

EMG-Guided Human-Machine Interaction Training Develops New Intermuscular Coordination Patterns in Stroke: A Pilot Study

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Abstract

Background

Stroke survivors often experience impaired upper extremity motor function due to abnormal muscle synergies. This pilot study evaluated the feasibility and preliminary effectiveness of electromyography-guided human-machine interaction training designed to expand the repertoire of intermuscular coordination patterns and improve upper extremity motor function in chronic stroke survivors.

Methods

Four chronic stroke survivors with mild-to-moderate upper extremity motor impairment and three age-matched healthy controls participated in a six-week electromyography-guided training intervention. Participants practiced selectively activating one elbow flexor muscle while suppressing another (brachioradialis or biceps brachii). Throughout the course of the intervention, the effect of the training on intermuscular coordination, task performance, and motor function and impairment level of stroke-affected upper extremity were assessed.

Results

Participants in both the control and stroke groups successfully learned to selectively activate targeted muscles, expanding their repertoire of habitual intermuscular coordination patterns. Stroke survivors demonstrated improvements in force generation, reaching ability, wrist rotation, and clinical measures of upper extremity motor function and spasticity. Participants also reported improved ease in performing daily activities.

Conclusions

This pilot study demonstrated the feasibility of using electromyography-guided human-machine interaction training to expand the repertoire of habitual intermuscular coordination patterns and improve upper extremity motor function in chronic stroke survivors. These findings highlight the potential of electromyography-guided human-machine interaction training as a neurorehabilitation approach to address motor deficits associated with abnormal intermuscular coordination following stroke.

Trial registration:

The study was registered at the Clinical Research Information Service of Korea National Institute of Health (KCT0005803).

Introduction

In the field of human motor control, it has been investigated that the coordination of spatiotemporal activity of muscle groups is facilitated by neuronal networks in the central nervous system (CNS) to achieve successful limb movements [1–4]. Harnessing the concept of muscle synergies, which are distinct patterns of activation across a muscle group that underlie a specific motor behavior, prior studies have utilized computational methods to delineate the modular organization of multi-muscle activities [5–9]. Through dimensionality reduction methods applied to electromyographic (EMG) signals,

muscle synergies have been modeled as a linear combination of time-invariant synergy composition components multiplied by time-varying activation profiles [6–14]. Human studies have demonstrated that a limited number of muscle synergies can effectively encapsulate the global patterns of muscle activation associated with lower and upper limb movements. [12–18]

Given that muscle synergies can underlie a neural strategy for motor control, expanding the repertoire of muscle synergies can potentially enhance motor performance. Following previous studies that have demonstrated the modulation of muscle synergies via conditioning or physical training in healthy adults [19, 20], our recent study [21] further showed an increase in the repertoire of upper extremity (UE) muscle synergies within a relatively short period through an isometric EMG-guided human-machine interaction in healthy young adults. The development of a new muscle synergy positively affected the motor control of the trained UE muscles. This finding suggests the potential of expanding the muscle synergy repertoire as a tool that can be further applied to develop a rehabilitation protocol targeting motor deficits induced by neurological injuries, such as stroke.

Stroke, which affects 800,000 individuals in the United States annually [22], leaves 80% of survivors with various motor deficits, including abnormal intermuscular coordination [23]. Prior studies have applied muscle synergy analysis to pinpoint disruptions in intermuscular coordination in stroke-affected UE [24–34]. Abnormalities in stroke-induced UE muscle synergies can usually be characterized by atypical coupling of activation between elbow flexors and shoulder abductors [24–26], along with anomalous co-activation of the three fibers of the deltoid muscle [28–29].

Aberrant muscle synergies can negatively affect motor output after stroke. Relatively recent studies have shown that abnormalities in muscle synergy are more frequently observed in stroke patients with severe impairment than in those with mild impairment during voluntary movements [27, 30]. Similarly, Roh et al. [29] showed that as the severity of motor impairment in the UE increased after stroke, the prevalence of abnormal muscle synergies also increased under isometric conditions. Supporting this result from Roh et al. [29], Pan et al. [31] demonstrated that the similarity in the synergy composition between stroke and the age-matched control group was positively correlated with the level of UE recovery after stroke. Li et al. [32] also showed a negative correlation between the alteration of muscle synergy and the quality of reaching movement in the stroke-affected UE. Furthermore, our previous study [33] demonstrated that stroke-affected muscle synergies contributed to abnormal end-point force control under isometric conditions in severely impaired UE. Overall, these findings suggest that the activation of abnormal synergistic muscle coordination induces impaired biomechanical outputs, which emphasizes the importance of targeting abnormal muscle synergies as a new direction for stroke rehabilitation [34].

Considering the feasibility of expanding the muscle synergy repertoire in young healthy adults [21] and its potential as a novel approach for stroke motor rehabilitation, this study was designed to further answer the questions: Is it possible to evoke new muscle synergies through human-machine interaction guided by myoelectric signals even in stroke-affected UE in the chronic stage? If feasible, do new synergistic muscular coordination patterns replace habitual muscular coordination that would not be

used anymore after motor learning? Can developing new intermuscular coordination help reduce post-stroke motor impairments and enhance motor function? As a continuation of our recent study on young healthy adults [21], we developed an isometric EMG-guided training protocol via human-machine interaction to target the modification of habitual elbow flexor synergy in stroke survivors and neurologically intact adults of matched ages. In this pilot study, four stroke survivors and three healthy, age-matched control volunteers participated in a six-week training to independently control the activation of a pair of elbow flexor muscles that naturally tend to co-activate. Throughout the course of the exercise, the effect of the training on intermuscular coordination, task performance, and motor function and impairment level of stroke-affected UE were assessed.

Methods

Participants

Four individuals with unilateral chronic stroke (two females; 59 ± 8.98 years (mean $\pm$ SD) of age) showing moderate-to-severe UE impairment (UE Fugl-Meyer assessment (FMA-UE) score: 27 ± 13 out of 66) were enrolled and completed the six-week training period. Only stroke survivors who had experienced a single stroke, had no other motor deficits, and had not received Botox injections within the three months prior to participation were recruited. As a control group, three neurologically healthy males (average age 56 ± 13 years) with no history of muscle or orthopedic injuries in their UE participated as an age-matched control group. The investigation complied with the principles outlined in the Declaration of Helsinki and was approved by the Institutional Review Board of the University of Houston. The study was registered at the Clinical Research Information Service of the Korea National Institute of Health (KCT0005803), and participant recruitment was conducted at the University of Houston. Each participant provided informed consent before each training and evaluation session.

EMG Recording

The stroke group used their impaired arm for both the training and assessment visits, whereas the age-matched control group employed their dominant arm. During the task, the activation of 10 major UE muscles used to perform the task was measured using a wireless EMG recording system (Trigno Avanti Platform; Delsys Inc., Natick, MA, USA) at a sampling rate of 1 kHz with onboard bandpass filtration (20–450 Hz) and amplification ($\times 1000$). The recorded muscle set included the brachioradialis (BRD), biceps brachii (BI), triceps brachii (long and lateral heads; TRl long and TRl lat), deltoids (anterior, middle, and posterior fibers; AD, MD, and PD), pectoralis major (clavicular fibers; PECT), trapezius (upper fibers; UpTrp), and infraspinatus (InfSp). Following the guidelines provided in the Surface Electromyography for the Non-Invasive Assessment of Muscles (SENIAM)–European Community project [35, 36], the bipolar EMG sensors were properly placed on each muscle's belly. To ensure the uniformity of sensor placements over the six-week period of the study, each participant wore a custom-made long-sleeve compression shirt that featured openings at the site of each muscle's belly identified during the first visit.

Experimental Setup

The overall experimental approach and procedure adhered to a previous study involving a young, healthy group [21]. A custom-designed apparatus, known as the KAIST Upper Limb Synergy Investigation System (KULSIS) [37], was employed for isometric exercises via human-machine interaction during the training and assessment sessions (Fig. 1A). Three-dimensional end-point forces produced on a gimbal handle affixed to a load cell were captured at a sampling frequency of 1 kHz in sync with the EMG signal. The acquired EMG and force signals were subsequently linked to the movement of a cursor on a screen for the participants during training and assessment.

To maintain a consistent seated posture and arm location across participants and sessions, the participant's acromion was aligned with the central point of the gimbal handle, while ensuring that the distance between the handle and acromion was maintained at 60% of the total arm length. To further minimize upper body movement during isometric exercise, the participant was securely strapped to the KULSIS seat.

Isometric EMG-Guided Training and Force Matching Assessment

The six-week training involved isometric EMG-guided exercises across 18 sessions (three weekly, with at least one resting day between sessions). The seated participant guided a cursor, whose horizontal and vertical movements were mapped to the activation magnitudes of the EMGs from the BRD and BI, respectively (Fig. 1B). The main goal was to consciously elevate the activation of a muscle while suppressing another muscle, chosen randomly for each trial: BRD as an activation-targeted (ACT) muscle and BI as a suppression-targeted (SUP) muscle in BRD-ACT trials, and vice versa in BI-ACT trials. Successful target matching requires strategically modulating muscle activation to direct the cursor from the baseline location to a square target area and maintain it in the area for 1 s (Hold period). Prior to each training session, the activation magnitudes of the BRD and BI during maximum voluntary contraction (MVC) were measured and used to optimize the target area. The square target area was defined by 40–70% of the ACT muscle's MVC level and 0–30% of the SUP muscle's MVC level. Each session, lasting an hour, consisted of three 15-minute training blocks and short rests, aiming to match as many targets per block as possible. To compare task performance across participants, the number of targets matched in each session was normalized to each individual's maximum number of targets matched across all training sessions.

