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QUANTIFYING THE EFFECTS OF MOTOR TASKS ON CORTICOKINEMATIC COHERENCE IN PARKINSON'S DISEASE

Debanjan Borthakur
University of Rhode Island, dborthakur@my.uri.edu

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QUANTIFYING THE EFFECTS OF MOTOR TASKS ON
CORTICOKINEMATIC COHERENCE IN PARKINSON'S DISEASE

BY

DEBANJAN BORTHAKUR

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DEBANJAN BORTHAKUR

APPROVED:

Thesis Committee:

Major Professor Kunal Mankodiya

Yalda Shahriari

Leslie Mahler

Joan Peckham

Nasser H. Zawia

DEAN OF THE GRADUATE SCHOOL

UNIVERSITY OF RHODE ISLAND

2018

ABSTRACT

Parkinson's disease (PD) is a neurodegenerative disorder. Researchers are investigating ways to identify neural and behavioral markers for PD that can lead to earlier diagnosis and more effective treatments. The goal of this research is to quantify the effects of motor tasks on corticokinematic coherence (CKC) in PD. We can consider this research as a proof of concept study. This research can eventually help us quantify the motor symptoms related to PD using the measurement process called CKC. Brain muscle synchrony can be quantified as corticomuscular coherence (CMC) and corticokinematic coherence (CKC). Surgical and Pharmacological treatments have not been shown to have consistent, positive effects on PD, although improvements in limb function have been reported. In this research, we studied neural responses during motor tasks using electroencephalography (EEG). Specifically, a finger tapping test which is widely used in motor screening exam such as Unified Parkinson's Disease Rating Scale - UPDRS was used at two different frequencies, with and without metronome support in maintaining the correct pacing frequency which has been found to influence perceptual processing by entraining endogenous neural oscillations. This allows for investigation of CKC variation between movement frequencies of 1 Hz and 2 Hz in participants. We had 10 neurotypical individuals and 4 People with PD (PwPD), of which we analyzed results from 8 neurotypical individuals and 3 PwPD. Both groups showed prominent CKC at the frequency of finger tapping in the contralateral sensorimotor cortex. We also explored mu rhythm suppression as a result of finger tapping using wavelet-based time-frequency analysis. The use of a Smart Glove with Flex sensors which is explicitly designed to measure subtle irregularities in finger kinematics was an additional novel approach towards measuring CKC in people with Parkinson's which allows comparisons of neural activity at the finger tapping frequencies and thereby

can be helpful in quantifying the motor-related symptoms associated with Parkinson. This is a first of its kind of study that investigates synchrony between neural oscillations and finger kinematics recorded by Smart Glove Flex sensors paced by auditory cue.

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CHAPTER 1

Introduction

More than 10 million people worldwide are living with PD [1]. To date, there is no cure for Parkinson's. PD is characterized by slowness of movement, increased tone/stiffness (rigidity), tremor, and the loss of postural reflexes. The sequence of beta desynchronization and resynchronization is impaired in PwPD. In addition, cortical oscillations are coherent with muscle contraction and muscle movement [2]. This coupling between brain activity and limb kinematics is called Corticokinematic coherence (CKC). CKC in involuntary limb movement originates mainly from the primary sensorimotor (SM1) cortex. That is, hand velocity and acceleration are coupled with Magnetoencephalographic/Electroencephalographic signals recorded from the contralateral primary sensorimotor (SM1) cortex. Changes in corticomuscular coherence have been documented for people with Parkinsons. This thesis, therefore, aims to explore the use of corticokinematic coherence in motor exercises for PwPD. The aims of this research is to investigate the Corticokinematic coherence between hand kinematics and EEG for People with Parkinsons with the Smart Glove [3] designed explicitly for Parkinson disease. The glove can quantify movements of the fingers by recording the activities of the finger using the flex sensors attached to the glove. The questions examined in this research are :

- Is there any clinically significant difference in brain activity during motor tasks like finger flexion and extension in healthy controls, or in people with PD?
- Is the combination of the Smart Glove with flex sensors and neuroimaging,

such as the EEG, effective in measuring motor activity during finger tapping in PwPD and healthy controls?

- Can the combination of EEG and Smart Glove data analysis serve as a useful quantification method for motor tasks in PwPD and healthy controls?

We used finger tapping tasks [4], [5] which is one of the widely used motor screening exams. The discipline of neurology has standardized finger tapping test in the clinical practice to make decisions for diagnosis and treatments. Moreover visible changes in performance on this task in people with Parkinson's are comparatively well understood. Bradykinesia, or slowness of movement, is an important symptom of PD which causes reduced speed, reduced amplitude, and the presence of pauses in the finger tapping task. People with Parkinsons have slower and less rhythmic finger tapping movements than healthy people [6]. This is the motivation behind CKC studies with finger tapping, which might help us discover new behavioral and neural markers for Parkinson's disease. The Smart Glove played an important role in this research work. In Abtahi et al. [7] researchers designed a MagicSox to quantify the gait abnormalities in remote settings. We tried to leverage the Smart-Glove and EEG to quantify finger tapping motor tasks which is widely used in motor screening exams for Parkinson disease. The contribution of this thesis mainly focuses on the simultaneous use of neuro-imaging and Smart Glove [8] sensors. For neuroimaging technique we have used EEG. The ultimate goal is to design a unified metric for quantification of motor related symptoms in Parkinson disease. Based on the previous research, we have focused on Corticokinematic coherence (CKC) as a measurement of synchrony and results that we have found makes it a useful proof of concept study.

This thesis is divided into six sections. After the introduction 1, section 2 discusses Parkinson disease, EEG, the Smart Glove, Corticomuscular coherence,

and Sensorimotor synchronization. The methodology section 3 discusses the participants, tasks, and stimuli used. Section 4 discusses the findings. Section 5 is the conclusion, and it provides insights into future work. We have also included an appendix section in this thesis at the end.

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CHAPTER 2

Background

2.1 Parkinson's disease

Parkinson's disease (PD) is a progressive neurodegenerative disorder and second most common neurodegenerative disease in western populations. Shaking, rigidity, slowness of movement, and difficulty walking are some early symptoms of PD. Sometimes behavioral problems may also occur. Depression, anxiety, and dementia are also common as the disease progresses [1]. Other possible symptoms include sensory, sleep, and emotional problems. The main motor symptoms are collectively called 'parkinsonism', or a 'parkinsonian syndrome' although one-quarter of subjects treated for Parkinson's disease did not show any clinical evidence of parkinsonism according to Meara et al. [2]. The cause of Parkinson's disease is still unknown, but both genetic and environmental factors play a role [3]. The death of dopaminergic neurons in the substantia nigra, a region in the midbrain, limits the dopamine available in the area, leading to motor symptoms. While this cell death, however, is not well understood, lewy bodies [4] can be found in the neurons. Neuroimaging is broadly used in PD diagnosis, like CT, PET scans etc [5]. The clinical features include tremor, bradykinesia, and rigidity. Patients with more advanced PD exhibit a characteristic gait with stooped posture and small shuffling steps. Several types of tremors are associated with PD.

- Resting tremors occur when muscles are relaxed.
- Action tremors occur with voluntary muscle movement which might overlap with kinetic tremors that occur with voluntary movement, such as finger tapping.
- Postural tremors occur when a person maintains a position against gravity.

Typical appearance of Parkinson's disease



Figure 1. People with Parkinson disease with different symptoms. The image is adapted from <http://www.tpgonlinedaily.com/>.

People with Parkinson also exhibit reduced facial expressions [6]. Figure 2 portrays a simplified model of basal ganglia. In PD, the firing of neurons in the basal ganglia, with changes in firing rates, abnormal burst patterns are seen. These abnormalities usually take place together, as mentioned in [7].

Studies investigating changes in firing rates in the basal ganglia of monkeys in response to 1-Methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) treatment showed increased activity in the subthalamic nucleus (STN) and Internal globus pallidus (GPi), as well as reduced activity in External globus pallidus (GPe) [8].

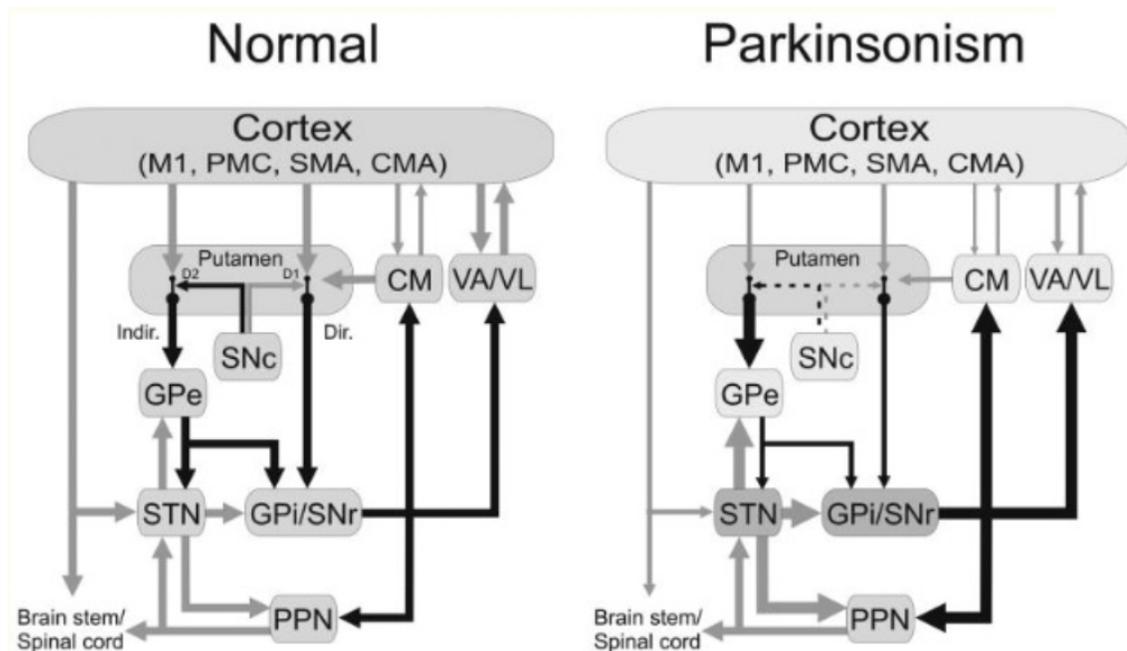


Figure 2. The basal ganglia-thalamocortical motor circuit: black arrows indicate inhibitory connections; gray arrows indicate excitatory connections. The thickness of the arrows corresponds to their presumed activity. Note Parkinsonism-related changes in overall activity (rate model) in the circuit. Adapted from [7]

Exaggerated oscillatory synchronization in the β frequency band has been associated with bradykinesia in patients with PD. High-frequency stimulation (HFS) of the STN has been shown to suppress local β activity. β power is diminished during STN High frequency stimulation (HFS) and recurs shortly after the end of High frequency stimulation [9]. Brown et al.[10] showed power spectra of local field activity recorded from the contacts of a DBS electrode in the subthalamic nucleus of a patient with PD on and off their anti-parkinsonian medication. They observed that during the off medication period, the Local field potentials (LFP) is dominated by β band oscillations with a frequency around 20 Hz. Post treatment with levodopa, the β band suppression and a new oscillation peaking at 75 Hz has been seen in the gamma-band. There are some studies on corticomuscular coherence and Parkinson Disease. Caviness et al. [11] measured Corticomus-

cular electroencephalographic-electromyographic (EEG-EMG) coherence elicited by speech and non-speech oromotor tasks in healthy participants and those with Parkinson's Disease (PD). They found that corticomuscular coherence existed for both groups and for all tasks, but to varying degrees in primary sensorimotor cortex and SMA. In [12] authors asserted that Parkinsonian and essential tremors and also Parkinsonian tremor imitated by healthy subjects induce CMC at the tremor frequency and its first harmonic and similar phenomenon is observed in CKC induced by voluntary movements [13].

2.2 EEG

Electroencephalography (EEG) is an electrophysiological monitoring method that records the electrical activity of the brain. It is noninvasive, with the electrodes placed over the scalp. EEG measures voltage fluctuations resulting from ionic current within neurons. Neural oscillations or Brainwaves and stimulus-driven time-locked activity both are studied in EEG. It is recorded from multiple scalp electrodes. Event-related potentials and the spectral content of EEG are mostly used for diagnostic purposes. One application of EEG is in epilepsy. It is also used to diagnose sleep disorders, depth of anesthesia, comas, encephalopathies, brain death, tumors, stroke, and other focal brain disorders [14]. EEG has lower spatial resolution than CT, PET, or MRI but provides a millisecond-range temporal resolution which is not possible in other technologies. In Fig 3 120 Hz EEG waveforms are subdivided into bandwidths known as alpha, beta, theta, and delta to signify the majority of the EEG used in clinical practice.

- Delta: Delta waves have frequency 3 Hz and below. They are both the slowest and highest amplitude brain waves. These are typically the dominant frequency in infants up to one year of age, and for people in sleep stages 3 and 4. Subcortical lesions may also cause focal delta waves.

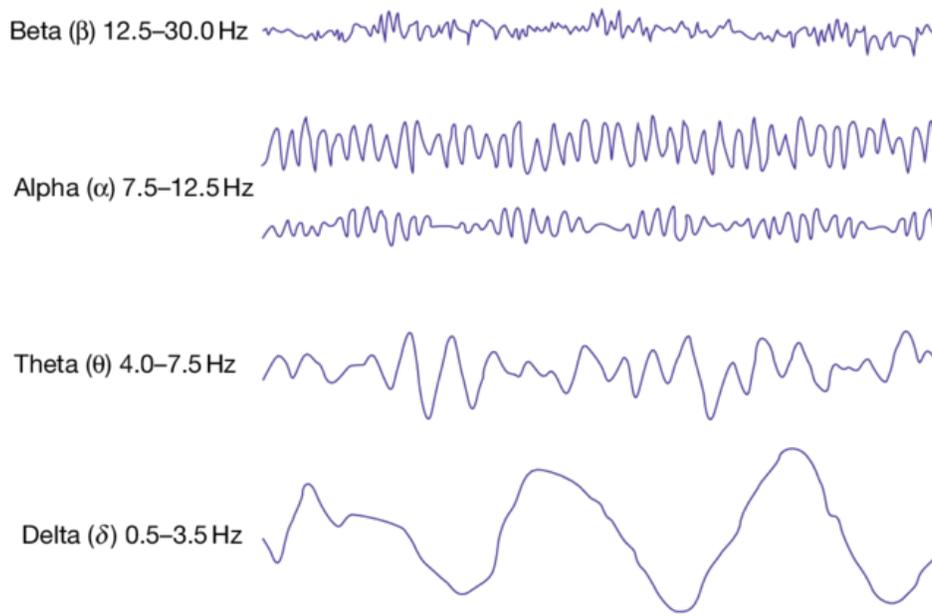


Figure 3. EEG frequency band plot adapted from [15]

- Theta: Theta waves of 4-7Hz are considered “slow” waves. They normally appear in sleep, or in waking children up to 13 years of age, but are considered abnormal in waking adults. Subcortical lesions can cause focal theta waves, while diffuse disorders such as metabolic encephalopathy or some instances of hydrocephalus. can cause more widespread theta in waking adults [16].
- Alpha: Alpha waves have frequencies between 8 and 13 Hz. They are usually best seen in both posterior regions. It is the major rhythm seen in normal relaxed adults. It is present during most of life, especially after the thirteenth year [16].
- Beta: Beta activity is a ”fast” activity. 14 Hz and faster waves are considered Beta waves. It is accentuated by sedative-hypnotic drugs. Generally regarded as a normal rhythm, it is dominant in people who are alert, have open eyes, or are anxious. [16].

- Gamma: Gamma oscillations are 25 to 100 Hz and are associated with subjective awareness. Human gamma oscillations were maximally coherent during slow-wave sleep.

EEG is best suited for analysis that demands temporal precision. This research work uses EEG signals to investigate the synchrony between the Brain Oscillations arising from the firing of neurons and finger kinematics.

2.3 Smart Glove

The Smart Glove was designed in the Wearable Biosensing Lab at URI. The Smart Glove we are using is similar to the one shown in the picture adapted from [17]. It is a wearable wireless device transmitting the data recorded by the micro-controller Arduino 101 to a smartphone or computer via Bluetooth. Spectra Symbol flex sensors are integrated into the Smart Glove. Flex sensors are analog resistors which act as variable analog voltage dividers. The voltage across the flex sensors changes when they are bent, and thus angular displacement can be measured. The experiment of finger tapping is a common practice in the diagnostic treatment procedures for Parkinsons disease. Smart Glove data can reveal how much and how quickly participants bend their fingers to do the finger tapping task in [17] , [18]. The Smart Glove is shown in Figure 4. Flex or bend sensors measure deflection or bending as the sensor element's resistance is directly proportionate to the amount of bending. It can also be called a goniometer or flexible potentiometer. Two flex sensors are embedded in the Smart Glove, as shown in figure 4. The index finger flexion and extension at the metacarpophalangeal joints produces a voltage that is then recorded. The Smart Glove plays a major role in this research. The Smart Glove is also synchronized with the BCI2000 software used for EEG signal acquisition so there is no time delay between the Smart Glove and EEG signal data.

