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Final Report: Electrocorticography Workshop

ABSTRACT

see attached report

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(a) Papers published in peer-reviewed journals (N/A for none)

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Number of Presentations: 0.00

Non Peer-Reviewed Conference Proceeding publications (other than abstracts):

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TOTAL:

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Peer-Reviewed Conference Proceeding publications (other than abstracts):

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TOTAL:

Number of Manuscripts:

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TOTAL:

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This section only applies to graduating undergraduates supported by this agreement in this reporting period

The number of undergraduates funded by this agreement who graduated during this period: 0.00

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Number of graduating undergraduates who achieved a 3.5 GPA to 4.0 (4.0 max scale):...... 0.00

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Sub Contractors (DD882)

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see attached report

Technology Transfer

10th Intl. Workshop on Advances in Electrocorticography

SUMMARY

The tenth International Workshop on Advances in Electrocorticography (ECoG) took place on November 10-11, 2016, in San Diego, CA. Sixteen distinguished members of the global ECoG community presented their latest research comprising the recent advances and state of the art in the field, encompassing engineering, basic science, translational, and clinical domains. Interactive panel discussions were held on both days of the workshop to provide perspectives on the presented material and to consider future directions. This year's workshop was attended by 80 largely senior academics from leading academic institutions and medical device companies. Over the past 10 years, approximately one third of all ECoG-related research published in peer-reviewed scientific journals has been conducted by past and present faculty of the ECoG Workshop series.

DAY 1 – THURSDAY, NOVEMBER 10, 2016

Introduction

Antony Ritaccio: He introduced this meeting as an extraordinary multidisciplinary program. He thanked the supporters and observed that about half of the meeting attendees are new. He talked about the expanding potential applications of ECoG and international research.

Gerwin Schalk: He identified the scope of this meeting as an opportunity for scientists, clinicians, and engineers to come together and be educated on ECoG. He was enthusiastic about the current worldwide recognition of ECoG as an important neuroimaging method, whereas even five years ago it was hardly mentioned, and its potential applications in basic neuroscience and clinical settings.

Distributed Bi-directional Brain-Computer-Interface Technologies and Conceptual Applications

Tim Denison - Medtronic

This talk kicked off with a video showing the immediate effects of a DBS device on an intention tremor patient. Even though this setup already shows impressive results, the challenge for the neurologist remains to control the side-effects and short-comings of current technology. The main issue with brain-computer interfaces (BCIs) is performance and the goal is to integrate currently used instrumentation into a device that will allow us to move from the operating room to ambulatory monitoring.

Potential BCI applications can be classified into 3 types: 1) use of "normal" signals to control an actuator with existing motor signals (e.g. Utrecht UNP communicator); 2) use of "normal" brain signals to control an implanted device (e.g. ET controller at U Florida); and 3) measure deviations from "normal" brain signals and stimulate to nudge them back into a more normal state (e.g. PD beta/gamma "thermostats"). The Medtronic pulse generator (sense and stimulation system) is an example of a type 3 device and its modulatory architecture is the key factor to the device success.

Promising neurophysiological signals are emerging that will enable BCIs to implement a “thermostat” type of dynamic control of the brain. For example the presence/absence of gamma oscillations in ECoG recordings in Parkinson’s disease (Swann, Starr et. al., 2016). Other key milestones to be conquered towards BCI design are: developing large databases (to conquer the difficulty of establishing a ground truth), early risk management, active probing and networks mapping.

ECoG-based Implant for Communication in the Locked-in State

Nick Ramsey – University Medical Center Utrecht

His work focuses on BCIs for locked-in patients; people who have lost the ability to communicate their thoughts while their cognition remains intact. BCIs need to always work, produce few errors, require minimal effort, not require caregiver training, and be aesthetic. He has chosen implantable BCIs as they deliver high-quality signals, are always available, and more aesthetic.

The first patient to test the paradigm suffers from ALS and was implanted in 2015. The pre-implantation preparation was strict and arduous (use of fMRI and practicing on a 3D printed brain), as the electrode location is important (i.e. implantation on blood vessels and unrelated areas would compromise system performance). They implanted four ECoG electrode strips and the Medtronic ACTIVA RC device, while the core of the software is BCI2000. The recorded signals are filtered and subsequently, the correlation between filtered signals and task (index finger and thumb touching each other) is computed. The result of the correlation is used to effectively control the BCI with success rate larger than 90%, even in noisy environments.

This innovative technology has allowed the patient to communicate her thoughts and regain some of her independence. She is using it at home and outside, to call her caregiver, and for entertainment purposes.

