NeuroImage 54 (2011) 1289–1296

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg

Electrocortical activity is coupled to gait cycle phase during treadmill walking

Joseph T. Gwin [a,*], Klaus Gramann [b], Scott Makeig [b], Daniel P. Ferris [a]

[a] Human Neuromechanics Laboratory, School of Kinesiology, University of Michigan, Ann Arbor, MI 48109-2214, USA
[b] Swartz Center for Computational Neuroscience, Institute for Neural Computation, University of California San Diego, La Jolla, CA 92093-0961, USA

ARTICLE INFO

Article history:
Received 23 June 2010
Revised 23 August 2010
Accepted 29 August 2010
Available online 9 September 2010

Keywords:
Electroencephalography
Locomotion
Motor control
Walking
Independent components analysis
Mobile brain imaging

ABSTRACT

Recent findings suggest that human cortex is more active during steady-speed unperturbed locomotion than previously thought. However, techniques that have been used to image the brain during locomotion lack the temporal resolution necessary to assess intra-stride cortical dynamics. Our aim was to determine if electrocortical activity is coupled to gait cycle phase during steady-speed human walking. We used electroencephalography (EEG), motion capture, and a force-measuring treadmill to record brain and body dynamics while eight healthy young adult subjects walked on a treadmill. Infomax independent component analysis (ICA) parsed EEG signals into maximally independent component (IC) processes representing electrocortical sources, muscle sources, and artifacts. We calculated a spatially fixed equivalent current dipole for each IC using an inverse modeling approach, and clustered electrocortical sources across subjects by similarities in dipole locations and power spectra. We then computed spectrograms for each electrocortical source that were time-locked to the gait cycle. Electrocortical sources in the anterior cingulate, posterior parietal, and sensorimotor cortex exhibited significant ($p<0.05$) intra-stride changes in spectral power. During the end of stance, as the leading foot was contacting the ground and the trailing foot was pushing off, alpha- and beta-band spectral power increased in or near the left/right sensorimotor and dorsal anterior cingulate cortex. Power increases in the left/right sensorimotor cortex were more pronounced for contralateral limb push-off (ipsilateral heel-strike) than for ipsilateral limb push-off (contralateral heel-strike). Intra-stride high-gamma spectral power changes were *evident in anterior cingulate, posterior parietal, and sensorimotor cortex*. These data confirm cortical involvement in steady-speed human locomotion. Future applications of these techniques could provide critical insight into the neural mechanisms of movement disorders and gait rehabilitation.

Introduction

Vertebrate legged locomotion requires dynamic interaction between peripheral sensors, central pattern generators, and supraspinal locomotion centers (Grillner et al., 2008; Rossignol et al., 2006). It is generally accepted that humans use a multifaceted locomotion control strategy, including descending, peripheral, and central inputs (Dietz, 2003; Dietz and Duysens, 2000; Drew et al., 2004; Nielsen, 2003; Yang and Gorassini, 2006). Spinal locomotor networks in humans and other vertebrates are capable of generating rhythmic muscle activity (Dietz, 2003; Dimitrijevic et al., 1998; Grillner, 1985; Rossignol, 2000; Rossignol et al., 2006; Shik and Orlovsky, 1976). However, activating this network in humans without functional descending motor pathways has proven to be difficult (Dietz et al., 1995; Ferris et al., 2004; Fong et al., 2009; Wirz et al., 2001). Some supraspinal locomotor centers are organized hierarchically in the brainstem, cerebellum, and cortex. This hierarchical structure facilitates integration of multi-sensory information for dynamic control during gait (Fong et al., 2009; Rossignol et al., 2006). However, primates (including humans) also have a monosynaptic corticospinal pathway connecting the motor cortex to spinal motoneurons.

Several research areas have provided indirect evidence of *cortical* involvement in human locomotion. Dual-task experiments have demonstrated that balance during walking can be negatively affected by concomitant information processing (Woollacott and Shumway-Cook, 2002). Positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) have demonstrated that during rhythmic foot or leg movements the primary motor cortex is activated, consistent with expected somatotopy, and that during movement preparation and anticipation frontal and association areas are activated (Christensen et al., 2000; Dobkin et al., 2004; Heuninckx et al., 2005, 2008; Luft et al., 2002; Sahyoun et al., 2004). Furthermore, electrophysiological studies of similar tasks have demonstrated lower limb movement related electrocortical potentials (Wieser et al., 2010), as well as coherence between electromyographic and electroencephalographic signals (Hansen and Nielsen, 2004; Raethjen et al., 2008). These studies can be extrapolated to make predictions about locomotion.

* Corresponding author. University of Michigan, School of Kinesiology, 401 Washtenaw Ave., Ann Arbor, MI 48109-2214, USA.
E-mail address: jgwin@umich.edu (J.T. Gwin).

1053-8119/$ – see front matter © 2010 Elsevier Inc. All rights reserved.
doi:10.1016/j.neuroimage.2010.08.066

Direct evidence for cortical involvement in human locomotion comes from studies using functional near-infrared spectroscopy (fNIRS) and PET. Using fNIRS, researchers demonstrated increases in oxygenated hemoglobin in the frontal, premotor, and supplementary motor cortex during walking (Harada et al., 2009; Miyai et al., 2001; Suzuki et al., 2008; Suzuki et al., 2004). In a recent study using PET before and immediately after imagined and real walking, researchers found that imagined 20-s bouts of walking beginning from stance activated an indirect pathway via the supplementary motor cortex and basal ganglia loop, while 20 min of real steady speed walking activated a direct corticospinal pathway via the primary motor cortex (la Fougere et al., 2010). The authors suggested that the direct corticospinal pathway is responsible for execution of steady-speed locomotion while the indirect pathway is responsible for planning and modulation of locomotion. In that framework, intra-stride phasic cortical activity associated with integration of afferent sensory information and maintenance a steady gait might be expected. However, it is difficult to disentangle differences between real and imagined locomotion from differences between short bouts of walking initiated from stance and long bouts of stead speed walking.

Transcranial magnetic stimulation (TMS) facilitates direct study of intra-stride modulations in corticospinal excitability. Studies using transcranial magnetic stimulation (TMS) have shown that activation of inhibitory circuits in the motor cortex during steady walking disrupts ongoing cortico-muscular interaction and reduces lower limb (plantar- and dorsi-flexor) activity (Capaday et al., 1999; Christensen et al., 2001; Petersen et al., 2001; Schubert et al., 1999, 1997), as well as upper-limb (posterior deltoid) activity (Barthelemy and Nielsen, 2010). In addition, motor evoked potentials (MEPs) in plantar- and dorsi-flexors evoked by TMS are evident only during phases of the gait cycle where a particular muscle is active; for example, MEPs in the soleus are present during stance and absent during swing (Capaday et al., 1999; Schubert et al., 1997). At least part of this MEP modulation is caused by changes in excitability of monosynaptic corticospinal cells (Petersen et al., 2001).

