Unilateral Walking Surface Stiffness Perturbations Evoke Brain Responses: Toward Bilaterally Informed Robot-assisted Gait Rehabilitation

Jeffrey Skidmore and Panagiotis Artemiadis*

Abstract—Gait impairment due to neurological disorders has become an important problem of the 21st century. Stroke is a leading cause of long-term disability with approximately 90% of stroke survivors having some functional disability, with mobility being a major impairment. Despite the growing interest in using robotic devices for rehabilitation of sensorimotor function, their widespread use remains somewhat limited, as results so far in gait rehabilitation do not generally show improved outcomes over traditional treadmill-based therapy. This work focuses on understanding the mechanisms of inter-leg coordination, and based on that, proposing novel methods for gait rehabilitation. Using a novel robotic device, the Variable Stiffness Treadmill (VST), we apply walking surface stiffness perturbations to one leg, and analyze the response of the human nervous system in both low- (muscle) and high- (brain) levels, focusing on the mechanisms involved in the response of the other (unperturbed) leg. We show that the unperturbed leg uniquely responds to unilateral stiffness perturbations, while we provide solid evidence that the brain is involved in this observed inter-leg coordination. From a clinical prospective, the results of this study can be disruptive since they suggest that supraspinal neural activity can be evoked by altering the stiffness of the walking surface. Moreover, our methods provide a safe and targeted way to provide gait rehabilitation in hemiparesis since direct manipulation of the paretic side is not required. The present work provides for the first time evidence that specific robotic intervention in gait rehabilitation can have direct and predictable effects on the brain, opening a new avenue of research on targeted robot-assisted gait rehabilitation.

I. INTRODUCTION

Gait impairment due to neurological disorders has become an important problem of the 21st century. Stroke is a leading cause of long-term disability with approximately 90% of stroke survivors having some functional disability, with mobility being a major impairment. Despite the growing interest in using robotic devices for rehabilitation of sensorimotor function, their widespread use remains somewhat limited by a number of factors, including the assessment of the true cost-to-benefit ratio relative to other types of rehabilitation approaches and parameters that would optimize their long-term efficacy.

Body-weight-supported treadmill has been widely used and standardized for rehabilitation of patients with gait impairments [1], [2]. The advantages of using a treadmill in such cases include adequate mobility of the walker, partial body-weight support, as well as controlled experimental environment equipped with many monitoring devices. However, most of the currently used methods consider gait as a kinematic process. Based on this, the state of the art devices for gait rehabilitation impose gait kinematics on the impaired legs using either hard or soft means, ranging from kinematically controlled exoskeletons [3] to impedance controlled orthotic devices [4], [5].

The assist-as-needed approach has been applied as a control strategy for robot-assisted walking rehabilitation in order to adapt the robotic device to varying gait patterns and levels of support by means of implementing control of mechanical impedance. Zero-impedance control mode has been proposed to allow free movement of the limb segments, referred to as “path control”, implemented to the Lokomat orthosis [6]. The concept of a “virtual tunnel” that allows a range of free movement has been evaluated with stroke patients in the lower limb exoskeleton ALEX [7]. A treadmill-based robotized therapy has been also proposed using the Gait Trainer [2]. However, according to recent studies, there is moderate evidence of improvement in walking and motor recovery using robotic devices, including systems for body-weight supported treadmill training (BWSTT), when compared to conventional therapy [8]–[10].

What previous methods fail to take advantage of is that locomotion can be mainly characterized as a dynamical process that involves inter-leg coordination and sensory feedback mechanisms from the environment. More specifically, locomotion results from intricate dynamic interactions between a central program, the plant (body) dynamics and feedback mechanisms. The central program relies fundamentally on a genetically determined spinal circuit capable of generating the basic locomotion pattern [11], and on various descending pathways that can trigger, stop and steer locomotion. Recent work has stressed the importance of peripheral sensory information [12] and descending inputs from motor cortex [13] in shaping the Central Pattern Generator function and particularly in guiding post-lesional plasticity mechanisms. In fact it has been shown that for over-ground walking, a spinal pattern generator does not appear to be sufficient. Supraspinal control is needed to provide both the drive for locomotion as well as the coordination to negotiate a complex environment [14], [15]. The latter is further supported by neuroimaging studies showing that rhythmic leg movements recruit the primary motor cortex [16], [17]. Therefore, the role of supraspinal (brain) mechanisms in
inter-limb coordination and gait in general has to be taken advantage of when designing robot-assisted rehabilitation protocols.

