33rd Annual International Conference of the IEEE EMBS
Boston, Massachusetts USA, August 30 - September 3, 2011

Towards a non-invasive brain-machine interface system to restore gait function in humans

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Abstract— **Before 2009, the feasibility of applying brain-machine interfaces (BMIs) to control prosthetic devices had been limited to upper limb prosthetics such as the DARPA modular prosthetic limb. Until recently, it was believed that the control of bipedal locomotion involved central pattern generators with little supraspinal control. Analysis of cortical dynamics with electroencephalography (EEG) was also prevented by the lack of analysis tools to deal with excessive signal artifacts associated with walking. Recently, Nicolelis and colleagues paved the way for the decoding of locomotion showing that chronic recordings from ensembles of cortical neurons in primary motor (M1) and primary somatosensory (S1) cortices can be used to decode bipedal kinematics in rhesus monkeys. However, neural decoding of bipedal locomotion in humans has not yet been demonstrated. This study uses non-invasive EEG signals to decode human walking in six nondisabled adults. Participants were asked to walk on a treadmill at their self-selected comfortable speed while receiving visual feedback of their lower limbs, to repeatedly avoid stepping on a strip drawn on the treadmill belt. Angular kinematics of the left and right hip, knee and ankle joints and EEG were recorded concurrently. Our results support the possibility of decoding human bipedal locomotion with EEG. The average of the correlation values (*r*) between predicted and recorded kinematics for the six subjects was 0.7 (±0.12) for the right leg and 0.66 (±0.11) for the left leg. The average signal-to-noise ratio (SNR) values for the predicted parameters were 3.36 (±1.89) dB for the right leg and 2.79 (±1.33)** dB **for the left leg. These results show the feasibility of developing non-invasive neural interfaces for volitional control of devices aimed at restoring human gait function.**

I. INTRODUCTION

In the United States, there are approximately 1.7 million people persons living with limb loss (National Limb Loss Information Center, 2008). Lower limb amputations accounted for 97% of all dysvascular limb loss discharges (133,735) from 1988-1996, and increased at a rate of 27% over this period. In addition, spinal cord injury, ALS and stroke affect locomotor capabilities and the quality of life of about 2 million people in the USA. Moreover, the socio-economic burden imposed on patients, relatives and caregivers is enormous. Therefore, restoration of gait function has been a long-standing focus of rehabilitation research worldwide. Recently, Nicolelis and colleagues have shown that primary motor cortex carries information about bipedal locomotion [1]. They demonstrated for the first time that chronic recordings from ensembles of cortical neurons in primary motor (M1) and primary somatosensory (S1) cortices can be used to predict the kinematics of bipedal walking in rhesus macaques. These results support the feasibility of BMI systems to restore locomotion. However, an important challenge of that study is its invasiveness. Electrodes implanted directly in the cortex might pose a serious risk for the patient, and may result in complications due to loss of signal integrity. Alternatively, it may be possible to use noninvasive scalp electroencephalography (EEG) to decode gait parameters in humans. Recently, our laboratory showed that the critical information needed to decode the kinematics of natural multijointed movement is available in the EEG signals in the lower frequencies (< 4 Hz) [2-4]. In light of these promising results and of the feasibility of decoding locomotion proven by Nicolelis' work, we show in this paper that EEG signals recorded from healthy subjects can be used to accurately decode kinematics extracted from lower limbs using linear neural decoders.

Manuscript received March 30, 2011. This work was supported by the University of Maryland College Park-University of Maryland-Baltimore Seed Grant Program to JLCV and LF. Support by the VA Maryland Exercise & Robotics Center of Excellence (VA RR&D B3688R) is gladly acknowledged.

