Impulses of activation but not motor modules are preserved in the locomotion of subacute stroke patients

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Impulses of activation but not motor modules are preserved in the locomotion of subacute stroke patients. J Neurophysiol 106: 202–210, 2011. First published April 20, 2011; doi:10.1152/jn.00727.2010.—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 wk) and compared it with that of 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 the 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 activation 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.

stroke; gait; motor control

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 (Bizzi et al. 2002, 2008; d’Avella et al. 2006, 2008; Hart and Giszter 2010; Muceli et al. 2010; Wakeling and Horn 2009), including human locomotion (Ivanenko et al. 2004; Monaco et al. 2010; Prentice et al. 1998). A number of motor modules (usually 4 or 5) have been identified to describe the muscle activation patterns of human locomotion (Cappellini et al. 2006; Jo et al. 2008; Ivanenko et al. 2004; Monaco et al. 2010; Prentice et al. 1998). 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 model of control of muscles in stroke patients. Cheung et al. (2009) analyzed the muscular activity of chronic poststroke 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 also identified a modular organization for walking in chronic stroke patients (on average, 57 mo poststroke). In that study (Clark et al. 2010), the walking of stroke patients, which was investigated from eight muscles of the lower limb, could be represented by a number of motor modules in the range from two to four, depending on the patient, whereas the dimensionality for healthy controls was usually four. 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 wk; subacute stroke) than in previous work (Clark et al. 2010) and whether the modules correspond to those in healthy controls. The second aim was to investigate whether the activation signals in subacute stroke patients are impulses distributed along the gait cycle, as has been observed in healthy subjects (Ivanenko et al. 2004), and therefore whether the impulsive control of gait, which seems a characteristic 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 (2 females and 8 males; age, 45.9 ± 16.5 yr; body mass, 77.3 ± 15.4 kg; height, 174.4 ± 6.2 cm; time since the event, 12 ± 5 wk) and 10 healthy controls (3 females and 7 males; age, 42.4 ± 14.5 yr; body mass, 75.5 ± 12.6 kg; height, 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 ethics 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, 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. Kinectics and electromyogram (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, Ballerup, Denmark), placed with 22 mm of center-to-center spacing. Before electrode placement, the skin was shaved, if necessary, and gently abraded with abrasive paste. EMG signals were amplified with a gain of 2,000 (EMG-USB; LISIN-OT Bioeletronica, Torino, Italy), band-pass filtered (8th-order Bessel filter, bandwidth 10–750 Hz), sampled at 2,048 Hz, and analog-to-digitally 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 (GM), 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), which 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 five 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 to match the walking speeds.

Model of motor modules. The EMG signals recorded from M muscles can be expressed as

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

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, in general, less than the number of muscles ($N < M$):

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

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

$$X(k) = X_s(k) = S \cdot P(k)$$

where $X_s(k)$ 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, passband 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, cutoff frequency 10 Hz) to obtain the muscular activation patterns. Signals were then time-interpolated to obtain 200 samples per segment. The envelope of each muscle signal was normalized by its maximal value for each stride (Clark et al. 2010; Ivanenko et al. 2004). To take into account the intersubject and trial-to-trial variability, the extraction of muscle modules was performed (with nonnegative matrix factorization, NMF) for each stride of each individual (left and right for control subjects, paretic and nonparetic side for stroke patients) after signal concatenation (Clark et al. 2010). To avoid confounding effects due to acceleration and deceleration, the first and last two gait cycles were removed from the data set. 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 al. 1999). Modules were extracted according to the model in Eq. 3. The number of motor modules needed for accurate description of the movement was assessed using the dimensionality analysis proposed by d’Avella et al. (2003). According to this procedure, the quality in reconstruction of the muscle activation pattern is analyzed as a function of the number of modules, and the minimum number of modules is identified as the point at which this curve changes slope (for details, see d’Avella et al. 2003, 2006). However, a minimum threshold for reconstruction quality was set to quantitatively indicate a satisfactory amount of variation (Clark et al. 2010); therefore, the number of modules was chosen so that the reconstruction quality was not lower than 80%. For quantifying the quality in reconstruction, the estimated muscular activation pattern was compared with the recorded pattern by means of 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) is the total variation of the data (Clark et al. 2010). The matrices of motor modules extracted from each individual were compared among individuals of the same group and between the two body sides by computing the scalar product between pairs of motor modules. This corresponds mathematically to the product of pairs of columns of the matrix $S$, normalized by the product of the norms of the columns (d’Avella et al. 2003; Muceli et al. 2010). Because vectors of modules are nonnegative, 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 that were due to chance, structureless signals, characterized by the same empirical amplitude distribution, were generated starting from the original data set of each subject by shuffling muscles and samples. Randomly generated data were low-pass filtered at 10 Hz 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 for each stroke 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 to the modules extracted from the original data were computed (d’Avella et al. 2006). To address the first aim of the study (i.e., whether the modularity of control persists and whether 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 data set of control subjects. For this analysis, a modified version of the NMF algorithm (Muceli et al. 2010), referred to in the following as nonnegative 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 and Seung (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 being nonnegativity. 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.

