Study of Synergy Patterns during the execution of Stroke Rehabilitation Exercises

O. Urra [1,2], A. Casals [1,2], R. Jané[1,2,3]

[1] Institute for Bioengineering of Catalonia, Barcelona, Spain,{ourra, acasals, rjane}@ibecbarcelona.eu

[2] Universitat Politècnica de Catalunya - BarcelonaTech, Barcelona, Spain

[3] CIBER de Bioingeniería, Biomateriales y Nanomedicina, Spain

Abstract

Stroke is a leading cause of disability, being motor impairments its major consequence. Despite rehabilitation, more than 60% of the patients report upper-limb motor dysfunction. The design of novel rehabilitation strategies requires objective measures to assess motor impairment and recovery. In a previous study, we proposed to use the synergy components of the unaffected limb as a reference to be targeted by rehabilitation, since they are proven to explain healthy motor control and to be altered after stroke. We demonstrated that healthy subjects have very similar control structures (synergies and activation vectors) in their right and left arms. Here, we investigate the existence of movement-specific control strategies. To do so, we analyze the inter-subject similarity of the healthy control structure in twelve common stroke rehabilitation exercises and we evidence that motor control is movement specific and generalizes across different subjects and their limbs. However, the similarity degree depends on the movement, suggesting that novel training protocols should purposely choose the rehabilitation exercises to ensure maximum control similarity with the reference pattern.

1. Introduction

Stroke is a leading cause of permanent and complex-long term disability in adults, with upper limb hemiparesis being one of the primary consequences [1]. Even with intensive rehabilitation two thirds of the patients remain without function in their upper limb [2]. The establishment of standards to study post-stroke functional recovery is essential to promote the development of successful therapies. However, available scales such as Fugl-Meyer Assessment of motor recovery or the Barthel Index are often not enough, since they rely on therapist expertise and non-quantitative measures [3]. In a previous study we proposed the use of the healthy limb synergies as a reference to be targeted by rehabilitation [4]. Synergies are conceptualized as muscle modules that the Central Nervous System recruits following specific activation patterns to control the motor function [5-7]. Thus, synergies constitute a meaningful physiological marker of healthy motor control. In addition, it has been demonstrated that stroke alters synergies - including associated activations - of the impaired limb while leaving the synergies of the other limb intact [8]. These results indicate that synergy alteration may explain at least to a certain extent the motor abnormalities exhibited by the paretic arm. In the aforementioned study, we proved that in healthy subjects right and left arm synergies and activation patterns are very similar, suggesting that restoring the synergy components of the healthy limb on the impaired limb may restore the normal motion. In this study, we investigate the existence of movement specific synergy and activation patterns in the population and whether these are conserved in both limbs, so that rehabilitation paradigms could be designed for each movement based on common synergy and activation traits. To do so, we asked six healthy subjects to perform twelve common stroke rehabilitation exercises involving elbow and shoulder and we compared the extracted synergies and activation patterns of each movement. We provide evidence that despite a certain degree of inter-subject variability, each movement is controlled by a specific synergy and activation pattern that generalizes across different subjects and their both limbs.

2. Methods

2.1. Experimental protocol

Six neurologically intact subjects (right-handed males, age 25-35) participated in this study. Written informed consent was required for participation in the protocol, approved by the Institutional Review Board of the Institute for Bioengineering of Catalonia. Subjects were asked to perform 30 repetitions of 12 common stroke rehabilitation movements to train elbow and shoulder, each involving 1-2 degrees of freedom. The experiment was carried out with both arms. In order to avoid learning effects, the arm order was randomly chosen for each subject.

2.2. Data acquisition

EMG signals were recorded using a pair of disposable disc Ag-AgCl electrodes (1 cm in diameter, 1.5 cm inter-electrode distance; Foam electrode 50/PK – EL501, Biopac Systems Inc.) for each muscle on right and left arms according to published guidelines [9]. Registered muscles were Infraspinatus (IS), Trapezius Superior (TS), Deltoid Anterior (DA), Deltoid Medial (DM), Pectoralis Major (PM), Biceps Brachii (BB), Triceps Brachii Long Head (TBL) and Brachioradialis (BRD), plus the reference electrode placed at the corresponding wrist. Registration was done through the EMG 100C acquisition system (BIOPAC Systems, Inc.) at a sampling rate of 1000 Hz and a gain of 500. A Notch filter was used to remove 50Hz interference.

