Motor modules and activation signals in subacute stroke

Submitted to: *Journal of Neurophysiology*

18th April 2011

**IMPULSES OF ACTIVATION BUT NOT MOTOR MODULES ARE PRESERVED IN THE**

**LOCOMOTION OF SUBACUTE STROKE PATIENTS**

Leonardo Gizzi¹,², Jørgen Feldbæk Nielsen¹, Francesco Felici², Yuri P. Ivanenko⁴, and Dario Farina¹

¹Department of Neurorehabilitation Engineering, Bernstein Center for Computational Neuroscience, University Medical Center Göttingen, Georg-August University, Göttingen, Germany

²Dept. Human Movement and Sport Sciences, University of Roma Foro Italico, Piazza Lauro De Bosis 6, Roma 00196 (Italy)

³Regionshospitalet Hammel Neurocenter, Aarhus University, Voldbyvej 15, 8450 Hammel, Denmark

⁴Laboratory of Neuromotor Physiology, Scientific Institute Foundation Santa Lucia, 00179 Rome, Italy

**Grants:** Supported by the EU project BETTER (Brain-Neural Computer Interaction for Evaluation and Testing of Physical Therapies in Stroke Rehabilitation of Gait Disorders) (contract # 247935) and by the Danish Research Council for Technology and Production Sciences (contract nr. 2117-05-0083; “Enhancing the ability of re-learning motor tasks after stroke with brain-computer interface technology”) (DF).

**Running title:** Motor modules and activation signals in subacute stroke

**Corresponding author:**

* Dario Farina, PhD
Department of Neurorehabilitation Engineering
Bernstein Center for Computational Neuroscience
University Medical Center Göttingen
Georg-August University
Von-Siebold-Str. 4, 37075 Göttingen, Germany
Tel: + 49 (0) 551 / 3920100; Fax: + 49 (0) 551 / 3920110
Email: dario.farina@bccn.uni-goettingen.de
ABSTRACT

It has been hypothesized that the coordinated activation of muscles is controlled by the central nervous system by means of a small alphabet of control signals (also referred to as activation signals) and motor modules (synergies). We analyzed the locomotion of 10 patients recently affected by stroke (maximum of 20 weeks) and compared it with healthy controls. The aim was to assess whether the walking of subacute stroke patients is based on the same motor modules and/or activation signals as healthy subjects. The activity of muscles of the lower and upper limb, and trunk was measured and used for extracting motor modules. Four modules were sufficient to explain the majority of variance in muscle activation in both controls and patients. Modules from the affected side of stroke patients were different from those of healthy controls and from the unaffected side of stroke patients. However, the activation signals were similar between groups and between the affected and unaffected side of stroke patients, and were characterized by impulses at specific time instants within the gait cycle, underlying an impulsive controller of gait. In conclusion, motor modules observed in healthy subjects during locomotion are different from those used by subacute stroke patients, despite similar impulsive activation signals. We suggest that this pattern is consistent with a neuronal network in which the timing of activity generated by central pattern generators is directed to the motoneurons via a premotor network that distributes the activity in a task-dependent manner determined by sensory and descending control information.

Keywords: stroke, motor modules, gait, motor control
INTRODUCTION

The planning and execution of movements implies a considerable computational load by the central nervous system (CNS). This complexity may be reduced by the activation of motor modules (also referred to as loadings or muscle synergies) in the spinal cord by means of a small number of activation signals (also referred to as factors or primitives or activation coefficients). This hypothesis has been confirmed in animal and human studies during a variety of tasks (d’Avella et al. 2006; Wakeling and Horn. 2009; d’Avella et al. 2008; Muceli et al. 2010, Bizzi et al. 2002, 2008; Hart and Giszter 2010), including human locomotion (Prentice et al. 1998; Monaco et al. 2010; Ivanenko et al. 2004). A small number of motor modules (usually 4-5) has been identified to describe the muscle activation patterns of human locomotion (Prentice et al. 1998, Jo et al. 2008, Ivanenko et al. 2004, Cappellini et al. 2006, Monaco et al. 2010). Moreover, Ivanenko et al. (2004) showed that the locomotor activation signals are invariant with respect to walking speed and shared among individuals. These results were confirmed by Cappellini et al. (2006) and partly by Monaco et al. (2010). Although the number of studies on modular organization of locomotion is vast, the pathological walking pattern has been less extensively investigated.

