

SUPPLEMENTARY DIGITAL MATERIAL 1

Supplementary Table I.— Main information of the studies selected in this scoping review: study characteristics and clinical results.

First author, year	Aim	Participants	Age (years)	Time since stroke	Stroke Type	Affected side	Motor impairment (baseline)	Device	Protocol of treatment	Timing	Outcome measures	Clinical results
<i>Robotic treatments</i>												
Pierella et al.¹, 2020	To develop a multivariate analysis method to couple clinical evaluations with multimodal instrumental evaluations in order to provide a deeper characterization of the neurobiomechanical status of stroke patients undergoing different rehabilitation protocols.	6 subacute stroke patients 6 healthy	68 ± 18 stroke (34-82) 58 ± 16 healthy	2-6 weeks	6 I	6 R	FMA-UL 5-54	Arm Light Exoskeleton Rehab Station, ALEx RS	The training sessions involved a 3D point-to-point reaching task using an upper-limb exoskeleton, with visual feedback and assistance mode.	Treatment: 30 min/session 3 sessions/weeks 4 weeks 12 total sessions +habitual physical and occupational therapy Assessment: A1: 2 weeks before the beginning of the training A2: 1 week before the beginning of the training A3: 1 weeks after the end of the training A4: 1 months after the end of the training	FMA-UL Grip strength EEG Kinematics (device) [mean tangential velocity (MV); movement accuracy; smoothness; spectral arc-length metric (SAL); workspace explored; robot assisted frequency] sEMG	Significant improvements in clinical scores, such as FMA (p<0.001) and grip strength (p=0.02) across all assessment. Motor performances improved in all patients except for workspace dimension. At A3 mean velocity and smoothness of the arm's trajectory length (SAL) reached levels comparable with those of healthy subjects. Patients performed straighter movements in a shorter amount of time along the four assessments. The spinal maps (reflect motoneuronal activity) of stroke patients became more similar to healthy controls. The cortical activity of stroke patients showed closer coefficients of variation to healthy controls.
Scotto di Luzio et al.², 2022	To investigate in chronic stroke patients and evaluate some possible benefits in the robot-aided rehabilitation treatment of the hand in these subjects.	7 chronic stroke patients	59.6 ± 12.8	52.7 ± 28.1 months	3H; 4I	NA	FMA-UL 26-45	Gloreha hand exoskeleton	The subject performed four different grasps selected randomly, shown by means of a purposely developed user interface. They had to grab and hold the following objects: a can, a pencil, a sheet, and a tennis ball. The subjects were required to perform the grasp and to hold the object for ten seconds, followed by a pause of at least ten seconds. Non paretic hand start movement and paretic hand follows the same movement with active assisted mode.	Treatment: 5 sessions /week 4 weeks 20 total sessions Assessment: T0: Before training T1: After training	FMA UE Motor Power (MP) sEMG	All the patients showed a significant increase in the FM and MP scores between T0 and T1 (p< 0.05).

Tropea et al.^{3, 2013}	To verify if the expected improvements in motor performance of subacute stroke patients due to the combination of spontaneous recovery and intense robot mediated neuro-rehabilitation treatment are reflected in the modular coordination of muscular activity.	6 subacute stroke patients 10 healthy	71.8 ± 5.4 (66–82)	14-37 d	5L; 1H	5 L; 1 R	FMA-UL 8 - 36	InMotio n2	Each patient completed at least 65 turns per sessions moving the handle from one target to another in the 8 cardinal directions while keeping the trajectory as straight as possible. Assisting force was provided by the robot when subjects were not able to reach specified targets.	Treatment: 45 min/session 5 sessions / week 6 weeks 30 total sessions Assessment: T0: 0 week - before training T1: 3 weeks - at middle T2: 6 weeks - after training	MAS FMA UE Motricity Index sEMG Kinematic (device) [number of Peaks; smoothness; movement accuracy; hand path error]	Improvement in FMA score of 72.8% (range 33.3-147.4 %) between T0 and T1 across all patients. Moreover, patients were also characterized by a positive variation of the Motricity index. Not significant change in MAS score. Improvement in motor performance, but significant difference only in number of Peaks.
Belfatto et al.^{4, 2018}	To apply a combined multi-domain assessment to evaluate the treatment outcome in a robot-assisted upper limb rehabilitation scenario.	5 chronic stroke patients	61 ± 11	>6 m	NA	NA	FMA-UL sections A–D 11 - 61	Mitsubishi Pa10-7 robot	The therapy consisted of the execution of 3D point-to-point reaching movements and hand-to-mouth movements.	Treatment: 40 min/session 3 sessions /week 4 weeks 12 total sessions Assessment: T0: Before training T1: After training	EEG sEMG Kinematics [duration of forward phase; shoulder flexion angle; elbow flexion angle; smoothness] FMA-UL WMFT	Not significant improvement in FMA-UL and WMFT in all patients (p= 0.06). Improvement of shoulder flexion angle, elbow flexion angle, duration of execution and smoothness. Pre-post differences resulted not significant for all the parameters other than smoothness (p<0.05). All patients show a decrease in event-related desynchronization post-treatment in the alpha band. The desynchronization occurred symmetrically in the ipsilateral and contralateral side, with a shift towards a physiological condition
Nerea Irastorza-Landa et al.^{5, 2021}	To investigate a Functional synergy recruitment index (FSRI) to measure the ability to elicit correct temporal recruitment patterns of a common set of functional synergies during paretic limb motor control in comparison to the healthy one before and after intensive BMI-based motor rehabilitation combined with physiotherapy.	18 chronic stroke patients: 10 experimental 8 control	54.66 ± 12.01	14 - 232 m	NA	NA	modified FMA-UL (0-54) [hand/fingers (hFMA, 0–24), + upper-arm (aFMA, 0–30)] 2 - 33,50	Brain machine interface (BMI) controlled robot	All patients received hand-BMI therapy by controlling a hand orthosis that performed the extension/flexion of the fingers. Some patients additionally received arm-BMI training using an arm orthosis attached to their paretic upper- and fore-arm that enabled the extension/flexion of the arm and the elbow. EG: received a contingent positive feedback CG: (n = 8) received either a random or contingent negative feedback.	Treatment: Daily 1h/session + 1h behavioral physiotherapy for 17 ± 1.8 days (5 days/week). Some patients additionally received arm-BMI training (mean sessions): 5.11 ± 4.27 sessions (max 11) Assessment: T0: 2 months before training T1: Before training T2: After training	modified FMA for the hand/fingers (hFMA), for the upper-arm (aFMA) and their combination (cFMA) (0-54) MAS sEMG	Significant improvement in cFMA (p = 0.012) and aFMA (p = 0.026) non-significant increase in hFMA (p=0.054). Not present a significant reduction in the level of spasticity (MAS, p = 0.29) after the intervention.
Lencioni et al.^{6, 2021}	To investigate the muscle synergies changes due to the strengthening of brain plasticity and connectivity functions related to the type of therapy,	32 stroke patients (RG: 15;UCG: 17); 10 Healthy	RG: median 68.0 y (54.5–74.5) UCG: median 59.0	RG: median 7.76 m UCG: median 5.8 m	RG: 4H; 11I 6H; 11 I	RG: 7R; 8L 6R; 11L	FMA-UL sections A–D RG: median 45	Braccio di ferro	RG: The robot-assisted treatment (BRACCIO DI FERRO) consisted of controlling the position of the end-effector of a planar robot with paretic	Treatment: 45 min/session 5 sessions /week 4 weeks 20 total sessions	FMA UE Kinematics [elbow extension; wrist pronation; angle of trunk; angle	Improvement (non-significant) in motor ability as measured by FMA-UL score in both groups. Kinematics: At T0, the contralesional arm of stroke