2.3. Synergy extraction

EMG signals were manually segmented to exclude segments resting periods and remaining segments were highpass filtered using a zero-phase Butterworth (n=6) filter, with a cutoff frequency of 50Hz. After demeaning, linear envelopes were computed and normalized to the maxima to estimate the mean envelope. Signal length was temporally normalized to 100 points. A synergy model was extracted for each subject's arm and movement using the nonnegative matrix factorization (NMF) algorithm [10]. NMF models the EMG signal of the recorded muscles as a linear combination of time invariant muscle synergies, each activated by a time-varying activation pattern which can be mathematically expressed as:

$$D(t) = \sum_{i=1}^{N} H_i(t) \cdot W_i + \varepsilon \quad (1)$$

where D(t) is the EMG signal at time t, N is the number of muscle synergies extracted, W_i is the *i-th* muscle synergy, H_i is the nonnegative activation vector for the *i-th* synergy and ε is any residual activity unexplained by linear combination. To set N, we successively increased the number of synergies extracted, from one to the number of muscles recorded, and selected the minimum number of synergies required for an EMG reconstruction VAF (Variance Accounted For) of 90%.

2.4. Synergy and activation comparison

Similarity between pairs of synergies was quantified via the scalar product after normalizing the vector norm of each synergy (W_i) to one. Arm synergies were matched to the synergy on the opposite arm resulting in a higher scalar product. Inter-subject synergy similarity was assessed with the mean Pearson's correlation coefficient (R^2) computed between the synergies of all possible subject pairs. Inter-subject synergies were matched using 2-node hierarchical cluster trees based on the Minkowski distance.

Activation vectors were matched following the order established by their corresponding synergies. Similarity between activation vectors was quantified by Pearson's correlation coefficient of the muscle activation vectors (H_i). Inter-subject activation similarity was also estimated with the mean Pearson's correlation coefficient between the activations of all possible subject pairs.

Statistical significance of the differences of synergies and activation vector similarities was determined by the Wilcoxon signed rank-test ($p<0.05$). Statistical significance on the variability differences of each muscle contribution to the mean synergy was determined by the Friedman test ($p<0.05$).

3. Results

Synergy extraction resulted on an average of 2 synergies needed to model the EMG recorded during the execution of the 12 rehabilitation movements for either the right or the left arm. Some subjects needed three synergies to explain at least the 90% of the variance of some movements, which varied from subject to subject. However, the VAF accounted by the corresponding 2-synergy model in these cases was almost 90% and never less than 85%, so in order to ease comparisons we considered the 2-synergy models for all subjects and movements.

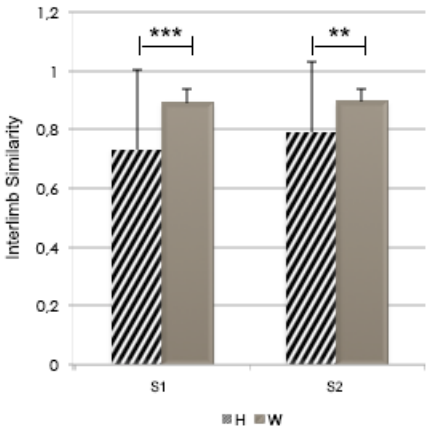

Figure 1 *Mean inter-limb activation (stripped bars) and synergy (solid bars) similarity* between the left and right arm of the same subject. *Activation similarity measure is R^2 and synergy similarity measure is the normalized scalar product. **: p <0.01, ***:p <0.001. Error bars are SD.*

Interlimb synergy comparison revealed that for a given movement both synergies and activations are highly conserved within the same subject, with similarity degrees ranging from 73.16 ± 27.05% to 79.01 ± 24.01% in the case of activations and from 89.03 ± 9.44% to 89.49 ± 10.51% in the case of synergies (Figure 1). However, synergies are significantly more conserved than activation vectors, both in synergy 1 ($p<0.001$) and synergy 2 ($p<0.01$). Similarly, synergies were less variable than their corresponding activations.

