EEG CHARACTERIZATION DURING MOTOR TASKS THAT ARE DIFFICULT FOR MOVEMENT DISORDER PATIENTS

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TITLE: EEG Characterization During Motor Tasks that are Difficult for Movement Disorder Patients

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ABSTRACT

EEG Characterization During Motor Tasks that are Difficult for Movement Disorder Patients

Adam Aslam

Movement disorders are a group of syndromes that often arise due to neurological abnormalities. Approximately 40 million Americans are affected by some form of movement disorder, significantly impacting patients' quality of life and their ability to live independently. Deep brain stimulation (DBS) is one treatment that has shown promising results in the past couple decades, however, the currently used open-loop system has several drawbacks. By implementing a closed-loop or adaptive DBS (aDBS) system, the need for expensive parameter reprogramming sessions would be reduced, side-effects may be relieved, and habituation could be avoided. Several biomarkers, for example signals or activity derived from electroencephalogram (EEG), could potentially be used as a feedback source for aDBS. Here, we attempted to characterize cortical EEG potentials in healthy subjects performing six tasks that are difficult for those with movement disorders. Using a 32-channel EEG cap with an amplifier sampling at 500 Hz, we performed our protocol on 11 college-aged volunteers lacking any known movement disorder. For each task, we analyzed task-related power (TRP) changes, spectrograms, and topographical maps. In a finger movement exercise, we found task-related depression (TRD) in the delta band at the F4 electrode, as well as TRD at the C3 electrode in the alpha band during a pencil-pickup

task, and TRD at the F3 electrode in the beta band during voluntary swallowing. While delta-ERD in the finger movement exercise was likely due to ocular artifact, the other significant results were in line with what relevant literature would predict. The findings from the work, in conjunction with a future study involving movement disorder patients, can provide insight into the use of EEG as a feedback source for aDBS.

Keywords: EEG, electroencephalography, neurostimulation, deep brain stimulation, movement disorders, closed-loop DBS, adaptive DBS, aDBS

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Lastly, I'd like to thank my family and friends for standing by my side through my years of schooling. My grandpa Eddie taught me that education outside and inside the classroom is priceless, while my mom and Gram always supported me to follow whatever interests were important to me. My sister Natalie and my wrestling family, the Langes, the Yozzos, the O'Learys, and Kevin Gallagher, made me the person I am today. From them I learned that the best things in life take the most amount of work. My friends Nick Bergam, Joanne Medrano, Youlen Ghazalian, Maddy Ramos, Diana Orozco, and Michael Woodson are the best support group I could have ever imagined! These people all helped make this 6(+) year process both an enjoyable and unforgettable one. Their belief in my success pushed me to work as hard as I have. It's because of these people that I have this document I am very proud to have written.

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CHAPTER 1: INTRODUCTION

In order to establish appropriate background knowledge for this project, we must understand the disorders we are attempting to treat, the related physiology and anatomy, and the various treatment options available and being researched.

1.1 MOVEMENT DISORDERS

Movement disorders are neurological syndromes that can be disabling and very difficult to manage. There is a wide variety of movement disorders described, however this section will cover essential tremor (ET), Parkinson's disease (PD) and Primary Generalized Dystonia (PGD), the most common movement disorders, which are often treated with DBS [1,2].

1.1.1 Types and Pathophysiology

The most common movement disorder is ET [3]. ET is a progressive disease that is often inherited and begins later in adulthood [3]. Patients experience tremor due to abnormal electrical signals generated as a signal travels through the cerebellum, red nucleus, globus pallidus internus (GPi), thalamus, and cortex, on its way to muscle [3]. It is difficult to accurately describe the pathophysiology of ET as it is not a specific disease, but rather a clinical syndrome [4].

Another common movement disorder is PD, which affects about one million Americans [5]. PD is a progressive disease in which patients often suffer from movement abnormalities, including tremor, muscle rigidity, bradykinesia (akinesia), and postural instability, and also non-movement related symptoms, such as depression, sleep disturbances, and hallucinations [6]. The typical progression of symptoms is shown in **Figure 1.1**. The exact cause of PD is unknown, but the symptoms are thought to be caused by the loss of dopaminergic neurons in the substantia nigra and the development of Lewy Bodies in dopamine-producing cells [5,7,8]. The substantia nigra produces the neurotransmitter dopamine, which is involved with muscle movement and motivation [3]. Lewy Bodies, abnormal intracellular aggregates, contain various proteins that interfere with neural function [5]. When the substantia nigra is deteriorated, the subthalamic nucleus (STN) becomes overactive, which affects the GPi [9]. The GPi being overstimulated leads to thalamic inhibition, thus tremor, and when the GPi is inhibited, bradykinesia and rigidity can occur [10].

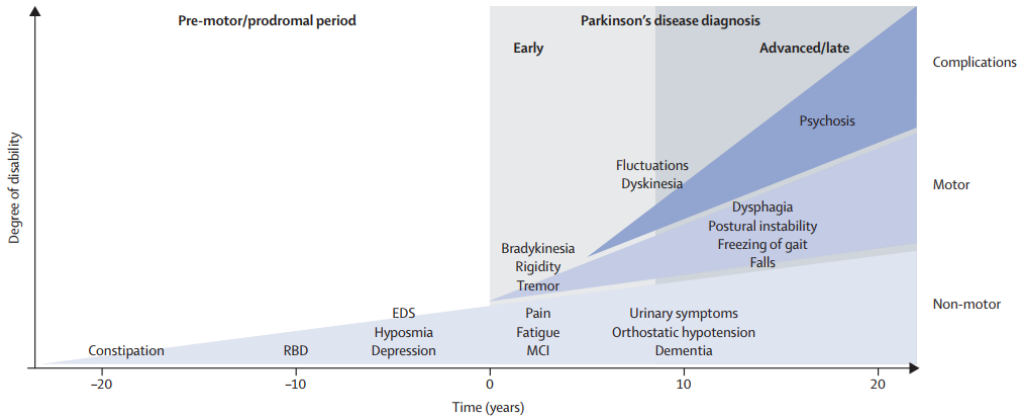

Figure 1.1: Progression of PD. The diagnosis of PD (time=0 years) can be preceded by symptoms occurring over a period of 20 years or more. The progressive nature of PD is shown as motor abnormalities and other complications take over. EDS=excessive daytime sleepiness. MCI=mild cognitive impairment. RBD=REM sleep behavior disorder [11].

There are three proposed models that explain the pathophysiology of PD [12,13]. In the "firing rate model", GPi and substantia nigra pars reticulata (SNr) neurons fire more rapidly than in healthy individuals [13]. This is due to dopamine depletion reducing inhibitory inputs through the striato-GPi/SNr *direct* pathway and elevating excitatory inputs through the striato-GPe-STN-GPi/SNr *indirect* pathway [13,14]. This decreases thalamic and cortical activity, resulting in bradykinesia and/or bradykinesia-like symptoms, while excess involuntary movements are caused by the reduction of thalamus inhibition by the GPi [13]. The "firing pattern model" is based on dopamine depletion enhancing connections between the globus pallidus externus (GPe) and the STN, increasing basal ganglia electrical activity [13,15]. In the "dynamic activity model", dopamine depletion

reduces movement-related GPi inhibition through the cortico-striato-GPi/SNr direct pathway and increases GPi excitation through the cortico-STN-GPi/SNr hyperdirect pathway and cortico-striato-GPe-STN-GPi/SNr indirect pathway (See **Figure 1.2**) [12,13]. This reduces GPi inhibition which in turn reduces inhibition of the thalamus and cortex, leading to bradykinesia and/or bradykinesia-like symptoms [13]. Excess involuntary movement is caused by increased GPi inhibition through the direct pathway and reduction of GPi excitation in the hyperdirect and indirect pathways.

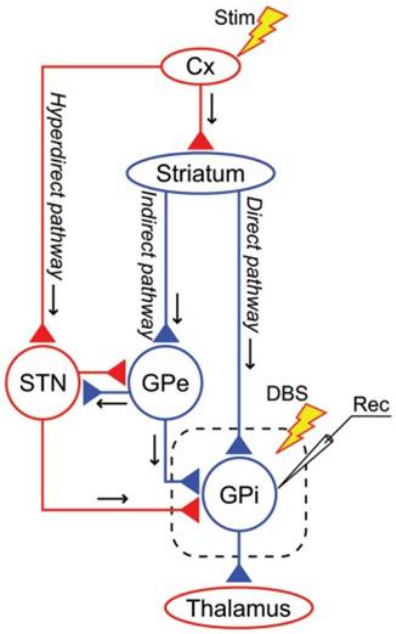

Figure 1.2: Basal Ganglia Pathways. The cortico-striato-GPi/SNr direct pathway, cortico-STN-GPi/SNr hyperdirect pathway, and cortico-striato-GPe-STN-GPi/SNr indirect pathways are shown [13].

PGD is another common movement disorder, in which muscle contractions lead to repetitive involuntary movements or abnormal postures [16]. Various genes related to dystonic syndromes have been identified. The "primary" in PGD refers to a patient that has no other neurological disorders and is thought to have an autosomal dominant pattern of inheritance [16,17]. PGD is thought to be a basal ganglia disorder due in part to patients' inability to effectively synthesize dopamine, however the exact pathophysiology is obscure [18]. More recent evidence also points toward other brain regions being involved, namely the cerebellum [18-20]. Imaging of dystonic patients showing basal ganglia abnormalities often show cerebellar abnormalities as well [19].

1.1.2 Current Treatments

No treatments slow the neurodegenerative process, however, there are a variety of ways movement disorder patients relieve symptoms [11]. ET patients may treat symptoms with non-medical solutions, medications, and/or surgery. Non-medical solutions include weighing down limbs to dampen tremor, for example with wrist weights, as well as managing anxiety, which can worsen symptoms [3]. Some choose to take anti-seizure and/or β-adrenergic inhibitor (e.g. β-blocker) medications [3]. If the previously mentioned treatments lose effectiveness, surgery is considered. A ventral intermediate thalamus (VIM) lesion has been shown to help 80-90% of patients [3]. A more reversible surgery with similar results is VIM-DBS [3].

As with many movement disorders, PD is often treated with a combination of pharmacotherapy and non-pharmacological alternatives [3,5]. Since psychological symptoms such as psychosis and depression are common in PD patients, treatments such as support groups and therapy are especially important [5]. A whole array of medications can be used to treat the various symptoms of PD such as sleep symptoms, behavioral disturbances, and hallucinations [3]. Many of these pharmacological treatments produce their own side-effects which too must be managed [3]. Levodopa, a drug that is used as a precursor to dopamine, has been considered the mainstay for PD therapy since 1970 [21].

PGD begins the earliest in life out of the three movement disorders described here, as its onset is common in childhood or as young adults [16,17]. PGD patients are frequently misdiagnosed for years and told they are suffering from a psychiatric problem [22]. Education and counseling are key in order to ease the often young dystonic patients and convince them to accept medical advice after being misdiagnosed for so long [22]. Oral medications are prescribed in many PGD cases in order to augment or suppress dopamine producing cells in the basal ganglia, to block acetylcholine receptors in the basal ganglia, or to amplify transmission through GABA receptors [22].

Although there are ways for ET, PD, and PGD patients to treat their symptoms, these conditions are ultimately progressive [11,16]. Medications and lifestyle changes are often sufficient in early stages of syndrome development, however as symptoms worsen despite pharmacotherapy, surgery is considered [11,16,23]. For ET, PD, and PGD patients, DBS is a potential treatment when other solutions fail (see section 1.3.1) [16,22,23,24,25].

1.2 ELECTROPHYSIOLOGY

Neural activity produces electrical potentials that can be analyzed with various measurement techniques. Neurotransmitters such as dopamine relay information between neurons and are released into the synaptic cleft as an action potential propagates from cell to cell. Abnormal activity can be related to the pathophysiology of certain disorders. By understanding and characterizing both normal and atypical electrophysiology, we can develop better therapies.

1.2.1 The Brain

Various regions in the brain are specialized centers that control different activities and processes. The four major lobes of the brain, frontal, parietal, temporal, and occipital have different functions for which they are primarily responsible.

1.2.1.1 The Lobes of the Brain and Their Functions

Understanding exact neuronal localizations is challenging, however several neuroimaging techniques have provided insight into which areas of the brain influence certain actions. EEG, MRI, fMRI, and MEG are a few techniques that have helped further the field [26].
The frontal lobe, located in the anterior part of the brain, influences many areas, for example, emotional control, forming our personality, influencing our decisions, cognition,

problem solving, speech, pre-initiation and execution of movement, impulse control, and planning [27,28]. The parietal lobe, which mainly functions as a sensory information processer for cognitive processes and spatial reasoning, is located posteriorly to the frontal lobe. More specifically, the parietal lobe senses pain, pressure, and touch, as well as regulates spoken and written word comprehension [28,29]. The temporal lobes are located on each side of the brain and their main function is to process auditory information [28]. Other functions of the temporal lobes include helping to form long-term memories and process new information, formation of visual and verbal memories, and interpreting smells [30]. Most posterior is the occipital lobe which is responsible for visual processing and color recognition [28]. These various regions in the brain can be visualized in **Figure 1.3**A.

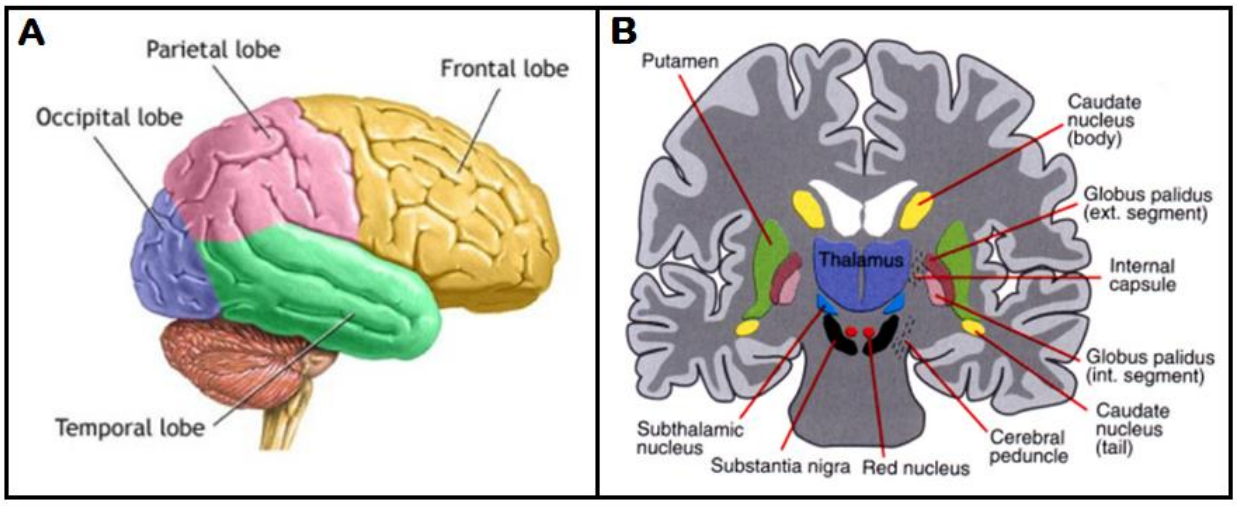

Figure 1.3: Brain Anatomy. A. All four major brain lobes are depicted [28]. B. Basal ganglia nuclei structures in relation to the thalamus are displayed [31].

1.2.1.2 Motor Function Control Centers

The basal ganglia (**Figure 1.3**.B) are a collection of subcortical nuclei that are primarily responsible for motor control [32]. Some of the nuclei can be categorized as input nuclei, which receive information mainly from the cortex, thalamus, and substantia nigra [32]. These include the caudate nucleus and the putamen. The GPi is an example of an output nucleus, which send information to the thalamus [32]. Intrinsic nuclei, for example the STN, are situated between output and input nuclei in the signal transmission pathway, and serve to modulate incoming information [32]. This pathway can be visualized in **Figure 1.4**. Proper dopamine release at input nuclei is key for normal basal ganglia function [32]. When this is interrupted, problems can arise such as development of movement disorders, namely PD, ET, and PGD [5,7,32,33].

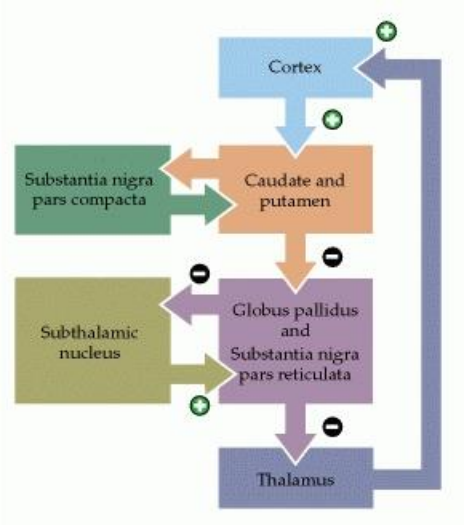

Figure 1.4: Signal Pathway of Brain Regions Related to Movement. Here, the signal transmission pathway depicting inputs and outputs of basal ganglia components, cortex, and thalamus is shown [34].

A region of the cerebral cortex that contains motor neurons, called the motor cortex, mediates the planning and initiation of voluntary movement [34]. Basal ganglia information is sent through the thalamus to the motor cortex to initiate muscle action [34]. Here, cortical signals involved with movement can be analyzed by recording EEG, which is of great importance for this study.

1.2.2 Neuron Behavior

Individual neurons are arranged into networks that are responsible for the various functions of the different brain regions. There are three critical levels of membrane potentials that occur during a neuronal action potential When the neuron is at rest, the transmembrane potential, which describes the potential difference between the inside and outside of the neuron, maintains a value of approximately -70 mV [35]. The threshold potential, approximately -55 mV, is the transmembrane potential that the neuron must reach in order for an action potential to occur [35]. An action potential is the period in which the cell potential rises and falls quickly to propagate a neural signal [36]. The peak potential during this time is approximately 40 mV and is the maximum value the potential reaches during depolarization (see **Figure 1.5**) [35].

