Neurophysiology of Brain-Machine Interface Rehabilitation

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***Abstract*— Long-lasting cortical re-organization or neuroplasticity depends on the ability to synchronize the descending (voluntary) commands and the successful execution of the task using a neuroprosthetic. This talk will discuss the neurophysiological mechanisms of brain-machine interface (BMI) controlled neuroprosthetics with the aim to provide implications for development of technologies for rehabilitation.**

I. INTRODUCTION

Functional electrical stimulation (FES) neuroprosthetics can be used to applying short electric impulses over the muscles or the nerves to generate hand muscle contractions and functional movements such as reaching and grasping. Our work has shown that recruitment of muscles using FES goes beyond simple contractions, with evidence suggesting re-organization of the spinal reflex networks and cortical-level changes after the stimulating period [1,2]. However, a major challenge remains in achieving precise temporal synchronization of voluntary commands and activation of the muscles [3]. Brain-machine interface (BMI) technologies can synchronize voluntary commands from the brain and movements generated by FES. This is hypothesized to be vital for inducing cortical level re-organization (neuroplasticity). Therefore, the objectives of the proposed research are to investigate how precise synchronous activation of muscles with FES and activation of the cortical networks: (a) using non-invasive brain stimulation and (b) motor imagery can affect corticospinal facilitation.

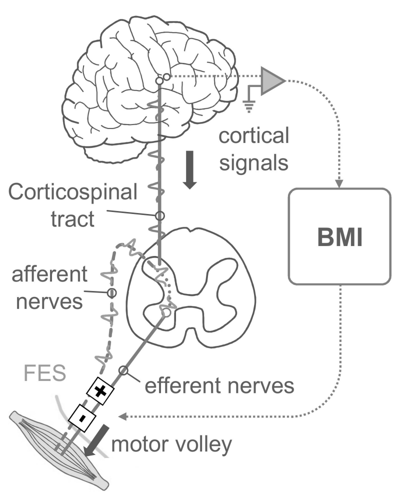

Figure 1. Neurophysiological basis for how BMI can be used to synchronize cortical signals and FES to induce neuroplasticity.

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II. METHODS

Stimulation of muscles with FES was delivered using a constant current biphasic waveform with a 300μs pulse width at 50 Hz frequency via surface electrodes. First, repetitive transcranial magnetic stimulation (rTMS) intermittent theta burst protocol (iTBS) was used to induce cortical facilitation. iTBS protocol consists of pulses delivered intermittently at a frequency of 50 Hz and 5 Hz for a total of 200 seconds. Moreover, motor imagery protocol was used to display a virtual reality hand opening and closing sequence of movements (hand flexion/extension) while subject's hands remained at rest and out of the visual field.

III. RESULTS

Our first results showed that motor imagery can affect corticospinal facilitation in a phase-dependent manner, i.e., hand flexor muscles during hand closing and extensor muscles during hand opening. Moreover, when iTBS was used to activate the cortical motor circuits, FES activation of hand flexors was more effective in facilitating the corticospinal tract, compared to when either iTBS or FES was delivered alone. Therefore, it seems that cortical facilitation is essential for inducing neuroplasticity

IV. DISCUSSION & CONCLUSION

Neuroplastic changes require engagement of both descending commands and afferents to facilitate execution of intended tasks. Such positive reinforcement, known as Hebbian learning, depends on precise spatiotemporal synchronization of voluntary signals and activation of FES and it can be achieved through use of BMI technology.

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Why Brain Machine Interface Should Be Used to Control Functional Electrical Stimulation Therapy?