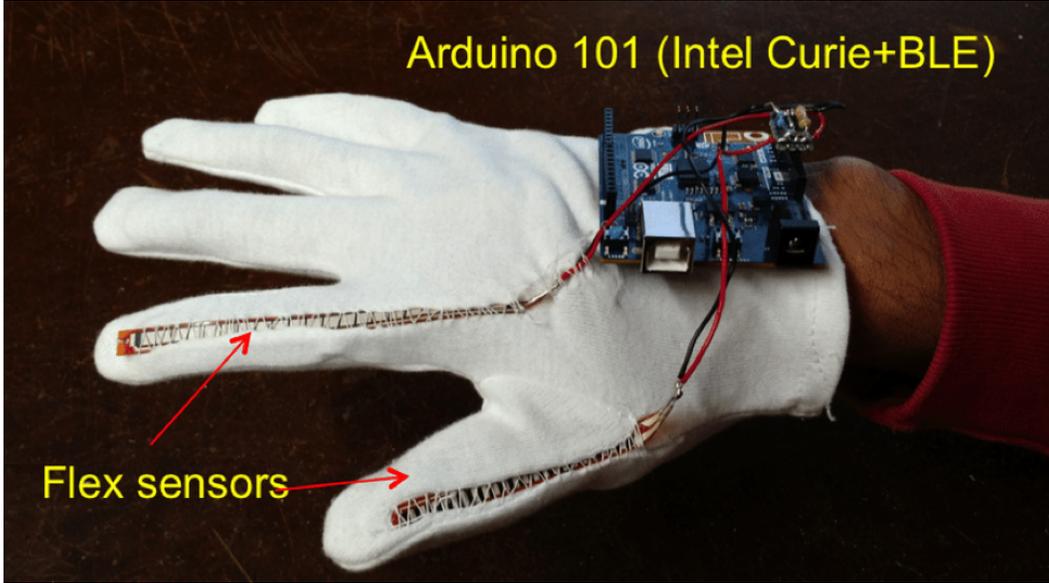


Figure 4. The Smart Glove designed to measure subtle irregularities in finger tapping in people with PD, adapted from [17].

2.4 Coherence

The spectral coherence is used to examine the relationship between two signals. It can also be used to estimate the causality between the input and output. It's a practical way to study motor functions by correlating cortical signaling with peripheral signals such as EMG [19]. Coherence is sometimes called magnitude squared coherence, which is a measure of frequency domain correlation of two signals. The magnitude-squared coherence is a function of the power spectral densities, $P_{xx}(f)$ and $P_{yy}(f)$, and the cross power spectral density, $P_{xy}(f)$, of x and y :

$$C_{xy}(f) = \frac{|P_{xy}(f)|^2}{P_{yy}(f) * P_{xx}(f)} \quad (1)$$

In our study, we used EEG as the cortical signal and flexion as the peripheral signal. Coherence measures can provide linear correlations between signals of interest. This thesis focuses on cortikokinematic coherence, but we will discuss both cortikokinematic and corticomuscular coherence. Similar algorithms have been used previously [19], but we have the Smart Glove with flex sensors for the peripheral

signal and EEG as the cortical signal in our analysis of corticokinematic coherence.

Here $P_{xy}(f)$ is the cross-spectral density between x and y , $P_{xx}(f)$ and $P_{yy}(f)$ are the auto-spectral densities of x and y respectively. Coherence functions estimate the extent to which $y(t)$ may be predicted from $x(t)$ by an optimum linear least squares function, and always range from zero to one. If the value of relative phase difference remains constant then they will have a higher coherence, while signals with opposite coherence will produce zero coherence score. Spectral coherence is scaled by the amplitudes of the individual spectra so the difference in units of amplitude will not affect the coherence analysis between two signals.

2.4.1 Corticomuscular coherence

Communication through corticospinal pathways between the primary motor cortex and muscles underpins the idea of corticomuscular coherence. Corticospinal pathways are associated with conscious motor control of skeletal muscles. When coherence is calculated between MEG and EMG, it is called MEG-EMG coherence or corticomuscular coherence. EEG can be used in place of MEG. Gwin and colleagues computed coherence between electrocortical source signals and EMG [20]. They found significant coherence between contralateral motor cortex electrocortical signals and lower limb EMG in the beta- and gamma-range for all exercise types. They documented that gamma-range coherence was significantly greater for isotonic exercises than for isometric exercises. They concluded active muscle movement modulates the speed of corticospinal oscillations. Specifically, isotonic contractions shift corticospinal oscillations toward the gamma-range while isometric contractions favor beta-range oscillations. The Figure 5 shows coherence plots from their study [20].

They found beta- and gamma-range coherence between contralateral motor cortex electrocortical source signals and lower-limb EMG was significant for all

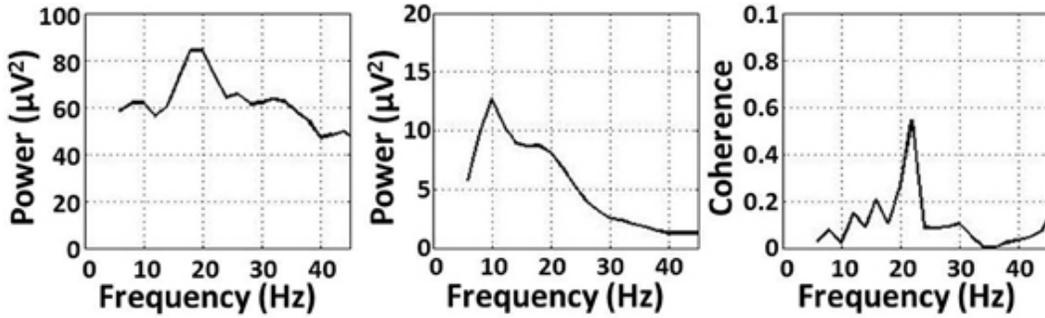


Figure 5. (Left) EMG power, (middle) EEG power, and (right) coherence for a representative subject performing an isometric exercise, adapted from [20]

exercises. In Conway et al. [21] authors observed that coherence was prominent outside the beta band. In the figure above coherence peaks at 20 Hz is clearly visible. Corticomuscular coherence is also documented in PD studies. Defective MEG-EMG coherence at the beta band is seen in PD [19]. Significant coherence is not observed in PD, although treatment with levodopa helped restore the peaks. CMC increased when Deep Brain Stimulation is applied during moderate strength isometric contraction [22]. In Kristeva et al. [23] researchers investigated whether beta-band CMC on C3 electrode varies with attention resources. Safri et al. [24] investigated beta-band CMC on c3 electrode variation with visual stimuli. Safri et al. [25] investigates brain's division in attention during a motor task using beta-band CMC on electrode C3. In Witt et al. [26] subjects had to periodically modulate dynamic isometric force output. They found an increase in the magnitude of static force output associated with enhanced beta-CMC on C3 electrode. However, our focus was oriented towards delta band activities associated with the finger movement frequency, rather than the beta band.

2.4.2 Corticokinematic Coherence

CKC or Corticokinematic Coherence is usually calculated between a Cortical signal (MEG or EEG) and an accelerometer signal recording the kinematics of

movement. In our research, we instead used flex sensors. Coherence peaks are seen at the movement frequency and its harmonics. Postural tremors are a hallmark of Parkinson disease which can be detected using sensitive accelerometers or Flex sensors. As mentioned in Lehti et al. [19] CKC can be an ideal tool for studying the differences in motor function between patients and healthy controls. Authors also calculated CMC along with CKC in their work whereas we have kept us restrained to the use of CKC in our analysis. In [27] researchers studied the possibility of eliciting cortical responses in newborns with simple passive hand movements said to be associated with proprioception. Authors observed statistically significant CKC along with activities over the brain in all infants at twice the movement frequency. Authors also have seen contralateral dominance on the central scalp. This work shows passive movements elicit cortical responses.

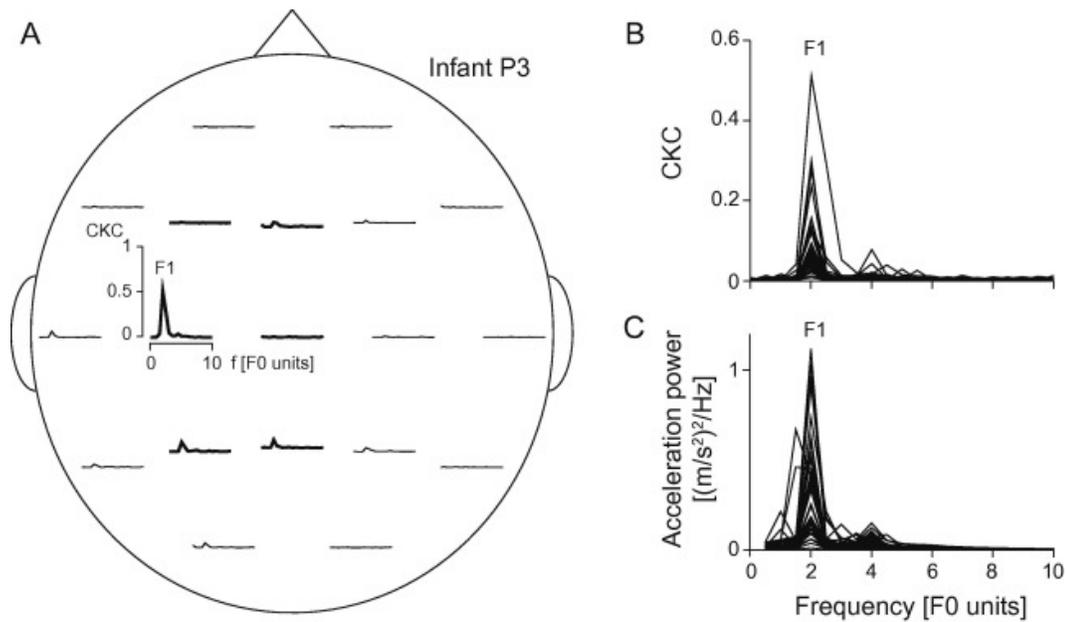


Figure 6. CKC and Acceleration spectra. A) CKC spectra of one infant from all EEG channels during right-hand movement at 1Hz. The most prominent peak is shown T F1 that is the first harmonic of movement frequency. B) CKC spectra from all infants and all stimulation run in the EEG channel with the highest CKC peak. C) Power spectra of the acceleration signals. Adapted from [27].

Researchers in [27] computed the phase-locking value (PLV) between the euclidean norm of the acceleration signals and the band-pass-filtered EEG signals. PLV and CKC both represent the consistency of the phase difference between two signals, and they showed similar results. Piitulainen et al. [13] perform CKC with MEG and 3-axis accelerometer. Authors recorded CKC during active and passive right index-finger movements. There were active-touch, active-no-touch, passive-touch, and passive-no-touch conditions based on whether the fingertips touched in the movement. Authors used the accelerometer to study the kinematics of the index finger. Authors used Beamformer analysis to locate brain activations for the movements. All active and passive movements resulted in statistically significant CKC at the movement frequency (F0) and its first harmonic (F1). Authors, also observed hemispheric lateralization. It was mentioned that at the first harmonic the coherence was two thirds stronger for passive than active movements, with no difference between touch vs. no-touch conditions. They showed the acceleration of index finger is coherent with the contralateral SM1 cortex during both active and passive index-finger movements. It is also asserted that CKC seems to be mainly driven by proprioceptive feedback, with no major indication of the effect of cutaneous input in their data. The study, [28] investigates the effect of movement rate on the coupling between cortical magnetoencephalographic (MEG) signals and the kinematics of repetitive active finger movements, or the corticokinematic coherence (CKC). They calculated CKC in subjects performing repetitive flexion-extension of the right-hand fingers in three different movement rate conditions: slow (1Hz, duration: 11min), medium (2Hz, duration: 5min) and fast (3Hz, duration: 3min). Authors found significant coherence at the movement frequency or its first harmonics in all subjects and movement conditions. They noted that movement rate had no effect on coherence levels or the location of coherent sources. Thus they

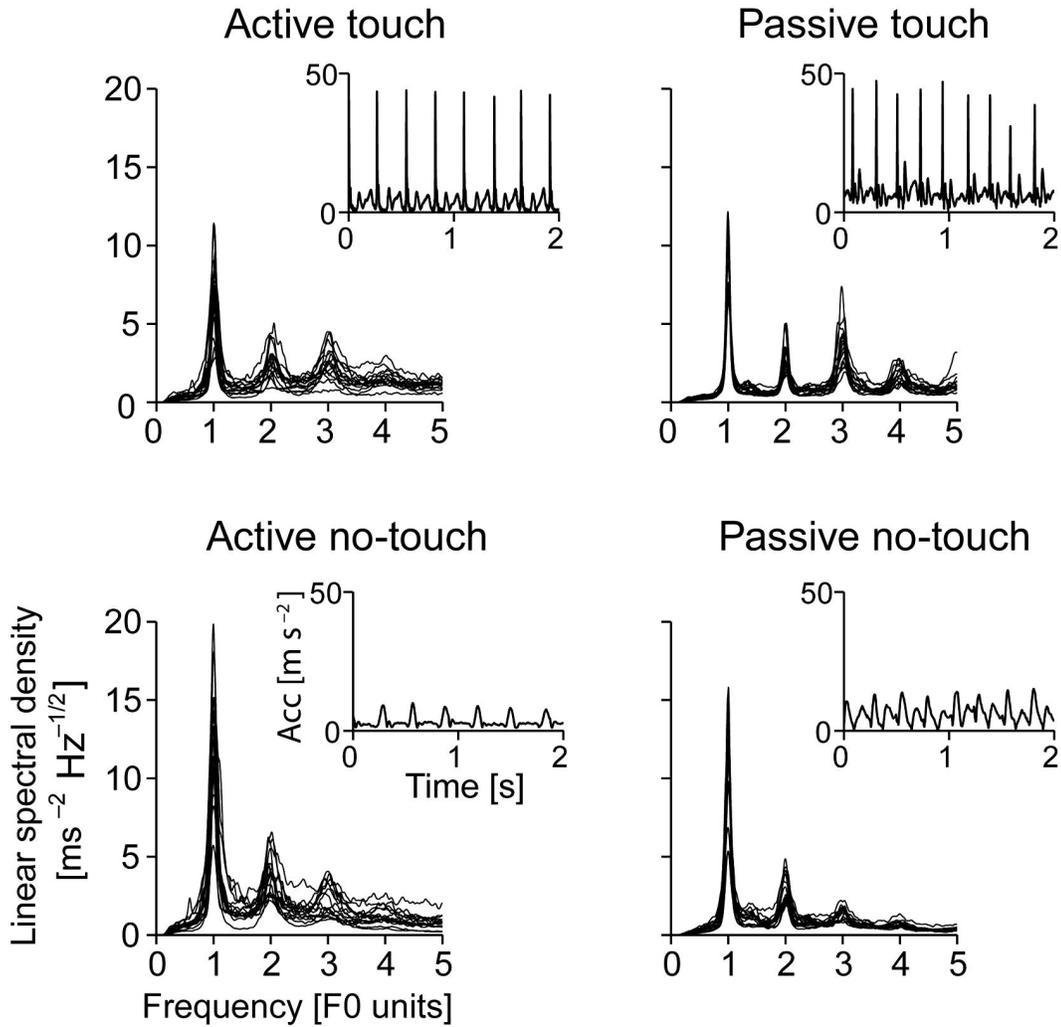


Figure 7. Linear spectral densities of hand acceleration as a function of frequency normalized according to individual movement frequency (F0); superimposed traces are from different subjects ($N = 15$) and data are given for all conditions. Inserts depict 2-s epochs of the Euclidian norm (Acc) of hand acceleration for each condition. Adapted from [13].

affirm that movement rates do not affect coherence levels or CKC source location during active finger movements. These findings have direct implications for CKC functional mapping applications and studies investigating the pathophysiology of central nervous disorders affecting proprioceptive pathways.

2.5 Sensorimotor Synchronisation

Sensorimotor synchronization (SMS) is defined as the rhythmic coordination of perception and action [29]. It occurs in many contexts, particularly in music performance and dance. It is studied with finger tapping to a sequence of auditory stimuli. We used a metronome, a device that produces an audible click a regular interval set by the user, usually in beats per minute. Sensorimotor synchronization has been studied in PD research, as dopamine plays an important role in temporal processing and prediction. Rat studies demonstrated that lesions of the hippocampus result in increased dopamine release to the striatum which disrupts the timing of temporal events [30]. Motor synchronization to external stimuli in PD is therefore of interest.

