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Involuntary paretic wrist/finger flexion forces and EMG increase with shoulder abduction load in individuals with chronic stroke

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Abstract

Objective—Clinical observations of the flexion synergy in individuals with chronic hemiparetic stroke describe coupling of shoulder, elbow, wrist, and finger joints. Yet, experimental quantification of the synergy within a shoulder abduction (SABD) loading paradigm has focused only on shoulder and elbow joints. The paretic wrist and fingers have typically been studied in isolation. Therefore, this study quantified involuntary behavior of paretic wrist and fingers during concurrent activation of shoulder and elbow.

Methods—Eight individuals with chronic moderate-to-severe hemiparesis and four controls participated. Isometric wrist/finger and thumb flexion forces and wrist/finger flexor and extensor electromyograms (EMG) were measured at two positions when lifting the arm: in front of the torso and at maximal reaching distance. The task was completed in the ACT^{3D} robotic device with six SABD loads by paretic, non-paretic, and control limbs.

Results—Considerable forces and EMG were generated during lifting of the paretic arm only, and they progressively increased with SABD load. Additionally, the forces were greater at the maximal reach position than at the position front of the torso.

Conclusions—Flexion of paretic wrist and fingers is involuntarily coupled with certain shoulder and elbow movements.

Significance—Activation of the proximal upper limb must be considered when seeking to understand, rehabilitate, or develop devices to assist the paretic hand.

1. Introduction

Stereotypical movement patterns in the paretic upper limb that emerge following hemiparetic stroke (Brunnstrom, 1970; Twitchell, 1951) may be attributed to neural coupling between upper limb joints (Dewald et al., 1995, 2001; Ellis et al., 2005, 2007; Sukal et al., 2007). Such coupling reduces the capacity to control the joints independently, especially in individuals with moderate to severe motor impairment. While clinical

observations of the flexion synergy, the most prevalent movement pattern in chronic stroke, have described coupling of shoulder abduction (SABD) with elbow, wrist, and finger flexion during movement (Brunnstrom, 1970; Twitchell, 1951), scientific investigations aiming to quantify the flexion synergy have focused on coupling between the shoulder and elbow joints alone (Dewald and Beer, 2001; Dewald et al., 1995, 2001; Ellis et al., 2005, 2007; Sukal et al., 2007; Yao et al., 2009).

Of the upper limb joints, the paretic hand and wrist typically display the greatest motor control impairment (Colebatch and Gandevia, 1989; Lang et al., 2006; Turton et al., 1996). They have also been the focus of extensive research. Much of this research has been approached from two main perspectives: (1) to understand and characterize the physiologic and/or mechanical mechanisms contributing to dysfunction of the paretic hand (Chae et al., 2002; Cruz et al., 2005; Kamper et al., 2001, 2003, 2006; Kamper and Rymer, 2000, 2001; Li et al., 2006; Seo et al., 2010), and (2) to rehabilitate the paretic hand through the development of novel robot-assisted rehabilitation protocols (for a review see (Balasubramanian et al., 2010)).

These investigations have provided important insights; however, because the paretic hand was often studied in isolation or during externally supported arm movements, it is difficult to generalize the results to behavior of the paretic hand during unsupported movements of the proximal upper limb. The effects of concurrent activation of the shoulder and elbow on the wrist and fingers following stroke have not yet been studied rigorously. The primary goal of this study was to quantify the behavior of paretic wrist and fingers during activation of the rest of the upper limb, that is, within the context of the expression of the whole-limb flexion synergy.

The design of the study was based on the understanding that the expression of the flexion synergy changes with motor demand. When the physical environment increases the motor demand required to achieve or maintain a desired limb posture, the nervous system must be able to respond by adequately recruiting the necessary resources. Such a response will be referred to as the descending motor drive necessary to complete a given task. Two possible ways to modulate required descending motor drive are utilized in this study: progressive SABD loading and forward reaching. The term 'SABD loading' refers to a research paradigm in which a robotic device applies vertical forces to the user's limb in order to vary the amount of SABD torque required to lift the limb.

The effects of SABD loading on the expression of the flexion synergy at the elbow have been well characterized. Specifically, it has been shown that increasing levels of SABD load lead to increased involuntary elbow flexion torque (Beer et al., 1999; Dewald and Beer, 2001; Lum et al., 2003) and elbow flexor muscle activity (Dewald et al., 1995) and a reduced capacity to volitionally generate elbow extension (Beer et al., 2004, 2007; Kamper et al., 2002; Sukal et al., 2007) and elbow extension torque (Beer et al., 1999). The effects of SABD loading on paretic hand behavior, however, are not well understood. There is only one known study to specifically examine the effect of SABD load on paretic hand function, and it showed an increased delay in grip termination when participants were required to lift their own limb rather than have it supported by an orthosis device (Seo et al., 2009). Consequently, the first purpose of this study was to determine whether progressive increases in SABD load would result in increased expression of the flexion synergy at the paretic wrist and fingers.

Forward reaching (i.e., shoulder flexion and elbow extension) is a functional task that, like increasing SABD load, necessitates an increase in descending motor drive. This is especially true following stroke when the paretic limb is required to produce shoulder and elbow

muscle activation patterns that are outside the compulsory activation patterns of the flexion synergy (as well as those of its companion—the extension synergy). Therefore, the second purpose of the study was to examine whether the expression of the flexion synergy at the paretic wrist and fingers would increase as a result of reaching.

This investigation will provide information with which to evaluate potential neural mechanisms underlying stroke-induced movement synergies. It also has important implications for rehabilitation strategies, assistive devices, and neuroprostheses for the paretic hand. Portions of the data have been reported in abstract form and in a technical paper validating the wrist/finger force-sensing device used in this study (Miller and Dewald, 2008, 2009a,b; Miller et al., 2009).

