Spinal Cord Maps of Spatiotemporal Alpha-Motoneuron Activation in Humans Walking at Different Speeds

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Ivanenko, Y. P., R. E. Poppele, and F. Lacquaniti. Spinal cord maps of spatiotemporal alpha-motoneuron activation in humans walking at different speeds. J Neurophysiol 95: 602–618, 2006. First published November 9, 2005; doi:10.1152/jn.00767.2005. Functional MRI (fMRI) imaging of motoneuron activity in the human spinal cord is still in its infancy, and it will remain difficult to apply to walking. Here we present a viable alternative for documenting the spatiotemporal maps of α-motoneuron (MN) activity in the human spinal cord during walking, similar to the method recently reported for the cat. We recorded EMG activity from 16 to 32 ipsilateral limb and trunk muscles in 13 healthy subjects walking on a treadmill at different speeds (1–7 km/h) and mapped the recorded patterns onto the spinal cord in approximate rostrocaudal locations of the motoneuron pools. This approach can provide information about pattern generator output during locomotion in terms of segmental control rather than in terms of individual muscle control. A striking feature we found is that nearly every spinal segment undergoes at least two cycles of activation in the step cycle, thus supporting the idea of half-center oscillators controlling MN activation at any segmental level. The resulting spatiotemporal map patterns seem highly stereotyped over the range of walking speeds studied, although there were also some systematic redistributions of MN activity with speed. Bursts of MN activity were either temporally aligned across several spinal segments or switched between different segments. For example, the center of mass of MN activity in the lumbosacral levels generally shifted from rostral to caudal positions in two cycles for each step, revealing four major activation foci: two in the upper lumbar segments and two in the sacral segments. The results are consistent with the presence of at least two and possibly more pattern generators controlling the activation of lumbosacral MNs.

INTRODUCTION

Locomotion is a basic motor activity that requires the coordination of many limb and trunk muscles. The activation of motoneurons during locomotion seems to occur in bursts at discrete times in the step cycle that depend on the speed and on limb loading (Ivanenko et al. 2004). Activation timing is likely to reflect the activity of underlying pattern generators as well as both central and proprioceptive modulation. Spinal pattern generators that are assumed to provide the basic timing of muscle activation for locomotion have been described in many vertebrates. Studies in lower vertebrates, e.g., the lamprey, have lead to a model for locomotion that is driven by a chain of coupled central pattern generators (CPGs) along the spinal segments (Orlovsky et al. 1999; Wallen and Williams 1984). A phase shift from segment to segment gives rise to a traveling wave of activity along the lamprey body associated with swimming. The evidence in mammals favors instead a concentration of CPG activity in the cervical and lumbar enlargements, basically one or more half-center CPGs for each limb (Brown 1911; Forssberg and Grillner 1973; Grillner and Zanger 1979). More recent data from in vitro preparations suggests a major site for CPG activity may be located in the upper lumbosacral segments and perhaps separate generator sites in more caudal segments (Cazalets and Bertrand 2000; Kremer and Lev-Tov 1997; Lev-Tov et al. 2000). The exact organization of CPGs is still largely unknown in humans (Barbeau et al. 1999; Duysens and Van de Crommert 1998; Lacquaniti et al. 1999). They are thought to comprise a network of interneurons linked to the output stage of α-motoneurons, but opinions diverge as to whether the mammalian CPGs are localized or distributed (Dimitrijevic et al. 1998; Grasso et al. 2004a; Kiehn et al. 1998; Orlovsky et al. 1999; Shapkova and Schomburg 2001).

Changes in locomotion speed are accompanied by changes in both the timing and distribution of muscle activity. We showed previously that the major muscle activation during locomotion could be accounted for by five basic activation components that are nearly invariant when normalized to the step cycle duration (Ivanenko et al. 2004). This suggests that pattern generators scale the cycle duration rather than the activation phase with speed changes. However, data from both human and animal studies have shown that swing and stance phases are modulated with speed. In fact, the swing phase tends to remain relatively constant as the duration of the step cycle shortens with increasing speed (Forssberg and Grillner 1973; Murray 1967). This suggests that activation phase changes with speed changes.

The aim of this study was to explore α-motoneuron (MN) activation in the human spinal cord during locomotion by visualizing its spatiotemporal distribution and the way that changes with locomotion speed. We mapped the recorded patterns of muscle activity onto the approximate rostro-caudal location of the motoneuron pools in the human spinal cord (Kendall et al. 1993; Sharrard 1955; Wilbourn and Aminoff 1998). Yakovenko et al. (2002) used a similar approach to provide the first demonstration of the spatiotemporal activation of MN ensembles in the cat lumbosacral spinal cord during locomotion. We recently performed a similar analysis in normal and spinal cord–injured humans (Grasso et al. 2004a).
However, that analysis was limited to 20 limb muscles during locomotion at a very low speed (0.7 km/h) with substantial body weight support (75%). This study expands this analysis to a much larger sample of ipsilateral limb and trunk muscles in 13 normal human subjects during treadmill locomotion using a wide range of natural walking speeds (1–7 km/h). The maps based on these EMG recordings do not directly show the organization of the CPG circuitry, but they do show the organization of the output directed to the muscles.

METHODS

Subjects

Thirteen healthy subjects (8 males and 5 females, between 26 and 43 yr of age, 64 ± 14 (SD) kg, 1.70 ± 0.07 m) volunteered for the experiments. The studies conformed to the Declaration of Helsinki, and informed consent was obtained from all participants according to the procedures of the Ethics Committee of the Santa Lucia Institute.