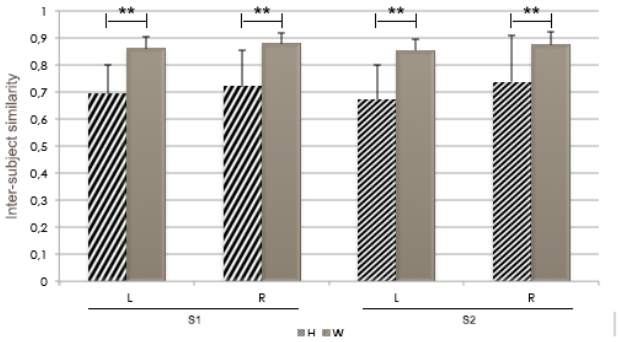

Figure 2 *Mean activation (stripped bars) and synergy (solid bars) similarity of synergy 1 (S1) and synergy 2 (S2) of left (L) and right (R) arm* across subjects. *Activation similarity measure is R^2 and synergy similarity measure is the normalized scalar product. **: p <0.01. Error bars are SD.*

Left and right arm synergies of a given movement are also significantly more conserved than their corresponding activation vectors across subjects ($p<0.01$). Averaged similarity measures of the 12 movements are shown in Figure 2. Inter-subject similarity is slightly lower than intra-subject similarity: activation similarity ranges from 69.31 ± 10.31% to 67.16 ± 12.88% for the left arm and from 71.75% ± 13.92% to 73.80 ± 16.90%

for the right arm; and synergy similarity ranges from 86.06 ± 4.54% to 85.25 ± 4.17% for the left arm and 87.84 ± 3.84% and 87.44 ± 4.65% for the right arm. Although right arm inter-subject synergy and activation similarity was slightly higher than left arm similarity, no statistically significant differences were found. Again, right arm variability was lower than left arm variability.

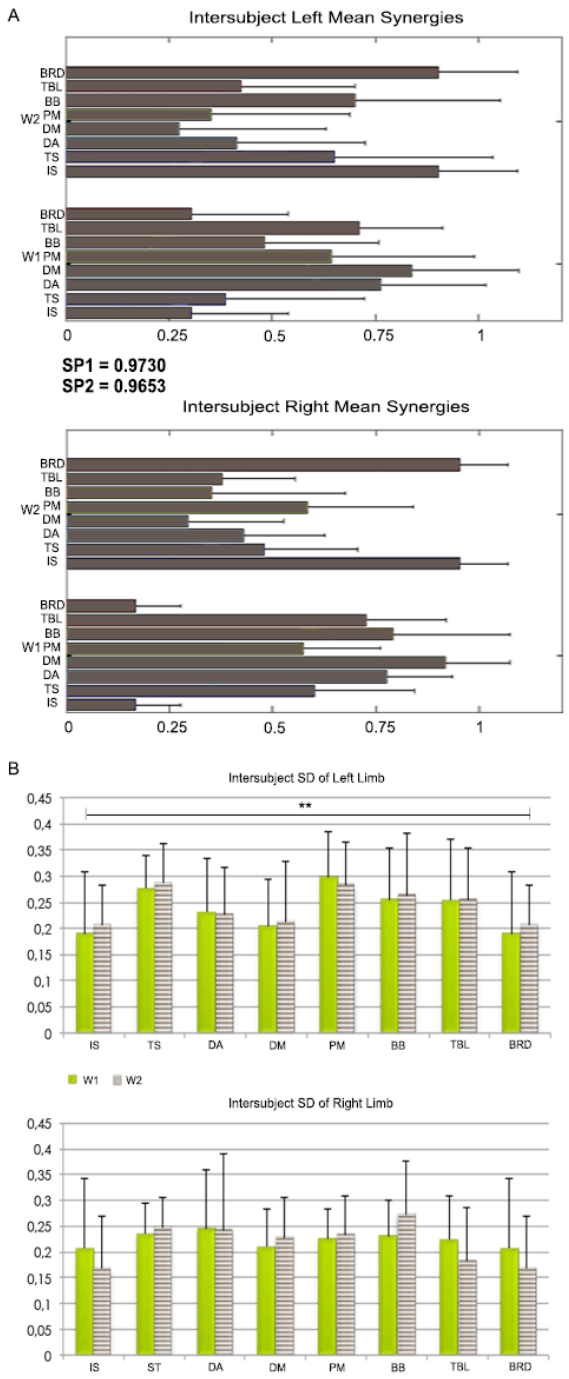

Figure 3 **A** *Mean population synergies of forward shoulder flexion for left and right arms. W1 – synergy 1, W2 = synergy 2.* ***SPi*** *is the scalar product between the i-th synergy of right and left arms. Muscles are IS – Infraspinatus, TS – Trapezius Superior, DA - Deltoid Anterior, DM - Deltoid Medial, PM - Pectoralis Major, BB - Biceps Brachii, TBL - Triceps Brachii Long Head and BRD – Brachioradialis. B – Mean intersubject standard deviation (SD) of muscle contributions to mean synergies W1 (solid bars) and W2 (stripped bars) of left and right arms. Error bars are SD.*