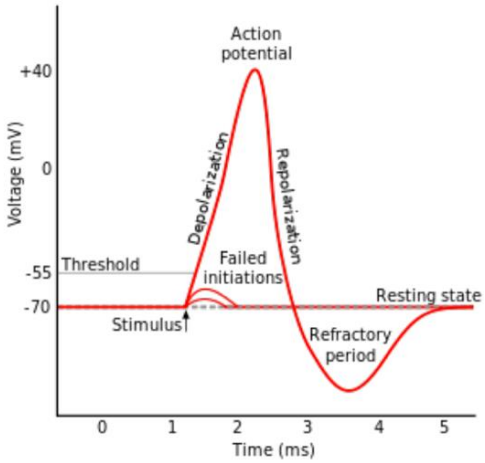

Figure 1.5: Neuron Action Potential. Curves labeled as "Failed initiations" show the transmembrane potential for a neuron that does not reach the threshold voltage , and thus, does not produce an action potential. The curve labeled "Action potential" shows the transmembrane potential for a neuron that undergoes rapid depolarization and reaches the maximum voltage before repolarizing and returning to its resting potential [36].

The process of depolarization begins with a stimulus which could come from a conformational change in a peripheral neuron receptor or from the transmission and reception of neurotransmitters within the brain [35]. This process could be caused, inhibited, or otherwise affected by an applied electrical stimulus as with DBS (see section 1.3.3 for more information) [13].

1.2.3 EEG Characteristics

Brain activity can be visualized by measuring voltages on the scalp, known as EEG. A modern EEG system is comprised of an array of electrodes measuring voltage over time,

an amplifier, an analog to digital converter, and a personal computer. Analysis of various EEG characteristics is important in clinical diagnosis and research.

1.2.3.1 EEG Signals

Scalp EEG electrodes primarily measure a sum of the synaptic potentials of cortical neurons in an open field geometrical arrangement [37,38]. Since EEG is a noninvasive measure taken on the scalp, we don't record individual neural activity, but rather the coordination of many neurons. In response to a stimulus, we are able to visualize brain activity as a function of time, known as an event-related potential (ERP). Pyramidal cells, the main type of cell in the cortex, are oriented perpendicular to the cortical surface. When stimulated, a strong dipole is formed, which can then be measured by scalp electrodes [37]. EEG shows a graphical representation of voltage differences between a scalp location and either another scalp location, a scalp potential average, or some combination of one or more referential electrodes (see section 1.2.3.4 for more information). EEG contains the summation of both excitatory postsynaptic potentials (EPSPs), which are positive potentials that make an action potential more likely, and inhibitory postsynaptic potentials (IPSPs), which make action potentials less likely [39]. It is important to note that scalp potentials are not necessarily a reflection of the activity directly under the electrode (see **Figure 1.6**) [40].

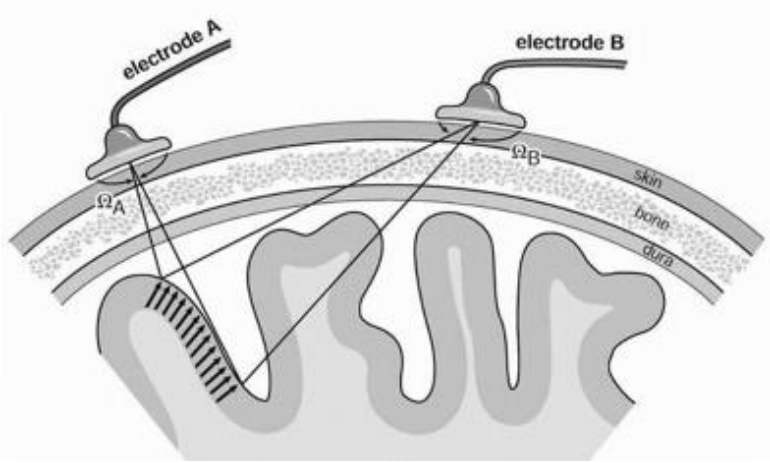

Figure 1.6: The Influence of Cortex Geometry on EEG. Due to the dipole nature of cerebral pyramidal cells and the complex geometry of the cerebral cortex, electrodes may not record the activity directly underneath the scalp. Here, electrode B measures the signal depicted as a higher amplitude than measured by electrode A despite electrode A being closer to the signal generation site [40].

There are five major classifications of EEG frequency bands. From lowest frequency to highest frequency, the waves are as follows: delta, theta, alpha, beta, and gamma bands (see **Figure 1.7**). The frequency cutoffs that define each band vary slightly depending on the study [41]. Here, frequency cutoffs were selected based on recent literature [41-44].

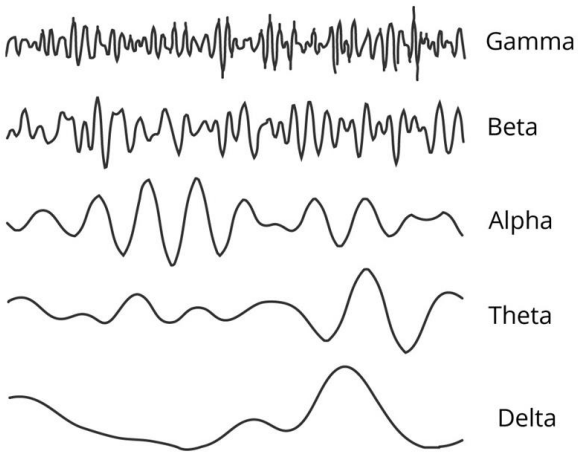

Figure 1.7: EEG Frequency Bands. EEG voltages are shown over a period of about one second for each major wave frequency class [45].

Delta waves have a frequency of approximately 1.5 Hz to 4 Hz with dominant rhythms occurring in infants and in the deepest stages of sleep. When elevated in adults, delta activity is considered a marker for brain damage or a pathological condition such as in schizophrenia patients [46].

Theta waves have a frequency between approximately 4 Hz and 8 Hz. These waves occur infrequently in adults who are awake, however are normal in children [43]. Along with delta waves, slow theta waves are common during sleep. Activity in this frequency range is likely related to drowsiness [43,44].

Alpha waves have a frequency from around 8 Hz to 12 Hz and are common over the occipital lobes [43,47]. Alpha activity is related to attentiveness and creative ideation [43,47,48,49]. Mu rhythms are centered over the sensorimotor cortex and are due to motor

activity in the same frequency as the alpha band [50]. During preparation of movement and/or during movement, mu activity is attenuated, whereas alpha activity is not, neither by movement nor movement planning [43,50,51].

Beta waves have a frequency from about 12 Hz to 30 Hz and they occur equally on both sides of the brain in the frontal region. These waves are dominant in people who are trying to solve problems [44]. During movement, people experience beta event-related desynchronization (ERD) and then a subsequent rebound of beta power after cessation of movement [50,51,52]. This event-related synchronization (ERS) of beta power after movement is likely involved in the termination of movement, which may be of particular importance for treating some symptoms of motor disorders such as tremor [52]. Elevated beta activity limits information coding capacity and the processing of new information is impaired, leading to the current motor state being favored, disallowing new movements [53]. This heightened beta activity of PD patients is what is thought to cause bradykinesia, which is a slowness in the initiation of movements [53,54]. The discovery that levodopa use by PD patients decreases the amount of beta activity suggests that beta waves regulate dopaminergic activity in response to internal cues as well as external cues like movement [54-56].

A fifth category, gamma waves, have a frequency between approximately 30 Hz and 50 Hz and are likely involved in working memory and attention [57,58]. Still, researchers debate whether gamma oscillations are directly linked to these functions or if they are just an epiphenomenon or byproduct of other waveforms [58]. In this frequency band, extra

caution should be taken when drawing results, as EMG is sensitive to cognitive processes [59,60]. Further, temporal, occipitofrontal, and auricular muscles on the head can produce signals in the gamma band that constitute the majority of the total gamma power [60].

Noise reduction is a primary concern when recording EEG. Noise sources can be patient related or from technical sources. Patient-related sources include minor body movements, EMG, ECG, eye movements or blinking (**Figure 1.8**) and sweating. Technical sources of noise include 50 or 60 Hz line noise, electrode impedance fluctuations, cable movements, broken wire contacts, over-application of conductive gel, dried conductive gel, and/or low battery [61].

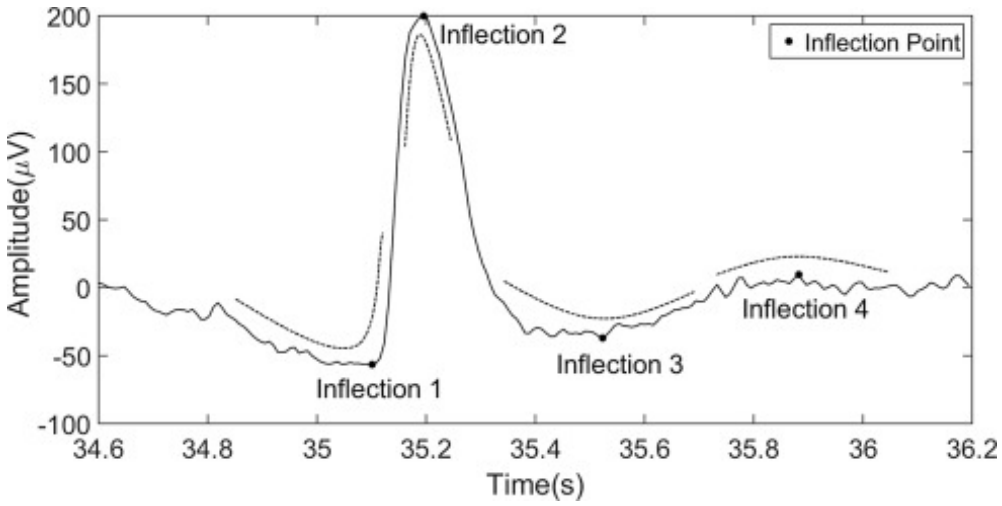

Figure 1.8: Ocular Artifact. EEG data shown has been corrupted by an eye blink, which introduces noise and overshadows useful information [66].

Approximately 90% of EEG spectral power falls between 1 and 30 Hz, which overlaps with potentially much larger EMG signals, which range from 5 to 450 Hz [62]. Physical movement can also alter coupling of the signal to EEG electrodes in the delta band. This indicates that motion artifact can easily corrupt the entire spectrum of EEG signal, so movement should be kept to a minimum while testing. Techniques such as independent component analysis (ICA) are sometimes used to separate important signals from noise sources such as eye blinks [63-65]. Artifact removal can also be done visually by ridding of data that is corrupted, either by marking artifact time during testing or while analyzing raw EEG data.

1.2.3.2 Components of an EEG System

An EEG system is comprised of electrodes with conductive media, amplifiers with filters, an analog to digital converter, and a recording device [61]. Data flows from activity within the brain (mainly cortical signals) to the electrodes placed on the scalp [38]. Typically, amplitudes are very small compared to other biosignals like ECG, usually in the 0.5 to 100 μV range [61]. Due to the low amplitude of the signals naturally created in the brain, amplifiers are required to increase the signal amplitude to levels usable by devices such as analog-to-digital converters, recorders, and displays [61]. Amplifiers and filters boost the important physiological signal to a range that can be accurately converted to digital data. Channels of analog signal are sampled at the sampling frequency to obtain digitalized EEG data which can later be analyzed much more effectively than the outdated paper analog

data [61,67,68]. The analog to digital converter converts the signal to be read and displayed by a recording device, such as a personal computer [67].

Neural activity in the brain results in changing potentials measured between a signal electrode and reference electrode. A third electrode is used to ground the system [68]. In this study, the location for a ground electrode is the earlobe. Types of electrodes include disposable electrodes, reusable disc electrodes, saline-based electrodes, dry electrodes, and needle electrodes [61,69]. Needle electrodes penetrate through the scalp which can cause irritation or pain for the user and are thus best used only for long duration readings [61]. One study compared the offset voltage, resistive and capacitive behavior over time, drift, and low-frequency noise of various electrode types [69]. In this study, six types of reusable electrodes (silver, tin and gold cup electrodes, sintered silver–silver chloride (Ag|AgCl), platinum, stainless steel), six disposable Ag|AgCl electrode models, and nine gels and pastes were analyzed and found the best results using reusable Ag|AgCl electrodes [69]. In some systems, dry electrodes are used for convenience. These do not require the use of conductive paste, which minimizes preparation and clean up time. The performance of these systems has been shown to be as effective as commercially available wet electrodes [70]. Multi-channel EEG analysis favors using an electrode cap as it secures electrodes in place on the scalp [71]. Some studies have praised the use of electrode caps, which contributed to our decision to implement an electrode cap in this study [71,72].

When using standard wet electrodes, a conductive gel is required to maintain electrical contact with the scalp [73]. This poses a minor problem, as many gels adhere tightly to the

hair when dry [74]. This can lead to uncomfortable cap removal, and washing the scalp and hair is recommended after testing. Rather than using dry electrodes or needle electrodes which have the potential to injure subjects, the best alternative is to simply warn study participants of possible discomforts related to gel use [61,74].

1.2.3.3 Important EEG System Specifications

Different applications of EEG may require different specifications and features depending on the experimental objectives. Below are several criteria which were considered in order to determine the most appropriate specifications for our study.

Frequency bandwidth: In the study we performed, frequencies related to the analysis of motor tasks were chosen as the most important frequency bands. Alpha and beta waves are likely the most important frequencies for this study (See section 1.2.3.1), which encompass the 8 to 30 Hz range.

Sampling rate: The rate of data acquisition varies widely from approximately 125 to 1000 Hz depending on the system [61]. Movement related studies used a sample rate between approximately 250 and 1000 Hz [75-79]. Faster sampling rates allow for the analysis of high frequency signals. The sampling rate must be at least double the highest frequency of interest in order to avoid aliasing. This is described by the Nyquist Theorem, which is shown below in EQ. 1.1 [73].

$$2f_{Max} \leq f_{Sampling} \quad \text{EQ. 1.1}$$

If this equation is true, then sampling is occurring fast enough to avoid aliasing. The highest frequency we are interested in is the upper limit of the gamma band, which we define as 50 Hz. It is also desirable to compare signal amplitudes to noise. One prominent source of noise is 60 Hz due to electrical activity. Therefore, we require a sampling rate of at least 120 Hz, although higher sampling rates can provide more accuracy.

Number of electrodes: Depending on the application and research group, the number of channels used usually ranges from about 4 to 256 [80]. For clinical applications, a low number of electrodes is usually utilized, while some research applications require much higher spatial resolution [80,81]. EEG research studies involving movement use a variety of number of electrodes, from about 5 to 128 [50,75,76,78,79]. Analysis of electrodes over the frontal cortex such as, Fz, the fronto-central region such as FCz, the frontal pole such as Fp1, the central brain region such as C3, Cz, and C4, the parieto-central region such as CP3 and CP4, the occipital lobe such as O1 and O2 are useful in understanding movement according to studies that have protocols similar to ours [50,76,77,79]. Of the literature we reviewed, the Cz electrode was analyzed in every study with a similar protocol to ours, making it especially interesting for our purposes.

Standard filters: In movement related research, typically a low and high pass filter are applied [50,75,78]. Sometimes, a notch filter is applied to remove 50/60 Hz noise as well

[78]. A high pass filter can be set to as low as about 0.1 Hz, and a low pass filter is usually (but not necessarily) set to a value under the line noise value (50 or 60 Hz) [50,61,75,78].

Electrode material: Reusable Ag|AgCl electrodes are a commonly used material in many EEG applications and provide the best results compared to electrodes made with other commercially available materials [69].

Electrode placement: Standard electrode locations such as 10/20, 10/10, or 10/5 placement are used in literature and clinical settings [84]. The first and second numbers refer to the percentages of the total scalp distance between each electrode (**Figure 1.9**) [82]. In a 10/20 system for example, distances between adjacent electrodes are either 10% or 20% of the total front-back or right-left distance. The standard 10/20 placement has been expanded upon in the 10/10 and 10/5 placements, which have more electrodes [82,83].

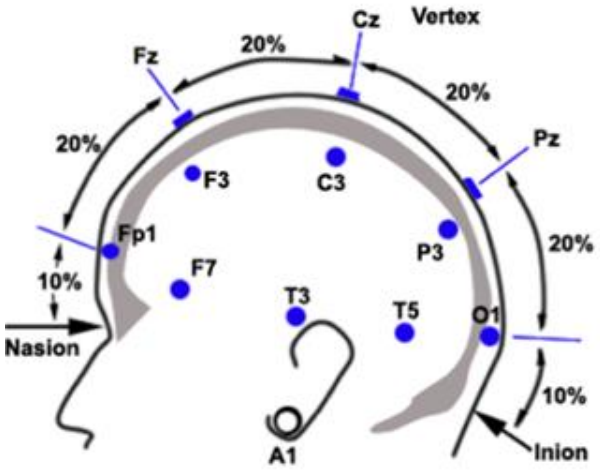

Figure 1.9: International 10/20 Electrode Placement System. Each letter preceding the numbers indicate the location of the brain on which the electrode is placed. The number refers to its side, with odd numbers being on the left of the brain, and even numbers on the right. Also shown are the placement of a reference electrode (A1), in this case, on the earlobe [84].

Impedance: Electrode impedance should be kept to a minimum to reduce noise and ensure important physiological signals are measured. It is recommended that impedance be kept under approximately 5-10kΩ [50,61,75,76,84].

1.2.3.4 EEG Montages

EEG can be visualized in different ways depending on which electrode is used as the negative input to the differential amplifier. For example, we can visualize EEG as a voltage differences between a scalp location of interest and either another scalp location, a scalp

potential average, a referential electrode, multiple referential electrodes, or an average of referential electrodes. Each of these electrodes summated with the negative of another electrode is called a channel. The F7-T7 channel shown in **Figure 1.10** may be referred to as the F7 electrode, but it is important to keep in mind that it is really a channel that represents the difference of two voltages over time [68].