Li et al. (2008) analyzed reaching tasks of the dominant hand and, with the use of a bayesian network, revealed a modular control of muscles in stroke patients. Cheung et al. (2009) analyzed the muscular activity of chronic post-stroke survivors during a reaching task, and found that motor modules did not differ between affected and unaffected side in patients and were similar to those found in healthy controls. Only one study investigated the modular organization of locomotion in stroke patients (Clark et al. 2010) by means of the motor modules/activation signals representation. Consistent with the results obtained during reaching by Cheung et al. (2009), Clark and colleagues identified a modular organization also for walking in chronic stroke patients (on average 57 months post stroke). In that study (Clark et al. 2010), the walking of stroke patients, which was investigated from 8 muscles of
Motor modules and activation signals in subacute stroke

The lower limb, could be represented by a number of motor modules in the range 2-4, depending on the patient, whereas the dimensionality for healthy controls was usually 4. These authors also showed that the lower dimensionality observed in some of the patients could be explained by two or more motor modules being merged in a single module.

The first aim of the present study was to investigate whether locomotion in stroke patients can be described by a small number of motor modules, with the analysis of a larger number of muscles and for patients less distant from the stroke event (<=20 weeks; subacute stroke) than in previous work (Clark et al. 2010) and if the motor modules correspond to those in healthy controls. The second aim was to investigate if the activation signals in subacute stroke patients are impulses distributed along the gait cycle, as it has been observed in healthy subjects (Ivanenko et al. 2004), and therefore if the impulsive control of gait, which seems a characteristics of gait invariant across conditions and tasks in healthy humans (Ivanenko et al. 2004, 2006), is maintained in subacute stroke patients.

METHODS

Subjects

Ten stroke patients (two females and eight males; age, 45.9 ± 16.5 yrs; body mass, 77.3 ± 15.4 kg; stature, 174.4 ± 6.2 cm; time since the event, 12 ± 5 weeks, Table 1) and 10 healthy controls (three females and seven males; age, 42.4 ± 14.5yrs; body mass 75.5 ± 12.6 kg; stature 175.1± 7.5 cm) volunteered in the study. The characteristics of the patients are described in Table 1. The lesions were located by CT or MRI-scans. All subjects gave written informed consent to participate in the study. The local ethical committee approved the study (M-20090018) and the experiments were conducted according to the standards set by the Declaration of Helsinki. Healthy subjects did not present any neurological disease in their clinical history.

Kinematics
The kinematics of locomotion was acquired by means of a VICON stereophotogrammetry system (Vicon Motus, Vicon Motions Systems, Centennial, CO), capturing frames at 100 samples/s. Four markers were located on each foot at the ankle, toe, and heel (the Plug-in-gait, Vicon Motion Systems Ltd., Oxford, UK), and at the base of the big toe. Foot kinematics was used to separate strides during walking trials. A stride was identified as the period between two heel strikes on the same side. The stride starting and ending samples were marked on a timeline; stride duration, cadence and speed were computed using a VICON built-in algorithm for the extraction of stride parameters. Kinematics and EMG recordings were synchronized offline.

**EMG**

Surface EMG signals were recorded in bipolar derivation with pairs of Ag/AgCl electrodes (Ambu® Neuroline 720 01-K/12, Ambu A/S, Ballerup, Denmark), placed with 22 mm of centre-to-centre spacing. Before electrode placement, the skin was shaved, if needed, and gently abraded with abrasive paste. EMG signals were amplified with gain 2000 (EMG-USB, LISiN – OT Bioelettronica, Torino, Italy), band-pass filtered (8th order Bessel filter, bandwidth 10-750 Hz), sampled at 2048 Hz, and A/D converted on 12 bits. A reference electrode was placed on the subject’s wrist.

A total of 32 muscles (16 for each body side) were investigated: Tibialis Anterior (TA), Gastrocnemius Medialis (GA), Soleus (SOL), Vastus Lateralis (VL), Rectus Femoris (RF), Biceps Femoris (BF), Gluteus Maximum (GM), Rectus Abdominis (RA), Erector Spinae (ES2), Latissimus Dorsi (LD), Biceps Brachii (BB), Triceps Brachii (TB), Anterior Deltoid (AD), Upper Trapezius (UT), Sternocleidomastoideus (ST) and Splenius Capitis (SPL). Electrodes for EMG recordings were placed according to the SENIAM recommendations (Hermens et al. 1999) for all muscles, except for RA and SPL (not described by SENIAM) that were analyzed following the recommendations of Ng et al. (1998) and Joines et al. (2006).
Experimental procedure

At the beginning of each experiment, the EMG electrodes and the markers for the kinematic analysis were mounted on the subject. The patients and control subjects were asked to perform a 6-m long walk without constraints, in a straight path. Each patient was asked to walk at a comfortable speed whereas, because motor modules may be influenced by speed (Ivanenko et al. 2004), the healthy controls were asked to walk at slow speed for comparison with the stroke patients. Each walking test was repeated 5 times by both patients and control subjects, separated by 5-10 min of rest, during which the subjects were seated. These resting periods were introduced to prevent fatigue in the stroke patients. The trials of healthy controls were analyzed offline and those with speed exceeding twice the standard deviation (SD) of the speed of the stroke patient group were excluded from the analysis in order to match the walking speeds.