Training based on rhythmic auditory stimulation (RAS) can improve gait in people with Idiopathic Parkinsons disease (IPD) [31]. They observed increased gait speed and stride length in non-cued gait after training with patients, though there were individual differences in these results. They concluded that sensorimotor timing skills underpinning the synchronization of steps to an auditory cue may predict the success of RAS in idiopathic Parkinsons disease [31]. People with PD demonstrate specific difficulties when trying to accurately synchronize their movements to a beat [32]. People with Parkinson’s disease show an inability to reproduce isochronous (occur at the same time) intervals. Relevant tasks include *finger tapping* and *circle drawing*. In one study, participants moved their index finger back and forth between two targets displayed in front of them in such a way that the arrival of the finger matches with the sounding of the beat [32]. This allowed investigation of the synchrony of finger movement with the auditory cue. They concluded degeneration of basal ganglia circuitry might undermine the temporal prediction ability, or the ability to anticipate when something is going to

happen [32]. Patients suffer from event-based timing or synchronization with an external acoustic beat. They also concluded that decreases in temporal movement control seem to be linked to impaired ability to predict when something will happen [32]. A frequency tagging approach has been used to test rhythm processing in infants with EEG, measuring neural entrainment to rhythmic patterns [33]. They also showed that music training can effect this entrainment. Sensorimotor synchronization studies can be done using a frequency-tagging approach where EEG is recorded while participants listen to an auditory beat and tap their hand synchronously with the beat. SS-EP based frequency domain analysis can be used to study neural entrainment underlying sensorimotor synchronization to beats [34]. They showed clear SS-EP's associated with the auditory beat with binary and ternary meter imagination. The goal was to understand the functional and neural mechanisms of neural entrainment to music. The frequency tagging approach is useful because when a stimulus is repeated at a fixed rate, it generates periodic change in voltage amplitude in EEG. As EEG is stable in phase and amplitude over time, SS-EP based methods are used for this analysis.

In our study the metronome was used as a cue with tapping happening either at 1 Hz or 2 Hz frequency. The subjects tapped their index finger while listening to the auditory stimulus beeping at the same rate. Studying sensorimotor synchronization entirely is beyond the scope of this master's research, but we sought to introduce it into our research in order to pave the way for future exploration. This research might in future help find neural and behavioral signatures of Parkinson or symptoms related to parkinson. We can see a future prospect with this kind of study that takes into account the sensorimotor synchronization with cortikokinematic coherence.

2.6 Time Frequency Analysis

Time-frequency analysis was performed for repetitive finger tapping. Along with coherence analysis, we have included Time-Frequency analysis in this research to explore the modulation of synchronized neuronal activity with dynamic voluntary movements. Stavrinou et al. investigated cortical activation and connectivity relating to real and imaginary rhythmic finger tapping using EEG signal processing [35]. The most reactive frequencies were 18 to 20 Hz. The ipsilateral hemisphere showed constant ERS and the contralateral electrodes showed ERD. Mu-rhythms were found to be detectable in a conventional finger-tapping task, and vocalization [36]. They also observed ERD/ERS patterns with right index finger tapping. [37] Smit et al. mentioned that beta oscillations showed a clear modulation at around the tapping rate, whereas alpha/mu showed a sustained depression in power compared with eyes-open rest in their paradigm. In both right and left finger tapping tasks, a grand average spectrogram ERD peak ERD is seen around in 10Hz six bipolar channels [38].

In our study we used wavelet based Time Frequency analysis to investigate the activity at different frequencies over time. Our region of interest was the mu band where reduction in power is documented in literature related to motor tasks, or motor imagination. The activity related to the finger movement is also investigated at their specific frequency of 1 Hz and 2 Hz. The reduction in power at the range of 8 to 13 Hz was seen in our analysis along with the activity associated with the 1 Hz or 2 Hz finger tapping for both people with PD and with control subjects. kiymik et al. [39] compared Short term Fourier transform (STFT) and Continuous wavelet transform. They found that the STFT was more applicable for real-time processing of EEG signals, due to its short process time, they also mentioned that the CWT had good resolution and performance high enough. We

have not explored STFT in our analysis.

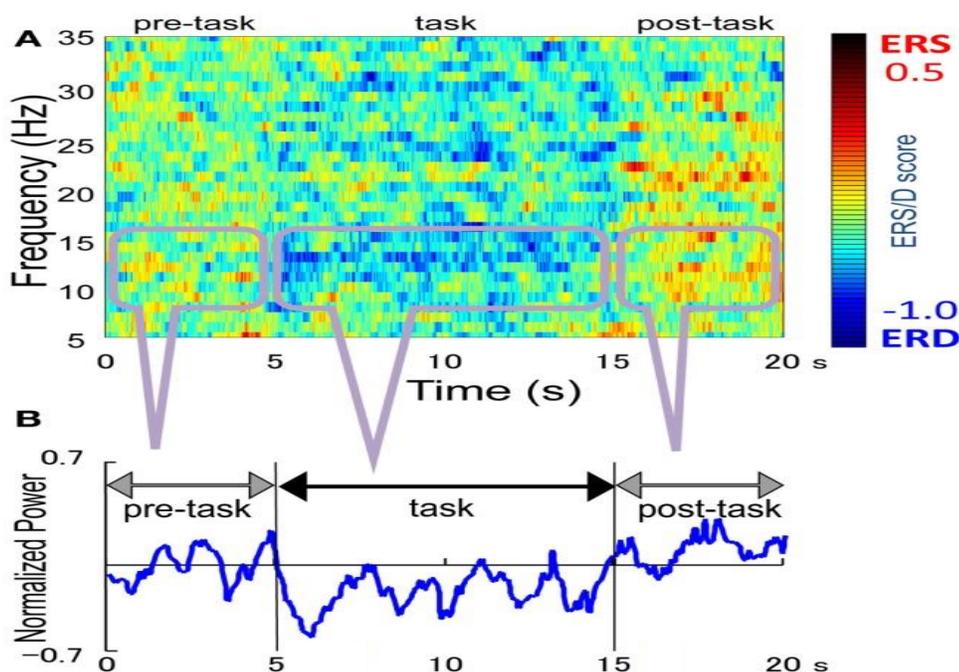


Figure 8. The plot shows the peak and average frequency analysis during right finger-tapping. (A) Shows the normalized power spectrum obtained by a fast Fourier transform (FFT) at channel C3, (B) Shows an example of the averaged power of the EEG oscillation at C3, Adapted from [36].

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CHAPTER 3

Methodology

3.1 Participants

This study had 10 neurotypical controls, 2 women and 8 men between the ages of 18-33. Four Participants with Parkinson disease participated in our study. Three of them were on medication and one is not taking any medication, the fourth subject was having tremors that made the data unreliable for analysis for some runs. All participants, signed an informed consent form before participating. The study was approved by University of Rhode Island IRB, IRB reference : 1239763-4, Local reference : HU1718-185. Ages were confirmed with valid ID. No monetary compensation was given to the participants. Participants with Parkinson's are screened using the Montreal Cognitive Assessment (MoCA) test. People with PD must score 23 or greater to sign the consent form and participate. All participants with PD have scored above the required score in MoCA.

Table 1 shows the information collected from the consent forms and HIPAA (The Health Insurance Portability and Accountability Act). None of the subjects were on Deep Brain Stimulation (DBS). Age ranges between 69 to 76. Some of the symptoms reported by the people with PD were tremor, slow walking, uneven gait issues, micro writing and dystonia etc.

Participants	Sex	MoCA	Age	Medication	DBS	Symptoms
PD1	F	30	69	Yes	No	Slowness, Dystonia, Tremor
PD2	F	29	72	Yes	No	Tremor, Slow walking
PD3	F	25	71	No	No	Uneven gait, Micro writing
PD4	M	24	76	Yes	No	Gait problem, Tremor

Table 1. The table provides the information for all the subjects with Parkinson's disease

3.2 Task and Stimuli

The participants sit in a comfortable chair and a cap with EEG electrode is placed on their head. The cap follows the standard 10-20 pattern of electrode placements. Participants are instructed to tap their finger when a green ball appears on the screen in front of them on a computer screen. An additional auditory cue (metronome) is also introduced in some of the runs of the experiment. The following section describes the experiments and associated systems.

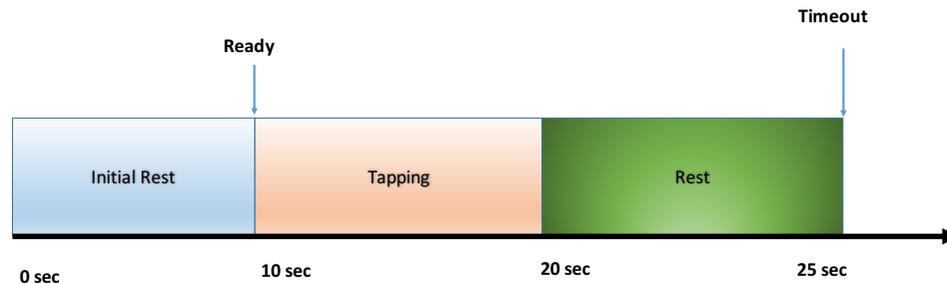


Figure 9. Finger Tapping with 1 or 2 Hz pacing is shown. The Tapping starts after 10 sec of initial rest followed by 5 sec of rest

3.2.1 MoCA

We have performed the Montreal Cognitive Assessment (MoCA) test on four PD subjects. MoCA is designed as a rapid screening instrument for mild cognitive dysfunction [1]. The assessment is done on different cognitive domains such as attention and concentration, executive function, memory, language, visuoconstructional skills, conceptual thinking, calculations and orientation. The total possible score is 30, we have set the cut off at 23. The specific tasks we have used were :

- Alternating Trail Making : The subject needs to draw a line going from a number to a letter in ascending order.
- Visuoconstructional Skills (Cube): The subject has to draw a cube as instructed.
- Visuoconstructional Skills (Clock): The subject has to draw a clock and set the time to 10 after 11.
- Naming : The subject has to tell the name of an animal, as instructed.
- Memory : The subject has to remember the words uttered by the instructor.
- Attention : It consist of forward digit span, backward digit span, scoring,vigilance.
- Sentence repetition : The subject has to repeat a sentence.
- Verbal fluency : The subject has to tell the names of objects starting with a specific letter.
- Abstraction : The subject has to explain how two objects are similar or different, such as how an orange and banana are alike.
- Delayed Recall : The subject is asked to recall previously read words.
- Orientation : The subject is asked to tell today's date.

All the subjects have scored more than 23 out of total 30 marks.

3.2.2 Finger Tapping

Finger tapping is commonly used in the study of the human motor system using functional neuroimaging [2]. It can be used in normal control subjects as well as those with neuropathologies affecting the motor system. The task is flexible

with numerous modifications possible. Use of a pacing stimulus is common and comparisons with self-paced and cue-based pacing can provide interesting results. Pacing stimuli helps participants perform a finger tapping task at a predetermined rate. The results from studies investigating the effects of auditory stimuli show different networks of active brain regions, but these results are not consistent across different studies [2]. We have used a metronome as auditory cue to externally pace the finger tapping. Participants were asked to tap their finger wearing the Smart Glove designed for this specific task. In our first paradigm, we asked the participants to tap their finger at a fixed pacing rate of 1 Hz for a period of 10 sec followed by a 5 sec rest period. This process continues for 10 trials. Similarly, in the next run, we asked the participants to tap their finger at a self-pacing rate of 2 Hz. The second paradigm introduced a metronome as a pacing stimulus. The metronome was fixed at 1 Hz and 2 Hz respectively. Participants completed runs of both paradigms, at both tapping rates, with both their dominant and non-dominant hands, for a total of 8 runs.

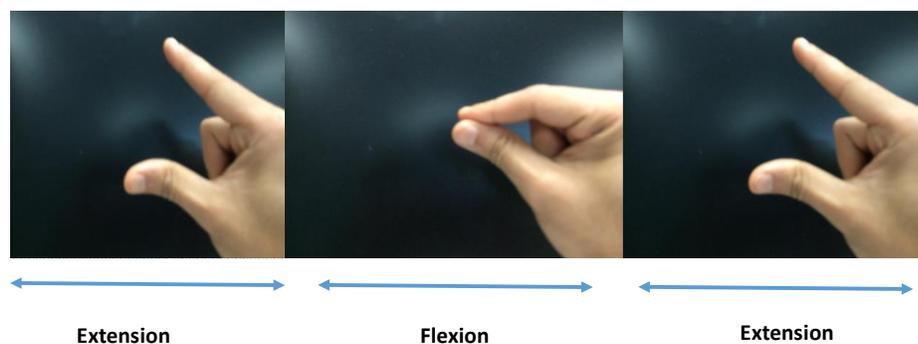


Figure 10. The picture shows finger Tapping with 1 or 2 Hz pacing. The first image shows the finger extension and the next image shows the flexion at the metacarpophalangeal joint of the index finger.

Figure 10 shows a hand with the index finger tapping at the specified frequency of 1 Hz or 2 Hz. The subject both PD and control follows the same protocol. A green ball appears in the screen in front of the subject. When the ball appears the subject starts tapping using the right or left index finger.

3.2.3 Metronome

A metronome is a device that produces an audible click at a regular interval. Musicians use the device to practice rhythm and improve their timing. Metronomes can also include synchronized visual motion such as a blinking light or swinging pendulum. We used an online metronome which produces clicks at the user-specified frequency. In Nozaradan et al. [3] researchers used auditory stimulus with finger tapping imagery. They have investigated and found beat- and meter-related SS-EPs were elicited by the 2.4 Hz auditory beat in the control condition, in the binary meter imagery condition, and the ternary meter imagery condition. In our research, we set the metronome click at 1 Hz and 2 Hz respectively. The following conditions were used in the experiment :

- 1 Hz tapping with metronome
- 2 Hz tapping with metronome
- 1 Hz tapping without metronome
- 2 Hz tapping without metronome.

3.3 Measurement

We collected electroencephalographic (EEG) signals and Flex signals from the Smart Glove throughout our experiments.

3.3.1 EEG

EEG signals were collected using gUSBamp (g.tec, Austria), this device is for brain signal acquisition. We used this device to record and amplify the brain signals from the surface of the scalp and is being considered as a non-invasive recording measure. We used the software BCI2000 for recording the data. The amplifier is compatible with BCI2000 software. The electrode positions are shown in figure 11. The electrodes cover the somatosensory and motor areas of the brain. The electrode positions respectively are : FC3, FC4, C1, CZ, C2, C3, C4, CP1, CP2, CP3, CP4, P3, PZ and P4. The colored electrodes in Figure 11 show the positions of the placed electrodes. The EEG data collection took place in Neural PC lab at the University of Rhode Island. 14 active electrodes were used for signal acquisition. The impedances of the electrodes were kept below $5K\Omega$. FCZ was considered as the ground and earlobe as the reference. The sampling rate was considered as 256Hz for the signal acquisition. The online filter uses a notch filter for power line interference suppression and we have used a cut off frequency of 0.5 Hz. The offline analysis will be explained in the later sections.

In Figure 12 one of the control is performing the finger tapping task. The EEG cap is placed on his head. The subject is wearing the glove in his right hand and performing the finger tapping task as instructed. The screen in-front of the subject provides the instruction of Tapping and Rest conditions. Consent has been achieved from the subject to use his picture in this thesis. Fourteen electrodes as shown in the Figure 11 montage are placed accordingly in the cap. The EEG signals are collected using the software BCI2000 and similarly from the Smart Glove the Flex data has also been collected from the Smart Glove as explained in the next section.

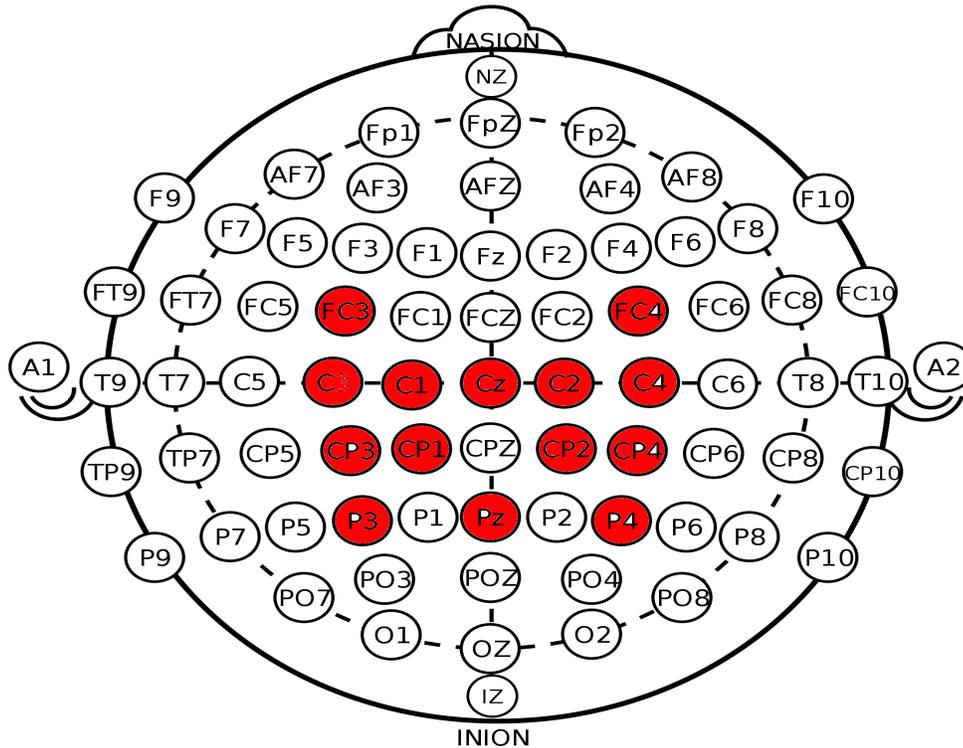


Figure 11. The EEG electrode positions are shown in the figure.