Experimental setup

Subjects walked on a treadmill (EN-MILL 3446.527, Bonte Zwolle BV, Zwolle, Netherlands) at different controlled speeds (1, 2, 3, 5, and 7 km/h). They were asked to swing their arms normally and to look straight ahead, without paying attention to the contact with the treadmill belt. Subjects walked with their shoes on. The walking surface of the treadmill was 1.5 m long, 0.6 m wide, and 0.15 m above the ground. Before the recording session, subjects practiced for a few minutes by walking on the treadmill at different speeds. To show overall continuous alterations in the EMG patterns with walking speed, we also used a computer controlled speed program that linearly increased and then decreased the belt speed between 1 and 7 km/h (ramp speed condition, deceleration and acceleration was set to 0.4 km/h/s). Three subjects participated in this experiment. The subjects were instructed to follow the changes in speed by remaining in place (Ivanenko et al. 2004). The wires were bent back to form hooks and insert the wires and subsequently withdrawn to leave the wires in place (Basmajian and De Luca 1985) to record the activity within the following 9 leg muscles: TA, LG, PERL, RF, Vlat, GM, ST, ADDL, and OE (Table 1). The wires were bent back to form hooks and insert the wires and subsequently withdrawn to leave the wires in place (Basmajian and De Luca 1985) to record the activity within the following 9 leg muscles: TA, LG, PERL, RF, Vlat, GM, ST, ADDL, and OE (Table 1).

The EMG activity was recorded by means of surface electrodes from 16 to 32 muscles simultaneously on the right side of the body in each of the 13 normal subjects. We recorded from slightly different sets of muscles in the 13 subjects (Table 1). The following 16 muscles were recorded from 9 to 12 subjects: tibialis anterior (TA), gastrocnemius lateralis (LG), soleus (Sol), peroneus longus (PERL), vastus lateralis (VLat), rectus femoris (RF), sartorius (SART), biceps femoris (long head, BF), semitendinosus (ST), adductor longus (ADDL), tensor fascia latae (TFL), gluteus maximus (GM), erector spinae, recorded at L2 (ESL2), rectus abdominis (RA), external oblique (OE), and latissimus dorsi (LD). The following 16 muscles were recorded from two to six subjects (Table 1): flexor digitorum brevis (FDB), gastrocnemius medialis (MG), vastus medialis (Vmed), iliopsoas (ILIO), gluteus medius (Gmed), internal oblique (OI), erector spinae, recorded at T1 and T9 (EST1 and EST9, respectively), biceps brachii (BIC), triceps brachii (TRIC), deltoideus, anterior and posterior portions (DELTA and DELTP, respectively), trapezius, inferior and superior portions (TRAPS and TRAPI, respectively), splenius capitis (SPLE), and sternocleidomastoid (STER). The activity was recorded using active Delsys electrodes (model DE2.1, Delsys, Boston, MA) applied to lightly abraded skin over the respective muscle belly. Electrode placement for the ES muscle was 2 cm lateral to the spinous process, about 2 cm distal to the medial head of the gastrocnemius for Sol, and about 3 cm lateral of the umbilicus for RA (also see Winter 1991). Before the electrodes were placed, the subject was instructed about how to selectively activate each muscle (Kendall et al. 1993), while EMG signals were monitored, so as to optimize the EMG signal and minimize cross-talk from adjacent muscles during isometric contractions. The signals were amplified (×10,000), filtered (20–450 Hz; Bagnoli 16, Delsys), and sampled at 1,000 Hz. Sampling of kinematic and EMG data were synchronized.

Some of the deeper muscles around the hip have a rather complex architecture depending on the hip joint angle (Delp et al. 1999), and we cannot rule out a possibility that there might be some cross-talk in our recordings of muscles like ILIO. Nevertheless, our averaged records (the major peak of activity around lift-off) are consistent with those reported in the literature (Rab 1994) and obtained using a simulated biomechanical model of bipedal stepping (Zajac et al. 2003).

In addition, we recorded intramuscular leg EMGs in one subject (YI) to control the effectiveness of cross-talk rejection by our surface recordings and to reconstruct the resulting maps of MN activity in the lumbosacral enlargement from the intramuscular records. We used a single-needle technique (Basmajian and De Luca 1985) to record activity within the following 9 leg muscles: TA, LG, PERL, RF, Vlat, BF, ST, SART, and TFL. Twisted 50-μm-diam wire pairs were threaded through a 27-gauge hypodermic needle that was used to insert the wires and subsequently withdrawn to leave the wires in place (Ivanenko et al. 2004). The wires were bent back to form hooks on the opposite sites of the shaft to prevent their direct contact and to provide a desirable orientation of the electrodes along the muscle fibers. The recording system bandwidth was 20–1,000 Hz with an overall gain of 1,000; signals were digitized at 2,000 Hz. Surface

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EMG electrodes were also placed within 2–3 cm of the intramuscular insertion points along the direction of muscle fibers.