Model of motor modules

The EMG signals recorded from $M$ muscles can be expressed as:

$$X(k) = [x_1(k), x_2(k), \ldots, x_M(k)]^T$$

(1)

where $x_m(k)$ is the activity of the $m$th muscle at the time instant $k$.

The electrical activation of each muscle depends on the summation of the contributions from the motor neurons innervating the muscle. The control signals that are weighted for each muscle can be represented as the activation signals $P(k)$ which are, in general, less than the number of muscles $(N<M)$:

$$P(k) = [p_1(k), p_2(k), \ldots, p_N(k)]^T$$

(2)
The muscle activities are obtained from the activation signals by linear transformation with gain factors $s_{mn}$. The matrix whose columns are the weights of each activation signal for each muscle is denoted as $S$ and referred to as the matrix of motor modules (Lee et al. 2001). The relation between $X(k)$ and $P(k)$ is described as follows:

$$X(k) \approx X_r(k) = S \cdot P(k)$$  \hspace{1cm} (3)$$

where $X_r(k)$ is the muscle activity vector reconstructed by the matrix of motor modules and the activation signals.

**Signal processing**

Electromyographic signals were segmented for each stride, as identified from the kinematics analysis, and band-pass filtered (4th order zero-lag Butterworth digital filter, pass-band 20-400 Hz) to attenuate DC offset, motion artifacts, and high frequency noise (Hermens et al. 1999). The filtered signals were full-wave rectified and low-pass filtered (4th order, cut off frequency 10 Hz) to obtain the muscular activation patterns. Signals were then time-interpolated in order to obtain 200 samples per segment. The envelope of each muscle signal was normalized by its maximal value for each stride (Ivanenko et al. 2004; Clark et al. 2010). To take into account the inter-subject and trial-to-trial variability, the extraction of motor modules was performed (with NMF) for each stride of each individual (left and right for control subjects, paretic and non paretic side for stroke patients), after signal concatenation (Clark et al. 2010). In order to avoid confounding effects due to acceleration and deceleration, the first and last two gait cycles were removed from the dataset. On average each subject performed 30 complete gait cycles.

The NMF algorithm was applied to extract the matrix $S$ of motor modules and the activation signals $P(k)$ (Eq. 3) from the normalized data (d’Avella and Bizzi 2005; Lee and Seung 2001; Tresch et
Motorkomponenter och aktiveringssignaler i subakut stroke

al. 1999). Komponenter extraherades på grund av modell i Eq. (3). Antalet komponenter
nödvändiga för en korrekt beskrivning av bevegelsen var bedömt med dimensionality analysen
proponerad av d’Avella et al. (2003). Enligt denna procedur, kvaliteten på bevegelse
activation pattern analyseras som funktion av antalet komponenter och minsta antalet
modules som identifieras som det punkt i vilket denna kurva förändrar lutning (se d’Avella et al.
2003, 2006). dock, ett minimalt sätt för kvalitetsmätning av rekonstruktion var ställt in ordre
to quantitativt indikera en tillfredsställande mängd variation (Clark et al. 2010), därför
antalet komponenter var valt så att kvaliteten på rekonstruktion inte var lägre än 80%.
Kvaliteten på rekonstruktion mättes genom variation beräknad för (VAF) värdet, definierat
som variation som kan förklaras av modellen: \( VAF = 1 - \frac{SSE}{SST} \), där SSE
(sum of squared errors) är den unutplägna
variation och SST (total sum of squares) är total variation av data (Clark et al. 2010). De
matriser av komponenter extraherade från varje individen jämfördes mellan individer i
samma grupp och mellan de två kroppssidan genom att beräkna skalaproddet mellan par av
komponenter. Det motsvarar matematiskt produkten av kolonnar av matrisen \( S \),
normaliserat med produkten av normerna av kolonnarna (D’Avella et al. 2003; Muceli et al. 2010).

Because vectors of modules are non-negative, this operation provides a value that ranges between 0 and
1. The degree of similarity between modules extracted from the left and right body side of the controls
and from the affected and unaffected side of the patients was computed. To test for the levels of
reconstruction accuracy and similarity among modules which were due to chance, structureless signals
–characterized by the same empirical amplitude distribution– were generated starting from the original
dataset of each subject by shuffling muscles and samples. Random generated data was low pass filtered
at 10Hz to match the frequency content of the original signal (D’Avella et al. 2006). The process of
data randomization was performed 50 times for each healthy control on the left leg and each stroke
patient.
patient for both sides. On each run of the randomization process, the motor modules were extracted from the unstructured data and the VAF index and the similarity with the modules extracted from the original data were computed (D’Avella et al. 2006).