Changes in intermuscular coordination during the training period were measured via untrained isometric reaching in a three-dimensional virtual force space using KULSIS at Weeks 0, 2, 4, and 6. Seated participants, in the same position as during training, navigated a virtual ball toward one of 54 target directions in three-dimensional space on a display by applying force at the handle (Fig. 1C). Each trial presented a randomly ordered target; participants guided the ball to the target and held it within a logical radius of the target for 1 s (Hold period) before the designated 7-second window elapsed. The assessment had two conditions: "Habitual" and "As-Trained", where participants followed their usual motor strategies or applied the trained strategies, respectively. For the Week 0 As-Trained session, general verbal advice was provided, as no new strategies had yet been developed (For facilitating BI

activation, participants received verbal instructions to 'squeeze the handle outward while generating force medially.' For BRD activation, verbal instructions to 'squeeze the handle inward while generating force upward' were provided prior to the assessment.). Participants who were already able to activate BRD and BI independently before training were excluded from the study. Our previous study provides more details about the training and assessment [21].

Signal-to-Signal Ratio (SSR) Analysis

To assess the training's influence on the activation of the targeted muscle pair derived from the raw EMGs, the signal-to-signal ratio (SSR) [21] was computed as follows for each training session:

$$SSR = \left(\frac{RMS(|EMG_{ACT}| / \max(|EMG_{ACT}|))}{RMS(|EMG_{SUP}| / \max(|EMG_{SUP}|))} \right)^2$$

1

In the equation, EMG_{ACT} is the concatenated Hold period EMGs of the ACT muscle across matched trials, while EMG_{SUP} is that of the SUP muscle. Before each concatenation, all EMGs were adjusted to be zero-mean and rectified. Following concatenation, the EMG amplitude for each muscle was normalized with respect to its maximum value.

Muscle Synergy Analysis

Muscle synergies were identified from the recorded EMGs during isometric force matching assessments using the NMF method, as outlined in previous studies [9, 11, 21, 28, 29, 33]. Before applying NMF, the raw EMGs underwent several preprocessing steps: noise filtering using a level-7 sym4 wavelet method to remove electrocardiogram (ECG) artifacts, demeaning to subtract baseline amplitude, and full-wave rectification and low-pass filtering (using a 4th order Butterworth filter with a 10 Hz cutoff frequency). After preprocessing, the EMGs of each trial were segmented from the start of the Hold period to the end. The segmented EMGs were then concatenated into a single matrix and normalized to achieve a unit variance.

Utilizing the NMF algorithm, the normalized EMG matrix was reconstructed into a linear combination of a muscle synergy set (W) and its corresponding activation coefficients (C) as expressed by

$$EMG_{reconstructed} \cong W_{M \times S} \bullet C_{S \times N}$$

2

In this equation, W is an M (total muscles) by S (muscle synergies) matrix, and C is an S by N (data sample) matrix. For any given S value, W and its corresponding C were derived from a randomly chosen 60% of the given EMG data, whereas the remaining 40% was reconstructed using the selected subset [30, 50]. After 100 iterations of this identification-reconstruction cycle, the muscle synergy set with the highest global variance accounted for (gVAF) was selected from the 100 sets.

The optimal S value corresponding to a given EMG dataset was estimated using three criteria: gVAF, diffVAF (the difference in gVAF, calculated by adding an extra synergy to a given S), and mVAF (the VAF value for each muscle). The estimate for the number of muscle synergies was based on the S value that met the conditions of $gVAF > 90\%$, $diffVAF < 3\%$, and $mVAF > 65\%$ [21].

Changes in muscle synergy composition were quantified using a similarity score (R), calculated using the scalar product of comparative W values [21, 28, 29, 33]. The average similarity scores of the total muscle synergy set and the trained muscles (BRD & BI) dominant synergies were analyzed over weeks for both Habitual and As-Trained conditions. With respect to the C values, the mean value of each trial was calculated to produce an activation profile of the corresponding W. Each C value was multiplied by the normalized force components to study the force mapping of the activation profile.

Behavior Outcomes and Clinical Measurements

Before each training session, the maximum forward pushing and backward pulling forces (MFF and MBF) were measured under isometric conditions using the KULSIS to assess the training effect on force generation levels for all participants. The backward pulling direction was specifically chosen because the targeted muscles (BRD and BI) are primarily involved in elbow flexion, which requires pulling backward under our isometric conditions. Forward pushing force was also measured to evaluate any indirect training effects on the antagonistic muscle groups. Additionally, for the stroke group, the maximum upward and forward arm reaching distances (MUR and MFR) relative to the center of the shoulder were assessed to examine training effects on shoulder function, as previous findings from our study with young healthy participants indicated shoulder involvement [21]. Lastly, maximum wrist pronation and supination angles (MPA and MSA) relative to the neutral resting position were specifically measured, given that the targeted muscles (BRD and BI) also contribute to wrist rotation. In addition to the behavior outcomes, anecdotal data were collected from each stroke participant to capture any noticeable changes in their daily life motor function. Before and after the six-week training period, the FMA-UE, Wolf Motor Function Test (WMFT), and Modified Ashworth Scale (MAS) were performed on the stroke group to quantify the training effect on their motor function and impairment levels.

Statistical Analyses

To test the normality of data distribution, the Kolmogorov-Smirnov test ($\alpha = 0.05$) was used, and the estimated number of muscle synergies satisfied the condition of normality, while the rest of the outcome measurements had a non-normal distribution. Therefore, a two-way ANOVA was used to test the statistical significance of the change in the estimated number of muscle synergies. Friedman tests and Wilcoxon Signed Rank tests with Bonferroni corrections were used to test the non-normally distributed features. For the significance of the similarity score of the muscle synergies in comparison, a similarity threshold ($Th_{sim}=0.76$), calculated as described in previous studies [21, 28, 29, 33], was further applied to ensure significance ($\alpha = 0.05$).

Results

Improvement in the Performance of the Training Task

Over the course of the six-week training period, improvements in the motor control of each targeted muscle (BRD and BI) were observed in both the age-matched control and stroke groups. During this training, the participants learned how to consciously amplify the activation of the ACT muscle while concurrently suppressing the activation of the SUP muscles (Fig. 2A). Compared to the first training session (T1), a distinct enhancement in SSR was noted from Week4 (T13) in both groups, regardless of the targeted muscle (age-matched control: 14 ± 0.25 (BRD-ACT at T13), 13 ± 0.25 (BI-ACT at T13), 1.9 ± 0.43 (BRD-ACT at T18), 1.7 ± 0.18 (BI-ACT at T18); stroke: 14 ± 0.13 (BRD-ACT at T13), 16 ± 0.16 (BI-ACT at T13), 1.18 ± 0.16 (BRD-ACT at T18), 2.1 ± 0.45 (BI-ACT at T18); Wilcoxon Rank-Sum test, $p < 0.05$) (Fig. 2B). This rise in SSR conspicuously led to an improvement in training task performance, expressed as an increased number of matched targets (age-matched control: 0.1 ± 0.05 (T1) & 0.9 ± 0.05 (T18); stroke: 0.29 ± 0.28 (T1) & 0.81 ± 0.21 (T15)) (Fig. 2C).

Muscle Synergy Analysis (1) - Number of Muscle Synergies

The optimal number of muscle synergies estimated based on the VAF criteria for each participant typically ranged from four to five in both groups. As summarized in Table 1, the average number of muscle synergies identified before training started (Week0) was 5.0 ± 0.82 for the age-matched group, regardless of the assessment condition. For the stroke group, 5.3 ± 1.1 and 5.0 ± 1.0 were obtained for Week0 Habitual and As-Trained conditions, respectively. Post-training (after six weeks), the average count in the age-matched control group rose to 5.2 ± 1.3 (Habitual) and 5.2 ± 0.96 (As-Trained) and reduced to 4.7 ± 1.1 (Habitual) and 4.7 ± 0.58 (As-Trained) in the stroke group. However, these changes were not statistically significant (ANOVA; $p = 0.43$). Similarly, no statistical difference was observed in the average number of muscle synergies during the intermediate weeks (Week2 and Week4) compared to Week0 for both group (ANOVA; $p > 0.18$). Therefore, the remainder of the muscle synergy analysis focused on five synergies.

Table 1
Estimated number of muscle synergies (mean $\pm$ SD).

Groups	Conditions	Week0	Week2	Week4	Week6
Age-Matched Control (n = 3)	Habitual	5.0 ± 0.82	5.7 ± 1.3	5.0 ± 0.82	5.2 ± 1.3
	As-Trained	5.0 ± 0.82	5.0 ± 0.82	4.7 ± 0.50	5.2 ± 0.96
Stroke (n = 4)	Habitual	5.3 ± 1.1	4.7 ± 0.58	4.7 ± 1.1	4.7 ± 1.1
	As-Trained	5.0 ± 1.0	4.7 ± 1.1	4.3 ± 0.58	4.7 ± 0.58

Muscle Synergy Analysis (2) - Muscle Synergies Composition

Typically, a set of five muscle synergies reflects the intermuscular coordination involved in the control of the elbow, shoulder joint, and scapula. The muscle synergies identified in age-matched control participants under Habitual at Week0 included (1) elbow flexor (E-Flex_{AC}; BRD and BI), (2) elbow extensor (E-Ext_{AC}; TRlLong and TRlLat), (3) shoulder adductor/flexor (S-AF_{AC}; AD, MD, and PECT), (4) shoulder abductor/extensor (S-AE_{AC}; MD and PD), and (5) scapula retractor (SR_{AC}; UpTrp and InfSp). Under the As-Trained condition at Week0, the muscle synergies generally shared a similar composition with the Habitual muscle synergies. Following two weeks of training, modifications in muscle synergies began to manifest and consolidate through Weeks 4 and 6. The muscle synergy set with the newly developed synergies included (1) a combination of BRD, S-AF_{AC}, and SR_{AC} (BSS_{AC}); (2) BI dominant E-Flex with minor MD and PECT (BI-EF_{AC}); (3) E-Ext_{AC}; (4) S-AF_{AC}; and (5) S-AE_{AC}. Initially at Week2, TRlLong and AD were involved in the development of BI-EF and S-AE. However, they stabilized in E-Ext_{AC} and S-AF_{AC}, respectively, as training progressed (Fig. 3A).

