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Ankle Robotics Training with Concurrent Physiological Monitoring in Multiple Sclerosis: A Case Report

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Abstract—In this paper, we investigate the feasibility of employing robotics, high-density electroencephalography (EEG), and surface electromyography (EMG) for ankle rehabilitation in a subject with multiple sclerosis (MS). A single session of seated, interactive ankle robot ("Anklebot") training with concurrent 60-channel EEG and 2-channel EMG monitoring was conducted. The task entailed pointing with the ankle while playing a video game that synchronized ankle movements to guide a screen cursor through 560 moving gates. Practice-induced improvements in multiple motor control measures were accompanied by changes in EEG measures of activation and networking, and in EMG measures indicating greater muscle activity. Our results suggest that Anklebot training and concurrent EEG-EMG monitoring is a feasible approach that may be deployed clinically to advance understanding of the neurophysiological mechanisms in motor-learning based recovery in persons with ankle motor deficits secondary to MS and other neurologic injuries.

I. Introduction

In recent years we have investigated a novel impedance-controlled ankle robot ("Anklebot") [1] interfaced with a visually-evoked, visually-guided task as a motor learning (ML) platform, to train paretic ankle function of chronic [2] and early sub-acute [3] stroke survivors. The overarching aim of this seated joint-specific approach has been to improve ankle function with the idea that reduction of these impairments might translate to benefits in walking function. Findings from these studies showed improved paretic ankle motor control that translated to increased independent floor-walking speeds [2] and more symmetric walking [3]. In addition, we reported baseline intra-session improvements in paretic ankle motor control of participants with chronic stroke, as indexed by gains in speed, smoothness, and accuracy of unassisted targeted ankle movements. These were retained at a 48-hour retest, indicative of short-term ML [4]. In another cohort of chronic stroke survivors, electroencephalography (EEG) was used to monitor changes in cortical activity as seated Anklebot training was conducted under either high (HR) vs. low reward (LR) conditions [5]. The results supported the feasibility of integrating EEG into Anklebot therapy and showed that augmented reward (HR) fosters a more rapid ML profile that was concomitant with reduced contralesional-frontoparietal theta coherence and reduced left-temporal spectral power in the gamma bandwidth. Collectively, these findings suggest that the Anklebot is a useful ML training and testing tool and that interactive visual Anklebot training provides an effective platform for improving ankle and gait function across the spectrum of stroke. We now ask whether seated, interactive Anklebot training can elicit similar benefits in people with other neurologic deficits that impair lower extremity (LE) motor control and function.

One candidate population is multiple sclerosis (MS), a chronic demyelinating disease of the brain and spinal cord that frequently causes LE spasticity and weakness at the ankle. These impairments often result in foot drop and other derangements of gait patterning (e.g., "scissor"-type asymmetric walking). To our knowledge only two studies have employed the Anklebot in MS; as a clinical measurement instrument to characterize ankle impairment i.e., static ankle impedance [6] and for seated, interactive therapy for 6 week (2xweekly, 12 sessions) [7]. The latter study reported significant benefits in volitional ankle torque generation and in the accuracy of unassisted ankle targeting [7], improvements that carried over to gains in walking function (10-m timed walks). What remains unclear is whether those functional changes were accompanied by changes in brain and muscle measures, and whether a single bout of progressive Anklebot regimen can elicit gains in key indices of motor control beyond movement accuracy alone. Hence, the purpose of this case report was to determine in a subject with MS: (1) the feasibility of acquiring physiological measures (EEG, EMG) during seated, interactive Anklebot training, (2) whether a single session of training leads to improvements in ankle motor control, and (3) if any changes in volitional ankle motor performance are

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concordant with changes in physiological measures. While recognizing the distinct mechanisms (e.g., brain insult versus demyelination) and functional (e.g., unilateral versus bilateral) differences underlying these conditions, and the notion that the effects of Anklebot training may differ, yet this type of therapy may positively impact the quality of life in MS. Hence, this case study will constitute a 1st but important step toward the design of individualized Anklebot interventions aimed at improving ankle motor control and function in neurologic injuries other than stroke.

II. METHODS

A. Subject characteristics

This case study reports on a single 61 year-old participant with MS as defined by the modified McDonald Criteria [8]. The volunteer had adequate language and neurocognitive function. The subject had completed all conventional physical therapy and was clinically assessed as having moderate ankle spasticity and mild weakness at the left ankle, resulting in gait disturbances (Table I). The subject agreed to participate and signed informed consent as approved by the University of Maryland Baltimore Institutional Review Board, the VA Research and Development Committee, and the Massachusetts Institute of Technology Committee on the Use of Humans as Experimental Subjects. Following informed consent he underwent a battery of neurocognitive tests (MMSE, CES-D, and Edinburgh Handedness Inventory).