	robot-assisted or usual care rehabilitation. .		y (46.9–68.4)				UCG: median 21		limb, while taking it forward and backward from a central position to five targets placed randomly around a circumference. The robotic system allowed the execution of reaching movements in two force modes, assist-as-needed or resistive, based on subject's residual skill/improvement. UCG: usual care arm-specific physiotherapy. The physiotherapy consisted of passive and active mobilization of scapula, shoulder, elbow, and wrist, followed by task-oriented exercises. Exercises were tailored to patients' abilities.	Assessment: T0: Before training T1: After training	of shoulder; smoothness] sEMG	patients showed statistically significant differences from healthy subjects in several kinematic parameters, including elbow extension, movement smoothness, and wrist pronation. After T1: In the object placing task, the RG showed a larger elbow extension and a larger improvement in the trunk movement compared to UCG. No significant difference between groups for the ipsilesional arm. In the forearm pronation task, the RG showed a larger Wrist Pronation compared to UCG. The UCG showed a decrease of the deviation from the normative curves in the Mean RMS of Shoulder Angle parameter. No significant difference between groups for the ipsilesional arm. RG was significantly improved in the smoothness of the movement than the UCG group.
<i>Non robotic</i>												
Niu et al.⁷, 2019	To evaluate the feasibility and the effectiveness of the synergy-based FES treatment in stroke patints.	5 subacute and 1 chronic stroke patients (3 patients for each experiment)	Exp 1: 38 to 71 Exp 2: 61 - 71	4 ± 3,16 m Exp 1: 3 (2-3 m) Exp 2: 2 (2-5 m) 1 chronic (10 m)	6 I	Exp 1: 1 L; 2 R Exp 2: 3 L	Brunnstrom stage III-IV Local infarction: atypical FMA-UL 15-28 (Exp 2)	FES	Parameters of FES were based on Muscle Synergies. The movement task was to extend the arm away from the trunk on a horizontal surface, reaching movements of 36 cm in forward direction (forward reaching) or 48 cm in lateral direction (lateral reaching). The home position and the goal position were marked on the table. Participants were allowed to use their vision to guide the movement. Patients were instructed to move as fast as possible without sacrificing accuracy.	Treatment: Experiment 1: 1 day session (30-50 movements) Assessment: pre and post test Experiment 2: 60 min/session (120 movements) 5 sessions /week 1 week 5 total session + conventional therapy Assessment: T0: 3 days before training T1: After training	Kinematics (peak velocity; endpoint variability; bell-shape profile; reaction time) surface EMG FMA-UL (only for Exp 2)	Exp 1: synergy-based FES had an instantaneous effect on movement kinematics, with increased peak velocities observed in some patients and patterns. Exp 2: patients showed improved peak velocity and bell-shaped time profiles, with patterns becoming more similar to those of normal controls for forward-reaching and lateral-reaching movements. Fugl-Meyer scores also increased for all 3 patients.
Hesam Shariati et al.⁸, 2017	To quantify poststroke muscle synergies during therapy and to use muscle synergies as a neurophysiological indication to distinguish the level of impairment and the effect of therapy on coordinated muscle activation	24 chronic stroke patients (8 low, 8 moderate, 8 high) 11 drop out at follow up	57.9 ± 12.1	3-88 m	16 I; 8 H	dominant side: 7 non-dominant side: 17	FMA-UL A-D low 25.3 ± 3.4 moderate 53.1 ± 3.0 high 61.6 ± 1.5	Nintendo Wii	Wii-based Movement Therapy uses the Nintendo Wii and Wii-Sports games of golf, baseball, bowling, tennis, and boxing as a rehabilitation tool in a structured protocol that	Treatment: 60 min/session 7 sessions /week 10 total sessions + home practice Assessment: T0: Before	sEMG WMFT-tt FMA-UL. MALQOM MAS	Improvement over time for WMFT-tt (p = 0.008), FMA (p = 0.001), and MALQOM (p < 0.001) sustained at 6-month follow-up. There were no changes in MAS score at wrist (p =