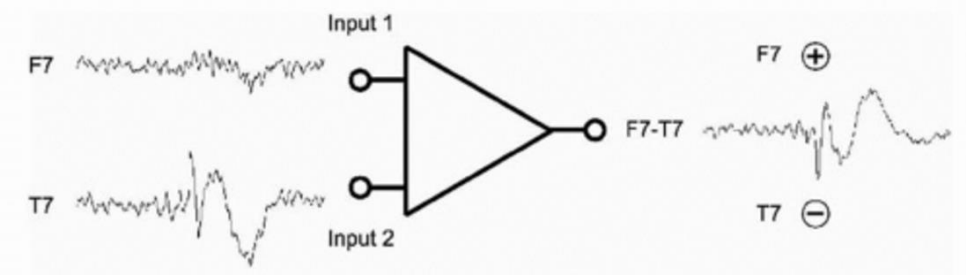

Figure 1.10: Differential Amplifier and Polarity Convention. Here, the electrode F7 is visualized as a voltage difference between F7 and T7. The difference between these readings is taken over time and amplified in an EEG device [85].

How the configuration of channels is laid out is referred to as a montage [68]. Selection of a montage is not purely a hardware decision. Many different montages can be analyzed using software by altering which electrode is used as the negative input to the differential amplifier (see **Figure 1.10**). One common type of montage is a bipolar montage, in which EEG can be visualized as an electrode of interest minus an adjacent electrode (**Figure 1.11**A and **Figure 1.11**B) [84]. This montage is beneficial, as noise that is present at one electrode can likely be canceled out by subtracting an adjacent electrode's signal. This also presents a problem, since important signals may be cancelled out if they occur at a similar amplitude in both electrodes in that channel [86]. There are two commonly used bipolar

montages, the anterior-posterior bipolar montage, and the transverse bipolar montage. For the anterior-posterior bipolar montage, the negative input to each channel is another electrode's voltage located posteriorly or anteriorly to it. For the transverse bipolar montage, the negative input to each channel is another electrode located transversely to it. The referential montage (**Figure 1.11**C) uses one common reference electrode for all channels [85]. This concept is commonly adapted from using a scalp location as the subtracted signal to using a mastoid or earlobe electrode as the negative input [87]. This avoids the problem of cancelling out important physiological signals, however, EMG or strong focal brain activity can corrupt signals if the reference is placed in a location that is particularly sensitive to muscular activity or prone to motion [86]. Sometimes multiple reference locations are used depending on the electrode being analyzed, or an average of multiple electrodes is used as a reference. Also used is an average of all scalp electrodes, or an average of signals from both earlobes or both mastoids [87,88]. The averaging of all other electrodes, called common average referencing, is useful for eliminating noise that is expected to be common though all electrodes, such as 60 Hz noise [88]. However, an outlier can strongly contribute to the averaged signal, so extra care must be taken to ensure impedances are kept low [88]. Another type of montage, the Laplacian montage (**Figure 1.11**D), subtracts an average of the surrounding electrodes' voltages. Its ability to localize focal activity easier than both referential and bipolar montages makes it a desirable setup, although it is worse at picking up generalized discharges [89].

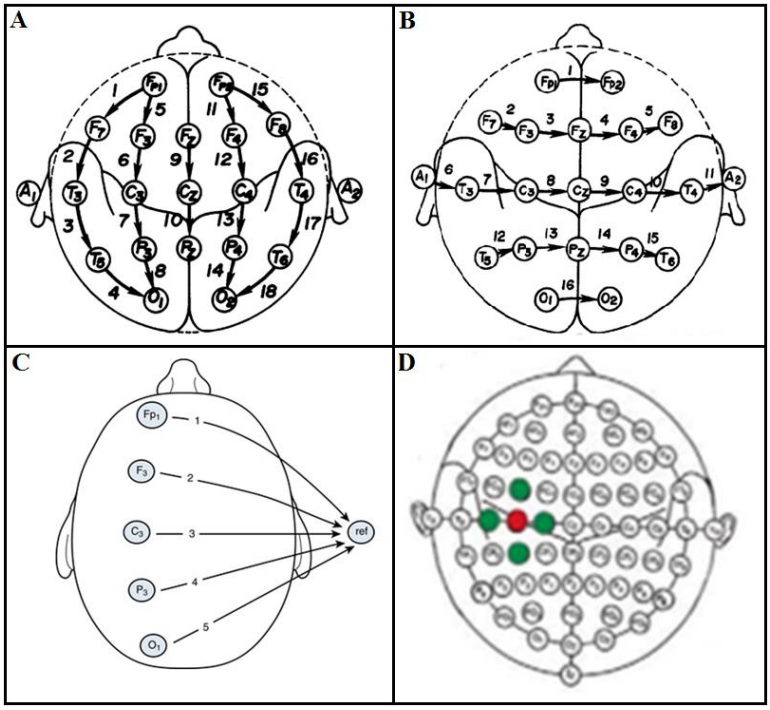

Figure 1.11: Montage Layouts. A. An anterior-posterior bipolar montage is shown [90]. B. Displayed here is a transverse bipolar montage.[90]. C. Each channel in a referential montage consists of an electrode of interest minus a reference electrode. [86]. D. A Laplacian montage is shown. Here the central electrode in red uses an average of the four surrounding green electrodes' signals [91].

1.3 DBS

DBS is a relatively recently developed technology that can provide a drastic improvement for symptomatic management of many movement disorder patients. Despite its mechanisms being poorly understood, DBS is a highly effective treatment of neurological and psychiatric disorders [92].

1.3.1 Overview

DBS as we know it today was first used in 1987 to treat tremor by targeting the motor thalamus [1,93]. In DBS for movement disorders, a lead is implanted in the brain, usually in the thalamus, STN, or the GPi depending on the patient's condition [94]. In PD patients, DBS is considered when other treatments become less effective, usually with the STN as the main target [16,24,25]. The GPi is the most common target for DBS for PGD [22,23]. PGD patients with DBS usually have bilateral electrodes placed in the GPi [95]. Since PGD often begins in childhood, GPi-DBS is an especially effective treatment for PGD because it can be reversed and somewhat easily revised, compared to brain lesioning [16]. GPi-DBS has proven much more effective for patients with PGD than for those with secondary dystonia [23]. Ventral intermediate (VIM) thalamic stimulation is the most common location for DBS to be implemented in ET patients [16,22]. Typically, unilateral VIM-DBS only treats limb tremor, however, bilateral stimulation has been shown to also improve head and voice tremor [16]. DBS stimulation locations for the disorders described here are shown below in **Figure 1.12**.

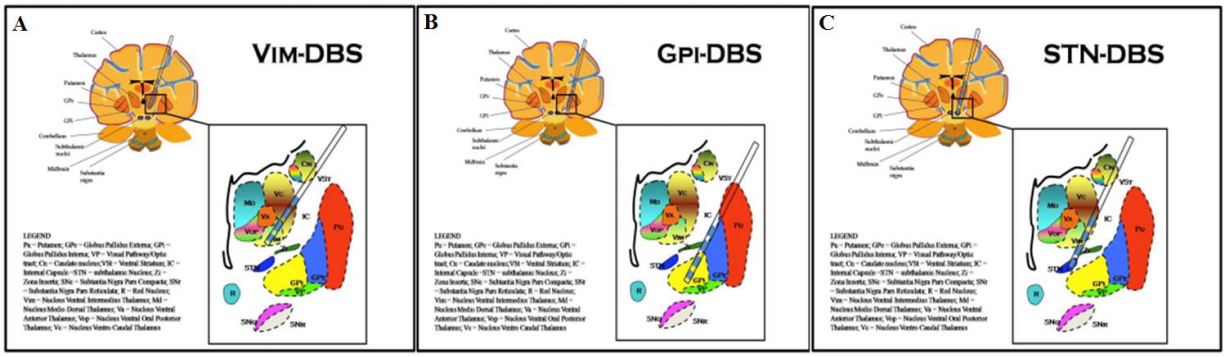

Figure 1.12: Common DBS Implantation Sites. A. VIM thalamus DBS electrode implantation for ET is shown. B. Here, GPi implantation of DBS electrode for PGD is displayed. C. STN-DBS for PD is shown [94].

1.3.2 Components

An implantable pulse generator (IPG) is implanted beneath the skin, usually in the upper portion of the chest but sometimes in the abdomen, and is connected by a subcutaneous wire to the DBS lead in the brain via an extension and cap that sits on the skull at the burr hole site (see **Figure 1.13**) [92,96].

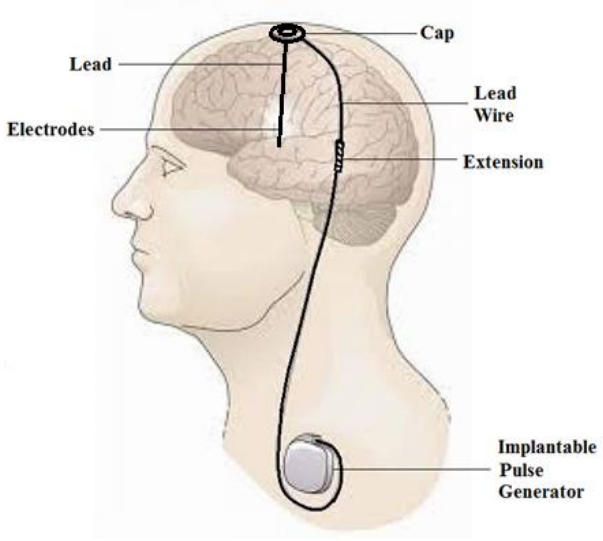

Figure 1.13: DBS Components. The major components of a DBS system are labeled [99].

The targeted location of electrode placement is in the neural circuit of the abnormal signal source for the disorder being treated [96]. IPG parameters such as voltage or current amplitude, frequency, and pulse width are programmed to deliver stimulation to the electrodes [24,97]. Most current DBS systems utilize a four or eight contact lead, however future electrodes will likely have more contacts to allow for more precise stimulation [98]. New lead technology allows for "current steering" which means that current will not have to be applied concentrically to the lead [97]. Electrodes are usually placed bilaterally, but are sometimes placed unilaterally due to clinical needs [96].

1.3.3 Mechanism

The exact mechanism behind DBS is not fully understood, however, it is thought that abnormal signals can effectively be altered by certain pulses if placed correctly in the brain [3]. In most applications, DBS has been found to be most effective at high frequencies (>130 Hz), but how this signal physiologically affects various brain structures is not known [96].

The "inhibition hypothesis" developed from the discovery that STN-DBS produced similar effects to STN-lesions and agrees with two models for movement disorders, the "firing rate model" and the "firing pattern model" (see section 1.1.1) [13,100]. In this way, DBS was thought to act as a reversible lesion because stimulation could be activated or turned off [96]. The inhibitory response can be explained by depolarization block, inactivation of voltage-gated currents, or activation of inhibitory afferents [13]. Movement disorder models disagree with the results of some therapies, such as the fact that thalamic lesions don't worsen bradykinesia or rigidity and that GPi-lesions don't lead to hyperkinetic disorders [101]. It was found that GPe-lesions worsen bradykinesia of parkinsonian monkeys, yet GPe-DBS improves bradykinesia, which goes against the "inhibition hypothesis" [102]. Still, it is possible that stimulation in one area results in the inhibition of a completely different structure [101].

Another hypothesis is the "excitation hypothesis" that states that DBS excites local neurons to produce its therapeutic effects, which fits well with the "firing rate model" of movement disorders [13]. This hypothesis suggests that despite stimulation possibly inhibiting neurons, the overall effect of the overall structure is that of excitation [101].

A recently proposed DBS mechanism suggest the "disruption hypothesis" in which the stimulation site cannot receive abnormal information due to the dissociation effect of DBS on output and input signals [13]. Another recent review proposes that there are several mechanisms for DBS depending on the stimulation site and the condition being treated [96].

Walker et al. found that DBS of the VIM and STN in patients with ET and PD, respectively, synchronizes cortical activity to its frequency or one of its subharmonics and that VIM-DBS and STN-DBS activates the cortex approximately one millisecond after stimulation [103,104]. This indicates that DBS may relieve motor disorder symptoms by synchronizing the motor network to a specific frequency.

There is much debate on which mechanism hypothesis is correct as there is conflicting evidence for each proposed view [13,96,101]. It is clear is that DBS has the potential to create a profound change in how we treat a host of neurological disorders. Even as it is so

poorly understood, DBS delivered to an appropriate site has been observed to relieve symptoms of movement disorders for many patients.

1.3.4 Reasoning for Using EEG for DBS Feedback

Currently, DBS is usually applied as a continuous high frequency stimulation at a set amplitude, pulse width, and frequency [96]. Other waveforms are currently being investigated in hopes of providing more effective treatments such as nonrectangular and biphasic pulses [97]. Due to the high cost, potential habituation of therapy over time, and side-effects, DBS must be improved in order to attain broader acceptance for treatment of the symptoms of movement disorders [24]. In PD for example, STN-DBS is most often operated continuously as an open-loop system delivering 1-4 volts at over 130 Hz with a pulse width of 60 μs [24,105]. These parameters lead to a short battery life and can result in habituation and side effects [24]. As DBS may become less effective in the years after implantation, parameter adjustment is needed which is expensive and a lack of standardized programming techniques can reduce performance [106].

DBS can theoretically be improved upon with the use of a closed-loop system that incorporates a feedback system, known as adaptive DBS (aDBS). The hope is that a functional feedback system will fix or at least better the shortcomings of modern DBS. Amplifier improvements have allowed for the possibility of recording very low voltage physiological signals while simultaneously delivering high frequency stimulation [56,107].

This has opened the possibility of using local field potentials (LFPs) as a feedback source. There are several articles that have performed small pilot studies looking into the use of DBS in a closed loop system [24,108,109,110]. One study in MPTP-treated monkeys suggests that using feedback from spikes in a single motor cortical neuron for controlling GPi-DBS was more effective at reducing motor symptoms than continuous open loop GPi-DBS [108]. Another study that applied STN-DBS to PD patients when their beta-LFP increased above a threshold level resulted in a 50% improvement of motor symptoms compared to continuous high-frequency DBS [109].

Several biomarkers can potentially be used as feedback sources for aDBS [111]. Electrocorticography potentials use electrodes that contact the cortex and have moderately high spatial resolution, but are invasive as they must penetrate the skull [105,111]. LFPs provide long term stability, can use the same recording system as the DBS, and provide high spatial resolution [105,109,111,112]. Action potential feedback from individual neurons is possible and would provide possibly the highest spatial resolution possible, however this would be very invasive and long term monitoring could lead to neural death, and therefore loss of signal [108,111]. Another potential feedback source is EMG signals [105,111]. ET has been successfully treated using aDBS with EMG as a feedback source, however, EMG is highly prone to noise and spatial resolution is poor [111,113]. Biochemical potentials, for example voltage changes related to adenosine neurotransmitter release in the brain, can also be used as a feedback source [111,114]. This would be very invasive, but have high spatial resolution and would likely be unaffected by external artifacts such as movement, talking, and thinking [105,111]. Lastly, EEG has potential to

be used to provide feedback for aDBS [104,105,111]. Noise and poor spatial resolution are issues, however the large amount of literature on the subject and its non-invasive nature make it an appropriate choice for further investigation [105,111]. Differences between EEG signals in early stage PD patients and healthy subjects have been shown during rest and while performing a tracing task [115,116]. This is promising for the possibility of using EEG as feedback for DBS, as it may be possible to alter DBS parameters during abnormal brain activity to alleviate movement disorder symptoms.

EEG has been successfully recorded during DBS with a handful of various post-processing techniques. It has been shown that during bipolar DBS, artifact due to stimulation is low and physiological signals can be easily collected [117]. However, in most cases, DBS is operated in a unipolar fashion, so the artifact amplitude can surpass EEG by a factor of 10 [118]. In past experiments, EEG has been recorded just as DBS is turned off to observe brain activity in response to stimulation. However, it is possible that the immediate after-effects of DBS on EEG aren't the same as activity during stimulation [118,119]. One simple technique to remove DBS artifact is to place a notch filter on the EEG data at the DBS frequency [120]. This technique is useful if the stimulation frequency isn't near a physiological frequency of interest. In addition, it is not necessarily true that recording of low frequency EEG bands is unaffected by high frequency stimulation, which is likely due to aliasing if appropriate filters are not used prior to data collection [118,120,121]. Aliasing leads to artifact being present in various frequencies given by the following equations:

$$f_{Alias} = \left| m f_{Sample} - n f_{Stimulation} \right|$$

$$\text{if } \left| m f_{Sample} - n f_{Stimulation} \right| \leq \frac{f_{Sample}}{2} \qquad \text{EQ. 1.2 [121]}$$

where m=1,2,3,…. & n= 1,2,3,…

In the case that DBS frequency is in the range of important EEG, more complicated methods are required. One method is implementing a Hampel filter which uses the fast Fourier Transform (FFT) and replaces outliers in the real and imaginary spectra with interpolated values [122]. Another technique is to use a matched filter based on EQ. 1.2 in which DBS artifact and alias frequencies can be identified and removed, although this has only been performed on generated data and not yet with EEG of DBS patients [121].

There is still much work to do before EEG can be used as an efficient clinical feedback source for DBS. EEG signals could potentially be a better feedback source than LFPs because this noninvasive measurement taken far from the DBS lead would avoid some stimulation artifact, decreasing the need for low pass filtering and thus allowing for a greater frequency band to be used as biomarkers in feedback control [123,124]. Another reason EEG could be a more desirable feedback source than from LFPs is that EEG's non-invasive nature allows us to more easily develop a suitable and safe measurement device. Use of feedback in aDBS from individual basal ganglia structure activity measured by LFPs could be coupled with feedback from EEG global field potentials to develop an effective closed-loop system [124].

1.4 OVERVIEW AND PROJECT AIMS

Movement disorders are a group of debilitating syndromes that are difficult to treat and usually progressive in nature. Once conservative treatment options are exhausted and lose effectiveness, surgery may be considered, especially for PD, ET and PGD. A common surgery used to treat the motor symptoms of these movement disorders is DBS, which is currently operated in an open-loop system. The effectiveness of DBS can potentially be improved with the use of a closed-loop system. One potential feedback source is scalp potential activity, measured with an EEG system.