For the stroke group, the muscle synergies identified under the Habitual condition at Week0 were (1) E-Flex_{ST}, (2) E-Ext_{ST}, (3) S-AF_{ST} (AD and MD), (4) S-AE_{ST} (PD and InfSp), and (5) SR_{ST} (PECT, UpTrp, and InfSp). Similar to the age-matched control group, changes in muscle synergy progressively emerged from Week2 under the As-Trained condition. The newly acquired synergy set consisted of (1) BRD dominant E-Flex (BR-EF_{ST}), (2) BI dominant E Flex with E-Ext_{ST} (BEE_{ST}), (3) E-Ext_{ST}, (4) S-AE_{ST}, and (5) SR_{ST} (UpTrp and InfSP with minor AD and MD). BEE_{ST} started with a form of BI-triceps (TRlLong and TRlLat) co-activation, but the involvement of the triceps was mitigated from BEE_{ST} and increased in E-Ext_{ST} after six weeks of training. Simultaneously, AD and MD interfered with E-Ext_{ST} when the new muscle synergies were introduced at Week2 but contributed more to SR_{ST} at Week6 (Fig. 3B).

According to the group mean similarity index, the overall composition of the Habitual muscle synergies in the age-matched control group remained consistent throughout the training period ($R > Th_{sim}$). However, distinct compositional changes were evident in As-Trained muscle synergies from Week2 ($R = 0.47$ at Week2, 0.38 at Week4, and 0.29 at Week6) and showed a markedly different composition compared to Habitual muscle synergies by Week6 ($R = 0.32$). Similarly, the stroke group showed conserved muscle synergy composition under Habitual condition from Week0 to Week6, and significant dissimilarity was observed in As-Trained muscle synergy composition from Week2 ($R = 0.66$ at Week2, 0.69 at Week4, and 0.60 at Week6; Fig. 4A). Even when considering only BRD and BI dominant synergies, the similarity index of As-Trained synergy composition decreased in Week6 for both age-matched control and stroke groups ($R = 0.57$ for age-matched control, $R = 0.61$ for stroke). Moreover, both groups exhibited a significant difference in the similarity index between the Habitual and As-Trained synergy composition at Week6 ($R = 0.71$) (Fig. 4B).

Muscle Synergy Analysis (3) - Muscle Synergies Activation Profile

The muscle synergy activation profile captures the development and preservation of new intermuscular coordination from the perspective of the biomechanical actions of the muscles in three-dimensional

force generation. In the age-matched control group under the Habitual condition, E-Flex_{AC} was primarily activated while matching targets in the medial-backward-upward directions, whereas its antagonistic counterpart, E-Ext_{AC}, was employed for targets in the opposite directions. Shoulder muscle synergies, S-AF_{AC} and S-AE_{AC}, were engaged for targets positioned in the up and down regions of the force space, respectively. The SR_{AC} was mainly activated to match the medial-lateral and upward targets. Under the As-Trained condition, BSS_{AC} and BI-EF_{AC}, which emerged from Week2, displayed an activation profile tuned towards the upward-backward and medial directions, respectively (Fig. 5A, Supplementary Fig. 1).

The stroke group's activation profiles of the Habitual muscle synergies exhibited characteristics similar to those of the age-matched control group, but with a lower magnitude in S-AF_{ST}, S-AE_{ST}, and SR_{ST}. The As-Trained muscle synergies, prior to training, presented activation profiles mirroring the Habitual muscle synergies. Upon the modulation of the muscle synergy set starting from Week2, the newly developed muscle synergies, BR-EF_{ST} and BEE_{ST}, revealed activation profiles that recapitulated the features of E-Flex_{ST} and a combination of E-Flex_{ST} and E-Ext_{ST}, respectively. In the case of SR_{ST}, as the contributions of AD and MD within its composition increased during the later stages of training, the activation profile was tuned more towards the upward force directions (Fig. 5B, Supplementary Fig. 2).

Changes in the Motor Function and Clinical Measurements

The six weeks of training influenced not only muscle synergy composition and activation but also upper extremity (UE) motor function of the participants. In the isometric force generation assessment, the age-matched control group demonstrated an overall significant improvement in the MBF across 18 training sessions (Friedman test; $\chi^2=36$, $p = 0.021$). For the stroke group, a significant overall improvement was observed in the MFF (Friedman test; $\chi^2=29$, $p = 0.026$; Fig. 6A). Additionally, stroke participants showed significant improvements in the maximum upward (MUR) and forward (MFR) reaching distances of the more affected UE (Friedman test; $\chi^2=46$, $p = 0.0001$ for MUR, $\chi^2=37$, $p = 0.0021$ for MFR). Notably, the increase in MUR was more pronounced throughout the six-week period (at T9: MUR increased by 8.7 cm and MFR by 4 cm; at T18: MUR increased by 27 cm and MFR by 6 cm; Fig. 6B). Regarding wrist rotation, stroke participants exhibited significant improvements in both MPA and MSA starting from the early stages of training (Friedman test; $\chi^2=41$, $p = 0.0005$ for MPA, $\chi^2=31$, $p = 0.0146$ for MSA). Compared to baseline (T1), MPA and MSA improved by 14 ° and 7.3 °, respectively, at T9, further increasing to 37 ° and 14 °, respectively, at T18 (Fig. 6C). None of the measures met the criteria for significance in the Wilcoxon signed-rank test at any individual assessment point during training.

Improvements in the motor function of stroke-affected upper extremities (UE) were also consistent with anecdotal data gathered during the training period. As summarized in Table 2, all four stroke participants reported that they started to experience stronger pushing and pulling with the more affected side of the UE during Week1. Regarding arm outreach and retraction speed, two participants (ST001 and ST004) noted significant improvement during Week1, with another participant (ST003) reporting the same at the end of Week2. In a similar vein, three participants (ST001-3) found that they were able to elevate their more affected UE higher than before in everyday life during Week1, with one participant (ST004)

recognizing this improvement in the Week2. Interestingly, the three patients who reported elevation enhancement by Week1 also indicated reduced UE pain or spasticity within the same week. When asked about long-term arm usage leading to fatigue, two stroke participants reported improvement: one (ST002) at the end of Week1 and the other (ST001) at the end of Week2. Finally, three participants (ST001, 3, and 4) observed that dressing became easier either during Week1 or Week2.

Table 2

Time points when stroke participants first noticed motor function changes in daily life activities. The number indicates the participant ID (ST00X).

	Training Sessions											
	T1	T2	T3	T4	T5	T6	T7	T8	T9	T10	T11	T12
Stronger pushing				2	1,3,4							
Stronger pulling				2	1,3,4							
Faster reaching out movement				1	4				3			
Faster pulling back movement				1	4				3			
Higher arm lifting				2	1,3			4				
Reduced pain when arm lifting/reaching				2	1							
Reduced spasticity in shoulder or arm					1,3	2						
Less tiring when using arm for a long time						2				1		
Easier dressing					1,3			4				

Clinical assessments further emphasized the positive changes in the trained upper extremity (UE) in stroke participants. Three of these participants (ST002-4), who completed pre- and post-training clinical assessments, exhibited marked improvement in several aspects of UE, including impairment level (FMA-UE), motor function (WMFT), and spasticity (MAS). Based on the FMA-UE results, the total scores for ST002 and ST003 increased by 14 points from the respective initial scores of 41 and 55, while the score for ST004, who had a more severe initial impairment, improved by 5 points from 13. More specifically, in the case of ST002, the upper extremity, wrist, hand, and coordination/speed subscores increased by 8, 3, 2, and 1 points, respectively. Similar increments of 7, 3, 2, and 2 points were observed in the same subscores for ST003. For ST004, though, improvements were confined to the upper extremity and hand subscores, by 3 and 2 points respectively (Fig. 7A). As for the WMFT outcomes, ST002 showed an increase from 60 to 61 points, while ST003 and ST004 manifested 8-point and 4-point increases from initial scores of 43 and 27, respectively (Fig. 7B). Correlatively, the MAS score readings indicated the

most significant improvement for ST003, dropping from 34 to 21, while the other two cases showed either no difference (ST002) or a marginal improvement (ST004; from 9 to 7), as shown in Fig. 7C.

Muscle Synergy and Clinical Measurements

Preliminary observations suggest a potential association between alterations in the composition of muscle synergies and outcome measures from clinical assessments within the stroke group. Regarding the FMA-UE score, stroke participants ST002 and ST003, who showed relatively moderate impairment before training, exhibited more significant changes in the composition of BRD&BI dominant muscle synergies after training than ST004, the participant with severe impairment (Fig. 7D). Additionally, the two participants with a relatively low similarity index of synergy composition demonstrated greater improvement in their FMA-UE scores (Fig. 7E). Considering the analysis between the similarity index and the WMFT and MAS, only ST003 and ST004 manifested an association similar to that observed in the FMA-UE vs similarity index analysis (Figs. 7F-G).