									can be individually tailored to the level of motor-function and progress of each patient. Patients used only the more-affected upper limb during therapy activities. When unavoidable, assistance was provided either with the less-affected hand or by the therapist.	training T1: After training T2: 6 months after training	0.355), elbow (p = 0.796), or shoulder (p = 0.592) at post-therapy	
Maistrello et al.⁹, 2021	To identify whether muscle synergies and clinical scales convey the same information or not.	50 subacute (32) and chronic (18) stroke patients	63.62 ±12.29	6.99 ± 13.07 [15pt: 2.32 ± 0.42 m 17pt: 4.25 ± 0.87 m 18pt: 20.61 ± 19.83 m]	5 H; 45 I	25 L; 25 R	FMA-UL 117.20 ± 24.57 MAS 1.92 ± 2.69 RPS 24.4 ± 11.19	Virtual Reality Rehabilitation System (VRRS)	Patients were asked to perform a defined set of exercises, including shoulder flexion–extension, abduction–adduction, internal–external rotation, circumduction, elbow flexion–extension, forearm pronation–supination, and hand–digit motion.	Treatment: 60 min/session 5 sessions /week 4 weeks 20 total sessions Assessment: T0: Before training T1: After training	MAS FMA-UL RPS sEMG MAS and N-aff. FMA-UL and RPS correlated positively both with Nsh-naff after treatment and with Median-sp .	Improvement of FMA-UL score by 6% (p<0.001) and RPS score by 4% (p<0.001). Not significant change in MAS. Positive correlation between MAS and N-aff. FMA-UL and RPS correlated positively both with Nsh-naff after treatment and with Median-sp .
Niu et al.¹⁰, 2022	To evaluate whether the instantaneous effects of FES would sustain or accumulate after repetitive training and to answer whether synergy-based FES could alter the patterns of muscular control.	16 subacute (13) and chronic (3) stroke patients (9 EG FES, 7 CG Sham)	57.00 ± 8.76	4.67 ± 3.54 m	16 I	FES: 8 L 1 R Sham: 5 L 2 R	FES group FMA- UL: 18-49 Sham group FM UL 13-56	FES	EG: Synergy based UL-FES interventions. The movement task was to extend the arm away from the trunk on a horizontal surface, reaching movements of 36 cm in forward direction (forward reaching) or 48 cm in lateral direction (lateral reaching). The home position and the goal position were marked on the table. Participants were allowed to use their vision to guide the movement. Patients were instructed to move as fast as possible without sacrificing accuracy. CG: Sham interventions were applied with all electrodes attached identically, but without actual stimuli.	Treatment: 60 min/session 5 sessions /week 1 week 5 total sessions +120 min PT and 60 min OT Assessment: T0: Before training T1: After training	sEMG FMA-UL Kinematics (peak velocity, movement duration)	Improvement in FMA-UL scores significantly higher after FES intervention (28.13%) compared to Sham intervention (7.32%). Kinematics: In forward-reaching, both groups showed increased peak velocity and decreased movement duration, but the effect was more significant in the FES group. The ratio between peak velocity and movement duration also increased significantly more in the FES group. In lateral-reaching, both groups showed increased peak velocity and movement duration, with no significant difference between the groups. The ratio between peak velocity and movement duration increased significantly more in the FES group.
Dash et al.¹¹, 2020	To evaluate the usability of the GripX system and its applicability to stroke rehabilitation.	12 chronic stroke patients; 8 healthy	44 ± 15	1 - 4 y	NA	8 R; 4 L	NA	VR-enabled sEMG-triggered grip exercise platform .GripX	Participants are exposed to VR-based tasks with sEMG-based biofeedback, and perform a power grip using maximum voluntary contraction to calibrate the GripX before the actual execution of the VR-based tasks. Then, the participant was asked to perform power grips in each hand that activated two Virtual objects to	Treatment: 45 min/session 2-3 sessions /week 6-7 weeks 12-21 total sessions Assessment: T0: Before training T1: After training	sEMG CTEC score Dynamometer-based grip strength Computation of Task Performance Indices	Improvement in overall grip ability. Both the indices of grip strength improved from the first exposure to the last exposure. Some participants exhibited varying improvements in CTEC scores with no noticeable improvement in others.

									move in the VR environment.			
Seo et al.¹², 2022	To investigate the feasibility and effectiveness of a personalized robot-assisted rehabilitation protocol for improving upper-limb function in stroke patients as well as to determine to what extent MyoCI training changed intermuscular coordination.	32 chronic stroke patients (3 groups: 12 60I; 11 90I; 9 90M)	27 to 75	11 - 314 months	NA	24 L; 8 R	FMA-UL sections A-D 60I: 17.0±2.4 90I: 19.6±3.0 90M: 18.7±2.0	Myoelectric computer interface (MyoCI) training	The MyoCI training protocol involves using electromyogram (EMG) signals from targeted muscle pairs to move a cursor in a custom-built game. Only activating muscle in isolation would move the cursor along the cardinal axis, while a co-activation moves the cursors along diagonal. Participants need to reach the target for 0.5seconds. Three groups: a) isometrically (restraining the arm) 60 min b) isometrically 90 min per session c) movement group for 90 min per session (90M). Participants trained 3 muscle pairs for six sessions over two weeks.	Treatment: 60 -90 min/session 3 sessions /week 6 weeks 18 total sessions Assessment: T0: 2 weeks before training T1: Before training T2: 2 weeks after start of training T3: End of training (6 weeks) T4: 4 weeks after the end of training (10 weeks)	FMA-UL WMFT Motor Activity Log (MAL) MAS sEMG Kinematics (20 subjects) [elbow angular position]	FMA-UL score and WMFT score improved significantly at week 6 and week 10. Quality of movement (MAL-Quality) and Amount of movement (MAL-Amount) improved significantly at week6 and 10. MAS declined significantly at week 6 and not significantly at week 10 Elbow angles during each reach improved significantly only at week 6
Alnajjar et al.¹³, 2019	To investigate the changes in motor control strategies and movement coordination in stroke survivors as they recovered motor function over time.	10 subacute stroke patients; 9 Healthy	EG: 66.5 ± 11.6 Healthy: 38.1 ± 7.8	1.5- 2 m	9 I; 1 H	NA	SIAS: Motor function UE Proximal (knee-mouth task) (score, 2-4 out of 5)	NA	Regular rehabilitation program (specifics were not described)	Treatment: 11 weeks Assessment: T0: week 1 T1: week 7 T2: week 11	sEMG SIAS	SIAS did not significant improvement in in patients' motor function.
Zendehbad et al.¹⁴, 2023	To evaluate the effect of a novel underlining mechanism of visual biofeedback based on muscle synergy pattern on upper extremity motor functions for subacute stroke patients.	24 subacute stroke (12 EG 12 CG); 12 healthy	EG: 63.25±15,5 3 CG: 64.16± 15.43 Healthy: 24 - 70	EG: 3.16 ±1.40 d CG: 2.19± 1.44 d	24 I	24 R	FMA-UL 21.66 ± 7.37 and 21.91 ± 6.51 NIHSS 8.41 ± 3.55 and 7.66 ± 3.98 MRS 3.25 ± 0.62 and 3.08 ± 0.66	Synergy based-visual biofeedback trajectory	EG: arm movement exercises using a visual biofeedback trajectory designed based on muscle synergy patterns. The visual biofeedback trajectory was projected on a screen in front of the participant, and the participant was instructed to follow the trajectory with their arm movement. The trajectory was adjusted based on the participant's performance to ensure that it was challenging but achievable. CG: conventional rehabilitation training, which consisted of passive range of motion exercises, stretching, and strengthening exercises.	Treatment: EG: 30 min/session 2 sessions /week 5 weeks 10 total sessions + 30 min/session Conventional therapy CG: 60 min/session Conventional therapy Assessment: T0: Before training T1: After training	Correlation coefficient (CC) FMA-UL MRS NIHSS	Statistically significant increase in the FMA-UL, NIHSS, and MRS scores at T1 (P < 0.001). No statistically significant difference between the EG and CG regarding the NIHSS and FMA-UL scores.