2. Methods

2.1. Participants

A departmental research database was used to recruit eight individuals with chronic hemiparetic stroke to complete this study (seven males, one female; mean age: 62.0 years; Table 1). Acceptable stroke lesion locations were cortical or sub-cortical (non-brainstem) that had occurred at least 1 year prior (mean: 8.5 years; range: 1.8–22.5). All participants had severe to moderate upper limb motor impairment according to the Fugl-Meyer Motor Assessment (FMA; upper extremity portion) (Fugl-Meyer et al., 1975) with scores ranging from 10 to 37 of 66 possible (mean: 21.8). Participants also had severe to moderate hand motor impairment according to the Chedoke-McMaster Stroke Assessment (CMSA; hand portion) (Gowland et al., 1993) with scores ranging from 2 to 5 of a possible 7 (mean: 2.9). Five participants had left-sided hemiparesis and three had right-sided hemiparesis.

Participation required full passive range of motion at the elbow, 15° or more of passive wrist extension (fingers fully extended), and at least 90° of passive shoulder flexion and abduction. Exclusion resulted from FMA scores outside of the 10–44 range (0–9 indicating near paralysis and 45–66 indicating mild impairment), from CMSA scores greater than 5 (indicating mild impairment), from significant impairment of vision or upper extremity tactile somato-sensation, or from the use of botox in the paretic upper limb.

Four control participants without stroke (three males, one female; mean age = 48.8 years) were included for comparison with the non-paretic limb of participants with stroke. Control participants completed the protocol with their right dominant arm.

Participants gave informed consent for participation in the study, which was approved by the Institutional Review Board of Northwestern University.

2.2. Experimental apparatus

An isometric setup with a 6 degree-of-freedom load cell (JR3, model 45E15A) measured each participant's maximum SABD torque and elbow flexion (EF) torque (Dewald et al., 2001; Ellis et al., 2005, 2007; McPherson et al., 2008).

Limb movements were completed in the ACT^{3D} haptic device (Sukal et al., 2006, 2007), which varied the amount of SABD torque required to lift the limb. The ACT^{3D} includes a Biodex experimental chair with shoulder/waist restraints to prevent shoulder girdle and trunk motion and a computer monitor to provide a real-time avatar of the limb (Figs. 1a and 1b).

To measure isometric wrist, finger and thumb forces, the ACT^{3D} forearm-hand orthosis included the Wrist/Finger Force Sensing module (WFFS), in which the forearm is tightly

secured in mid pronation-supination (Miller et al., 2009). The WFFS consists of a one degree-of-freedom tension–compression load cell placed under the fingers (Omega Engineering, LC201) and a one degree-of-freedom compression load cell placed under the thumb (LC302). The fingers and thumb are secured to stiff measurement plates attached to the load cells. Measurements from the load cell underneath the fingers reflect forces generated by wrist, fingers, or both. In this experiment, it was not possible to separate them. Therefore, forces measured by the WFFS will be referred to as ‘wrist/finger’ and ‘thumb’ forces.

Electromyographic (EMG) activity was recorded using active differential surface electrodes with a 1-cm interelectrode distance (16-channel Bagnoli EMG System; Delsys Inc.; 1000 × gain, 20–450 Hz bandpass). A signal conditioner (Frequency Devices, Model 9064) filtered (8th order Butterworth low-pass, 500 Hz) and amplified EMG and force data before digitization at a sampling frequency of 1 kHz. A handgrip dynamometer and key-pinch gauge collected maximum forces used for descriptive purposes.

2.3. Experimental protocol

2.3.1. Preliminary measurements—Each participant's maximum SABD torque was measured in the isometric setup with a limb configuration of 85° SABD, 40° horizontal adduction (HADD), 90° EF, and forearm mid pronation-supination. The limb was fully supported by the testing apparatus during the measurement. Each participant's maximum EF torque was measured in the same way for calculation of residual strength.

Surface EMG electrodes were placed over the flexor digitorum superficialis (FDS) and extensor digitorum communis (EDC) muscle bellies. Maximum voluntary isometric wrist/finger and thumb flexion forces and corresponding maximum voluntary contraction (MVC) of the FDS were measured using the WFFS and surface EMG. Most participants with stroke had little to no voluntary wrist and finger extension, and the effort to extend often resulted in flexion (a phenomenon described previously (Kamper et al., 2003). Therefore, the MVC value for the EDC was obtained by calculating the largest value produced during the experimental session. Because of the limited spatial resolution of surface EMG electrodes and the high density of muscles within the forearm, recordings in this experiment could also include signals from wrist flexors or extensors adjacent to the FDS and EDC, respectively.

2.3.2. Main protocol—During reaching, the most functionally relevant components for the hand are in preparation for the reach, with the arm close to the torso, and at terminal reach, with the arm maximally extended toward the desired target. Therefore, the experimental task required reaching between two arm positions within the horizontal plane while maintaining an SABD load. Visual feedback on the ACT^{3D} monitor displayed a real-time avatar of the limb to verify desired timing and limb positioning (Figs. 1a and 1b). The first position, the ‘lift position’ of 85° SABD, 40° HADD, and 90° EF, was indicated on the ACT^{3D} monitor by a green sphere, the ‘lift target’. Participants were instructed to move the distal tip of the limb avatar into the lift target to achieve the lift position and to hold the position for 0.5 s. The lift target then disappeared and a blue sphere, the ‘reach target’, appeared located in the sagittal plane through the virtual shoulder and at a distance just beyond the length of the virtual arm. Participants were instructed that, when the reach target appeared, they should reach in the horizontal plane as fast and as far as possible toward the target and hold their maximal reach distance to achieve the second position, the ‘max-reach position’. They were encouraged to hold the max-reach position as long as they could until the remainder of the trial; the hold duration was typically 1–3 s. Participants were told to keep their hand relaxed during the entire trial.