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II. METHODS

A. Experimental setup and procedure

Six healthy adults aged 18-45 (3 male, 3 female) with no history of neurological disease or lower limb pathology and free of injury participated in the study after giving informed consent. The study was conducted with approved protocols from the Institutional Review Boards at the University of Maryland College Park, the University of Maryland Baltimore, and the Baltimore VA Research and Development Committee. Participants were first asked to walk on a treadmill, to establish their comfortable speed during a 5-minute familiarization period that preceded the beginning of the recordings. Next, resting eyes-open EEG was collected during a 2-minute period (baseline) of quiet standing on the treadmill. This was followed by 5-minutes of *precision walking*, when subjects were instructed to walk on the treadmill at their comfortable speed while receiving real time visual feedback (30 frames/sec) of their lower limbs and told to avoid stepping on the white stripe drawn in the treadmill's belt by using the monitor's video to keep track of foot placement relative to the white stripe. This increased the attentional demands during treadmill walking [5], a condition that can be considered to mimic walking in a novel environment or under novel conditions (e.g., after brain injury).

B. Limb movement and EEG recordings

The three-dimensional (3D) joint kinematics of the hip, knee and ankle joints were recorded using an infrared optical motion capture system (Optotrak, Northern Digital, Ontario, Canada @ 100 Hz) with foot switch data (Koningsberg Instrumentation, Pasadena, CA, @ 100 Hz). Precision manufactured 5 cm diameter disks (Innovative Sports Training, Chicago, IL), each embedded with three infrared diodes that formed an equilateral triangle (~3 cm sides), were affixed with adhesive and secured with foam wrap at the second sacral vertebra (S-2) and on the thigh, shank, and foot segments of each lower limb. A segmental model of the lower limbs was then determined by digitizing joint centers for the hip, knee and ankle joints of each limb. Gait kinematics were derived from the model using motion analysis software (Motion Monitor, Innovative Sports Training, Chicago, IL) and exported as ascii files containing time histories of the joint angular positions and joint angular velocities for the hip, knee and ankle joints of the right and left leg. Whole scalp 60-channel EEG (Neuroscan Synamps2 RT, Compumedics USA, Charlotte, NC, USA) and electro-ocular activity were recorded (sampling rate of 500 Hz; band-pass filtered from 0.1 to 100 Hz; right ear lobe (A2) was used as a reference) and time-locked with the movement kinematics using the footswitch signals.

C. Signal preprocessing

All the data analysis, decoder design and cross-validation procedures were performed off-line using custom software written in MATLAB (Mathworks Inc., Natick, MA). Twelve electrodes covering the most critical brain areas involved during locomotion were used for decoding: pre-frontal (F3, Fz, F4), motor (C3, Cz, C4), parietal (P3, Pz, P4) and occipital (O1, Oz, O2). The choice of 12 out of 60 electrodes is also due to the fact that for a real-time analysis (our ultimate goal) a small number of sensors is desirable for computational reasons. Signals from each EEG electrode were decimated by a factor of 5 (to 100 Hz), then filtered with a zero-phase, 3rd order, band-pass Butterworth filter (0.1 – 2 Hz) and normalized by subtracting their mean and dividing by their standard deviation [3]. Kinematic data were filtered with a zero-phase, 3rd order, band-pass Butterworth filter (0.1 – 3 Hz), as this frequency range accounted for 90% of the signal power.

D. Muscle and eye artifacts

It has been shown that electromyographic (EMG) and ocular artifacts do generally occur mainly at frequencies higher than 8 Hz, which is 4 times higher than our frequency cutoff of 2 Hz used for reconstruction [6]. Moreover, frontal and temporal electrodes were removed from the analysis, as those electrode sites are prone to facial EMG and eye-blinking artifacts [6]. Recently [4] showed that eye movements don't positively affect the decoding accuracy.