Towards a Platform for Integrating ECoG and Other Multimodal Data

Zack Ives – University of Pennsylvania

Researchers spend 69% of their time for data acquisition, curating and management. A database is needed that will allow to better use and reuse datasets collected by the community, exploit richer, multimodal data in learning and modeling and combine expertise from different communities (i.e. neuroscience, statistics, software) into teams.

In collaboration with Mayo Clinic, University of Pennsylvania launched two separate challenges for detection and prediction of epileptic seizures. Hundreds of teams, worldwide, came together to compete for a solution and the products were detection and prediction algorithms that outperform state-of-the art algorithms.

This "experiment" provides further proof of the need for a unified platform. The key tasks involved in building this platform are: centralizing data access, careful partition between private and public data, building a big library of file format readers, and building intuitive data viewing. The key aspects of the database model are: the website format needs to be adaptable, and linking and co-registration are imperfect.

To materialize these concepts, he and his colleagues have launched Blackfynn, a data management platform integrating complex neuroscience data. Blackfynn enables to upload diverse datasets, integrate findings, analyze data, access curated datasets, facilitate collaborations, and ultimately to create better drugs, devices and clinical care.

Intracranial Signatures of the Perception and Memory of Spoken Sentences

Christopher Honey – Johns Hopkins University

For understanding and decoding brain states, temporal structure matters. To reveal functional hierarchy patterns, information needs to be linked over time and across multiple scales. Working memory is considered a top-down maintenance process, having limited capacity and protecting items from interference. However, this paradigm only works well when introduced with completely new information.

A parallel processing model is proposed, when prior knowledge is at play. To test this hypothesis, a segment of information is presented to the subject either in meaningful content or in scrambled mode. In early sensory region, the scrambling has little effect, but moving towards higher regions (prefrontal cortex) the scrambling influences time scales.

This shows that timescales of information are processed hierarchically across the cortex. The derived model of information integration over time is threefold: 1) controlled maintenance for sequences of unrelated items, 2) distributed hierarchical process memory for coherent sequences, and 3) process memory is reflected in timescales of neural dynamics.

Research, additionally, tried to answer the questions of how we remember sequences of words and why coherent sentences are easier to recall than random words. Their approach is based on the recall by regeneration model, introduced by Potter and Lombardi in 1990, according to which the previous input can be generated via semantic and synaptic representations.

The task that was presented to the subject was to repeat coherent versus incoherent sentences. The performance difference was 97% vs 93%, but the major difference was shown in the neural response (broadband high frequency power). Significantly larger power was demonstrated for incoherent sentence. To discard the possibility that the higher power is a loading side-effect, a decoder was used.

Computational Models of ECoG Signals in Human Visual Cortex

Jon Winawer – New York University

Visual perception and mapping has long intrigued researchers. Perception of an image is subject to its peripheral contents enabling the creation of visual illusion by manipulation of factors such as background grey-scaling.

The main focus of this talk was how information is mapped into the visual cortex. Visual pathways preserve the spatial structure of an image. In 2008, Dumoulin and Wandell used a linear model of population receptive fields to predict BOLD time series. This model works well on larger objects. The work presented in this meeting expanded this model by adding non-linearity, thus enabling its use for scaled down objects and prediction of ECoG time series.

Furthermore, they explored the effect of electrical brain stimulation on visual perception showing increase in the spatial extent of the activated cortex. Activation around each stimulation electrode increases with larger injected charge density and can be an order of magnitude larger than the electrode itself.

Neuronal Synchrony and the Relation Between ECoG Signal and the BOLD Response

Dora Hermes – University Medical Center Utrecht

Different neuroimaging modalities are used to access information in the brain. This study focuses on the spatial match, spatial correlation, and correlations across conditions between ECoG and BOLD, and how the features for each are derived from underlying neurophysiology. The approach that was taken was two-fold.

First, the correlations between ECoG and BOLD signals were computed. As expected, during the task, a decrease in alpha band and an increase in gamma manifested. Fitting a linear regression model between the changes in BOLD and changes an ECoG, a positive correlation is observed. Moreover, comparison of the broadband activity between the two imaging modalities revealed negative correlation in the alpha band and no significant correlation in the gamma band.

The second step was to successfully replicate the correlations using simulated signals. The main conclusion is that ECoG, unlike BOLD, is influenced by the firing synchrony of the underlying neurons (i.e. BOLD is a measure of how many neurons are firing and ECoG is a measure of how many neurons are rhythmically firing).

Engineering Approaches to Understanding Control in Brain Networks

Danielle Bassett – University of Pennsylvania

The brain can be viewed as a network system. As such, it can be constrained by structural architecture or functional dynamics and it comprises both internal processes (cognitive control and homeostasis) and external perturbations (stimulation and neurofeedback). The networked nature of the brain inherently changes how we think about control.