The overall goal of the project was to characterize important features of healthy brain activity during tasks that are difficult for PD patients by analyzing EEG. This was done to establish a control group that can later be compared to patients with movement disorders. This will provide insight into the use of EEG as a feedback mechanism for DBS. This was an exploratory study that will aim to investigate a variety of analysis techniques, mainly by classifying the spectral characteristics of several tasks. Our protocol and analysis were based on a thorough literature search and we have attempted to take the advice of leaders in the field. Our first aim was to select an EEG system suitable for our research goals. Next, we aimed to develop a protocol that would test subjects during tasks that are difficult for movement disorder patients. In a future phase of this project, our protocol and data analysis techniques can be used in a study testing subjects with DBS for movement disorders, in order to compare EEG to healthy subjects. Our final aim was to characterize recorded data in a way that quantifies the EEG signals of interest. To our knowledge, there are no studies

investigating the use of EEG as a feedback mechanism for DBS although some mention this as a possibility [24,105,109-111].

CHAPTER 2: METHODS

After considering various EEG amplifiers and caps, we selected the system best suited to our research goals and cost restraints. We then developed a protocol aimed to measure EEG for future analysis. To characterize data, a few approaches were considered, all based on frequency analysis techniques. Statistical analysis was performed to determine if results were significant.

2.1 STUDY PARTICIPANTS

We wrote a protocol that recorded EEG of healthy subjects during tasks that are difficult for movement disorder patients. Our protocol (see **Appendix E**) was reviewed and approved by the Institutional Review Board at California Polytechnic State University San Luis Obispo (see **Appendix D**). Volunteers were emailed an informed consent form, W9 Form, protocol, and demographics form, and were warned about discomforts they may experience via email before the testing date (see **Appendices B**, **C**, **E**, **G**, and **H**). Eight subjects were recruited by our team, while three subjects participated as an assignment for an undergraduate psychology class (see **Appendix A**). In total, eleven subjects took part in the study, five men and six women (range: 18-23 years old $\{\mu: 21, \sigma: 1.5\}$). All participants were Cal Poly students that were offered monetary disbursement for their time (see **Appendices B** and **C**). Each subject was assigned an ID in order to maintain confidentiality. Each ID consisted of "EEG" followed by the year the testing took place (e.g. "2016"), followed by a letter. The letter for the first subject tested was "A" and each subsequent

volunteer's ID letter was labeled as the following letter (e.g. "A", "B", "C"…). Alertness level was self-assessed on a scale from one to ten by each participant depending on how alert they felt just prior to testing, with ten being most alert. Race, sex, age, and relevant health information was self-reported if the subject was comfortable sharing that information with us. After the data collection period, it was decided that handedness is an important piece of information as different sides of the brain may be more active during right or left body movement. In order to collect this information, an IRB extension was approved and subjects were emailed. All volunteers replied that they were right handed. Subject details are provided in **Table 2.1**.

Table 2.1: Subject Demographics and Health Information. Demographic and health information was collected before the start of the data collection period.

Subject	Age	Sex	Race	Handedness	Alertness Level (1-10)	Health Conditions
EEG2016A	19	M	Caucasian	R	8	None
EEG2016B	18	F	Caucasian	R	9	None
EEG2016C	18	M	Caucasian	R	8	Recovering from concussion
EEG2016D	21	M	Asian	R	10	None
EEG2016E	21	F	Asian	R	3	None
EEG2016F	19	F	Asian	R	9	None
EEG2016G	23	M	Caucasian	R	8	None
EEG2016H	21	F	Hispanic origin	R	6	None
EEG2016I	20	M	Hispanic origin	R	9	None
EEG2016J	22	F	Hispanic origin	R	9	None
EEG2016K	21	F	Caucasian/Asian	R	8	None

2.2 EEG RECORDINGS

Subjects sat in a comfortable chair in a dim room with their arms on the table in a way that allowed them to move freely through the duration of the tasks (see section 2.3). They were asked to avoid unnecessary movements, thinking about things other than the task at hand, and blinking during trials. Before beginning recordings, the subjects were trained on how to properly perform the task. Each subject performed all trials of all six tasks (see section 2.3). EEG cap setup duration was approximately 15-30 minutes per patient, while testing usually lasted 40-60 minutes.

A data acquisition software (EEG Studio, Mitsar Ltd, St. Petersburg, Russia) was used to visualize data on a personal computer. Both a high pass filter of 0.08 Hz and a low pass filter of 150 Hz were implemented on the digitized data. EEG was acquired using an amplification system (Mitsar-EEG 202-31, Mitsar Ltd, St. Petersburg, Russia) sampling at 500 Hz. This system met or exceeded the specifications listed in section 1.2.3.3 and was within our budget. A 32-channel cap (EasyCap, Brain Products GmbH, Munich, Germany) was used to hold electrodes in position. This cap included all 19 electrodes in the international 10/20 montage with additionally placed electrodes for more spatial resolution. Electrodes were also placed on the earlobes to serve as reference and ground electrodes (see **Figure 2.1**A). Some electrode cap locations did not align with the labels on the amplifier due to the products being purchased separately. A key is provided that describes which electrodes correspond to each amplifier position (**Figure 2.1**B and **Figure 2.1**C).

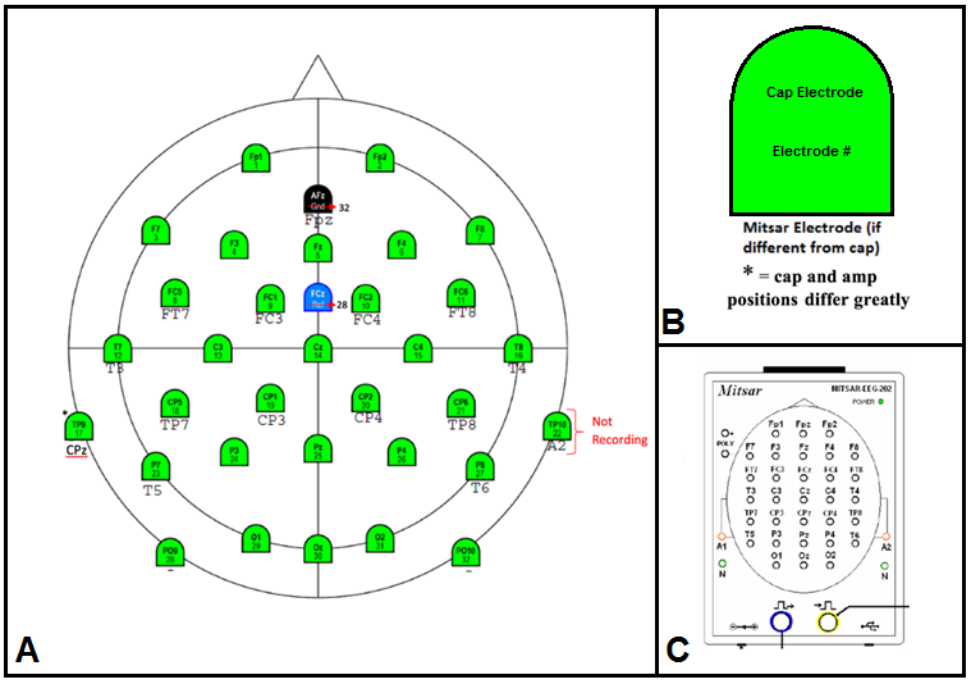

Figure 2.1: EEG Cap and Amplifier Locations. A. Scalp electrode locations are shown with the nose pointing up. B. A key is shown which provides information on each electrode. The top letter(s) and number(s) refer to the actual electrode position on the cap. The next entry corresponds to the labels placed on the electrode cap's rubber electrode holders. The number under some of the shapes corresponds to where the electrode wire plugs into the amplifier, in cases where the electrode and amplifier had different labels. C. The amplifier box used in our study is shown.

Before beginning recording, electrode impedance was measured using EEG Studio. Electrodes were adjusted with the goal of obtaining impedance below 10 kΩ. A screenshot was taken to record values (see **Figure 2.2**). In order to lower impedance values, a conductive gel (SuperVisc, Brain Products GmbH, Munich, Germany) was injected

between the scalp and electrode contact in order to maintain electrical continuity (see **Figure 2.3**). Recordings were started approximately five seconds before the task "go" cue and stopped about five seconds after the final action of interest for each trial. During testing, notes were taken to identify times when excess movement may have led to artifact (**Appendix F**).

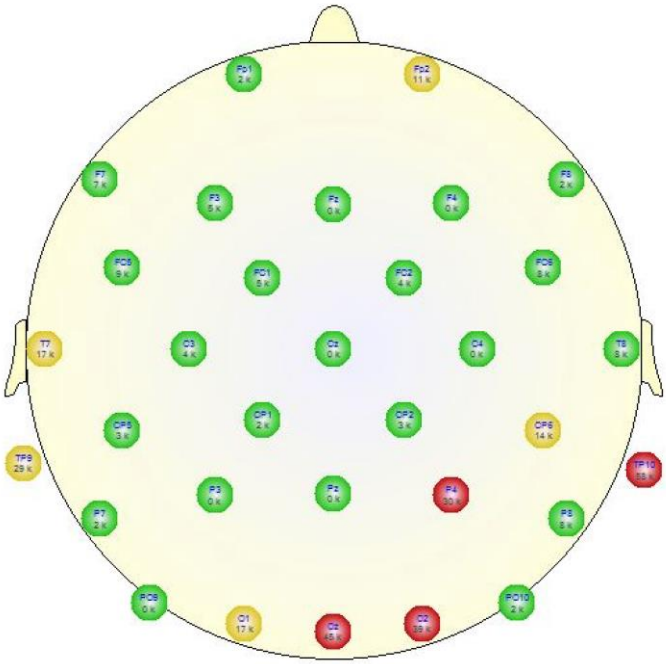

Figure 2.2: Impedance Map. Scalp locations are shown with their impedance levels, which was measured prior to testing. Here, "good" electrodes were shown as green, meaning their impedance was below 10 kΩ. "Bad" electrodes labeled in red had an impedance over 30 kΩ, while electrodes in between these values were labeled in yellow.

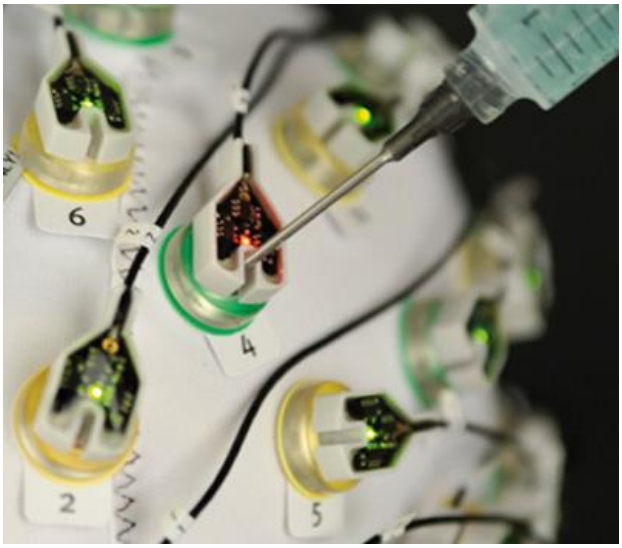

Figure 2.3: ActiCap Active Electrodes Being Injected with Conductive Gel. Electrodes used in this study have LEDs that can be activated to show impedance levels. Here, an electrode with poor electrical continuity was injected with conductive gel in order to lower impedance [125].

The full system used in our study consisted of an electrode cap with inserted electrodes injected with conductive gel, an analog to digital converter and amplifier system, and a laptop. Additional materials for the 6 tasks included a writing utensil, white computer paper, plastic cups for water sipping, and a chair. The experimental setup can be seen in **Figure 2.4**.

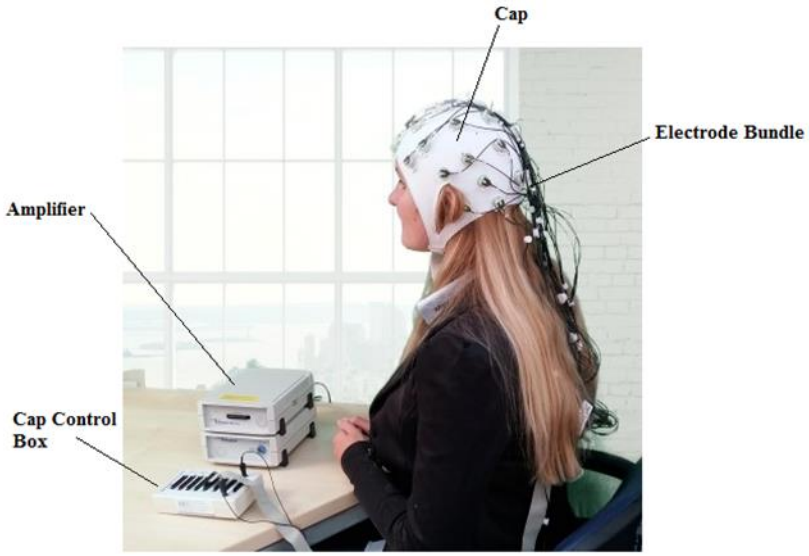

Figure 2.4. EEG System Components. Our EEG experimental setup consisted of an electrode cap, electrodes that plug into the cap and maintain electrical continuity using conductive gel, an amplifier, a cap control box that relays information from electrodes to the amplifier, and a laptop to visualize signals (not shown) [126].

2.3 EXPERIMENTAL TASKS

Our tasks were designed to collect EEG on healthy subjects performing tasks that are difficult for movement disorder patients. This was done with the intent of establishing a baseline for future comparison to patients with movement disorders. This preliminary work can potentially lead to a DBS feedback system using EEG biomarkers. Specific tasks included the pencil-pickup task, writing/drawing task, swallow task, standing task, postural tremor task, and bradykinesia task, which are described below.

2.3.1 Pencil-Pickup Task

In this task, subjects were instructed to place their hands on the table comfortably in front of them. At arm's length, a writing utensil was placed on the table, which the participant reached for upon a "go" cue (**Figure 2.5**A), grabbed (**Figure 2.5**B), lifted about six inches off the table (**Figure 2.5**C), and set back down (**Figure 2.5**D), before returning their hands to a resting position in front of them (**Figure 2.5**E).

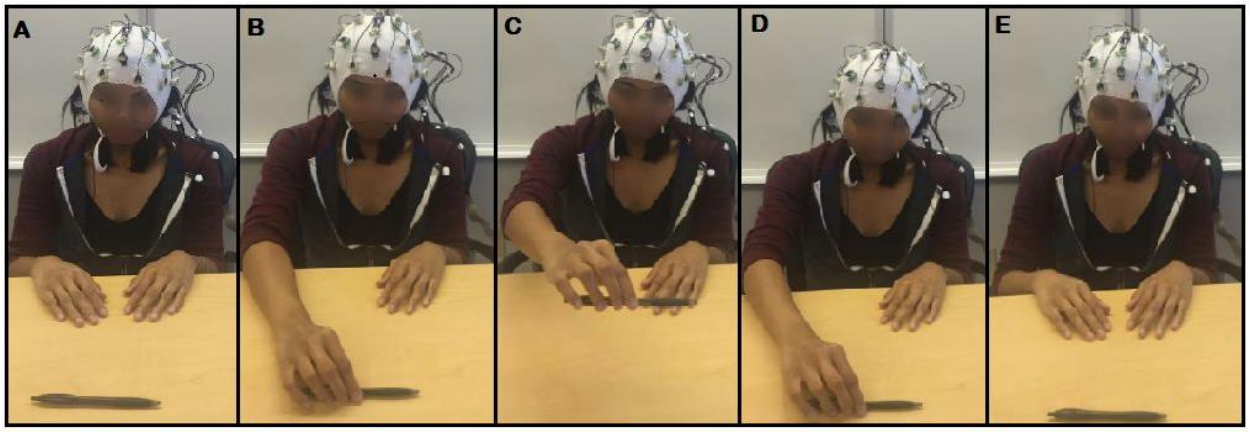

Figure 2.5: Pencil-Pickup Task. A. The pencil-pickup task began with the subject seated comfortably with their hands on the table. B. The subject then reached for and grabbed the writing utensil. C. They then lifted the writing utensil. D. Next, the volunteer set the utensil down. E. Lastly, the subject returned to a comfortable resting position.

This task was repeated five times with approximately twenty seconds between each trial. Data was marked when the subject began reaching, picked up the pencil, set it down, and

stopped moving to conclude the trial. Many movement disorder patients would experience symptoms during this task, for example, tremor and/or bradykinesia.

2.3.2 Writing/Drawing Task

The writing/drawing task consisted of two parts, a 30 second writing exercise in which the subject repeatedly wrote their name on a piece of paper with a writing utensil (**Figure 2.6**A), followed by a 10 second drawing exercise that required drawing an outward circling spiral (**Figure 2.6**B).

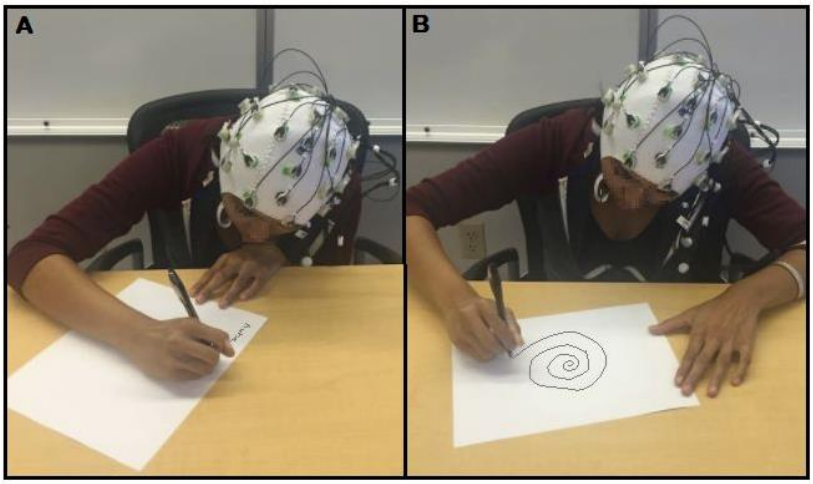

Figure 2.6: Writing/Drawing Task. A. The subject repeatedly wrote their name for 30 seconds. B. They then drew an outward circling spiral for 10 seconds.

