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Impaired Coordination and Recruitment of Muscle Agonists, But Not Abnormal Synergies or Co-contraction, Have a Significant Effect on Motor Impairments After Stroke

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Abstract

Movement synergies, muscle co-contraction, and decreased motor drive to muscle agonists were suggested to be major factors in motor impairments after stroke. The purpose of this study was to investigate the major muscle mechanisms contributing to motor impairment after stroke. Twelve healthy and 13 post-stroke patients participated in this observational study. Both groups participated in a single experimental session, performing hand pointing movements in multiple directions, during which EMG was assessed. Additionally, the patients underwent the Fugl-Meyer assessment. A set of features from the electromyography (EMG) signal and co-contraction ratios were used to compare the capacity to modulate the muscle activity between the two groups of participants. A correlation analysis was applied between the Euclidian distances of each target and the Fugl-Meyer scoring assessment in the post-stroke patients. We found that impaired modulation of muscle activity in post-stroke patients was characterized by significantly increased Euclidian distances between the EMG features of different target directions and by a higher variability between muscle activation compared to healthy subjects. Impaired capacity to modulate muscle activity significantly correlated with the impairment status. In conclusion, impaired motor performance post-stroke systematic disturbance in the control signal to limb muscles, which manifests as decreased capacity to modulate muscle activity, rather than co-contraction of muscle antagonists or stereotyped movement patterns.

Keywords

Electromyography · Motor drive · Motor performance · Muscle activity · Muscle contraction · Stroke

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1 Introduction

Brunnstrom (1970) has described six stages of recovery of voluntary movements post-stroke, reflecting the patient's capacity to isolate a movement of a particular limb segment. According to the magnitude and location of the lesion, the restoration of arm motor function begins with flaccid paralysis, followed by return of reflexes, voluntary movement within a synergy, movements out of synergy, and finally restoration of normal movement patterns. The movement synergy is here understood as the stereotypical movement patterns emerging during voluntary movement execution, reflecting the incapacity to dissociate limb segment movements from one another (Levin et al. 2009; Krakauer 2005).

The Fugl-Meyer scale enables the classification of post-stroke patients' impairment based on the recovery stages (Fugl Meyer et al. 1975). The scale is widely used in clinical settings (Nelson et al. 2018; Harris–Love et al. 2015; Mirela Cristina et al. 2015; Ohn et al. 2013). It has been validated to represent the motor impairment status post-stroke, mainly through construct validity studies that correlate the score with those of other clinical scales (Wei et al. 2011) or with activities of daily living status (Gladstone et al. 2002). Movement synergies of different severity are commonly seen in post-stroke patients and are suggested to reflect the degree of motor impairment. However, most studies focus on the chronic stage of post-stroke recovery, when the majority of recovery had already took place (Wagner et al. 2007). In the first post-stroke month, when motor recovery is substantial, movement synergies may not be pronounced as spasticity is not yet developed. Moreover, muscle activation pattern does not necessarily reflect the capacity to move out of synergies. Beer et al. (2000) have reported that impaired modulation of muscle activity post-stroke should neither be attributed to movement synergies nor to co-contraction ratios, but rather to systematic disturbance in the control signal to limb muscles. Wagner et al. (2007), on the other hand, have suggested the changes in muscle activity in the subacute post-stroke phase reflect improvements in hand reaching. Hand reaching movements require simultaneous activation of multiple muscles upon two joints, as opposed to stereotypical movement patterns, which makes the execution of such movements difficult for post-stroke patients. When reaching to different locations, healthy subjects change the activation amplitude of muscles in the time domain. For instance, reaching across the body may require a greater involvement of the pectoralis and anterior deltoid muscles than when reaching to the body side typically executed by the middle deltoid muscle and scapular stabilizers (Israely et al. 2017a, b). Likewise, reaching to the body top involves a greater involvement of the deltoid muscles than when reaching to a lower body target.

In the present study, we set out to investigate the muscle mechanisms contributing to the motor post-stroke impairment whose degree was evaluated on the Fugl-Meyer scale. In detail, we investigated the notion that clinical manifestations of motor impairment could have to do with muscle activation pattern during a hand reaching task. We reasoned that different movement strategies and impaired coordination in post-stroke patients might be captured by the time domain properties of the electromyography (EMG) signal. Therefore, the ability to change the activation properties of muscles during different motor tasks could be inferred from the EMG signal modulation. Figure 1 illustrates the proposed concept of muscle activity modulation during movements targeted to different locations, in both post-stroke and healthy subjects.

2 Methods

2.1 Participants

The study was conducted at the Bait-Balev Rehabilitation Center in Nesher, Israel. There were two groups of participants: 13 post-stroke patients and 12 control healthy subjects. Both groups participated in a single experimental session with the EMG assessment. In addition, the patients underwent the Fugl-Meyer assessment to enable the evaluation of a correlation between