In order to address the first aim of the study (i.e., whether the modularity of control persists, and if motor modules are shared between the control and patient group), the muscle activation pattern of each stroke patient was reconstructed with the matrix of motor modules extracted from the entire dataset of control subjects. For this analysis, a modified version of the NMF algorithm (Muceli et al. 2010), referred in the following to as non-negative reconstruction (NNR), was used. With NNR, the matrix $S$ of motor modules was fixed and, at each iteration, the activation signal matrix $P$ was updated with the Euclidean update rules described by Lee et al. (2001). The accuracy in reconstructing the muscular activation pattern of stroke patients with this procedure represents the maximal accuracy when using the matrix of motor modules of healthy controls across all the possible choices of activation signals, with the only constraint of non-negativity. This analysis therefore provides direct evaluation of the possibility to describe the walking muscular patterns of stroke patients with the same motor modules of healthy subjects.

In order to address the second aim of the study (i.e., whether the activation signals are preserved in the patients and if they maintain an impulsive structure during the gait cycle), the degree of similarity between activation signals of the two groups was computed as the value of the cross-correlation function at zero lag. Before computing the cross-correlation, the activation signals were ordered to obtain the maximal similarity with the Gaussian-like waveforms proposed by Ivanenko et al. (2004). Motor modules were ordered following the association with the respective activation signals.

For comparison with a previous study (Clark et al. 2010), the analysis was repeated on a subset of 7 muscles of the lower limb (TA, GA, SOL, VL, RF, BF, GM), which are functionally matched to
Motor modules and activation signals in subacute stroke

The muscles studied by Clark et al. (2010). The reconstruction quality and comparison of motor modules between groups were computed as for the case of the 16 muscle dataset.

Statistical analysis

Differences between groups in walking cadence and speed were analyzed with a Student t-test for independent samples. The degrees of similarity between motor modules and between activation signals were tested with Student t-tests. Significance level was set at $P < 0.05$ and values are reported as mean and SD.

RESULTS

Stride cadence and speed

The two groups were not different for stride cadence and speed (control subjects cadence: 73.5 ± 37.5 step/min; speed: 2.15 ± 0.6 km/h; stroke patients cadence: 74.8 ± 20.51 step/min, speed: 1.9 ± 0.9 km/h) (controls: $P = 0.67$, patients: $P = 0.61$). The toe off event occurred at 62.9±3.0% of the gait cycle for healthy controls, and at 63.7±4.9% ($P= 0.34$) and 64.0±2.9% ($P=0.08$) for affected and unaffected side of stroke patients, respectively. The speed and cadence for the selected trials of healthy controls were comparable with those of stroke patients ($P = 0.31$).

Motor modules

From the analysis of dimensionality, the accuracy in reconstruction of the muscular patterns (average over all subjects in each group) was >80% with 4 modules in both the controls (80.6±2.9%) and stroke patients, for the affected (81.5±3.1%%) and unaffected side (80.7±3%) (see Fig.1). The accuracy in reconstruction of structureless data resulted in significantly lower values (27.8±3.6% for control group, 25.4±3.5% for stroke patients unaffected side and 26.0±4.6% for stroke patients affected side, respectively). This result indicates that walking can be expressed by a small number of motor modules for healthy subjects as well as subacute stroke patients.
In the healthy subjects the modules extracted from the left and right side had similarity of 0.79±0.11 (average similarity over 10 subjects using 4 modules). Accordingly, when using the modules extracted from one side to reconstruct the muscle activation pattern of the other side with the NNR algorithm in healthy subjects, the accuracy was 79 ± 7% with 4 modules. Therefore, in the following, for the healthy subjects only the results of the left side are reported (results from the right side are equivalent).

The motor modules extracted from different subjects in the control group had mean similarity of 0.67 ± 0.07, which was significantly greater than the level of similarity between modules extracted from structureless data (0.49±0.09) (P<0.05). Moreover, the modules extracted from individual subjects in the control group presented a similarity of 0.75 ± 0.06 with respect to the modules extracted from the entire dataset of healthy subjects. Therefore, for the walking speed investigated, similar motor modules are used by different healthy individuals during walking (Fig. 2A).

In healthy subjects, walking was characterized by the simultaneous activation of GA and SOL, alternated to the activation of the TA and VL (and RF), as represented in the motor modules 2 and 3, respectively (Fig. 2A). The RF was represented in the motor module 3, whereas the BF muscle was mainly represented in the motor module 4 (Fig. 2A). Trunk and upper limb muscles showed a high variability among different subjects, presumably due to a lower signal-to-noise ratio of the EMG of trunk muscles with respect to lower limb muscles during walking (Shiavi et al. 1985, Ivanenko et al. 2006).