Subjects were reminded to only use muscles involved in moving the wrist to avoid excess artifact. This task was designed this way because of the difficulty that movement disorder patients often have while writing. Additionally, there is evidence that the use of a spiral test can screen for movement disorders [127]. Times were marked when writing or drawing began and after the corresponding pre-determined exercise duration. These two exercises were repeated three times each for a total of six trials with approximately twenty seconds between each trial.

2.3.3 Swallow Task

Dysphagia, or a difficulty in swallowing, is a common symptom of movement disorders such as PD [128]. In order to characterize voluntary swallowing, we instructed study participants to raise a cup of water to their mouth, take a sip, set the cup down, and wait for our "go" cue to swallow the water (**Figure 2.7**).

Figure 2.7: Swallow Task. Here, the subject raised a water bottle to their mouth after the "go" cue.

Time markers were placed when the water contacted their mouth and then again when we visually observed them swallowing. Enough time was given for them to set the cup on the table and return to a comfortable position before initiating the "go" cue, in order to avoid excess noise due to motion artifact. This process was repeated five times with approximately twenty seconds between each trial. Results from this task should be taken with care as muscles involved in swallowing were expected to potentially produce EMG artifact in EEG electrodes, although most past swallowing EEG studies did not consider artifact removal [129].

2.3.4 Standing Task

Movement disorders can make the act of standing up from a chair difficult. The five-times-sit-to-stand time is a clinical test that evaluates PD patients' risk of falling [132]. We attempted to characterize this activity that is difficult for movement disorder patients by recording EEG while the participant stood slowly from the sitting position. The task began while the subject was seated comfortably in a chair with their hands in their lap (**Figure 2.8**A). When prompted by the "go" cue, the subject slowly stood to a standing position with their hands by their side (**Figure 2.8**B). Motion artifact was a major concern in this task, so an effort was made to keep cables as still as possible and that the participant moved slowly and steadily. This sit-to-stand exercise was performed five times with approximately twenty seconds between each trial.

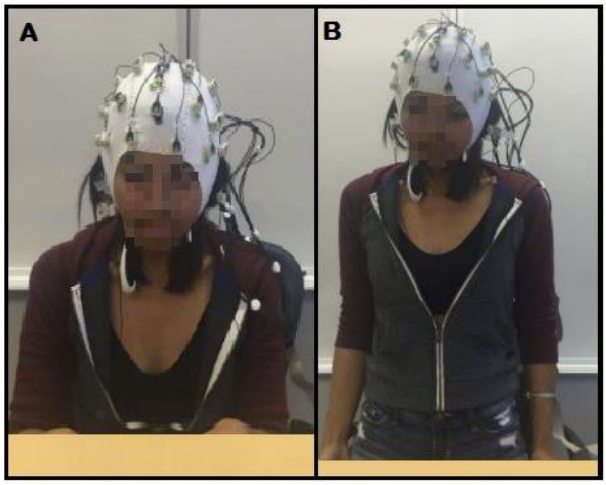

Figure 2.8: Standing Task. A. The subject began the task sitting comfortably in a chair. B. The subject stood slowly when prompted to.

2.3.5 Postural Tremor Task

Postural tremor, a cardinal symptom of PD that is often present in other movement disorders, is tremor that is present while maintaining a position against gravity [133]. In this task, subjects were asked to hold their dominant arm extended parallel to the ground palm up (**Figure 2.9**A) and rotate their hand 180° at approximately one cycle per two seconds (**Figure 2.9**B). This was repeated for approximately ten seconds, and then this trial was repeated five times with approximately twenty seconds between each trial. Times were marked at every 180° rotation.

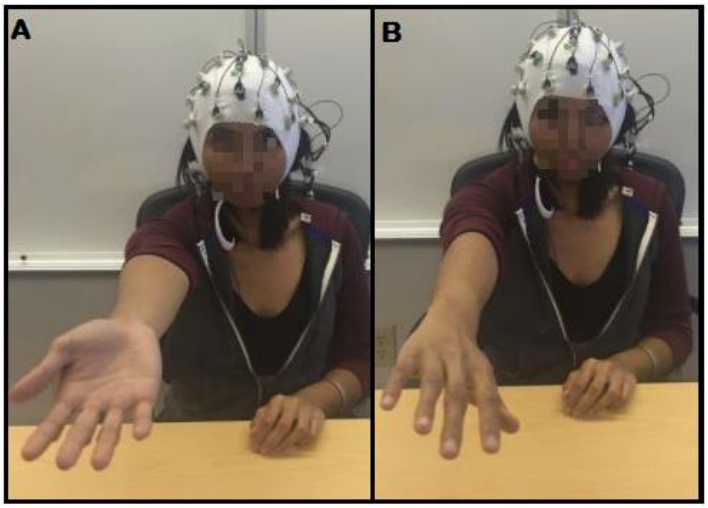

Figure 2.9: Postural Tremor Task. A. The task began with the subject holding their hand palm facing up and their arm extended. B. The volunteer then slowly rotated their hand 180° until their palm faced down. This was repeated for about 10 seconds.

2.3.6 Bradykinesia Task

Bradykinesia is another common symptom of movement disorders in which patients experience difficulty or slowness of movement [5]. This task was developed to analyze EEG during a time when patients may experience bradykinesia, during fine motor performance of the dominant hand's fingers. We instructed subjects to have their dominant hand placed comfortably on the table in front of them while seated with their pointer finger and thumb outstretched (**Figure 2.10**A). At approximately 1 Hz, participants touched their pointer finger and thumb together, while keeping the rest of their body still (**Figure 2.10**B).

This process was repeated five times with approximately twenty seconds between each trial. Times were marked at every time their finger and thumb made contact.

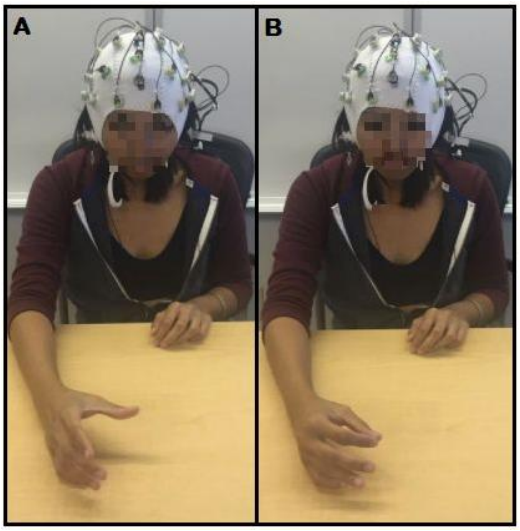

Figure 2.10: Bradykinesia Task. A. The subject sat in a chair with their hand on the table and their pointer finger and thumb stretched away from each other. B. They then touched their pointer finger and thumb together slowly. This process was repeated for about 10 seconds.

2.4 ANALYSIS

All EEG data were processed using MATLAB R2016a (The Mathworks, Inc., Natick, MA, USA) and custom-made MATLAB scripts or functions in EEGLAB, a widely used open-source software toolbox for EEG signal processing. As discussed in section 1.2.3.1, alpha and beta waves are likely the most important frequencies for this study. However, as this is an exploratory experiment, we also considered lower and higher frequencies, from the delta band to the gamma band (1.5 to 50 Hz).

2.4.1 TRP Changes

Our protocol consisted of the following:

1. A two-minute-long baseline period.
2. Five trials of the pencil-pickup task.
3. Three trials of the writing/drawing task.
4. Five trials of the standing task.
5. A minute-long baseline period.

6. Five trials of the postural tremor task.

7. Five trials of the bradykinesia task.

8. A minute-long baseline period.

The baselines were collected while the subject sat still and was asked to remain relaxed without concentrating on anything and to avoid moving and excess amounts of blinking. . The cleanest portion from any baseline, defined as the section with the least amount of artifact as determined by visual inspection of raw data, was selected to be used as the TRP change baseline to be subtracted from task power. For each task, all trials across all subjects were shortened to the length of the shortest trial time. For example, all pencil-pickup trials, which ranged from about 3.3-4.5 seconds depending on the subject and trial, were cut to 3.3 seconds in order to make accurate comparisons. For each trial, an equal length period from the baseline period was also selected to create a set of trials and trial-matched baselines.

The analysis period for the pencil-pickup task started when the subject began reaching for the writing utensil and ended when they were back in a resting position after setting it down. For TRP analysis, the writing/drawing task began when the subject started moving their writing utensil and ended after the predetermined trial time length of 30 seconds for the name writing exercise and 10 seconds for the spiral exercise. For the swallow task, we analyzed EEG from 0.25 seconds before the swallowing movement was visually detected

up until the swallowing motion itself. The stand task analysis period was the entire time the subject was moving from the seated position to completely standing. Both the postural tremor and bradykinesia task analyses began when the subject started moving after the "go" cue and ended after the predetermined trial time length of 10 seconds.

A custom MATLAB script converted raw EEG into the frequency domain by the FFT. Parameters related to this conversion are shown in **Table 2.2**.

Table 2.2: FFT Parameters. For each task, various parameters are listed. Included is the number of time points used in analysis of each trial, its corresponding time length, the number of FFT sample points derived from the time sample points, and the frequency bin width of the FFT results.

	Number of Time Sample Points	Time Length (s)	Number of FFT Sample Points	Frequency Bin Width (Hz)
Pencil-Pickup Task	1757	3.51	880	0.28
Writing/Drawing Task	4500	9.00	2251	0.11
Swallowing Task	250	0.500	126	2.0
Stand Task	424	0.848	213	1.18
Postural Tremor Task	4074	8.15	2038	0.13
Bradykinesia Task	4325	8.65	2164	0.12

Each trial and trial-matched baseline period was normalized by dividing its power spectra by the total power from the beginning of the theta band to the end of the gamma band (4-50 Hz). This accounted for differences in impedance and shifting electrodes during testing.

For all trials in a given task and subject, the set of trial-matched baseline periods were averaged (shown by the solid red line in **Figure 2.11**).

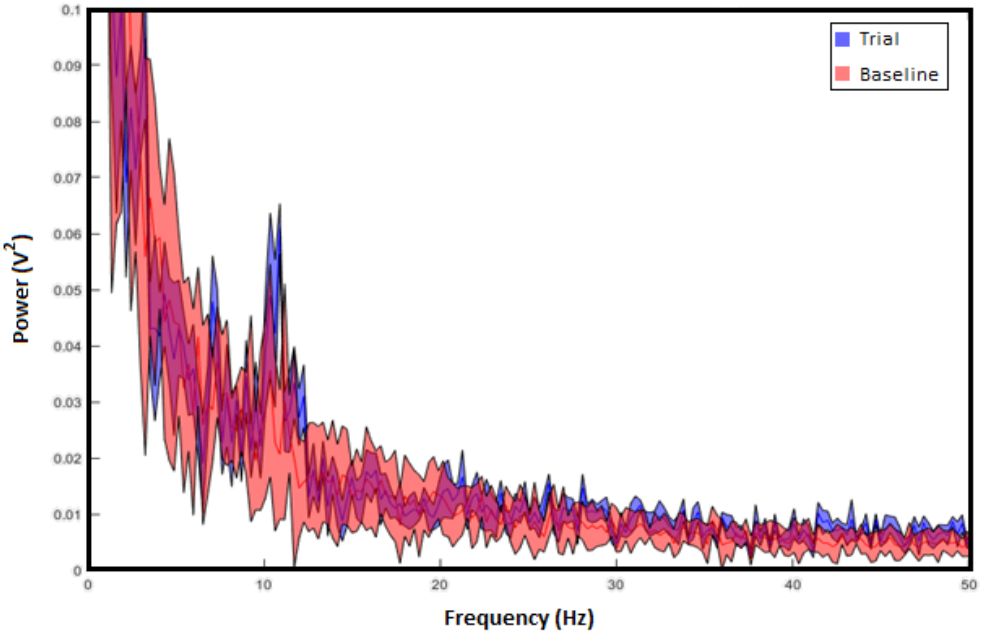

Figure 2.11: Power Spectra Curve. Solid blue line represents the average power spectra of the pencil-pickup task for one subject at the Cz electrode. The solid red line represents the average power spectra of the baseline period samples, which was subtracted from each trial power value to obtain TRP change for a given frequency band. The shaded areas represent the standard error of the mean about each solid line.

This baseline average curve was subtracted from each trial power spectra to produce a set of power spectra that represented the change from baseline to task. For each frequency band of this difference curve, the integral was taken to produce TRP change for each trial in a subject. For a subject, these trial TRP changes were averaged for each task and frequency band. In this way, each subject was treated as a single data point, instead of

treating each trial as an individual sample point. In each task, channel, and frequency band, all subjects' TRP was averaged.

On this data, thirty one-way unbalanced ANOVAs were run to compare the interaction between TRP change in each frequency band across nine electrodes most likely to be related to movement (Cz, C3, C4, FCz, FC1, FC2, Fz, F3, and F4). Each ANOVA focused on the TRP change relative to a baseline period for a specific task (six total) and frequency band (five total) across the nine electrodes of interest. Initially, we intended to include an analysis of types of task and frequency bands, along with electrodes in the ANOVA, however we later deemed these variables unfit to compare. The different tasks were not compared to each other because they include different amounts of data points in each trial due to the differing lengths of time the tasks were run for. Comparing frequency bands to each other was also avoided due to the presence of 1/f noise in EEG. Looking across electrodes within each frequency band, a threshold p-value of 0.0014 or less was necessary to declare significance. This value was calculated by dividing a standard p-value of 0.05 by a Bonferroni correction of 36, as there are 36 comparisons being made between all electrodes in a frequency band.

Comparing the TRP change at each electrode to zero for all trials allows us to see if that individual electrode measured a significant change in TRP from the baseline period. This analysis was done in MATLAB using the "ttest" function which ran one-sample t-tests. For these comparisons, we use a threshold p-value of 0.0056 or less. This was obtained by

dividing a standard p-value of 0.05 by a Bonferroni correction of 9, as there are 9 electrodes being analyzed individually.

2.4.2 Spectrograms

A spectrogram was created for each trial using the EEGLAB function “pop_newtimef”. This tool allows for visualizing power changes across time and different frequencies. This technique gives similar results to power spectra and TRP changes; however, we also gain temporal information. Raw data was converted to the frequency domain by the FFT and then compared to a baseline period just before the trial began. At each time and frequency, power levels were compared to a bootstrapped baseline with a bootstrap significance level of 0.01. This bootstrapping method constructs a surrogate baseline data distribution by averaging spectrogram data from randomly selected time windows within the selected baseline period [63]. This distribution provides the percentiles that are used for significance thresholds [63]. Each spectrogram was made with 400 time sample points to maintain consistent resolution across trials, 200 randomly selected time windows for the bootstrapped baseline, and a pad ratio of two.

2.4.3 Topographical Maps

Another technique used to visualize EEG data is the use of topographical maps, which display power levels at various frequencies across a spatial map of the head. By generating topographical maps during a trial, we can see which areas of the brain are most active for that task. This tool was also helpful in identifying eye blink artifact, which led to cleaner baseline data in our TRP analysis.

For each trial, topographical maps were created that displayed power maps at approximately the middle of every frequency band of interest. This was accomplished by implementing an adapted version of the "spectopo" EEGLAB function in MATLAB. This function computes a power spectrum for each channel by using the FFT on raw EEG. Power values at each frequency band midpoint were used to create a distribution of power values across the scalp. Often times, there are channels with poor impedance that would interfere with topographical maps if not addressed. This was addressed by replacing bad channels with EEG signals from a random channel that has low impedance [134]. A custom script identified channels with poor impedance by comparing the amount of power from 8-30 Hz (the beginning of the alpha band to the end of the beta band) to the amount of power from 58-62 Hz (line noise). Channels with poor impedance were replaced with better channels if they were identified as bad by the following equations:

$$if \quad \frac{Power_{58-62\ Hz}}{Power_{8-30\ Hz}} \geq 0.7, \ then\ channel\ is\ bad \quad \text{EQ. 2.1}$$

$$if \quad \frac{Power_{58-62\ Hz}}{Power_{8-30\ Hz}} < 0.7, \ then\ channel\ is\ good \quad \text{EQ. 2.2}$$

Previously recorded EEG coupled with impedance maps allowed us to determine what a sufficient cutoff level would be for excluding electrodes. This cutoff ratio was set to 0.7.

CHAPTER 3: RESULTS

Performing various analysis techniques allowed us to characterize EEG during our various tasks of interest. Our major findings were related to TRP changes, while spectrograms and topographical maps helped to validate our TRP change results.

3.1 TRP CHANGES

ANOVA results show that we did not reject the null hypothesis that there is no difference between different electrodes' TRP values for any task comparison. Nevertheless, there was significant TRD compared to baseline during the bradykinesia task in the delta band at electrode F4, during the pencil-pickup task in the alpha band at electrode C3, and during the swallow task in the beta band at electrode F3. Two subjects had poor continuity for some electrodes analyzed (Cz, C4, FC2, and F4). Their data was omitted from TRP change analysis.

First we analyzed the delta band across our nine electrodes of interest and six tasks. During the pencil-pickup task, little change was observed at any electrode, and power increases or decreases was not consistent across electrodes. ERD was observed at all electrodes during the writing/drawing task. During the swallow task, we found high amplitude task-related

synchronization (TRS) across all electrodes. During the stand task, we saw TRD or a very slight power increase in all electrodes. Similar results were found for the postural tremor task. All electrodes showed TRD during the bradykinesia task. The only significant result in the delta band was TRD during the bradykinesia task at electrode F4.

Next we analyzed the theta band across our nine electrodes of interest and six tasks. During the pencil-pickup task, power increase or decrease was not consistent across electrodes. During the writing/drawing task, swallow task, and stand task, TRD were observed at almost every electrode. During the postural tremor task, ERS was found at all electrodes besides Cz and F4. Similar results were found during the bradykinesia task, however power change at most electrodes was smaller in amplitude. All data analyzed in this band had very high variance and no significant results were found.

Alpha TRP was also analyzed across nine electrodes. TRS was only found in some electrodes located centrally (electrodes ending in "z") or on the right side of the brain (electrodes ending in even numbers), while electrodes over the left side of the brain (electrodes ending in odd numbers) generally experienced more TRD during the bradykinesia task. All other tasks only experienced TRD at every electrode of interest. The tasks which experienced the strongest amplitude power changes were the pencil-pickup task and the writing/drawing task. The only significant result found was TRD during the pencil-pickup task at electrode C3.