In order to rule out the presence of mechanical artifacts introduced by motion of the EEG cables or walking itself, we computed the phase-locking value (PLV) among sensors. The rationale was that potential motion artifacts due to EEG wires or the subject's motion would affect all sensors equally. To assess the phase-locking value using wavelet analysis, the significance threshold value was set based on the values calculated by [7]. We applied such analysis to both the baseline EEG and the walking EEG conditions. Our results suggest that mechanical artifacts did not play a role in decoding

E. Decoding method

A time-embedded (10 lags, corresponding to 100 ms in the past) linear Wiener filter [1,3,8] was independently designed, optimized, and cross-validated for each extracted gait parameter. The linear model was given by:

$$y(t) = a + \sum_{n=1}^{N}\sum_{k=0}^{L} b_{nk} S_n(t-k) + \varepsilon(t)$$

where $y(t)$ is the gait parameter measured time series representing the angular kinematics $(\phi, d\phi/dt)$, for the hip, knee and ankle joints; L and N are the number of lags and the number of electrodes, respectively; $S_n(t-k)$ is the standardized voltage measured at EEG electrode n at lag time k, a and b are weights obtained through multiple linear regression and $\varepsilon(t)$ is the residual error. The parameters of the model were calculated using the standard GLM functions in MATLAB under the Gaussian distribution using the Matlab's linear *link* function.

F. Model performance metrics

In order to assess and compare the predictive power of each decoder, a 5-fold cross validation procedure (80% training, 20% testing) was employed. The Pearson correlation coefficient (r) was calculated between the known measured signal and the predicted decoder's output as follows:

$$r(x,\hat{x}) = \frac{\mathrm{cov}(x,\hat{x})}{\sigma_x \sigma_{\hat{x}}}$$

where x is the actual measured parameter, $\hat{x}$ is the prediction of that parameter and σ_x and $\sigma_{\hat{x}}$ are the standard deviations of x and $\hat{x}$ respectively.

The SNR (signal-to-noise ratio of the decoder's output) was calculated according to [1].

$$SNR(x,\hat{x}) = 10\log_{10}\left(\frac{Var(x)}{MSE(\hat{x})}\right)$$

where the variance (Var) of the actual measured parameter (signal x) was calculated by subtracting out the mean of the signal, then squaring and averaging the amplitude. The noise or error ($\hat{x}$) was the difference between the predicted and actual measured signal. The mean squared error (MSE) was calculated by squaring the difference, then averaging to get the MSE, or the power of the noise. The ratio between $Var(x)$ and $MSE(\hat{x})$ was converted into a decibel (dB) scale. A *SNR* with a value of "0" means that the signal and the noise are equally present in the reconstructed kinematic parameter. A $SNR < 0$ (poor prediction) indicates a noisy reconstruction, while a $SNR > 0$ (good prediction) indicates a high-quality reconstruction of the signal.

G. Sensor dropping analysis

A sensor dropping analysis (SDA) was used to evaluate the importance of groups of sensors of different sizes to decoding accuracy (e.g., [1,8]). First, decoder models were trained by using each lag of each sensor (one lag at a time) with the above mentioned 5-fold cross validation procedure. Sensors were ranked based on the maximum value of the correlations calculated at each lag.

III. Results

Our EEG decoding method was able to reconstruct 3D angular kinematics of the ankle, knee and hip joints with high accuracy. In order to quantify the level of accuracy, we computed the Pearson's *r* and the *SNR* between measured and predicted joint angles and angular velocities across

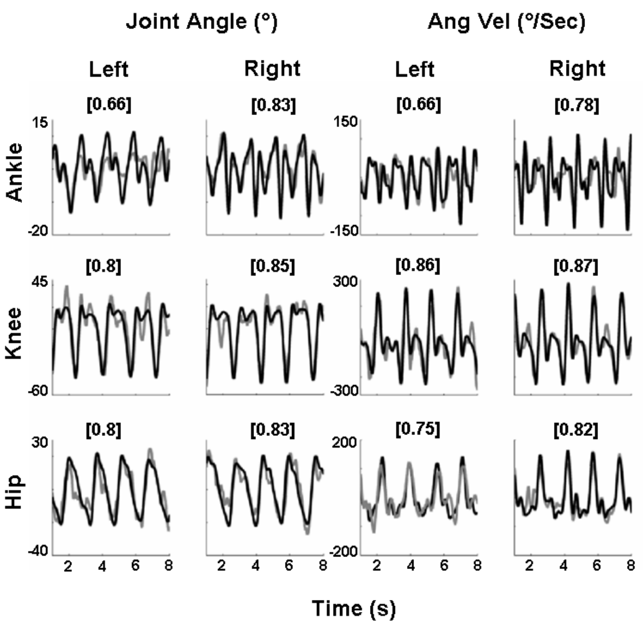

Fig. 1. Reconstructed left and right leg kinematics from EEG for the 'best' (S4) decoded subject. Rows represent ankle, knee and hip joints. Each column represents comparison of reconstructed (gray) and actual (black) measured kinematic trajectories for joint angle and angular velocity time series. R values are reported between square brackets.