In the stroke patients, the mean similarity of motor modules extracted from the two sides (affected and unaffected) was lower (0.58 ± 0.18) than the similarity between sides observed among the healthy individuals (P < 0.05). However, the similarity of motor modules among different stroke patients was comparable with that observed in the control subjects (mean similarity: 0.68 ± 0.07 for
Motor modules and activation signals in subacute stroke

affected, 0.63 ± 0.06 for unaffected side) and higher than the similarity among modules extracted from
structureless data generated from the two datasets (0.5±0.09 for unaffected and 0.49±0.1 for unaffected
side, respectively). For a direct comparison, the modules extracted from stroke patients were compared
with those extracted from the healthy individuals (mean similarity: unaffected side vs controls
0.65±0.09, affected side vs controls 0.59±0.1, P>0.05).

The motor modules of the unaffected side of stroke patients showed activation of the BF and
GM (module 3) concomitant with VL and RF, differently from healthy controls (Fig. 2B,C). The
affected side was characterized by high level of concomitant activation of knee flexors and extensors,
as seen in motor module 2, whereas the TA was alternatively active in module 3, as in healthy controls
(Fig. 2).

Finally, for comparison with previous results on a smaller set of muscles (Clark et al. 2010), the
procedure of extraction of motor modules was also performed on the lower limb muscles only (7
muscles per body side). The reconstruction quality of the signals from the 7 muscles was not sufficient
to meet the criteria adopted when using only 2 (VAF = 42.3%) or 3 (VAF = 68.0%) modules. Thus, it
was necessary to use 4 modules also for describing the activity of the 7 muscles. With 4 modules, the
variation accounted for in the case of 7 muscles was 89.4±3.6% for the control group and 87.9±4.5%
for the patients affected side, and 86.5±4.6% for the patients, unaffected side. Three of the 4 motor
modules extracted from the subset of 7 lower limb muscles were similar between stroke patients and
healthy controls (Fig. 2; similarity in the range 0.76-0.89 for the first three modules), however the
fourth module was very different between groups (similarity between healthy controls and patients
unaffected side, 0.32, and between healthy controls and patients affected side, 0.28). Therefore, even
reducing the muscle set, it was not possible to reduce dimensionality to less than 4 for the patient group
analysed in this study and the motor modules (at least one of them) differed from healthy controls.
The above observations on similarities between motor modules, indicate that the motor modules extracted from stroke patients differed from those obtained from healthy controls. However, this may also be a consequence of the extraction method. To further investigate the possibility of existence of the same motor modules in stroke patients and healthy subjects, we fixed the matrix of motor modules obtained from healthy individuals and used it to reconstruct the muscular activation pattern of stroke patients, as described in the following.

**Description of the muscular activation patterns with the modules of healthy subjects**

The matrix of motor modules of the healthy subject group was used to reconstruct the muscular activation pattern of each stroke patient for the entire muscle set and for the subset of lower limb muscles. This was done to verify if there was a combination of activation signals that could explain the walking patterns of subacute stroke patients with the same motor modules used by the healthy individuals. The accuracy in reconstruction depended on the number of modules but was anyway lower than the result for the control group (mean and SD values for VAF in healthy controls 67.8±1.3; patients unaffected side 40.2±2.6%; patients affected side 40.9±5.7% with 4 modules). A similar result was found when repeating the analysis for the 7 muscles subset (healthy controls: 69.3±1.7%; stroke patients unaffected side 54.0±1.1%; stroke patients affected side: 53.6±1.2% with four modules). This result suggests that, with the possibility of varying the activation signals with only the non-negativity constraint, the muscular activation pattern of stroke patients was not well explained by the motor modules of the controls.

Fig. 3 shows the activation signals for the reconstruction of muscular signals in the two subject groups (healthy controls, stroke patients for affected and unaffected side). The correlation between
Motor modules and activation signals in subacute stroke

activation signals of individuals in the same group revealed a comparable degree of homogeneity which did not differ between controls and stroke patients (healthy controls: 0.78 ± 0.05; stroke patients, affected side, 0.74 ± 0.07, and unaffected side, 0.75 ± 0.06; P > 0.05 for controls vs patients for both affected and unaffected side and for stroke patients between affected and unaffected side).

Accordingly, the average value for SD of the activation signals was similar among groups (normalized units): 0.137 for healthy controls, 0.137 and 0.138 for stroke patients for affected and unaffected side). Therefore, the activation signals of stroke patients did not show greater inter-subject variability when compared to the controls. Moreover, as can be seen in Fig. 3, the activation signals were very similar between groups (correlation, control vs patients affected: 0.76 ± 0.09; control vs patients unaffected: 0.77 ± 0.09). Therefore, despite the different motor modules in the two groups (Fig. 2), the activation signals were maintained in the stroke patients (Fig. 3).