EG: experimental group; CG: control group; RG: robotic-assisted group; UCG: usual care group; FMA-UL; Fugl Meyer assessment upper limb; FES: Functional electrical stimulation; CTEC: Complex Task Execution Capacity; WMFT: Wolf motor function task; MRS: Modified Rankin Scale MAL: motor activity log; MAS: modified Ashworth Scale; sEMG: surface electromyography; NIHSS: National Institutes of Health Stroke Scale; SIAS: Stroke Impairment Assessment Set; I: ischemic; H: hemorrhagic; L: left; R: right; d: days; m: months; y: years; Exp: experiment; *some data have been extracted from the previous study on same population¹⁵

Supplementary Table II.— Main information of the studies selected in this scoping review: muscle synergies.

First author, year	Muscles	Baseline postures	Movement analyzed	Protocol for synergy extraction	Extraction Algorithms	Metrics	Number of synergies	Synergy composition variation	Temporal component variation
Robotic treatments									
Pierella et al. ¹ , 2020	15 muscles: upper TRAP, TRAPM, AD, MD, PD, PECM, LD, INFRA, RHO, BBLH, BBSH, BRAD, TRILA, TRILH, PT	Seated posture with the upper body, and the arm in a starting position dictated by the exoskeleton's design with the elbow bent	3D point Reaching task involving reaching of 18 outer targets in a spherical workspace of 19 cm radius. Device movement - only affected limb	The subjects were instructed to reach as many targets as possible within 30 minutes starting from the center of work space, reaching one of the targets and moving back to the start position while wearing the exoskeleton with the paretic right arm. Visual feedback was provided through a monitor displaying a yellow sphere for the position of the exoskeleton's end-effector and a red sphere for the target to be reached. For the healthy subjects the total number of movements was 30, while for the stroke subjects it depended on the level of residual mobility at each assessment.	NMF VAF > 95%	Synergy similarity was computed with the scalar product between synergies from patients and synergies from healthy subjects	Stroke subject: Significant increase in the number of synergies from A1 to A4 (p = 0.036). A1 (NA) A2 (4.1 ± 0.4) A3 (5.0 ± 0.3) A4 (5.4 ± 0.4). Healthy controls: 5.8 ± 0.5	The structure of the synergies in stroke subjects became more similar to that of healthy controls over time and training. The similarity of muscle synergies between stroke subjects and healthy controls, significantly improved over time and continued to evolve even at follow-up.	NA
Scotto di Luzio et al. ² , 2022	6 muscles: FDS, EDS, FPB, APB, ADM, EDM	The specific upper body and arm posture is described with a figure. Subjects were seated with the upper body upright, maintaining a good vertical alignment in front of a computer monitor. The arms are bent at the elbows, positioned at about a 90-degree angle. The forearms are held horizontally, and the wrists in a neutral position. Different grasps were used for each object Tripod Grip for pencil The thumb and index finger typically grasp the object, while the middle finger supports it from below, . Lateral Pinch for sheet involves the thumb pressing against the side of the index finger, as if holding a key. Spherical Grip for tennis ball The fingers and thumb wrap around the object in a spherical shape, with all fingers and the thumb involved to some extent, Palmar Pinch for the can involves the thumb, index, and middle fingers.	Grasping and holding the objects (pencil, can, sheet, tennis ball) Free movement - affected and unaffected limb	Patients seated in a comfortable position in front of a screen that showed the task to perform. The subjects were required to perform the grasp and to hold the object (pencil; sheet; cylinder; ball) for ten seconds, followed by a pause of at least ten seconds. The sEMG data were recorded during the ten seconds of grasp execution. The subjects were asked to perform the same task with the injured limb and subsequently with the healthy limb.	NMF R ² > 80%	Synergies from the same patient were compared in the three conditions (before rehabilitation, after rehabilitation, healthy limb) with Cosine similarity (CS), computed as the scalar product between matched synergies, and Similarity index (SI), that is the weighted sum of the difference between matched synergies	3 fixed synergies were extracted from the EMG signal in the three condition BR: before rehabilitation AR: after rehabilitation H: healthy	The patients show a very high degree of similarity of the involved synergies after intervention between healthy and injured limb and between before and after treatment (mean SI values: H-BR: 0.88±0.03; H-AR: 0.94±0.03; BR-AR: 0.89±0.05). Statistically significant (p = 0.018) increase in CS in H-BR, H-AR, and BR-AR comparisons (mean CS values: H-BR: 0.74±0.09; H-AR: 0.91±0.06; BR-AR: 0.82±0.09).	NA
Tropea et al. ³ , 2013	10 muscles: BB; BRAC;	(figure) The baseline posture is not explicitly	Planar reaching tasks executed from	Patient moved with the paretic limb the position of	FA – the	Scalar product normalized to the	4 muscle synergies (S1-S4) accounting	Muscle synergies were qualitatively similar to	Comparison between groups showed that post-