In a more strict mathematical definition of the networked brain, the brain is represented by a linear model $x(t+1) = Ax(t)+Bu(t)$, where x is the state of brain regions, A is the strength of connection between brain areas (brain areas modeled as oscillators), B is the number of regions being controlled, and u is the control energy. For simulated ECoG dynamics, non-linearity needs to be added to the above equation.

This model was successfully applied to simulate epileptic seizures. More specifically, push-pull control was used to simulate a focal epileptic network versus a distributed epileptic network. Interestingly, distributed epileptic networks show stronger synchronization prior to the seizure.

Closed-loop Neurofeedback Paradigms Using LFP and ECoG Signals in Monkey and Man

Jose Carmena – University of California, Berkeley

Current BMIs are usually bulky and confined in laboratory or clinical settings. The ultimate goal is to move towards chronic multi-electrode recording, scaling up in performing tasks of daily living. In this project, neural activity (single neuron activity and LFPs) is used as the input to a musculoskeletal model of the arm (translating neural activity into kinematic and stiffness parameters) to volitionally control a prosthetic device.

The BMI is not exclusively a decoding product but rather a closed loop system with visual feedback. This feedback has demonstrated improvement on motor control 30% larger than the state-of-the-art Kalman filter.

In another project, they take advantage of the inhibitory properties of the beta rhythm as recorded using ECoG. More specifically, they use neurofeedback to selectively manipulate beta oscillations in peritoneal dialysis patients (implanted with the ACTIVE PC+S device) to study real-time effects on arm reaching.

DAY 2 – FRIDAY, NOVEMBER 11, 2016

Intracortical Neural Interfaces for the Restoration of Communication and Mobility

Leigh Hochberg, MD, PhD, FANA, FAAN, Brown University

There are a variety of signals that are of interest for neuroscientific investigations. These can be electrical, chemical, blood flow, and more specialized measures such as saliva pH. These signals can be studied and decoded from a variety of perspectives, e.g. clinical neurophysiology and cognitive neuroscience. To advance neural interfaces to be able to restore communication and mobility in subjects with paralysis, a combination of these perspectives is required.

An overview of the current achievements and future aims of the BrainGate project and ongoing trials of intracortically-based BCIs for people with paralysis was provided. Dr.

Hochberg's studies have utilized microelectrode arrays such as the Utah array in more than a dozen subjects with a total of more than eight thousand implant days. Neural control of a robotic arm was demonstrated in a subject with tetraplegia, allowing the subject to perform actions such as moving a drink from a table to their mouth (Hochberg et al., 2012). Advances in neurally-driven point-and-click applications was also shown including the BrainGate iBCI-controlled tablet computer.

One of the main problems identified in this work is finding optimal array position on the brain. Typically, devices are implanted in the pre-central gyrus on the dominant hemisphere. Use of functional magnetic resonance imaging (fMRI) is not ideal in the patient population, but has been found to be beneficial with recent subjects. Similarly, venograms can also prevent sub-optimal placement of microelectrode arrays.

Attempts to make the patient cable wireless were detailed, leading to a proposed wireless subcutaneous chronic implant. Several challenges in developing this type of technology were described and potential solutions presented. Ultimately, the project aims to be able to restore or replace function, or assist subjects without the need for an engineer to be present.

Multi-site ECoG: What We Can Learn from the Restoring Active Memory Trial

Kathryn Davis, MD, MSTR, University of Pennsylvania

Dr. Davis gave a comprehensive overview of the Restoring Active Memory (RAM) project and dataset, the largest publicly available ECoG dataset containing data from approximately two hundred subjects and over ten thousand memory mapping sessions. The dataset provides total coverage of brain across all subjects.

Results were presented to demonstrate the effect of stimulation on behavior and how this is dependent on brain state. Some of the findings from the project revealed that stimulation of the hippocampus can impair memory, contrary to findings in earlier studies. A number of strategies were employed to study memory including stimulation only during poor memory performance, stimulation during memory retrieval, and multi-channel stimulation.

Details of a new fully implantable device for memory impairment were presented, similar to the NeuroPace device for epilepsy. Other results demonstrated seizure prediction, web-based visualization of surface and volume data for multi-site collaboration, and network analysis to improve memory. These results revealed ideal activity for improved memory performance. This analysis allows the prediction of optimal control points in the brain based on the structural and functional networks that can now be determined.

Intracortical Insights into the Human Sense of Smell

Jay Gottfried, MD, PhD, Northwestern University

ECoG-related neuroscience approaches for studying human and animal olfactory systems were introduced. These described how breathing, sniffing, and smelling shape olfactory cortical oscillations. The advantages of using odors to assess limbic system physiology and function in humans was also explained. Experiments in rodents demonstrated that respiratory oscillations provide an olfactory signature and oscillations in the theta band are tied to breathing rate. Beyond the olfactory system, effects are also observable in the hippocampus and whisker barrel cortex.