3.3.2 Smart Glove Flex

The Flex glove data collection system consists of the glove, Arduino processing unit, and the laptop for receiving data over serial communication. Using a prototype Smart Glove from Wearable Biosensing Lab, URI, the subject inserts their hand into the glove properly positioning the Flex sensors of the index finger metacarpophalangeal joint. As the subject taps their index finger, the flexion causes a change in resistance values, thus altering the electrical potential values being collected. These changes in potential indicate the motor movement activity levels occurring during the test procedure. This data was collected by the Arduino Uno processing unit, sampling at approximately 250 Hz or 250 entries over the span of one second. When electrical potential is collected in the analog pins,



Figure 12. The Subject with EEG electrodes placed in his head is shown in the figure. The subject is also wearing the Smart Glove in his right hand. The Smart Glove is also shown in the figure .

that voltage is also altered by an op-amp and voltage divider before the initial five-volt output is returned. This safety precaution serves to protect not only the processing unit but the laptop that is also connected to the serial connector. This wiring setup on the printed circuit board also allows for easy additions of more sensors including additional Flex sensors for the other four digits, as well as acceleration and gyroscopic sensors, which were considered during development. As the test procedure is conducted and flexion patterns are collected, the values are then transmitted via serial cable to the recording laptop. For real-time data collection, the PLX-DAQ freeware extension package of Microsoft Excel is used. This freeware allows excel to continuously stream the serial data as it is being collected into columns at the same frequency of approximately 250 samples a second. Then, at the end of each trial, the thousands of columns of voltage and time stamp data are saved as .csv files for further analysis in MATLAB. We used the Flex data for coherence analysis with the brain data collected from the BCI2000 software. The

Smart Glove used is shown in Figure 12. The subject has to flex and extend the index finger with the pace assigned. This task is performed with or without the auditory cue of metronome clicks at 1 Hz or 2 Hz.

3.4 Analysis

We developed MATLAB scripts for the analysis. For the coherence analysis, we have used an 'mscohere' function that finds the magnitude-squared coherence estimate of the input signals. We will discuss the analysis associated with the EEG, the Smart Glove flex sensors, time-frequency analysis using wavelet transform, spectral analysis using fast Fourier transform and coherence analysis using magnitude squared analysis.

3.4.1 EEG

The EEG signals were collected using the software BCI2000 [4]. The signals were band passed to .5 and 200 Hz online. And again filtering is applied offline and band passed to .5 and 100 Hz. We used z-score to normalize the signal. z-score can be calculated using $z = (X - \mu) / \sigma$, where z is the z-score, X is the value of the element, μ is the population mean, and σ is the standard deviation Epochs of the desired length are taken that was giving proper peaks. Then averaging is done to get the power spectrum of the signals and also for the coherence analysis etc. We used EEGLab [5] to visually inspect the artifacts related to motion. Those artifacts, if any, were removed after inspecting them visually. The same portion of data is removed from Flex sensor data.

3.4.2 Smart Glove Flex

Flex data was collected from the Smart Glove had a sampling rate of approximately 250 Hz. We used resampling method to make the sampling frequency of Flex equal to EEG, that is 256 Hz. Standard preprocessing steps associated with

EMG, Accelerometer data was applied to the Flex data. We used detrend on the Flex data Detrend removes the mean value or linear trend from a vector or matrix. Standard MATLAB function detrend is used for this purpose. Similar z score normalization and epoching have been done on the Flex data.

3.4.3 Power Spectral Analysis

Power Spectral Density estimation was performed on both EEG and Flex data for all the subjects. Fast Fourier transform determined the frequency components in the signal. We used MATLAB, $Y = \text{fft}(X,n)$ function which returns the n-point DFT. We not specified the value of n so the length of Y is same as that of X. We calculated FFT over the epochs and averaged the results. The same procedure is applied to the Flex data also. The power spectral density provided the spectral energy distribution for the data.

3.4.4 Corticokinematic Coherence Analysis

For studying the coupling between finger movement and neural oscillations the metric we used was CKC or corticokinematic coherence. The MATLAB function mscohere was used to find the magnitude-squared coherence estimate between the EEG and Flex data. The function is applied to the resampled, epoched data to visualize the significant frequency-domain correlation at the specific frequencies. We also used topographic plots of the scalp data field in a 2-D circular view for investigating the hemispheric lateralization associated with the finger tapping.

3.4.5 Time Frequency Analysis

Time-Frequency analysis is generalization and refinement of Fourier analysis. We use Time-Frequency analysis when the signal frequency characteristics are varying with time. Time-Frequency analysis has a wide scope of applications. We used wavelet transform based Time-Frequency analysis for this research. Baseline

correction is often needed as power decreases as frequency increases which follows the 1/f power law scaling. We used decibel conversion based baseline correction for this purpose. which is defined as :

$$dBconversion = 10\log_{10}\left(\frac{activity}{baseline}\right)$$

The selection of baseline was an issue as different subjects showed different responses to the choice of baseline. This was mainly due to the recording conditions of the data, while the subjects might have induced some artifacts like an eye blink, motion etc. The width of the Gaussian was taken as the variable of 3-10 cycles for the wavelet convolution to deal with the trade off of frequency and temporal precisions for the signal which was bandpass filtered at 5-40 Hz.

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CHAPTER 4

Results and Discussions

4.1 Time Series Analysis

For time series analysis in Figure 13, we have visualized the raw EEG signals and Flex signals collected from the Smart Glove. The signals are plotted for both resting and tapping duration. The resting duration was 10 sec initial rest and then followed by 10 sec tapping and 5 sec rest. We have shown in the plot, the rest and rapping period. Finger tapping starts at the end of 10 sec. Clear activity is

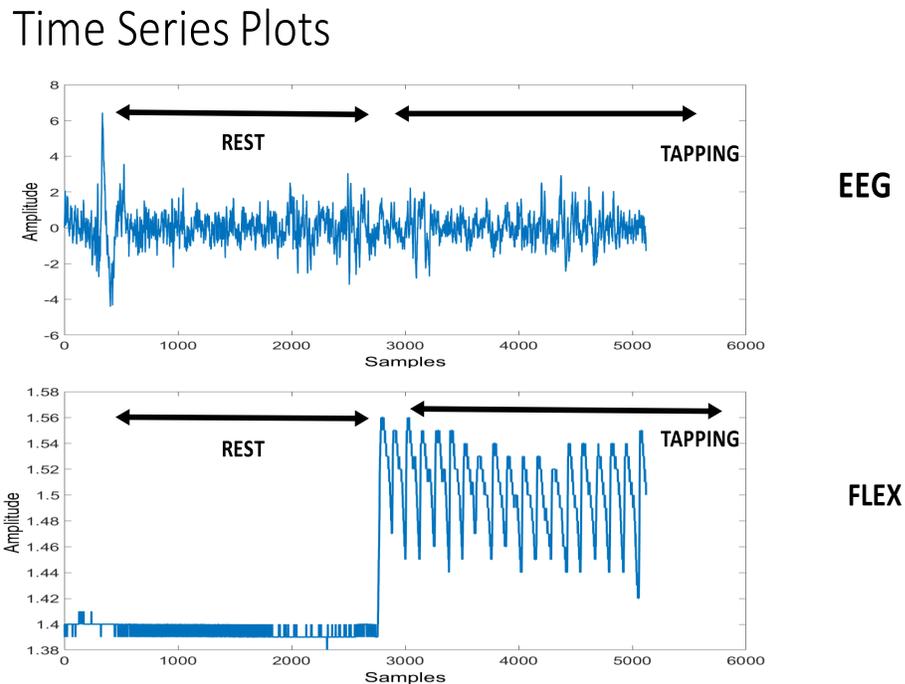


Figure 13. The plot shows the time series for EEG for one channel for one subject, and Flex sensor data for same subject for both Resting and Tapping condition

seen in the Flex sensor data as shown the the figure 13. The EEG signal is shown

for the channel C2 for one subject data for one particular condition. Although no clear signatures are visible for rest vs tapping condition in the time domain signal. Which demands the frequency domain analysis to investigate the signatures associated with the finger tapping in EEG data, which we have investigated using power spectrum, Time-Frequency and Coherence analysis.

4.2 Time Frequency Analysis

Event-related resynchronization and desynchronization is often seen with finger movement tasks. Tamura et al. [1] has shown a reduction in power at μ band. μ band is a range of electroencephalography oscillations from 8 to 13 Hz. Finger tapping tasks were performed at 1 Hz and 2 Hz pacing rates. Figures 14, 15, 16 shows the Time-Frequency plots for the 2 Hz left-hand finger tapping condition. Results for 1 Hz and/or right-hand tapping were similar. For the sake of simplicity, we have not presented all the results. Usually, the frequency spectrum of data tends to show decreasing power at increasing frequencies, which is also termed as the 1/f power law. To avoid this, we performed one type of baseline normalization called decibel conversion. It is defined as,

$$dBconversion = 10\log_{10}\left(\frac{activity}{baseline}\right)$$

The mid of the rest period was chosen as the baseline. In the Figure 14, Figure 15, Figure 17 reduction in power at the μ band is seen in both people with Parkinson's disease (PwPD) and controls. We have shown three PD subjects and three healthy controls. The finger tapping starts at 5000 ms and ends at 150000 ms. A clear reduction in power was seen in 8-15 Hz range after the finger tapping starts. Beta oscillations are associated with Parkinson Disease, we have seen such oscillations in the Time-Frequency plots although no further investigations were done on this. For creating the Time-Frequency plots we used wavelet transform method using Morlet wavelets with a variable width of the Gaussian ranging from 3-10 cycles to adjust

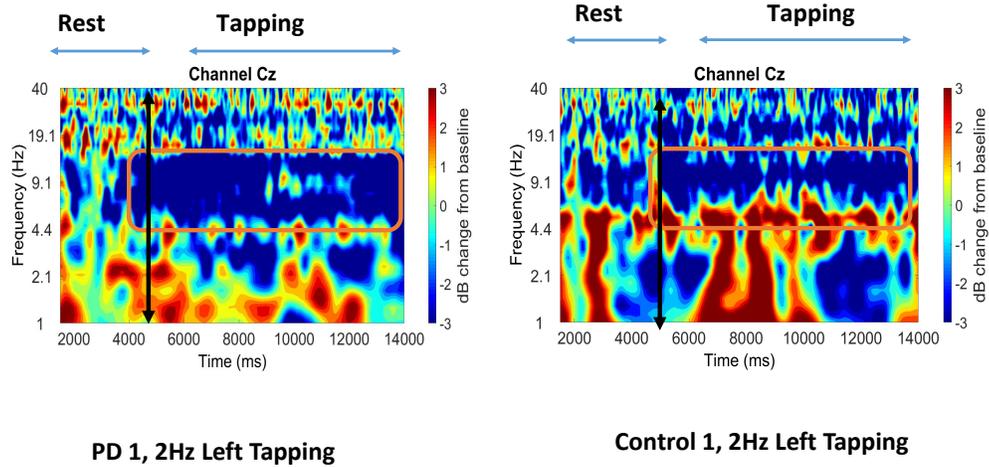


Figure 14. The figure shows the Time-Frequency plots for the finger tapping for PD 1 and control 1. Reduction in mu rhythm is visible. Both the subjects were doing 2 Hz left hand finger tapping

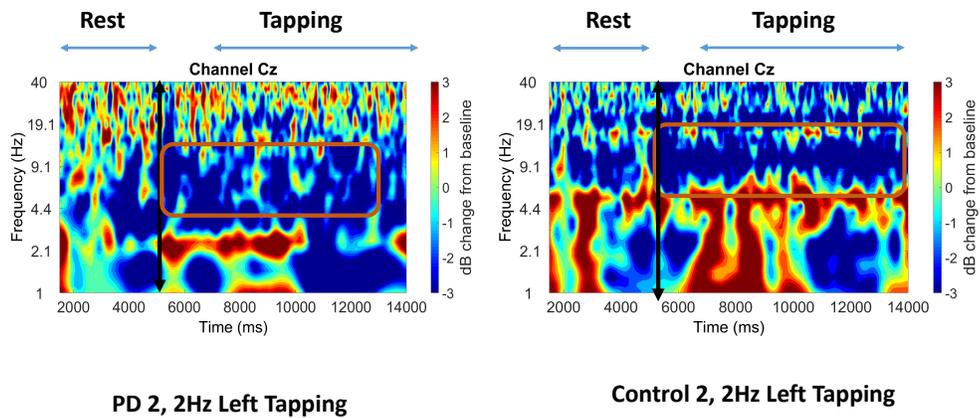


Figure 15. The figure shows the Time-Frequency plots for the finger tapping for PD 2 and control 2. Reduction in mu rhythm is seen. Both the subjects were doing 2 Hz left hand finger tapping

the trade-off between temporal and frequency precision. We used frequencies from 1 Hz to 40 Hz and dB change from -3 to +3. The 2 Hz tapping activity is also seen

as a red color region. Control 3 does not show clear activity pattern around 2 Hz although a clear reduction in activity is seen in the μ region. Control 3 has shown more reduction beyond mu band as shown in Figure 16. Very clear reduction in mu power is seen in PD 1 in Figure 14, although the Control subject did not show such clear activity. The 2 Hz activity is also visible from the plots.

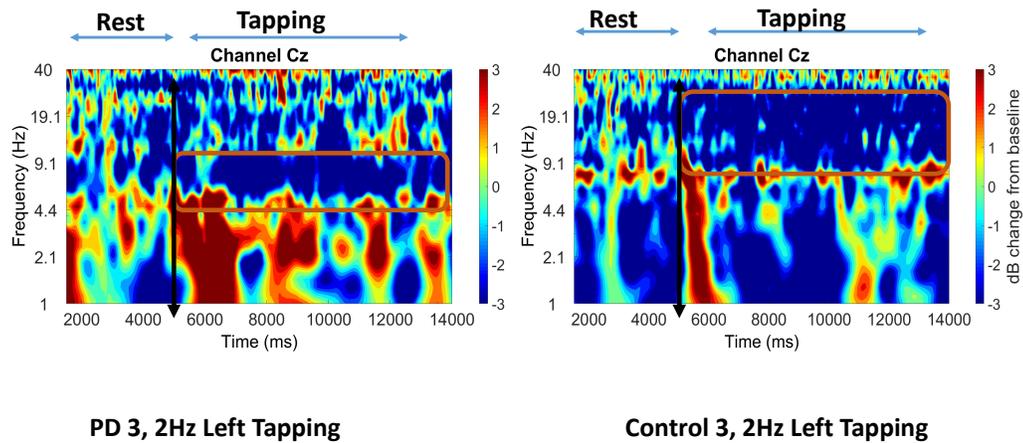


Figure 16. The Figure shows the Time-Frequency plots for the finger tapping for PD 3 and control 3. Reduction in mu rhythm is seen. Both the subjects were doing 2 Hz left hand finger tapping

The Figure 17 shows how the power in the μ band is reduced when the subject starts tapping his finger. The results from Wilcoxon signed rank test indicate that the test rejects the null hypothesis of zero medians in the difference at the default 5% the significance level for control rest vs tapping condition. We have seen with Wilcoxon rank sum test that P value of 0.024 from the results indicates that rank sum rejects the null hypothesis of equal medians at the default 5% the significance level for PD vs Control rest and tapping conditions in mu power.

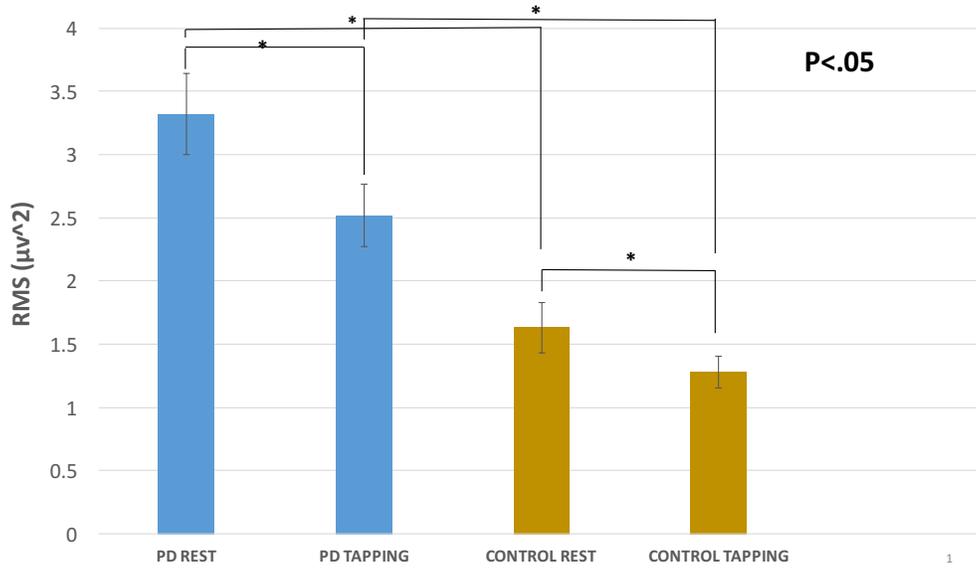


Figure 17. The Figure shows the average RMS bar plots for the finger tapping of people with PD and control for 2 Hz finger tapping with the left hand. Reduction in mu rhythm power is quantified using RMS values of the voltage. Asterisk indicate statistical significance at $P < 0.05$ level.