Data analysis

The body was modeled as an interconnected chain of rigid segments: IL-GT for the pelvis, GT-LE for the thigh, LE-LM for the shank, and LM-VM for the foot. The elevation angle of each segment in the sagittal plane corresponds to the angle between the projected segment and the vertical. These angles are positive in the forward direction (i.e., when the distal marker is located anterior to the proximal marker). The limb axis was defined as GT-LM. Gait cycle was defined as the time between two successive maxima of the elevation angle of the limb axis. The time of maximum and minimum elevation of the limb axis corresponds to heel-contact and toe-off (stance to swing transition), respectively, in healthy subjects (Bianchi et al. 1998). These time markers were used to identify stance and swing phases. In previous experiments in which a force platform (Kistler 9281B) was used to monitor the contact forces during ground walking, we found that this kinematic criterion predicts the onset and end of stance phase with an error <3% of the gait cycle duration (Borghese et al. 1996). The data were time-interpolated over individual gait cycles on a time base with 200 points.

EMG ANALYSIS. Raw data were numerically rectified, low-pass filtered with a zero-lag Butterworth filter with cut-off at 15 Hz, time-interpolated over a time base with 200 points for individual gait cycles, and averaged. Each trial for a given speed included ≥10 consecutive gait cycles (typically 15). Factor analysis of a subset of these data has been previously reported (Ivanenko et al. 2004).

SPATIOTEMPORAL PATTERNS OF MN ACTIVITY IN THE SPINAL CORD. The recorded patterns of EMG activity were mapped onto therostro-caudal location of ipsilateral MN pools in the human spinal cord (for a related application to cat locomotion data, see Yakovenko et al. 2002). This reconstruction is based on the approximate rostro-caudal localization of MN pools innervating different muscles in the human spinal cord based on published charts of segmental localization. In general, each muscle is innervated by several spinal segments. Many myotomal maps have been published, derived from various sources, including autopsy, clinical, neuroimaging, and electrophysiologic studies (see Wilbourn and Aminoff 1998 for a review). Nevertheless, the root innervation of many muscles remains debatable, and all myotomal charts can usually be considered as “approximate guides” only, because anomalous innervation occurs so frequently that caution should be used in attributing any pattern of clinical or EMG findings to a specific spinal level (Phillips and Park 1998 for a review). Nevertheless, the root innervation of many muscles remains debatable, and all myotomal charts can usually be considered as “approximate guides” only, because anomalous innervation occurs so frequently that caution should be used in attributing any pattern of clinical or EMG findings to a specific spinal level (Phillips and Park 1998 for a review). Nevertheless, the root innervation of many muscles remains debatable, and all myotomal charts can usually be considered as “approximate guides” only, because anomalous innervation occurs so frequently that caution should be used in attributing any pattern of clinical or EMG findings to a specific spinal level (Phillips and Park 1998 for a review). Nevertheless, the root innervation of many muscles remains debatable, and all myotomal charts can usually be considered as “approximate guides” only, because anomalous innervation occurs so frequently that caution should be used in attributing any pattern of clinical or EMG findings to a specific spinal level (Phillips and Park 1998 for a review).
### TABLE 2. Muscle innervation

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Results are from Kendall et al 1993.
segments, as the Kendall data tend to do. The anatomical data were taken as multiple slices within each spinal segment. To this end, we subdivided each segment (Table 3) into six subsegments and applied the same formulas 1 and 2 for each \( j \text{th} \) subsegment. The resulting spinal cord maps of activation were not smoothed as in the case of the Kendall chart but instead they contained 36 discrete bands (6 subsegments \( \times \) 6 segments; C2–L2; see Fig. 3C).

**CALCULATION OF THE CENTER OF MN ACTIVITY IN THE LUMBOSACRAL ENLARGEMENT.** The temporal locus of MN activity in the lumbosacral spinal cord was estimated using a method similar to that of Yakovenko et al. (2002). We calculated the center of activity (CoA) of the six (from L2 to S2) most active lumbosacral segments using the following formula

\[
\text{CoA} = \frac{\sum_{j=1}^{k} S_j \times j}{\sum_{j=1}^{k} S_j}
\]

where \( S_j \) is the estimated activity (from formula 1 or 2) of the \( j \text{th} \) segment (the origin for the CoA and for the vector \( j \) being defined as the caudal-most segment) and \( N \) is the number of segments (\( n = 6 \) for the Kendall charts and \( n = 36 \) for the Sharrard charts). Thus the center of activity was expressed in terms of absolute position within the lumbosacral enlargement. At any time there was typically only one dominant locus of activity in the lumbosacral enlargement (see RESULTS). Nevertheless, the CoA can only be considered as a qualitative parameter because averaging between distinct foci of activity (for instance, L2 and S2) may lead to misleading activity in the midsegments (\( \sim \)L5). Therefore we compared qualitatively the spatiotemporal dynamics of the CoA both across speeds and with that in the cat (Yakovenko et al. 2002).

**Published EMG data**

We also examined the patterns of muscle activation from a set of muscle recordings published by Winter (1991), in which the average EMG activity from 25 leg and upper and lower trunk muscles was determined for a standard step cycle (data from 18 normal subjects were pooled and averaged). The subjects walked over ground at a natural speed (~5 km/h; Winter 1991). The published records included the average and SD of filtered EMG activity (3-Hz cut-off) for one step cycle beginning with ipsilateral heel strike. Published graphs were each scanned, digitized manually (in ~30–50 points) and

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**TABLE 3. Innervation of the lower limb muscles**

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<td></td>
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Results redrawn from Sharrard, 1964. (Copyright The Royal College of Surgeons of England. Reproduced with permission.)
time-interpolated to fit a normalized 200-point time base, referred to as the Winter data (see also Ivanenko et al. 2004).