In animal models, microwire electrode arrays implanted into the cortex have provided evidence of intra-stride modulations of neuronal firing rates. In feline posterior parietal cortex (Andujar et al., 2010; Beloozerova and Sirota, 2003; Lajoie et al., 2010) and motor cortex (Armstrong and MarpleHorvat, 1996; Drew, 1993; Drew et al., 2002; Widajewicz et al., 1994) neuronal firing rates exhibit peaks that are synchronized to the gait cycle. These studies suggest that feline posterior parietal cortex likely plays a role in visuo-motor integration during locomotion while motor cortex contributes to gait execution. Additionally, lower limb muscle activations and joint angles have been decoded from motor cortex neuronal firing rates in rhesus monkeys during bipedal walking (Fitzsimmons et al., 2009). Taken together these studies demonstrate the existence of intra-stride modulations in cortical activity in various vertebrate animals.

Electroencephalography (EEG) is the only non-invasive brain imaging modality that uses sensors that are light enough to wear during ambulation and have sufficient time resolution to record intra-stride changes in brain activity (Makeig et al., 2009). Independent component analysis (ICA) combined with magnetic resonance based head models can be used to overcome electromyographic, electro-ocular, movement artifact, and line noise contamination of EEG signals (Delorme and Makeig, 2004; Delorme et al., 2007; Gwin et al., 2010; Jung et al., 2000a,b; Makeig et al., 1996, 2009; Onton et al., 2006). We have previously demonstrated that high-density EEG can be used to record electrocortical dynamics associated with cognitive tasks during walking and running (Gwin et al., 2010). Specifically, we identified a visually evoked target response in human electrocortical activity during walking and running that was similar to the visually evoked target response during standing. The purpose of this study was to use high-density EEG to examine patterns of intra-stride electrocortical dynamics during steady-speed human walking. Our hypothesis was that electrocortical dynamics, particularly in the sensorimotor cortex, would exhibit intra-stride patterns of activation and deactivation. In addition to providing insight into how the human central nervous system coordinates locomotion, we believe that in the long run these dynamics may be of use for brain-machine interface (BMI) based neurorehabilitation (Daly and Wolpaw, 2008; Yang and Gorassini, 2006) and that future applications of these techniques could provide critical insight into the neural mechanisms of movement disorders and gait rehabilitation.

Materials and methods

Data collections

Eight healthy volunteers with no history of major lower limb injury and no known neurological or locomotor deficits completed this study (seven males and one female, age range 21–31 years). All subjects provided written informed consent prior to the experiment. All procedures were approved by the University of Michigan Internal Review Board and complied with the standards defined in the Declaration of Helsinki.

Subjects stood, walked (0.8 and 1.25 m/s), and ran (1.9 m/s) on a force measuring treadmill (Collins et al., 2009) facing a monitor placed at eye level about 1 m in front of them while we recorded 248-channel electroencephalography (EEG), lower limb kinematics, and ground reaction forces. One objective of this data collection was to test the feasibility of recording cognitive brain processes during human locomotion (Gwin et al., 2010). In order to do this standard (80%) and target (20%) stimuli (vertical or 45° rotated black crosses on a white background, respectively) were displayed on the monitor for 500 ms with a random inter-stimulus interval between 500 and 1500 ms. For each gait condition (standing, slower walking, faster walking, running) subjects performed an experimental block wherein they were asked to press a handheld button whenever the target stimulus appeared and a control block wherein no manual response to the target stimulus was required. Each session began with the standing condition, followed by the other three conditions in random order. The standing blocks lasted 5 min each while the walking and running blocks lasted 10 min each. For the present study we analyzed data from the walking control conditions. Data collected during running were not used due to the presence of large mechanical artifacts in the EEG signals.

We recorded EEG using an ActiveTwo amplifier and a 248-channel active electrode array (BioSemi, Amsterdam, The Netherlands). The BioSemi software sampled the EEG signals at 512 Hz per channel. Prior to data collection, we measured electrode impedance and used electrode gel to ensure that the impedance was less than 20 kΩ for each channel. After data collection we high-pass filtered the EEG signals above 1 Hz. As in Gwin et al. (2010) EEG signals exhibiting substantial noise throughout the collection were removed from the data in the following manner: 1) channels with std. dev. $\geq$ 1000 μV were removed, 2) any channel whose kurtosis was more than 5 std. dev. from the mean was removed, and 3) channels that were uncorrelated ($r \leq 0.4$) with nearby channels for more than 1% of the time-samples were removed. On average 130.4 EEG channels were retained for analysis (range, 89–164; std. dev., 24.6). These remaining channel signals were then re-referenced to an average reference. All processing and analysis was performed in Matlab (The Mathworks, Natick, MA) using scripts based on EEGLAB 7.1.4 (sccn.ucsd.edu/eeglab), an open source environment for processing electrophysiological data (Delorme and Makeig, 2004).

We recorded the positions of 25 reflective markers on the lower limbs and the pelvis using an eight-camera motion capture system (Motion Analysis Corporation, Santa Rosa, CA). Marker positions were sampled at 120 Hz and low pass filtered at 6 Hz to remove movement

artifact. Visual-3D software (C-Motion, Germantown, MD) computed the kinematics of the ankle, knee, and hip joints based on these marker positions. Event detection algorithms within Visual-3D determined when heel-strike and toe-off occurred based on vertical ground reaction forces and lower limb kinematics (Stanhope et al., 1990).

Data analyses

We applied an adaptive mixture independent component analysis (ICA) algorithm [AMICA] (Palmer et al., 2006, 2008) that generalizes infomax (Bell and Sejnowski, 1995; Lee et al., 1999a) and multiple mixtures (Lee et al., 1999b; Lewicki and Sejnowski, 2000) ICA approaches, to parse EEG signals into spatially static, maximally independent component (IC) processes (Makeig et al., 1996). Prior to performing ICA decomposition, time-periods of EEG with substantial artifact, as defined by z-transformed power across all channels in a given time window being larger than 0.8, were rejected using EEGLAB.

DIPFIT functions within EEGLAB (Oostenveld and Oostendorp, 2002) computed an equivalent current dipole model that best explained the scalp topography of each IC using a boundary element head model based on the Montreal Neurological Institute (MNI) template (the average of 152 MRI scans from healthy subjects, available at http://www.mni.mcgill.ca). We excluded ICs from further analysis if the projection of the equivalent current dipole model to the scalp accounted for less than 80% of the scalp map variance, or if the topography and time-course of the IC was reflective of eye movement artifact (Jung et al., 2000a,b). The remaining ICs were classified as electrocortical sources or muscle sources based on inspection of their power spectra and the locations of their equivalent current dipoles. Next, electrocortical sources were clustered across subjects using EEGLAB routines implementing k-means clustering on vectors jointly coding differences in equivalent dipole locations and power spectra; the resulting joint vector was reduced to 10 principal dimensions using principal component analysis (Gramann et al., 2009; Jung et al., 2001).