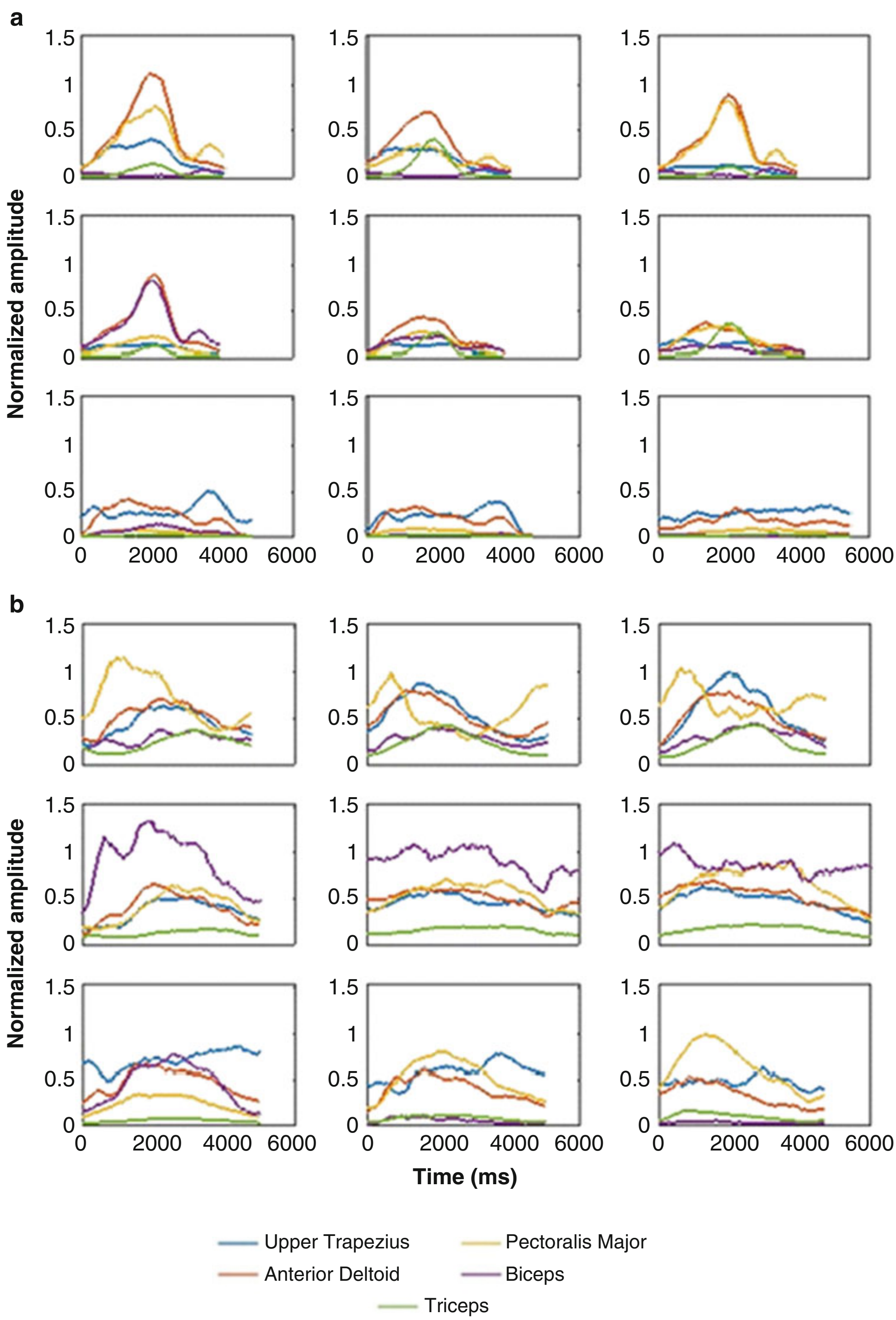


Fig. 1 Changes in muscle activation in the time domain for different movement directions, referred herein as modulation of muscle activity. Participants executed hand pointing movements to nine targets located in front of them while monitored by EMG. (**a**) EMG tracings of five muscles in a healthy subject while executing the movements to nine targets; (**b**) same traces in a post-stroke individual. Note that muscle activation in the healthy subject is more phasic, especially in the upper six movement targets, the overall exertion is smaller, and the time to

clinical score and EMG data. Cerebral stroke and hemiparesis of the upper extremity. Exclusion criteria, other central nervous system disease, and significant visual or hearing deficits. Participants' characteristics are summarized in Table 1. Post-stroke patients had mild (Fugl-Meyer score > 38; $n = 4$)-to-moderate (Fugl-Meyer score > 50; $n = 9$) motor impairment. Control subjects were contacted over the phone. The groups were about matched by the number of participants and sex, but differed by age ($p = 0.027$).

2.2 Study Protocol

Post-stroke patients were tested using the affected arm, whereas healthy subjects were tested using their self-reported dominant arm. Maximum voluntary contractions (MVC) were measured by standard muscle testing (Hislop and Montgomery 2002). The subject sat in front of a table with his forearm resting on it comfortably. The hand reaching spatial device was located as indicated in Fig. 2a. Subjects were requested to point to each target five times with a voice cue activated by EMG software every 10 s, for 45 pointing movements. The target pointing order was constant for all participants. Figure 2b illustrates the target order for a subject with a right-hand dominance. The order for the left-hand dominant subjects was horizontally mirrored but the same in the vertical dimension.

The hand reaching spatial device was composed of two vertical rods to which there were attached three semicircular shelves. Each shelf contained three movable pointing pins adjustable left- and rightward. The three shelves were located 10, 35, and 60 cm above the table. The device was positioned at the maximum hand reaching distance in front of the tested shoulder, with the middle pin (target 5) aligned with the shoulder in the sagittal plane. The side pins were positioned at a 45° angle to the shoulder joint at either side.

2.3 Electromyography

Surface EMG was recorded from eight muscles of the shoulder girdle and arm: trapezius; deltoid anterior, medial, and posterior fibers; pectoralis major; infraspinatus; biceps; and triceps (Trigno 8 setup, Delsys; Boston, MA). Electrodes were placed in accordance with the guidelines of the Surface Electromyography for the Non-Invasive Assessment of Muscles (SENIAM)–European Community Project (Hermens et al. 1999). MVC were performed prior to data collection. A 1-min rest period followed each MVC assessment to limit the possibility of fatigue. EMG signals were band-pass filtered at 20–450 Hz and were sampled at 2000 Hz.

