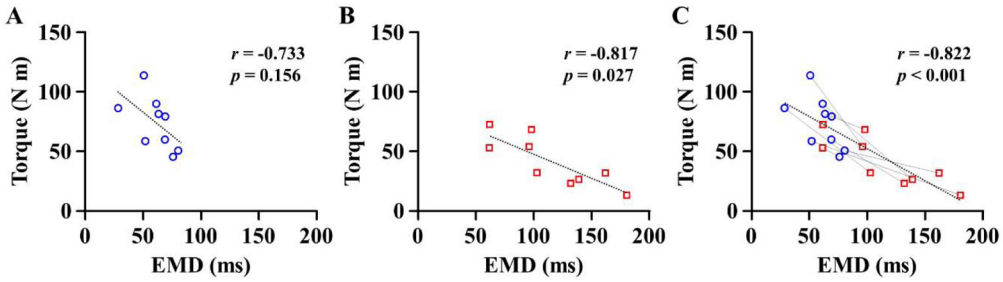

Figure 3.

Relationship between maximum ankle plantarflexion torque and electromechanical delay (EMD) on non-paretic (**A**) and paretic (**B**) sides. There is a strong negative correlation on the paretic side ($p < 0.05$), but not on the non-paretic side ($p > 0.05$). (**C**) Pooled data from both sides also show a strong negative correlation ($p < 0.001$) between the maximum torque and the EMD (gray lines indicate paired data). Each marker indicates an individual. The non-paretic data side is in blue, and the paretic data in red.

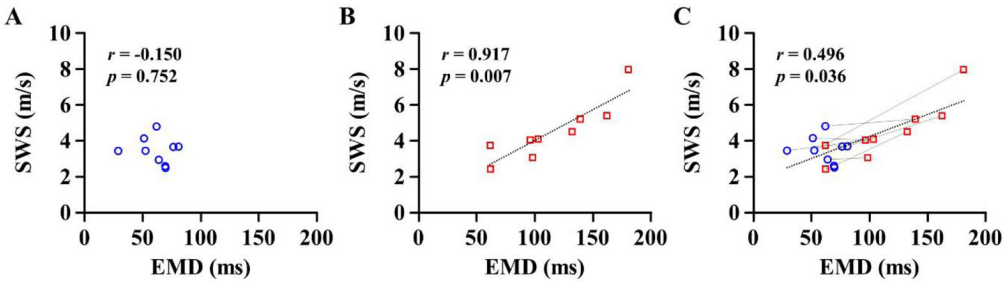

Figure 4.

Relationship between shear wave speed (SWS) and electromechanical delay (EMD) on non-paretic (**A**) and paretic (**B**) sides. A strong positive correlation ($p < 0.01$) is found only on the paretic side. (**C**) Pooled data from both sides also show a positive correlation ($p < 0.05$) between the SWS and the EMD (gray lines indicate paired data). Each marker indicates an individual. The non-paretic data side is in blue, and the paretic data in red.

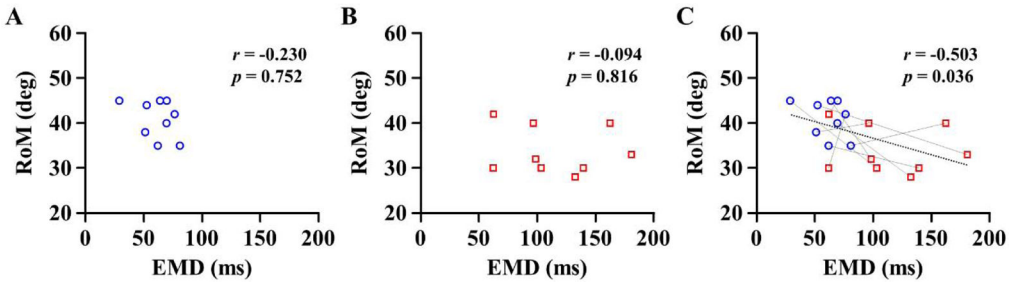

Figure 5.

Relationship between ankle joint range of motion (RoM) and electromechanical delay (EMD) on non-paretic (**A**) and paretic (**B**) sides. No significant correlation ($p > 0.05$) is found on both sides. (**C**) Pooled data from both sides show a negative correlation ($p < 0.05$) between the RoM and the EMD (gray lines indicate paired data). Each marker indicates an individual. The non-paretic data side is in blue, and the paretic data in red.

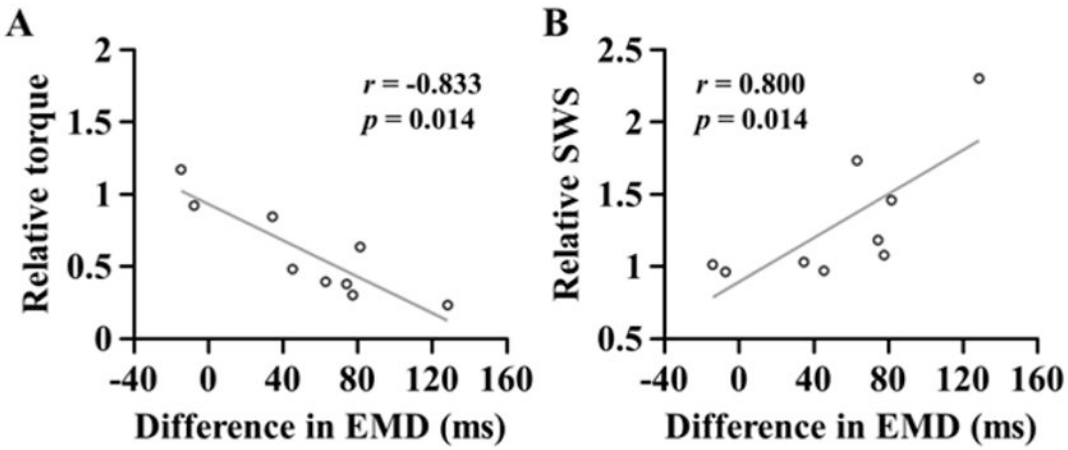

Figure 6.

Relationship of difference (paretic – non-paretic) in electromechanical delay (EMD) with relative (paretic / non-paretic) maximum plantarflexion torque (**A**) and shear wave speed (SWS) (**B**). As the EMD on the paretic side is longer, the maximum torque on the paretic side is smaller ($p < 0.05$) and the SWS on the paretic side is greater ($p < 0.05$).