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Abstract— **In this study we examined how different control strategies for the functional electrical stimulation therapy (FEST) may influence the rehabilitation process and the efficacy of FEST. We tested three different FEST control strategies: (i) push button, (ii) electromyogram (EMG) and (iii) brain-machine interfaces (BMI) control. This study suggests that the BMI control strategy appears to be the most effective control strategy for FEST, as it promotes neuroplasticity considerably more than the competing approaches.**

I. Introduction

Over the past two decades, our team at the KITE Research Institute, Toronto Rehabilitation Institute – University Health Network, has developed a therapy that is now better known as functional electrical stimulation therapy (FEST). This treatment uses functional electrical stimulation (FES) as a tool to restore voluntary arm and hand function in stroke and spinal cord injured individuals with severe upper limb deficits. This therapy works as follows. The client is asked to perform a particular reaching and/or grasping task. Since the client is paralyzed and is unable to perform the task voluntarily, while the client is struggling to perform the requested function/task, the FES is delivered to her/his arm muscles to generate the desired arm/hand movements. The simultaneous imagination and striving to perform the desired task(s), plus activation of the muscles in the physiologically correct manner to execute the desired task(s), with the help of FES, helps reprograms the central nervous system of the client and enables her/him to relearn how to reach and grasp objects voluntarily.

Although this therapy works well in cognitively intact clients, it is not as effective in clients who are unable to focus on the task at hand. Therefore, we proposed to conduct a study to examine how different control strategies for FEST may influence the learning and motor function recovery. In this article, we studied three different FEST control strategies and examined which one is the most effective.

II. Methods

The objective of the study was to compare (i) push button, (ii) electromyogram (EMG) and (iii) brain-machine interfaces (BMI)-controlled FEST. At the same time the neuroplasticity induced by these three FEST modalities, was also compared to voluntary grasping (VOL) and BMI-guided grasping. Ten able-bodied participants underwent one hour of each of five grasping training modalities. Assessments, including motor-evoked potential, grip force, and maximum voluntary contraction, were conducted.

III. Results

Motor-evoked potential-based outcome measures were more upregulated following BMI-FEST and EMG-FEST as compared to VOL, push-button-controlled FEST or BMI-guided grasping. No significant changes were found in the more functional outcome measures.

IV. Discussion & Conclusion

These results provide preliminary evidence suggesting the potential of BMI-FEST and EMG-FEST to induce greater neuroplastic changes than conventional FEST, although the precise mechanism behind these changes remains speculative.

Following this discovery our team spent 5+ years testing BMI-controlled FEST. The results of the BMI-controlled FEST are encouraging and will be presented in this symposium by Dr. Cesar Marquez-Chin.

Acknowledgment

The authors wish to thank Carolyn Gunraj for assistance in developing the motor-evoked potentials methodology and the study participants for their dedication

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EEG-Triggered Functional Electrical Stimulation Therapy for Restoration of Movement in Chronic Severe Hemiplegia

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Abstract— **Functional electrical stimulation therapy has become an important tool available to therapists treating individuals with spinal cord injury and stroke to improve voluntary movement after paralysis. We present here a new version of the intervention that uses EEG-based indicators of motor attempt to trigger the electrical stimulation. Two individuals with chronic severe hemiplegia improved their level of impairment by 6 and 17 points in the Fugl-Meyer Upper Extremity score after 40 and 80 treatment sessions, respectively. Both participants were unresponsive to every other treatment, including state-of-the-art functional electrical stimulation therapy, during the six prior to their participation in our studies. These encouraging results suggest that the integration of brain-computer interfacing technology and functional electrical stimulation may be effective in cases for which every other therapeutic intervention has failed.**

I. INTRODUCTION

Paralysis can have devastating consequences on the independence and quality of life of those who experience it. Stroke, which results from the death of brain tissue caused by an interruption of blood flow, is an important cause of paralysis. An important tool to improve the ability to move after paralysis is functional electrical stimulation therapy (FEST) [1]. In this intervention, patients are asked to perform a functional task with their affected limb. After a few seconds of trying, a therapist triggers a train of electrical pulses producing a contraction of muscles that are selected specifically to produce the practiced movement. This process is repeated multiple times in each of the 40 one-hour sessions, a common length for and FEST intervention, and multiple movements can be practiced in a single session.

FEST has been demonstrated effective for the rehabilitation of individuals with hemiplegia [2]. Importantly the intervention has been shown effective in cases of severe impairment in the chronic stage; a population that is often unable to benefit from other forms of therapy.