Insert Figure 3 here

The activation signals in the two groups were characterized by an impulsive pattern. The first impulse had the peak associated to the heel strike (HS) phase, the second occurred immediately before the toe off (TO), the third during the swing phase, and the fourth immediately before the next HS. For all groups, the timing of these impulses of activation signals was consistent with the results reported by in literature (Ivanenko et al. 2004, 2006; Clark et al. 2010; Monaco et al. 2010) for healthy subjects, where a sequenced Gaussian-like activation was associated with the discharge from different loci in the spinal cord.

Individual motor modules and activation coefficients for a representative healthy control and stroke patient are reported in Fig. 4.
DISCUSSION

We investigated the muscle activation pattern of stroke patients and healthy controls during walking. Previous findings in spinal animals and intact and pathologic humans indicated that the CNS could accomplish the control of a large number of degrees of freedom by means of few motor modules. Our findings confirm these results in healthy controls and extend them to subacute stroke patients. A similar relation between activation signals and motor modules was previously reported for other walking conditions, such as different walking speeds and surfaces (Ivanenko et al. 2004, 2008). The findings by Ivanenko et al. (2008) show consistent activation signals (referred to as factors in that report) even in presence of stride perturbations, such as kicking a ball or stepping an obstacle. An overview of these results ensures the substantial reliability of an activation signal-based representation of human walking. Recent results have shown a modular organization of walking and reaching also in stroke patients (Clark et al. 2010, Cheung et al. 2009). In the present study, despite confirming the presence of modularity, the results showed that it is not possible to accurately describe the muscular activation pattern of subacute stroke patients using the same motor modules of healthy controls, whereas the characteristics of the activation signals are strongly maintained. The results showed that the timing of bursts are consistent with those seen in controls, as might be expected for activity generated by a central pattern generator.

Dimensionality

The number of modules required to describe the muscular activation pattern during walking was 4 for both stroke patients and healthy controls. This result is qualitatively in agreement with those presented by Ivanenko et al. (2004), Cappellini et al. (2006), and Monaco et al. (2010), although in
some of these previous studies the minimal number of modules was 5. This difference in
dimensionality among studies may be due to the number of muscles analyzed, which was up to 32
ipsilateral muscles in Ivanenko et al. (2004, 2006). Interestingly, despite the present study analyzed a
greater number of muscles, Clark et al. (2010) also found that 2-4 motor modules were sufficient to
describe the leg muscle activation patterns of stroke patients. This result was confirmed in the current
study by the analysis of a subset of the measured muscles to match the muscle set measured by Clark et
al. (2010), despite the dimensionality needed was 4. Moreover, the current study extends those results
to muscles of the trunk and neck and indicates that low dimensionality in muscle control is a feature of
human walking maintained with stroke despite severe motor impairments. The dimensionality of
control in the current study was the same for all patients and controls, even reducing the number of
muscles in the analysis to 7. Conversely, Clark et al. (2010) differentiated their group of patients on the
basis of the dimensionality in the range 2-4. This difference with respect to our study is likely
explained by the more inhomogeneous sample of stroke patients investigated by Clark et al. (2010),
which included patients with time from stroke in the range 7 to 411 months; although smaller, the
sample of stroke patients in the present study was homogeneous in terms of both time distance after
stroke (8-20 weeks), level of impairment, and absence of previous rehabilitation (Tab. 1).

Comparison between motor modules

In the healthy subjects, similar motor modules were observed between sides and among
individuals. This conclusion was substantiated by both the computation of the degree of similarity
between modules and by the result that the healthy modules could reconstruct the muscular activation
pattern of each individual subject. This result confirms previous observation during reaching with the
upper limb (d’Avella et al. 2005; Cheung et al. 2009; Muceli et al. 2010). The motor modules of stroke
patients differed from those of controls although the activation signals were similar.
A previous study (Clark et al. 2010) investigated the similarity in motor modules between stroke patients and controls during walking and concluded that similar modules were used in both the affected and unaffected side despite they appeared collapsed. In order to separate the influence of upper body muscles on motor modules extraction, in the current study the analysis was repeated with a subset of 7 muscles of the lower limb. This analysis also needed 4 modules for accurate reconstruction, as for the full muscle dataset and contrary to the case of chronic patients analysed by Clark et al. (2010). The modules of stroke patients in the case of 7 muscles were similar between sides, contrary to the case of the full muscle set, but one of them differed substantially with respect to controls. A possible explanation for this difference can be that the patients analyzed by Clark et al. (2010) experienced the stroke on average 57 months before the measures whereas the patients analyzed in the present study were observed not more than 20 weeks after stroke (Tab. 1). No correlation between time from stroke and/or rehabilitation therapies administered to the patients were directly tested in that work. It is thus possible that adaptations in motor control have occurred more extensively in the patients analyzed by Clark et al. (2010) than in our study.