Figure 3A shows the left and right mean population synergies that result from averaging the synergies of the six subjects extracted for the forward shoulder flexion. Synergies from different subjects were matched using cluster analysis. Despite a substantial inter-subject variability in individual muscle contributions, averaged right and left synergies are strikingly similar, with scalar products for synergy 1 being 0,9730 and for synergy 2 0,9653. This high interlimb similarity degree is observed in the 12 movements, with all of them having scalar products exceeding 0.90, except for the synergy 2 of the shoulder extension movement which has an scalar product of SP = 0.5491.

The inter-subject mean variability of muscle contributions to the mean synergies of the 12 movements is shown in figure 3B. Left arm synergies are significantly more variable (SD = 0.24 ± 0.01) than right arm synergies (SD = 0.22 ± 0.01) with $p < 0.001$. In addition, Friedman's test revealed that left synergy variability differs significantly from muscle to muscle, with Trapezius Superior (TS) and Pectoralis Major (PM) been the most variable muscles. In right arm synergies, differences in muscle contributions are not significant.

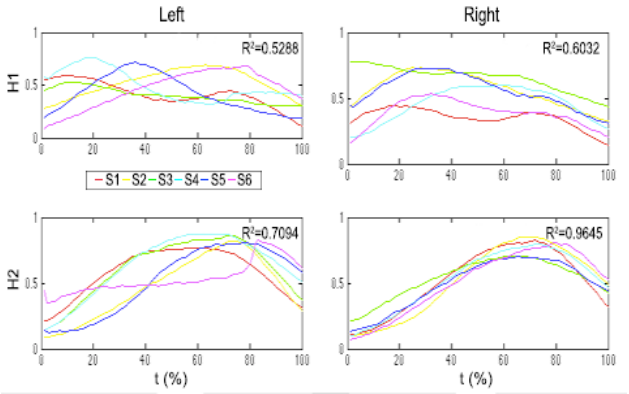

Figure 4 *Activation vectors of forward shoulder flexion for left and right arms corresponding to synergy 1 (H1) and synergy 2 (H2). Each color represents a different subject.* R^2 *indicates the inter-subject similarity of movement-specific activations.*

Figure 4 shows the activation vectors of right and left arms during shoulder forward flexion. Activation vectors are also quite conserved across subjects, however, the similarity degree drops in comparison with synergies for the same movement. It has to be noted that activation similarity depends on the movement: some, such as shoulder forward extension, have very similar activations with R^2 values of 0.9281 / 0.9185 and 0.8794/0.9054 for synergy1/synergy2 of left and right arm respectively, while others, such as shoulder forward flexion exhibit poorer inter-subject similarity with R^2 values of 0.5288 / 0.7094 and 0.6032/0.9645 for synergy1/synergy2 of left and right arm respectively. Regarding interlimb consistency, right arm activations were in general more conserved than left arm activations. However, taking into account the inter-subject similarity of the twelve movements in average, these differences were not found to be significant.

4. Discussion

This study demonstrates that 1) healthy subjects exhibit common control structures (synergies and activations) that are movement specific and generalize across subjects and limbs; 2) synergies are significantly more conserved than activations, both across subjects and limbs; 3) right arm control structure is more robust than its equivalent left arm structure; 4) in this last case, synergy variability depends on individual muscles and 4) however, inter-subject control structure similarity across limbs is still very high.

Every analyzed movement is characterized by a specific synergy and activation vector set that generalizes across subjects but also across limbs. Thus, the control structure (synergy and activation vector) dedicated to coordinate the execution of a movement seems to be specific of that movement, which is to a certain extent logical, taking into consideration that each movement has its own kinematic requirements. However, it seems that regardless the inherent redundancy that defines the human motor system, which allows an individual to perform a movement in thousands of different ways, subjects tend to follow the same motor control strategy when executing a given motor task. Therefore, it may be possible to define standard healthy control structures that could be targeted by motor rehabilitation protocols.