The Winter data included average EMG recordings from the following leg muscles: GM, GMed, ADDL, adductor magnus (ADDM), SART, TFL, BF, ST, RF, Vlat, Vmed, extensor digitorum longus (EDL), PERL, peroneus brevis (PERB), TA, SOL, LG, and MG.

Statistical analysis of EMG patterns

To determine the basic set of temporal activation components, we applied a factor analysis (FA) to each of several data sets consisting of normalized EMG patterns over a step cycle. Factor analysis used here has been thoroughly described in our previous papers (Ivanenko et al. 2003–2005). Briefly, the steps involve calculation of the correlation matrix, extraction of the initial principal components (PCs), application of the varimax rotation, calculation of activation components (factor scores), weighting coefficients (factor loadings), and percent of variance accounted for (VAF) by each component in the total data set. The PCs were expressed using a varimax rotation to minimize the number of variables with high loadings on each component. The aim of FA is to represent the original EMG data set \( E \) (\( m \times t \) matrix, where \( m \) is the number of muscles and \( t = 200 \) for all speeds, because EMG data were time-interpolated over individual gait cycles to fit a normalized 200-point time base) as a linear combination of \( n \) basic temporal components (\( n < m \))

\[
E = WC + \text{residual} \quad (4)
\]

where \( W \) are weighting coefficients or loadings (\( m \times n \) matrix) and \( C \) are basic components (\( n \times t \) matrix).

Recently we used other statistical approaches (independent component analysis and nonnegative matrix factorization) that have also been successful in extracting independent components from data like the EMG patterns (Ivanenko et al. 2005). The different algorithms seemed to converge to a similar solution about the temporal structure of the EMG activity pattern during human locomotion even though they are based on different sets of assumptions. The common temporal patterning elements each consisted of a relatively narrow peak of activation (Gaussian-like) at a specific timing point in the gait cycle. The width of the main peak estimated as full-width at half-maximum (FWHM) was relatively invariant across components (~14% of the cycle duration). Therefore in this study, the activity was initially fitted (using multiple linear regression; Eq. 4) with five Gaussian activation components having a SD of 6% of the cycle duration (equivalent to a half-width of 14%, FWHM = SD × 2.35). The timing of the Gaussian peaks was determined from peaks in the combined map data presented in Fig. 3A.

Statistics

The data analysis and spinal MN activity map construction were performed with software written in Matlab (v.7, The Mathworks). A FA was performed using Statistica v6.0 (StatSoft). To compare individual activation waveshapes in the lumbosacral enlargement with averaged waveforms, simple linear correlations (\( r \) values) of activation waveforms were calculated. Statistics on correlation coefficients was performed on the normally distributed, Z-transformed values.

RESULTS

Muscle activity patterns

Muscle activity during locomotion occurs in bursts that change in both amplitude and duration as a function of locomotion speed (den Otter et al. 2004; Ivanenko et al. 2002; Nilsson et al. 1985). This is shown in Fig. 1, which shows a typical example of the EMG patterns in 17 ipsilateral leg and trunk muscles from one representative subject as treadmill
speed was slowly increased from 1 to 7 km/h and then decreased again. Many muscles showed a very nonlinear behavior with these changes. For instance, some muscles (i.e., RF, Vlat, SART, LD, Vmed, Bic, Tric) were basically silent at low speeds (less than ~4 km/h) and very active at higher speeds (>4 km/h).

We examined these effects more systematically by determining the average EMG activity for ≤32 ipsilateral muscles in 13 subjects walking at constant speed on a treadmill at five different speeds (Table 1; Fig. 2). The overall effect of speed on the average EMG activity is consistent with that reported in the literature (den Otter et al. 2004; Hogue 1969; Ivanenko et al. 2002; Murray et al. 1984; Nilsson et al. 1985). Distal leg activity had about the same intensity and overall pattern at all five speeds, although mean activity increased with speed. Proximal leg activity became more robust at the higher speeds, and patterns of activity were often different at different speeds (see also Ivanenko et al. 2002; Winter and Yack 1987). The patterns of activity in trunk and abdominal muscles also tended to change dramatically as a function of speed. Cervical muscle activity, which was quite small at the lowest speeds, became significant at the higher speeds (Fig. 2).
Spatiotemporal patterns of MN activity along the rostro-caudal axis of the spinal cord

We used the EMG data to construct maps of spinal MN activity by adding up the contributions of each muscle to the total activity in each spinal segment (Fig. 3, A and B). We used the myotomal maps of Kendall et al. (1993) to determine the approximate rostro-caudal location of MN pools in the human spinal cord (Table 2; METHODS). These data indicate only the segments innervating each muscle and not the fraction of total motor pool output that can be assigned to a segment. To estimate how much this might distort the maps, we also applied the myotomal data of Sharrad (1964) (Table 3) to the leg EMG data because it does include that information for the lumbosacral segments (Fig. 3C). The maps generated with these two data sets have the same features, suggesting that the distortion introduced by the Kendall data are minimal in these segments, although the sacral activation may appear slightly stronger with the Kendall data.