Next, we analyzed beta TRP change. TRD occurred at every electrode during the pencil-pickup task and all electrodes besides FC2 during the swallow task. TRS was observed at all electrodes during the writing/drawing task and all electrodes besides F4 for the stand task. Postural tremor and bradykinesia tasks were difficult to characterize in the beta band as amplitudes were relatively low and no trends were found across electrodes. Significant TRD decrease compared to baseline was found during the swallow task at electrode F3.

In the gamma band, the pencil-pickup task, writing/drawing task, swallow task, and stand task all experienced TRS at every electrode of interest, with the swallow task having the highest amplitude at each electrode. For both the postural tremor and bradykinesia tasks, there was little power change from baseline. No significant results were found in the gamma band.

3.2 SPECTROGRAMS

A tremendous amount of information is generated with each spectrogram; however, it is incredibly difficult to sift through results. Analyzing each frequency band of every subject's trials for our nine electrodes of interest means sifting through over 3000 graphs. Therefore, in this study, we rely on spectrograms only to validate TRP findings. The three

significant results from the TRP analysis were validated by the spectrograms produced, as they did not point to any external noise sources that may have caused a false positive.

3.3 TOPOGRAPHICAL MAPS

Like spectrograms, topographical maps are visually analyzed trial-by-trial, making them useful as a qualitative tool in this study. Topographical maps were produced to visualize important electrodes at various frequencies. This technique was used to show that one result obtained in this study was likely due to artifact (see section 4).

CHAPTER 4: DISCUSSION

Our significant findings include TRD during the bradykinesia task in the delta band at electrode F4, during the pencil-pickup task in the alpha band at electrode C3, and during the swallow task in the beta band at electrode F3. Due to a low sample size of this study, some results may become significant with more data collection.

Results for the bradykinesia task indicated that the delta band was suppressed during finger movement exercises at the F4 electrode. Similar results in literature, however, were not found.. It is unlikely that this is a new finding in this field, as similar movements during EEG are fairly widely researched [50-52]. One potential reason why this finding did not align with literature is the presence of artifact. It is possible that eye blinks contaminated EEG to a degree that we obtained a false positive result. Eye blinks are known to have a great effect on the delta band, so our results should be interpreted with caution [130]. Analyzing topographical maps at the midpoint of the delta band at electrode F4 shows approximately 13% of the trials appearing to be contaminated by ocular artifact. This noise source is not eliminated through our custom script, which is designed to rid of line noise and poor continuity. An example of this artifact is shown in **Figure 4.1**.

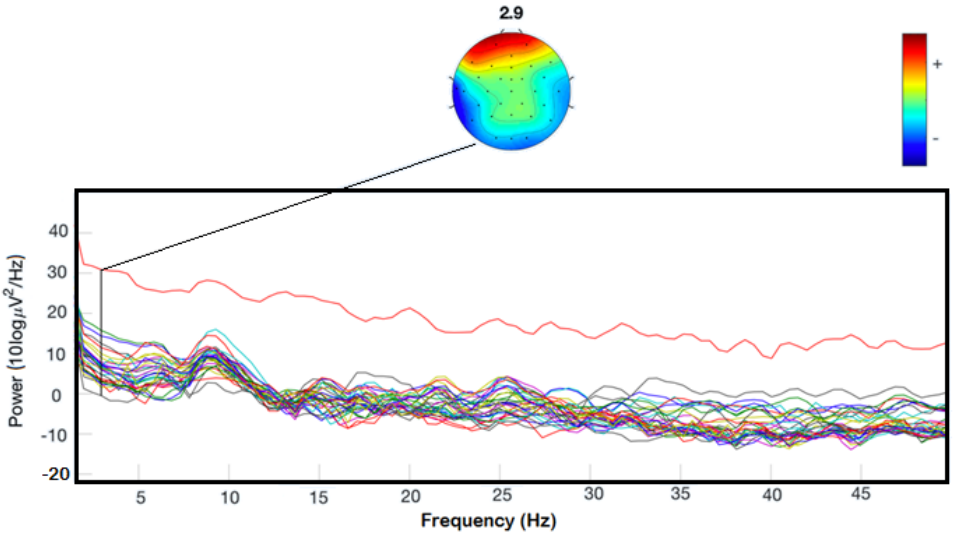

Figure 4.1: Blinking Artifact Present in Topographical Map. Ocular artifact can be detected by the presence of extreme power values at the front of the head, nearest to the eyes.

CHAPTER 5: CONCLUSION

First, an extensive literature review gave us insight needed to properly carry out our study. Literature also led us to select an EEG system capable of acquiring data suitable to our needs. We gained IRB approval to execute our protocol, which was performed on eleven healthy students at Cal Poly. After gathering data, we began the data analysis phase of the project. Many analysis techniques were investigated, and one of the most powerful for our purposes was determined to be TRP change relative to baseline. This analysis was augmented with other tools such as spectrograms and topographical plots. These tools helped lead us to our significant results, that we found ERD in the delta band at the F4 electrode during the bradykinesia task, ERD at the C3 electrode in the alpha band during a pencil-pickup task, and ERD at the F3 electrode in the beta band during the swallowing task. These findings were expected other than delta band ERD during the bradykinesia task, which was likely due to ocular artifact. If results found here in healthy subjects differ from results of movement disorder patients, we will gain more insight into the possibility of using EEG-derived biomarkers as a feedback source in aDBS.

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APPENDICES

APPENDIX A: PSYCHOLOGY RUBRIC

PSY 202 WRITING ASSIGNMENT

PROMPT FOR THE STUDY:

How Electrical Signals in the Brain Impact Movement

The question below relates to the study *How Electrical Signals in the Brain Impact Movement.* It is possible that the question may be only indirectly related to your experience in the study.

Your paper must be 2–3 pages long (not counting the title page), printed (in 12-point font), double spaced, with one-inch margins and a title page that includes the following…

- the title of your paper,
- your first and last name,
- the number of your discussion section,
- your Cal Poly e-mail address,
- last two digits of your EMPL ID,
- the date you are actually turning in your paper, and
- the question below fully typed out.

For full credit, the text on the second page must take up at least ¾ of the page. Anything less and your paper will not be considered the proper length. You might wish to place a backup copy of your paper on the course PolyLearn site.

Your essay may express your own ideas on the question, and you may use personal examples to support your ideas. But a largely narrative (story-oriented) paper limits development and will be graded accordingly. Keep in mind that your grade on the essay will be based not only on your ideas but also on how well you organize, develop, express, and understand the topic. Be sure to review the grading criteria on the PSY 202 web site.

Background:

Your textbook discusses brain-mapping techniques in chapter four and direct brain intervention in chapter twelve. Review this material and use it to help you answer the questions below.

Question:

As you have learned, neurons are little electrochemical generators, and they support all brain function from the production of physical movement to abstract thought. Describe the two techniques of deep brain stimulation (DBS) and transcranial magnetic stimulation (TMS). What are their similarities and differences? In what clinical ways are these techniques used? What are your thoughts about using a procedure or drug in a manner other than its originally intended/studied application? Does potential benefit always justify risk?

APPENDIX B: INFORMED CONSENT FORM

Informed Consent Form

INFORMED CONSENT TO PARTICIPATE IN A RESEARCH PROJECT, "Electroencephalography Measurement During Motor Tasks"

A research project studying brain signals in healthy subjects is being conducted by Adam Aslam, Charlie Aylward, and Sara Wier, students in the Department of Biomedical Engineering at Cal Poly, San Luis Obispo, under the supervision of Dr. Kristen Cardinal. The purpose of the study is to measure brain activity in healthy individuals performing daily motor tasks, in order to observe relationships between brain activity and movement.

You are being asked to take part in this study by allowing the researchers listed above to record brain signals while you perform daily tasks such as lifting a pencil or holding your arms in certain positions. You will be asked to wear an electroencephalography (EEG) recording cap, which is placed on your head like a helmet and is connected by wires to recording equipment in order to measure brain activity. The EEG merely collects the electrical activity produced by your brain and then displays this on output devices. Conducting gel will be added between the cap and your hair or scalp to improve signal quality. Your participation will take approximately 1 to 1 ½ hours. Please be aware that you are not required to participate in this research and you may discontinue your participation at any time without penalty.

The possible risks associated with participation in this study include minor discomfort due to the electrode cap or the conducting gel, and a very minor risk of low voltage electric shock due to static electricity. If you should experience any discomfort or emotional distress, please be aware that you may contact the Cal Poly Health Center at (805) 756-1211 or Cal Poly Counseling Services at (805) 756-2511 at any time for assistance.

Your confidentiality will be protected by maintaining restricted access to each subject's personal information and study data. Also, an anonymous patient identifier will be used in place of your name or any other identifying information in study documents. Your name will not be used in any reports of this research without your permission.

Your participation may help contribute to an understanding of brain function. In addition, you will be offered a $40 gift card at the end of the data collection period.

If you have questions regarding this study, please feel free to contact Charlie Aylward, Adam Aslam, or Sara Wier at eegcalpoly@gmail.com or at (805) 756-2675. If you have concerns regarding the manner in which the study is conducted, you may contact Dr. Michael Black, Chair of the Cal Poly Human Subjects Committee, at (805) 756-2894, mblack@calpoly.edu, or Dr. Dean Wendt, Dean of Research, at (805) 756-1508, dwendt@calpoly.edu.

If you agree to voluntarily participate in this research project as described, please indicate your agreement by signing below. Please keep one copy of this form for your reference, and thank you for your participation in this research.

_____ _____

Signature of Volunteer Date

_____ _____

Signature of Researcher Date

APPENDIX C: W9 TAX FORM

Form **W-9**
(Rev. December 2014)
Department of the Treasury
Internal Revenue Service

Request for Taxpayer Identification Number and Certification

Give Form to the requester. Do not send to the IRS.

Print or type See **Specific Instructions** on page 2.

1 Name (as shown on your income tax return). Name is required on this line; do not leave this line blank.

2 Business name/disregarded entity name, if different from above

3 Check appropriate box for federal tax classification; check only **one** of the following seven boxes:

☐ Individual/sole proprietor or single-member LLC ☐ C Corporation ☐ S Corporation ☐ Partnership ☐ Trust/estate

☐ Limited liability company. Enter the tax classification (C=C corporation, S=S corporation, P=partnership) ▶ _____

Note. For a single-member LLC that is disregarded, do not check LLC; check the appropriate box in the line above for the tax classification of the single-member owner.

☐ Other (see instructions) ▶

4 Exemptions (codes apply only to certain entities, not individuals; see instructions on page 3):

Exempt payee code (if any) _____

Exemption from FATCA reporting code (if any) _____

(Applies to accounts maintained outside the U.S.)

5 Address (number, street, and apt. or suite no.)

Requester's name and address (optional)

6 City, state, and ZIP code

7 List account number(s) here (optional)

Part I Taxpayer Identification Number (TIN)

Enter your TIN in the appropriate box. The TIN provided must match the name given on line 1 to avoid backup withholding. For individuals, this is generally your social security number (SSN). However, for a resident alien, sole proprietor, or disregarded entity, see the Part I instructions on page 3. For other entities, it is your employer identification number (EIN). If you do not have a number, see *How to get a TIN* on page 3.

Note. If the account is in more than one name, see the instructions for line 1 and the chart on page 4 for guidelines on whose number to enter.

Social security number

☐☐☐ – ☐☐ – ☐☐☐☐

or

Employer identification number

☐☐ – ☐☐☐☐☐☐☐

Part II Certification

Under penalties of perjury, I certify that:

1. The number shown on this form is my correct taxpayer identification number (or I am waiting for a number to be issued to me); and
2. I am not subject to backup withholding because: (a) I am exempt from backup withholding, or (b) I have not been notified by the Internal Revenue Service (IRS) that I am subject to backup withholding as a result of a failure to report all interest or dividends, or (c) the IRS has notified me that I am no longer subject to backup withholding; and
3. I am a U.S. citizen or other U.S. person (defined below); and
4. The FATCA code(s) entered on this form (if any) indicating that I am exempt from FATCA reporting is correct.

Certification instructions. You must cross out item 2 above if you have been notified by the IRS that you are currently subject to backup withholding because you have failed to report all interest and dividends on your tax return. For real estate transactions, item 2 does not apply. For mortgage interest paid, acquisition or abandonment of secured property, cancellation of debt, contributions to an individual retirement arrangement (IRA), and generally, payments other than interest and dividends, you are not required to sign the certification, but you must provide your correct TIN. See the instructions on page 3.

Sign Here **Signature of U.S. person** ▶ **Date** ▶

General Instructions

Section references are to the Internal Revenue Code unless otherwise noted.

Future developments. Information about developments affecting Form W-9 (such as legislation enacted after we release it) is at *www.irs.gov/fw9*.

Purpose of Form

An individual or entity (Form W-9 requester) who is required to file an information return with the IRS must obtain your correct taxpayer identification number (TIN) which may be your social security number (SSN), individual taxpayer identification number (ITIN), adoption taxpayer identification number (ATIN), or employer identification number (EIN), to report on an information return the amount paid to you, or other amount reportable on an information return. Examples of information returns include, but are not limited to, the following:

- Form 1099-INT (interest earned or paid)
- Form 1099-DIV (dividends, including those from stocks or mutual funds)
- Form 1099-MISC (various types of income, prizes, awards, or gross proceeds)
- Form 1099-B (stock or mutual fund sales and certain other transactions by brokers)
- Form 1099-S (proceeds from real estate transactions)
- Form 1099-K (merchant card and third party network transactions)
- Form 1098 (home mortgage interest), 1098-E (student loan interest), 1098-T (tuition)
- Form 1099-C (canceled debt)
- Form 1099-A (acquisition or abandonment of secured property)

Use Form W-9 only if you are a U.S. person (including a resident alien), to provide your correct TIN.

If you do not return Form W-9 to the requester with a TIN, you might be subject to backup withholding. See *What is backup withholding?* on page 2.

By signing the filled-out form, you:

1. Certify that the TIN you are giving is correct (or you are waiting for a number to be issued),
2. Certify that you are not subject to backup withholding, or
3. Claim exemption from backup withholding if you are a U.S. exempt payee. If applicable, you are also certifying that as a U.S. person, your allocable share of any partnership income from a U.S. trade or business is not subject to the withholding tax on foreign partners' share of effectively connected income, and
4. Certify that FATCA code(s) entered on this form (if any) indicating that you are exempt from the FATCA reporting, is correct. See *What is FATCA reporting?* on page 2 for further information.

Cat. No. 10231X Form **W-9** (Rev. 12-2014)

Note. If you are a U.S. person and a requester gives you a form other than Form W-9 to request your TIN, you must use the requester's form if it is substantially similar to this Form W-9.

Definition of a U.S. person. For federal tax purposes, you are considered a U.S. person if you are:

- An individual who is a U.S. citizen or U.S. resident alien;
- A partnership, corporation, company, or association created or organized in the United States or under the laws of the United States;
- An estate (other than a foreign estate); or
- A domestic trust (as defined in Regulations section 301.7701-7).

Special rules for partnerships. Partnerships that conduct a trade or business in the United States are generally required to pay a withholding tax under section 1446 on any foreign partners' share of effectively connected taxable income from such business. Further, in certain cases where a Form W-9 has not been received, the rules under section 1446 require a partnership to presume that a partner is a foreign person, and pay the section 1446 withholding tax. Therefore, if you are a U.S. person that is a partner in a partnership conducting a trade or business in the United States, provide Form W-9 to the partnership to establish your U.S. status and avoid section 1446 withholding on your share of partnership income.

In the cases below, the following person must give Form W-9 to the partnership for purposes of establishing its U.S. status and avoiding withholding on its allocable share of net income from the partnership conducting a trade or business in the United States:

- In the case of a disregarded entity with a U.S. owner, the U.S. owner of the disregarded entity and not the entity;
- In the case of a grantor trust with a U.S. grantor or other U.S. owner, generally, the U.S. grantor or other U.S. owner of the grantor trust and not the trust; and
- In the case of a U.S. trust (other than a grantor trust), the U.S. trust (other than a grantor trust) and not the beneficiaries of the trust.

Foreign person. If you are a foreign person or the U.S. branch of a foreign bank that has elected to be treated as a U.S. person, do not use Form W-9. Instead, use the appropriate Form W-8 or Form 8233 (see Publication 515, Withholding of Tax on Nonresident Aliens and Foreign Entities).

Nonresident alien who becomes a resident alien. Generally, only a nonresident alien individual may use the terms of a tax treaty to reduce or eliminate U.S. tax on certain types of income. However, most tax treaties contain a provision known as a "saving clause." Exceptions specified in the saving clause may permit an exemption from tax to continue for certain types of income even after the payee has otherwise become a U.S. resident alien for tax purposes.

If you are a U.S. resident alien who is relying on an exception contained in the saving clause of a tax treaty to claim an exemption from U.S. tax on certain types of income, you must attach a statement to Form W-9 that specifies the following five items:

1. The treaty country. Generally, this must be the same treaty under which you claimed exemption from tax as a nonresident alien.
2. The treaty article addressing the income.
3. The article number (or location) in the tax treaty that contains the saving clause and its exceptions.
4. The type and amount of income that qualifies for the exemption from tax.
5. Sufficient facts to justify the exemption from tax under the terms of the treaty article.

Example. Article 20 of the U.S.-China income tax treaty allows an exemption from tax for scholarship income received by a Chinese student temporarily present in the United States. Under U.S. law, this student will become a resident alien for tax purposes if his or her stay in the United States exceeds 5 calendar years. However, paragraph 2 of the first Protocol to the U.S.-China treaty (dated April 30, 1984) allows the provisions of Article 20 to continue to apply even after the Chinese student becomes a resident alien of the United States. A Chinese student who qualifies for this exception (under paragraph 2 of the first protocol) and is relying on this exception to claim an exemption from tax on his or her scholarship or fellowship income would attach to Form W-9 a statement that includes the information described above to support that exemption.

If you are a nonresident alien or a foreign entity, give the requester the appropriate completed Form W-8 or Form 8233.