The task was performed 11 times at each of six SABD load levels (table and 5%, 15%, 25%, 35%, 50% of SABD max), and the order of completion of load levels was randomized for each participant. During the 'table' condition, the arm was fully supported by a horizontal, frictionless, stiff haptic surface. During the other six levels of SABD loading, the arm was not supported. The amount of vertical force the ACT^{3D} imposed on the arm varied so that participants had to generate 5%, 15%, 25%, 35%, or 50% of their maximum SABD torque to lift the arm above the table. The design of the ACT^{3D} interface ensured that the SABD torque required to lift the arm did not change between the two reach positions.

2.3.3. Data analysis—A Jacobian-based algorithm converted endpoint forces and moments collected from the isometric setup to shoulder and elbow joint torques. Wrist/finger and thumb forces and full-wave rectified EMG were smoothed using a two-sided moving average filter (window length: 250 ms) and were normalized by the appropriate force or EMG value obtained during maximum voluntary exertions. Before normalization, force and EMG data were baseline corrected using resting values so that any muscle tone present at rest would not factor into subsequent analyses of experimental data.

Wrist/finger and thumb forces and EMG, generated while participants held the lift position and max-reach position, were identified for analysis. Verification of the lift and max-reach positions was done offline using position data collected by the ACT^{3D} at 250 Hz. The maximum forces generated in the lift and max-reach positions were calculated and averaged across trials of each SABD load for use with group analyses, as were EMG values 50 ms prior to the maximum force value, to account for the electromechanical delay inherent in skeletal muscle.

To compare the relative strength deficits of the components of the flexion synergy at proximal and distal paretic upper limb joints, residual strength was calculated as a ratio of paretic to non-paretic values at the shoulder, elbow, and hand. Residual strength for the hand was comprised of averaged values for the wrist, fingers, and thumb.

2.3.4. Statistical analysis—Two-sided paired (paretic vs. non-paretic) and independent (non-paretic vs. control) *t*-tests were computed on maximum voluntary forces/torques. Polynomial contrasts were used to test for a linear trend in residual strength across upper limb joints, proximal to distal.

The general linear mixed model approach was used to analyze main protocol data instead of a repeated measures ANOVA because of the ability to include random effects. Interpretation of model results is similar to an ANOVA. A $2 \times 2 \times 7$ linear mixed model with repeated factors was used to determine fixed repeated main effects of limb (paretic, non-paretic), reach position (lift, max-reach), and SABD load (table and 5%, 15%, 25%, 35%, and 50% of maximum SABD), as well as interaction effects of SABD load by limb and reach position by limb on each dependent variable. To model the variation of the main effects due to individual participants, limb, SABD load, and reach position were also included as random factors along with a random intercept. Next, a similar model with repeated factors was used to examine differences between paretic FDS and EDC muscles on EMG activity, with a fixed repeated main effect of muscle (FDS, EDC) instead of limb.

Finally, a similar model was used to compare the non-paretic and control limbs with a fixed non-repeated factor of group (non-paretic, control) instead of limb and a random factor of SABD load. For all three linear mixed models, a first-order autoregressive co-variance structure was used for repeated effects, and a scaled identity co-variance structure was used for random effects, chosen based on evaluation of -2 restricted log likelihoods, Wald statistics, information criteria, and underlying experimental design.

For correlations that involved ordinal data, Spearman's rank correlation coefficient was computed. For correlations based on interval data, Pearson's product moment correlation coefficient was computed. All statistical analysis was completed using IBM SPSS Statistics version 19 (SPSS Inc.). A p -value of 0.05 was considered statistically significant for all tests.

3. Results

3.1. Preliminary measurements

Table 2 displays strength measurements for the major components of the flexion synergy: maximum voluntary wrist/finger flexion forces (WFFS and grip force) and thumb flexion forces (WFFS and key-pinch forces) and SABD and EF torques. Limb weight expressed as a percentage of maximum SABD torque is also shown in order to give clinical relevance to the SABD loading paradigm. To account for inter-subject variability in strength when analyzing data from the experimental protocol, each participant's wrist/finger and thumb forces were normalized to the participant's maximum voluntary force. However, paired t -tests revealed that the wrist/finger and thumb strength measurements of the paretic group were significantly smaller than those of the non-paretic group. Therefore, because normalizing the data from the paretic group involves dividing by smaller numbers than those of the non-paretic and control groups, there is the possibility of generating an inaccurate trend. To evaluate whether this occurred, un-normalized forces were also analyzed. As will be discussed in subsequent sub-sections, the linear mixed model results for normalized and un-normalized forces were similar.

The residual strength of the paretic limb was calculated for the major components of the flexion synergy: SABD, EF, and wrist/finger/thumb flexion. The most proximal component, SABD, had the highest mean residual strength (0.566), and residual strength means decreased at each subsequently distal component (EF = 0.474; wrist/finger/thumb flexion = 0.398). Results from the polynomial contrasts showed a significant linear trend ($p = 0.048$) moving from proximal to distal or vice versa. These ordered strength deficits are consistent with the proximal to distal increasing gradient of cortico-spinal innervation that has been reported (Colebatch and Gandevia, 1989; Palmer and Ashby, 1992).

3.2. Experimental data

Because the main comparison of interest in this study is between the paretic and non-paretic limb, the next three sub-sections will address analyses from the linear mixed model involving only the paretic and non-paretic limbs. Figs. 2–4 present data broken down by all experimental conditions, and control data are included for visual comparison. Subsequently, differences found between the non-paretic and control limbs will be presented in sub-Section 3.2.4.