cross-validation folds. SNR proved to be a more sensitive measure compared to *r*, which describes the correspondence of signal waveforms, but is insensitive to amplitude scaling and offsets. The averages of the correlation values (*r*) and signal-to-noise ratio (SNR) of the right and left legs for each subject were: S1 ($r_{right} = 0.6 \pm 0.11$, $SNR_{right} = 2.21 \pm 1.02$; $r_{left} = 0.55 \pm 0.12$, $SNR_{left} = 1.73 \pm 0.9$), S2 ($r_{right} = 0.75 \pm 0.1$, $SNR_{right} = 4.1 \pm 1.82$; $r_{left} = 0.69 \pm 0.06$, $SNR_{left} = 3 \pm 0.77$), S3 ($r_{right} = 0.61 \pm 0.05$, $SNR_{right} = 2.08 \pm 0.47$; $r_{left} = 0.59 \pm 0.04$, $SNR_{left} = 1.86 \pm 0.43$), S4 ($r_{right} = 0.83 \pm 0.03$, $SNR_{right} = 5.18 \pm 0.68$; $r_{left} = 0.75 \pm 0.08$, $SNR_{left} = 3.95 \pm 1.27$), S5 ($r_{right} = 0.62 \pm 0.06$, $SNR_{right} = 1.8 \pm 0.89$; $r_{left} = 0.67 \pm 0.07$, $SNR_{left} = 2.38 \pm 1.05$), S6 ($r_{right} = 0.77 \pm 0.14$, $SNR_{right} = 4.81 \pm 2.38$; $r_{left} = 0.73 \pm 0.12$, $SNR_{left} = 3.82 \pm 1.61$). The average of the *r* values between predicted and recorded kinematics across the six subjects was 0.7 (±0.12) for the right leg and 0.66 (±0.11) for the left leg. The average of the SNR values for the right leg was 3.36 (±1.89) and 2.79 (±1.33) for the left leg. Figure 1 shows examples of the measured (black) and the reconstructed (gray) kinematics for the best (S4) subject in terms of decoding accuracy.

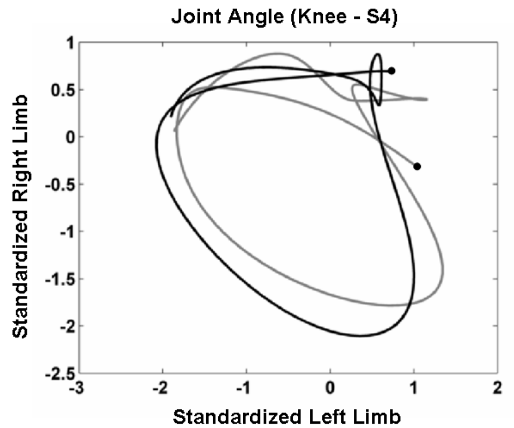

Fig. 2. Standardized predicted (gray) and actual (black) trajectories of the knee joint angle for the best subject (S4). X and Y axes represent respectively the standardized joint angle of the left and right knee. The black circles represent the starting points. The predicted trajectory has been filtered with a zero-phase, 3rd order, band-pass Butterworth filter (0.1 – 3 Hz) before being plotted for comparison to the 3Hz filtered measured data.