Discussion

Building upon our recent study on young healthy adults [21], this pilot study further demonstrated the feasibility of developing new intermuscular coordination patterns and expanding the repertoire of muscle synergies in chronic stroke through an EMG-guided exercise, facilitated by human-machine interaction, as well as its positive influence on post-stroke motor function and impairment. The six-week training targeted developing new intermuscular coordination patterns by decoupling a pair of the two natural elbow flexor muscles, BRD and BI. Both stroke and age-matched, healthy control groups successfully learned how to consciously amplify the activation of the ACT muscle while concurrently suppressing the activation of the SUP muscle. Although the exercise did not affect the number of muscle synergies, changes in synergy composition progressively emerged from Week2 and consolidated through Week4 and 6. As a new muscle synergy was developed, improvements in motor function of the trained UE were observed, along with evident post-training gains in clinical assessment scores within the stroke group.

The impact of rehabilitation training on stroke survivors, specifically on their muscle synergy attributes, has been the focus of several recent studies. For instance, the utilization of an assistive exoskeleton in a rehabilitation protocol, as shown by Pierella et al. [38] and Luzio et al. [39], resulted in clinical improvement in stroke-affected UE. This clinical progress positively correlated with the similarity of muscle synergy to healthy individuals or the less-affected UE. Pierella et al. also noted an increase in the number of muscle synergies in the affected UE following training. Another stroke study, which showed improved UE kinematics after a robot-assisted rehabilitation, found that the activation profiles of the affected UE after training were mostly modified, while the number and the composition of muscle synergies were preserved [40]. Similarly, in a pilot study done by Tropea et al. [41], the number of muscle synergies remained consistent, although subtle changes in synergy composition occurred among stroke participants after a 6-week robot-assisted treatment. Other studies involving stroke neurorehabilitation

through functional electrical stimulation [42] and brain-machine interface [43] associated enhanced motor function of the impaired UE with increased similarity between muscle synergy in the affected UE and those in controls. Notably, these studies used muscle synergies as a measure of a training protocol's efficacy, not as a direct target within the training itself.

To our knowledge, there has been scant research focused on fostering new intermuscular coordination patterns in the stroke-affected upper extremity (UE) to improve motor function. Recent studies have concentrated on reducing pairwise co-activation of UE muscles using a myoelectric-controlled interface (MCI) in stroke patients. For instance, Jian et al. [44] explored the effects of one-dimensional and two-dimensional MCI training on elbow muscle pair co-activation in stroke patients. Their study showed that increasing MCI dimensionality effectively reduced antagonist muscle activation while enhancing activation in the prefrontal and primary motor cortices. Additionally, Mugler et al. [45] conducted a six-week MCI training under isometric and unrestricted movement conditions with chronic stroke survivors who had moderate-to-severe arm impairments. This intervention successfully reduced co-activation in targeted muscle pairs, resulting in improved motor function and reduced impairment levels. This finding was further investigated through muscle synergy analysis in a follow-up study by Seo et al. [46]. Although no consistent changes were observed in synergy composition across participants, responders showed increased disparity in muscle weights of targeted muscle pairs within synergy composition vectors after training. In addition to studies focused on pairwise muscle co-activation, Seo et al. [47] also investigated modifying the activation patterns of four muscles in the more affected arm of stroke survivors. This study aimed to mimic the activation patterns of the less affected arm using an MCI protocol and documented improvements in arm motor function. Collectively, these studies illustrate the potential to modify intermuscular coordination patterns through targeted rehabilitation protocols. By demonstrating the feasibility of eliciting new muscle synergies and expanding the repertoire of muscle synergies readily available in the stroke-affected UE and their beneficial effects on motor function and impairment, our study further supports muscle synergy as a potential target for enhancing motor recovery in stroke patients.

In this study, the development of new muscle synergy in the stroke-affected UE was not associated with an increase in the number of synergies required to accomplish the task. Instead, it was acquired through expanding the repertoire of naturally expressed intermuscular coordination patterns. As investigated in the studies mentioned earlier [38–43], the debate continues regarding whether an increase in the number of muscle synergies effectively improves motor outcomes post-stroke. This lack of relationship between the number of muscle synergies and motor function was observed even in the age-matched control group as well as in the young healthy group from our previous study [21]. Additionally, when comparing the stroke and age-matched control groups, no statistically significant differences in the number of synergies were observed throughout the training period. A previous stroke study [33] utilizing a three-dimensional isometric force generation setup similar to the KULSIS system used in the current study also reported minimal differences in the number of UE muscle synergies between stroke and control groups. This consistency in the number of UE muscle synergies across different groups may be

attributed to the nature of the isometric task, which involves constrained UE movements and compensation for gravity.

While the number of muscle synergies remained consistent, the composition of the naturally expressed (Habitual) muscle synergy also did not show significant modulation throughout the training period in either group. No clear differences in the composition of Habitual synergies involving the elbow joint were observed between the control and stroke groups. However, the stroke group's Habitual SR_{ST} synergy included an atypical co-activation of PECT and the back muscles (UpTrp and InfSp), compared to the age-matched control group's Habitual SR_{AC} composition. This abnormal co-activation aligns with findings from Silva et al. [48], who reported higher co-activation ratios of the sternal head of the pectoralis major and latissimus dorsi on the contralesional side of stroke-affected UEs compared to healthy controls. Due to the involvement of PECT in back muscle activation after stroke, the SR_{ST} activation profile showed reduced involvement in force generation in the upward direction (Fig. 5B, Supplementary Fig. 1).

Both healthy control and stroke groups successfully developed muscle synergies through decoupling BRD and BI after training; however, abnormalities in muscle synergies of the stroke-affected UE prior to training could have led stroke survivors to develop new synergies with different characteristics. When BRD was decoupled from BI in the healthy control group, it formed a new synergy (BSS_{AC}) with the back muscles, contributing to greater upward and lateral force generation. In contrast, the newly developed elbow flexor synergy in the stroke group ($BR-EF_{ST}$) involved isolated BRD activation only. The back muscles remained as a separate synergy (SR_{ST}) with minor AD and MD involvement, while PECT contributed to the newly formed BI-dominant synergy (BEE_{ST}). The decoupling of PECT and the addition of the shoulder abductor/flexor muscles in SR_{ST} could affect its activation profile to focus more on the upward direction in the force space (Fig. 5B, Supplementary Fig. 2).

The targeted muscle pair, BI and BRD, is primarily involved in elbow flexion; however, each muscle also contributes to forearm supination and pronation, respectively. Therefore, wrist control could be crucial for isolating these targeted muscles from each other within our protocol. Under our isometric condition, in which hand and wrist movements were restricted by the gimbal handle of the KULSIS system, wrist supination required participants to generate medial-directed force with the palm while simultaneously pulling the handle in the opposite direction with the fingers. As a result, PECT, primarily activated during medial force generation, became strongly associated with BI activation, as observed in the age-matched group's newly developed BI-dominant muscle synergy ($BI-EF_{AC}$).

A similar approach for BI isolation was observed even in the stroke group. However, for the stroke-induced UE motor impairment, not just the PECT-back muscles (UpTrp and InfSp) coactivation but also the wrist impairment, appeared to disrupt learning new motor strategies aimed at dissociating BI activations from BRD activation. Previous studies have shown that stroke can cause spasticity and contractures at the wrist [49, 50], and stroke survivors who participated in this study exhibited wrist

impairment at baseline (FMA-UE wrist subscore; ST002: 6, ST003: 3, ST004: 0). To compensate for these impairments during isolating BI activation, the triceps were additionally recruited to support medial force generation, leading to the development of the BEE_{ST} synergy.

These stroke-induced motor impairments in the UE also likely affected the rate of developing new intermuscular coordination patterns. Specifically, the stroke group required a longer training period to consolidate the composition of newly developed muscle synergies reflecting BRD-BI decoupling. While the age-matched healthy participants clearly established their new synergies (BSS_{AC} and $BI-EF_{AC}$) within four weeks, stroke participants needed six weeks for their new muscle synergies ($BR-EF_{ST}$ and BEE_{ST}) to stabilize. Considering that young healthy participants required only two weeks to develop new muscle synergies [21], aging may also be an important factor influencing motor learning speed in this training protocol. Moreover, even within the stroke group, the initial severity of impairment appeared to influence the development of new muscle synergies differently. Specifically, participants who exhibited relatively more severe impairment at baseline showed changes in synergy composition after training less clearly compared to participants with mild-to-moderate impairment. This suggests that individuals with severe impairment may require a longer training period to consolidate newly developed synergy patterns.