Backup Withholding

What is backup withholding? Persons making certain payments to you must under certain conditions withhold and pay to the IRS 28% of such payments. This is called "backup withholding." Payments that may be subject to backup withholding include interest, tax-exempt interest, dividends, broker and barter exchange transactions, rents, royalties, nonemployee pay, payments made in settlement of payment card and third party network transactions, and certain payments from fishing boat operators. Real estate transactions are not subject to backup withholding.

You will not be subject to backup withholding on payments you receive if you give the requester your correct TIN, make the proper certifications, and report all your taxable interest and dividends on your tax return.

Payments you receive will be subject to backup withholding if:

1. You do not furnish your TIN to the requester,
2. You do not certify your TIN when required (see the Part II instructions on page 3 for details),
3. The IRS tells the requester that you furnished an incorrect TIN,
4. The IRS tells you that you are subject to backup withholding because you did not report all your interest and dividends on your tax return (for reportable interest and dividends only), or
5. You do not certify to the requester that you are not subject to backup withholding under 4 above (for reportable interest and dividend accounts opened after 1983 only).

Certain payees and payments are exempt from backup withholding. See *Exempt payee code* on page 3 and the separate Instructions for the Requester of Form W-9 for more information.

Also see *Special rules for partnerships* above.

What is FATCA reporting?

The Foreign Account Tax Compliance Act (FATCA) requires a participating foreign financial institution to report all United States account holders that are specified United States persons. Certain payees are exempt from FATCA reporting. See *Exemption from FATCA reporting code* on page 3 and the Instructions for the Requester of Form W-9 for more information.

Updating Your Information

You must provide updated information to any person to whom you claimed to be an exempt payee if you are no longer an exempt payee and anticipate receiving reportable payments in the future from this person. For example, you may need to provide updated information if you are a C corporation that elects to be an S corporation, or if you no longer are tax exempt. In addition, you must furnish a new Form W-9 if the name or TIN changes for the account; for example, if the grantor of a grantor trust dies.

Penalties

Failure to furnish TIN. If you fail to furnish your correct TIN to a requester, you are subject to a penalty of $50 for each such failure unless your failure is due to reasonable cause and not to willful neglect.

Civil penalty for false information with respect to withholding. If you make a false statement with no reasonable basis that results in no backup withholding, you are subject to a $500 penalty.

Criminal penalty for falsifying information. Willfully falsifying certifications or affirmations may subject you to criminal penalties including fines and/or imprisonment.

Misuse of TINs. If the requester discloses or uses TINs in violation of federal law, the requester may be subject to civil and criminal penalties.

Specific Instructions

Line 1

You must enter one of the following on this line; **do not** leave this line blank. The name should match the name on your tax return.

If this Form W-9 is for a joint account, list first, and then circle, the name of the person or entity whose number you entered in Part I of Form W-9.

a. **Individual.** Generally, enter the name shown on your tax return. If you have changed your last name without informing the Social Security Administration (SSA) of the name change, enter your first name, the last name as shown on your social security card, and your new last name.

Note. ITIN applicant: Enter your individual name as it was entered on your Form W-7 application, line 1a. This should also be the same as the name you entered on the Form 1040/1040A/1040EZ you filed with your application.

b. **Sole proprietor or single-member LLC.** Enter your individual name as shown on your 1040/1040A/1040EZ on line 1. You may enter your business, trade, or "doing business as" (DBA) name on line 2.

c. **Partnership, LLC that is not a single-member LLC, C Corporation, or S Corporation.** Enter the entity's name as shown on the entity's tax return on line 1 and any business, trade, or DBA name on line 2.

d. **Other entities.** Enter your name as shown on required U.S. federal tax documents on line 1. This name should match the name shown on the charter or other legal document creating the entity. You may enter any business, trade, or DBA name on line 2.

e. **Disregarded entity.** For U.S. federal tax purposes, an entity that is disregarded as an entity separate from its owner is treated as a "disregarded entity." See Regulations section 301.7701-2(c)(2)(iii). Enter the owner's name on line 1. The name of the entity entered on line 1 should never be a disregarded entity. The name on line 1 should be the name shown on the income tax return on which the income should be reported. For example, if a foreign LLC that is treated as a disregarded entity for U.S. federal tax purposes has a single owner that is a U.S. person, the U.S. owner's name is required to be provided on line 1. If the direct owner of the entity is also a disregarded entity, enter the first owner that is not disregarded for federal tax purposes. Enter the disregarded entity's name on line 2, "Business name/disregarded entity name." If the owner of the disregarded entity is a foreign person, the owner must complete an appropriate Form W-8 instead of a Form W-9. This is the case even if the foreign person has a U.S. TIN.

Line 2

If you have a business name, trade name, DBA name, or disregarded entity name, you may enter it on line 2.

Line 3

Check the appropriate box in line 3 for the U.S. federal tax classification of the person whose name is entered on line 1. Check only one box in line 3.

Limited Liability Company (LLC). If the name on line 1 is an LLC treated as a partnership for U.S. federal tax purposes, check the "Limited Liability Company" box and enter "P" in the space provided. If the LLC has filed Form 8832 or 2553 to be taxed as a corporation, check the "Limited Liability Company" box and in the space provided enter "C" for C corporation or "S" for S corporation. If it is a single-member LLC that is a disregarded entity, do not check the "Limited Liability Company" box; instead check the first box in line 3 "Individual/sole proprietor or single-member LLC."

Line 4, Exemptions

If you are exempt from backup withholding and/or FATCA reporting, enter in the appropriate space in line 4 any code(s) that may apply to you.

Exempt payee code.

- Generally, individuals (including sole proprietors) are not exempt from backup withholding.
- Except as provided below, corporations are exempt from backup withholding for certain payments, including interest and dividends.
- Corporations are not exempt from backup withholding for payments made in settlement of payment card or third party network transactions.
- Corporations are not exempt from backup withholding with respect to attorneys' fees or gross proceeds paid to attorneys, and corporations that provide medical or health care services are not exempt with respect to payments reportable on Form 1099-MISC.

The following codes identify payees that are exempt from backup withholding. Enter the appropriate code in the space in line 4.

1—An organization exempt from tax under section 501(a), any IRA, or a custodial account under section 403(b)(7) if the account satisfies the requirements of section 401(f)(2)

2—The United States or any of its agencies or instrumentalities

3—A state, the District of Columbia, a U.S. commonwealth or possession, or any of their political subdivisions or instrumentalities

4—A foreign government or any of its political subdivisions, agencies, or instrumentalities

5—A corporation

6—A dealer in securities or commodities required to register in the United States, the District of Columbia, or a U.S. commonwealth or possession

7—A futures commission merchant registered with the Commodity Futures Trading Commission

8—A real estate investment trust

9—An entity registered at all times during the tax year under the Investment Company Act of 1940

10—A common trust fund operated by a bank under section 584(a)

11—A financial institution

12—A middleman known in the investment community as a nominee or custodian

13—A trust exempt from tax under section 664 or described in section 4947

The following chart shows types of payments that may be exempt from backup withholding. The chart applies to the exempt payees listed above, 1 through 13.

IF the payment is for . . .	THEN the payment is exempt for . . .
Interest and dividend payments	All exempt payees except for 7
Broker transactions	Exempt payees 1 through 4 and 6 through 11 and all C corporations. S corporations must not enter an exempt payee code because they are exempt only for sales of noncovered securities acquired prior to 2012.
Barter exchange transactions and patronage dividends	Exempt payees 1 through 4
Payments over $600 required to be reported and direct sales over $5,000[1]	Generally, exempt payees 1 through 5[2]
Payments made in settlement of payment card or third party network transactions	Exempt payees 1 through 4

[1] See Form 1099-MISC, Miscellaneous Income, and its instructions.

[2] However, the following payments made to a corporation and reportable on Form 1099-MISC are not exempt from backup withholding: medical and health care payments, attorneys' fees, gross proceeds paid to an attorney reportable under section 6045(f), and payments for services paid by a federal executive agency.

Exemption from FATCA reporting code. The following codes identify payees that are exempt from reporting under FATCA. These codes apply to persons submitting this form for accounts maintained outside of the United States by certain foreign financial institutions. Therefore, if you are only submitting this form for an account you hold in the United States, you may leave this field blank. Consult with the person requesting this form if you are uncertain if the financial institution is subject to these requirements. A requester may indicate that a code is not required by providing you with a Form W-9 with "Not Applicable" (or any similar indication) written or printed on the line for a FATCA exemption code.

A—An organization exempt from tax under section 501(a) or any individual retirement plan as defined in section 7701(a)(37)

B—The United States or any of its agencies or instrumentalities

C—A state, the District of Columbia, a U.S. commonwealth or possession, or any of their political subdivisions or instrumentalities

D—A corporation the stock of which is regularly traded on one or more established securities markets, as described in Regulations section 1.1472-1(c)(1)(i)

E—A corporation that is a member of the same expanded affiliated group as a corporation described in Regulations section 1.1472-1(c)(1)(i)

F—A dealer in securities, commodities, or derivative financial instruments (including notional principal contracts, futures, forwards, and options) that is registered as such under the laws of the United States or any state

G—A real estate investment trust

H—A regulated investment company as defined in section 851 or an entity registered at all times during the tax year under the Investment Company Act of 1940

I—A common trust fund as defined in section 584(a)

J—A bank as defined in section 581

K—A broker

L—A trust exempt from tax under section 664 or described in section 4947(a)(1)

M—A tax exempt trust under a section 403(b) plan or section 457(g) plan

Note. You may wish to consult with the financial institution requesting this form to determine whether the FATCA code and/or exempt payee code should be completed.

Line 5

Enter your address (number, street, and apartment or suite number). This is where the requester of this Form W-9 will mail your information returns.

Line 6

Enter your city, state, and ZIP code.

Part I. Taxpayer Identification Number (TIN)

Enter your TIN in the appropriate box. If you are a resident alien and you do not have and are not eligible to get an SSN, your TIN is your IRS individual taxpayer identification number (ITIN). Enter it in the social security number box. If you do not have an ITIN, see *How to get a TIN* below.

If you are a sole proprietor and you have an EIN, you may enter either your SSN or EIN. However, the IRS prefers that you use your SSN.

If you are a single-member LLC that is disregarded as an entity separate from its owner (see *Limited Liability Company (LLC)* on this page), enter the owner's SSN (or EIN, if the owner has one). Do not enter the disregarded entity's EIN. If the LLC is classified as a corporation or partnership, enter the entity's EIN.

Note. See the chart on page 4 for further clarification of name and TIN combinations.

How to get a TIN. If you do not have a TIN, apply for one immediately. To apply for an SSN, get Form SS-5, Application for a Social Security Card, from your local SSA office or get this form online at *www.ssa.gov*. You may also get this form by calling 1-800-772-1213. Use Form W-7, Application for IRS Individual Taxpayer Identification Number, to apply for an ITIN, or Form SS-4, Application for Employer Identification Number, to apply for an EIN. You can apply for an EIN online by accessing the IRS website at *www.irs.gov/businesses* and clicking on Employer Identification Number (EIN) under Starting a Business. You can get Forms W-7 and SS-4 from the IRS by visiting IRS.gov or by calling 1-800-TAX-FORM (1-800-829-3676).

If you are asked to complete Form W-9 but do not have a TIN, apply for a TIN and write "Applied For" in the space for the TIN, sign and date the form, and give it to the requester. For interest and dividend payments, and certain payments made with respect to readily tradable instruments, generally you will have 60 days to get a TIN and give it to the requester before you are subject to backup withholding on payments. The 60-day rule does not apply to other types of payments. You will be subject to backup withholding on all such payments until you provide your TIN to the requester.

Note. Entering "Applied For" means that you have already applied for a TIN or that you intend to apply for one soon.

Caution: *A disregarded U.S. entity that has a foreign owner must use the appropriate Form W-8.*

Part II. Certification

To establish to the withholding agent that you are a U.S. person, or resident alien, sign Form W-9. You may be requested to sign by the withholding agent even if items 1, 4, or 5 below indicate otherwise.

For a joint account, only the person whose TIN is shown in Part I should sign (when required). In the case of a disregarded entity, the person identified on line 1 must sign. Exempt payees, see *Exempt payee code* earlier.

Signature requirements. Complete the certification as indicated in items 1 through 5 below.

1. Interest, dividend, and barter exchange accounts opened before 1984 and broker accounts considered active during 1983. You must give your correct TIN, but you do not have to sign the certification.

2. Interest, dividend, broker, and barter exchange accounts opened after 1983 and broker accounts considered inactive during 1983. You must sign the certification or backup withholding will apply. If you are subject to backup withholding and you are merely providing your correct TIN to the requester, you must cross out item 2 in the certification before signing the form.

3. Real estate transactions. You must sign the certification. You may cross out item 2 of the certification.

4. Other payments. You must give your correct TIN, but you do not have to sign the certification unless you have been notified that you have previously given an incorrect TIN. "Other payments" include payments made in the course of the requester's trade or business for rents, royalties, goods (other than bills for merchandise), medical and health care services (including payments to corporations), payments to a nonemployee for services, payments made in settlement of payment card and third party network transactions, payments to certain fishing boat crew members and fishermen, and gross proceeds paid to attorneys (including payments to corporations).

5. Mortgage interest paid by you, acquisition or abandonment of secured property, cancellation of debt, qualified tuition program payments (under section 529), IRA, Coverdell ESA, Archer MSA or HSA contributions or distributions, and pension distributions. You must give your correct TIN, but you do not have to sign the certification.

What Name and Number To Give the Requester

For this type of account:	Give name and SSN of:
1. Individual	The individual
2. Two or more individuals (joint account)	The actual owner of the account or, if combined funds, the first individual on the account[1]
3. Custodian account of a minor (Uniform Gift to Minors Act)	The minor[2]
4. a. The usual revocable savings trust (grantor is also trustee)	The grantor-trustee[1]
b. So-called trust account that is not a legal or valid trust under state law	The actual owner[1]
5. Sole proprietorship or disregarded entity owned by an individual	The owner[3]
6. Grantor trust filing under Optional Form 1099 Filing Method 1 (see Regulations section 1.671-4(b)(2)(i)(A))	The grantor*
For this type of account:	**Give name and EIN of:**
7. Disregarded entity not owned by an individual	The owner
8. A valid trust, estate, or pension trust	Legal entity[4]
9. Corporation or LLC electing corporate status on Form 8832 or Form 2553	The corporation
10. Association, club, religious, charitable, educational, or other tax-exempt organization	The organization
11. Partnership or multi-member LLC	The partnership
12. A broker or registered nominee	The broker or nominee
13. Account with the Department of Agriculture in the name of a public entity (such as a state or local government, school district, or prison) that receives agricultural program payments	The public entity
14. Grantor trust filing under the Form 1041 Filing Method or the Optional Form 1099 Filing Method 2 (see Regulations section 1.671-4(b)(2)(i)(B))	The trust

[1] List first and circle the name of the person whose number you furnish. If only one person on a joint account has an SSN, that person's number must be furnished.

[2] Circle the minor's name and furnish the minor's SSN.

[3] You must show your individual name and you may also enter your business or DBA name on the "Business name/disregarded entity" name line. You may use either your SSN or EIN (if you have one), but the IRS encourages you to use your SSN.

[4] List first and circle the name of the trust, estate, or pension trust. (Do not furnish the TIN of the personal representative or trustee unless the legal entity itself is not designated in the account title.) Also see *Special rules for partnerships* on page 2.

*Note. Grantor also must provide a Form W-9 to trustee of trust.

Note. If no name is circled when more than one name is listed, the number will be considered to be that of the first name listed.

Secure Your Tax Records from Identity Theft

Identity theft occurs when someone uses your personal information such as your name, SSN, or other identifying information, without your permission, to commit fraud or other crimes. An identity thief may use your SSN to get a job or may file a tax return using your SSN to receive a refund.

To reduce your risk:

- Protect your SSN,
- Ensure your employer is protecting your SSN, and
- Be careful when choosing a tax preparer.

If your tax records are affected by identity theft and you receive a notice from the IRS, respond right away to the name and phone number printed on the IRS notice or letter.

If your tax records are not currently affected by identity theft but you think you are at risk due to a lost or stolen purse or wallet, questionable credit card activity or credit report, contact the IRS Identity Theft Hotline at 1-800-908-4490 or submit Form 14039.

For more information, see Publication 4535, Identity Theft Prevention and Victim Assistance.

Victims of identity theft who are experiencing economic harm or a system problem, or are seeking help in resolving tax problems that have not been resolved through normal channels, may be eligible for Taxpayer Advocate Service (TAS) assistance. You can reach TAS by calling the TAS toll-free case intake line at 1-877-777-4778 or TTY/TDD 1-800-829-4059.

Protect yourself from suspicious emails or phishing schemes. Phishing is the creation and use of email and websites designed to mimic legitimate business emails and websites. The most common act is sending an email to a user falsely claiming to be an established legitimate enterprise in an attempt to scam the user into surrendering private information that will be used for identity theft.

The IRS does not initiate contacts with taxpayers via emails. Also, the IRS does not request personal detailed information through email or ask taxpayers for the PIN numbers, passwords, or similar secret access information for their credit card, bank, or other financial accounts.

If you receive an unsolicited email claiming to be from the IRS, forward this message to *phishing@irs.gov*. You may also report misuse of the IRS name, logo, or other IRS property to the Treasury Inspector General for Tax Administration (TIGTA) at 1-800-366-4484. You can forward suspicious emails to the Federal Trade Commission at: *spam@uce.gov* or contact them at *www.ftc.gov/idtheft* or 1-877-IDTHEFT (1-877-438-4338).

Visit IRS.gov to learn more about identity theft and how to reduce your risk.

Privacy Act Notice

Section 6109 of the Internal Revenue Code requires you to provide your correct TIN to persons (including federal agencies) who are required to file information returns with the IRS to report interest, dividends, or certain other income paid to you; mortgage interest you paid; the acquisition or abandonment of secured property; the cancellation of debt; or contributions you made to an IRA, Archer MSA, or HSA. The person collecting this form uses the information on the form to file information returns with the IRS, reporting the above information. Routine uses of this information include giving it to the Department of Justice for civil and criminal litigation and to cities, states, the District of Columbia, and U.S. commonwealths and possessions for use in administering their laws. The information also may be disclosed to other countries under a treaty, to federal and state agencies to enforce civil and criminal laws, or to federal law enforcement and intelligence agencies to combat terrorism. You must provide your TIN whether or not you are required to file a tax return. Under section 3406, payers must generally withhold a percentage of taxable interest, dividend, and certain other payments to a payee who does not give a TIN to the payer. Certain penalties may also apply for providing false or fraudulent information.