	BRAD; AD; MD; PD; LD; PECM; upper TRAP; TRI	<p>stated (only with a figure). The individual is seated with the back upright, facing the monitor.</p> <p>The shoulder is in the rest position (slightly abducted). The elbow bent at a roughly 90-degree angle. The forearm horizontal on a support leading to a neutral wrist position while handling the joystick.</p>	<p>a central target in 8 directions around a circumference of radius of 0.14 m.</p> <p>Device Movement - only affected limb</p>	<p>an end effector back and forward from a central target carrying out 16 subsequent sub-movements (full turn). No robotic assistance or resistance was used during trials. EMG signals were recorded in an additional section every two weeks for each of the 8 directions (i.e., N, NE, E, SE, S, SW, W, and NW). Healthy subjects performed 5 full turn, constrained by the beat of a metronome at the following frequencies: 24, 30, 40, 60, and 80 beats per minute.</p>	<p>eigenvalue > 1 criterion;</p> <p>– the number of synergies at which the slope of the cumulative variance drops below the 75% of the slope related to the shuffled dataset.</p>	<p>Euclidean norm (dot) of two homologous muscle synergies was adopted to define a synthetic measure of their degree of similarity.</p> <p>a) intra-group similarity (dotintra)</p> <p>b) inter group similarity between patients and healthy subjects (dotinter)</p> <p>Pearson correlation coefficient (r) was used to compare the temporal components</p> <p>a) intra-group similarity (rintra)</p> <p>b) inter group similarity between patients and healthy subjects (rinter)</p>	<p>for about 70% of the cumulative variance.</p>	<p>healthy subjects with some specific differences. The intra-group similarity of muscle synergies decreased with the number of retained synergies, with lower mean values in post-stroke patients compared to healthy subjects. The rehabilitative treatment significantly decreased the intra group similarity (dot intra) for synergies S1, S2, and S4 in post-stroke patients (p-values < 0.05).</p> <p>The similarity between healthy subjects and post-stroke patients was highest for S1, lower for S3 and S4, and increased for S2 with the ongoing of the treatment.</p> <p>The rehabilitative treatment did not modify similarity between groups (dot inter) for all synergies (p-values > 0.05).</p>	<p>stroke patients at the beginning of treatment had lower values of rintra and rinter compared to healthy subjects, which increased with ongoing treatment, suggesting improved consistency of related temporal components.</p> <p>The anisotropic behavior of rinter was in accordance with data related to healthy subjects.</p>
Belfatto et al. ⁴ , 2018	8 muscles: upper TRAP, PECM, AD, MD, PD; TRIM, BBLH, BRAD	<p>The individual maintains an upright seated position. The shoulder is relaxed and not elevated. There is a slight shoulder abduction.</p> <p>The elbow is extended. The wrist maintains a neutral position, in line with the forearm, to avoid strain. The hand grasps a part of the robotic arm</p>	<p>Hand to mouth movement (shoulder flexion elbow flexion).</p> <p>Device movement - only affected limb</p>	<p>Patients seated and moved the robotic handle with paretic arm from the start position (hand on the thigh and shoulder slightly extended) to final position (elbow fully flexed and shoulder flexed around 30°) completing an Hand to mouth movement. The Hand to mouth movement trajectory was predetermined and the patient was unable to modify it during the motor execution. Only the forward phases when the subject bring the hand toward the mouth were considered (involving shoulder flexion in the sagittal plane and elbow flexion). No assistance was provided.</p>	<p>NMF VAF > 80%</p>	<p>Scalar product between spatial components was used to compare synergies extracted before and after rehabilitation from the same patient. Pearson's correlation coefficient between temporal components was used to compare synergies extracted before and after rehabilitation from the same patient</p>	<p>2 fixed synergies were considered for pre and post treatment evaluation</p>	<p>High similarity (t0-t1) in spatial synergies both for the first and the second synergy for all the subjects, with a dot product mean score 0.86 for the first and 0.90 for the second synergy.</p>	<p>The temporal components of the first synergy showed high or very high Pearson's correlation coefficient (r > 0.79).</p> <p>The temporal components of the second synergy showed varying correlation values ranging from 0.56 to 0.87, with one patient showing even negative correlation (-0.15).</p>

Nerea Irastorza-Landa et al. ⁵ , 2021	11 muscles: ECU, ED, FCR, PL, FCU, BB, TRI, AD, MD, PD, INFRA	Subjects were seated or positioned relaxed position with both hands resting on their lap.	Five bilateral simultaneous movements of the upper limbs (paretic and healthy): Shoulder flexion (SF) Shoulder external rotation (SER) Elbow extension (EE) Wrist extension (WE) Finger extension (FE) Free movement - affected and unaffected limb	The patients were seated in front of a screen and instructed to perform five different movements using auditory and visual cues with E-prime software. They performed 10 trials per movement type (40-60 trials in total) starting from a relaxed position with both hands resting on their lap. 6 s was given to attempt to reach and maintain the instructed final posture by eliciting isometric co-contraction of muscles. Then 4 and 7 s were given to return to the initial resting position. Compensatory movements were discouraged.	NMF Mean VAF > 95% and adding another synergy did not increase global VAF > 3%	Functional synergy recruitment index (FSRI) was computed to compare temporal activations of synergies extracted from the paretic and the healthy limb Preservation, merging and fractionation indexes were computed to compare the structure of synergies extracted from the paretic and the healthy limb	Eight and seven groups of muscle synergies represent the general modular organization of the healthy and paretic muscle activations. No significant differences were found in the inter-limb synergy preservation, merging or the fractionation indexes between pre and post-therapy time points.	No significant variation in clustered weightings of synergy structures between pre and post-treatment evaluations in healthy or paretic limbs. The paretic limb exhibited lower complexity in modular control than the healthy limb. Inability for selective fingers or wrist extensor activation was observed in the paretic limb, with larger antagonist flexor and biceps muscles activations.	General increase in FSRI Global (temporal similarity) as an effect of the intervention ($p = 0.015$). The experimental group increased their FSRI value during FE movement, whereas the control group was characterized by a decrease in the correct temporal recruitment of functional synergies during this gesture.
Lencioni et al. ⁶ , 2021	16 muscles: TRILH, TRIMH, BBSH, MD, PD, UTRAP, RHO, BRAD, SUP, BRAC, PT, PECMI, INFRA, TEMA.	Object placing task: the subject kept both hands in the middle of own thighs. Forearm pronation task: the subject kept the elbow angle at 90°, the wrist fully supinated and the shoulder laterally rotated so that the forearm was approximately 45° relative to the thigh.	3D motor task Object placing (reaching) and pronation tasks Free movement - affected and unaffected limb	Tasks were performed with both arms (ipsilesional and contralesional) separately. The subject was seated in front of a screen grasping the VRRS electromagnetic sensor with the examined hand and moved a virtual object (a ball and a donut) performing the object placing (move a virtual ball forward and vertical distance of 36 and 26 cm) and pronation task (move and rotate a virtual donut and placed inside a yellow cube medial and vertical distance of 52 cm and 12 cm).	NMF $R^2 > 90\%$	Module similarity, computed as the scalar product between matched synergies, and activation profile similarity, computed as the Pearson's correlation coefficient between temporal activation profiles of matched synergies, were used to compare patients and healthy subjects.	2 synergies for each task were retained for all subjects for both arms. No significant difference in the number of extracted synergies between healthy and post-stroke subjects latter both the pre- and the post-treatment evaluation.	At baseline the comparison of similarity of motor weightings and activation profiles between treatment groups (UCG vs RG) showed not significantly different values ($P > 0.05$) for both arms and tasks, with the exception of motor weightings of synergy 1 (W1) in the ipsilesional arm for the object placing task. After treatment a) synergy 1 object placing task: not significantly differ value for the muscle weightings, with the exception of the similarity of muscle weightings of ipsilesional arm in favor of the RG group ($F(1,29) = 3.38, P = 0.07$). b) synergy 2 object placing task: there was a significantly greater effect in muscle weighting ($P < 0.01$) in the RG than in the UCG group, for the contralesional arm only. c) synergy 1 and 2 forearm pronation task: a comparable positive effect of the two interventions in the weightings (W).	At baseline the activation profiles were altered with the exception of the activation profiles of the ipsilesional side during the object placing task. The comparison of similarity of activation profiles between treatment groups (UCG vs RG) showed not significantly different values ($P > 0.05$) for both arms and tasks. After treatment a) synergy 1 object placing task: not significantly differ value in the activation profile for both arms. b) synergy 2 object placing task: there was a significantly greater effect in activation profile ($P = 0.07$) in the RG than in the UCG group, for the contralesional arm only. c) synergy 1 and 2 forearm pronation task: both interventions had a negative effect on the activation profile of both muscle synergies for both arms in the forearm pronation task.