One of the contributions of this study is also to have tested the hypothesis of shared motor modules directly considering the possibility of different modules being extracted only because of the mathematical procedure applied to different data sets. The motor modules of the healthy controls were indeed fixed leaving the activation signals to vary without constraints (except for the non-negativity), to explain the muscular patterns of the patients. The result of this analysis indicated that the accuracy in reconstruction of the muscular activity in stroke patients using the matrix of motor modules of the controls was low and this result was confirmed also for the smaller subset of 7 muscles.

A possible interpretation of the results observed could be that stroke causes a misdirection of descending control signals so that different motor modules are activated instead of those usually
involved during walking. Motor modules may be encoded at the spinal level but different sets of
modules may be elicited by the CNS in conditions of stroke. Alternatively, it is also possible that spinal
plasticity occurs very early after stroke. Accordingly, previous studies (Rogers et al. 2004, Hidler et al.
2007) reported that during a leg push task in individuals after stroke, the ability to coordinate muscular
activity was preserved, even if a difference in the direction of the force exerted was evidenced with
respect to the control group. Similar activation signals after stroke may be achieved through
interhemispheric and pyramidal-extrapyramidal transmission and augmented influence of reticulospinal
and bulbospinal tracts on movement (Dewald et al. 2001, Lum et al. 2003), although it is not possible
to exclude a contribution of sensory modulation directly affecting spinal central pattern generators (i.e.,
stretch reflex-induced spasticity). For partly excluding this possibility we selected stroke patients after
a much shorter period from stroke than in previous studies (Clark et al. 2010). However, 8-20 weeks
separated the measures from the stroke event and this period may have been sufficient for plastic
reorganization of spinal modules (Liepert et al 2000). Interestingly, the motor modules extracted from
the investigation of 7 muscles of the lower limb of the patients were similar between sides (although
one module was different from the controls) whereas the modules extracted from 16 muscles, including
upper limb and trunk muscles, were different between sides (Fig. 2). Because the changes in motor
modules in the unaffected side of stroke patients with respect to controls were likely due to
compensatory strategies to balance strength loss in the paretic side during walking, the difference
between sides evidenced with the analysis of the full muscle set may indicate specific compensatory
mechanisms of the upper limb and trunk musculature.

The presence of a specific timing structure above a pattern shaping structure was already
proposed for the description of natural behaviours in amphibian (Giszter et al. 2007; Hart and Giszter
2010) and mammalian locomotion (McRea and Rybak 2007). According to this interpretation, motor
modules may be encoded at the spinal level but different sets of modules may be elicited by the CNS in
conditions of stroke. The small variability in activation signals in the stroke patients (similar to the variability among controls) is in agreement with this interpretation.

It is interesting to note that the characteristic bursts of activation during the gait cycle were maintained in subacute stroke patients, with the same variability as in controls (Fig. 3), despite substantial differences in the muscular activity. This impulsive control of motor modules and its timing have been shown to be robustly maintained in a variety of conditions, such as walking at different speeds (Prentice et al. 2008; Ivanenko et al. 2005, 2008) and in case of chronic stroke at least in some cases (Clark et al. 2010). The present study indicates that this impulsive control is preserved in subacute stroke.

We suggest that this pattern is consistent with a neuronal network in which the timing of activity generated by central pattern generator neurons is directed to the motoneurons via a premotor network that distributes the activity to motoneurons in a task dependent manner, determined by sensory and descending control information (Rossignol et al. 2006). Results from animal experiments (Grillner 1975) and human reflex and coordination studies (Zehr et al. 2004) (Kawashima et al. 2008) as well as treadmill and overground locomotion (Ivanenko et al. 2005) discuss the muscular control for both the upper and lower limbs as consequence of CPG activity. In accordance, a wider dataset (i.e., including upper limb and trunk muscles) with respect to a previous study (Clark et al. 2010) did not influence the number of motor modules needed for an accurate reconstruction of surface EMG patterns for both controls and stroke patients.