Figs. 2–4 show the group mean normalized wrist/finger flexion forces, FDS and EDC EMG, respectively, that were generated during each of the six SABD loads at both lift and max-reach positions. For all dependent variables (normalized and un-normalized wrist/finger flexion forces, normalized and un-normalized thumb flexion forces, FDS and EDC EMG), the main effects of limb ($p = 0.000$), SABD load ($p = 0.000$), and reach position (ranging from $p = 0.000$ to $p = 0.030$) were statistically significant in the paretic vs. non-paretic comparison. For brevity, un-normalized wrist/finger flexion forces and normalized and un-normalized thumb flexion forces are not shown. For the un-normalized wrist/finger flexion forces, the overall trends are similar to Fig. 2 (appreciable paretic forces and virtually no non-paretic and control forces), except that at the 50% SABD load the non-paretic and control forces increased to approximately half and one quarter of the paretic forces, respectively. The trend was also similar for the thumb: the non-paretic and control values

were all virtually zero and the paretic normalized forces were, on average across SABD loads, 6% and 11% lower than paretic wrist/finger forces for lift and max-reach, respectively.

3.2.1. Effect of shoulder abduction load—Increasing the SABD load was hypothesized to cause an increase in wrist/finger and thumb flexion forces and FDS EMG in the paretic limb but not the non-paretic limb. This was tested by examining the two-way interaction of SABD load by limb. As seen in the upper middle panel of Table 3, this interaction was statistically significant for these dependent variables. The paretic EDC EMG was hypothesized not to differ from the non-paretic EDC EMG across SABD load, and accordingly, the SABD load by limb interaction for EDC EMG was not significant. The differences between FDS and EDC EMG are discussed in sub-Section 3 below.

As shown in Figs. 2–4, values generated by the paretic wrist/finger progressively increased with each heavier SABD load for both reach positions. For the most strenuous experimental condition, max-reach position with 50% SABD max, values reached 72.7% of normalized wrist/finger flexion force and 53.4% of FDS EMG. The pattern of progressive and substantial increases in forces and EMG was not observed in the non-paretic limb. The 35% SABD max experimental condition is roughly equivalent to participants supporting their own limb against gravity (requiring 37.8% SABD-max, on average).

3.2.2. Effect of reach position—Moving from the lift position to the max-reach position was hypothesized to cause an increase in wrist/finger and thumb flexion forces and FDS EMG in the paretic limb, but not the non-paretic limb. This was tested by examining the two-way interaction of reach position by limb. This interaction was statistically significant for all dependent variables, with the exception of FDS EMG (right panel, Table 3).

As shown in Figs. 2–4, values generated by the paretic wrist/finger increased consistently from lift to max-reach at all SABD loads. On average across SABD loads, values increased approximately 24.7% of normalized wrist/finger flexion force and 15.5% of FDS EMG. The pattern of increase from lift to max-reach was also observed in the non-paretic limb FDS EMG, albeit to a lesser extent (7.4% of FDS EMG), which may explain why the reach position by limb interaction was not significant.

As mentioned, the ACT^{3D} interface was designed so that SABD load would not change with changes in forearm position (i.e., elbow angle), which allowed the independent examination of forward reaching against the flexion synergy. Under normal biomechanical conditions, however, SABD load does change as the forearm is moved away from the body. Therefore, it is likely that participants would experience an even greater expression of the flexion synergy when outside of the ACT^{3D} due to the increase in SABD load with reaching.

3.2.3. FDS vs. EDC EMG—Within the paretic limb, FDS and EDC EMG were compared to see whether differences in their activation might explain the wrist and finger flexion coupling seen as part of the flexion synergy. Examining Figs. 3 and 4, the paretic limb overall had greater FDS than EDC EMG, with marginal means of 27.2% compared to 12.6% MVC (main effect of muscle; $p = 0.000$).

Increasing SABD load and moving from the lift position to the max-reach position were hypothesized to increase FDS EMG activity more than EDC EMG activity. This was tested by examining the two-way interactions of muscle by SABD load and muscle by reach position. As seen in the bottom row of Table 3, the former was statistically significant whereas the latter was not. Examining the significant interaction graphically in Figs. 3 and 4, it can be seen that FDS EMG increased across the 7 SABD loads more than EDC EMG did.

3.2.4. Non-paretic vs. control comparisons—Comparing the non-paretic and control limbs, there was a significant effect of reach position by group for normalized wrist/finger flexion force and FDS EMG ($p = 0.025$ and $p = 0.049$, respectively). This interaction is reflected in Fig. 2 by a slight increase in normalized wrist/finger flexion force from the lift position to the max-reach position in the non-paretic limb and a slight decrease in the control limb. The same pattern appeared in the unnormalized wrist/finger flexion force as well as normalized and unnormalized thumb flexion forces but was not significant in these variables. Fig. 3 shows that the non-paretic limb had more FDS EMG (7.2%) on average at the max-reach position compared to the lift position than did the control limb (1.4%). The EDC EMG on average at the max-reach position compared to the lift position was similar for both groups (non-paretic: 1.5%; control 1.8%); the interaction was not significant ($p = 0.135$).

Examining the overall FDS EMG, there are slight increases in FDS EMG at the 35% and 50% SABD load levels for both groups. From the table to 25% SABD load, however, the control values are virtually zero whereas the non-paretic values are between 10% and 20% MVC. Reflecting this phenomenon statistically, there was a significant main effect of group ($p = 0.005$). The overall EDC EMG was similar between groups.

Comparing the FDS vs. EDC EMG within each limb, the non-paretic group had a greater overall FDS than EDC EMG (marginal means of 10.5% and 4.1%, respectively; main effect of muscle: $p = 0.017$), similar to the paretic limb. The control group, however, had less overall FDS than EDC EMG, but the difference was not statistically significant (2.1% and 5.0%; main effect of muscle: $p = 0.137$).