We generated spectrograms for each electrocortical source during each gait cycle for each subject. For comparison purposes we selected a subset of muscle sources located around the left and right mastoid processes (possibly representing left and right sternocleidomastoid EMG) and computed similar spectrograms. The single-trial spectrograms were then linearly time-warped so that both right and left heel-strikes occurred at the same adjusted latencies in each epoch (Makeig et al., 2007). To visualize intra-stride changes in the spectrograms, we subtracted the average log spectrum for all gait cycles from the log spectrogram for each gait cycle. We refer these changes from baseline as gait event related spectral perturbations (ERSP) (Makeig, 1993). We generated grand average mean ERSP plots for each cluster of electrocortical sources at each walking speed. Significant gait ERSPs ($p<0.05$) were identified using a bootstrapping method available within EEGLAB (Delorme and Makeig, 2004). In order to visualize the relative timing of spectral power fluctuations we computed the average gait ERSP for each electrocortical source in the alpha (8–12 Hz), beta (12–30 Hz), and high-gamma (50–150 Hz) frequency bands. We displayed these average ERSPs in separate line plots for each frequency band.

Results

Clusters of electrocortical sources that were identified by ICA and inverse source modeling were spatially localized to the prefrontal cortex (5 electrocortical sources), left and right sensorimotor cortex (7 and 6 sources), anterior cingulate cortex (9 sources), and posterior parietal cortex (13 sources) (Fig. 1). Electrocortical sources were also identified in the left premotor cortex, left/right temporal lobe, and left/right occipital lobe, but these sources were found in less than half of our subjects and so were not included in subsequent analysis. Gait ERSPs revealed small but significant modulations of spectral power within IC clusters localized in or near the anterior cingulate, posterior parietal, and left/right sensorimotor cortex (Fig. 2). Finding no significant differences between gait ERSPs for 0.8 and 1.25 m/s walking, we averaged the gait ERSPs across walking speeds.

Cortical local field potential activity represents net potentials within complex local thalamocortical and cortico-cortical networks with many modulatory influences. Cortically generated far-field EEG activity recorded at scalp electrodes reflects partial synchrony of local field potentials across a compact cortical domain (on the order of a cm^2) that is far larger than a few neurons. Increased EEG power relative to the mean baseline, shown in Fig. 2 by warm colors, may reflect a mean increase in the degree of local synchrony within the source domain, a change in the size of the source domain, and/or stronger local field activity within the source domain. Decreased power is indicated by cool colors.

Significant alpha- and beta-band power increases in or near the left/right sensorimotor and dorsal anterior cingulate cortex occurred during the end of stance as the leading foot was contacting the ground and the trailing foot was pushing off. Power increases in the left/right sensorimotor cortex were more pronounced for contralateral limb push-off (ipsilateral heel-strike) than for ipsilateral limb push-off (contralateral heel-strike) (Fig. 2). Within the alpha- and beta-bands, spectral fluctuations for all four electrocortical sources were in phase with each other. Peaks in beta-band spectral power preceded peaks in alpha-band spectral power by roughly 8% of the gait cycle; beta-band peaks occurred at heel-strike while alpha-band peaks occurred roughly half-way through the double support phase (Fig. 3). Power increases in the high-gamma band occurred for all clusters (Fig. 2). With the exception of the right sensorimotor source, high-gamma spectral fluctuations across the electrocortical domains were in phase with each other and exhibited more peaks per gait cycle than the alpha- and beta-band spectral fluctuations. High-gamma spectral fluctuations in the right sensorimotor source were out of phase with high-gamma fluctuations in the other electrocortical domains (Fig. 3).

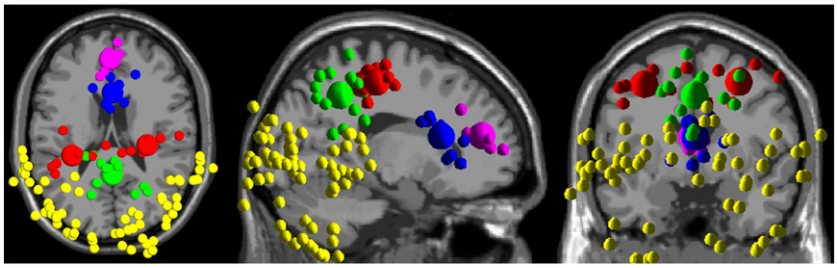

Fig. 1. Clusters of electrocortical sources localized to the anterior cingulate (blue), prefrontal cortex (purple), posterior parietal cortex (green), and sensorimotor cortex (red). Small spheres indicate the equivalent current dipole locations for single electrocortical sources for single subjects; larger spheres indicate geometric cluster centroids. The locations of the equivalent current dipoles for muscle sources are shown in yellow.