Other Interventions

Niu et al. ⁷ , 2019	7 muscles: BB, TRILA, TRILH, AD, PD, PECM, BRAD	The baseline posture likely involved subjects seated with electrodes placed on the upper limb to facilitate FES during motor tasks. The shoulder in a neutral to slightly abducted position. The elbow flexed at an angle close to 90 degrees. The wrist is in a neutral position, aligned straight with the forearm.	Planar reaching movements of 36 cm in forward direction or 48 cm in lateral direction (joint rotations in the elbow and the shoulder)	The home position and the goal position were marked on the table. Participants were allowed to use their vision to guide the movement and followed verbal cues. The patients were encouraged to practice each movement for 20~40 times before the experiment until they could comfortably accomplish the task. Patients were instructed to move as fast as possible without sacrificing accuracy.	NMF VAF (threshold N/A)	Similarity of synergy, similarity of synergy time profile, common similarity in synergy were computed between synergies extracted before and after treatment	3 fixed synergies a priori	Composition did not change after treatment. Trends in similarity in synergy varied among patients and tasks.	More similar to synergy time profiles for forward-reaching and lateral-reaching movements, except for a marginal decrease in one case.
Hesam Shariati et al. ⁸ , 2017	6 muscles: Middle TRAP, MD, BB, FC, ECR, FDI	The baseline posture Therapy was performed standing wherever possible, and time spent standing was progressively increased for those who began seated.. Patients with unstable balance begin by holding on to a support with one hand and the level of support is progressively reduced. For patients with lower-limb disabilities, Wii therapy can be undertaken seated or in a wheelchair if necessary. All games can be effectively played in either position, with increased standing as locomotion, balance and endurance improve. *	Wii-baseball swings.	Mean baseline EMG was measured over 1 s prior to the beginning of the Wii-baseball game, while the muscles were at rest. The mean was subtracted from the signal of the same game for each patient. EMG of each muscle was normalized to its peak amplitude, then averaged over 10 consecutive Wii-baseball swings for each patient.	NMF VAF > 97% and VAF increased by less than 2% when another synergy was added	Scalar product of synergy timing profiles was used to compare patients with the same level of motor function	At early therapy significant difference ($p = 0.036$) in number of muscle synergies between low motor-function (3.38 ± 0.2) and high motor-function (4.00 ± 0.3). At late therapy, not statistically significant increase in the number of synergies for patients with low and moderate motor-function. No change for patients with high motor-function. At 6-month follow-up data, no significant changes in the number of synergies over time.	Muscle weightings are categorized into 10 or 11 clusters at early and late therapy respectively No significant difference in incidence of muscle synergies based on level of motor function at early therapy. Synergy muscle weighting changed from early to late therapy except for the first four clusters.	Synergy timing profiles were similar for patients in each level of motor-function. Differences pre and post treatment were not reported
Maistrello et al. ⁹ , 2021	16 muscles: TRI MH, TRILH, BBSH, BBLH; AM, MD, PD, UTRAP, RHO, BRAD, SUP, BRAC, PT, PECM, INFRA; TEMA	NA	Seven standardized motor tasks involving interaction with a Virtual Reality Rehabilitation System (VRRS®): shoulder flexion-extension, abduction-adduction, internal-external rotation, circumduction, elbow flexion-extension, forearm pronation-supination, and hand-digit motion.	Subjects executed seven standardized motor tasks (not specified), each repeated 10 times, by interacting with a Virtual Reality Rehabilitation System by means of a 3D motion-tracking system fixed on the back of the hand.	NMF $R^2 > 90\%$	Number of synergies of the affected limb and of the unaffected limb; scalar product between synergies of the affected and unaffected limb; median scalar product between the affected and unaffected synergies (Median-sp); mean number of unaffected synergies merging in every affected synergy (P1)	Number of synergies (8) and other related parameters don't change significantly after treatment.	Median-sp showed no significant change after the treatment. there was a strong positive correlation between the Median-sp values and the FMA and RPS. The general linear regression model found that Median-sp was significantly associated with Reaching Performance Scale at T0.	NA
Niu et al. ¹⁰ , 2022	7 muscles: BB, TRILH,	The baseline posture likely involved subjects seated	Planar reaching movements of 36cm	Patient is seated comfortably in front of a	NMF VAF	SV: similarity of synergy vectors, ST: similarity of	3 fixed synergies a priori	Linear regression analysis showed a significant	Individual data showed more concentrated