3.2.5. Correlations—Correlations were computed to determine the linear relationships among standard clinical assessments (FMA, CMSAh) and higher resolution objective laboratory measurements from the paretic limb (normalized wrist/finger force at the most strenuous experimental condition: max-reach, 50% SABD load). The clinical assessments were each statistically significantly and highly correlated with normalized wrist/finger force ($\rho = -0.74$, $p = 0.046$ (FMA); $\rho = -0.93$, $p = 0.002$ (CMSAh)). These correlations indicate that the severity of flexion synergy expression at the wrist/fingers varies with clinically determined motor control impairment level. Additionally, the FMA and CMSAh were correlated with each other ($\rho = 0.85$, $p = 0.011$).

4. Discussion

The overall goal of this study was to quantify the behavior of the paretic wrist and fingers during movement of the shoulder and elbow in order to characterize the expression of the flexion synergy at the hand. Previously, progressive SABD loading has been used to quantify flexion synergy expression at the elbow, showing that strength of coupling between shoulder abduction and elbow flexion has a direct relationship with required descending motor drive (Sukal et al., 2007); however, the paretic hand has typically been examined in isolation from the proximal upper limb. In the present study, six SABD loads (table and 5%, 15%, 25%, 35%, 50% SABD max) and two reach positions (lift, max-reach) were used to increase required descending motor drive. Paretic, non-paretic, and control wrist/finger and thumb flexion forces and FDS and EDC EMG were used to quantify wrist and finger behavior.

Our hypotheses that increased SABD load and forward reaching would augment the expression of the flexion synergy at the wrist and fingers were confirmed. All paretic measurements increased substantially, while those of the non-paretic and control limbs increased only slightly. The results of this study suggest that the expression of the flexion

synergy at the paretic hand may be due to neural coupling with the shoulder and elbow. Furthermore, movements of the proximal paretic upper limb must be considered when seeking to understand, rehabilitate, or develop devices to assist the paretic hand. Finally, the descending motor drive required to complete a proximally-driven task will influence paretic hand behavior and should therefore be taken into account in clinical and research settings.

4.1. Increased influence of bulbospinal pathways

One mechanism that has been postulated to underlie the expression of abnormal synergistic movement patterns at the shoulder and elbow following stroke is an increased influence of medial descending bulbospinal pathways, such as the reticulospinal tract (Dewald and Beer, 2001; Dewald et al., 1995, 1999; Ellis et al., 2007, 2009; Lum et al., 2003; McPherson et al., 2008; Riddle and Baker, 2010; Riddle et al., 2009; Schwerin et al., 2008; Sukal et al., 2007; Yao et al., 2009). Based on animal preparations, bulbospinal pathways are thought to project diffusely to several vertical segments of the spinal cord, to terminate bilaterally on intermediate zone interneurons and motoneurons responsible for innervation of axial and proximal musculature, and to activate multiple motoneuron pools for grouped postural and body orienting movements (Drew and Rossignol, 1990b; Lawrence and Kuypers, 1965; Matsuyama et al., 1997, 2004; Peterson, 1979; Schepens and Drew, 2004, 2006). This classical understanding of bulbospinal anatomy does not include projections to distal upper limb musculature in primates. Rather, the lateral corticospinal tract is thought to be the primary motor pathway to innervate the distal upper limb, mono-synaptically projecting to motoneurons controlling the forearm and hand (Brouwer and Ashby, 1990; Palmer and Ashby, 1992) and giving rise to fractionated movements and fine motor control (Lawrence and Kuypers, 1968a; Porter and Lemon, 1993).

However, recent work in the monkey has revealed neuro-anatomical connections between reticulospinal pathways and hand and wrist motoneurons, engendering a new perspective for the role of these pathways in upper limb motor control (Davidson and Buford, 2006; Davidson et al., 2007; Riddle and Baker, 2010; Riddle et al., 2009). These studies together have shown that a significant number of motoneurons and interneurons controlling forearm and intrinsic hand muscles receive convergent mono- and di-synaptic input from both corticospinal and reticulospinal tracts. See Baker (2011) for a review of the role of the reticulospinal tract in hand function.

Despite the anatomical convergence of corticospinal and reticulospinal pathways on distal musculature, these pathways are not thought to control the hand in the same way. Rather, it is likely that they work in precise concert with one another, the reticulospinal system coordinating the gross multi-joint movements and postural control necessary to support the dexterous, goal-directed movements of the corticospinal tract (Lawrence and Kuypers, 1968b; Riddle and Baker, 2010; Riddle et al., 2009; Schepens and Drew, 2006). Therefore, if bulbospinal pathways such as the reticulospinal tract have more influence following lesion of the corticospinal tract in humans, their diffuse connections to multiple motoneuron pools may, in part, explain the coupling of paretic wrist, fingers, and thumb with movements of the proximal upper limb. Although the measurements of the current study are only indirect probes into the nervous system, the results are compatible with such a theory.

The reticulospinal tracts may also have differential effects on upper limb flexors vs. extensors. Selective stimulation of the origin of reticulospinal axons in the pontomedullary reticular formation in the monkey was found to simultaneously facilitate ipsilateral shoulder, elbow, and wrist flexors while suppressing their antagonistic extensors (Davidson and Buford, 2006; Davidson et al., 2007). Analogous findings were seen with pontomedullary reticular formation stimulation in the cat (Drew and Rossignol, 1990a,b; Kably and Drew, 1998; Schepens and Drew, 2006; Sprague and Chambers, 1954). In the present study, a

similar preference for flexors was seen when the FDS EMG increased much more quickly over SABD load than did EDC EMG, providing further support for involvement of the reticulospinal pathway in the flexion synergy. Unlike the two aforementioned studies, some EDC EMG was seen in the current study. However, we speculate that this may be due to the broader activation of fibers under physiological conditions than the selective stimulation performed during the experiments. Additionally, the EDC EMG presented here is normalized data; examination of the raw EMG voltage from the paretic limb generated during the experimental protocol reveals near negligible amounts of EDC EMG compared with the non-paretic and control limbs.