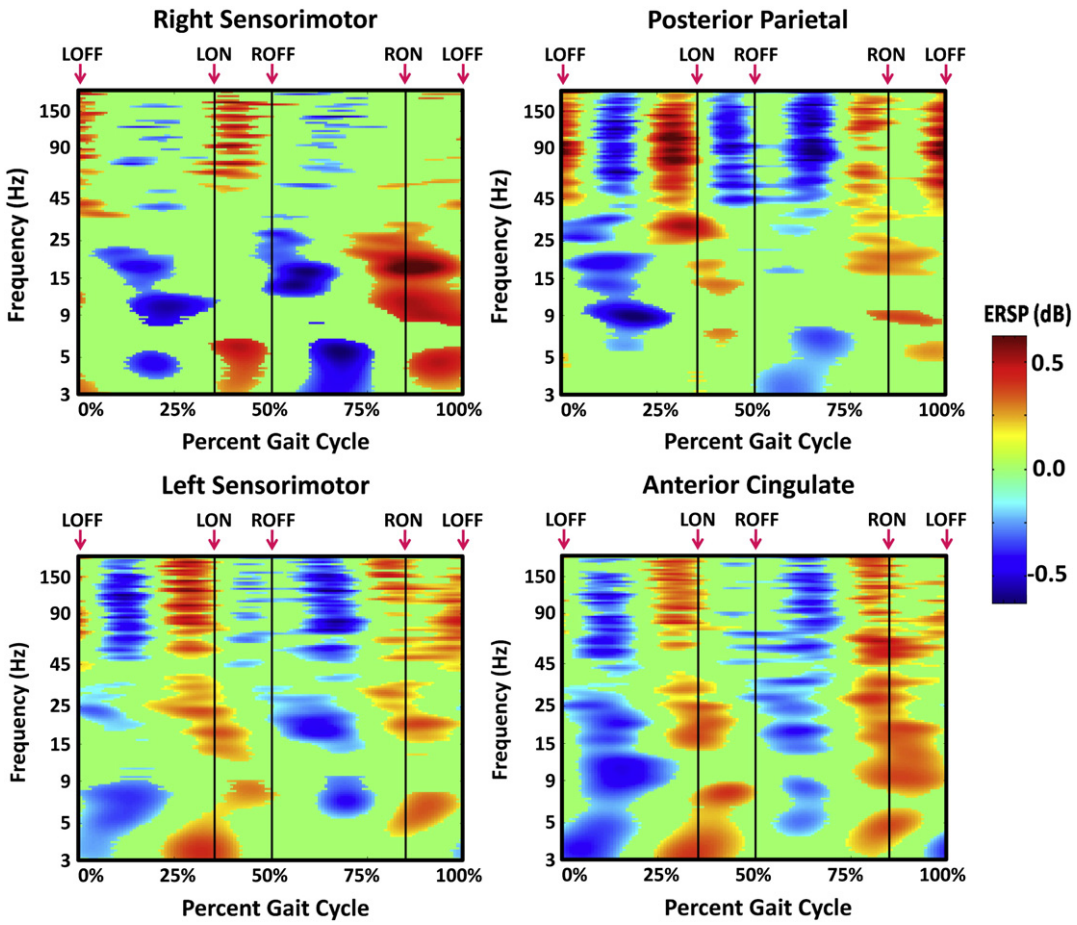

Fig. 2. Gait event-related spectral perturbation (ERSP) plots showing average changes in spectral power during the stride cycle relative to the full gait cycle baseline for (top left) the right sensorimotor cluster, (top right) the posterior parietal cluster, (bottom left) the left sensorimotor cluster, and (bottom right) the anterior cingulate cluster. The gait cycle begins and ends with left toe-off (LOFF). Vertical lines indicate the timing of left heel-strike (LON), right toe-off (ROFF), and right heel-strike (RON). Non-significant differences ($p<0.05$) have been set to 0 dB (green).

To highlight the importance of extracting neck muscle contributions from the EEG signals, we have also shown gait ERSP plots for groups of muscle sources that were localized to the region around the left/right mastoid processes (Fig. 4). Muscle sources exhibited larger intra-stride spectral power changes than electrocortical sources; as such, the color scale in Fig. 4 is four times coarser than in Fig. 2. The broad spatial distribution of all neck muscle sources (Fig. 1) is reflective of the fact that many neck muscles contribute to head stabilization during walking (Cromwell et al., 2001). Only one subset of these neck muscle sources is represented in Fig. 4, with the intent of demonstrating that the magnitude of electromyographic spectral fluctuations can be at least 4× greater than the magnitude of electrocortical spectral fluctuations.

Discussion

To our knowledge, this is the first study to report intra-stride patterns of spatially resolved human brain activation during walking. ICA decomposition parsed scalp EEG into activities generated in separate cortical domains, individual neck and scalp muscles, and

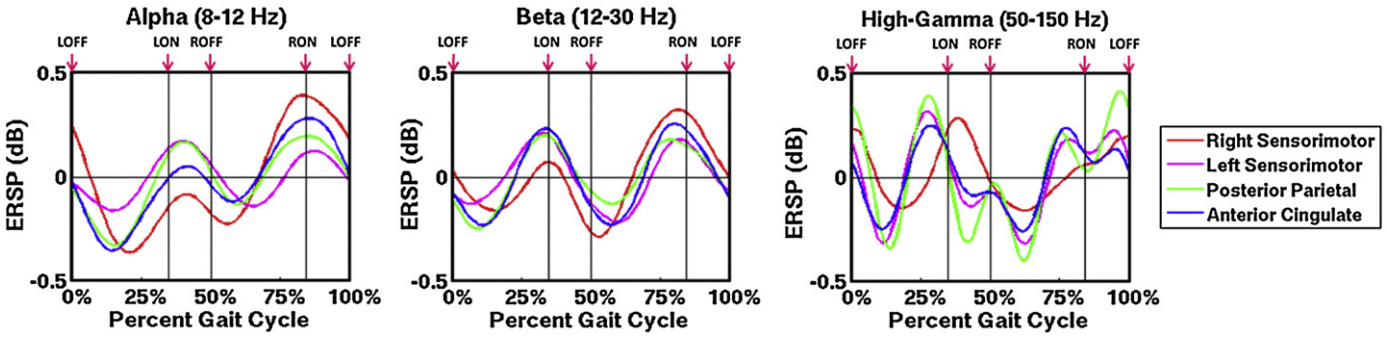

Fig. 3. Average gait event-related spectral perturbation (ERSP) line plots showing the average gait ERSP for the (left) alpha (8–12 Hz), (middle) beta (12–30 Hz), and (right) high-gamma frequency bands. Each cluster of electrocortical sources is represented by a colored trace: (red) right sensorimotor cluster, (magenta) left sensorimotor cluster, (green) posterior parietal cluster, and (blue) anterior cingulate cluster. The gait cycle begins and ends with left toe-off (LOFF). Vertical lines indicate the timing of left heel-strike (LON), right toe-off (ROFF), and right heel-strike (RON).

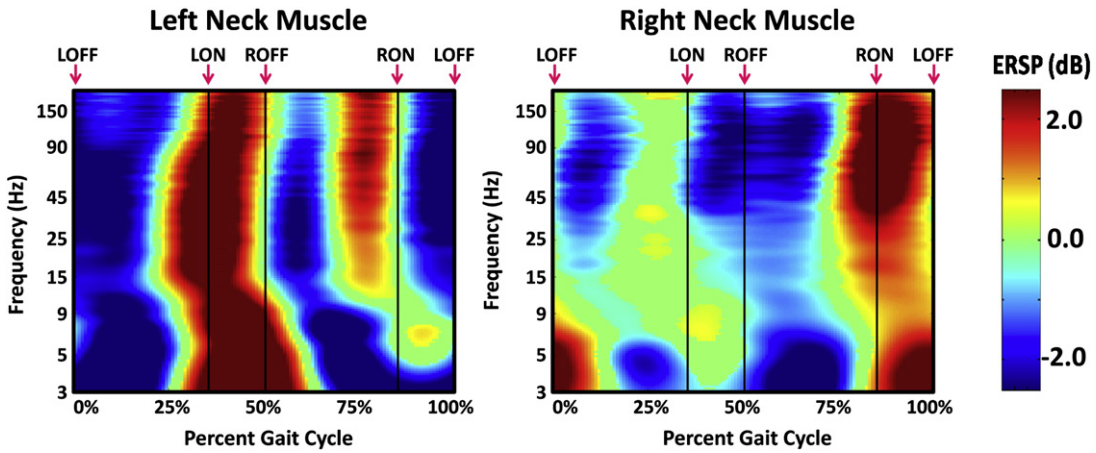

Fig. 4. Gait event-related spectral perturbation (ERSP) plots showing average changes in spectral power during the stride cycle relative to the full gait cycle baseline for a subset of neck muscle components localized to the region around the left (shown left) and right (shown right) mastoid processes. These clusters may represent left and right sternocleidomastoid EMG and are shown for comparison with Fig. 2. Note that the color scale is coarser than Fig. 2. The gait cycle begins and ends with left toe-off (LOFF). Vertical lines indicate the timing of left heel-strike (LON), right toe-off (ROFF), and right heel-strike (RON). Non-significant differences ($p<0.05$) have been set to 0 dB (green).

other non-brain artifact sources (eyes, heart, line noise, etc.). We found that small but significant changes in the power spectra of various electrocortical processes, which were disentangled from scalp EEG by ICA, occurred during particular phases of the gait cycle.