EMG recordings were organized as an 8 by T matrix X^{8XT} for each target, where 8 was the number of muscles and T was the number of time samples. Net noise was filtered out at 50 Hz, followed by a mean subtraction. This was followed by root mean square calculations using overlapping windows of 50 samples. The mean baseline EMGs for each trial were subtracted from the averaged data. EMG data were normalized in accordance with the 70% MVC for each muscle.

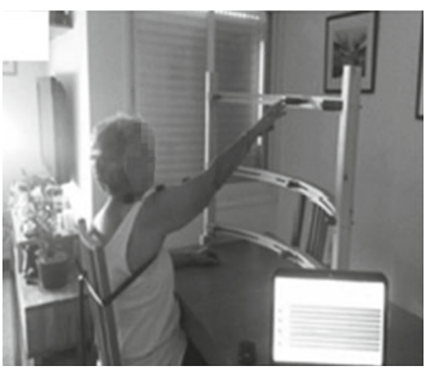
Each muscle from each EMG dataset and from each of the 9 movement directions was expressed by 12 constant features. Extracted features were chosen according to the authors' considerations to construct a good low dimensional representation of the original EMG data matrix. Figure 3 details

Fig. 1 (continued) task completion is shorter when compared with those in the post-stroke individual. The post-stroke activation pattern is more tonic, especially for the six lower targets of movement. The pectoralis muscle (yellow trace) is highly activated on all of the nine movement directions. In contrast, in the healthy subject, the pectoralis muscle is strongly activated in phasic pattern for the upper three targets of movement and for the mid-left target, which corresponded to the across-body movement, and is barely active in the three lower targets

Table 1 Participants' demographics and baseline measures

Post-stroke patients	Age	Sex	Dominant hand	Side affected	Stroke type	Location	Time since stroke (days)	FM (score)	Shoulder pain (score)
1	78	F	R	L	Ischemic	R-MCA	22	53	44
2	67	F	R	R	Ischemic	L-MCA	32	51	40
3	78	M	R	L	Ischemic	R-IC	20	54	60
4	81	F	R	L	Ischemic	R-IC and Th	13	58	35
5	68	F	R	R	Ischemic	L-Tl	13	53	7
6	76	M	R	L	Ischemic	R-IC and BG	25	51	27
7	68	F	R	R	Ischemic	L-IC	9	54	0
8	89	M	R	R	Ischemic	L-pons	25	42	0
9	79	M	R	L	Hemorrhagic	R-Th	14	38	2
10	71	M	R	R	Ischemic	L-MCA	20	60	0
11	63	M	R	L	Ischemic	R-MCA	15	46	0
12	82	F	R	L	Ischemic	R-BG	26	41	0
13	81	M	R	L	Ischemic	R-MCA	20	59	0
Control subjects									
1	78	M	R	R					
2	71	F	R	R					
3	74	M	R	R					
4	54	M	R	R					
5	58	M	L	L					
6	65	M	R	R					
7	67	F	R	R					
8	70	F	L	L					
9	78	F	R	R					
10	79	M	L	L					
11	70	F	R	R					
12	67	M	R	R					

R right *L* left, *MCA* middle cerebral artery, *IC* internal capsule, *Th* thalamus, *Tl* temporal lobe, *BG* basal ganglia, *FM* Fugl-Meyer score. The Fugl-Meyer scale evaluates the degree of motor impairment with 0 (maximum) and 66 (minimum impairment). Shoulder pain was assessed on a visual analogue scale (VAS) with 100 (maximum) and 0 (no pain)



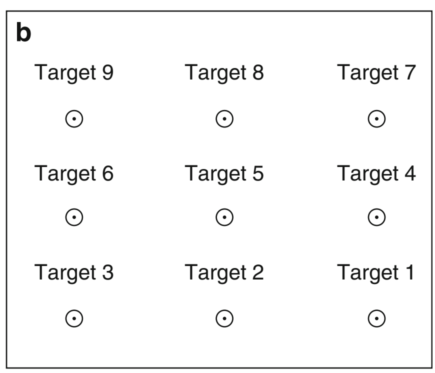


Fig. 2 The hand reaching spatial device. (**a**) Subjects were asked to reach with their dominant hand (control group) or the impaired hand (patient group) to nine different targets that were located in each participant's maximum hand reaching range of motion. (**b**) Representation of the order and direction of the targets for a subject with a dominant right hand