To address the second aim of the study (i.e., whether the activation signals are preserved in the patients and whether 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 the cross-correlation was computed, 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 seven muscles of the lower limb (TA, GA, SOL, VL, RF, BF, and GM), which are functionally matched to 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 data set.

**Statistical analysis.** Differences between groups in walking cadence and speed were analyzed with a Student’s $t$-test for independent samples. The degrees of similarity between motor modules and between activation signals were tested with Student’s $t$-tests. Significance level was set at $P < 0.05$, and values are means and SD.

**RESULTS**

**Stride cadence and speed.** The two groups were not different in stride cadence and speed (control subjects: cadence, 73.5 ± 37.5 steps/min; speed, 2.15 ± 0.6 km/h; stroke patients: cadence, 74.8 ± 20.51 steps/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 the 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 (81.5 ± 3.1% for the affected side and 80.7 ± 3% for the unaffected side) (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 the unaffected side of stroke patients, and 26.0 ± 4.6% for the affected side of stroke patients). 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 a similarity of 0.79 ± 0.11 (average similarity over 10 subjects using 4 modules). Accordingly, when the modules extracted from one side were used 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).

![Fig. 1. Reconstruction quality for healthy controls (solid line), the unaffected side of stroke patients (dashed-dotted line), and the affected side of stroke patients (dashed line) with respect to 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) is the total variation of the data.](http://jn.physiology.org/content/106/1/204/F1.large.jpg)
The motor modules extracted from different subjects in the control group had a mean similarity of \(0.67 \pm 0.07\), which was significantly greater than the level of similarity between modules extracted from structureless data \((0.49 \pm 0.09)\) \((P < 0.05)\). Moreover, the modules extracted from individual subjects in the control group presented a similarity of \(0.75 \pm 0.06\) with respect to the modules extracted from the entire data set 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 motor modules 2 and 3, respectively (Fig. 2A). The RF was represented in motor module 3, whereas the BF muscle was mainly represented in 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 (Ivanenko et al. 2006; Shiavi et al. 1985).

In the stroke patients, the mean similarity of motor modules extracted from the two sides (affected and unaffected) was lower \((0.58 \pm 0.18)\) 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 to that observed in the control subjects (mean similarity: \(0.68 \pm 0.07\) for affected side, \(0.63 \pm 0.06\) for unaffected side) and higher than the similarity among modules extracted from structureless data generated from the two data sets \((0.5 \pm 0.09\) for affected side, \(0.49 \pm 0.1\) 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, \(0.65 \pm 0.09\); affected side vs. controls, \(0.59 \pm 0.1\); \(P > 0.05)\).

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. 2, B and C). The affected side was characterized by a 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 seven muscles was not sufficient to meet the criteria adopted when using only two \((\text{VAF} = 42.5\%)\) or three modules \((\text{VAF} = 68.0\%)\). Thus it was necessary to also use four modules to describe the activity of the seven muscles. With four modules, the variation accounted for in the case of seven muscles was \(89.4 \pm 3.6\%\) for the control group, \(87.9 \pm 4.5\%\) for the affected side of stroke patients, and \(86.5 \pm 4.6\%\) for the unaffected side of stroke patients. Three of the four motor modules extracted from the subset of seven lower limb muscles were similar between stroke patients and healthy controls (Fig. 2; similarity in the range \(0.76 – 0.89\) for the first 3 modules); however, the fourth module was very different between groups (similarity between healthy controls and the unaffected side of patients, \(0.32\); and between healthy controls and the affected side of patients, \(0.28\)). Therefore, even after reducing the muscle set, it was not possible to reduce dimensionality to less than four for the patient group analyzed in this study, and the motor modules \((\geq 1)\) of them) differed from those of 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 below.

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 whether 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 in any case lower than the result for the control group (mean ± SD values for VAF: healthy controls, 67.8 ± 1.3; unaffected side of stroke patients, 40.2 ± 2.6%; and affected side of stroke patients, 40.9 ± 5.7% with 4 modules). A similar result was found when the analysis was repeated for the seven-muscle subset (healthy controls, 69.3 ± 1.7%; unaffected side of stroke patients, 54.0 ± 1.1%; affected side of stroke patients, 53.6 ± 1.2% with 4 modules). This result suggests that, with the possibility of varying the activation signals with only the nonnegativity constraint, the muscular activation pattern of stroke patients was not well explained by the motor modules of the controls.