TABLE I
PATIENT DEMOGRAPHICS

VARIABLE	VALUE
Age (yrs.)	64
Gender (M/F)	M
MS Type, Diagnosis Date	SPMS, 1984
Ankle Weakness	Left, 4/5*
Spasticity	Moderate
Ambulatory Function	Single Point Cane
Spasticity Medication	Baclofen 10mg TID
25-Foot Walk (sec)	16.4
CESD	9
MMSE	30
Edinburgh Handedness Inventory	Strongly Right

*On manual muscle test score (0-5). CESD: Center for Epidemiologic Studies Depression Scale, MMSE: Mini Mental State Exam, SPMS: Secondary Progressive MS.

B. Training device (Anklebot)

The modular VA-MIT ankle robot (Anklebot) has been a subject of numerous investigations (e.g., [1-5]). Here, we briefly describe two of its key features (impedance control, backdrivability) pertinent to the protocol. The Anklebot provides assistance "as-needed" during execution of motor tasks such as playing a video game. To be more specific, "assist-as-needed" feature stems from using an impedance controller that consists of a programmable reference position, a programmable proportional gain (approximating a controllable torsional stiffness), and a programmable derivative gain (approximating a controllable torsional damping in parallel with the stiffness. During the visually-evoked task, when a target appears an impedance virtual slot is created whose back-wall moves toward the desired direction (i.e., toward the target). If the human is ahead of the moving back-wall, the robot is compliant (i.e., provides no assistance); however, if the user fails to initiate movement within a pre-established time latency, or is unable to complete the prescribed movement at any point in time, the robot provides "gentle nudge" toward the target. The amount of assistance provided depends on the stiffness and damping settings of the impedance controller, and ongoing movement (ankle kinematics – angular displacement and velocity). Hence, this impedance control allows subjects to reach targets unassisted and automatically tracks their performance; however, if subjects cannot initiate movement in time or are unable to reach a target, the robot provides assistive ankle torques.

The Anklebot is also backdrivabile, a feature of the actuators that allows an elderly or impaired individual with diminished function to easily move the robot endpoint and allows the robot to interact stably and safely with the environment (individual) at all times; in other words, the Anklebot has the capability to "get out of the way" when appropriate. Backdrivability is achieved when the forces produced at the robot endpoint as a result of endpoint motions are low, so that they do not impose a force or position on the individual; i.e., the robot "easily gets out of the way." Backdrivability thus allows individuals to train their own movements, and is essential in keeping the individuals engaged in an interactive task and enables them to observe their attempts at motion.

C. Anklebot training with EEG-EMG protocol

This was a single-session experiment during which the subject played 8 blocks of an ankle targeting videogame with the Anklebot while in a seated position (Fig. 1 top row) as applied in our previous Anklebot studies in stroke [2-5]. The goal of the training activity was to dorsiflex (DF) and plantarflex (PF) her left ankle to move a robot-controlled cursor "up/down" in order to pass through "gates" that migrated across the screen at different vertical locations, each scaled to individual ankle range of motion (Fig.1 bottom row). The first and last blocks (40 targets each) were unassisted, i.e., the robot only recorded the participant's movements. Six intermediate blocks consisted of 80 assist-as-needed targets that progressively decreased the level of robotic assistance every other block. Specifically, robotic assistance was progressively decreased every two blocks in an "easy-to-difficult" sequence [2-5], with stronger assistance during the first two blocks (K = 100 Nm/rad), reduced assistance in the next two blocks (K = 50 Nm/rad), and minimum assistance during the last two blocks (at K = 25 Nm/rad). This was done to maintain enthusiasm and avoid frustration while providing and sustaining challenge in order to avoid performance ceiling effects. Throughout, 60 channels of EEG were acquired at a sampling rate of 2 kHz using a linked ears reference (Compumetics, USA). During recordings, electrode impedances were maintained below 10 kΩ with bandpass filters set at .01-100 Hz. The recorded EEG signal was digitized using SynaAmps RT amplifier linked to Neuroscan Acquire software (v4.5). Two bipolar channels of electromyography (EMG) were also collected at 2 kHz from the gastrocnemius and tibialis anterior muscles via the same EEG amplifier. Figure 1 shows the experimental setup.