	TRILA, AD, PD, PECM, BRAD	with electrodes placed on the upper limb. The shoulder in a neutral to slightly abducted position. The elbow flexed at an angle close to 90 degrees. The wrist is in a neutral position, aligned straight with the forearm.	forward direction or 48cm lateral direction.	desk with affected arm resting on lubricated elbow cast. The home position and the target were marked on the table. Participants were allowed to visually guide the movement and followed verbal cue. They were also instructed to move as fast as possible without sacrificing accuracy. A total of 120 movement trials, which were divided into 2 blocks of forward-reaching (FR) and 2 blocks of lateral-reaching (LR), 30 trials per block. A mandatory 5-minute break was given between blocks.	(threshold NA)	time profiles, SCOM: index of combined similarity, which was averaged from SV and ST were used to compare synergies extracted before and after treatment.		correlation between the change in elbow flexion and the change in synergy similarity for the FES group ($p < 0.05$, slope = 0.022) in lateral reaching movement, no significant linear relationship was found for the Sham group ($p = 0.661$). Similar relations were found between the combined similarity and the change of elbow flexion.	activation in muscle vector and higher magnitude and clearer bursts time profile, particularly in FR movement. t. Pre-FES intervention, muscle vectors showed clear co-activation, but post-intervention, the muscle vector exhibited more concentrated activation from individual muscles, making it easier to form a canonical "tri-phasic" pattern of muscle activation. Post-intervention time profiles showed higher magnitude and clearer bursts. synergy-based FES might have incurred benevolent changes in muscle synergy.
Dash et al. ¹¹ , 2020	4 muscles: ECRL, FCR, FDS, ED	The user is seated upright on a chair that supports an erect posture. The upper arms appear to be hanging vertically and relaxed. The elbows are bent at a 90-degree angle. The forearms are horizontal and parallel to the ground. The wrists maintain a neutral position, aligned with the forearms. The hands are engaged with controls.	Grasping and lifting a glass task	The table was marked with two positions, labeled Pos1 and Pos2, which were approximately 40cm apart. A glass was placed on Pos1, which was on the side of the table corresponding to the participant's affected hand. The participant was then asked to use their affected hand to grasp and lift the glass, and move it from Pos 1 to Pos2 while keeping their elbow resting on the armrest.	NMF The threshold of the extracted synergies was not reported	Synergy stability index (SSI) was computed over the trials to evaluate the consistency of synergies. SSI was computed before and after training.	2 fixed synergies	The 5 patients (out of 12) who completed the training with GripX platform showed statistically significant ($p < 0.05$) Pre-to-Post increase in the SSI values.	N/A
Seo et al. ¹² , 2022	8 muscles: AD, MD, TRILH, TRILA, BRAD, PECM	The user maintains an upright seated position, The shoulder is relaxed with a slight elevation. The elbow is bent approximately at a 90-degree angle. The forearm is extended forward, positioned horizontally. The wrist in a neutral position.	Reaching task in forward and lateral direction (only away-from-body reaches) to six targets (approximately 4" in diameter and spaced 1ft apart),	The task involved three reaches to each of six targets, placed at waist and shoulder height, in front of and lateral to the impaired arm. Participants were asked to reach to the target as best as they could (self-paced speed), and after each reach, they were asked to bring the arm back to the rest position. The resting period in between each reach was at least 3 seconds.	NMF VAF > 90%	Disparity index was computed to compare synergy weights before and after training.	Average number of synergies across all participants and weeks was 2.41 (from 2 to 4). No consistent pattern of change in number of muscle synergies was observed after training in each group. 40.6% of participants preserved their number of synergies, 37.5% decreased, and 21.9% increased.	No significant change in group-wise overall composition of muscle synergies due to MyoCI training. Inter-subject variability of synergy composition within the same group was observed. There was a notable change, within individual synergies, in the disparity of muscle weights of the trained muscles in responders to the training: there was a reduction in co-activation of the first muscle pair in responders, but not typically observed in non-responders. Mean similarity of norm synergies between pre- and post-training was 0.98 ± 0.01 and 0.99 ± 0.01 for responders and	NA

								non-responders, respectively.	
Alnajjar et al. ¹³ , 2019	5 muscles : PECM, AD, INFRA, BB, BRAD	The baseline posture likely involved subjects seated or positioned shoulder abducted 90° elbow extended forearm in neutral position hand holding a robotic manipulandum	Bimanual shoulder flexion task	Simple bimanual shoulder flexion task A set of 10 to 15 trials for each session was conducted by each patient, to avoid fatigue.	NMF VAF > 90%	NA	1 synergy in the affected upper limb before and after treatment, there were notable changes in the level of VAF, which resembled the formation of 2 synergies. 2 synergies in the unaffected upper limb.	NA	NA
Zendehbad et al. ¹⁴ , 2023	4 muscles: PD, PECM, Middle TRAP, and Lower TRAP	The participants sat on a chair during the experiment. The visual interface monitor was within one meter of the chair. Shoulders are Flexed forward. This positioning can lead to tension in the shoulders and upper back. The elbows are extended. The forearms are likely parallel to the ground or sloping slightly downwards toward the wrists, depending on the height of the table relative to the chair. The wrist is in a neutral position.	Horizontally shoulder movement with internal and external rotation	Five fast movements (duration time: 10 seconds) and three slow movements (duration time: 20 seconds) were recorded with a 10-second break between them to prevent muscle fatigue. The participants were asked to sit on a chair during the experiment. The visual interface monitor was placed within one meter of the chair.	HALS R ² > 0.9	NA	3 fixed synergies	NA	NA

TRI MH: triceps medial head, TRILH: triceps lateral head, BBSH: biceps brachii short head, BBLH: biceps brachii long head; AD: anterior deltoid, MD: middle deltoid, PD: posterior deltoid, UTRAP: upper trapezius, MTRAP: middle trapezius and LTRAP: lateral trapezius RHO: rhomboid, BRAD: brachioradialis, SUP: supinator, BRAC: brachialis, PT: pronatores teres, PECM: pectoralis major, INFRA: infraspinatus; TEMA: teres major; ECRL: extensor carpi radialis longus, FCR: flexor carpi radialis, FDS: flexor digitorum superficialis, ED: extensor digitorum; FPB: flexor pollicis brevis, APB: abductor pollicis brevis, ADM: abductor digiti minimi, EDM: extensor digiti minimi; FDI: first dorsal interosseus; NA: not available; NMF: non negative matrix factorization; VAF: variance accounted for; HALS: Hierarchical Alternating Least Squares. *data provided from the previous study¹⁶