The EMG data have obvious temporal patterns (Fig. 2) that are also evident in the maps projected onto the spinal segments (Fig. 3). The maps cover spinal levels C_3 to S_2 corresponding to the levels of the MNs innervating the recorded muscles (Table 2). Figure 3B shows the derived spatiotemporal pattern of MN activity along the rostro-caudal axis of the spinal cord over one cycle of walking at 3 km/h. At least five discrete activity periods appear as vertical bands in the map (Fig. 3B, dashed lines). Each of these periods can be approximated with a Gaussian activation component having a SD of ∼6% of the cycle duration (see METHODS). The first activation component is centered near the origin (time of heel strike) at ∼10% of the cycle, and the four other activation periods are centered at ∼45, 55, 75, and 95% of the cycle, respectively. Figure 4 shows the muscles that are activated by each of these components (METHODS, Fig. 4B), and the corresponding spinal segments activated (Fig. 4C). The initial activity in the cycle (component 1) appears primarily in the mid and upper lumbar segments (L_4–L_2) and extending into the lower thoracic segments. This is followed by component 2 activity in the sacral segments (S_1, S_2) at ∼45% of the cycle, when activity in the lumbar segments becomes silent or much reduced. Muscles are also activated during this period in the upper thoracic and cervical segments. A stronger activation of muscles in these segments corresponds to component 3 occurring just before lift-off at ∼55% of the cycle. These bursts are related to trunk...
stabilization activity (Thorstensson et al. 1982; Waters and Morris 1972). Lift-off at 60–70% of the cycle precedes component 4 muscle activity in the mid and upper lumbar segments. Finally, near the end of the cycle, preceding heel strike, muscles are activated by component 5 in nearly all spinal segments.

The five Gaussian components are very similar to the components derived from EMG records using FA (Fig. 5) (Ivanenko et al. 2004; Olree and Vaughan 1995). Unlike the Gaussian components, some of the FA components have minor activity peaks in addition to a main peak (Fig. 5A, thick traces). These features may account for some of the muscle activity not well captured by the Gaussian components, which may therefore provide a somewhat less complete representation of the total activity. For example, a consistent activity in triceps surae muscles between 10 and 30% of the cycle (Fig. 2, during stance) does not correspond to a Gaussian component. Even so, the total EMG variance accounted for by five Gaussians was 90% compared with 92% by the five FA components. In fact, the main peaks of the Gaussian components (Fig. 5A, thin traces) are basically the same as those of the FA components (thick traces). Some of the activity in the early stance phase not accounted for by the Gaussian components does not seem to

FIG. 4. Five gaussian activation components and their distribution along the rostrocaudal axis of the spinal cord during walking at 3 km/h. A: Gaussian components. B: their weighting coefficients across muscles. C: extent of activation by each component in the spinal cord obtained by mapping the Gaussian component for each muscle multiplied by its weighting coefficient (rescaled according to absolute EMG amplitude) onto Kendall’s chart of segmental localization. Same format as in Fig. 3B.

FIG. 5. Comparison of Gaussian components with factor analysis (FA) components. A: 5 Gaussian components (thin lines) and 5 FA components (thick lines) that account for ~92% of total EMG variance. Corresponding timing of main peaks for each component is indicated by vertical dashed lines. B: total EMG variance accounted for by each FA component.
increase with speed and may be associated more with postural support than with stepping (e.g., LG, PERL in Fig. 2).

It is also worth noting that an arbitrary temporal distribution of five Gaussians within a cycle cannot fully account for the EMG variance (range 60–80% for uniform distributions depending on initial phase), whereas the most variance (90%) is explained only when the Gaussian peaks are aligned with the main peaks of the FA components. The amount of EMG variance explained by each of the FA components also corresponds reasonably well to the extent of activation by each Gaussian component (correlation of Gaussian weighting coefficients with FA loadings, $r = 0.91 \pm 0.04$).

**Bilateral coordination of MN activity**

A remarkable feature of the bilateral coordination of MN activity is that four of the five activation components are temporally synchronized on both sides of the body, each side being phase-shifted by half a cycle. This was discovered by Olree and Vaughan (1995), who recorded from leg muscle on both sides of the body. They found basically the same five FA components shown in Fig. 5, but they noted that two of the components (3 and 5 in Fig. 5) were phase-shifted copies of the components corresponding to 1 and 2 (Fig. 6A). They also found that the phase-shifted components were loaded primarily on muscles in the contralateral leg, whereas those corresponding to components 1 and 2 were loaded primarily on ipsilateral leg muscles, whereas their fifth component (our component 4) was comparably loaded on muscles in both legs. Figure 4 shows that the components described as “ipsilateral” (components 1 and 2) correspond primarily to the activation of muscles in the lumbosacral segments, whereas those described as “contralateral” (components 3 and 5) account mostly for ipsilateral activation in the thoracic and cervical segments. Thus the ipsilateral activity in these spinal areas is likely to be coincident with the contralateral activation of leg muscles. In contrast, component 4, which explains the least variance (Fig. 5) and is associated with the ipsilateral foot lift or swing, has no contralateral analog (Fig. 6B).

**Effect of locomotion speed**

The spinal activation pattern observed at 3 km/h is also clearly evident with stronger activations at 5 and 7 km/h (Fig. 7). The patterns are also similar at the lower speeds (1 and 2 km/h), but the initial activity tends to occur later in the cycle (15–25%), and it occurs in more caudal segments. The low-speed patterns are also weaker than those seen at higher speeds.

The major leg muscle activity at 1 km/h occurs in the midstance during weight support and just before lift-off and results from activity in the sacral and lower lumbar segments. With increasing speed, leg muscle activity shifts to progressively earlier phases at the beginning of the cycle and becomes more prominent at the end of the cycle (Fig. 7).