APPENDIX D: CAL POLY HUMAN SUBJECTS COMMITTEE APPROVAL FORM

HUMAN SUBJECTS PROTOCOL APPROVAL FORM
Cal Poly, San Luis Obispo

All Cal Poly faculty, staff, and student research with human subjects, as well as other research involving human subjects that is conducted at Cal Poly, must be reviewed by the **Cal Poly Human Subjects Committee** for the protection of human subjects, the researchers, and the University. Human subjects research is defined as any systematic investigation of living human subjects that is designed to develop or contribute to generalizable knowledge. While the ethical guidelines for research are applicable to classroom activities, demonstrations, and assignments, the Human Subjects Committee does not review classroom activities unless data will be collected and used in a systematic investigation.

Researchers should complete all items on this approval form and submit it, along with a research protocol (containing the information detailed in Guidelines for Human Subjects Research Protocol), to the Office of Research and Economic Development (Debbie Hart, Bldg. 38, Room 154). Please feel free to attach an additional page if your responses to any of the items require more space. Your answers to the items on this form, as well as the research protocol, should be typed. The Committee will make every effort to respond to your submission within two to four weeks. Committee approval should be received prior to contacting prospective subjects and collecting data. Please read carefully Cal Poly's Policy for the Use of Human Subjects in Research prior to completing this application.

If you require assistance in completing this form, contact the Office of Research and Economic Development at (805) 756-1508.

1. Date: January 1, 2016

2. Title of Research Project:
Electroencephalography (EEG) measurement during motor tasks

3. Type of Research:
- [ ] Senior project
- [ ] Master's thesis
- [ ] Faculty research
- [X] Other:

please explain: MEDITEC Research Project

4. Name(s) of Researcher(s)

Principal Investigator:	Adam Aslam		
Department or other affiliation:	Mechanical Engineering		
Phone:	(925)336-7603	Email:	aaslam@calpoly.edu
Position:	[ ] Faculty	[X] Student	
	[ ] Other: *please explain*		
Additional Researcher:	Charlie Aylward		
Department or other affiliation:	Computer Engineering		
Phone:	(530)774-6696	Email:	caylward@calpoly.edu
Position:	[ ] Faculty	[X] Student	
	[ ] Other: *please explain*		
Additional Researcher:	Sara Wier		
Department or other affiliation:	Biomedical Engineering		
Phone:	(406)750-3526	Email:	swier@calpoly.edu
Position:	[ ] Faculty	[X] Student	
	[ ] Other: *please explain*		

Any additional researchers involved in the project should be listed with the descriptive information requested above on a separate sheet.

5. Faculty Advisor (if applicable)

Name:	Dr. Kristen Cardinal	Email:	kohallor@calpoly.edu
Department or other affiliation:	Biomedical Engineering Department	Phone:	(805)756-2675

Other thesis committee members if the research is a thesis:

Name:		Email:	
Department or other affiliation:		Phone:	
Name:		Email:	
Department or other affiliation:		Phone:	
Name:		Email:	
Department or other affiliation:		Phone:	

6. Is there an *external* funding source for the project:

X	Yes, and the source is:	St. Jude Medical and MEDITEC budget
	No	

7. Is this a modification of a project previously reviewed by Cal Poly's Human Subjects Committee?

X	Yes, and the approximate date of the last review was:	3/15/15
	No	

8. Estimated duration of the project:

Starting date: 1/15/2016 Completion date: 12/31/2016

9. Describe *any* risks (physical, psychological, social, or economic) that may be involved.
See Specific Ethical Criterion #1 in Policy for the Use of Human Subjects in Research for a description of the types of risks.

1) There is a slight risk of discomfort due to wearing the EEG electrode cap and conductive gel.
2) There is a very minor risk of possible low voltage electric shock generated by the EEG measurement hardware or from static electricity.

10. Indicate what measures will be taken to minimize risks. *See Specific Ethical Criterion #1 in Policy for the Use of Human Subjects in Research for a discussion of strategies for minimizing risks.*

1) The EEG system safety guidelines specified by the system manual will be precisely followed.
2) EEG system setup and operation will be practiced prior to conducting research on subjects.
3) Subjects will be asked periodically about any discomfort that they are experiencing, and measures will be taken to try to mitigate any discomfort.

11. Explain how subjects' *confidentiality* will be protected. *See Specific Ethical Criterion #5 in Policy for the Use of Human Subjects in Research for a discussion of strategies for minimizing risks.*

1) The confidentiality of the test subjects will be protected by replacing patient names with an anonymous unique identifier consisting of a letter followed by the year that the subject participated in the study (e.g. A15, B15, etc.). Any study documents and publications will refer to patients by anonymous identifier only.
2) Although demographic information and EEG tracings may be published along with findings from the study, the identity of subjects participating in the study will not be disclosed.
3) Paper copies of research paperwork, consent forms, and data with subjects' information will be stored in a locked cabinet.

12. Describe any *incentives* for participation that will be used. *See Specific Ethical Criterion #2 in Policy for the Use of Human Subjects in Research for a discussion of the use of incentives in research.*

Subjects who participate will be offered a $40 gift card from the MEDITEC budget to be used for purchase of a meal.

13. Will *deception* of subjects be involved in the research procedures?

[ ] Yes* [X] No

If so, explain the deception and how it will be handled.* ***See Specific Ethical Criterion #3 in Policy for the Use of Human Subjects in Research* *for a discussion of the use of deception in research:*

14. Type of review requested:

[ ] Exempt from further review* [X] Expedited review [ ] Full review

See ***Types of Review*** in Policy for the Use of Human Subjects in Research for a discussion of the criteria for exempt, expedited, and full reviews.

**The research protocol submitted for a project presumed to be exempt may be abbreviated but should contain sufficient information to support the conclusion that the project meets the criteria for exemption.*

15. Signatures:

Your signature below indicates that the information presented in this application (the approval form and research protocol) is accurate and that you have read, understand, and agree to follow the Policy for the Use of Human Subjects in Research.

Name of Primary Researcher: Adam Aslam

Signature: _____

Cal Poly Faculty Advisor's Signature (Required if this is student research)

I have reviewed this research proposal which has been prepared by my advisee(s) in accordance with the Guidelines for Obtaining Human Subjects Approval.

Name of Faculty Advisor: Kristen Cardinal

Signature _____

Return to the Human Subjects Committee homepage.

APPENDIX E: PROTOCOL

Protocol: Electroencephalography Measurement During Motor Tasks

Objective

This study conducted at California Polytechnic State University involves the use of an electroencephalography (EEG) system to measure brain signal data from healthy subjects. Our interest is to analyze this EEG while subjects perform tasks that are difficult for patients with movement disorders such as Parkinson's Disease. Our hope is that results can then be used to give more insight on the function of deep brain stimulation in movement disorder patients.

Materials

EEG systems consist of a cap, electrodes, recording circuitry, and connecting wires. We will be using the Mitsar-EEG 202-31 system with the 19 standard 10/20 layout electrodes with 12 additional electrodes for added spatial resolution. This system has a 500 Hz sampling rate and includes the amplifier, a USB cable, a power supply unit, and WINEEG data analysis software. The cap and electrode system used will be a 32-channel BrainProducts actiCAP with active electrodes. This also comes with the SuperVisc gel that is used to increase conductivity at the electrode. For use in our tests seen in the Methods section, we will use paper cups, pencils, and binder paper.

Methods

The 18-24 year old students being studied will be asked for basic demographic information, including age, sex, race, and relevant health history. Before testing begins, the subject will be asked to review and sign the informed consent form, and any questions that he or she has about the study will be addressed. The subject will be told that they have the option to opt out of the study at any time.

The study will take approximately 1 hour to complete. The first step is EEG system setup, which includes placement of the EEG cap and will take 10-15 minutes total to complete. The camera will be set up to view the subject's upper body, head, and the table in front of him/her. At this time, an optional accelerometer may also be set up in the appropriate location. The setup of the EEG includes adjusting the electrode cap to fit the user's head and injecting the conductive gel. The subjects will then be asked to relax and sit still for 2 minutes. Each test will have the subject wait for a verbal cue to begin the indicated activity. A research supervisor will begin a timer at the start of each test. During each test, subjects will be asked to avoid blinking, thinking, or moving, other than that required for the test.

1. Pencil-Pickup Test

    The first test has the subject reach for an object placed on a table within arm's reach. The subject will be asked to sit comfortably with their arms resting on the table. Then he/she will reach for a pencil on the table, pick it up, and place it back on the table. This test will be repeated five times by each subject with 20 seconds between each test.

2. Writing/Drawing Test

This test looks into writing/drawing. The subject will be given a pencil and binder paper to write their name repeatedly for 30 seconds and then stop for 10 seconds. The subject will then be asked to draw an outwardly expanding spiral for 10 seconds. This will be repeated 3 times with 20 seconds between each test.

3. Swallow Test

This test has the subject take sips of water from a paper cup. We are looking at the swallowing action, so the subject will be asked to remain still with a small amount of water in their mouth for 2 seconds before swallowing. This will be repeated 5 times with 20 seconds between tests.

4. Stand Test

This test has the subject stand up. He/she will be asked to stand up for 5 seconds after being verbally prompted. We will attempt to keep all wires and other parts stationary since we expect noise to interfere with our signal. We will ask the subject to perform this task 5 times with 20 seconds between each test.

5. Postural Tremor Test

This test has the patient hold their dominant arm parallel to the floor and pause for 5 seconds. With their arm held out, the subject proceeds to rotate their wrist alternating between facing the hand up and down for 10 seconds. This test will be repeated 5 times with 20 seconds between each test.

6. Bradykinesia Test

This test has the subject place their arm on a table and tap their thumb to their index finger. The subject will sit at rest with their arm resting on the table. Once verbally prompted, the subject taps their thumb to their index finger 10 times at 1-second

intervals using a stopwatch for assistance. This test will be repeated 5 times with 20 seconds between each test.

Once the testing is finished, the cap will be removed, which will take roughly 5 minutes. Subjects will be advised to wash out the conductive gel using water and shampoo.

Each measurement will begin with the subject at rest and continue through the duration of the exercise. A new sample is recorded for each test including repeated tests. The aim of the recordings at different conditions is to determine characteristics of the EEG while the subject is at rest, and changes that occur with typical voluntary motions or actions. These tests represent the control group which serves as a baseline for the tasks performed. Data that will later be conducted on patients with Parkinson's Disease can be compared to this control group.

Data Interpretation

The 32-channel EEG being used will follow the standard 10/10 electrode layout. The number of electrodes acquiring signals provides sufficient freedom to observe responses in different sections of the brain during the tests. The focus of the tests performed in the experiment procedure will be on movement related activity. The corresponding electrodes used for analysis will be primarily in the C, F and P regions of the 10/10 scheme and will vary depending on the activity performed by the subject.

The EEG manufacturer software will manage the signal acquisition from the EEG electrodes. Raw signals will be analyzed using Matlab with the EEGLAB Toolbox. The acquisition software provided by the EEG manufacturer, EEGStudio, provides filtering of

common noise signals including the power frequency (60Hz). EEGStudio also provides adjustment of individual electrode sensitivity and filtering. The preprocessed data obtained from EEGStudio can then be exported to a Matlab compatible file format for extended analysis. EEG signals existing in the time domain will be converted to the frequency domain using Fast Fourier Transform techniques provided by the EEGLAB software to observe the power spectra produced by each activity. The power spectra will be observed to identify signal peaks of interest associated with each movement related activities. Subject data will then be compared to find peak frequencies common to multiple subjects. Further analysis will include spatial filtering to produce a scalp map of peak signals during the activities with the help of the EEGLAB software.

Data for each subject will be stored anonymously using the following format: "EEG2016A" to represent EEG data from subject 'A' taken in the year 2016. Any publication or distribution of the data will not reveal name or any identifying information about any of the subjects.

APPENDIX F: PROTOCOL TIME MARKERS AND PROTOCOL DEVIATIONS

1. Baseline: 2 minutes of silence, where subject is asked to sit still and clear their mind.
    a. First click: start of baseline
    b. Second click: end of baseline

2. Task 1: Pencil-Pickup (5 trials)
    a. First click: Initial movement reaching for pencil
    b. Second click: Motion picking the pencil up
    c. Third click: Setting the pencil down
    d. Fourth click: Hand placed back on table directly in front of subject

3. Task 2: Writing/Drawing (3 trials)
    a. First click: Begin name writing
    b. Second click: End name writing
    c. Third click: Begin drawing a spiral
    d. Fourth click: End drawing a spiral

4. Task 3. Swallow (5 trials)
    a. First click: Sip is taken (water hits mouth)
    b. Second click: Mouth movement indicating swallowing

5. Task 4. Stand (5 trials)
    a. First click: Begin standing motion

b. Second click: Fully stood up

6. Baseline: 1 minute of silence, where subject is asked to sit still and clear their mind.

a. First click = baseline start

b. Second click = baseline end

7. Task 5. Postural Tremor (5 trials)

a. First click: Start of rotation (begin with palm up)

b. Next clicks: Every 180 degree rotation

8. Task 6. Bradykinesia (5 trials)

a. Every click: thumb and index finger touch

9. Baseline: 1 minute of silence, where subject is asked to sit still and clear their mind.

a. First click = baseline start

b. Second click = baseline end

Deviations/Notes by subject:

EEG2016A:

- Electrode 17 was left unplugged.
- Impedance lights were left on during first approximately 80 seconds of the recording period, making that data useless.

- A loud printer turned on from approximately 30-60 (s) of the second baseline.
- We took a second baseline after the fourth task instead of after the third task.
- Later, we revised the protocol to have baselines before the first, fifth, and sixth tasks.

EEG2016B:

- An extra 1 minute baseline was taken after the second task.
- Second task was done very slowly. There were few number of names written and spirals drawn.
- Ignore the second click of the second trial of the swallow task, only look at first and third clicks.
- The cap was adjusted after the third task.
- First trial of bradykinesia test had very slow finger touches. All other trials were slow.

EEG2016C:

- A new laptop was used, but about 5 times, trials would cease recording because of amp error.
- The second baseline (approximately 3:00-4:06 mins) has no second click because of amp error.
- Ignore the Second click of the Second trial of the name writing.
- A baseline was taken after each task and before the first task.

- The first click of the first swallow test was accidental.
- During the third baseline (after the swallow task), the amp malfunctioned so we restarted the baseline. Ignore that first click. Malfunction was followed by normal 2 click baseline.

EEG2016D:

- The first baseline measurement failed. Ignore the first click.
- During the first baseline, the subject blinked a lot.
- Ignore the third click of the first trial of pencil-pickup.
- Ignore the second trial of the name writing task, the program failed.
- Accidental first click of first swallow task trial.
- Ignore all five swallow trials and the first standing because the impedance lights were on.
- The first trial of postural included a lot of blinking.
- The first trial of bradykinesia should have double the clicks.

EEG2016E:

- All testing was performed during a class so there were lights on, noise/distractions, close proximity to electronics.
- For approximately the first 40 seconds of recording, the patient was moving/fidgeting.

- There was an accidental small recording between trials 2 and 3 of the pencil-pickup task.
- At approximately 9:49.5, there was an extra click between arm rotations.

EEG2016F:

- All testing was performed during a class so there were lights on, noise/distractions, close proximity to electronics.
- The third drawing trial had lots of arm movement.

EEG2016G:

- Recording was made with the lights off.
- During the fourth swallow trial, there was a loud knocking outside the room.

EEG2016H:

- The initial 30 seconds of the first baseline recording was conducted with the laptop power cable right next to the cap (usually, the baseline laptop power cable is about 4'-5' away). This was done to compare the two cases (no difference was found).
- The right hemisphere had poor impedance (due to long hair).

EEG2016I:

- No deviations or notes to report.

EEG2016J:

- The second click of the first trial pencil-pickup task was late by approximately .25 seconds.
- Postural tremor trials were somewhat close together.
- Trials were not recorded separately.

EEG2016K:

- During the fourth and fifth trial of the swallow task, the subject blinked. Perhaps during previous trials as well, but it was not observed.
- For the first 8 seconds and last 9 seconds of the third baseline, there was loud clapping next door. Also, the subject had an itch starting in the middle of the third baseline.
- Trials were not recorded separately.

APPENDIX G: SUBJECT DEMOGRAPHIC FORM

How Electrical Signals in the Brain Impact Movement

Subject Demographic Form

Name: _____ Age:_____

Sex: _____ Race: _____

Do you have any relevant medical history that you feel comfortable sharing with us? If so, please list below.

On a scale of 1 to 10, how alert do you feel right now (10 being most alert)? Please circle one number.

1 2 3 4 5 6 7 8 9 10

APPENDIX H: POTENTIAL SUBJECT EMAIL TEMPLATE

Hello research participant,

Thank you for volunteering for our study! We would like to go over some logistics before meeting. We are working on this project in collaboration with St. Jude Medical to provide valuable information to help treat Parkinson's Disease. We have Institutional Review Board (IRB) approval with Cal Poly that allows us to perform our study.

Before meeting with us, please review the attached protocol and informed consent. Before the study begins, you must fill out and sign the informed consent. To receive a $40 gift card to a restaurant or retailer of our choosing, you must fill out a W-9 form. The form requires a social security number and is submitted to the Sponsored Programs Department in 33-102. If you feel uncomfortable giving us this form, you can turn it into the department and when we receive confirmation that the form is received, you will in turn receive the gift card.

Taking EEG recordings requires electrical conduction to your scalp, which is accomplished through electrodes filled with gel. This can be somewhat messy, so we recommend washing your hair after the study is complete.

Should you feel uncomfortable and wish to leave, you are completely free to discontinue the study at any time. If you are a Psychology 202 student, you will receive your writing prompt upon completion of the study, which should take approximately 1 hours. We look forward to seeing you on **X, X** at **X:XX.** in **38-133**.

Sincerely,

Adam Aslam, Charlie Aylward, & Sara Wier