Significant alpha- and beta-band power increases in or near the left/right sensorimotor and dorsal anterior cingulate cortex occurred during the end of stance as the leading foot was contacting the ground and the trailing foot was pushing off. Findings from electrophysiological and imaging studies have suggested that dorsal anterior cingulate cortex may be the brain's center for error detection and correction (Bush et al., 2000; O'Connell et al., 2007; Walton et al., 2007). In our study, therefore, the increased beta activity in or near anterior cingulate during foot placement could be related to foot trajectory error detection and correction. A future experiment that examines a walking task requiring more controlled foot placement and step-to-step adjustment (e.g., walking on stepping stones or marks on the floor) could test this hypothesis. An alternate hypothesis is that medial frontal processes are implicated in the transition from flexion to extension (akin to the stance to swing transition in normal walking). This hypothesis is supported by a recent study of scalp EEG topography during a rhythmic multi-joint lower limb movement task designed to mimic walking (Wieser et al., 2010).

Power increases in the left/right sensorimotor cortex were most pronounced during the end of contralateral limb stance when maximum lower limb muscle power is required (Kuo et al., 2005) but somatosensory attention may shift from the contralateral limb to the ipsilateral limb about to be raised (Pfurtscheller et al., 1996). It is possible that increased sensorimotor cortex EEG power during push-off indexes stronger lower limb muscle recruitment. If so, future studies examining biomechanical perturbations to gait might identify correlations between muscle recruitment and electrocortical dynamics during walking. Interestingly, electrocortical sources were broadly distributed in the lower and upper limb regions of the somatosensory cortex. This may be reflective of different attentional strategies between subjects who are more or less accustomed to treadmill walking. Future studies examining simultaneous lower and upper limb motor tasks could test whether high density EEG and ICA can effectively disentangle sources in the upper limb region of the somatosensory cortex from sources in the lower limb region.

Broad high-gamma (50–150 Hz) changes in electrocortical power intra-stride were evident in all four electrocortical clusters including the posterior parietal cortex. Prior research has suggested that high-gamma activity is increased in human cortex during selective attention (Ray et al., 2008), in motor cortex accompanying finger movements (Pfurtscheller et al., 1996), and selectively in different cortical regions during various imagined emotion states (Onton and Makeig, 2009). Others have proposed that during rhythmic sensory tasks the brain favors a 'rhythmic mode of operation' that includes entrainment of lower-frequency oscillations to task dynamics and temporal alignment of high-frequency oscillations to attended rhythmic events as a means of enhancing responses that are in-phase with attended events and suppressing responses that are out-of-phase with attended events (Schroeder and Lakatos, 2009). It has also been suggested that during dynamic force production the sensorimotor system shifts towards gamma frequencies to rapidly integrate multi-sensory information that is required to produce the appropriate motor command (Omlor et al., 2007).

Posterior parietal cortex has been associated with visuo-motor integration and bimanual coordination. Prior research using functional magnetic resonance imaging has implicated the posterior parietal cortex in upper-limb reaching (Filimon et al., 2009) and in coordination of left and right wrist movements (Wenderoth et al., 2005). In addition, microwire arrays implanted into feline posterior partial and motor cortex during flat ground and precision walking have suggested that visuo-motor integration during locomotion is critically dependent on posterior parietal and motor cortex networks (Andujar et al., 2010; Beloozerova and Sirota, 2003; Drew et al., 2002; Lajoie et al., 2010). In our study, we found (with one exception) that within a given frequency band (alpha, beta, or high-gamma) spectral power fluctuations were synchronous across all four electrocortical domains but were not uniformly significant (i.e. periods of significant spectral fluctuations occurred in different regions of the gait cycle for different electrocortical domains, Fig. 2). The exception was that high-gamma fluctuations in the right sensorimotor cortex were out of phase with high-gamma fluctuations in the other three regions (left sensorimotor, anterior cingulate, and posterior parietal). This is consistent with convincing evidence that bilateral coordination preferentially recruits the left hemisphere and that the left hemisphere regulates limb position and posture (Serrien et al., 2006). Synchronous spectral power fluctuations across the anterior cingulate, posterior parietal and left sensorimotor cortex may be reflective of visuo-motor integration and error monitoring networks.

In this study we showed intra-stride changes in spectral power of neck and scalp muscle sources to demonstrate the importance of spatially filtering EEG signals. Muscle source spectral power

changes were substantially larger than electrocortical spectral power changes. Interestingly, neck muscle sources located around the left and right mastoid processes (possibly representing left and right sternocleidomastoid EMG) exhibited increased spectral power from ipsilateral heel-strike through contralateral toe-off, which may be reflective of head stabilization during locomotion. The sternocleidomastoid is only one of several muscles that contribute to head stabilization during walking (Cromwell et al., 2001). A more thorough analysis of neck muscle EMG, including EMG sources extracted from EEG by the methods presented herein, is needed to characterize intra-stride patterns of neck muscle activation and to assess the possibility of incomplete decontamination of electrocortical sources.

The intra-stride changes in electrocortical spectral power identified in this study are small, on the order of 0.5 dB (corresponding to a mean 2.5% amplitude increase). Nevertheless, the existence of significant intra-stride patterns of activation and deactivation suggests that the human cortex is actively engaged during steady-speed locomotion. Given that corticospinal excitability is modulated during the human gait cycle (Capaday et al., 1999; Petersen et al., 2001; Schubert et al., 1997) it is likely that direct corticospinal pathways contribute to locomotor execution. This hypothesis is also supported by a recent PET study of imagined and real walking (la Fougere et al., 2010). However, tonic descending inputs to spinal networks from the mesencephalic locomotor region of the brainstem can also generate rhythmic muscle activation and may be modulated by afferent sensory signals processed in the cortex (Rossignol et al., 2006). In an *in-vitro* isolated lamprey brainstem the mesencephalic locomotor region has recently been shown to modulate sensory transmission (Le Ray et al., 2010) and rhythmic motor task have been shown to active the sensorimotor cortex even when performed passively (Christensen et al., 2000). Given these prior results, our finding of intra-stride cortical spectral power fluctuations in humans, while novel, is not entirely surprising. Furthermore, our finding does not indicate whether human cortex is actively involved in controlling locomotion via direct pathways or whether human cortex processes sensory afferents that are used to modulate a descending signal to spinal generators via the mesencephalic locomotor region. We expect that human cortex in fact performs both of these functions. Studying walking under challenging conditions, with either increased or decreased sensory demands or availability, may provide a means of further testing these hypotheses. It may be easier to discern the precise nature of attended sensory events during challenging walking conditions than during normal locomotion. For example, close examination of these data revealed no relationship between the timing of intra-stride power increases and step-to-step changes in step duration for any of the clusters of electrocortical sources. We expect that 1) walking through more complex environments with obstacles and varied terrain requires more input from supraspinal centers than steady-speed treadmill walking, and 2) steady-speed treadmill walking on a flat consistent surface should demand less cortical control and adjustment, indexed by less within-stride variation in high-frequency EEG source activity. However, our data suggest that even under steady-speed walking conditions the cortex shows moment-to-moment adjustments in activity tone. The locations of the electrocortical sources that were active during walking are mostly consistent with results of prior studies using fNIRS and PET. Unlike recent PET results (la Fougere et al., 2010), but as expected for scalp EEG data, we did not detect EEG source activity in parahippocampal or cerebellar regions.