4.3 Corticokinematic Coherence

MATLAB based mscohere function was used to calculate magnitude squared coherence between Flex data collected from Smart Glove and EEG data. CKC peaks were observed for two different movement frequencies, they were at 1 Hz and 2 Hz. This result replicates the findings in [2]. They have found CKC peaks at the movement frequency. We have also observed prominent peaks at the movement frequency and at their harmonics. In Figure 18 three PD subjects and three control subjects were shown. They were doing 1 Hz finger tapping with the right hand with metronome. 'No metronome' conditions were not compared. Similar responses can be seen with right-hand finger tapping. The corticokinematic coherence peaks were seen at the movement frequency of 1 Hz and it's harmonics. Activity is more dominant in the right hemisphere as can be seen from the topographic distribution of the coherence magnitude. Control 2, did not show clear

hemispheric dominance in activity. It might be because of noisy trials and should not be related to endogenous neural activity associated with the finger tapping. In

1 Hz Finger Tapping Right Hand with Metronome

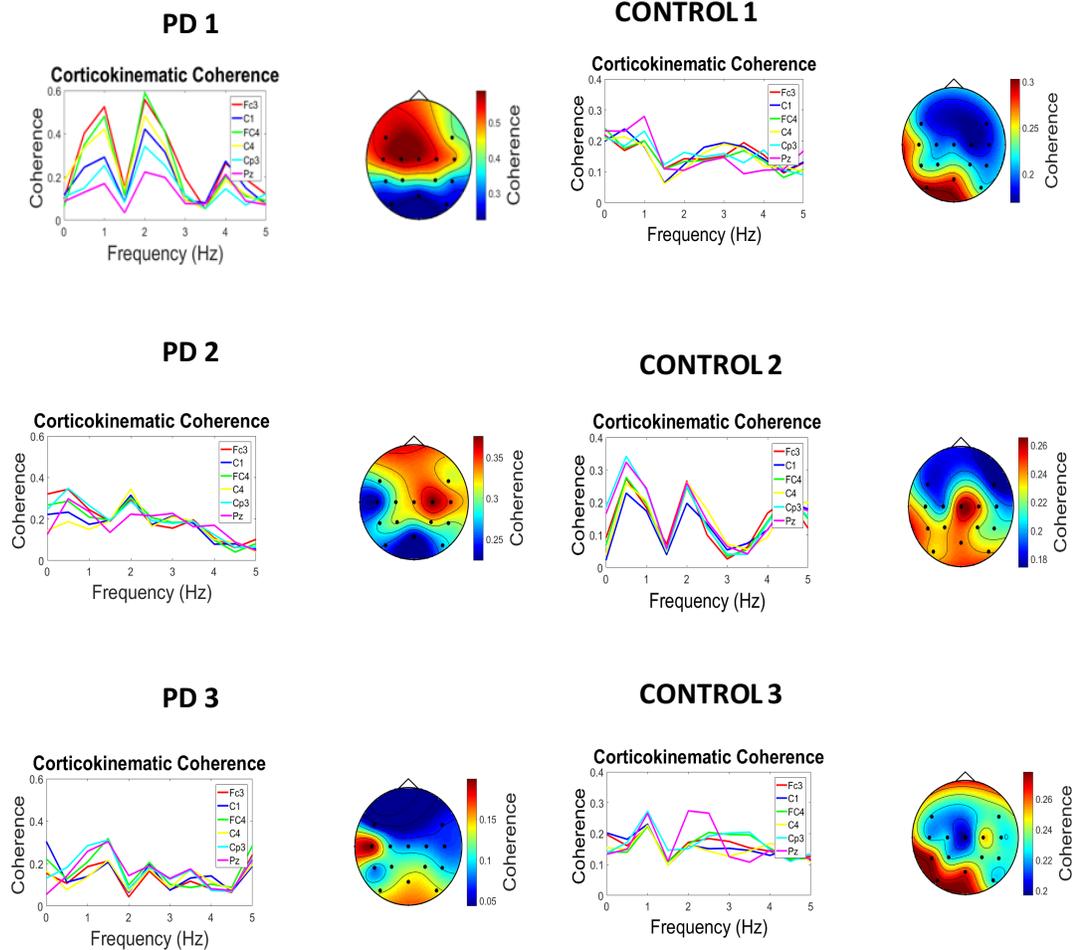


Figure 18. The figure shows the corticokinematic coherence for both Parkinson and control groups while they were doing 1 Hz tapping with the right hand.

Figure 19 three PD subjects and three control subjects were shown. Subjects were doing 2 Hz finger tapping with the left hand. Results from different hands were shown in order to investigate the activity of each hemisphere. The corticokinematic coherence peaks were seen at the movement frequency of 2 Hz and its harmonics.

Activity is more dominant in the contralateral hemisphere as can be seen from the topographic distribution of the coherence magnitude. All the controls have shown higher activity in the left hemisphere. Different channels with different

2 Hz Finger Tapping Left Hand with Metronome

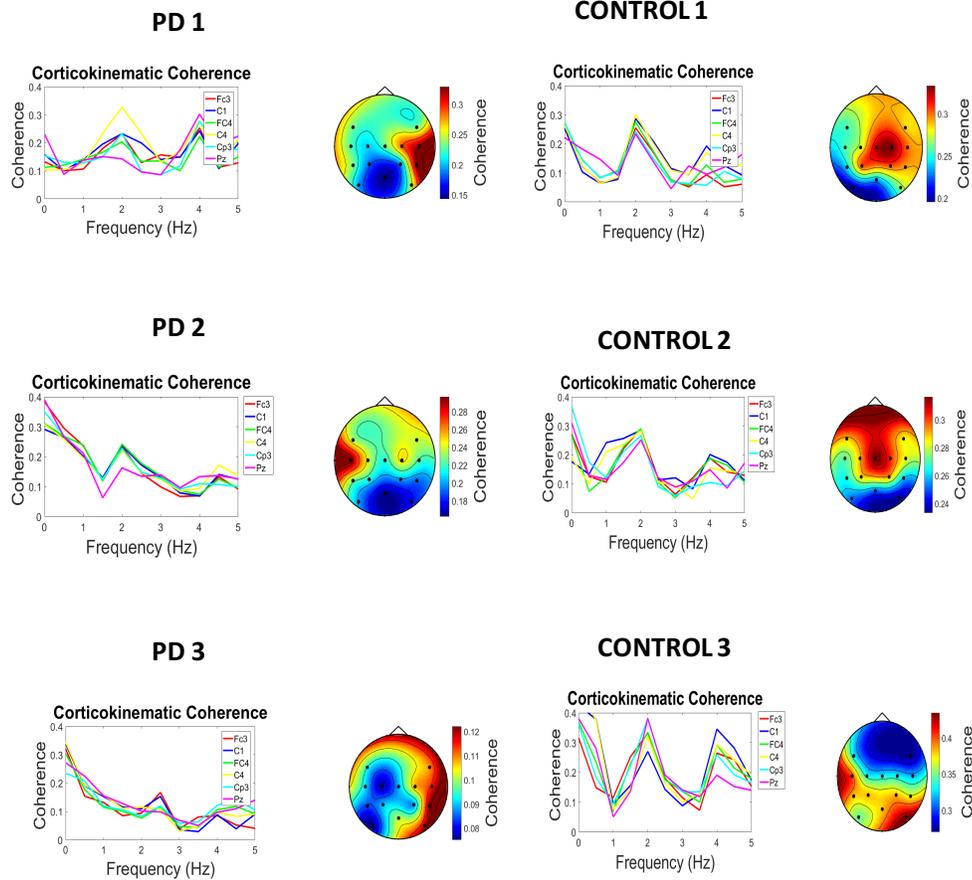


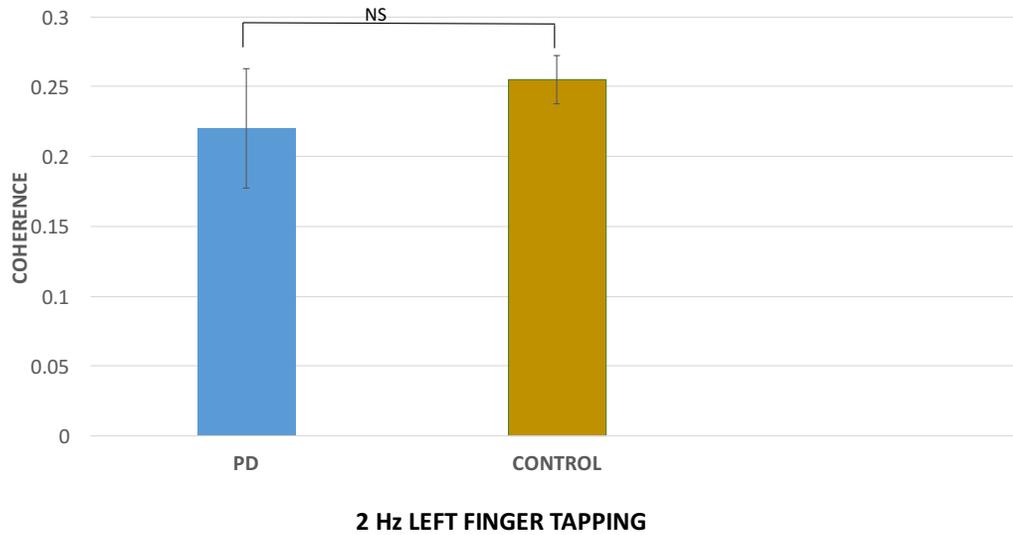
Figure 19. The figure shows the corticokinematic coherence for both Parkinson and control group while they were performing 2 Hz tapping with the left hand.

colors were shown in the coherence plot along with the topographic distribution of the coherence magnitude that ranges between 0 and 1. The values of coherence were averaged over all the trials for each subject. The channels shown are FC3,C1,FC4,C4,CP3 and PZ. [3] used wavelet coherence to investigate the neu-

rovascular coupling between NIRS and aEEG. We skipped the wavelet coherence analysis, although magnitude squared coherence and topographic plots are providing insights into the coupling between EEG and Flex sensor outcomes. We have shown results with metronome only, that was used as an auditory cue for externally pacing the finger movements. The contralateral hemispheric activity is not prominent in all the subjects but can be seen in the topographic plots. Statistical significance could not be achieved with wilcoxon rank sum test which is a non-parametric version of the two-sample t-test. The possible reason for not achieving significance can be the small number of sample size for Parkinson's subjects.

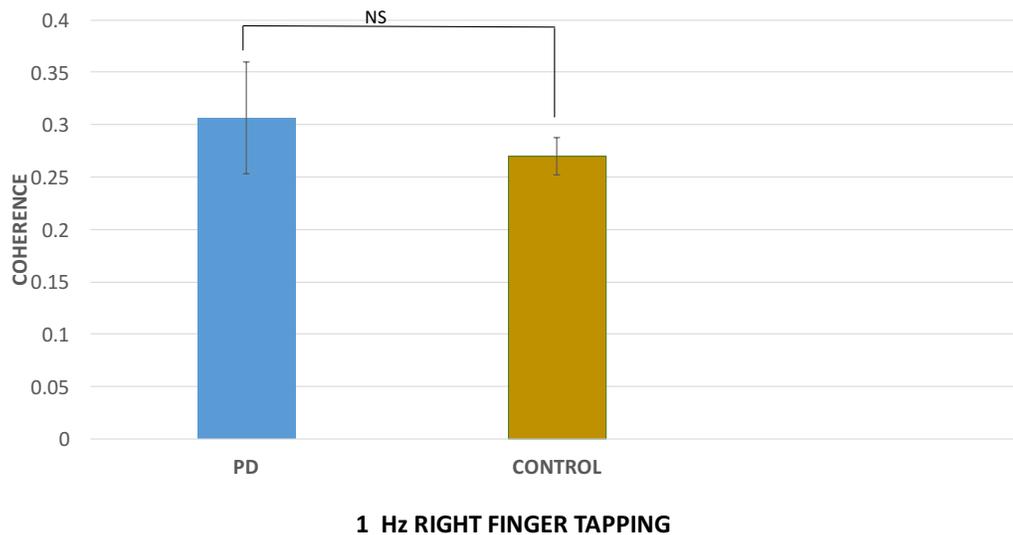
Figure 20, Figure 21 displays the comparative bar plots for 1 Hz right-hand tapping and 2 Hz left-hand tapping respectively. In the 1 Hz right hand tapping PD subject, subject 1 has a relatively higher peak that can account for the higher average peak value in PD group as compared to the control group. In the 2 Hz tapping of the left-hand plot, the mean coherence is found to be more in control group as compared to PD group.

The results from Wilcoxon rank sum test gives the P value greater than .05 for 2 Hz PD vs control coherence. Results indicate that there is not enough evidence to reject the null hypothesis of equal medians at the default 5% the significance level for PD vs Control, 1 Hz tapping conditions. Similarly, the P value of greater than .05 for 1 Hz PD vs control coherence was found with Wilcoxon rank sum test. Results indicate that there is not enough evidence to reject the null hypothesis of equal medians at the default 5% the significance level for PD vs Control 1 Hz Tapping conditions. The reason for not achieving statistically significant difference might be the low number of sample size for PD group. We had 3 people with PD and 8 control subjects chosen from initial 10 neurotypical subjects and 4 PD subjects. The last PD subject's results are shown in the appendix.



1

Figure 20. The figure displays the bar plots for 2 Hz left-hand tapping for PD and control groups.



1

Figure 21. The figure displays the bar plots for 1 Hz right-hand tapping for PD and control groups.

A higher number of PD subjects might provide better results with statistical testing which we could not see in this analysis probably due to low sample size. The error bars in Figure 20 and Figure 21 show overlapping between the two groups.

The mean coherence of .3067 for PD 1 Hz and .2700 for control 1 Hz tapping condition is seen. Similarly mean coherence of .22 and .25 is seen in 2 Hz tapping condition for PD and control groups respectively. The standard error was .0536 for PD 1 Hz and .0175 for control 1 Hz condition. Similarly, the standard error was .043 for PD 2 Hz tapping condition and 0.017 for the control group for 2 Hz tapping condition.

4.4 Power Spectrum Analysis

The power spectrum of the EEG signals and Flex signals are shown in Figure 22, Figure 23, Figure 26 and Figure 27. Motor related steady-state evoked potentials (SSEP) is seen at the movement frequency in both PD and control groups with both metronome and without metronome conditions. The results presented in this thesis includes only the metronome conditions which act as a pacing signal for endogenous neural oscillations [4]. Past researchers have seen the activity of accelerometer and EEG in the alpha and beta bands.