**Migration of the center of MN activity in the lumbosacral enlargement during the gait cycle**

We also used the locus of the center of mass of MN activity (CoA) to describe how activity centers changed in time through the step cycle (Fig. 8, solid lines). We focused on the lumbosacral enlargement because it contains the MN of all the leg muscles. In general, the CoA shows rostral and caudal movements with two cycles in each step. Just before and during heel strike (the beginning of the cycle), the CoA shifts rostrally toward the upper lumbar segments. This MN activity is associated with EMG activity in the proximal (thigh) leg muscles and ankle dorsiflexors. It is responsible for extending the leg before heel strike and for braking and weight acceptance at the beginning of stance. The CoA shifts caudally on the contralateral side. The midswing caudal shift of the CoA is absent at the lowest speed (1 km/h; Fig. 8A, top panels). This results in a pattern that has basically a single cycle per step. It reflects a change in the behavior of the hamstring muscle activity as a function of locomotion speed. Hamstring activity is attenuated at the
lowest speeds, and it increases with speed as it shifts from the end of swing to the beginning of stance (Fig. 2). These changes are caused by the modified biomechanical requirements and altered dynamics of the swinging limb at low and higher walking speeds (den Otter et al. 2004; Ivanenko et al. 2002).

The features of the CoA shifts were very similar across speeds from 2 to 7 km/h. However, there are some differences in the timing of the second rostral shift. At 2 and 3 km/h, the shift occurs at ~70% of the cycle, whereas at higher speeds (5 and 7 km/h), it occurs earlier. The basic features of the CoA did not seem to depend on the method we used to estimate the activity loci (Fig. 8A, columns 1 and 2, Sharrard data table; column 3, Kendall data table). In fact, even when a slightly different set of muscle recordings was used to generate the maps (Fig. 8B, Winter data), both the maps and the basic features of the CoA were strikingly similar to those prepared from our data. Thus our result also did not seem to depend strongly on which muscles we included in the analysis.

Intersubject variability

We also examined the spatiotemporal activation patterns in the lumbosacral enlargement for single subjects. Despite remarkable similarities, there were also systematic differences among subjects that could not be explained by anomalous root innervation in some subjects (Phillips and Park 1991; Stewart 1992), because the differences clearly depended on speed. In general, the map patterns were much more similar across subjects at the higher speeds than at low speeds (Fig. 9). At lower speeds, intersubject variability was associated with differences in the activity pattern of the proximal leg muscles (i.e., RF, Vlat, Vmed, SART, BF, ST; Ivanenko et al. 2002; Winter and Yack 1987). For example, quadriceps (RF, Vlat) activity was virtually silent in some subjects at low speeds (see Fig. 1), whereas it was still present in others. This gives rise to two different types of activation maps at 1 km/h, one with component 1 activity in the upper lumbar segments (Fig. 9A, subject 1) and another with no significant activity corresponding to component 1 (subject 2). Activity associated with components 1 and 3 was not evident in this subject at speeds <5 km/h. Activation in the lower lumbosacral segments was more consistent across subjects at all speeds.

Finally, because the accuracy of activation maps could theoretically be jeopardized by electrical cross-talk among adjacent muscle recordings, we also constructed activation maps using both surface and intramuscular EMGs for one subject. The surface electrodes recorded activity that was generally well correlated with the intramuscular recordings (waveform correlation coefficients ranged from 0.45 in SART to 0.96 in TA; see Ivanenko et al. 2004), although in some cases (e.g., TFL and SART), the intramuscular recordings may have recorded components not present in the surface recordings, due perhaps to some kind of intramuscular compartmentalization that was not seen at the surface (Chanaud et al. 1991; English et al. 1993; Windhorst et al. 1989). The maps derived from the recordings made from this subject for the nine intramuscular leg EMGs (TA, LG, PERL, RF, Vlat, BF, ST, SART, and TFL) plus seven surface EMGs (SOL, MG, FDB, ADDL, ILIO, GM, and Gmed) were compared with those using only surface leg muscle recordings. The recording site (intramuscular or surface) had no significant effect on the waveforms of L2–S2 segmental activation in the lumbosacral enlargement (r = 0.92 ± 0.05).

DISCUSSION

We computed spatiotemporal maps of spinal cord MN activation by combining two data sets: the averaged, rectified
EMG-waveforms recorded simultaneously during the step cycle and the approximate spinal segment location of human MN pools innervating the muscles. At least five discrete periods of muscle activity (Figs. 3–5 and 7), corresponding to activation components described previously (Ivanenko et al. 2004), account for the major activation pattern, and they are associated with the major kinematic and kinetic events in the gait cycle. A striking feature of the maps is that bursts of MN activity are

**FIG. 8.** Spatiotemporal patterns and the center of MN activity in the lumbosacral enlargement. ***A***: pattern at different walking speeds is plotted vs. normalized gait cycle. ***B***: results are compared with the Winter data (derived from 18 leg muscles; Winter 1991). Color scale denotes relative amplitude. White dotted lines denote stance-to-swing transition time. Positions of the center of mass of MN activity (CoA) were calculated at each time of the step cycle (black curves). Three different normalization procedures were used to assess parametric sensitivity. ***Left***: nonnormalized method (EMGs were expressed in μV) using Sharrard’s chart. ***Middle***: normalized method (EMGs were normalized to the maximum during gait cycle across all speeds after subtraction of minimum) using Sharrard’s chart. ***Right***: normalized method using Kendall’s chart. General features of rostrocaudal movement of the CoA were strikingly similar despite different normalizations and different data sets (except for very low speeds, for which heel-strike/weight-acceptance activity was highly attenuated). Migration of the CoA showed basically 2 waves throughout gait cycle, thus revealing 4 major loci of activation in the lumbosacral enlargement: rostral detours of activity at the beginning of stance and at swing-stance transition and caudal movement during midstance and midswing.
temporally aligned across spinal segments, with little evidence for a wavelike rostrocaudal progression. Instead, the patterns seem more consistent with the presence of discrete pattern generators having different phases in different spinal segments that are modulated by speed.