In a clinical setting, the ability to quantify brain activation patterns during gait in neurologically impaired patients could be helpful as it might allow clinicians to better diagnose subsets of patients with similar EEG symptomatology (Alexander et al., 2009; Boyd et al., 2007). Most behavioral variables of motor performance (e.g. over-ground preferred walking speed) have large inter-subject and intra-subject variability, making them coarse measures of motor learning and neural plasticity. Even when behavioral measures are robust enough to test the efficacy of therapeutic interventions, methods to quantify brain plasticity (versus spinal plasticity or muscle plasticity) are needed for studying the underlying mechanisms of motor recovery (Gorassini et al., 2009; Norton and Gorassini, 2006; Yang and Gorassini, 2006). Spatially resolved EEG measures might help clinicians choose rehabilitation strategies with a better chance of success and might also allow researchers and clinicians to track brain plasticity during interventions to gauge the success of an intervention (Boyd et al., 2007; Mielke and Szelies, 2003; Weiller, 1998; Yang and Gorassini, 2006). Another potential use of the technique presented here would be to identify neural mechanisms of freezing gait in Parkinson's patients.

In closing, our study suggests that high-density EEG recorded simultaneously with body motion capture during ambulation and then spatially resolved using independent component analysis can provide insight into the cortical contributions to locomotor control and might provide useful information regarding brain activation supporting gait in clinical settings.

Acknowledgments

We would like to thank Evelyn Anaka, Amy Sipp, and Sarah Weiss for their help during data collection. This work was supported by a grant from the Office of Naval Research (N000140811215), a gift from The Swartz Foundation (Old Field, NY), and an Air Force Office of Scientific Research (AFOSR) National Defense Science and Engineering Graduate (NDSEG) Fellowship, 32 CFR 168a.

References

Alexander, L.D., Black, S.E., Patterson, K.K., Gao, F.Q., Danells, C.J., McIlroy, W.E., 2009. Association between gait asymmetry and brain lesion location in stroke patients. Stroke 40, 537–544.

Andujar, J.E., Lajoie, K., Drew, T., 2010. A contribution of area 5 of the posterior parietal cortex to the planning of visually guided locomotion: limb-specific and limb-independent effects. J. Neurophysiol. 103, 986–1006.

Armstrong, D.M., MarpleHorvat, D.E., 1996. Role of the cerebellum and motor cortex in the regulation of visually controlled locomotion. Can. J. Physiol. Pharmacol. 74, 443–455.

Barthelemy, D., Nielsen, J.B., 2010. Corticospinal contribution to arm muscle activity during human walking. J. Physiol. Lond. 588, 967–979.

Bell, A.J., Sejnowski, T.J., 1995. An information-maximization approach to blind separation and blind deconvolution. Neural Comput. 7, 1129–1159.

Beloozerova, I.N., Sirota, M.G., 2003. Integration of motor and visual information in the parietal area 5 during locomotion. J. Neurophysiol. 90, 961–971.

Boyd, L.A., Vidoni, E.D., Daly, J.J., 2007. Answering the call: the influence of neuroimaging and electrophysiological evidence on rehabilitation. Phys. Ther. 87, 684–703.

Bush, G., Luu, P., Posner, M.I., 2000. Cognitive and emotional influences in anterior cingulate cortex. Trends Cogn. Sci. 4, 215–222.

Capaday, C., Lavoie, B.A., Barbeau, H., Schneider, C., Bonnard, M., 1999. Studies on the corticospinal control of human walking: I. Responses to focal transcranial magnetic stimulation of the motor cortex. J. Neurophysiol. 81, 129–139.

Christensen, L.O.D., Johannsen, P., Sinkjaer, T., Petersen, N., Pyndt, H.S., Nielsen, J.B., 2000. Cerebral activation during bicycle movements in man. Exp. Brain Res. 135, 66–72.

Christensen, L.O.D., Andersen, J.B., Sinkjaeer, T., Nielsen, J., 2001. Transcranial magnetic stimulation and stretch reflexes in the tibialis anterior muscle during human walking. J. Physiol. Lond. 531, 545–557.

Collins, S.H., Adamczyk, P.G., Ferris, D.P., Kuo, A.D., 2009. A simple method for calibrating force plates and force treadmills using an instrumented pole. Gait Posture 29, 59–64.

Cromwell, R.L., Aadland-Monahan, T.K., Nelson, A.T., Stern-Sylvestre, S.M., Seder, B., 2001. Sagittal plane analysis of head, neck, and trunk kinematics and electromyographic activity during locomotion. J. Orthop. Sports Phys. Ther. 31, 255–262.

Daly, J.J., Wolpaw, J.R., 2008. Brain–computer interfaces in neurological rehabilitation. Lancet Neurol. 7, 1032–1043.

Delorme, A., Makeig, S., 2004. EEGLAB: an open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. J. Neurosci. Meth. 134, 9–21.

Delorme, A., Sejnowski, T., Makeig, S., 2007. Enhanced detection of artifacts in EEG data using higher-order statistics and independent component analysis. Neuroimage 34, 1443–1449.