Our analysis focused on delta band activity mainly from .5 to 4 Hz. The subject performed index finger tapping with a 1 Hz and 2 Hz metronome as an auditory cue. FFT power spectral density for the 1 Hz finger tapping condition is shown for both PD and control groups in the plots. Clear peaks at 1 Hz have been shown by all three people with PD and eight out of ten control subjects. Power spectral density is estimated using the MATLAB 'fft' function that computes the discrete Fourier transform (DFT) of the signal using a fast Fourier transform (FFT) algorithm. For the n-point DFT, the value of n is chosen same as the length of the signal. The sampling frequency was 256 for all the conditions. Flex signals had a sampling frequency of 258Hz. So the Flex signals are down-sampled to match with the sampling rate of EEG signals. Individual variability in the peak amplitude is observed in all the cases and groups. No statistically significant difference has

been seen with EEG spectral peaks between PD and control groups. Small sample size might be the reason. Figure 24, Figure 25 shows the bar diagram with the error bars comparing peaks in the power spectrum averaged over all the subjects in both the groups. Similarly, with 2 Hz finger tapping condition, EEG signals power spectrum did not show any statistically significant difference between the groups in the 5% significance level. Figure 22 and 23 shows the power spectrum

1 Hz Finger Tapping Left Hand with Metronome

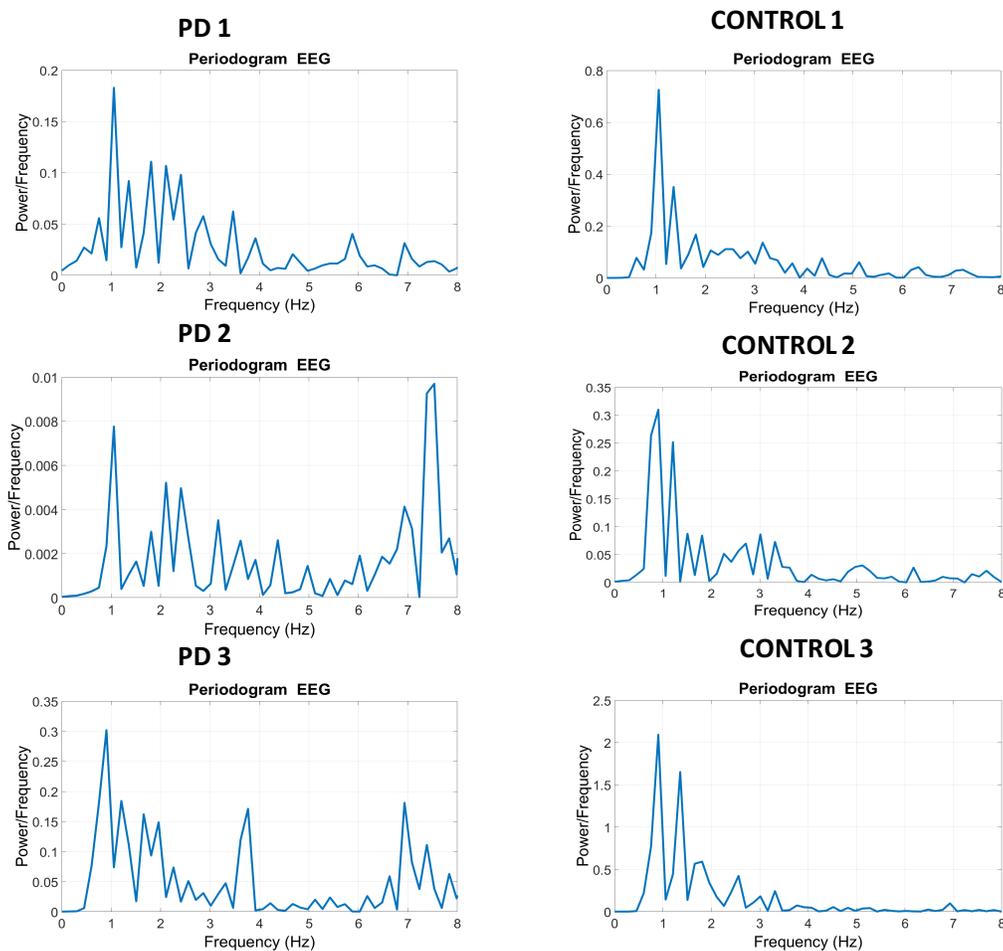


Figure 22. The figure shows the spectrogram of EEG for subjects performing 1 Hz left hand finger tapping.

for the 1 Hz, 2 Hz tapping condition for both the PD and control groups. The

peaks are seen clearly at the 1 Hz and 2 Hz in 22 and at 2 Hz and 4 Hz in 23 , that is the movement frequency and harmonics of the movement frequency. The plot displays the power spectrum density for channel C2 only. Although clear peaks were seen in other channels covering somatosensory and motor area. The Figure 24, 25 bar plots were generated with C2 peaks for left hand tapping. The power

2 Hz Finger Tapping Left Hand with Metronome

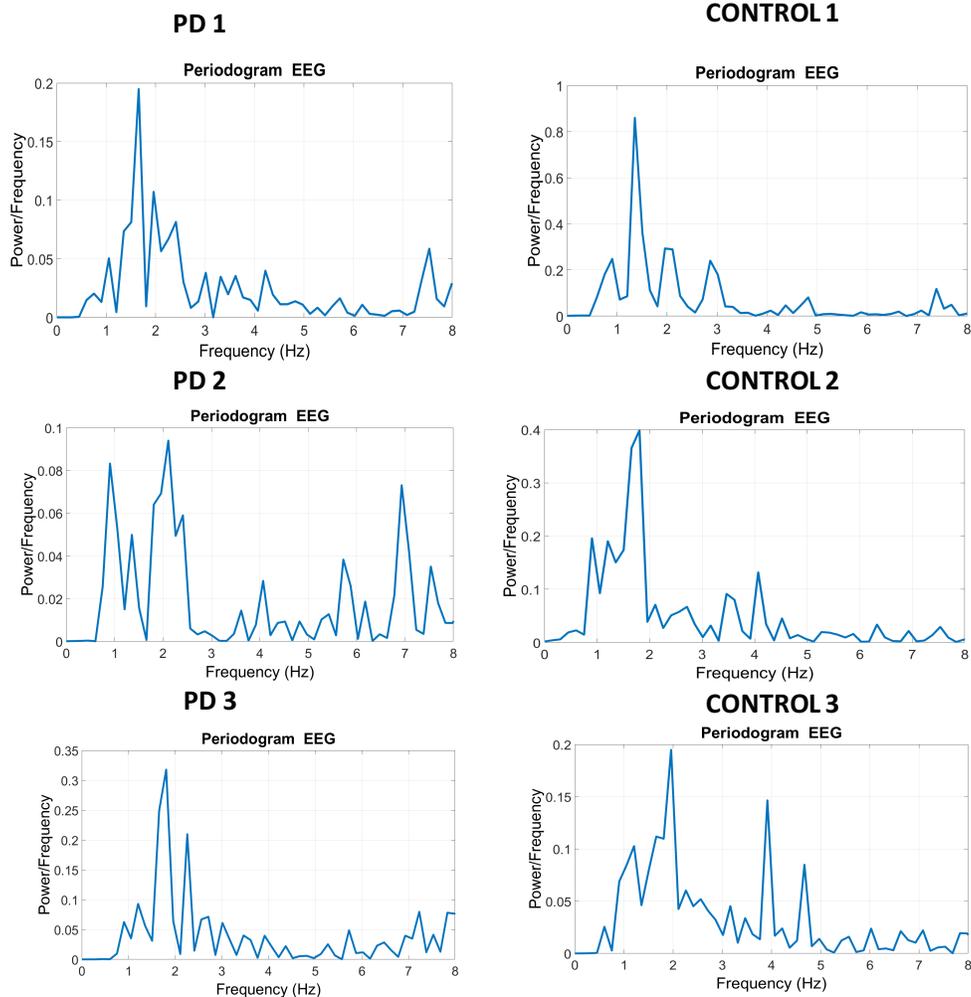


Figure 23. The figure shows the power spectrum with 2 Hz finger tapping left hand of PD and control groups for EEG.

spectrum for Flex 1 Hz and 2 Hz signals are shown in Figure 26 and in Figure 27. Clear peaks are seen at the movement frequency of 1 Hz and 2 Hz and with

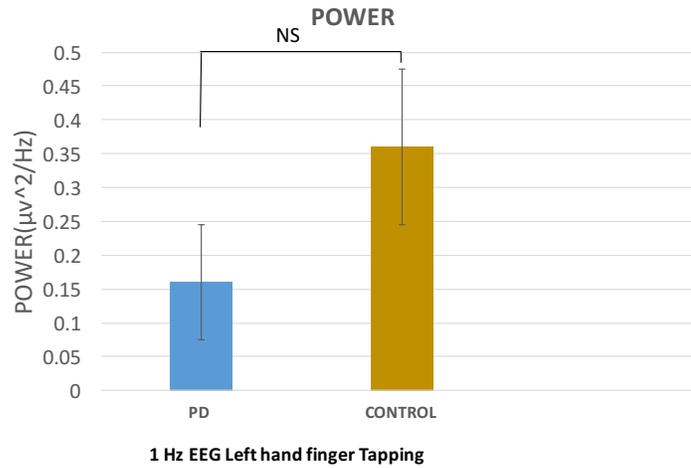


Figure 24. The figure shows the bar plots for the finger tapping left hand of PD and control groups with 1 Hz for EEG.

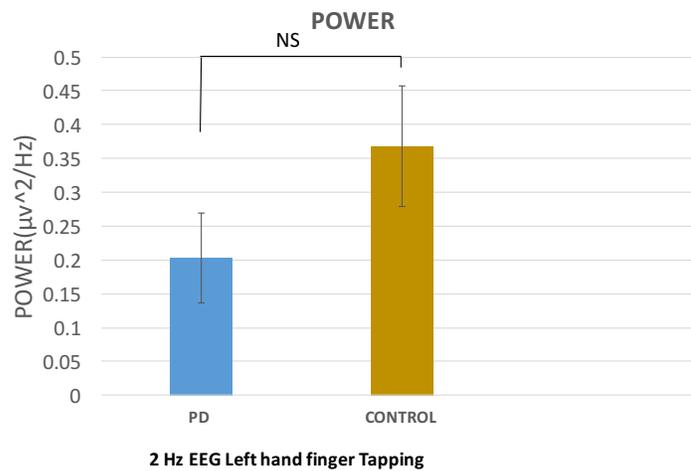


Figure 25. The figure shows the bar plots for the finger tapping left hand of PD and control with 2 Hz groups for EEG.

their harmonics respectively for 26 and 27 for both the PD and control groups. Flex signals were bandpass filtered at .5 to 100 Hz frequency band similar to EEG signals.

2 Hz Finger Tapping Left Hand with Metronome

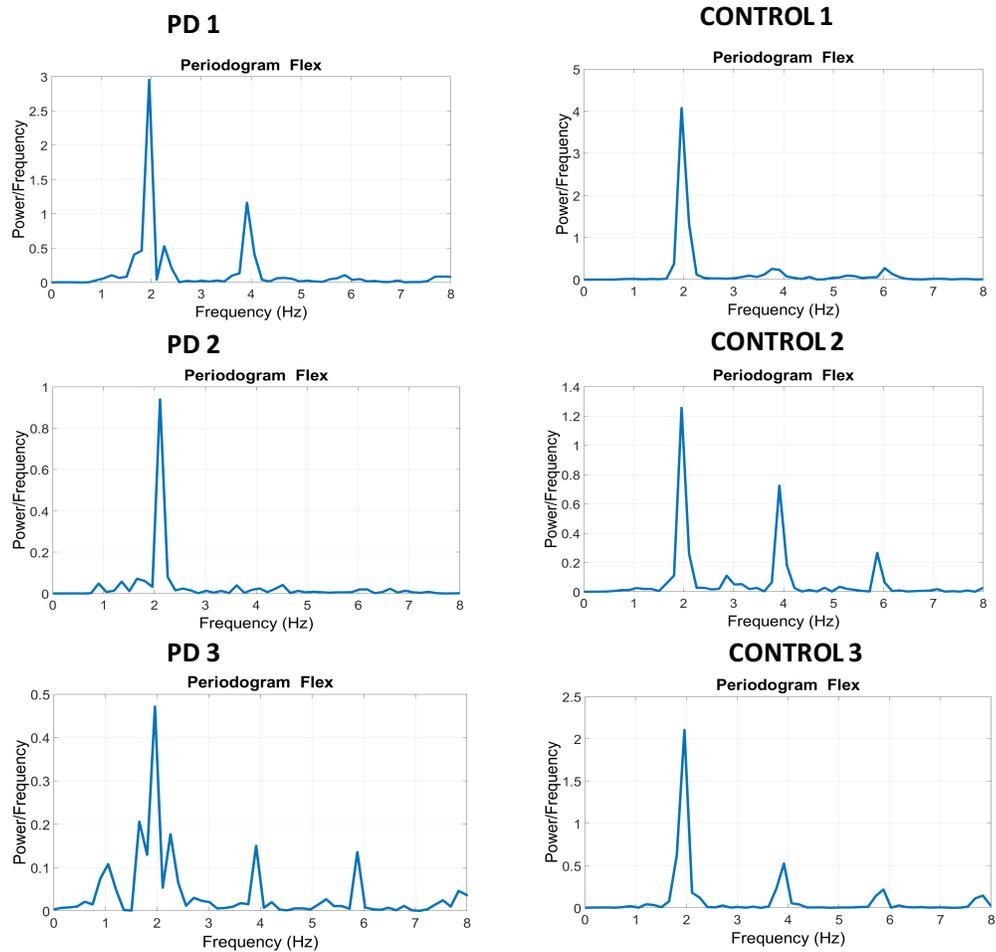


Figure 26. The figure shows the power spectrum with 2 Hz finger tapping left hand of PD and control groups for Flex signal.

The peaks for Flex were more clear and prominent as compared to the EEG spectrum. Mainly due to noise associated with EEG signals, which is absent with the Flex signal. Flex signals were detrended to remove any linear trend before processing. It removes the long-term trends in order to emphasize short-term changes in the signal. The sampling frequency was made equal to EEG sampling rate of 256 Hz. Epoch length of 8 sec was chosen for trial averaging of the signals. Fourier transform of the trials were averaged to get the spectrum. The plots show

results for single trials.

The results from Wilcoxon rank sum test gives the P value of .3758 for 2 Hz PD vs control FFT power spectral density amplitudes for Flex signals. Results indicate that there is not enough evidence to reject the null hypothesis of equal medians at the default 5% significance level for PD vs Control, 2 Hz tapping conditions. Similarly, a P value of 0.1818 for FFT power spectral density amplitudes for Flex signals were found with Wilcoxon rank sum test. Results indicate that there is not enough evidence to reject the null hypothesis of equal medians at the default 5% significance level for PD vs Control 1 Hz tapping conditions. The reason for not achieving statistically significant difference might be the low number of sample size for PD group as seen with EEG spectrum and Coherence spectrum. We had three people with PD and eight control subjects. A higher number of PD subjects might provide better results with statistical testing which we could not see in this analysis of spectral amplitudes.

One interesting observation from the power spectrum plots that can be seen is that the spectral peaks are localized almost exactly at the movement frequency, that is either 1 Hz or 2 Hz and at its harmonics. We also investigated power spectrum of EEG signal when the only metronome as an auditory cue was used and no finger tapping was there. We could see peaks at the tapping frequency but the amplitudes were much weaker. For PD subject 4, the power spectrum did not show prominent peaks, as shown in the appendix. This is due to the tremor the subject was experiencing while doing the finger tapping. Although for 1 Hz right hand condition, the subject has shown peaks at the movement frequency.

Statistical significance is not achieved but amplitudes for control subjects were seen larger than PwPD as shown in the bar graphs in Figure 28 and 29. This is also seen in Figure 25 and Figure 24. NS in the plots signify, not significant

difference between the groups. A larger sample size along with similar age group neurotypical study can yield better significant results. This is one of the limitations of this study. There was a significant gap between the age of healthy vs PwPD subjects. Despite this limitation, we could see nice and prominent peaks in the power spectrum of the EEG and Flex for both the groups.

1 Hz Finger Tapping Left Hand with Metronome

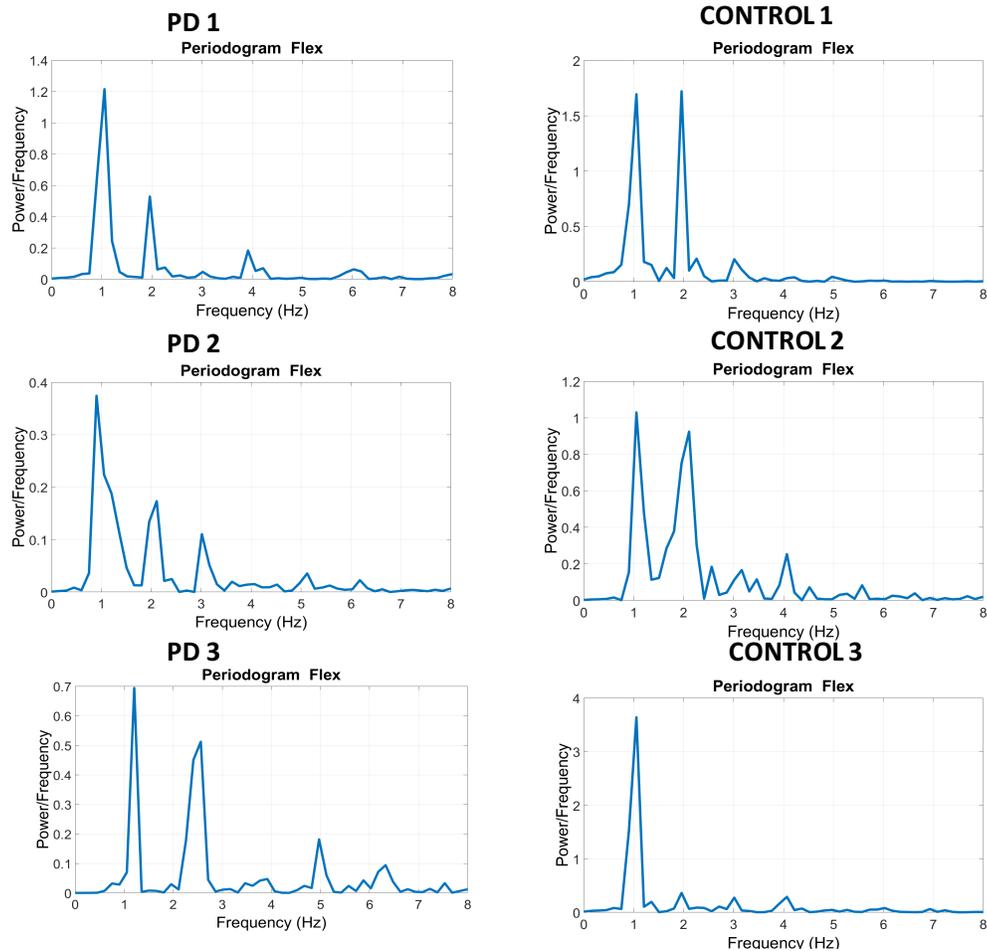


Figure 27. The figure shows the power spectral density for Flex signal for 1 Hz finger tapping with metronome as auditory pacing cue for both PD and control groups.