This paper presents an original robot-assisted effort in understanding inter-limb coordination in both low- (muscle) and high- (brain) levels, toward defining novel methods for gait rehabilitation. The analysis is performed using experimental protocols employing a unique robotic device, the Variable Stiffness Treadmill (VST). The VST can interactively change the walking surface stiffness of each side of a split-treadmill, and therefore investigate inter-limb coupling in a unique, safe, and repeatable way. In previous works we have shown that unilateral stiffness perturbations evoke contralateral muscle activations [18]–[20]. This paper focuses on the supraspinal level (brain), and the effect of the unilateral stiffness perturbations on that level. By employing EEG recordings in conjunction with EMG and leg kinematic analysis, we show for the first time robust and repeatable evoked activations on the brain, originating from the unilateral stiffness perturbations. Using our fully integrated experimental setup we correlate evoked brain activity with contralateral leg muscle activations evoked by unilateral stiffness changes. The latter provide original and strong evidence of the role of supraspinal circuits (brain) in inter-limb coordination. Moreover, the fact that our stiffness perturbations evoke activity in the brain provides strong evidence that our methods can be used for gait rehabilitation of stroke survivors.

The rest of the paper is organized as follows: Section II describes the experimental setup and protocol used for this study, Section III presents the effect of unilateral stiffness perturbations on the brain and muscle activation of the contralateral leg for healthy subjects. Section IV discusses the implications of the results and possible medical applications. Finally, section V concludes the paper with a brief summary of the contribution.

II. METHODS

A. Experimental Setup

In order to investigate the existence of supraspinal mechanisms of inter-leg coordination during human walking, unilateral stiffness perturbations were induced using the Variable Stiffness Treadmill (VST) system shown in Fig. 1. The system has been detailed in previous work [18], [19] and will not be described in this paper for brevity.

B. Experimental Protocol

Two healthy subjects [Subject 1: age 20 years, weight 130 lbs, height 70 in; Subject 2: age 25 years, weight 175 lbs, height 75 in] were supported by 30% BWS and walked on the treadmill at a speed of 0.60 m/s for at least 320 gait cycles. A speed of 0.60 m/s was chosen for comparison with previous work [20] and because gait therapy is usually conducted at slower speeds than normal walking speeds for healthy individuals. A value of 30% BWS was chosen for comparison with other studies that have used 30% BWS [20]–[22], and because this level of support minimizes vestibular input and mechanisms related to body balance and posture as seen in previous studies [23]. Since the goal of this experiment is to investigate interleg coordination, the right treadmill belt was not allowed to deflect for the duration of the experiment, thus preventing any direct perturbation of the right leg. The surface underneath the left leg was commanded to maintain a stiffness of 1 MN/m, which is very high and considered to be rigid, for 30 gait cycles at the beginning of the experiment. Then, after a random number n of steps, where n ∈ [4, 7], we immediately dropped the stiffness to a constant value of 60 kN/m. A stiffness level of 60 kN/m was chosen because it resembles that of a gym mat [24] and for comparison with previous work [20]. The low stiffness perturbation began shortly after heel strike (approx. 125 ms) and lasted for the duration of the left leg stance phase (ie. until toe-off) after which the stiffness was commanded back to 1 MN/m for the next n number of steps. A graphical representation of the timing of the stiffness perturbation is included at the bottom of Fig. 3. Each subject experienced 50 low stiffness perturbations. Informed consent from the subject was obtained at the time of the experiment, and the experimental protocol is approved by the Arizona State University Institutional Review Board (IRB ID#: STUDY00001001).

C. Data Collection and Processing

1) Kinematics: Kinematic data for both legs were obtained at 140 Hz using an infrared camera system that tracked 12 (6 on each leg) infrared LEDs placed as pairs on the thigh, shank, and foot. This data was also utilized in real time for timing of the stiffness perturbation.

2) Electromyography: The muscle activity of the unperturbed leg was obtained using surface electromyography (EMG) via a wireless surface EMG system (Delsys, Trigno Wireless EMG) and recorded at 2000 Hz. Electrodes were placed on the tibialis anterior (TA), gastrocnemius (GA) and soleus (SOL) of the right leg. After computing the EMG linear envelope, the data were normalized to the maximum value of that EMG signal. The EMG data corresponding to the gait cycles of walking on the rigid surface and the cycles pertaining to the low stiffness perturbations were found and categorized accordingly. Because muscle activity during walking is highly dependent on the phase of the gait cycle, the data were normalized temporally to percent gait cycle. The first 30 gait cycles and the cycles in between perturbations at rigid stiffness (except for one cycle following a perturbation to eliminate any residual effects from the perturbation) are included in the unperturbed data set. The normalized EMG signals were then resampled at the average duration of the gait cycle in order to plot the EMG activity over time, where time = 0 corresponds to the heel strike of the left leg.