Dietz, V., 2003. Spinal cord pattern generators for locomotion. Clin. Neurophysiol. 114, 1379–1389.
Dietz, V., Duysens, J., 2000. Significance of load receptor input during locomotion: a review. Gait Posture 11, 102–110.
Dietz, V., Colombo, G., Jensen, L., Baumgartner, L., 1995. Locomotor capacity of spinal cord in paraplegic patients. Ann. Neurol. 37, 574–582.
Dimitrijevic, M.R., Gerasimenko, Y., Pinter, M.M., 1998. Evidence for a spinal central pattern generator in humans. Ann. NY Acad. Sci. 860, 360–376.
Dobkin, B.H., Firestine, A., West, M., Saremi, K., Woods, R., 2004. Ankle dorsiflexion as an fMRI paradigm to assay motor control for walking during rehabilitation. Neuroimage 23, 370–381.
Drew, T., 1993. Motor cortical activity during voluntary gait modifications in the cat: 1. Cells related to the forelimbs. J. Neurophysiol. 70, 179–199.
Drew, T., Jiang, W., Widajewicz, W., 2002. Contributions of the motor cortex to the control of the hindlimbs during locomotion in the cat. Brain Res. Rev. 40, 178–191.
Drew, T., Prentice, S., Schepens, B., 2004. Cortical and brainstem control of locomotion. Prog. Brain Res. 143, 251–261.
Ferris, D.P., Gordon, K.E., Beres-Jones, J.A., Harkema, S.J., 2004. Muscle activation during unilateral stepping occurs in the nonstepping limb of humans with clinically complete spinal cord injury. Spinal Cord 42, 14–23.
Filimon, F., Nelson, J.D., Huang, R.S., Sereno, M.I., 2009. Multiple parietal reach regions in humans: cortical representations for visual and proprioceptive feedback during on-line reaching. J. Neurosci. 29, 2961–2971.
Fitzsimmons, N.A., Lebedev, M.A., Peikon, I.D., Nicolelis, M.A., 2009. Extracting kinematic parameters for monkey bipedal walking from cortical neuronal ensemble activity. Front. Integr. Neurosci. 3, 3.
Fong, A.J., Roy, R.R., Ichiyama, R.M., Lavrov, I., Courtine, G., Gerasimenko, Y., Tai, Y.C., Burdick, J., Edgerton, V.R., 2009. Recovery of control of posture and locomotion after a spinal cord injury: solutions staring us in the face. Prog. Brain Res. 175, 393–418.
Gorassini, M.A., Norton, J.A., Nevett-Duchcherer, J., Roy, F.D., Yang, J.F., 2009. Changes in locomotor muscle activity after treadmill training in subjects with incomplete spinal cord injury. J. Neurophysiol. 101, 969–979.
Gramann, K., Onton, J., Riccobon, D., Mueller, H.J., Bardins, S., Makeig, S., 2009. Human brain dynamics accompanying use of egocentric and allocentric reference frames during navigation. J. Cogn. Neurosci. 22, 2836–2849.
Grillner, S., 1985. Neurobiological bases of rhythmic motor acts in vertebrates. Science 228, 143–149.
Grillner, S., Wallen, P., Saitoh, K., Kozlov, A., Robertson, B., 2008. Neural bases of goal-directed locomotion in vertebrates—an overview. Brain Res. Rev. 57, 2–12.
Gwin, J.T., Gramann, K., Makeig, S., Ferris, D.P., 2010. Removal of movement artifact from high-density EEG recorded during walking and running. J. Neurophysiol. 103, 3526–3534.
Hansen, N.L., Nielsen, J.B., 2004. The effect of transcranial magnetic stimulation and peripheral nerve stimulation on corticomuscular coherence in humans. J. Physiol. Lond. 561, 295–306.
Harada, T., Miyai, I., Suzuki, M., Kubota, K., 2009. Gait capacity affects cortical activation patterns related to speed control in the elderly. Exp. Brain Res. 193, 445–454.
Heuninckx, S., Wenderoth, N., Debaere, F., Peeters, R., Swinnen, S.P., 2005. Neural basis of aging: the penetration of cognition into action control. J. Neurosci. 25, 6787–6796.
Heuninckx, S., Wenderoth, N., Swinnen, S.P., 2008. Systems neuroplasticity in the aging brain: recruiting additional neural resources for successful motor performance in elderly persons. J. Neurosci. 28, 91–99.
Jung, T.P., Makeig, S., Humphries, C., Lee, T.W., McKeown, M.J., Iragui, V., Sejnowski, T.J., 2000a. Removing electroencephalographic artifacts by blind source separation. Psychophysiology 37, 163–178.
Jung, T.P., Makeig, S., Westerfield, M., Townsend, J., Courchesne, E., Sejnowski, T.J., 2000b. Removal of eye activity artifacts from visual event-related potentials in normal and clinical subjects. Clin. Neurophysiol. 111, 1745–1758.
Jung, T.P., Makeig, S., Westerfield, M., Townsend, J., Courchesne, E., Sejnowski, T.J., 2001. Analysis and visualization of single-trial event-related potentials. Hum. Brain Mapp. 14, 166–185.
Kuo, A.D., Donelan, J.M., Ruina, A., 2005. Energetic consequences of walking like an inverted pendulum: step-to-step transitions. Exerc. Sport Sci. Rev. 33, 88–97.
la Fougere, C., Zwergal, A., Rominger, A., Forster, S., Fesl, G., Dieterich, M., Brandt, T., Strupp, M., Bartenstein, P., Jahn, K., 2010. Real versus imagined locomotion: a [18F]-FDG PET-fMRI comparison. Neuroimage 50, 1589–1598.
Lajoie, K., Andujar, J.E., Pearson, K., Drew, T., 2010. Neurons in area 5 of the posterior parietal cortex in the cat contribute to interlimb coordination during visually guided locomotion: a role in working memory. J. Neurophysiol. 103, 2234–2254.
Le Ray, D., Juvin, L., Boutin, T., Auclair, F., Dubuc, R., 2010. A neuronal substrate for a state-dependent modulation of sensory inputs in the brainstem. Eur. J. Neurosci. 32, 53–59.
Lee, T.W., Girolami, M., Sejnowski, T.J., 1999a. Independent component analysis using an extended infomax algorithm for mixed subgaussian and supergaussian sources. Neural Comput. 11, 417–441.
Lee, T.W., Lewicki, M.S., Girolami, M., Sejnowski, T.J., 1999b. Blind source separation of more sources than mixtures using overcomplete representations. IEEE Signal Process. Lett. 6, 87–90.
Lewicki, M.S., Sejnowski, T.J., 2000. Learning overcomplete representations. Neural Comput. 12, 337–365.
Luft, A.R., Smith, G.V., Forrester, L., Whitall, J., Macko, R.F., Hauser, T.K., Goldberg, A. P., Hanley, D.F., 2002. Comparing brain activation associated with isolated upper and lower limb movement across corresponding joints. Hum. Brain Mapp. 17, 131–140.
Makeig, S., 1993. Auditory event-related dynamics of the EEG spectrum and effects of exposure to tones. Electroencephalogr. Clin. Neurophysiol. 86, 283–293.
Makeig, S., Bell, A.J., Jung, T.P., Sejnowski, T.J., 1996. Independent component analysis of electroencephalographic data. Adv. Neural Inf. Process. Syst. 8, 145–151.