A lesion of the corticospinal pathway might disrupt the balance of converging contralateral corticospinal and reticulospinal input to paretic upper limb musculature; thus, the unchecked reticulospinal input could explain the emergence of abnormal synergies. However, when contralateral cortico–bulbar connections are lesioned along with corticospinal fibers, as they often are, the abnormal synergies are still present. Therefore, it is likely that the putative bulbospinal activation of flexion synergy musculature is elicited via cortico–bulbar connections from the contralesional (ipsilateral) hemisphere. Transcranial magnetic stimulation over the contralesional hemisphere has revealed motor-evoked potentials in ipsilateral paretic upper limb muscles with latencies suggestive of oligosynaptic activation of motoneurons (Netz et al., 1997; Schwerin et al., 2008, 2011), perhaps synapsing in the brainstem. These connections also appear to be present in healthy individuals as measured with transcranial magnetic stimulation, but motor-evoked potentials are difficult to elicit (Netz et al., 1997), suggesting that, following stroke, the pathways are disinhibited or otherwise upregulated.

When required descending motor drive (such as that required to maintain an SABD load) exceeds the capability of remaining ipsilesional corticofugal fibers, bulbospinal fibers may be recruited via contralesional cortico–bulbar connections. We hypothesize that the extent to which they are recruited is directly related to the quantity of corticospinal fibers that have been lost in the lesioned hemisphere. This would explain what we have observed—that the desired motor output is achieved, but at the expense of anatomical specificity. The significant and high correlation found in the present study between the amount of paretic wrist/finger coupling and FMA score supports this hypothesis, because a low FMA score can be predicted by loss of corticospinal tract integrity measured with diffusion tensor imaging (Globas et al., 2011; Qiu et al., 2011). Indeed, preliminary work in our laboratory using electroencephalography (EEG) suggests that cortical activity during forward reaching progressively shifts to the contralesional cortex as SABD load is increased and the expression of the flexion synergy at the elbow becomes more pronounced (Chen et al., 2007). Additionally, increases in connections to the paretic limb elicited by TMS of the contralesional hemisphere are associated with increased involuntary synergistic expression between the shoulder and elbow (Schwerin et al., 2008).

Recruitment of bulbospinal pathways to augment the corticospinal tract may also be a possibility in able-bodied individuals when high levels of descending motor drive are required. Facilitation of bulbospinal neuromodulatory pathways likely occurs during ‘fight or flight’ periods of high behavioral arousal (Heckman et al., 2003; Udina et al., 2010), resulting in two- to five-fold amplification of motoneuronal input (Heckman et al., 2003). It is possible that a similar effect occurs during maximal or substantial submaximal motor exertions. This concept could explain the slight increases in involuntary coupling of the control group wrist/finger flexion forces and FDS EMG at the highest SABD load, 50% SABD max. Furthermore, it would support the idea that normal motor control of the upper limb is dependent on the appropriate balance of corticospinal and bulbospinal pathways, and

that the loss of independent joint control following stroke is due to a disruption of this balance.

The increases in paretic limb wrist/finger flexion forces and EMG seen at the max-reach position are thought to reflect the influence of bulbospinal pathways recruited as a result of increases in descending motor drive required to move outside the flexion synergy. Alternatively, changes in afferent feedback from the position of the limb could have contributed in some way to the results observed. However, the increases in flexion forces and EMG from lift to max-reach remained relatively constant across SABD load, even though the distance participants could reach decreased with increasing loads. Reach distance data are not shown but are similar to previously published accounts (Chen et al., 2007; Sukal et al., 2007). Furthermore, for some participants, there was almost no change in limb position as they reached for the target at the heaviest SABD loads, because of the increased expression of the flexion synergy at the elbow. Therefore, we attribute the increased wrist/finger and thumb flexion coupling from before to after the reach to an increase in descending motor drive and subsequent bulbospinal recruitment rather than to changes in afferent feedback.

The instruction to reach as fast as possible was implemented in the experimental protocol in order to control for the amount of descending motor drive across participants. One potential complication of this strategy could have been the manifestation of spasticity that would result in an increased probability of self-evoked stretch reflexes in the paretic elbow flexors. If such reflexes were indeed evoked, it is possible that transient increases in wrist flexor EMG may have occurred due to activation of heteronymous reflex pathways (Lewis and McNair, 2010; Sangani et al., 2007; Trumbower et al., 2010). However, if any heteronymous reflexes were elicited in the wrist, their effects would have decayed before the data analysis window for the max-reach position. Furthermore, preliminary evidence from our laboratory suggests that reaching velocity decreases as the expression of the flexion synergy at the elbow increases; therefore, the likelihood that self-evoked stretch reflexes could appear in the paretic elbow flexors also decreases.