We present a new version of FEST in which the stimulation is triggered with the patients' intention to move as indicated by a decrease in power of their electroencephalographic (EEG) activity.

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II. METHODS

Two individuals with severe stroke hemiplegia resulting from stroke received the brain-computer interface-triggered FEST (BCI_FEST). The participants, A and B, were treated for 40 and 80 one-hour sessions, respectively. A single EEG channel was used to monitor and detect decreases in power indictive of the participants' attempt to move their arm and hand. Stimulation was delivered with a programable four-channel stimulator to facilitate reaching, grasping, and releasing (hand opening) movements.

III. RESULTS

The participants experienced an increase of 6 (participant A) and 17 points (participant B) in the Fugl-Meyer Upper Extremity Score (FMA-UE) [3]. The FMA-UE is a scale used clinically to measure the level of impairment after stroke. Changes of 5 points in this scale are considered clinically important (MCID = 5 points).

IV. DISCUSSION & CONCLUSION

Our initial results suggest that BCI_FEST may be viable and suitable for restoring reaching and grasping functions in individuals with chronic severe hemiplegia, a population which is often unable to participate in and benefit from most forms of therapy.

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Bimodal Neuronal Modulation in Deep Brain Structures

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***Abstract*— Electrical stimulation can be used to selectively suppress or facilitate neuronal activity. Here, we present experimental data and introduce a novel computational model capable of predicting these bimodal neuronal responses.**

I. Introduction

Deep brain stimulation (DBS) is an efficacious therapy for neurological disorders such as Parkinson's disease (PD), dystonia, and essential tremor (ET). Despite its clinical efficacy, the mechanisms of action have remained largely unknown. Many newer DBS applications (i.e. for Alzheimer's disease and depression) have applied the same stimulation paradigm that is used in subthalamic DBS for Parkinson's disease, but have suffered from limited clinical efficacy. Moreover, stimulation programming relies on a guess-and-check approach, rather than knowledge of how stimulation interacts with the brain.

II. Methods

During DBS surgery, microelectrode recordings are performed for electrophysiological verification of the MRI-defined implantation target region. We use a dual-microelectrode (MER) setup (600µm spacing), which enables recording from individual neurons during simultaneous delivery of electrical stimulation. In surgical patients with PD and ET, we have stimulated at various frequencies (1, 2, 3, 5, 10, 20, 30, 50, 100, 200Hz; 100uA; 150µs pulse width) while recording from 10-30 individual neurons in each of four clinically-relevant brain regions – subthalamic nucleus (STN; target for PD), substantia nigra pars reticulata (SNr; emerging target for PD axial symptoms), ventral intermediate nucleus (Vim; target for tremor in PD and ET), and reticular nucleus (Rt; potential target for epilepsy). Moreover, based on this experimental data, a biophysically realistic computational model was developed (with consideration for short-term synaptic plasticity dynamics and local microcircuitry) for the prediction of site-specific stimulus response functions of nearly any neuron within the brain (including the above).

III. Results

We have demonstrated that in the STN and SNr, structures with predominantly GABAergic (inhibitory) afferent inputs, neuronal firing was progressively suppressed with increasing stimulation frequency [1]. Here, we demonstrate that electrical stimulation can also upregulate neuronal activity in a frequency-dependent manner, but only when delivered to structures which contain primarily glutamatergic (excitatory) inputs such as the Vim and Rt. However, regardless of the afferent inputs, we also demonstrate that high-frequency (≥100Hz) stimulation leads to suppression of neuronal activity by way of synaptic depression. Thus, all structures can be downregulated, while only some can be upregulated.

