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Perturbation-induced electromyographic activity is predictive of flexion synergy expression and a sensitive measure of post-stroke motor impairment

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***Abstract*—The goal of this study was to explore whether the stretch reflex-induced muscle activity is correlated with the expression of the flexion synergy and, therefore, can serve as a quantitative indicator of post-stroke motor impairment. Eleven stroke participants stroke were recruited for this study. Their forearm was connected to a robotic device that applied continuous position perturbations to the paretic elbow joint. The magnitude of EMG activity of the spastic biceps brachii was measured. The expression of the flexion synergy was determined using the increase of synergistic elbow flexion torque when subjects were gradually lifting their paretic arm with two derived measures: normalized flexion synergy area (NFSA) and the mean slope of the expression of flexion synergy (ΔFS). Significant positive correlations were found between spastic biceps EMG (predictor variable) and the flexion synergy expression (response variables), i.e., NFSA ($\rho = 0.89$, $p < 0.001$) and ΔFS ($\rho = 0.73$, $p = 0.01$). This result indicates that the perturbation-induced EMG activity can serve as a sensitive indicator of post-stroke motor impairments related to the expression of spasticity and flexion synergy and demonstrates that these motor impairments may be mechanistically linked.**

Keywords—Electromyography, Flexion synergy, Muscle Contraction, Muscle Spasticity, Stretch reflex, Stroke.

I. Introduction

After a stroke, the loss of corticospinal and corticoreticular projections is postulated to result in an upregulation of descending monoaminergic pathways namely the ceruleospinal and raphespinal tracts which increases spinal motoneuron excitability [9][13]. The increased motoneuron excitability results in hyperactive stretch reflexes or spasticity [4] and strengthens the usage of the contralesional indirect cortico-reticulospinal motor pathways resulting in the expression of the flexion synergy. The upper extremity flexion synergy, defined as the abnormal co-activation between shoulder abductor and elbow/wrist/finger flexor muscles, limits arm/hand function post-stroke and significantly reduces reaching and hand opening during shoulder abduction [1][2][3]. This may imply a mechanistic link between the expression of flexion synergy and spasticity.

Hence, we hypothesized that a quantitative measure of the amount of muscle spasticity can indicate the severity of abnormal synergies (and therefore the extent of underlying maladaptive neuroplasticity) in chronic hemiparetic stroke. To test this hypothesis, we measured the flexion synergy at the elbow joint from 10-90% of the maximum shoulder abduction (SABD) loading in the paretic arm of individuals with chronic hemiparetic stroke. We also measured stretch reflex-related electromyographic (EMG) activity of biceps brachii elicited during continuous position perturbations to the elbow joint of the paretic arm (without any SABD load). We explored their relationship using stretch reflex-related EMG activity as the predictor variable and the expression of the flexion synergy as the response variable by applying a linear regression model.

II. Methods

Eleven participants with the following inclusion criteria were recruited in the study: (i) Unilateral ischemic stroke (not involving the brainstem or cerebellum), sustained at least 1 year earlier, were recruited for this study. (ii) Hemiparesis without severe wasting/contracture. (iii) Absence of muscle tone abnormalities and motor/sensory impairment in the non-paretic limb. All participants provided informed consent prior to their participation in the study (IRB No.: STU00021840). Their demographics and clinical characteristics including Fugl-Meyer Upper Extremity Motor Score (FM-UE, maximum = 66) are provided in **Table 1**.

We used an experimental setup similar to our previous studies (see **Figure 1A**) [5][6]. Participants were seated in a Biodex chair (Biodex Medical Systems, Shirley, NY), with their trunks restrained by belts across the shoulders and lap. A fiberglass participant-specific forearm-wrist-hand cast rigidly attached the forearm to a beam, which was connected to a six-degree-of-freedom load cell (JR3, Woodland, CA) and actuator

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(Peabody, MA, USA). The medial epicondyle of the humerus was aligned with the center of rotation of the actuator. The tested upper limb was positioned such that it retained 85° shoulder abduction, 45° shoulder flexion, 90° elbow flexion, and the forearm was casted and fixed in a mid-prone position with a Delrin cuff into a metal ring attached to a metal beam which was connected to the JR3 loadcell. EMG activity of biceps brachii was recorded using differential surface electrodes (Delsys EMG system, Boston, MA). All data were synchronized and collected at 1 kHz. First, maximum voluntary torques (MVT) in SABD and elbow flexion (EF) were measured [5]. The peak value was obtained from the data after filtering it with a moving average filter (1000 ms window with a 1-ms step) online. The MVT trials were repeated until the variance of the peaks of the last three consecutive trials were within 5% of each other. Subsequently, the trial with the highest SABD MVT (from the last three trials) was chosen for determining the expression of the flexion synergy. The trial data were smoothed using the same moving average filter, and then the segment of the trial from 10-90% SABD MVT was extracted for further analysis. Synergistic EF (normalized to the EF MVT) was plotted against voluntary SABD (normalized to the SABD MVT) and two measures were computed from this plot to estimate the extent of the flexion synergy expression: (i) the area under the curve indicating the total synergy generated during the period (Normalized Flexion Synergy Area, NFSA) and, (ii) the mean rate of expression of the flexion synergy (ΔFS) defined as follows:

$$\Delta FS = \frac{\sum_{i=\,10\%\,SABD}^{90\%\,SABD} \frac{\delta EF_i}{\delta SABD_i}}{n-1}$$

where δEF and δSABD were the instantaneous (i.e., between successive samples, $\delta t = 1$ ms) changes in normalized synergistic EF and voluntary SABD and n was the number of data samples (as illustrated in **Figure 1B**). NFSA measured the total amount of normalized elbow flexion impulse that was produced involuntarily due to voluntary shoulder abduction. ΔFS measured the mean rate of involuntary elbow flexion as a function of voluntary shoulder abduction. Therefore, both the measures estimated the extent of pathological flexion synergy produced during voluntary torque generation.

TABLE I. DEMOGRAPHICS AND CLINICAL CHARACTERISTICS OF PARTICIPANTS WITH STROKE

Subject No.	Age	Gender	Years Post-stroke	Lesion site*	Paretic Arm	FM-UE***
1	53	Male	31	NA**	Right	26
2	72	Male	8	R: IC, T, I	Left	49
3	48	Male	11	R: Th, IC, BG	Left	18
4	62	Male	6	R:IC	Left	39
5	66	Female	11	L: BG, IC, Th	Right	24
6	70	Female	15	R: Th, IC, BG	Left	18
7	59	Male	10	R: FC, PC, TC	Left	24
8	59	Male	3	L: TC, PC	Right	23
9	72	Male	25	L: I, IC, Th, BG	Right	12
10	65	Female	6	R: IC, BG	Left	43
11	78	Male	16	L: IC	Right	13
Mean ± std	**65 ± 9**	**-**	**11 ± 8**	**-**	**-**	**24 ± 12**

*L: Left, R: Right, IC: Internal Capsule, Th: Thalamus, BG: Basal Ganglia PC: Parietal Cortex, FC: Frontal Cortex, TC: Temporal Cortex; **Medical records unavailable, cerebellum and brainstem lesion excluded clinically; ***FM-UE: Fugl-Meyer Upper Extremity Motor Score (maximum = 66)

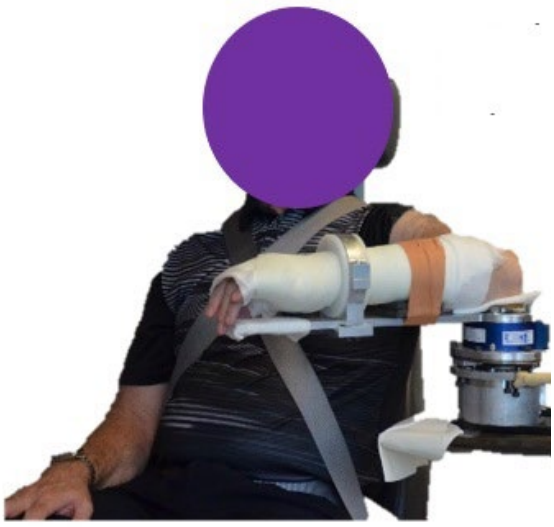

Figure 1A: Experimental setup.

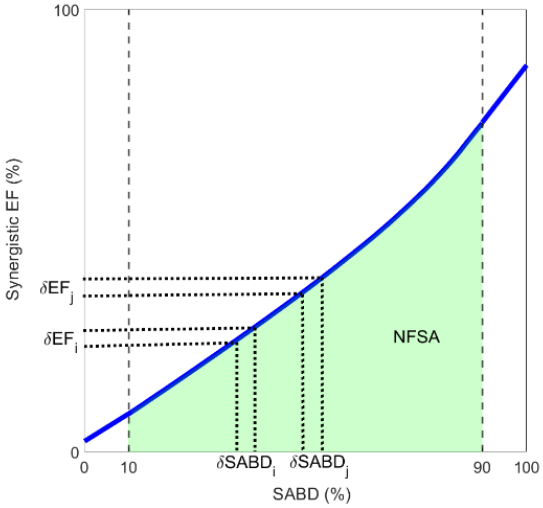

Figure 1B: Schematic of normalized voluntary shoulder abduction (SABD) vs. synergistic elbow flexion (EF) plot. The green shaded area is the normalized flexion synergy area (NFSA), δEF and δSABD were the instantaneous changes in normalized synergistic EF and voluntary SABD. They are used to calculate ΔFS as explained in the METHODS section.