In conclusion, although the muscular patterns of subacute stroke patients are highly variable, the patients investigated in this study showed a modular control of walking with low dimensionality. However, the motor modules were different between the two sides and with respect to those found in healthy controls. Moreover, the patients showed activation signals similar to those of healthy controls.
Motor modules and activation signals in subacute stroke

in both the unaffected and affected side and presented a control of locomotion based on bursts during specific times of the gait cycle, characteristic of healthy subjects. These results substantiate the evidence of modular organization of walking in healthy subjects and in subacute stroke patients. Moreover, the results indicate that the motor pattern in subacute stroke patients may be explained by similar activation signals as in healthy individuals, which however acts on different motor modules. The origin of these activation signals, largely invariant across conditions, is consistent with a neuronal network in which the timing of activity generated by central pattern generators is directed to the motoneurons via a premotor network.
Motor modules and activation signals in subacute stroke

REFERENCES


Motor modules and activation signals in subacute stroke


Motor modules and activation signals in subacute stroke


Motor modules and activation signals in subacute stroke

FIGURE CAPTIONS

FIG. 1. Reconstruction quality for healthy controls (full line), stroke patients unaffected side (dashed-dotted line) and affected side (dashed line) with respect of the number of motor modules extracted from 16 muscles. The index of reconstruction quality is the variation accounted for (VAF) value, defined as the variation that can be explained by the model: $VAF = 1 – \frac{SSE}{SST}$, where $SSE$ (sum of squared errors) is the unexplained variation and $SST$ (total sum of squares).

FIG. 2. Motor modules during walking in healthy subjects and stroke patients for the complete muscle set (16 muscles; left) and a subset of 7 muscles (right). A: Modules (mean and SD) obtained from the concatenation of signals from all healthy subjects. B: Modules (mean and SD) extracted from the unaffected side of stroke patients. C: Modules (mean and SD) extracted from the affected side of stroke patients. TA: Tibialis Anterior; GA: Gastrocnemius Medialis; SOL: Soleus; VL: Vastus Lateralis; RF: Rectus Femoris; BF: Biceps Femoris; GM: Gluteus Maximum; RA: Rectus Abdominis; ES2: Erector Spinae; LD: Latissimus Dorsi; BB: Biceps Brachii; TB: Triceps Brachii; AD: Anterior Deltoid; UT: Upper Trapezius; ST: Sternocleidomastoideus; SPL: Splenius Capitis. AU: Arbitrary Units.

FIG. 3. A: Activation signals for the healthy controls, B: for the stroke patients, unaffected side, and C: for the stroke patients, affected side. The signals are average values (solid line) and standard deviation (dashed line). The grey lines represent the activation coefficients for each subject and trial. AU: Arbitrary Units.

FIG. 4 Surface EMG (mean and standard deviation), motor modules and activation signals for a representative healthy control subject (A) and stroke patient for unaffected (B) and affected side (C).
Table 1. Description of patients.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Diagnosis</th>
<th>Affected side</th>
<th>Gender</th>
<th>Age</th>
<th>Weeks since event</th>
<th>FIM*</th>
</tr>
</thead>
<tbody>
<tr>
<td>S1</td>
<td>Infarction</td>
<td>Right</td>
<td>Male</td>
<td>53</td>
<td>12</td>
<td>111</td>
</tr>
<tr>
<td>S2</td>
<td>Hemorrhage</td>
<td>Right</td>
<td>Male</td>
<td>52</td>
<td>20</td>
<td>112</td>
</tr>
<tr>
<td>S3</td>
<td>Infarction</td>
<td>Left</td>
<td>Female</td>
<td>28</td>
<td>8</td>
<td>117</td>
</tr>
<tr>
<td>S4</td>
<td>Infarction</td>
<td>Right</td>
<td>Female</td>
<td>18</td>
<td>8</td>
<td>106</td>
</tr>
<tr>
<td>S5</td>
<td>Hemorrhage</td>
<td>Left</td>
<td>Female</td>
<td>27</td>
<td>8</td>
<td>100</td>
</tr>
<tr>
<td>S6</td>
<td>Hemorrhage</td>
<td>Right</td>
<td>Male</td>
<td>49</td>
<td>8</td>
<td>112</td>
</tr>
<tr>
<td>S7</td>
<td>Hemorrhage</td>
<td>Right</td>
<td>Male</td>
<td>58</td>
<td>20</td>
<td>106</td>
</tr>
<tr>
<td>S8</td>
<td>Infarction</td>
<td>Right</td>
<td>Male</td>
<td>64</td>
<td>8</td>
<td>116</td>
</tr>
<tr>
<td>S9</td>
<td>Infarction</td>
<td>Right</td>
<td>Male</td>
<td>37</td>
<td>12</td>
<td>110</td>
</tr>
<tr>
<td>S10</td>
<td>Infarction</td>
<td>Right</td>
<td>Male</td>
<td>49</td>
<td>16</td>
<td>101</td>
</tr>
</tbody>
</table>

* Functional Independence Measure, range (18-126).
Figure 2
Figure 3
Figure 4

(A) Healthy control

(B) Patient unaffected side

(C) Patient affected side

Gait Cycle (%)