1. Pierella C, Pirondini E, Kinany N, Coscia M, Giang C, Miehlbradt J, et al. A multimodal approach to capture post-stroke temporal dynamics of recovery. *J Neural Eng* [Internet]. 2020 Jul 8 [cited 2023 Apr 5];17(4):045002. Available from: <https://iopscience.iop.org/article/10.1088/1741-2552/ab9ada>
2. Di Luzio FS, Cordella F, Bravi M, Santacaterina F, Bressi F, Sterzi S, et al. Modification of Hand Muscular Synergies in Stroke Patients after Robot-Aided Rehabilitation. *Applied Sciences* 2022, Vol 12, Page 3146 [Internet]. 2022 Mar 19 [cited 2023 Mar 23];12(6):3146. Available from: <https://www.mdpi.com/2076-3417/12/6/3146/htm>
3. Tropea P, Monaco V, Coscia M, Posteraro F, Micera S. Effects of early and intensive neuro-rehabilitative treatment on muscle synergies in acute post-stroke patients: A pilot study. *J Neuroeng Rehabil* [Internet]. 2013 Oct 5 [cited 2023 Mar 22];10(1):1–15. Available from: <https://jneuroengrehab.biomedcentral.com/articles/10.1186/1743-0003-10-103>
4. Belfatto A, Scano A, Chiavenna A, Mastropietro A, Mrakic-Sposta S, Pittaccio S, et al. A Multiparameter Approach to Evaluate Post-Stroke Patients: An Application on Robotic Rehabilitation. *Applied Sciences* 2018, Vol 8, Page 2248 [Internet]. 2018 Nov 14 [cited 2023 Mar 22];8(11):2248. Available from: <https://www.mdpi.com/2076-3417/8/11/2248/htm>

5. Irastorza-Landa N, García-Cossio E, Sarasola-Sanz A, Brötz D, Birbaumer N, Ramos-Murguialday A. Functional synergy recruitment index as a reliable biomarker of motor function and recovery in chronic stroke patients. *J Neural Eng* [Internet]. 2021 May 18 [cited 2023 Feb 24];18(4):046061. Available from: <https://iopscience.iop.org/article/10.1088/1741-2552/abe244>
6. Lencioni T, Fornia L, Bowman T, Marzegan A, Caronni A, Turolla A, et al. A randomized controlled trial on the effects induced by robot-assisted and usual-care rehabilitation on upper limb muscle synergies in post-stroke subjects. *Scientific Reports* 2021 11:1 [Internet]. 2021 Mar 5 [cited 2023 Mar 22];11(1):1–15. Available from: <https://www.nature.com/articles/s41598-021-84536-8>
7. Niu CM, Bao Y, Zhuang C, Li S, Wang T, Cui L, et al. Synergy-Based FES for Post-Stroke Rehabilitation of Upper-Limb Motor Functions. *IEEE Transactions on Neural Systems and Rehabilitation Engineering*. 2019 Feb 1;27(2):256–64.
8. Hesam-Shariati N, Trinh T, Thompson-Butel AG, Shiner CT, McNulty PA. A longitudinal electromyography study of complex movements in poststroke therapy. 2: Changes in coordinated muscle activation. *Front Neurol*. 2017 Jul 20;8(JUL).
9. Maistrello L, Rimini D, Cheung VCK, Pregnotato G, Turolla A. Muscle Synergies and Clinical Outcome Measures Describe Different Factors of Upper Limb Motor Function in Stroke Survivors Undergoing Rehabilitation in a Virtual Reality Environment. *Sensors (Basel)* [Internet]. 2021 Dec 1 [cited 2023 Mar 18];21(23). Available from: <https://pubmed.ncbi.nlm.nih.gov/34884003/>
10. Niu CM, Chou CH, Bao Y, Wang T, Gu L, Zhang X, et al. A pilot study of synergy-based FES for upper-extremity poststroke rehabilitation. *Neurosci Lett* [Internet]. 2022 May 29 [cited 2023 Mar 23];780. Available from: <https://pubmed.ncbi.nlm.nih.gov/35395324/>
11. Dash A, Lahiri U. Design of Virtual Reality-Enabled Surface Electromyogram-Triggered Grip Exercise Platform. *IEEE Transactions on Neural Systems and Rehabilitation Engineering*. 2020 Feb 1;28(2):444–52.
12. Seo G, Kishta A, Mugler E, Slutzky MW, Roh J. Myoelectric interface training enables targeted reduction in abnormal muscle co-activation. *J Neuroeng Rehabil* [Internet]. 2022 Dec 1 [cited 2023 Apr 5];19(1):1–12. Available from: <https://jneuroengrehab.biomedcentral.com/articles/10.1186/s12984-022-01045-z>
13. Alnajjar FS, Moreno JC, Ozaki KI, Kondo I, Shimoda S. Motor Control System for Adaptation of Healthy Individuals and Recovery of Poststroke Patients: A Case Study on Muscle Synergies. *Neural Plast*. 2019;2019.
14. Zendeabad SA, Kobravi HR, Khalilzadeh MM, Razavi AS, Nezhad PS. Presenting a New Muscle Synergy Analysis based Mechanism to Design a Trackable Visual Biofeedback Signal: Applicable to Arm Movement Recovery after Ischemic Stroke. *IEEE Access*. 2023;
15. Hesam-Shariati N, Trinh T, Thompson-Butel AG, Shiner CT, McNulty PA. A Longitudinal Electromyography Study of Complex Movements in Poststroke Therapy. 1: Heterogeneous Changes Despite Consistent Improvements in Clinical Assessments. *Front Neurol*. 2017 Jul 28;8:340.
16. McNulty PA, Thompson-Butel AG, Faux SG, Lin G, Katrak PH, Harris LR, et al. The efficacy of Wii-based Movement Therapy for upper limb rehabilitation in the chronic poststroke period: a randomized controlled trial. *Int J Stroke* [Internet]. 2015 Dec 1 [cited 2024 May 25];10(8):1253–60. Available from: <https://pubmed.ncbi.nlm.nih.gov/26332338/>