While an increased recruitment of bulbospinal pathways may contribute to the expression of the flexion synergy, it is also possible that alterations in spinal networks may be a relevant factor. For example, the C3–C4 propriospinal pre-motoneuronal system that is involved in target reaching in the cat (Lundberg, 1999) has been suggested to contribute to upper limb motor control in higher primates and humans (Pierrot-Deseilligny, 2002). Specifically, it has been suggested that the oligosynaptic propriospinal system becomes more involved during reaching and stabilizing tasks than it does with fine, dexterous hand and finger tasks that require monosynaptic corticospinal control (Stinear and Byblow, 2004). These propriospinal interneurons are thought to synapse diffusely on multiple upper limb motoneuron pools and to receive convergent input from corticospinal and bulbospinal descending pathways as well as from peripheral afferents, providing a site for sensorimotor integration at the spinal level (Pierrot-Deseilligny, 2002; Stinear and Byblow, 2004). Several studies have shown presumed increases in propriospinal activity on the paretic side in individuals following hemiparetic stroke (Mazevet et al., 2003; Stinear and Byblow, 2004), potentially leading to a difference in the ability to activate wrist extensors vs. flexors during reaching (Stinear and Byblow, 2004). However, current evidence does not suggest that propriospinal activation leads to selective and simultaneous facilitation of shoulder abductors, elbow flexors and wrist flexors, whereas the evidence presented above suggests that reticulospinal activation does lead to such facilitation of these muscles. Therefore, the most compelling explanation for the results of the current study centers on the role of the reticulospinal tract as the primary contributor to the flexion synergy.

4.2. Differences between non-paretic and control limbs

While the main goal of this study was to examine differences in the paretic limb compared to the non-paretic limb, we also found subtle differences between the non-paretic and control limbs. The most striking finding was that the non-paretic group exhibited more FDS EMG over all experimental conditions than the control limb, but the same amount of EDC EMG. Similarly, the non-paretic group exhibited a greater increase in FDS EMG from the lift to max-reach position than the control limb.

Several previous investigations have found differences between non-paretic and control limbs in terms of strength (Colebatch and Gandevia, 1989) and performance of motor tasks (Haaland et al., 2004; Nowak et al., 2007; Schaefer et al., 2007; Seo et al., 2009). Such differences have been found for both proximal (Haaland et al., 2004; Nowak et al., 2007; Schaefer et al., 2007) and distal upper limb joints (Colebatch and Gandevia, 1989; Nowak et al., 2007; Quaney et al., 2005; Yarosh et al., 2004) and have been attributed to changes in intra- or inter-hemispherical connectivity (Nowak et al., 2007; Nudo, 2006; Strens et al., 2004) and loss of bilateral descending cortical projections (Colebatch and Gandevia, 1989).

However, the nature of the current results leads us to consider whether pathological recruitment of bulbospinal pathways becomes evident in control of the non-paretic limb in addition to the paretic limb. This possibility and the others mentioned above are not mutually exclusive. Previous results were obtained during voluntary tasks, but the pathological EMG generated by the non-paretic limb in this experiment is an involuntary phenomenon that was coupled to proximal limb movements. Furthermore, the FDS EMG was selectively increased in the non-paretic limb while the EDC EMG was similar to the control group. Both of these components are consistent with the anatomical pattern of bulbospinal pathways.

Because many cortico–bulbar tracts synapse bilaterally in the brainstem, it is possible that disruptions in either hemisphere could be contributors to the hypothesized increased influence of bulbospinal pathways in the non-paretic hand. For example, lost fibers in the lesioned hemisphere could result in disinhibition of ipsilateral cortico–bulbar projections. Alternatively, reorganization of the non-lesioned hemisphere could affect contralateral cortico–bulbar projections. At this time these suggestions are purely speculative, and the topic should be investigated further.

4.3. Implications for clinical research

Implications of studies that quantified behavior of the paretic hand in isolation should be reconsidered in the context of the current results. Within the last decade, Kamper and colleagues published a series of papers that elegantly quantified neural and biomechanical contributors to paretic hand dysfunction (Cruz et al., 2005; Kamper et al., 2001, 2003, 2006; Kamper and Rymer, 2000, 2001; Li et al., 2006; Seo et al., 2010). One paper concluded that neurally-mediated finger extensor weakness was the primary contributor to deficits in voluntary finger extension, compared with stiffness, spasticity, and flexor co-activation (Kamper et al., 2006). The present results suggest that while extensor weakness may prevail with the proximal upper limb at rest, reaching and increasing SABD load requirements cause increases in involuntary wrist/finger flexor activity that presumably dominate over extensor weakness. The progressive nature of the coupled wrist/finger flexion also suggests that passive tissue changes are not a primary component of the flexion synergy.

Our results may also provide empirical evidence to develop more effective rehabilitation strategies for the paretic hand. Ellis et al. (2009) showed that incorporating progressive SABD loading into upper limb reaching training provided increases in post-training work area that were not seen in the intensity and repetition-matched control group. Such a strategy

has potential for the paretic hand as well, insofar as recovery of hand function in the chronic state is possible.

Robot-assistive devices or electrical stimulation-based neuro-prostheses may be required for significant improvement of severe hand dysfunction post-stroke in patients for whom conventional rehabilitation is not successful. Being able to predict the patient-specific amount of wrist, finger, and thumb flexion coupling during arm movement, as measured in this study, would be beneficial to improve control of a custom assistive device. For example, Chae and Hart (2003) noted that a percutaneous hand neuroprosthesis system that overcame forearm flexor hypertonia while the arm was supported failed to do so when the arm was lifted by the participant or when task difficulty was otherwise increased. Similarly, Lin (2000) noted that increases in stimulation intensity were necessary to open the paretic hand when the participant performed a forward reach.

Finally, the significant correlations found between FMA/CMSAh and the amount of wrist/finger flexion force during the most strenuous experimental condition (max-reach position with 50% SABD max) suggest that our quantification of the flexion synergy at the wrist and fingers is a valid measure that provides higher resolution than standard clinical assessments.