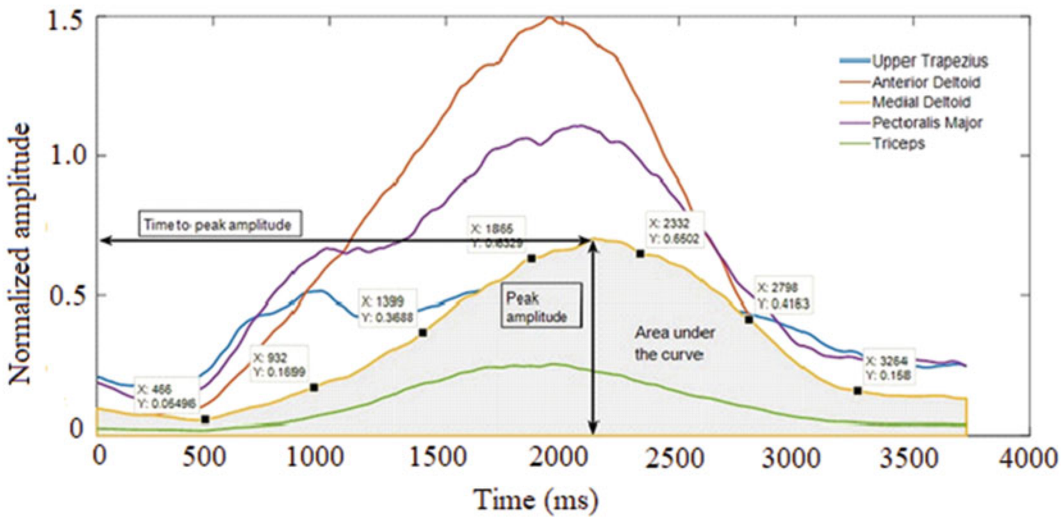


Fig. 3 A set of 12 features was extracted from the EMG signal of each muscle to compare inter-group differences in its modulation in response to different movement directions. The features comprised the time and amplitude of the first peak, the time and amplitude of the second peak, and the total area under the curve. In cases of more than two peaks or less than two peaks the relevant features were replaced as detailed in the method section. Additional seven features comprised the amplitude of seven data points equally distributed on the time domain plot. In the figure, only five muscles are shown and only one is marked by the set of features. In the study, features were extracted from eight muscles and for each movement direction. Accordingly, each subject was represented by a feature matrix for further analysis

the chosen features selected by the algorithm. The analysis was performed using Matlab (MathWorks Inc., Natick, MA).

2.4 Data

For each movement direction $i \in [1, 9]$, the EMG data $X^{8 \times T}$ was expressed as $X^{8 \times 12}$. For the first inter-group comparison, each $X^{8 \times 12}$ matrix was converted to $X^{1 \times 96}$, $f \in [1, 96]$ vector. Accordingly, each participant was expressed by $X^{9 \times 96}$ matrix ($X^{i \times f}$) for all nine movement directions. This was followed by calculating the Euclidian distance between all combinations of rows within the $X^{9 \times 96}$ matrix.

The first method applied for the comparison of differences in muscle function between the post-stroke patients and healthy subjects used the Euclidian distances between EMG features, the central fifth point of the reaching space, shown in Fig. 2b, all the other target directions (Table 2). A multivariate analysis of variance (MANOVA) was applied using the eight dependent variables in each subject for inter-group comparison. The Euclidian distance of a muscle feature for reaching each target was correlated with the Fugl-Meyer score. A second method for comparison between the two groups used the same features, however separately for each muscle (Table 3). Accordingly, each muscle tested of each subject was expressed as an eight-dimensional vector. The MANOVA was applied for each muscle separately. The third method of analysis compared the total exertion of individual muscles for each movement direction. An eight-dimensional vector represented each subject for each movement direction (Table 4). The MANOVA was again applied for comparison between the two groups.

In addition, five pairs of muscles were evaluated for co-contraction and compared between the two groups, according to previously proposed method of analysis (Israely and Carmeli, 2016; Kellis et al. 2003). Briefly, the minimum function and the maximum function of common muscle activities were calculated for each muscle pair. For each function, the total area

Table 2 Comparison of the mean Euclidian distances between EMG features for the central point of the reaching space and for all other target directions between post-stroke patients and control healthy subjects

Condition	Target 1	Target 2	Target 3	Target 4	Target 6	Target 7	Target 8	Target 9
Healthy	4.876	4.045	4.919	4.185	5.256	4.700	4.191	5.997
	(0.954)	(1.314)	(1.772)	(1.253)	(1.848)	(1.213)	(1.340)	(1.900)
Stroke	8.867	7.330	9.103	7.997	6.553	7.368	6.738	7.418
	(5.185)	(4.162)	(3.836)	(5.142)	(2.474)	(2.541)	(2.387)	(2.713)
p value	0.017	0.017	0.020	0.022	0.150	0.003	0.004	0.142

Data are means (SD); non-significant values are highlighted in gray. Note: values in the first two rows represent the Euclidian distances between two vectors as detailed in the methods section and accordingly have no units

Table 3 Differences in muscle activity, assessed by the mean Euclidian distances between EMG features of the central point of the reaching space and all other target directions, between groups

Muscle	*p* value	Target 1	Target 2	Target 3	Target 4	Target 6	Target 7	Target 8	Target 9
Upper trapezius	0.027	0.003	0.008	0.002	0.032	0.000	0.029	0.049	0.034
Anterior deltoid	0.119	0.105	0.033	0.006	0.066	0.938	0.246	0.361	0.154
Medial deltoid	0.004	0.010	0.003	0.001	0.013	0.001	0.005	0.011	0.013
Posterior deltoid	0.480	0.522	0.353	0.069	0.132	0.098	0.121	0.197	0.271
Pectoralis major	0.360	0.278	0.038	0.064	0.221	0.615	0.239	0.077	0.955
Infraspinatus	0.000	0.028	0.037	0.001	0.002	0.000	0.000	0.006	0.000
Biceps	0.189	0.438	0.218	0.239	0.100	0.191	0.063	0.012	0.005
Triceps	0.212	0.061	0.083	0.053	0.046	0.353	0.023	0.007	0.054

Multivariate analysis of variance MANOVA. The numbering of targets represents the movement directions depicted in Fig. 2

under curve was calculated. Then, the area of minimum function was divided by that of maximum function. The presence of a correlation between co-contraction indices and the Fugl-Meyer score was investigated.

The Fugl- Meyer scale, which assesses upper extremity motor function, was the main outcome measure. It consists of 33 items scored on a 3-point scale, where 0 represents the inability to complete the test, 1 represents a partial ability, and 2 represents full completion. The items assess reflexes, capacity to move in and out of synergy, and the ability to limit a movement to the shoulder, elbow, or wrist and to grasp various objects (Fugl Meyer et al. 1975). In addition, shoulder pain was assessed on a visual analogue scale (VAS) with 100 (maximum) and 0 (no pain).