3) Electroencephalography: The brain activity during the experiment was monitored using electroencephalography (EEG). The EEG data were collected using a BrainProducts ActiCHamp amplifier module and 128 active electrodes, as shown in Fig. 1. The electrodes were placed on the
subjects scalps based on the International 10-20 system using a BrainProducts ActiCAP cap. The data were recorded at 1000 Hz. The processing of the EEG data was done using the EEGLAB [25] and ERPLAB [26] packages which are available for the Matlab environment. First, a 6th order high-pass Butterworth filter at 1 Hz followed by a 6th order low-pass Butterworth filter at 40 Hz were applied to the data in order to remove any low frequency trends and high frequency noise, respectively. The filtered data were then re-referenced at average reference and epoched at 500 ms before and 1.2 s after the left heel-strike. Finally, channels and epochs that contained artifacts were removed from the data set. This was done using standard artifact rejection techniques implemented in EEGLAB that include detection of extremely large fluctuations in voltage levels, abnormal trends, improbable data and abnormal distributions. The corresponding results are presented in the next section where statistical significance between the perturbed and unperturbed data sets is calculated at the 95% confidence level using an independent t-test.

### III. RESULTS

The results of the experiment show significant changes in EEG activity, as well as the kinematics and muscle activity of the right leg, in response to the low stiffness perturbations on the left leg. Since the changes in contralateral kinematics and muscle activity have been discussed in previous works [20], [27], and the focus of this work is to understand supraspinal influences in inter-leg coordination by investigating the response of the brain to stiffness perturbations, kinematic data will not be presented and muscle activation will only be included in support of understanding supraspinal influences on inter-leg coordination. The kinematic and muscular responses recorded during this study are consistent with what would be expected from previous studies and the reader is referred to the previous works [20], [27] for the corresponding analysis. The results in this work will focus on the brain activity recorded with EEG.

Significant changes in EEG activity were seen between the event related potentials (ERPs) of the perturbed and unperturbed gait cycles throughout the data epochs. Statistically significant differences between the two cases were calculated for all channels at every 1 ms of the epoch using a two sample unpaired t-test at the 95% confidence level. Topological plots of statistical significance are shown at 25 ms intervals from -50 to 1050 ms (where \( t = 0 \) ms corresponds to left heel strike) for both subjects in Fig. 2. Significant differences are indicated in red while insignificant differences are designated by green. Other colors that are seen in the figure result from interpolation across the topology of values at the electrode locations.

As can be seen in the figure, there are time periods with little to no significant changes and but there are also noticeable regions with sustained levels of significance. Specifically, from approx. 150 to 575 ms for subject 1 and 350 to 525 ms for subject 2 there are generally sustained significant differences in the same regions of the brain. Generally speaking, these regions of activation are near the center of the brain with a bias to the left of the midline. This is the approximate location of the medial section of the primary motor and sensory cortices which lie just anterior and posterior of the central sulcus, respectively. Regions with concentrated significance and large gradients with very little activation elsewhere in the topology (ex. subject 1 at 800 ms) are also seen in the figure and are attributed to blinking artifacts and not actual brain activations.

In order to visualize the actual ERPs, the EEG potential recorded at location CP1 of the International 10-20 system (mean and standard deviation) over time under both conditions (perturbed and unperturbed) for both subjects is shown in Fig. 3. The normalized right leg TA EMG activity for both conditions and both subjects is also included for comparison between the central and peripheral neural activity.

As seen in the figure, there are statistically significant differences between the unperturbed and perturbed cases in both brain and muscle activation for both subjects. For subject 1 the EEG and EMG are significant from 200-729, 863-1083 and 291-1200 ms, respectively. For subject 2 the EEG and EMG are significant from 283-776 and 341-648 ms, respectively. Therefore, the latency from the onset of perturbation to significant changes in EEG and EMG are 71 and 162 ms, respectively, for subject 1, and 161 and 219 ms, respectively, for subject 2. The differences in onset of evoked muscle and brain activity between the two subjects results from subject 2 having a larger stride length than subject 1, and they walked at the same treadmill speed.
IV. DISCUSSION

The results presented in this paper suggest that supraspinal neural circuitry is involved in interleg coordination. This has strong potential for medical application in a novel approach to robot-assisted gait therapy for stroke patients. Discussion of the results indicating the presence of supraspinal circuits in inter-leg coordination and the potential for application in robot-assisted gait therapy will be presented below.