Fig. 1. (*Top*) Exemplar experimental set-up showing seated interactive Anklebot training with concurrent EEG-EMG monitoring. The subject was fitted with a 60-channel EEG cap and seated with the Anklebot mounted proximally onto a fixed plate and the affected leg resting at 45° on a padded support. Event markers generated by the Anklebot were used to synchronize the Anklebot, EEG, and EMG data streams; (*Bottom*) Screen capture of the video game and corresponding ankle movements. The task required the subject to move the on-screen cursor by dorsi- or plantar-flexing their ankle. The goal was to successfully maneuver through vertical gates approaching across the screen from left to right (arrows).

D. Anklebot-derived ankle motor control measures

As with the previous studies [2-5], ankle motor control measures were calculated from point-to-point ankle angle and velocity time series recorded by the Anklebot during the unassisted blocks. Velocity time series were rectified to compute speed profiles. Specifically, movement accuracy was defined as the average number of successful passages, movement speed by the average peak and mean angular speeds, and movement smoothness by the negative of average jerk (third time derivative of position) normalized to peak speed[1]. A measure related to movement smoothness, the mean arrest period ratio (MAPR) [9], was computed as the duration of movements below 5% peak speed as a proportion of actual movement time. For every motor control metric (except accuracy), actual movement was considered to occur when the speed was greater than a threshold (5% of peak speed).

E. EEG measures and analysis

The EEG measures consisted of spectral power and coherence, which reflect regional activation and networking, respectively. All signal processing of the EEG data was conducted using Neuroscan Edit software version 4.5 (Compumetics, USA). Time-series data from unassisted trials were offline-referenced to an averaged ears montage and then low-pass filtered at 55 Hz with a 48-dB roll off using a zero phase Butterworth filter.

The resulting epochs were baseline corrected using the entire sweep and then visually inspected to remove any remaining sweeps that contained artifact or amplitudes >75 μV^2. Epochs were then transformed using the discrete Fourier transform, employing a Hamming window with a 50% overlap. Spectral power (μV^2) was calculated across 1-Hz bins and averaged across the frequency bandwidths: theta (3–8 Hz), low-alpha (8–10 Hz), high-alpha (10–13 Hz), beta (13–30 Hz), and gamma (30–50 Hz). The same artifact-reduced epochs were used to compute coherence using the cross- and auto-spectral densities, then averaged across the theta, alpha, low-beta (13-20 Hz), high-beta (20-30 Hz). Specifically, coherence was computed between electrode[2] Fz, which overlies the motor planning region and electrodes F3, F4, C3, C4, T7, T8, P3, P4, O1, and O2, and between frontoparietal electrodes (F3-P3/P4 and F4-P3/P4). Spectral power was examined globally, i.e., across scalp topography.

III. RESULTS

Anklebot training with concurrent EEG-EMG monitoring was successfully completed in a participant with MS without adverse events or excessive self-reported fatigue. Improvements in ankle motor control were accompanied by changes in EEG coherence and power spectral density.

A. Ankle motor control

Figure 2 shows speed profile for a single unassisted movement made toward the same target (DF), before and after training. Both speed (mean: Δ = +34% peak: Δ = +16%) and smoothness (normalized jerk: Δ = -20%, MAPR: Δ = -43%) of unassisted ankle targeting movement showed improvements after training (Table II). These responses

[1]Strictly speaking, since jerk is a measure of non-smoothness, the negative of jerk is used to define smoothness (i.e., smoother movements have lower negative values of jerk and vice versa) – see Fig. 3.

[2]Electrode nomenclature [10]: "F" (frontal), "C" (central), "T" (temporal), "P" (parietal), "O" (occipital). A "z" (zero) refers to an electrode placed on the midline. Even (2,4,6,8) and odd (1,3,5,7) numbers refer to electrode positions on the right and left hemispheres, respectively. Higher numbers correspond to greater distance from the midline.