There were some missing data in the statistical analysis. Three out of the 13 post-stroke patients managed to reach for the 6 lower targets, but not for the upper 3. The mean amputation technique was applied for the three missing targets in these three participants (Schafer and Graham 2002). When the assumption of homogeneity of variance was violated, ANOVA Welch test was applied instead of the standard MANOVA. Spearman's rank correlation was applied between the Fugl-Meyer score and the mean Euclidian distance of each target direction. A p value <0.05 defined statistically significant differences. The analysis was performed using a commercial SPSS v23 package (IBM Corp, Armonk, NY).

3 Results

3.1 Changes in Muscle Activity Between the Middle of the Hand Reaching Space to Other Movement Directions

Table 2 summarizes the mean Euclidian distances from the middle fifth target to each other target direction in the two groups. Distances between the fifth target and other six targets were significantly different between the two groups

Table 4 Comparison of the mean muscle exertion index, measured as the normalized EMG amplitude for each muscle and for each target direction, between groups. Accordingly, the data are unitless

Muscle		Target 1	Target 2	Target 3	Target 4	Target 5	Target 6	Target 7	Target 8	Target 9
Upper trapezius	Healthy	2,360	1,844	1,918	2,814	2,616	2,543	3,503	3,589	3,652
		(1221)	(1522)	(1791)	(1445)	(1597)	(1763)	(1758)	(1612)	(1699)
	Stroke	7,307	8,643	8,160	11,370	10,422	10,126	9,420	9,399	9,677
		(4285)	(5523)	(5961)	(7431)	(6768)	(6785)	(4271)	(4203)	(5155)
	p value	0.001	0.001	0.003	0.001	0.001	0.002	0.002	0.002	0.005
Anterior deltoid	Healthy	1,569	2,138	2,751	2,036	2,575	3,650	2,371	3,101	4,380
		(734)	(1024)	(1067)	(663)	(1027)	(859)	(941)	(1040)	(977)
	Stroke	4,955	6,242	6,424	6,871	6,955	7,204	6,198	6,999	7,678
		(2137)	(3026)	(2890)	(3298)	(3059)	(3325)	(2563)	(3015)	(3641)
	p value	<0.001	<0.001	0.001	<0.001	<0.001	0.002	0.001	0.003	0.019
Medial deltoid	Healthy	1,504	1,254	1,019	2,049	1,800	1,516	2,744	2,621	2,186
		(334)	(425)	(497)	(658)	(599)	(568)	(906)	(748)	(645)
	Stroke	5,621	6,115	4,713	8,501	6,834	5,894	7,953	7,707	7,197
		(2781)	(4849)	(3626)	(6020)	(4492)	(4195)	(4594)	(5281)	(6281)
	p value	<0.001	0.004	0.003	0.002	0.002	0.003	0.006	0.014	0.033
Posterior deltoid	Healthy	535	345	462	765	436	355	847	534	404
		(293)	(226)	(713)	(638)	(457)	(322)	(364)	(276)	(230)
	Stroke	2,438	3,109	2,341	4,465	3,207	2,703	4,125	3,930	3,887
		(3089)	(5187)	(3104)	(6574)	(4815)	(3911)	(6050)	(6056)	(7183)
	p value	0.047	0.079	0.053	0.066	0.061	0.052	0.121	0.110	0.160
Pectoralis major	Healthy	1,091	1,525	3,441	1,271	1859	4,037	1,073	1,632	3,675
		(1132)	(1024)	(2974)	(1134)	(1729)	(3223)	(940)	(1086)	(2873)
	Stroke	3,742	5,676	8,087	4,441	4,897	6,825	3,138	4,238	5,570
		(4010)	(6234)	(6064)	(5586)	(4233)	(4795)	(3181)	(3604)	(3097)
	p value	0.038	0.035	0.024	0.063	0.030	0.100	0.075	0.051	0.156
Infraspinatus	Healthy	1,306	1,313	1,258	1,493	1,378	1,166	1,569	1,640	1,430
		(198)	(290)	(430)	(459)	(406)	(308)	(498)	(366)	(401)
	Stroke	4,972	5,996	6,307	7,196	6,716	6,755	6,090	6,312	6,474
		(2841)	(4375)	(4667)	(5174)	(4542)	(4944)	(3815)	(4207)	(5010)
	p value	0.001	0.002	0.002	0.002	0.001	0.002	0.005	0.007	0.011
Biceps	Healthy	440	483	462	500	478	454	495	488	441
		(198)	(265)	(231)	(232)	(266)	(236)	(208)	(262)	(205)
	Stroke	2,248	2,765	2,717	3,191	3,004	2,929	1,786	1,849	1,818
		(1670)	(2330)	(2062)	(3168)	(3134)	(2602)	(902)	(940)	(843)
	p value	0.002	0.004	0.002	0.010	0.013	0.005	0.001	0.001	<0.001
Triceps	Healthy	1,451	1,357	925	1,670	1,227	900	1,826	1,582	1,085
		(886)	(958)	(718)	(1228)	(853)	(838)	(1400)	(1187)	(997)
	Stroke	3,569	4,112	3,012	5,666	4,494	3,975	5,290	5,055	4,870
		(2764)	(4660)	(3277)	(5956)	(4465)	(3909)	(5357)	(5149)	(5480)
	p value	0.020	0.057	0.043	0.063	0.023	0.016	0.075	0.064	0.058

Data are means (SD); Welch's ANOVA was applied for comparisons. The numbering of targets represents the movement directions depicted in Fig. 2

($p < 0.05$) in that they increased post-stroke, reducing the possibility for movement synergies. Targets 6 and 9 were placed in such a way that the patients had to execute the hand pointing movements across the body and to the upper portion of the reaching space. These movements required a greater muscle exertion of deltoid and pectoralis muscles also in healthy subjects, assumingly leading to non-significant inter-group differences. Movements to other locations in space required a smaller effort in healthy subjects but were still demanding for post-stroke patients, which led to significant inter-group differences.