**Locomotion pattern generator output**

**TIMING PATTERNS.** The number of lumbosacral MN activity peaks in a locomotion cycle suggests that these MN may be activated by at least two pairs of bilateral pattern generators. One such generator may activate MNs located primarily in the upper lumbar segments (components 1 and 3) and another the MNs located primarily in the lower lumbar and sacral segments (components 2 and 5; Figs. 3 and 4). As a result, these segments undergo different periods of activation in the step cycle. The same timing extends to the thoracic and cervical segments as well with components 1, 3, 4, and 5 predominant in the lower thoracic and components 2, 3, and 5 in the upper thoracic and cervical segments.

There are also speed-dependent effects on the timing patterns. For example, component 1 may be nearly absent at the lowest speed because of a drastic decrease in EMG activity at the beginning of stance (weight acceptance) in muscles innervated from the upper lumbar region (RF, Vlat, Vmed, SART; Fig. 1). The EMGs recorded at the lower speeds may result from the activation of mostly smaller motor units, yet at higher speeds, the EMG may be dominated by the recruitment of large motor units (Wakeling 2004). Thus the activity maps based on EMG activity may provide a distorted representation of MN activation. For example, the highest activity level indicated by the map at 2 km/h (Fig. 8A, nonnormalized) occurs in the sacral segments at about 50% of the cycle, and there is much less apparent activation in the lumbar segments at the beginning of the cycle. However this might not accurately represent the intensity of MN activation in these segments. In fact, the maps based on normalized records, which emphasize EMG waveforms rather than amplitudes, indicate that the lumbar MN activation may actually be greater than the sacral activation at this speed.

Other speed-dependent differences are also evident in Fig. 8 during the transition to swing. At 2 and 3 km/h, the upper lumbar activity occurs just after lift-off, whereas at 5 and 7 km/h, it occurs at or before lift-off. These times correspond to different activation components. The earlier activation at 5 and 7 km/h corresponds to component 3, whereas the later one at 2 and 3 km/h corresponds to component 4. The shifts are also clear in the data from single subjects (Fig. 9), so it is not likely to be an artifact of the averaging across subjects. Moreover, components 3 and 4 are both evident in the maps for 5 km/h (Figs. 8, 9, and 11A).

**LOCALIZATION OF PATTERN GENERATORS.** It should be emphasized again that the maps represent MN activity loci and not the loci of spinal pattern generators. Therefore questions of pattern generator location and how they might be distributed, whether at discrete sites or in a more distributed manner, cannot be answered directly from our results. Evidence favoring both distributed and discrete distributions of pattern generators has been presented (Duyens and Van de Crommert 1998; Kiehn et al. 1998; Orlovsky et al. 1999). It has also been suggested that MNs are integral elements of CPGs (Marder 1991; O’Donovan et al. 1998).

The localization of mammalian spinal pattern generators has been explored extensively with in vitro rodent models, but a clear picture has not yet emerged. A time series of Ca$^{2+}$ images over a locomotion cycle showed a wave-like propagation of motoneuron activity in the neonatal mouse lumbar

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**FIG. 9.** Intersubject variability in spatiotemporal patterns of MN activity in the lumbosacral enlargement. **A**: spatiotemporal maps of activity in the 2 subjects at different speeds obtained using Kendall’s chart. **B**: correlations (mean ± SD) between individual activation waveforms (L2–S2 segments) with averaged waveforms as a function of speed. For a given speed, individual correlations were obtained for each segment and averaged across segments and subjects. Note comparable individual activations at high speeds and larger variability at low speeds.
spinal cord (Bonnot et al. 2002), and other data from the neonatal rat suggest that pattern generator activity may be localized near the relevant MN pools (Tresch and Kiehn 1999). However, data from adult animals suggest that dominant generators in the upper lumbar segments may drive the distributed neonatal generators (Cazalets and Bertrand 2000).

The evidence from rodent spinal cords also shows that oscillatory networks sensitive to different modulators (e.g., serotonin or acetylcholine) are in fact distributed throughout the cord, so the resulting MN activity might also depend on a dominant modulator (Kremer and Lev-Tov 1997). In fact, the interpretation of our results also suggests that different pattern generators controlling the same spinal segments might be differentially activated at different speeds.

While a functional organization might be evident from these results, the anatomical details might be quite different. For example, there is an extensive propriospinal network of reciprocal excitatory and inhibitory connections active during locomotion that may activate MNs far from the site of pattern generator (Nathan et al. 1996; Poppele and Bosco 2003). Finally, the role of sensory feedback in establishing MN activation patterns in addition to or in conjunction with pattern generators cannot be ignored.