It was revealed that respiratory oscillations can be identified in the human piriform cortex at 0.15-0.3 Hz, equivalent to 4-8 Hz in rodents. Odor-induced piriform theta was investigated with results indicating that the olfactory brain is indelibly associated with the limbic system and that theta phase-locking occurs in the presence of odor.

Application of Continuous Cortical and Deep LFPs for Adaptive DBS Control

Kelly Foote, MD, University of Florida

Dr. Foote explained the motivation behind adaptive deep-brain stimulation (DBS) and the different signal modalities that can be utilized. The hardware and neuroscientific challenges to advance adaptive DBS were also presented.

Combining ECoG and DBS provides unique opportunities for adaptive control of neural activity. Tourette syndrome, Parkinson's disease (PD), and essential tremor are ideal disorders for DBS intervention. Tourette syndrome was proposed as an ideal test bed for closed loop DBS however the technology currently has severe limitations. Existing devices are poor choices for continuous stimulation as they will require frequent replacement. However, by adaptively scheduling stimulation these concerns can be addressed to some extent.

Intraoperative tic mapping was demonstrated with very robust indication in central medial nucleus (CM) of thalamus. DBS was found to reduce phase-amplitude coupling (PAC) in PD. A combination of CM thalamic and cortical signals produces the best tic detection. Closed loop DBS was demonstrated to work in Tourette's. Results also show that PAC suppresses cortical function and that DBS diminishes PAC in hypokinetic PD, and increases PAC in hyperkinetic Tourette's.

Detecting Physiological Signatures of Disease States Using ECoG

Coralie De Hemptinne, PhD, University of California - San Francisco

Dr. De Hemptinne presented methods for closed-loop DBS treatment for movement disorders. ECoG provides significant advantages in identifying markers of PD. Open-loop continuous stimulation can potentially produce adverse effects and has limitations, such as being unresponsive to changing symptoms. However, closed-loop stimulation can circumvent many of these limitations. Stimulation was administered to subjects based on beta power in the subthalamic nucleus (STN). Local field potentials (LFPs) were found to be a biomarker of hypokinetic state, and peak gamma power is observed during dyskinesia. Application of stimulation shifted the peak activity to half the stimulation frequency. Additionally, beta power in orbitofrontal cortex was found to reflect the severity of anxiety. Using ECoG, putative electrophysiological markers of PD symptoms can be identified.

ECoG Signatures of Subcortical Input to the Brain Surface

Kai Miller, PhD, MD, PhD, Stanford University

Dr. Miller presented work concerned with visual processing, focusing on the human ventral temporal cortex. These studies explored how visual percepts are formed. It was found that peri-hippocampal areas respond to visual stimuli depicting houses, while the fusiform gyrus responds to visual stimuli depicting faces (Miller et al., 2016). Explanation of different types of prosopagnosia (the ability to recognize faces), e.g. associative and appreciative, was described and possible explanations for their occurrence was presented. Data and methods used for these studies has been made freely available online.

CorTec Brain Interchange – Developing a 32-Channel Implant System for Clinical Research

Joern Rickert, PhD, Founder and CEO of CorTec

Dr. Rickert presented the technical specification and requirements of the CorTec Brain Interchange (BIC) and potential applications of closed-loop therapies in the central nervous system (CNS). A main requirement of the system is that it must be wireless. This was achieved by making an implantable device with hermetic encapsulation that communicates wirelessly and is inductively powered. The device is expected to provide movement reconstruction from brain activity and have an expected lifetime of over fifty years. The device has also been developed to stimulate with an arbitrary waveform. To date, sheep have been utilized as a chronic animal model.

A Hybrid System Solution to ECoG Control of Prosthesis

Nathan Crone, MD, Johns Hopkins University

Dr. Crone presented current progress in ECoG prosthetic control, strengths and limitations of ECoG for prosthetic control and methods by which machine control can augment brain control of prosthetics. ECoG possesses various strengths for BCI applications. It offers good spatial resolution, improved signal-to-noise ratio, and long-term stability. High-density ECoG, for example providing sixteen electrodes where traditionally four would be used for the same area, can provide detailed functional mapping of the brain. Hybrid systems were demonstrated utilizing both BCI and eye tracking techniques using computer vision methods to integrate sensor data and enhance performance.

Finally, HARMONIE: A Hybrid Augmented Reality Multimodal Operation Neural Integration Environment was introduced, utilizing intelligent robotics providing the subject with supervisory control. A simulation of future applications of the system was presented to demonstrate the goals of the project.

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