Table 3 illustrates the modulation of each muscle activity in the time domain between different targets for both groups. Using single muscle activity for inter-group comparisons produced less consistent differences that were present only in the upper trapezius, medial deltoid, and infraspinatus but not in the other muscles. That might indicate that differences in muscle activity between the two groups depended on interactions between muscles and not only on the activity of single muscles. With reference to the previous assumption regarding the non-significant inter-group differences for targets 6 and 9, Table 3 does illustrate non-significant inter-group differences for the anterior and posterior deltoids and pectoralis muscles but significant differences for the medial deltoid. The first three muscles are highly active in movements across the body and in the top of the reaching space, i.e., for targets 6 and 9. The non-significant inter-group differences concerning these muscleswith our assumption. However, the significant difference between the medial deltoids was with the assumption.

3.2 Muscle Exertion for Different Movement Directions in the Healthy and Post-stroke Groups

The posterior deltoid, pectoralis major, and triceps demonstrated non-significant inter-group differences in some of the movement directions (Table 4). Non-significant differences in pectoralis for higher target directions were consistent with our assumption of non-significant inter-group differences in the first analysis method for targets 6 and 9. The posterior deltoid was less activated during hand reaching in both groups as indicated by lower exertion values compared to the other muscles, suggesting that this muscle did not play a key role in task completion. A non-significant difference in the triceps muscle was rather surprising, given its crucial role in extending the elbow, a movement reportedly shown to be significantly impaired post-stroke (Tomita et al. 2018; Beebe and Lang 2009). Dysfunction of elbow extension post-stroke may be aggravated due to impaired recruitment of muscle agonist (triceps) or hyperactivity of muscle antagonist (biceps). Both factors are related to the extent of the integrity of the corticospinal tracts, i.e., stroke severity (Lindenberg et al. 2010) and the time lapse from stroke (Harris–Love et al. 2015). In the present study, patients were in the subacute phase post-stroke with mild-to-moderate motor impairment, and they apparently sustained less biceps co-contraction, resisting the elbow extension by the triceps.

3.3 Correlation Between Muscle Activity and Fugl-Meyer Score

Correlation was investigated between the Fugl-Meyer score and Euclidian distances between targets. The mean of each individual modulation matrix, i.e., the Euclidian distance from each of the nine targets to all other eight targets, was calculated, so that each individual was represented by modulation vector. Table 5 illustrates the results in which significant negative correlations indicate that an increased Euclidian distance between target features corresponded to low Fugl-Meyer scores.

3.4 Muscle Co-contractions in the Healthy and Post-stroke Individuals

Muscle co-contraction ratios between pairs of muscles were calculated and compared between the groups of healthy and post-stroke individuals. Table 6 illustrates the p values of MANOVA evaluation, using the co-contraction ratios between five muscle pairs in both groups. The results were not significant in the three movement directions 4, 5, and 7. These three targets were

Table 5 Correlation between the mean Euclidian distance and the Fugl-Meyer score ($n = 13$)

	Target 1	Target 2	Target 3	Target 4	Target 5	Target 6	Target 7	Target 8	Target 9
Spearman's coefficient	−0.549	−0.527	−0.519	−0.554	−0.577	−0.596	−0.557	−0.546	−0.607
p value	0.052	0.064	0.069	0.049	0.039	0.032	0.048	0.053	0.028

Table 6 Comparison of co-contraction ratios for five muscle pairs between healthy subjects and post-stroke patients

	Pairwise comparisons; *p* values				
	Trapezius-anterior deltoid	Anterior deltoid-posterior deltoid	Pectoralis major-posterior deltoid	Anterior deltoid-biceps	Biceps-triceps
Target 1	0.007	0.879	0.781	0.058	0.138
Target 2	0.001	0.057	0.105	0.028	0.304
Target 3	0.021	0.192	0.751	0.025	0.076
Target 4	0.256	0.476	0.251	0.023	0.056
Target 5	0.074	0.757	0.741	0.052	0.028
Target 6	0.007	0.012	0.010	0.001	0.239
Target 7	0.019	0.685	0.043	0.075	0.063
Target 8	0.002	0.008	0.306	0.014	0.092
Target 9	0.001	0.004	0.006	0.002	0.330

located at the body side and required a shoulder horizontal abduction, in contrast to targets 6 and 9 that required reaching across the body with a horizontal adduction. Reaching across the body to targets 3, 6, and 9 showed significant differences in inter-group co-contraction ratios, due assumingly to greater exertions required to complete the task. There were non-significant inter-group differences in the co-contraction ratio in three pairs of muscles. This might reasonably justify the notion that the emergence of stereotyped movement patterns evolves later through recovery and does so in patients with a greater degree of motor impairment. The right-hand column in Table 5, for instance, illustrates that the ratio between the recruitment of the biceps and triceps muscles was preserved in the subacute phase. Accordingly, impaired elbow extension was probably not due to overactivity of the biceps antagonizing the triceps, but rather due to impaired recruitment of the triceps (Molina Rueda et al. 2012; Wagner et al. 2007). These findings suggest that the co-contraction ratios did not play a major role in motor impairments in the subacute phase of the post-stroke patients.