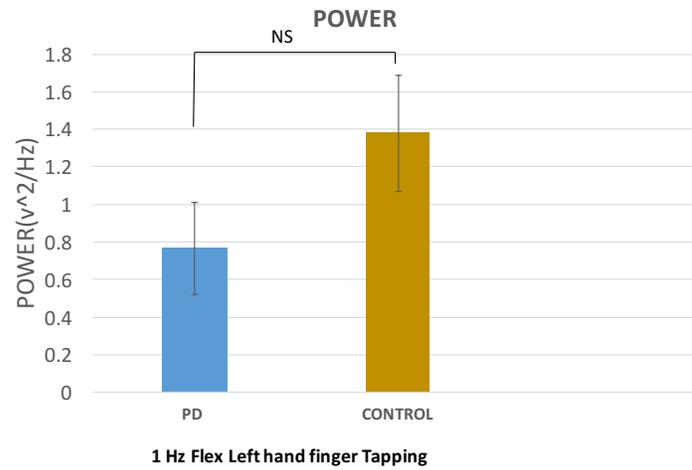


Figure 28. The figure shows the bar plots with error bars for the finger tapping of PD and control groups for Flex signals at 1 Hz tapping.

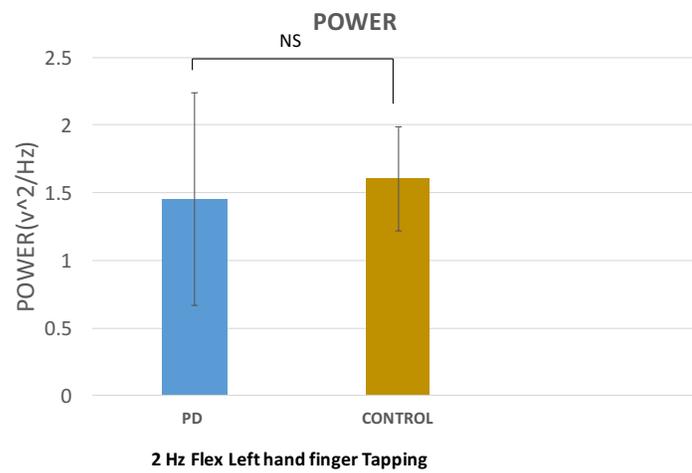


Figure 29. The figure shows the bar plots with error bars for the finger tapping of PD and control groups for Flex signals at 2 Hz tapping.

4.5 Discussion

We examined the coupling between finger kinematics and cortical signals for a finger tapping task in people with PD(PwPD) and healthy controls. Three out of the four PwPD were on medication. None of the participants had DBS surgery. All the participants from the PD group have scored more than 23 in the Montreal Cognitive Assessment Test (MoCA). Authors in [5] reported in their research about EMG power spectra peaks between 5-12 Hz for postural tremor peak in Parkinson disease. Our experimental paradigm does not investigate the small amplitude tremor associated with Parkinson disease, rather we have investigated corticokinematic coherence(CKC) between Smart Glove Flex signals and EEG at the movement frequency of simple finger flexion and extension task. As reported by Piitulainen et al. [2] in their research, they investigated CKC for active and passive index finger kinematics. They have seen CKC peaks at the movement frequency. In our analysis, Figure 18 and Figure 19 shows the CKC peaks at the movement frequency for both PD and control groups. But we could not see the statistically significant difference between the groups due to a smaller sample size of PD group as shown in Figure 20 and 21. We have also investigated time-frequency analysis on the EEG data. A clear reduction in power is seen at the mu band when the subject starts finger tapping. The extent of reduction was varied from subject to subject. Figure 14, Figure 15, Figure 16 shows the time-frequency plots generated using wavelet transform. The reduction at the frequency range of 8-15 Hz is apparent. In Figure 17 the RMS power plots were shown for PD and control group, Rest vs Tapping conditions. Individual variation is often reported in studies associated to EEG. While investigating the CKC and power spectrum, we have observed this variability. Different subjects showed different peak amplitude at the movement frequencies. The peaks at the movement frequency might provide insights into

the neural oscillations phase locked to movement frequency. Jerebi et al. [6] observed that 2 to 5 Hz cortical oscillations in human M1 neurons is increased in amplitude and became phase locked with hand speed during motor control. Such similar phenomenon must be happening with the extension and flexion task at the metacarpophalangeal joint of the index finger paced by metronome as an auditory cue. Further exploration of the neuro-scientific origin of such motor and cortical coupling is required.

This research can be considered as a proof of concept study. For significance in the comparison between PwPD and neurotypical, a larger sample size was needed. We have included the analysis of the fourth PwPD subject in the appendix. The fourth subject was seen to exhibit excessive tremor so EEG signals were contaminated with motion artifacts.

We have also investigated if there was any effect of the metronome as a cue. The figure A.16 in the appendix shows the comparison between finger tapping and only metronome and no tapping conditions. The peak for tapping was larger, and no prominent peak was seen with no tapping and only metronome condition.

As a future outlook, novel approaches using Machine learning and Deep learning might be useful in identifying the tremors in Parkinson, differentiate between Parkinson and Parkinsonism, stages of Parkinson disease etc from the features extracted using signal processing techniques such as the CKC and power spectrum explored in this research. This research introduces the use of Flex sensor based Smart Glove. This combination of neuro-imaging and Smart Glove can be helpful in finding quantifiable measurements like CKC to quantify motor-related symptoms in Parkinson disease, as we have shown with the finger tapping task. Thus we can say that this research validates the use of CKC as a metric for quantification of motor tasks in Parkinson disease.

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CHAPTER 5

Conclusion

Parkinson Disease is affecting millions of people throughout the globe. The objective of our research is to quantify the effects of motor tasks for finger tapping in Parkinson disease using a specially designed Smart Glove. We have investigated the coupling between neural oscillations and finger kinematics using cortikokinematic coherence (CKC) as a measurement. We have also investigated the suppression of power in mu band associated with the performance of a motor action that is finger tapping in our case. A clear reduction of power at the mu band frequencies was observed when the subjects started tapping the finger. CKC and power spectrum showed prominent peaks at the movement frequency of finger tapping with a metronome as pacing cue. We could not see any statistically significant difference in PD vs control groups neither in CKC nor in power spectrum. We assume that this is mainly due to the small sample size of PD participants and the difference in the age between the two groups can also be a factor.

This research will help the clinicians and researchers to investigate further. For example, quantification of motor-related symptoms can be extremely helpful for the people living with Parkinson. This research can be considered as a proof of concept study, which successfully demonstrated the use of CKC as a quantification measure with the help of specially designed Smart Glove. In the long run, this research work will certainly open up new scientific questions and will contribute to the Parkinson research community in developing new methods to quantify the symptoms associated with Parkinson and thereby might help in better diagnosis and treatment of Parkinson disease.

APPENDIX

A.0.1 Power Spectrum of EEG and Flex

The power spectrum of the EEG signals and Flex signals are shown in the plots. Figure A.1 shows the EEG and Flex signals for Left hand 1 Hz finger tapping condition. Figure A.2 displays the same for subject 7 and subject 8. Figure A.3 shows the EEG and Flex power spectrum for 2 Hz left hand tapping condition. All the conditions were with metronome. Figure A.4 displays the activity of subject 7 and subject 8 for EEG and Flex. Figure A.5 shows the power spectrum for right hand finger tapping. The channel chosen was C1 for right hand and C2 for left hand. Figure A.6 shows the finger tapping for right hand 1Hz. Figure A.7 displays the power spectrum for the subjects 4, subject 5, subject 6, while they were doing 2 Hz right hand finger tapping. Figure A.8 shows the same activity for control subject 7 and subject 8. Figure A.13 and A.14 displays the EEG and Flex power spectra for the 4 th PD subject.

A.0.2 Time Frequency Plots

Figure A.15 shows the time frequency plots for the PD subject 4, for left and right hand finger tapping at 1 Hz and 2 Hz respectively. Figure A.9 displays the Time Frequency plots of the EEG of the control subjects. The reduction in mu band is not prominent in all the subjects but can be seen clearly in a varying degree. Figure A.10 shows The Time Frequency plots for control subjects 7 and 8. Figure A.11 shows the similar time frequency plots for left and right hand 2 Hz activity. Figure A.12 shows the time frequency activity for control subjects 7 and 8 while they were tapping at 2 Hz.

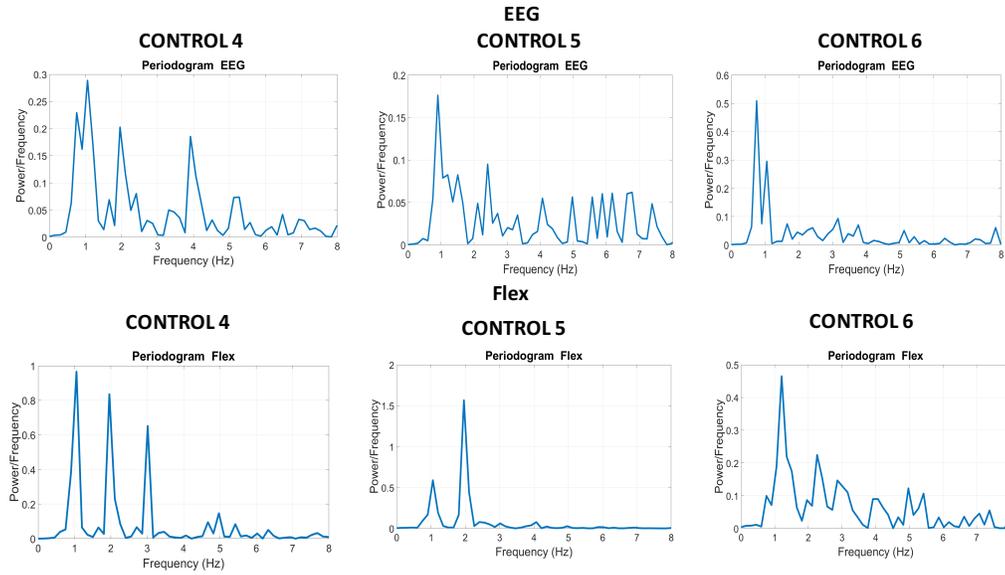


Figure A.1. Power spectrum EEG and Flex signals for left hand 1Hz finger tapping with metronome for control subjects 4 to 6.

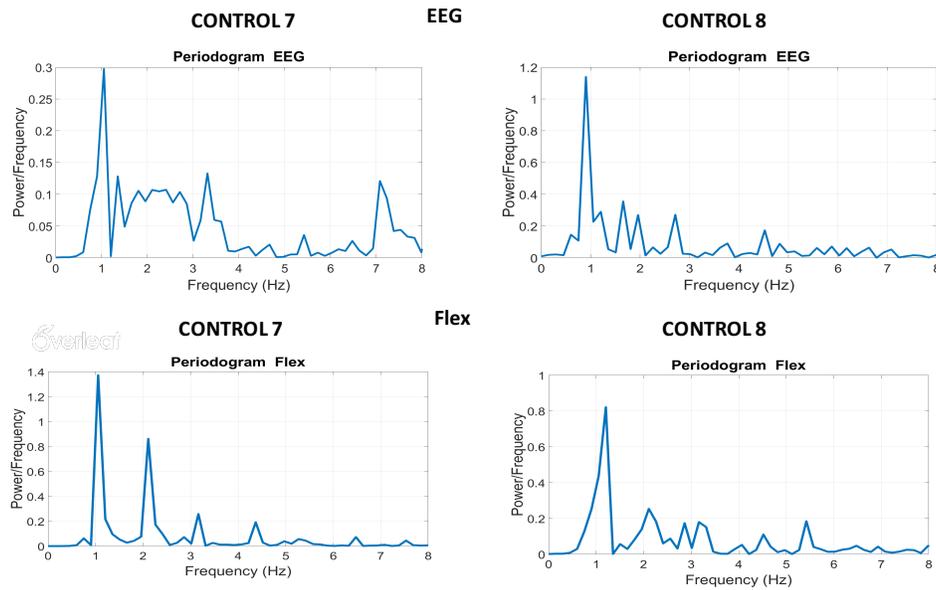


Figure A.2. Power spectrum EEG and Flex signals for left hand 1Hz finger tapping with metronome for control subjects 7 and 8.

A.0.3 Comparison between only metronome vs finger tapping

Figure A.16 shows the comparison of power spectrum for Tapping condition and only metronome and no tapping condition. The First plot displays the power

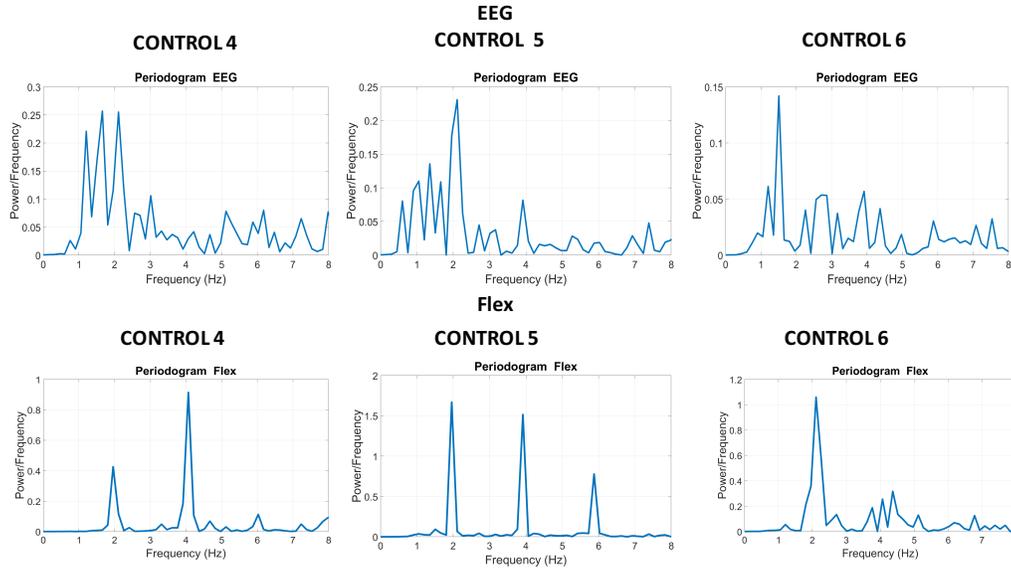


Figure A.3. Power spectrum EEG and Flex signals for left hand 2Hz finger tapping with metronome for control subjects 4 to 6.

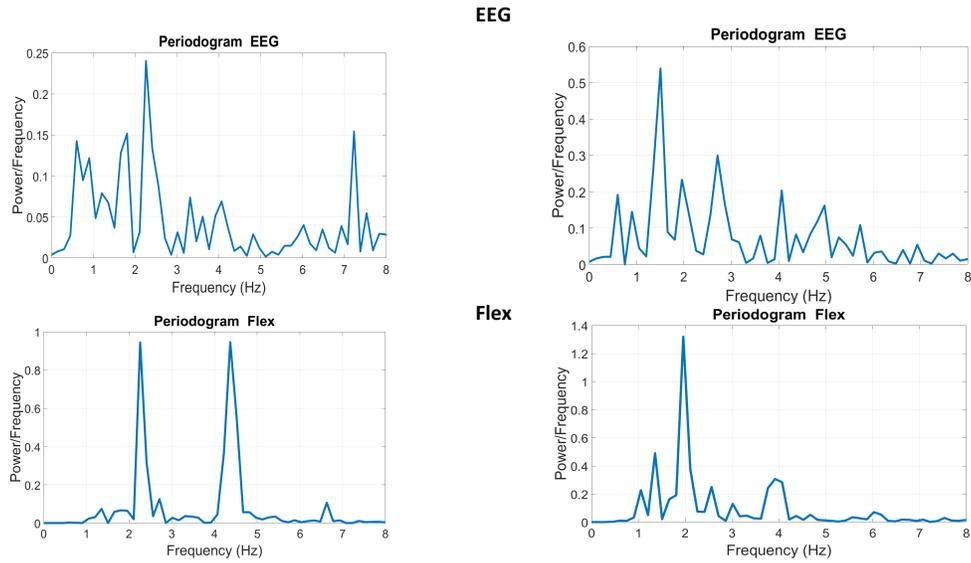


Figure A.4. Power spectrum EEG and Flex signals for left hand 2Hz finger tapping with metronome for control subject 7 and 8.

spectrum of EEG and second spectrum displays the power spectrum of flex.