The changes in the As-Trained muscle synergies in the stroke-affected UE were reflected in the changes in the motor function involved in the muscles that were directly or indirectly affected by the training. As stroke participants learned to intentionally dissociate BRD-BI coupling and developed new muscle synergies, their maximum wrist pronation and supination angles were noticeably improved. Given that BI and BRD play roles in forearm supination and pronation, respectively, training BI and BRD isolation could positively impact wrist impairment. Clinically, two stroke participants showed a 3-point increase in the FMA-UE wrist subscore, and an average 2-point decrease in the MAS forearm supination/pronation score. Moreover, as a byproduct of BEE_{ST} development, the As-Trained- SR_{ST} synergy with mitigated PECT involvement and increased AD and MD contribution possibly benefited the stroke participants' motor function in upward arm reaching. Compared to the pre-training performance, the maximum upward reaching distance improved significantly throughout the training, which was reflected in the increased shoulder-related FMA-UE subscores in all the stroke participants who completed the pre- and post-training clinical assessments (increase of 5, 4, and 3 points in ST002, ST003, and ST004, respectively). Two participants also displayed reduced spasticity in the shoulder (shoulder-related MAS score; 4 points decrease in ST003 and 2 points decrease in ST004). Interestingly, the FMA-UE joint pain score, assessed separately from the motor function score, indicated that ST002 and ST003 experienced less pain in their shoulder after training. (ST002 and ST003 had 3 and 4 points increased, respectively.) In the WMFT, all three stroke participants showed improvements specifically in tasks 1–6, which are timed functional tasks involving the shoulder, elbow, and forearm. (ST002, ST003, and ST004 improved 2, 10, and 3 points, respectively.) Anecdotal reports further indicated improved motor function and reduced pain in daily activities involving coordinated elbow and shoulder movements, even during the early stages of developing new intermuscular coordination patterns. Considering the clinically important differences for each clinical measure reported in previous studies (FMA-UE: 4.25–7.25 points [51];

WMFT functional ability score: 0.2–0.4 points [52]; MAS: 0.48–0.76 points [53]), our preliminary results suggest that training-induced changes in muscle synergies may positively influence motor impairment and function in the stroke-affected UE.

A potential neural mechanism underlying the development of new muscle synergies observed in our stroke participants may involve adaptive plasticity within motor pathways responsible for fractionated upper limb movements. After the stroke, damage to the corticospinal tract and increased reliance on the reticulospinal tract commonly result in abnormal muscle co-activation and reduced fractionation of movements [54–57]. Our training protocol possibly enabled stroke survivors not simply to reweight muscle activations within existing synergies, but rather to expand their repertoire of intermuscular coordination patterns by developing entirely new muscle synergy patterns. This finding suggests that participants possibly retained or regained some corticospinal tract functionality, allowing the development of new motoneuron networks to compensate for the impairment. Based on our preliminary transcranial magnetic stimulation (TMS) findings, we observed increases in the motor evoked potential (MEP) peak-to-peak amplitude of the BRD muscle following a six-week rehabilitation exercise intervention, in two stroke survivors and one healthy participant. (see Supplementary Fig. 3) Such findings could indicate modulation of corticospinal excitability in these individuals, along with a possible enhancement in corticospinal tract integrity to the BRD muscle in the stroke participants [58–61]. These neurophysiological changes, accompanied by improvements on the FMA-UE assessment, enhanced motor function, and an expanded repertoire of muscle synergies, suggest the intervention's potential to promote adaptive plasticity in the primary motor cortex (M1) and downstream motor pathways, thereby supporting functional recovery [58, 59, 62, 63]. However, interpretation and generalization of our TMS findings remain limited by the small sample size (two stroke survivors and one healthy participant) and the inherently high variability of MEP amplitude. Notably, MEP measurements are known to be influenced by various factors such as attention, sleep duration, arousal, and daily fluctuations in cortical excitability, making MEP amplitude a highly variable metric even within the same individual [64]. Lastly, findings from our previous study [65] provided preliminary evidence of enhanced intermuscular connectivity (coherence) between BRD and BI muscles in the beta-band frequencies for stroke patients following same training. This preliminary finding suggests an increased level of common descending neural drive to both muscles—likely cortical in origin [66]—as the synergy repertoire expanded through training.

Despite the limited number of participants, our preliminary results demonstrate the feasibility of developing new intermuscular coordination patterns in the stroke-affected upper extremity (UE) through isometric EMG-guided training, as well as the positive impacts of these patterns on motor function and impairment. To further validate these findings, testing with a larger participant sample is necessary. Additionally, following our previous study on young healthy adults [67], future studies could incorporate analyses of cortico-muscular and cortico-cortical connectivity, along with measures of corticospinal excitability and inter-muscular connectivity, to systematically explore the potential neural mechanisms underlying the development of new intermuscular coordination patterns in stroke-affect UE. Another limitation of our current study is the absence of follow-up sessions beyond the six-week training period, since our primary goal was to evaluate the feasibility of inducing new muscle synergies in stroke-

affected UEs. Including follow-up assessments in future research would allow us to investigate the retention of changes in muscle synergies and their long-term effects on motor function and impairment. Finally, given that we have demonstrated the feasibility of developing new muscle synergies through targeted training of a single muscle pair, future studies could extend this approach by targeting activation patterns involving larger muscle groups. This expansion could facilitate the development of new muscle synergies tailored more effectively to each stroke survivor's specific impairments.

Conclusions

Extending our recent findings from young healthy adults, this pilot study further demonstrated the feasibility of using EMG-guided human-machine interaction training to expand the repertoire of habitual intermuscular coordination patterns in chronic stroke survivors. Although the total number of muscle synergies remained unchanged, distinct changes in synergy composition emerged progressively during training. These newly developed coordination patterns were associated with meaningful improvements in UE motor function and clinical outcomes in stroke survivors. Future studies with larger samples and longer training periods are needed to confirm these preliminary findings and further explore their underlying neural mechanism and clinical implications.

Abbreviations

UE	
upper extremity	
KULSIS	
KAIST Upper Limb Synergy Investigation System	
ACT	
activation-targeted	
SUP	
suppression-targeted	
SSR	
signal-to-signal ratio	

Declarations

Ethics approval and consent to participate

The study protocol was approved by the University of Houston Institutional Review Board, and each participant gave written informed consent before the eligibility assessment.

Consent for publication

Not applicable.

Availability of data and materials

The data used in this study may be made available by the corresponding author upon a reasonable request.

Competing interests

J-HP, HL and H-SP are inventors of the issued patent (South Korea, 10-2246686) for the design of the experimental device, which produces isometric conditions for the study's muscle synergy assessment and EMG-guided training task.

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Authors' contributions

GS completed the data collection and analysis and made significant contributions to the manuscript writing. MPJ and MH helped with data collection, data analysis, and manuscript writing. J-HP developed training software and helped with manuscript writing. HL helped with manuscript writing. SL, YZ, H-SP, and JR further refined the study design, helped analyze and interpret results, and wrote the manuscript. JR originally developed the study design. All authors read and approved the final manuscript.

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Figures

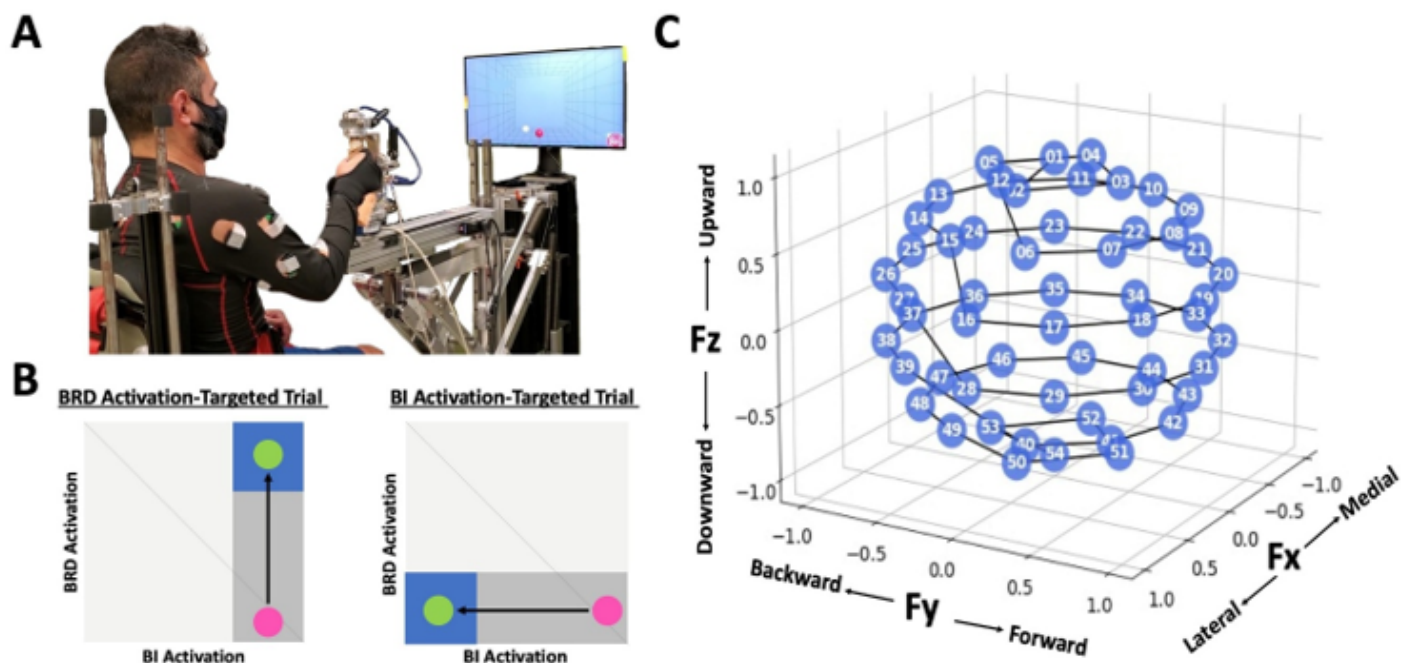


Figure 1

Experimental setup and overview of training and assessment tasks. **A**, KAIST Upper Limb Synergy Investigation (KULSIS). **B**, The EMG-guided training paradigm. The vertical and horizontal movement of a round cursor was mapped to the activation of the targeted muscle pair, brachioradialis (BRD) and biceps brachii (medial head; BI), respectively. The bottom right corner of the display indicates no activation of either targeted muscle, and the blue target zone represents the target area. (left: BRD activation-targeted trial, right: BI activation-targeted trial) **C**, The spatial distribution of 54 normalized force targets for the assessment. Fx, Fy, and Fz directions represent medial-lateral, backward-forward, and downward-upward directions, respectively. Each target has its own unique number assigned (1 to 54; top to bottom).