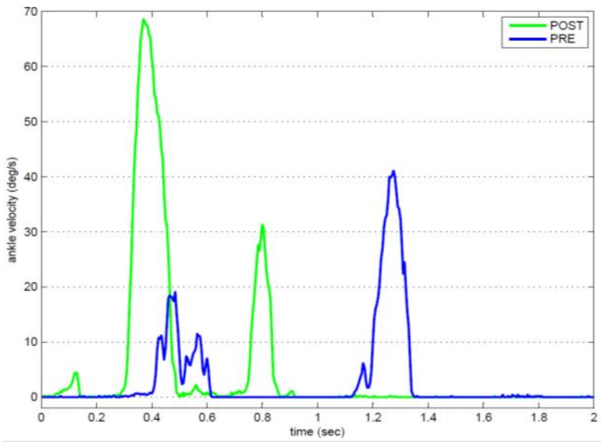

Fig. 2. Speed profile during a single exemplar unassisted ankle targeting movement, before (blue) and after (green) training. Note that less episodic movement (velocity reversals, number of local speed peaks) post-training indicates smoother movement.

were higher than (double in peak speed) or comparable to (mean speed, normalized jerk) chronic stroke subjects (n = 8) exposed to a single bout of Anklebot training [4] (Fig. 3). Movement accuracy (number of successful passages) also increased but to a far lesser degree than observed in stroke subjects (Δ = +6% vs. Δ = +59%).

TABLE II
CHANGES IN ANKLE MOTOR CONTROL MEASURES

METRIC	PRE	POST	%Δ*
Peak speed (°/s)	39.9 (20.6)	46.3 (19.1)	+16
Mean speed (°/s)	3.2 (6.7)	4.3 (3.6)	+34.4
Accuracy	32	34	+6.3
Normalized jerk (s^{-2})	309.5 (224.2)	248 (239.3)	-19.9
MAPR**	0.63 (0.31)	0.36 (0.27)	-42.8

Values depicted are mean (SD) of 40 unassisted movements at PRE and POST assessments. *Relative percent change **Mean arrest period ratio.

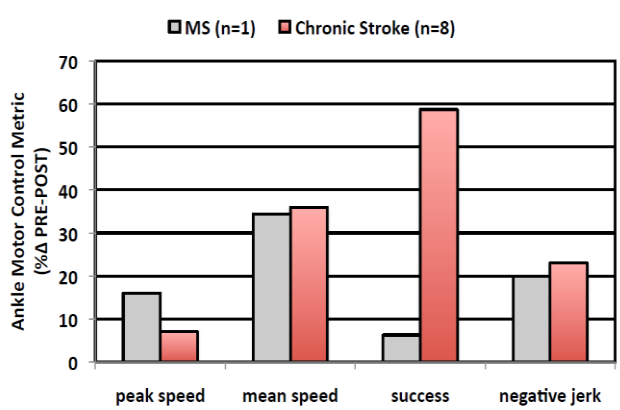

Fig. 3. Pre-post comparison of key motor control measures in this MS participant vs. those reported previously in a small cohort (n = 8) of hemiparetic stroke survivors (mean values) [4].

B. *Changes in psychophysiological measures (EEG, EMG)*

Decreased low alpha (8-10 Hz) spectral power was observed during the unassisted Anklebot trial after training (Fig. 4 top row). Further, increases in alpha (8-13 Hz) coherence were recorded between Fz (motor planning) and distributed cortical networks across both hemispheres post-training (Fig. 4 - bottom row). These were accompanied by greater muscle activation and higher co-contraction in both muscles (Fig. 5). The gains in ankle motor control and changes in spectral measures of EEG are consistent with previous reports from single-bout, as well as 3- and 6-week seated, interactive Anklebot studies in chronic stroke [2,4,5].

Previous studies [11-13] have demonstrated changes in EEG coherence due to learning and/or short-term motor adaptation. Task-relevant and regionally specific coherence increases during the early stages of learning, then decreases or streamlines as skill increases. Decreases in low-alpha (8-10 Hz) power have been associated with increases in general cortical arousal, indicative of relatively higher cortical resource management and effort, i.e., a "busier" brain [14].