Makeig, S., Onton, J., Sejnowski, T., Poizner, H., 2007. Prospects for mobile, high-definition brain imaging: spectral modulations during 3-D reaching. Hum. Brain Mapp. Chicago, IL.
Makeig, S., Gramann, K., Jung, T.P., Sejnowski, T.J., Poizner, H., 2009. Linking brain, mind and behavior. Int. J. Psychophysiol. 73, 95–100.
Mielke, R., Szelies, B., 2003. Neuronal plasticity in poststroke aphasia: insights by quantitative electroencephalography. Expert Rev. Neurother. 3, 373–380.
Miyai, I., Tanabe, H.C., Sase, I., Eda, H., Oda, I., Konishi, I., Tsunazawa, Y., Suzuki, T., Yanagida, T., Kubota, K., 2001. Cortical mapping of gait in humans: a near-infrared spectroscopic topography study. Neuroimage 14, 1186–1192.
Nielsen, J.B., 2003. How we walk: central control of muscle activity during human walking. Neuroscientist 9, 195–204.
Norton, J.A., Gorassini, M.A., 2006. Changes in cortically related intermuscular coherence accompanying improvements in locomotor skills in incomplete spinal cord injury. J. Neurophysiol. 95, 2580–2589.
O'Connell, R.G., Dockree, P.M., Bellgrove, M.A., Kelly, S.P., Hester, R., Garavan, H., Robertson, I.H., Foxe, J.J., 2007. The role of cingulate cortex in the detection of errors with and without awareness: a high-density electrical mapping study. Eur. J. Neurosci. 25, 2571–2579.
Omlor, W., Patino, L., Hepp-Reymond, M.C., Kristeva, R., 2007. Gamma-range corticomuscular coherence during dynamic force output. Neuroimage 34, 1191–1198.
Onton, J., Makeig, S., 2009. High-frequency broadband modulations of electroencephalographic spectra. Front. Hum. Neurosci. 3, 61.
Onton, J., Westerfield, M., Townsend, J., Makeig, S., 2006. Imaging human EEG dynamics using independent component analysis. Neurosci. Biobehav. Rev. 30, 808–822.
Oostenveld, R., Oostendorp, T.F., 2002. Validating the boundary element method for forward and inverse EEG computations in the presence of a hole in the skull. Hum. Brain Mapp. 17, 179–192.
Palmer, J.A., Kreutz-Delgado, K., Makeig, S., 2006. Super-Gaussian mixture source model for ICA. In: Rosca, J., Erdogmus, D., Principe, J.C., Haykin, S. (Eds.), Lecture Notes in Computer Science. Springer, Berlin, pp. 854–861.
Palmer, J.A., Makeig, S., Kreutz-Delgado, K., Rao, B.D., 2008. Newton method for the ICA mixture model. 33rd IEEE International Conference on Acoustics and Signal Processing, Las Vegas, Nevada, pp. 1805–1808.
Petersen, N.T., Butler, J.E., Marchand-Pauvert, V., Fisher, R., Ledebt, A., Pyndt, H.S., Hansen, N.L., Nielsen, J.B., 2001. Suppression of EMG activity by transcranial magnetic stimulation in human subjects during walking. J. Physiol. 537, 651–656.
Pfurtscheller, G., Stancak Jr., A., Neuper, C., 1996. Event-related synchronization (ERS) in the alpha band—an electrophysiological correlate of cortical idling: a review. Int. J. Psychophysiol. 24, 39–46.
Raethjen, J., Govindan, R.B., Binder, S., Zeuner, K.E., Deuschl, G., Stolze, H., 2008. Cortical representation of rhythmic foot movements. Brain Res. 1236, 79–84.
Ray, S., Niebur, E., Hsiao, S.S., Sinai, A., Crone, N.E., 2008. High-frequency gamma activity (80–150 Hz) is increased in human cortex during selective attention. Clin. Neurophysiol. 119, 116–133.
Rossignol, S., 2000. Locomotion and its recovery after spinal injury. Curr. Opin. Neurobiol. 10, 708–716.
Rossignol, S., Dubuc, R.J., Gossard, J.P., 2006. Dynamic sensorimotor interactions in locomotion. Physiol. Rev. 86, 89–154.
Sahyoun, C., Floyer-Lea, A., Johansen-Berg, H., Matthews, P.M., 2004. Towards an understanding of gait control: brain activation during the anticipation, preparation and execution of foot movements. Neuroimage 21, 568–575.
Schroeder, C.E., Lakatos, P., 2009. Low-frequency neuronal oscillations as instruments of sensory selection. Trends Neurosci. 32, 9–18.
Schubert, M., Curt, A., Jensen, L., Dietz, V., 1997. Corticospinal input in human gait: modulation of magnetically evoked motor responses. Exp. Brain Res. 115, 234–246.
Schubert, M., Curt, A., Colombo, G., Berger, W., Dietz, V., 1999. Voluntary control of human gait: conditioning of magnetically evoked motor responses in a precision stepping task. Exp. Brain Res. 126, 583–588.
Serrien, D.J., Ivry, R.B., Swinnen, S.P., 2006. Dynamics of hemispheric specialization and integration in the context of motor control. Nat. Rev. Neurosci. 7, 160–166.
Shik, M.L., Orlovsky, G.N., 1976. Neurophysiology of locomotor automatism. Physiol. Rev. 56, 465–501.
Stanhope, S.J., Kepple, T.M., McGuire, D.A., Roman, N.L., 1990. Kinematic-based technique for event time determination during gait. Med. Biol. Eng. Comput. 28, 355–360.
Suzuki, M., Miyai, I., Ono, T., Oda, I., Konishi, I., Kochiyama, T., Kubota, K., 2004. Prefrontal and premotor cortices are involved in adapting walking and running speed on the treadmill: an optical imaging study. Neuroimage 23, 1020–1026.
Suzuki, M., Miyai, I., Ono, T., Kubota, K., 2008. Activities in the frontal cortex and gait performance are modulated by preparation. An fNIRS study. Neuroimage 39, 600–607.
Walton, M.E., Croxson, P.L., Behrens, T.E.J., Kennerley, S.W., Rushworth, M.F.S., 2007. Adaptive decision making and value in the anterior cingulate cortex. Neuroimage 36, T142–T154.
Weiller, C., 1998. Imaging recovery from stroke. Exp. Brain Res. 123, 13–17.
Wenderoth, N., Debaere, F., Sunaert, S., Swinnen, S.P., 2005. The role of anterior cingulate cortex and precuneus in the coordination of motor behaviour. Eur. J. Neurosci. 22, 235–246.

Widajewicz, W., Kably, B., Drew, T., 1994. Motor cortical activity during voluntary gait modifications in the cat: 2. Cells related to the hindlimbs. J. Neurophysiol. 72, 2070–2089.
Wieser, M., Haefeli, J., Butler, L., Jancke, L., Riener, R., Koeneke, S., 2010. Temporal and spatial patterns of cortical activation during assisted lower limb movement. Exp. Brain Res. 203, 181–191.
Wirz, M., Colombo, G., Dietz, V., 2001. Long term effects of locomotor training in spinal humans. J. Neurol. Neurosurg. Psychiatry 71, 93–96.
Woollacott, M., Shumway-Cook, A., 2002. Attention and the control of posture and gait: a review of an emerging area of research. Gait Posture 16, 1–14.
Yang, J.F., Gorassini, M., 2006. Spinal and brain control of human walking: implications for retraining of walking. Neuroscientist 12, 379–389.