**Functional Organization.** The outputs from the spinal pattern networks can be represented functionally by a separate activation of MNs in the upper lumbar and lower lumbosacral spinal segments (Fig. 10). We propose that half-center oscillators with outputs directed to MNs in the two segments on each side of the spinal cord can represent the spinal pattern generators responsible for the main peaks of lumbosacral MN activity. The ipsilateral oscillators are postulated to drive ipsilateral MN either during stance or during swing (or the transition to swing), as depicted in Fig. 10 by the output arrows and by the diagrams of corresponding activity periods. The data suggest that, unlike classic half-center oscillators, the pattern generators have a short duty cycle, where each half is active for only ~15% of the cycle. The data also suggest that the oscillators on the two sides of the cord are coupled so that contralateral MNs are activated at the same time as the ipsilateral MNs, but in opposite phase. For example, ipsilateral stance activity corresponds to contralateral activation in swing or transition to swing.

While this may account for the basic pattern seen at 5 and 7 km/h, the timing of upper lumbar MN activation may be different at lower speeds where the timing of activation during the transition to swing corresponds to component 4 rather than component 3. This does not fit easily into the above interpretation because component 4 does not have a corresponding opposite side counterpart (Fig. 6).

**Component 4.** The studies of Olree and Vaughan (1995) noted above concluded that component 4 (their component 5) was different because, unlike the other activation components, there was no contralateral equivalent or paired component. However, it is still possible that a paired component exists, but occurs coincidently with another activation component already present (e.g., component 1; see also Ivanenko et al. 2005). This could happen if the timing between the half-center activity periods were slightly asymmetric, instead of occurring at half-cycle intervals as appears the case for the other activation components. If so, our results suggest that there may be a “component 1, 4 oscillator,” which is dominant at low speeds, whereas the “component 1, 3 oscillator” becomes dominant at higher walking speeds.

This interpretation is consistent with a shift in dominant oscillators with speed changes, in addition to any single oscillator phase shifts that may occur (e.g., Yakovenko et al. 2005). The presence of both components 3 and 4 in records from single subjects (Fig. 9A) shows that both oscillator phases can exist simultaneously. Thus the result is not simply an artifact of averaging across subjects. Moreover, we noted earlier that component 4 explained more response variance at 2 km/h than at 5 km/h, whereas component 3 explained more at 5 km/h than at 2 km/h (Ivanenko et al. 2004).

Although there are other possibilities to explain the timing of MN activity, including the influence of sensory input, this proposed organization of generators seems consistent with several other observations concerning timing and localization in pattern generating circuitry in mammals (see Localization of pattern generators).

**Comparison of spatiotemporal maps in human and cat**

Yakovenko et al. (2002) also reported spatiotemporal maps of MN activation for the cat lumbosacral spinal cord. They constructed the map from anatomical data on MN localization obtained by Vanderhorst and Holstege (1997) and from a compilation of published records of EMG activity during locomotion of intact cats. Interestingly, the
lumbosacral MNs contribute much earlier in stance, whereas levels are quite different in the two species. In the cat, lower patterns. The contributions of MNs at various lumbosacral siderable differences between human and cat activation times.

tivity jumps from one region to the other at the transition both sets of maps (Fig. 11), the CoA of MN activity of the same features as that of Yakovenko et al. (2002). In lumbosacral map we obtained in healthy humans has some

Nevertheless, despite such similarities there are also considerable differences between human and cat activation patterns. The contributions of MNs at various lumbosacral levels are quite different in the two species. In the cat, lower lumbosacral MNs contribute much earlier in stance, whereas L5 and L4 activity is seen later in stance. This is also evident in the sample EMG records in Fig. 11. LG activity, which corresponds to an activation peak late in stance at the lower lumbosacral in the human, occurs instead at the beginning of stance in the cat. Similarly, RF activity, which is most prominent at heel strike in the human, occurs mostly at mid-stance in the cat.

These differences can be accounted for by the different biomechanics of limb movement. In humans, the presence of a strong burst of activation at the upper lumbar spinal cord at the beginning of stance (Fig. 11A) is associated with the weight acceptance and is a specific feature of the activity of proximal leg muscles (Fig. 2). In the cat, the vertical ground reaction force peaks only once during the first third of stance (the paw remains digitigrade), and knee extensor activity is consistent with an extensor muscle torque at the knee joint for all but the initial segment of stance (Fowler et al. 1993; Zernicke and Smith 1996). Therefore in the cat, the ankle extensors are most active at the beginning of stance, resulting in a caudal locus of activation.

These differences serve to emphasize that peripheral feedback and perhaps also CPG organization are likely to play an important role in controlling locomotion in the human and the cat (Capaday 2002; Winter 1989).

Clinical implications

Spatiotemporal patterns of spinal cord activations (Figs. 7 and 8) may have important clinical implications. The network of MNs actively oscillating during the step cycle appears widely spaced over extensive regions of the spinal cord. This could imply that individual burst generators may be coupled by long propriospinal neurons to different pools of MNs across several spinal segments (as suggested by Nathan et al. 1996). After spinal cord injury, changes in the connections of the network are probably adaptive and learned because the corresponding spatiotemporal maps of MN activity are very different in patients with spinal cord injuries (Grasso et al. 2004a). The reorganization may involve a redistribution of activity to different limb and body muscles, creating new muscle synergies (Barbeau et al. 1999; Ivanenko et al. 2003; Pearson 2001; Pepin et al. 2003) that are specific to the learned task (de Leon et al. 1998; Grasso et al. 2004b). Thus the model of the net MN activity along the rostrocaudal axis of the human spinal cord may be used to monitor the output state and plasticity of the neural network in the course of recovery of locomotor function in patients with various motor disorders.

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