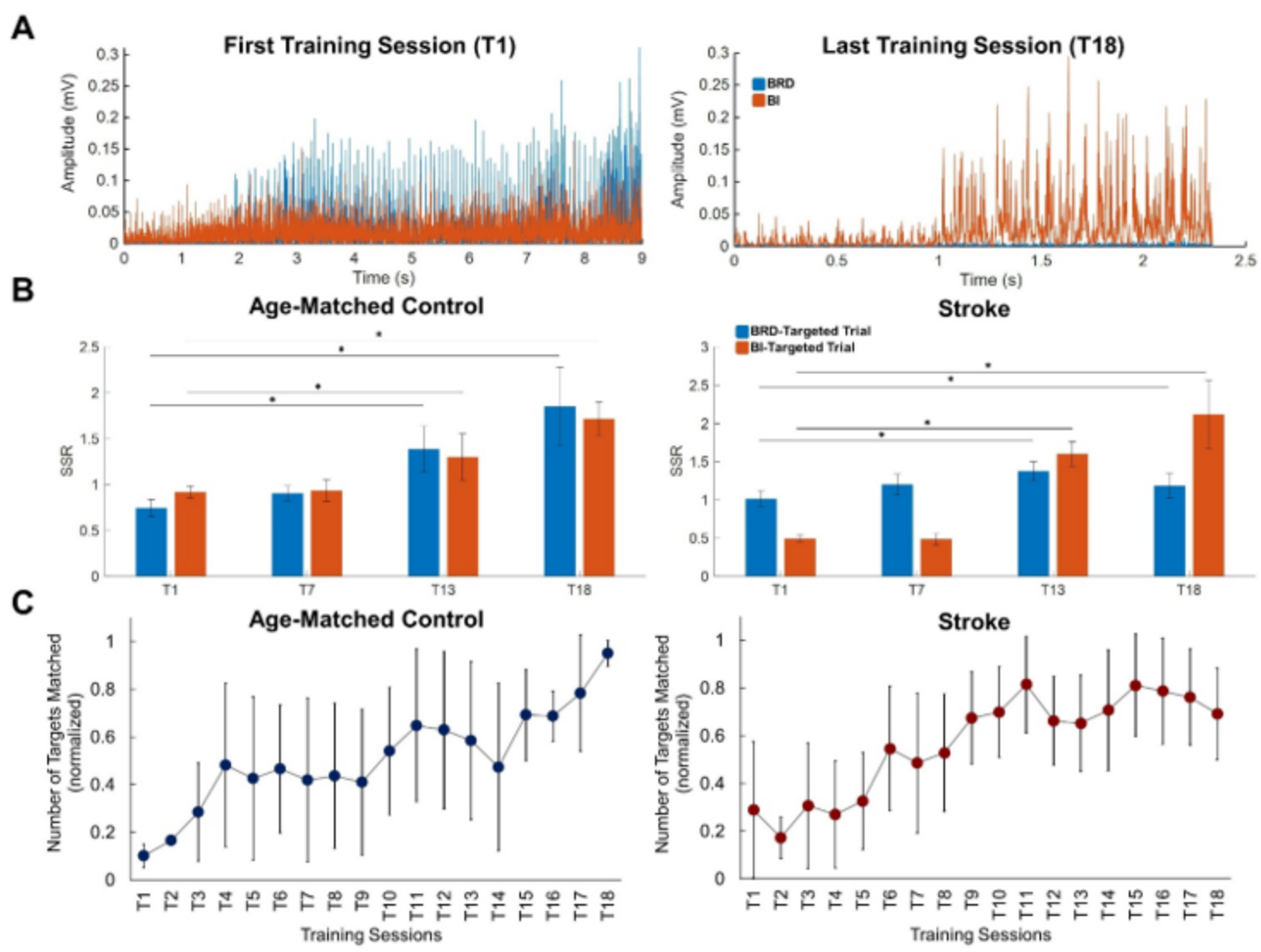


Figure 2

Changes in the targeted muscle activation and task performance across training sessions. **A**, Preprocessed EMG signals of brachioradialis (BRD; blue) and biceps brachii (BI; red) acquired from a

representative participant with stroke during the first (T1; left) and the last (T18; right) training sessions. **B**, Mean and SD of SSR measured at different training sessions for the age-matched control (left) and the stroke (right) groups (Wilcoxon Rank-Sum test; *, $p < 0.05$). **C**, Number of targets matched at each training session (T1-T18) (mean $\pm$ SD). The number of targets matched in each session was normalized to each individual's maximum number of targets matched across all training sessions.

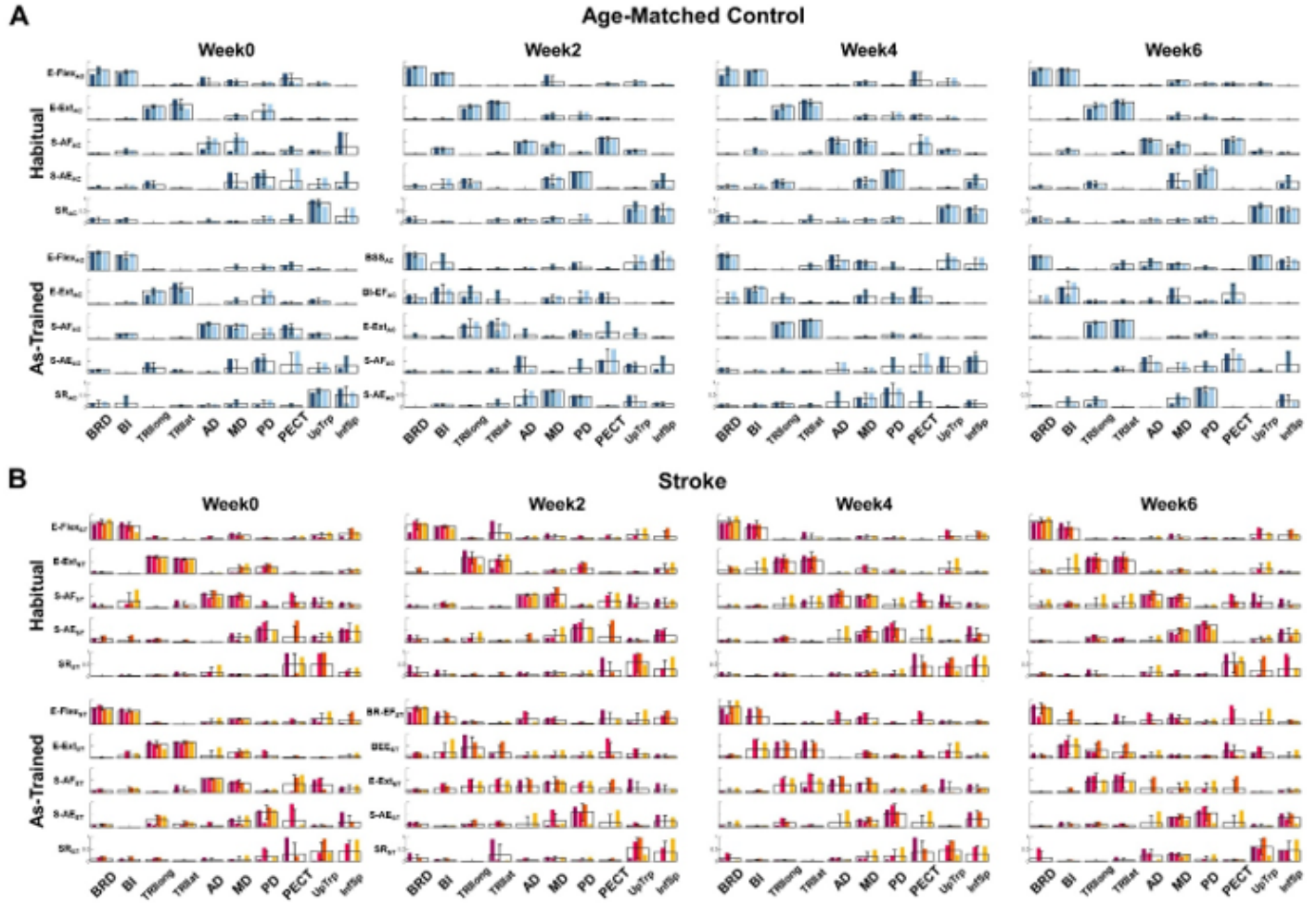


Figure 3

The composition of muscle synergies over the course of six weeks of training. The mean and SD of muscle weights, superimposed on the distribution of the muscle weights of participants, per each of five synergies identified in the assessment session at Weeks 0, 2, 4, and 6 under two conditions (Habitual and As-Trained). Each bar color represents each participant. The muscle set included brachioradialis (BRD), biceps brachii (BI), triceps brachii (long and lateral heads; TRlong and TRlat), deltoids (anterior, middle, and posterior fibers; AD, MD, and PD), pectoralis major (clavicular fibers; PECT), upper trapezius (UpTrp), and infraspinatus (InfSp). **A**, Five muscle synergies identified in age-matched control participants under Habitual and As-Trained conditions at each assessment week. Muscle synergies, identified under Habitual condition, included (1) elbow flexor (E-Flex_{AC}; BRD and BI), (2) elbow extensor (E-Ext_{AC}; TRlong and TRlat), (3) shoulder adductor/flexor (S-AF_{AC}; AD, MD, and PECT), (4) shoulder