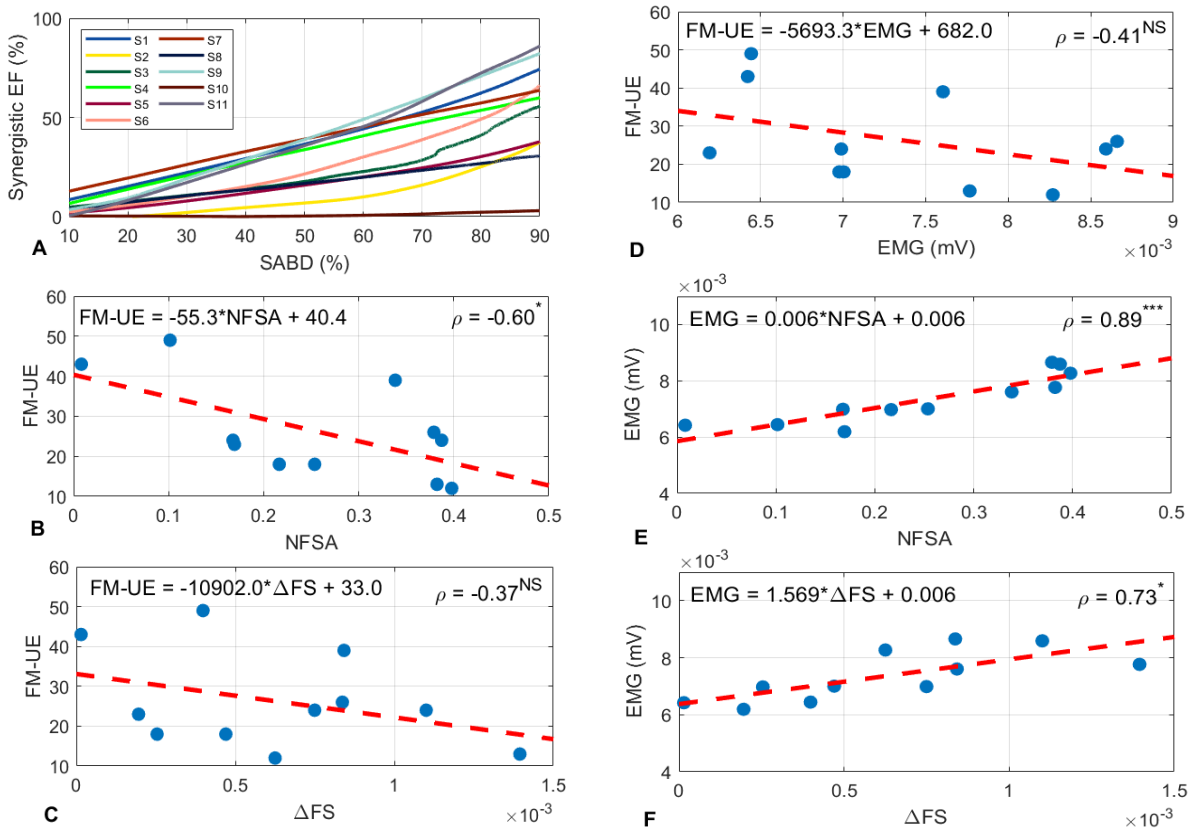

Figure 2: A. Synergistic elbow flexion (normalized to the maximum voluntary elbow flexion) vs. 10-90% of maximum voluntary shoulder abduction for 11 participants with stroke. B. Fugl-Meyer upper extremity motor assessment score (FMA-UE) vs. area under the curve of plot A (Normalized Flexion Synergy Area, NFSA) for each participant. C. FMA-UE vs. the mean rate of change of synergistic elbow flexion with voluntary shoulder abduction (ΔFS) for each participant. D. FM-UE vs. mean rectified epoch-averaged stretch reflex related electromyographic activity of biceps brachii during continuous position perturbations to the elbow joint (EMG) for each participant. E. EMG vs. NFSA for each participant. F. EMG vs. ΔFS for each participant. The red dashed lines in B-F are linear fits to the data. The Pearson correlation coefficient (ρ) along with its significance is indicated on the top right of each subplot in B-F. (NS = not significant, p > 0.05; * p <= 0.05; ** p < 0.01; *** p < 0.001).