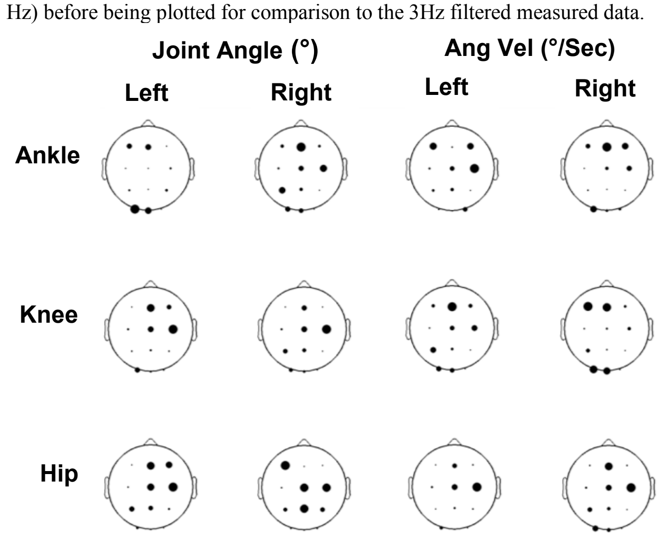

Fig. 3. Spatial distribution of r^2decoding accuracies across sensors for the best (S4) subject. Scalp maps represent the mean spatial distribution of r^2 across electrodes across all lags for each parameter resulting from the training of the linear model. The larger the circumference of each electrode, the higher its r^2value.

The quality of the reconstructions of the gait trajectories is shown in Figure 2, where an example of standardized actual and predicted angular angles, and their relative phasing, for the right and left knee for subject S4 are depicted in 2D. Figure 3 shows the spatial distribution of r^2 for the best subject.

IV. Discussion

The main result of this work is the first demonstration of the feasibility of decoding human bipedal locomotion from scalp EEG using linear decoders. Many studies using invasive and non-invasive recordings have already demonstrated the feasibility of decoding kinematic parameters such as angular velocity, joint angles from monkeys and humans [2,3,8,9,10,11,12,13] However, these techniques have been largely studied in, and applied to, upper limb function, perhaps due to the expected physiological and non-physiological artifacts during lower limb functional activities such as walking. As a consequence of this, little is known about the organization of cortical motor circuits for walking in humans [14]. Interestingly, neuroimaging studies show that rhythmic foot or leg movements recruit primary motor cortex [15], whereas electrophysiological investigations have shown electrocortical potentials related to lower limb movements [16], and greater involvement of human cortex during steady-speed normal locomotion than previously thought [17,18]. Moreover, studies using functional near-infrared spectroscopy (fNIRS) have shown involvement of frontal, premotor and supplementary motor areas during walking [19]. Recently, [17] have shown that meaningful changes during walking or running occur at low frequencies (< 10 Hz) in EEG. Encouraged by these findings, we decoded 3D joint kinematics using frequencies in the delta band (≤ 2 Hz). Our choice of input space is consistent with recent EEG, electrocorticographic (ECoG), and local field potential (LFP) upper limb movement decoding studies that use the fluctuations in the amplitude of highly smoothed signals for decoding [12,20,21]. In summary, this study demonstrates that non-invasive scalp electroencephalographic (EEG) signals can be used to decode kinematic parameters extracted during walking with high accuracy. Encouraged by promising decoding results obtained in our laboratory [2-4], we designed neural decoders by using time-domain EEG features extracted from the low-frequency delta band (0.1 – 2 Hz), the so-called slow cortical potentials. Remarkably, SNR and *r* values were comparable to the ones reported by [1], a result that, combined with observations drawn from the scalp map distribution, supports the hypothesis that the EEG signals in the low delta frequency band over a large but sparse cortical network contain decodable information that could be used to design EEG-based brain-machine interface systems for restoration of lower limb movement.

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Acknowledgement

We wish to thank Dr. Ronald Goodman for his help in collecting the data for this study.

Author Contribution

JLCV conceived the research; JLCV designed the experiment with assistance from LF; AP and LF performed the research at the VAMC; AP and JLCV designed the decoders, and analyzed the data at UMCP; AP wrote the paper; JLCV and LF edited the manuscript.