A. Supraspinal influences

This paper shows results for the first time that EEG activity changes during unilateral low stiffness perturbations. Our previous work [20] had shown a relatively long delay between the onset of left leg perturbation and the evoked right leg EMG activity. This latency was recorded at approximately 150 ms which suggested supraspinal involvement in inter-leg coordination. This current work shows for the first time that there is evoked brain activity that follows the perturbation and precedes contralateral leg EMG activity. More importantly, we show statistically significant changes in EEG activity for both subjects in similar regions of the brain.

The latency of response seen in previous studies (delay > 150 ms) is again seen for both subjects in the evoked TA activation shown in Fig. 3, which supports the hypothesis of supra-spinal circuitry. Furthermore, significant changes in EEG activation are seen prior to the evoked TA activity for both subjects. The latency of EEG response at location CP1 shown in Fig. 3 precedes the TA activation by 98 and 58 ms for subjects 1 and 2, respectively. Therefore, this finding provides stronger support that supraspinal mechanisms are involved in mechanisms of inter-leg coordination and participate in the evoked TA activation.

Moreover, as seen in Fig. 2, the main concentration of significant changes is seen in the medial side of the left brain near the mid-coronal plane. This is the approximate location of the medial section of the primary motor and sensory cortices which lie just anterior and posterior of the central sulcus, respectively. These areas are primarily involved in motor commands and sensory responses to and from the
right side of the body, respectively. Specifically, activations in the medial section of the primary motor cortex near the brain midline are associated with motor output in the lower limb of the right leg. Because the activation in the brain is seen before changes in muscle activity of the right leg (as described above), we conclude that the activations are associated with the motor output signal as opposed to the input sensory signal. Therefore, this provides some indication that the brain is influenced by the low stiffness stimulus to the left leg and then contributes to the evoked TA activity of the right leg.

B. Possible Medical Application

From a clinical perspective, the results of this study can be disruptive since they suggest that supraspinal neural activity can be evoked by altering the stiffness of the walking surface. Moreover, low stiffness perturbations to the ipsilateral leg evoke increased TA activation in the contralateral leg. These combined results suggest a possible novel approach to robot-assisted gait therapy for hemiparetic stroke patients, that would entail manipulation of the healthy leg through stiffness perturbations in order to provide therapy to the impaired leg.

The idea of providing therapy for stroke patients through supraspinal mechanisms of inter-leg coordination has several advantages over current rehabilitation protocols. The most significant advantage is the safety of the patient since there is no direct manipulation of the paretic leg. Moreover, other studies have stimulated the impaired TA via functional electric stimulation to improve functional outcome [28], [29], but that technique bypasses the brain which is the location of the root cause of the gait impairment created by stroke. On the other hand, the results of this work suggest the feasibility of an alternative approach to create desired contralateral TA activity by exploiting existing supraspinal neural circuits via regulation of the stiffness of the walking surface.

Moreover, a main deficiency in stroke survivors is insufficient TA activity (which is the primary muscle creating dorsiflexion) in the swing phase which results in decreased dorsiflexion (toe-up motion). Insufficient dorsiflexion during walking, referred to as drop-foot, is a problem that most impaired walkers suffer from, and is the leading cause of after-stroke falls [30]. The results presented above for healthy subjects show evoked EEG and EMG activity during swing phase (i.e., between toe-off and heel-strike) of the right leg which provides foundational indications suggesting the feasibility of a solution to drop-foot by manipulating the non-paretic leg in stroke patients through stiffness perturbations. Furthermore, stimulating the supraspinal mechanisms involved in TA activation that may have been damaged by stroke (leading to drop-foot) may induce neuroplasticity and recovery at the root cause of the drop-foot problem.

While the results of this study are for healthy subjects, there is strong potential for providing therapy through mech-
anisms of inter-leg coordination because research has shown that neural coupling exists in post-stroke patients as it does in healthy subjects [31]. In studies with post-stroke subjects with hemiparesis, it was found that neural decoupling between the lower limbs perturbs the paretic lower limb function [32]. It has been also shown that forceful interaction with the non-paretic leg elicits involuntary tension of the resting paretic leg when subjects are supine [33]. Therefore, providing therapy to the paretic leg via manipulation of the healthy leg may be a viable approach to gait rehabilitation after stroke.

V. CONCLUSIONS

This paper presented results of evoked brain activity in healthy walkers in response to unilateral low stiffness perturbations. Statistically significant changes in brain activity are seen prior to evoked muscle activity (by at least 50 ms) in the contralateral leg suggesting supraspinal influences in inter-leg coordination. Moreover, statistically significant changes in EEG activity are shown for the subjects in the medial region of the left primary motor cortex. This work provides evidence for the first time that specific robotic intervention during gait can have direct and predictable effects on the brain. These findings open a new avenue of research in targeted, bilaterally informed robot-assisted gait rehabilitation.

REFERENCES