abductor/extensor ($S-AE_{AC}$; MD and PD), and (5) scapula retractor (SR_{AC} ; UpTrp and InfSp). Under As-Trained condition, changes in the habitual muscle synergy set emerged from Week2: (1) a combination of BRD, $S-AF_{AC}$, and SR_{AC} (BSS_{AC}), (2) BI dominant E-Flex with minor MD and PECT ($BI-EF_{AC}$), (3) $E-Ext_{AC}$, (4) $S-AF_{AC}$, and (5) $S-AE_{AC}$. **B**, Five muscle synergies identified in stroke participants under Habitual and As-Trained conditions at each assessment week. Muscle synergies, identified under Habitual condition, included (1) $E-Flex_{ST}$, (2) $E-Ext_{ST}$, (3) $S-AF_{ST}$ (AD and MD), (4) $S-AE_{ST}$ (PD and InfSp), and (5) SR_{ST} (PECT, UpTrp, and InfSp). Under As-Trained condition, changes in the habitual muscle synergy set emerged from Week2: (1) BRD dominant E-Flex ($BR-EF_{ST}$), (2) BI dominant E Flex with $E-Ext_{ST}$ (BEE_{ST}), (3) $E-Ext_{ST}$, (4) $S-AE_{ST}$, and (5) SR_{ST} (UpTrp and InfSP).

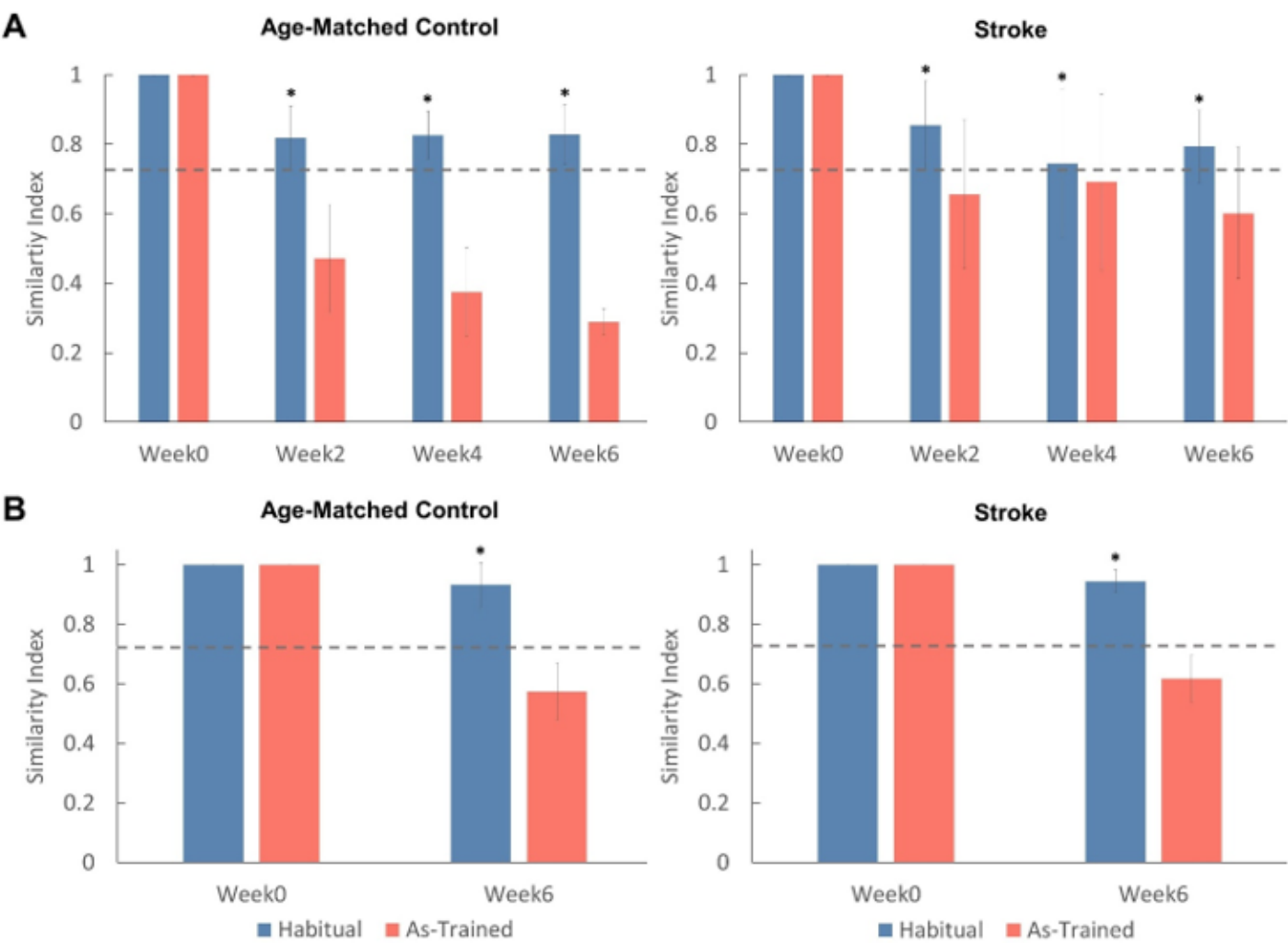


Figure 4

Quantification of changes in muscle synergy composition during training. **A**, The mean similarity of synergy composition (all five synergies) between the baseline (Week0) and the rest of the assessment weeks (Week2, 4 and 6) calculated for Habitual (blue) and As-trained (red) conditions. **B**, The similarity of

BRD & BI dominant synergy composition between Week0 and Week6. (mean $\pm$ SD). The dotted line indicates the similarity threshold ($Th_{sim}=0.76$); *, $p<0.05$.

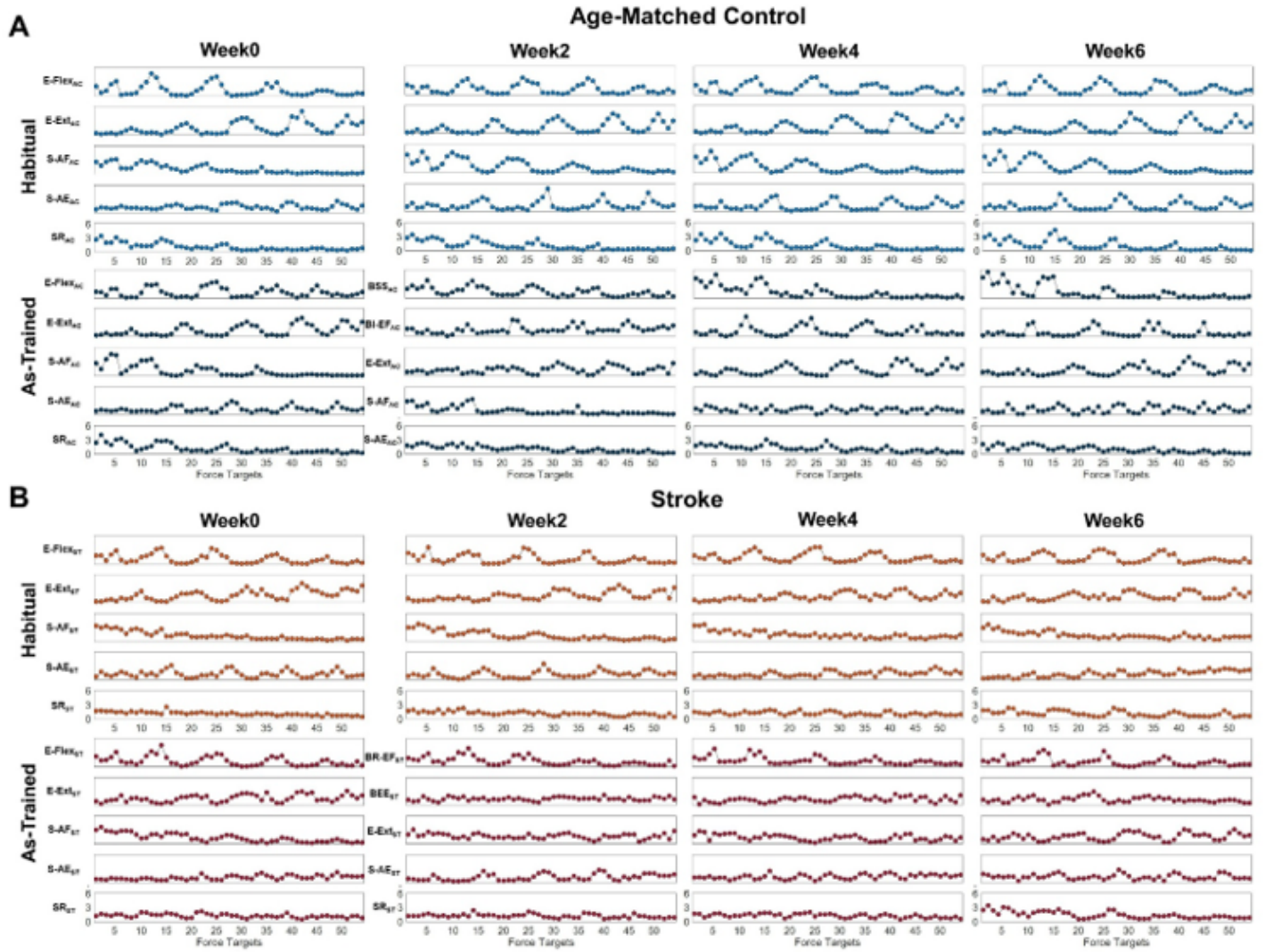


Figure 5

The group mean activation profile of muscle synergies during six weeks of the training period. **A**, Mean synergy activation coefficients of age-matched control group obtained during each target force matching under Habitual and As-Trained assessment conditions. **B**, Mean synergy activation coefficients of stroke group. Readers are referred to Fig.3 for abbreviations.