Figure 4 illustrates the means of co-contraction ratios for each pair of muscles separately. It emphasizes that apart from the co-contraction between the trapezius and the anterior deltoid, the other four pairs of muscles were recruited in a similar manner in both groups, despite a greater exertion of muscles in the post-stroke patients (Table 4). Significant inter-group differences between the trapezius and the anterior deltoid could assumingly result from overactivity of the trapezius to compensate for a weaker deltoid (Israely et al. 2017b; Levin et al. 2009; Wagner et al. 2007). Correlations between the Fugl-Meyer score and co-contraction for all of the muscle pairs were non-significant, which is compatible with the non-significant differences in co-contraction ratios between the two groups, reinforcing the assumption that mild-to-moderate motor impairments in the subacute phase of

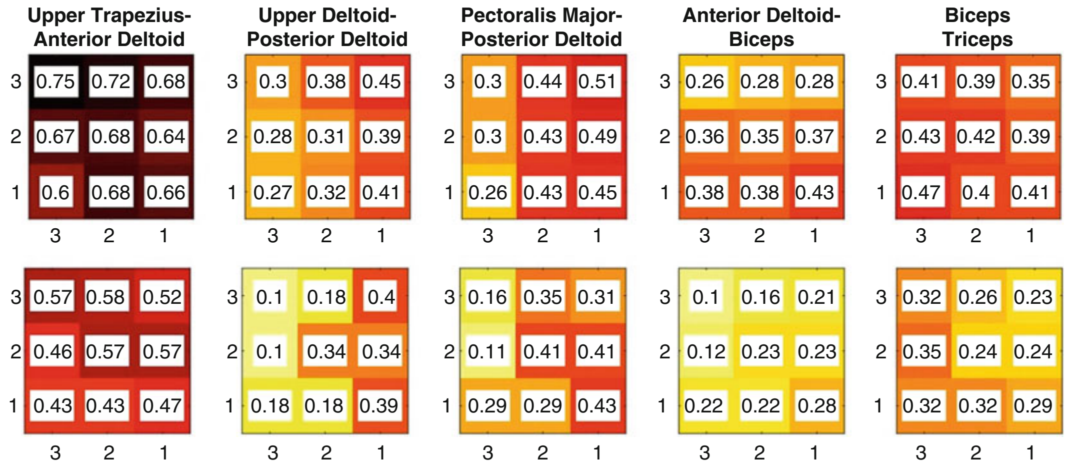


Fig. 4 Mean co-contraction ratios of post-stroke patients (upper row) and healthy subjects (bottom row) of five muscle pairs for nine movement directions. Each column refers to a different pair of muscles. Co-contraction between a pair of muscles was defined as the ratio between the minimum function of the two muscles and the maximum function of the two muscles and was accordingly graded on 0 to 1 scale. Dark colors indicate higher co-contraction ratios, which means that timing and amplitude of recruitment of the two relevant muscles were more similar. Lower values, marked by brighter colors, indicate different recruitment properties of the two muscles. The digits 1, 2, and 3 around the boxes indicate the order of targets executed during hand reaching by the right-handed participants. They applied hand reaching to the first row of targets, followed by the second row and then the third row. In each row, the first applied hand reaching was to column number 1, followed by column number 2 and then column 3. For example, the fifth target is the target in the second row in the second column

stroke patients are not due to increased co-contraction ratios.

4 Discussion

We investigated muscle mechanisms underlying motor impairments, in post-stroke patients, who were mostly categorized as suffering from mild motor impairments, in the subacute post-stroke phase. In this cohort, we evaluated their capacity for executing demanding task, which apparently could not be executed in patients with higher degrees of motor impairment. Three patients could execute hand reaching to only six targets instead of nine targets. During data collection, it was noticed that post-stroke patients struggled to execute this task. To minimize the use of compensation strategies, a trunk belt was used to eliminate trunk displacement, forcing the patients to complete the task without recruiting additional abnormal degrees of freedom. The aim was to study muscle mechanisms that contribute to motor impairments under these circumstances, knowing that the well-defined cohort may limit the generalization of results. Movement synergies were measured by the extent to which patients modulated their muscle activity in the time domain, for different directions. Since movement synergy is characterized by stereotypical movement pattern, we hypothesized that it would be reflected by decreased Euclidian distances between different directions in the post-stroke condition. The second mechanism investigated was co-contraction between five pairs of antagonistic muscles.

Post-stroke patients modulate muscle activity in a different manner than healthy subjects do. Contrary to our assumption, Euclidian distances between targets were significantly increased in post-stroke patients, when compared to healthy subjects. Increased Euclidian distances between targets showed large changes in the pattern of muscle activity between targets, suggesting that motor impairments were probably not due to stereotyped movement patterns. These findings are compatible with previous reports showing that pathologic movement synergies mostly appear in later stages of recovery (McPherson and Dewald 2019; Pandian and Arya 2012) and in patients with more pronounced motor impairments (Cirstea and Levin 2000). Capacity to move out of synergies and to execute isolated joint movements in the subacute phase of recovery may indicate a better prognosis for recovery of physiologic movement patterns (Krakauer and Marshall 2015; Winters et al. 2015).

In this study we revealed significant negative interactions between the Fugl-Meyer scores and muscle activity. The larger the Euclidian distance between targets, the lower the score. The validity of these interactions in mildly impaired patients should be cautiously considered due to the ceiling effect of proximity to the maximum Fugl-Meyer score. Significant differences in muscle activity modulation between the stroke patients and healthy subjects indicate that motor impairments are manifested by interactions between activities of different muscles rather than by activation properties of single muscles. Although muscle exertion was significantly higher in post-stroke patients (Table 4), co-contraction ratio was not a major factor in motor impairments.