Synergies tend to be more consistent than their activation patterns, both interlimb but also across subjects. In [11] such phenomenon is also described in patients with stroke suggesting that rehabilitation should focus on activation patterns since these may constitute the cause of motor impairment. Here, we demonstrate that inter-limb healthy activation patterns are conserved enough within a subject but also across subjects so as to use them as a reference for the impaired limb rehabilitation. It has to be noted that the degree of activation similarity differs from movement to movement, with some movements having similarity degrees of around 90% and others being as low as 50%. We attribute such differences to the kinematic particularities of each movement, as not every movement has the same length and degrees of freedom involved. For instance, in a previous study we noticed that the longer the movement trajectory was, the higher its inter-subject and intra-subject (trial-to-trial) variability was. Therefore, therapy design should take into account the kinematic nature of the movement used in rehabilitation in order to maximize the activation similarity between limbs.

Right arm control structure exhibits higher inter-subject robustness. In the case of synergies, inter-subject left arm synergies are more variable than right arm synergies, and this variability is muscle dependent. That is, some muscles are more variable than others in every left-arm movement. Analyzing the physiological causes of these differences goes beyond the scope of this study, but we hypothesized that the optimized motion control of the dominant limb can explain them. Be as it may be, we did not find significant differences between the mean inter-subject similarity degree of right and left arm control structures of the 12 movements. Consequently, this type of rehabilitation approach could be applied regardless if the affected arm corresponds to the dominant or nondominant side.

5. Conclusion

This study proves the existence of movement-specific control strategies that generalize across subjects and limbs. Thus, establishing standard patterns of motion control based on common synergy and activation traits may guide the design of more effective rehabilitation paradigms.

Acknowledgements

This work was supported by grants of La Caixa Foundation and the Spanish Ministry of Economy and Competitiveness (TEC2010-21703-C03-01) and developed in the frame of the HYPER project (CSD2009-00067 CONSOLIDER INGENIO 2010).

References

[1] Page JD, Sisto S, Johnston MV and Levine P. Modified constraint induced therapy after subacute stroke: a preliminary study. *Neurorehabilitation and Neural Repair,* vol 16, sup 3, 2002, pp 290–2 .

[2] Sunderland A, Tinson DJ, Bradley L, Langton Hewer RL. Arm function after stroke: an evaluation of grip strength as a measure of recovery and prognostic indicator. *J Neurol, Neurosurgery and Psychiatry,* vol 52, 1989, pp 1267–72.

[3] Maciejasz P, Eschweiller J, Gerlach-Hahn K *et al*. A survey on robotic devices for upper limb rehabilitation. *J Neuroeng Rehabil,* vol 11, sup 3, 2014.

[4] Urra O, Casals A and Jané R. Synergy Analysis as a Tool to Design and Assess an Effective Stroke Rehabilitation. 35th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC), Chicago, 2014

[5] Tresch MC, Saltiel P, Bizzi E. The construction of movement by the spinal cord. *Nat Neurosci,* vol 2, 1999, pp 162–167.

[6] Cheung VC, d'Avella A, Tresch MC, Bizzi E. Central and sensory contributions to the activation and organization of muscle synergies during natural motor behaviors. *J Neurosci,* vol 25, 2005, pp 6419–6434.

[7] d'Avella A, Bizzi E. Shared and specific muscle synergies in natural motor behaviors. *Proc Natl Acad Sci USA,* vol 102, 2005, pp 3076–3081.

[8] Cheung VC, Turolla A, Agostini A *et al*. Muscle synergy patterns as physiological markers of motor cortical damage. *Proc Natl Acad Sci USA*, vol 109, sup 36, 2012, pp 14652-6.

[9] Perotto AO. Anatomical guide for the electromyographer; the limbs and trunk. Springfield, 2005.

[10] Lee DD and Seung HS. Learning the parts of objects by non-negative matrix factorization, *Nature,* vol 401, 1999, pp. 788-791.

[11] Cheung VC, Piron L, Agostini M *et al*. Stability of muscle synergies for voluntary actions after cortical stroke in humans. *Proc Natl Acad Sci USA*, vol 106, sup 46, 2009, pp 19563-8.