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IV. Discussion & Conclusion

These findings demonstrate unequivocally that electrical stimulation of the brain is site specific, but also frequency-dependent. The net somatic effect is dependent on the weighted composition of inhibitory and excitatory inputs the stimulated brain region. This should be considered in the development of new stimulation paradigms and novel DBS indications. To date, most conventional high-frequency DBS applications work by suppression of neuronal activity [2,3]. However, the term 'neuromodulation' implies the ability to manipulate neural activity as desired, and should not be limited to the creation of a functional lesion. Thus, the novel findings of the ability to upregulate neuronal function are of therapeutic and clinical interest. Our novel computational model holds great power in its ability to predict neuronal responses to electrical stimulation based only on knowledge of the afferent inputs to the stimulated structure. This is important for understanding the effects of stimulation in potential novel therapeutic stimulation targets that have yet to be explored clinically or electrophysiologically.

Acknowledgment

The data were collected at Toronto Western Hospital in collaboration with and co-supervision from Dr. William D. Hutchison (Krembil Research Institute; KRI, Toronto). Dr. Milad Lankarany (KRI) was the collaborator for the presented model. Dr. Milos R. Popovic (KITE, Toronto) was involved in supervision and mentorship.

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A Hybrid Brain-Computer Interface Based on Electroencephalography and Functional Transcranial Doppler

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***Abstract*— In this talk, we introduce a novel hybrid brain–computer interface (BCI) system that measures electrical brain activity as well as cerebral blood velocity using electroencephalography (EEG) and functional transcranial Doppler ultrasound (fTCD) respectively. We will review the most recent results in this area.**

I. Introduction

BCI are typically used to aid individuals with neurological deficits, particularly those with motor or speech impairments, to communicate and interact with their surrounding environment. BCIs are also used to design rehabilitation and intervention techniques for individuals with disabilities to restore the lost functionalities. Such techniques are cost effective as they can be administered in clinics or at home without requiring additional supervision from a rehabilitation therapist.

While EEG represents a most commonly used BCI modality, its main drawback is a varying accuracy. To address this issue, hybrid BCI, that is EEG combined with another modality, are introduced to improve the accuracy and information transfer rates of EEG-based BCIs.

II. Methods

Data presented in this talk comes from a study approved by the by the local institutional review board at the University of Pittsburgh. Eleven healthy participants (three females, and eight males) provided informed consent and participated in this study with ages ranging from 25 to 32 years. None of the participants had a history of migraines, concussions, strokes, heart murmurs, or other brain related injuries.

EEG was collected using 16 electrodes placed according to the 10-10 system over frontal, central, and parietal lobes at positions Fp1, Fp2, F3, F4, Fz, Fc1, Fc2, Cz, P1, P2, C1, C2, Cp3, Cp4, P5, and P6. Left mastoid was used as the reference for all participants. A g.tec EEG system with g. USBamp, a bio-signal amplifier, was used in this study. It included 16 24-bit simultaneously sampled channels with an internal digital signal filtering and processing unit and sampling rate up to 38.4 kHz. The data were digitized with a sampling rate of 256 samples/sec and filtered by the amplifier's 8th order bandpass filter with corner frequencies 2 and 62 Hz in addition to 4th order notch filters with corner frequencies 58 and 62 Hz.

The fTCD data was collected with two 2 MHz transducers using SONARA TCD system of 145 Mw ultrasonic power. These transducers were placed on the left and right sides of the transtemporal window located above the zygomatic arch. Since the middle cerebral arteries provide approximately 80% of the brain with blood, the fTCD depth was set to 50 mm which is the depth of the mid-point of the middle cerebral arteries.

III. Results

To examine the performance of this novel hybrid BCI, we considered a motor imagery (MI) paradigm. Features derived from the power spectrum for both EEG and fTCD signals were calculated. Mutual information and linear support vector machines were employed for feature selection and classification.

Using the EEG-fTCD combination, average accuracies of over 80% were achieved for right arm MI versus baseline, left arm MI versus baseline, and right arm MI versus left arm MI respectively. Compared to performance measures obtained using EEG only, the hybrid system provided significant improvement in terms of accuracy by 4.48%, 5.36%, and 4.76% respectively. In addition, average transmission rates of 4.17, 5.45, and 10.57 bits/min were achieved for right arm MI versus baseline, left arm MI versus baseline, and right arm MI versus left arm MI respectively.