4.4. Limitations and future work

Several limitations of the study should be considered. Our sample was admittedly small; nevertheless, strong results were seen in all participants. Because participants were purposely chosen based on moderate-to-severe impairment of upper limb motor control, results for participants with mild impairment might be less pronounced. This is likely true given the significant correlations with clinical impairment level as previously discussed. Wrist and finger torque measurements could not be separated in the study, and we are currently investigating the relative amount of flexion coupling at the joints separately. Finally, the neuroscientific implications drawn from the results are speculative, given the indirect nature of our measurements. In future studies, we will pursue more direct ways to investigate neural mechanisms underlying the expression of the flexion synergy.

The current study addressed involuntary behavior of the paretic hand during voluntary activation of the shoulder and elbow. It would also be of interest to examine how voluntary activation of the paretic hand in hand opening or grip modulation tasks might change during SABD loading.

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Highlights

- For the first time, the paretic wrist and fingers of individuals with chronic hemiparetic stroke were investigated within the context of the upper extremity flexion synergy instead of in isolation.
- Involuntary paretic wrist and finger flexion forces and EMG were generated in proportion to descending motor drive requirements, modulated in this study by six levels of shoulder abduction torque and by forward reaching.
- Results support the hypothesis of an increased influence of bulbospinal motor pathways following stroke and suggest that activation of the proximal upper limb must be considered when seeking to understand, rehabilitate, or develop devices to assist the paretic hand.

Fig. 1.
1a. ACT^{3D} experimental setup, which includes a modified HapticMaster robot with Wrist/Finger Force Sensing module (WFFS), biodex chair, and real-time visual feedback display.
1b. Visual feedback display with real-time avatar of the limb. The left panel shows the limb in the lift position and the right panel shows the reach target.

Fig. 2. Normalized wrist/finger flexion forces generated by the paretic, non-paretic, and control groups during 6 SABD loads for the lift and max-reach positions (group mean + 95% CI).

Fig. 3. FDS EMG generated by the paretic, non-paretic, and control groups during 6 SABD loads for the lift and max-reach positions (group mean + 95% CI).

Fig. 4. EDC EMG generated by the paretic, non-paretic, and control groups during 6 SABD loads for the lift and max-reach positions (group mean + 95% CI).

Table 1

Demographics of the participants with chronic hemiparetic stroke.

Participant	Age	Sex	Affected/Dominant	Lesion location	Yrs post-stroke	FMA	CMSAh
1	52	M	L/R	N/A	1.8	25	3
2	56	F	R/R	BG, TH, IC, CFL, SFL	22.5	10	2
3	77	M	R/R	N/A	4.0	16	2
4	63	M	L/R	CR	5.3	37	4
5	61	M	L/R	CFL, CPL, BG, TH, IC, CR	5.8	34	3
6	62	M	R/L	BG, TH, IC	12.3	14	2
7	52	M	L/R	BG, IC, CL	14.0	10	2
8	73	M	L/R	N/A	2.4	28	5
Mean (SD)	62.0 (9.1)				8.5 (7.2)	21.8 (10.7)	2.9 (1.1)

FMA = upper extremity score of the Fugl-Meyer motor assessment (max = 66); CMSAh = hand portion of the Chedoke-McMaster stroke assessment (max = 7); BG = basal ganglia; TH = thalamus; IC = internal capsule; CFL = cortical frontal lobe; SFL = subcortical frontal lobe; CR = corona radiata; CPL = cortical parietal lobe; CL = claustrum; N/A = not available.

Table 2

Maximum voluntary strength measurements.

	Paretic	Non-paretic	Control
Wrist/finger flexion force (N)	63.0 ± 43.4 [*]	205.6 ± 147.2	180.5 ± 57.1
Thumb flexion force (N)	31.9 ± 18.0 ^{**}	71.2 ± 23.9	67.2 ± 24.2
Grip force (N)	92.5 ± 48.3 ^{***}	388.0 ± 92.2 [†]	519.8 ± 85.9
Key pinch force (N)	36.1 ± 9.8 ^{***}	93.1 ± 18.6	115.1 ± 22.6
EF torque (Nm)	28.7 ± 11.7 [*]	62.9 ± 16.6	77.1 ± 21.9
SABD torque (Nm)	25.3 ± 8.7 ^{**}	45.7 ± 16.1	56.6 ± 12.9
Limb weight (% max SABD torque)	37.8 ± 13.5 ^{**}	20.0 ± 4.0	17.7 ± 2.7

Values are mean ± standard deviation.

^{*} Significant difference between the paretic and non-paretic group means with $p = 0.05$.^{**} Significant difference between the paretic and non-paretic group means with $p = 0.01$.^{***} Significant difference between the paretic and non-paretic group means with $p = 0.001$.[†] Significant difference between non-paretic and control group means with $p = 0.05$.

Table 3

Linear mixed model results: two-way interactions.

Paretic vs. non-paretic limb	SABD load by limb	Reach position by limb
<i>Wrist/finger flexion forces</i>		
Normalized	$p = 0.001^{***}$	$p = 0.000^{***}$
Un-normalized	$p = 0.023^*$	$p = 0.000^{***}$
<i>Thumb flexion forces</i>		
Normalized	$p = 0.000^{***}$	$p = 0.000^{***}$
Un-normalized	$p = 0.048^*$	$p = 0.000^{***}$
FDS EMG	$p = 0.003^{**}$	$p = 0.107^{\dagger}$
EDC EMG	$p = 0.171$	$p = 0.000^{***}$
Paretic limb	Muscle by SABD load	Muscle by reach position
FDS vs. EDC EMG	$p = 0.011^*$	$p = 0.366$

* Significant difference between the paretic and non-paretic group means with $p < 0.05$.

** Significant difference between the paretic and non-paretic group means with $p < 0.01$.

*** Significant difference between the paretic and non-paretic group means with $p < 0.001$.

† Significant difference between paretic and control group means with $p < 0.05$ where paretic and non-paretic groups are not significantly different.