Concerning the movement components above outlined, the Fugl-Meyer score enables the quantification of motor impairment in a clinical setting. Since the Fugl-Meyer scale assesses sub-movements, and as such enables the isolation of segmental movements, a decreased score can be interpreted as movement synergies or increased co-contraction. The present findings were with this notion despite significant correlations between muscle activity modulation and the Fugl-Meyer score. The findings illustrate that larger movement impairments correlated with increased Euclidian distance between different target directions. Movement synergies were not the main source of motor impairments observed. This notion is reinforced by the Euclidian distances of the patients being significantly greater when compared to those of the control subjects. The present findings are in line with those of Beer et al. (2000) who have revealed abnormal spatial tuning of muscle torque at the elbow, used to initiate movements of the paretic limb in hemiparetic patients. Those authors suggest that spatial abnormalities result from systematic disturbances in the control signal to limb muscles rather than muscle weakness, spasticity, or muscle synergies. In the present study, co-contraction ratios between five pairs of muscles were not significantly different between the stroke patients and healthy subjects, suggesting that motor impairments were probably not related to co-contraction between antagonists. These findings are with those of other studies that investigated patients in the chronic stage of recovery from more severe motor impairments (Ohn et al. 2013; Leonard et al. 2006).

Significant correlations between our model of the assessment of muscle activity impairment post-stroke and the Fugl-Meyer scale are not settled with the underlying mechanisms causing motor impairments, i.e., movement synergies and increased co-contractions. In this study patients were examined approximately 3 weeks post-stroke and suffered from mild-to-moderate impairments. Spasticity was not strongly pronounced in these patients during recovery; therefore muscle activations were less prone to stereotypical movement patterns. It seems that during recovery from flaccid paresis, patients scan for a proper group of agonistic muscles to efficiently execute the movement manifest by increased Euclidian distances between targets. A larger task demand probably requires recruitment of additional synergistic muscles for task completion (Israely et al. 2017a).

Our present findings underscore the necessity for differentiation between a degree of motor impairment and the time elapsed since stroke, when formulating a suitable treatment program, as has also been suggested by others (Carmichael and Krakauer 2013). Twitchell (1951) and Brunnstrom (1970) have suggested that control over basic synergies should be achieved in order to execute more complex movements. Accordingly, during early stages of recovery, patients should be aided or encouraged to use these synergies (Cirstea and Levin 2000; Bobath, 1990; Carr and Shepherd 1989).

In the last decades, task-oriented training (TOT) has been indicated to promote functional independence. TOT was previously defined as treatment approach that focuses on meaningful complex movements, with real-life object manipulation in a real-life environment (Timmermans et al. 2010). Numerous studies have evaluated the efficiency of TOT, but controversies remain as yet unsettled regarding its efficiency for improving motor function (Thant et al. 2019; Almhdawi et al. 2016; Jeon et al. 2015; Pollock et al. 2014; French et al. 2007). The mechanisms for motor improvement, motor learning, and motor compensation remain unsettled as well (Krakauer and Cortés 2018; Kitago et al. 2013; Roby-Brami et al. 2003).

Animal experiments and human studies have demonstrated the necessity to focus on reducing motor impairment by enhancing motor learning in the first 6 months post-stroke (Krakauer et al. 2012; Moon et al. 2009). In that context, therapists should direct toward the execution of motor task with the right movement pattern. In severe cases of stroke, therapists may decrease the degrees of freedom to be used by the patient to ease the motor task or may use assisted approach to bridge the agonist recruitment deficits. Moreover, therapists should apply the commonly known rehabilitation principles for motor learning, which include distributed practice (frequent rest periods within a session), contextual interference (using different objects to manipulate), task specific variability (different textures, weights, arm range of motion, direction of movement), feedback by knowledge of results, and increased task demands (Israely et al. 2017b; Schweighofer et al. 2011; Krakauer 2006). In moderately to severely (Fugl-Meyer <45 points) impaired patients, with increased muscle tone 2 weeks post-stroke (Ashworth scale >2), a greater attention should be taken for preserving joint motion ranges and to decrease a chance for contractures in later stages of recovery (Triccas et al. 2019; Urban et al. 2010; Wissel et al. 2010). Platz et al. (2001) have introduced the arm ability training that implemented the above principles, tailored to post-stroke patients with mild impairment. TOT is considered the intervention of choice in patients with mild motor impairment, as long as the emphasis is placed on correct movement pattern and motor learning principles.

This study has several limitations. A rather small number of participants might affect between-group differences. It also could have an impact on the application of classification algorithms validating our findings. Patients had just mild-to-moderate motor impairments, which makes it difficult to generalize the findings for more severe post-stroke conditions. Nonetheless, we believe we have shown that impaired capacity for modulating muscle activity for different movement directions is a good indicator of the overall motor impairment of the upper extremity in milder post-stroke stages of motor impairment. Our findings suggest that in the subacute phase of recovery, motor impairment cannot be attributed to movement synergies or increased co-contraction between muscle antagonists, but rather to impaired coordination and recruitment of muscles agonists, resulting in increased demand on synergistic muscles. It might be assumed that corticospinal tract integrity may facilitate isolated joint movement out of movement synergies.

Conflicts of Interest The authors declare no conflicts of interest in relation to this article.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the Review Board of the Bait-Balev Rehabilitation Center in Nesher, Israel, and it was registered at ClinicalTrials.gov#NCT03063151.

Informed Consent Informed consent was obtained from all individual participants included in the study. In addition, the subject presented in the photo of Fig. 2 gave written informed consent permitting the reproduction of his body in both electronic and printed versions of the article.

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