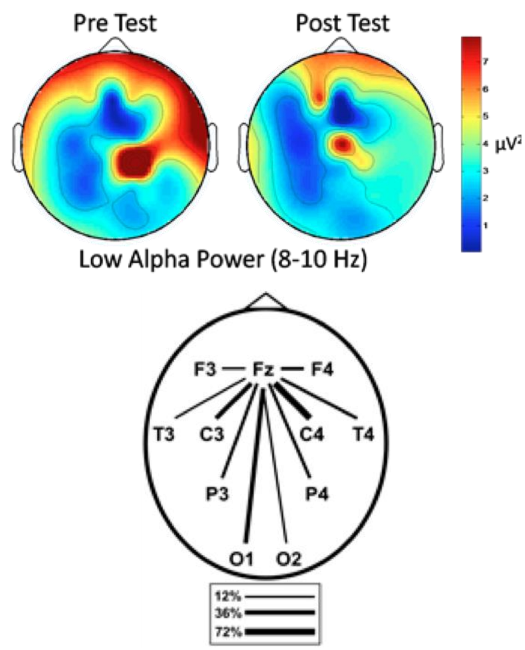

Fig. 4. (*Top*): Low alpha power across the topography during pre and post test. Cooler colors reflect less power, accordingly there is less low alpha power during post test compared to pre test suggesting an increase in cortical engagement as a result of training; (*Bottom*): Change in alpha coherence as from pre to post test between distributed regions of the cortex and the motor-planning region. The line thickness reflects increased in coherence implying an increase in networking to the motor-planning region from all regions.

This increased activation has also been linked to the early stages of ML [13]. However, as learning progresses, activation and coherence decrease in task-relevant brain areas [11-13], suggesting less neural effort and a more streamlined cortical network to accomplish the same task.

EMG data showed that heightened agonist amplitudes were accompanied by greater co-contraction (Fig. 5) - perhaps needed to overcome larger antagonist amplitudes. This may reflect spasticity or the onset of fatigue, even if the latter was not self-reported as being very high. While we do not have sufficient data to fully explore and support this qualitative line of reasoning, it could account for the pronounced difference in targeting success (overall task objective and instruction to the subject) in MS versus those observed in chronic stroke [4]. Hence, the "dosage" (task-specific variables, e.g., number of targets per trial, number of trials, level of robotic assistance and progression, etc.) warrants more careful investigation to minimize the EMG co-contraction and/or spasticity, and to potentially enhance ankle function recovery in those with MS.

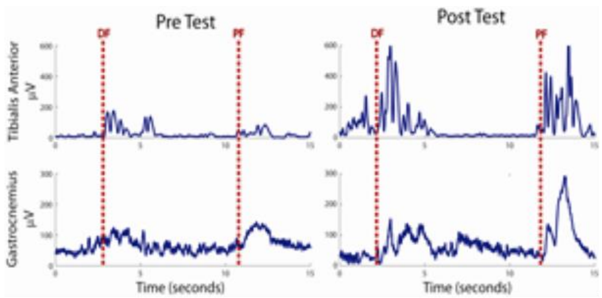

Fig. 5. Surface EMG signals from tibialis anterior (*Top panel*) and gastrocnemius (*Bottom panel*) muscles during unassisted targeted movement in dorsiflexion (DF) and plantarflexion (PF) before (*Left panel*) and after training (*Right panel*). Overlaid are target appearance event markers for exemplar targets in DF and PF. Note higher agonist amplitudes post-training with greater antagonist co-contraction.

IV. CONCLUSIONS AND FUTURE DIRECTIONS

Here, we presented a "three-prong" approach to a single bout of seated, interactive Anklebot training in a participant with MS. The training session was well tolerated by the subject, demonstrating that robotic training in concert with task-related monitoring of muscle and brain activity is feasible in this population. The subject responded positively with respect to intra-session gains in key indices of ankle motor control and brain (EEG) measures that were comparable to those reported in stroke [4]. Our own work has shown significant improvements in ankle motor control resulting from a single bout of seated, interactive Anklebot therapy in chronic stroke [4]. The comparison of findings from this protocol to those in stroke is relevant given the overlap of selected ankle function and gait deficits between the two conditions. Further, we speculate that single-session training and testing protocols could foster development of "responder-non responders" profiles, better informing treatment outcomes for long-term Anklebot training and advance more individualized (deficit-adjusted) interventions.

Of course, the results presented here are limited and must be expanded with more subjects and longer interventions to investigate the potential of the Anklebot to elicit long-lasting ankle motor gains, and assess whether those translate to improvements in gait function, as observed in chronic [2] and sub-acute stroke [3]. Apart from a more comprehensive investigation, future studies will also use Verbal Analog Scale (VAS) [15] to quantify self-reported fatigue. In addition, to assess whether short-term adaptations in key measures of ankle motor control translate to benefits in key aspects of walking function, we also plan to add to the clinical battery, timed-up-and-go [16] and 10-m walking [17] standardized tests.

In conclusion, we believe that this case report provides the first-of-its-kind pilot data with MS subjects, suggesting that the use of motor-learning based ankle robotics training in tandem with physiological (EEG, EMG) monitoring may advance our understanding of the underlying neuro-muscular mechanisms associated with training-induced recovery in MS and other neurological injuries that negatively impact lower extremity function.

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