IV. Discussion & Conclusion

Based on these results, we believe that the proposed hybrid BCI is a promising tool for developing real-time BCI applications, as in our subsequent studies, we obtained very similar results when it comes this novel hybrid BCI.

Acknowledgment

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Implantable Brain-Machine Interfaces: Towards Clinical Trials

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Abstract— **Implantable brain machine interfaces (BMI) enable severely disabled people high-performance real-time robot control and communication, utilizing high-quality intracranial neural signals. We established ECoG-based robot control and communication. Independent component analyses effectively extract neural information with dimensional reduction and contribute to improving decoding accuracy. Also, we are developing a fully implantable BMI for long-term home-use with 24/7 supports. We completed GLP tests and non-clinical long-term implantation. The next step is a clinical trial to confirm safety and efficacy of the implantable BMI.**

I. Introduction

Implantable brain machine interface is a promising new therapeutic modality to support motor and communication control for disabled people suffering from amyotrophic lateral sclerosis (ALS), spinal cord injury and stroke [1]. Electrocorticograms (ECoGs) are useful for brain machine interfaces (BMI) because of not only their zero time-lag property but also their high spatiotemporal resolution. ECoG-based BMIs enable severely disabled people real time robot control and communication [1].

Previously, we developed a wired type ECoG-based BMI system for human application. We performed clinical research of the BMI system in patients with intractable epilepsy or intractable pain who underwent the temporary placement of subdural electrodes. High gamma activity in the 80 – 150 Hz band was a good decoding feature for ECoG-based real time decoding and control. We performed clinical research of the BMI system in a paralyzed patient in minimal communication state (MCS) with amyotrophic lateral sclerosis (ALS). The participant successfully controlled a robot hand and a communication assistive device using the BMI. Also, we developed a fully implantable BMI device for long-term home-use with 24/7 supports [2]. This paper describes the present state of our project for the clinical trial.

II. ECoG-Based Decoding and Control

Quantitative decoding methods may be more appropriate than classification decoding methods for decoding arm trajectory. Therefore, we developed a decoding algorithm using sparse linear regression (SLR) to infer 3-dimensional trajectory of a robotic arm. As a result, we were able to decoded 3 dimensional trajectory of the arm and fingers from ECoGs in patients with intractable epilepsy or intractable pain [3]. In addition, we introduced independent component analysis (ICA) to improve decoding accuracy. We selected independent components specifically distributed over the sensorimotor area of the hand area to effectively extract neural information related to the sensorimotor processing with dimensional reduction, and we used only such sensorimotor-specific components to decode the arm trajectory. As a result, decoding accuracy of the arm trajectory using SLR was improved by 30 – 50 %. We also introduced a new task to obtain learning data for SLR applicable to paralyzed study participants. We instruct the participants to observe the motion of simulated robotic arm and to attempt to move their arm in the same way as the simulated robotic arm. Thus, ECoG data can be correlated to 3-dimensional trajectory of the simulated robotic arm.

III. A Fully Implantable Device for ECoG-Based BMI

We have been developing a fully implantable BMI device for long-term home-use. The previous prototype of the implantable device was separated into the head and body part [2]. We minimized the electronic modules to unify the head and body part. We also improved signal-to-noise ratio of the integrated analog amplifier module to clearly detect subtle high gamma activity without averaging or summation of neural data.

We completed GLP (Good Laboratory Practice) tests: skin sensitization test, subcutaneous reaction test, acute systemic toxicity test, subcutaneous implantation test, cytotoxicity test, reverse mutation test, chromosomal aberration test, and subacute systemic toxicity test. The GLP tests showed the implantable device was biologically safe. In addition, preclinical animal experiments were also performed to evaluate safety and efficacy.

IV. Discussion & Conclusion

This paper described the present state of our project of implantable BMI for clinical application. The next step is clinical trial to confirm safety and efficacy of the implantable BMI. If BMIs can reduce the decrease in quality of life (QOL) of severely disabled patients with ALS, they will change the way of thinking to decide more positively and to live with higher QOL under mechanical ventilation.

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