To assess the stretch reflex-related activity of the biceps muscle, participants were asked to fully relax but remain alert in the experimental setup while band-limited small-amplitude continuous position perturbations were applied to their elbow joint. To guide their behaviour, we provided visual feedback on a screen placed in front of the participant which indicated the level of voluntary elbow flexion before starting the perturbations. To further corroborate the absence of any unwanted voluntary activation of the biceps, we monitored the background EMG signal before starting the perturbations. The perturbation signal was designed as a sum of 10 zero-centered sinusoids (0.8-18.4 Hz) with a cycling period of 1.25s [5]. 15 trials were conducted for each participant (with 15s per trial). The biceps EMG activity during the perturbation was then epoched by the cycling period, rectified, and averaged across all the epochs. The mean magnitude of the processed EMG was computed to estimate the amount of biceps spasticity per participant.

Pearson correlation coefficients were computed between the extent of the flexion synergy expression (as measured by NFSA and ΔFS, see previous figure) and the stretch reflex-related biceps EMG activity. For comparison, we also computed the correlation coefficients between the FM-UE scores and (i) the extent of the flexion synergy expression (NSFA and ΔFS) and (ii) stretch reflex-related biceps EMG activity. A p-value of 0.05 was used to assess the significance of each correlation coefficient.

III. Results

The relationship between normalized synergistic elbow flexion and voluntary shoulder abduction is shown in **Figure 2A**. For all participants, the synergistic elbow flexion increased with voluntary shoulder abduction effort. However, the NSFA and ΔFS varied between participants based on their level of impairment. The FM-UE score exhibited weak to moderate negative correlations with the expressed synergy level as measured by NFSA and ΔFS, as well as the stretch reflex related biceps EMG (**Figure 2B-D**). Moreover, only the correlation between FM-UE score and NFSA was statistically significant. On the other hand, significantly strong positive correlations were found between stretch reflex related biceps

EMG and both the measures of expressed flexion synergy i.e., NFSA ($\rho = 0.89$, $p < 0.001$, **Figures 2E**) and ΔFS ($\rho = 0.73$, $p = 0.01$, **Figures 2F**).

IV. Discussion

The strong positive correlation between flexion synergy and spasticity, as shown in our results, supports and emphasizes the common neural mechanism of origin of post-stroke synergies and spasticity. Abnormal limb synergies and spasticity likely arise from an imbalanced usage of different motor pathways following damage to the corticofugal projections in a hemiparetic stroke. The pontomedullary reticular formation (PMRF) is the site of origin of the reticulospinal tract (RST) which projects ipsilaterally to the spinal cord. The corticoreticular tracts (CRT) from the primary motor cortex (M1) project predominantly contralaterally to the PMRF while those from premotor (PM) cortices and supplementary motor area (SMA) project predominantly ipsilaterally to the PMRF [7]. A previous study shows that M1 exerts both excitatory and inhibitory influences on the PMRF [8]. Thus, under normal conditions, there is a balance of excitatory and inhibitory influences on the PMRF from the M1. A M1 lesion or an internal capsule infarct disrupts both the crossed corticospinal tract and CRT because of their anatomical proximity. Consequently, the balanced modulation of the PMRF by the M1 is lost. Increased activation of the PMRF (caused by PM/SMA) amplifies the ionotropic post-synaptic potentials in spinal motoneurons due to the upregulated neuromodulatory metabotropic monoaminergic component of the RST via ceruleospinal (with neurotransmitter Norepinephrine) [9,10] and possibly raphespinal tracts (with Serotonin)[11]. Thereby, motoneurons become hyperexcitable to Ia afferent inputs during muscle stretching resulting in spasticity. Furthermore, motoneuron hyperexcitability will strengthen the effect of relying on normally weak indirect cortico-reticulospinal motor pathways from the contralesional hemisphere. Due to the diffuse and divergent projections of the RST, any attempt to voluntarily activate a hypertonic muscle is accompanied by the unwanted involuntary activation of other upper extremity flexor muscles as also shown by electrical stimulation of the origin of the RST in non-human primates i.e., the expression of the abnormal flexion synergy [12]. In short, the upregulated neuromodulatory metabotropic monoaminergic component of the RST results in an increased excitability of motoneurons resulting in spasticity and facilitates the effect of relying on the cortico-reticulospinal tract from the contralesional hemisphere resulting in post-stroke flexion synergy and spasticity.

We did not find a statistically significant correlation between the proposed measures and Fugl-Meyer Upper Extremity Motor Score. This is likely because Fugl-Meyer Upper Extremity Motor Score is a rough measure that is not as sensitive to the expression of flexion synergy and especially spasticity.

However, our proposed measure is sensitive enough even with this small sample size to indicate the relationship between the expression of flexion synergy and hyperactive stretch reflex related EMG activity. This result indicates that the perturbation-induced EMG activity can serve as a sensitive yet convenient marker for measuring pathological expression of upper extremity spasticity and flexion synergy that is strongly correlated with the ground truth using a readily available clinical tool i.e., surface EMG.

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