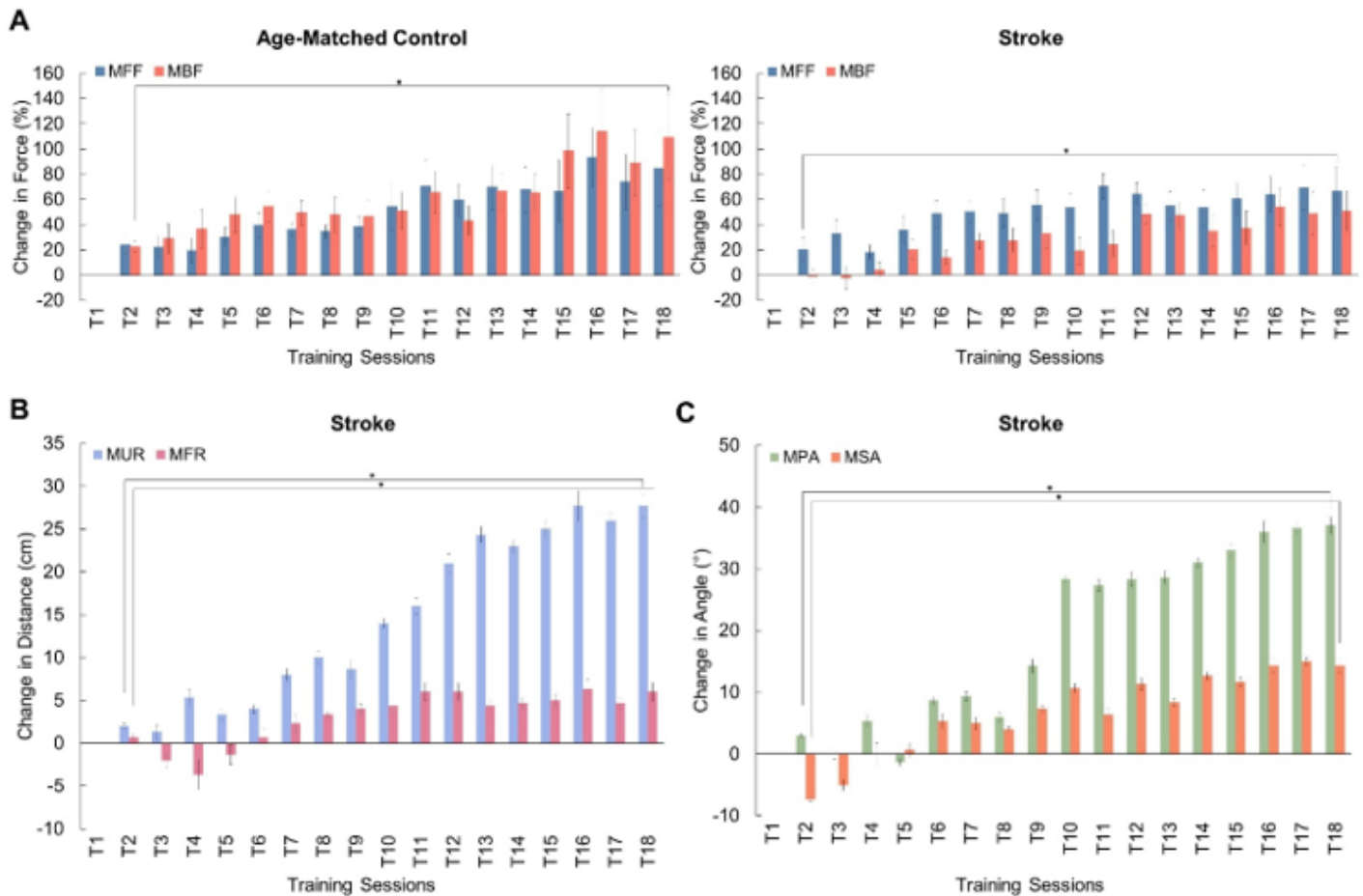


Figure 6

Changes in the motor functions during training compared to the initial training session. **A**, Percent change of the maximum forward pushing force (MFF; red) and maximum backward pulling force (MBF; blue) measured under isometric condition from age-matched control (left) and stroke (right) group. **B**, Changes in distance of the maximum upward arm reaching (MUR; purple) and maximum forward arm reaching (MFR; pink) in stroke group. **C**, Changes in angle of maximum wrist pronation (MPA; green) and supination (MSA; orange) in stroke (mean $\pm$ SE; Friedman test; *, $p < 0.05$).

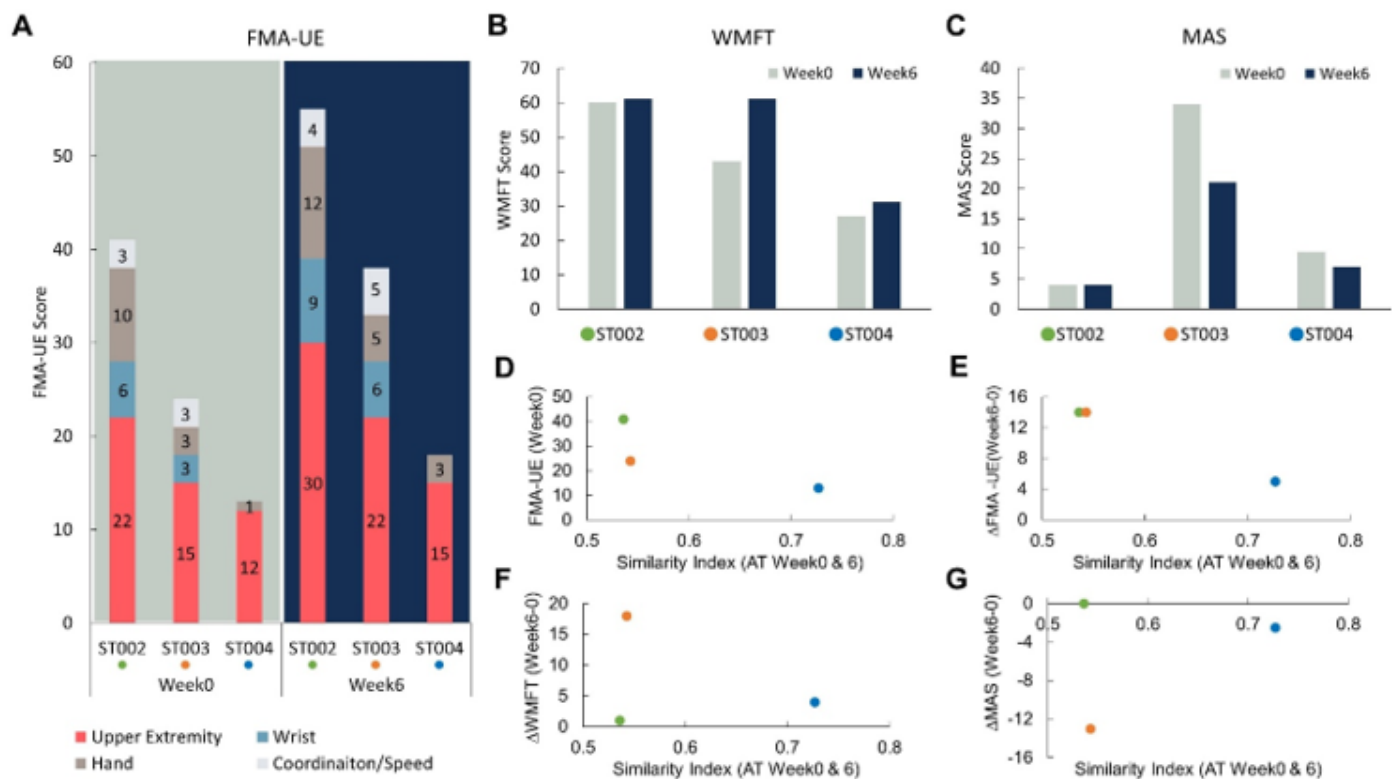


Figure 7

Clinical scores before and after training and correlation with muscle synergy similarity index. **A**, Total Fugl-Meyer Assessment Upper Extremity (FMA-UE) score and the subscores (Coordination/Speed; grey, Hand; brown, Wrist; blue, Upper Extremity; red). **B**, Wolf Motor Function Test (WMFT) score. **C**, Modified Ashworth Scale (MAS) score. **D**, The baseline FMA-UE at Week0 and the similarity of elbow flexion synergy composition measured under As-Trained condition at Week0 and Week6. **E**, The change in the FMA-UE score (Week6-Week0) and the similarity of elbow flexion synergy composition measured under As-Trained condition at Week0 and Week6. **F**, The change in WMFT score (Week6-Week0) and the similarity of elbow flexion synergy composition measured under As-Trained condition at Week0 and Week6. **G**, The change in MAS score (Week6-Week0) and the similarity of elbow flexion synergy composition measured under As-Trained condition at Week0 and Week6.

Supplementary Files

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