Figure 3 shows the activation signals for the reconstruction of muscular signals in the two subject groups (healthy controls and stroke patients for affected and unaffected sides). The correlation between activation signals of individuals in the same group revealed a comparable degree of homogeneity that did not differ between controls and stroke patients (healthy controls, 0.78 ± 0.05; affected side of patients, 0.74 ± 0.07; and unaffected side of patients, 0.75 ± 0.06; P > 0.05 for controls vs. patients for both affected and unaffected sides and for stroke patients between affected and unaffected sides). Accordingly, the average value for SD of the activation signals was similar among groups (normalized units): 0.137 for healthy controls and 0.137 and 0.138 for affected and unaffected sides of stroke patients, respectively. Therefore, the activation signals of stroke patients did not show greater intersubject variability compared with the controls. Moreover, as can be seen in Fig. 3, the activation signals were very similar between groups (correlation: control vs. affected side of patients, 0.76 ± 0.09; control vs. unaffected side of patients, 0.77 ± 0.09). Therefore, despite the different motor modules in the

![Figure 3](http://jn.physiology.org/)

Fig. 3. Activation signals for the healthy controls (A), the unaffected side of stroke patients (B), and the affected side of stroke patients (C). The signals are average values (solid line) and SD (dashed line). The shaded lines represent the activation coefficients for each subject and trial.
two groups (Fig. 2), the activation signals were maintained in the stroke patients (Fig. 3).

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 in the literature (Clark et al. 2010; Ivanenko et al. 2004, 2006; 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 in intact and pathological 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 the presence of stride perturbations, such as kicking a ball or stepping over an obstacle. An overview of these results ensures the substantial reliability of an activation signal-based representation of human walking. Recent results also have shown a modular organization of reaching and walking in stroke patients (Cheung et al. 2009; Clark et al. 2010). In the present study, despite confirming the presence of modularity, the results show 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 show 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 four 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),

Fig. 4. Surface electromyogram (left; means and SD), motor modules (middle), and activation signals (right) for a representative healthy control subject (A) and for the unaffected (B) and affected side of a stroke patient (C).
although in some of these previous studies the minimal number of modules was five. 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 fact that the present study analyzed a greater number of muscles, Clark et al. (2010) also found that two to four 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 fact that the dimensionality needed was four. 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 after the number of muscles in the analysis was reduced to seven. Conversely, Clark et al. (2010) differentiated their group of patients on the basis of the dimensionality in the range from two to four. 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 from 7 to 411 mo; although smaller, the sample of stroke patients in the present study was homogeneous in terms of time from stroke (8–20 wk), level of impairment, and absence of previous rehabilitation (Table 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 the result that the healthy modules could reconstruct the muscular activation pattern of each individual subject. This result confirms previous observations during reaching with the upper limb (Cheung et al. 2009; d’Avella et al. 2005; 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 the fact that they appeared collapsed. To separate the influence of upper body muscles on motor modules extraction, in the current study the analysis was repeated with a subset of seven muscles of the lower limb. This analysis also needed four modules for accurate reconstruction, as for the full muscle data set and contrary to the case of chronic patients analyzed by Clark et al. (2010). The modules of stroke patients in the case of seven 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 could be that the patients analyzed by Clark et al. (2010) experienced the stroke on average 57 mo before the measures, whereas the patients analyzed in the present study were observed not more than 20 wk after stroke (Table 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 occurred more extensively in the patients analyzed by Clark et al. (2010) than in our study.

One of the contributions of this study is to also 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 nonnegativity) 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 also was confirmed for the smaller subset of seven 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 (Hidler et al. 2007; Rogers et al. 2004) 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). To partly exclude this possibility, we selected stroke patients after a much shorter period from stroke than in previous studies (Clark et al. 2010). However, 8–20 wk 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 seven muscles of the lower limb of the patients were similar between sides (although 1 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 has already been proposed for the description of natural behaviors in amphibian (Giszter et al. 2007; Hart and Giszter 2010) and mammalian locomotion (MeRea 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),...
MOTOR MODULES AND ACTIVATION SIGNALS IN SUBACUTE STROKE

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 (Ivanenko et al. 2005, 2008; Prentice et al. 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 (Kawashima et al. 2008; Zehr et al. 2004), as well as treadmill and overground locomotion (Ivanenko et al. 2005), discuss the muscular control for both the upper and lower limbs as a consequence of central pattern generator activity. In accordance, a wider data set (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 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, act 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.

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DISCLOSURES

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REFERENCES