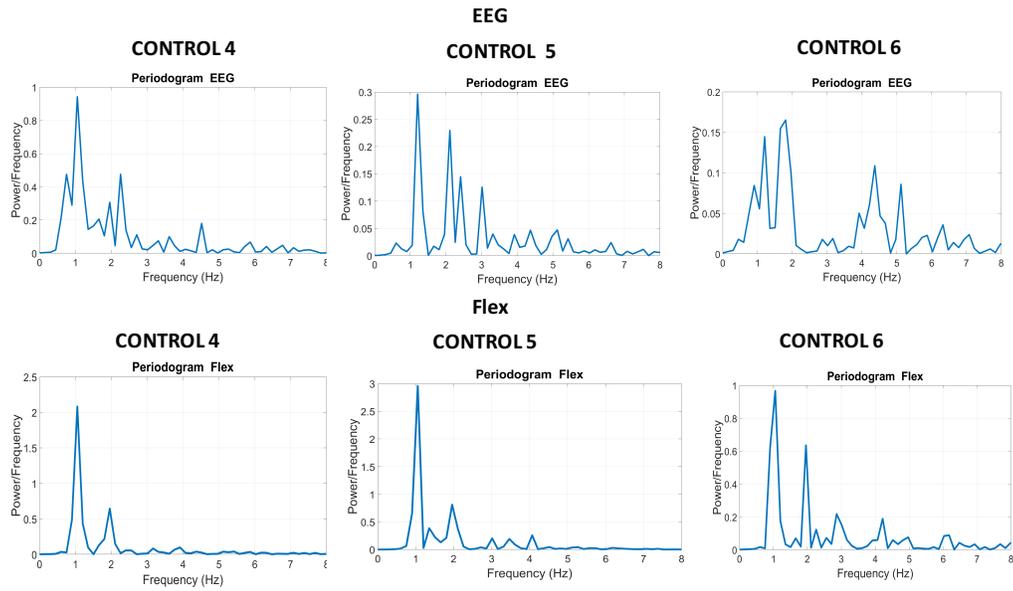


Figure A.5. Power spectrum EEG and Flex signals for right hand 1Hz finger tapping with metronome for control subject 4 to 6.

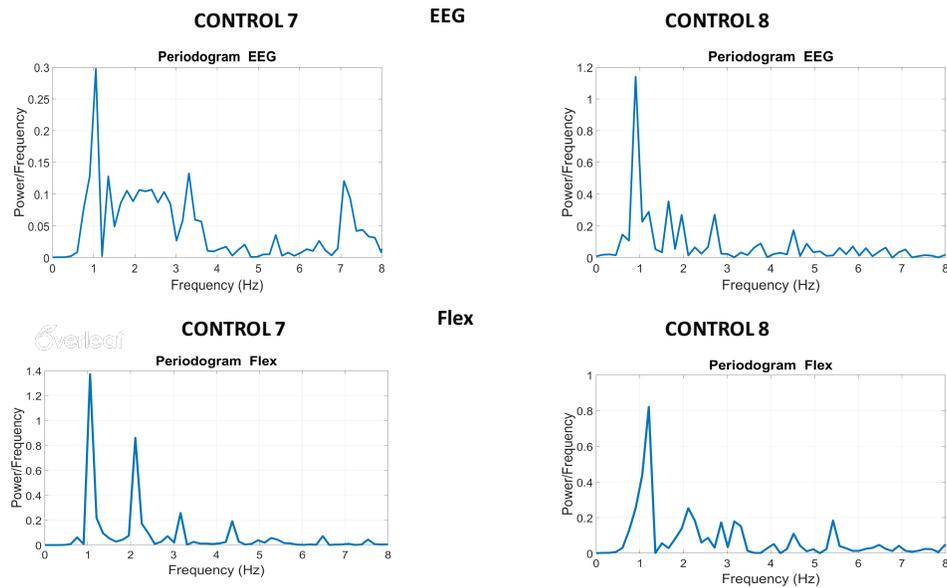


Figure A.6. Power spectrum EEG and Flex signals for right hand 1Hz finger tapping with metronome for control subject 7 and 8.

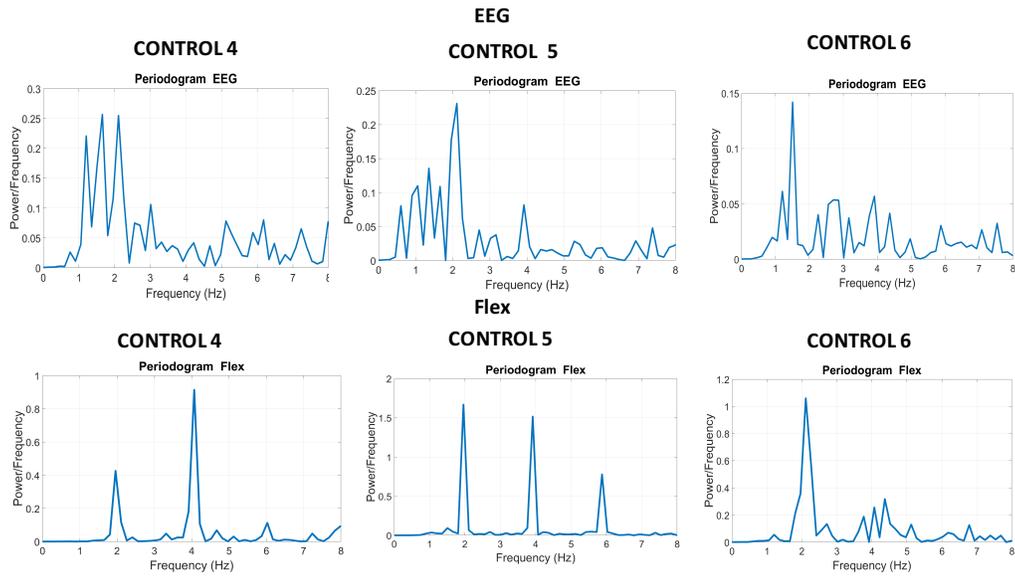


Figure A.7. Power spectrum EEG and Flex signals for right hand 2Hz finger tapping with metronome for control subjects 4 to 6.

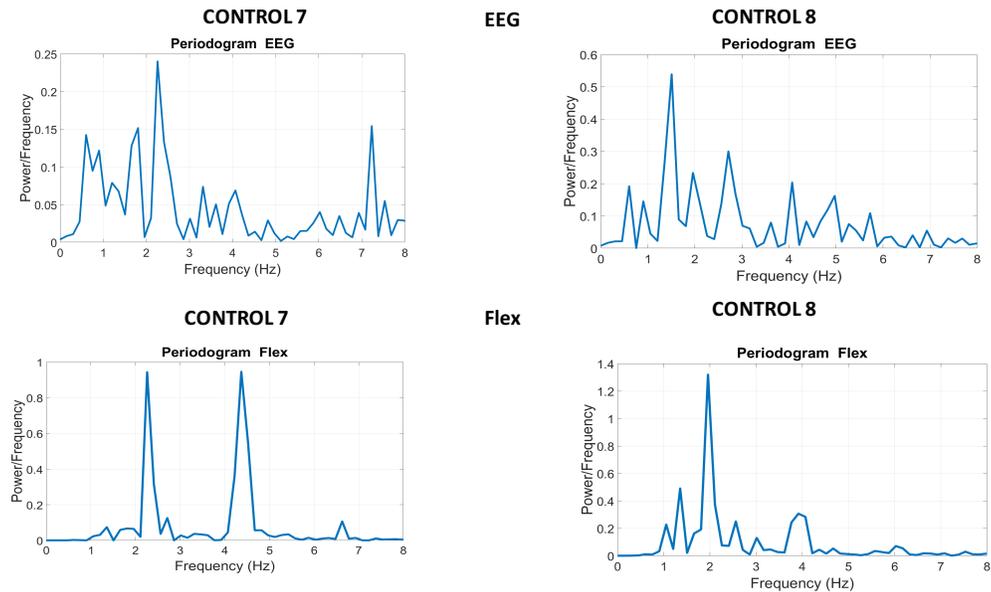


Figure A.8. Power spectrum EEG and Flex signals for right hand 2Hz finger tapping with metronome for control subjects 7 and 8.

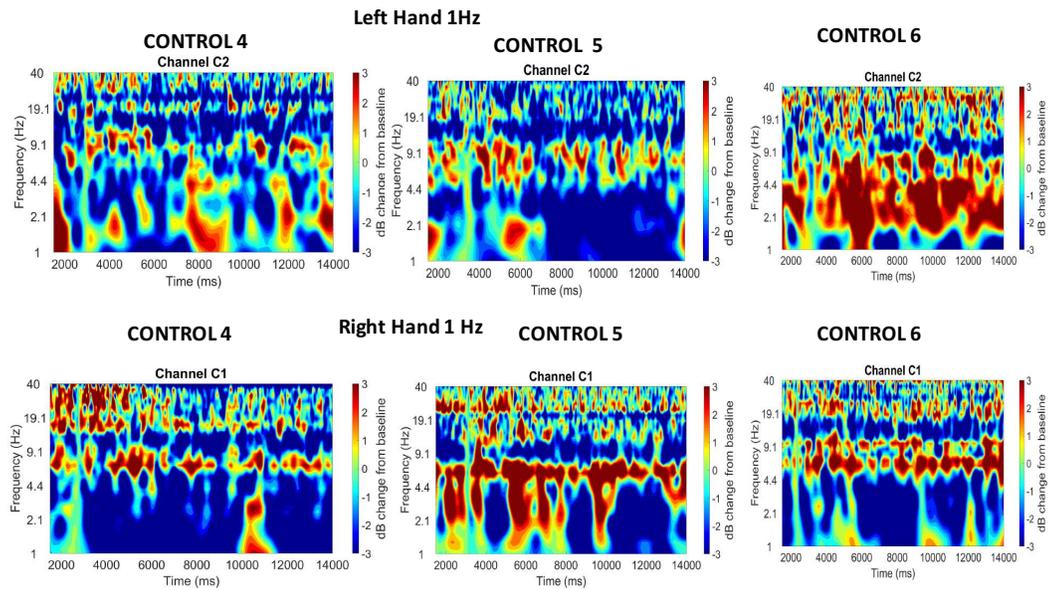


Figure A.9. The time frequency plots for EEG for control subjects 4 to 6, for both left and right hand 1 Hz tapping condition.

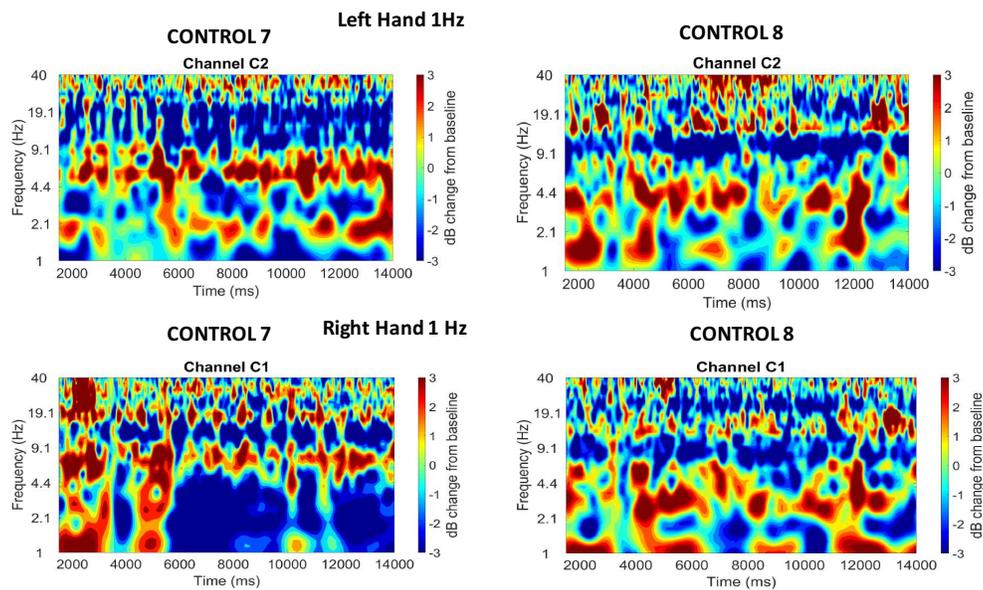


Figure A.10. The time frequency plots for EEG for control subjects 7 and 8, for both left and right hand 1 Hz tapping condition.

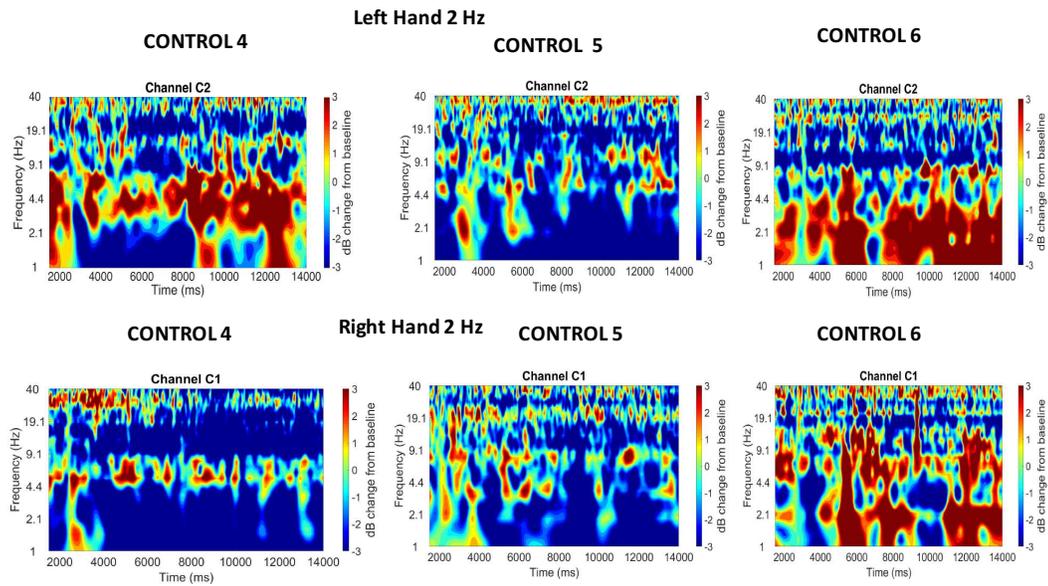


Figure A.11. The time frequency plots for EEG for control subjects 4 to 6, for both left and right hand 2 Hz tapping condition.

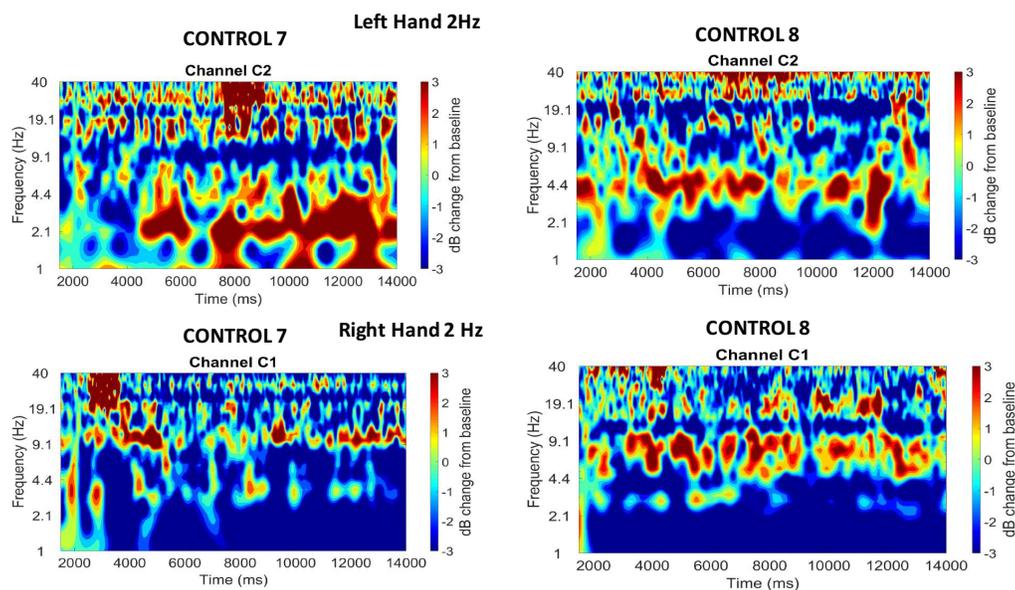


Figure A.12. The time frequency plots for EEG for control subjects 7 and 8, for both left and right hand 2 Hz tapping condition.

Finger Tapping with Metronome PD 4 EEG signal

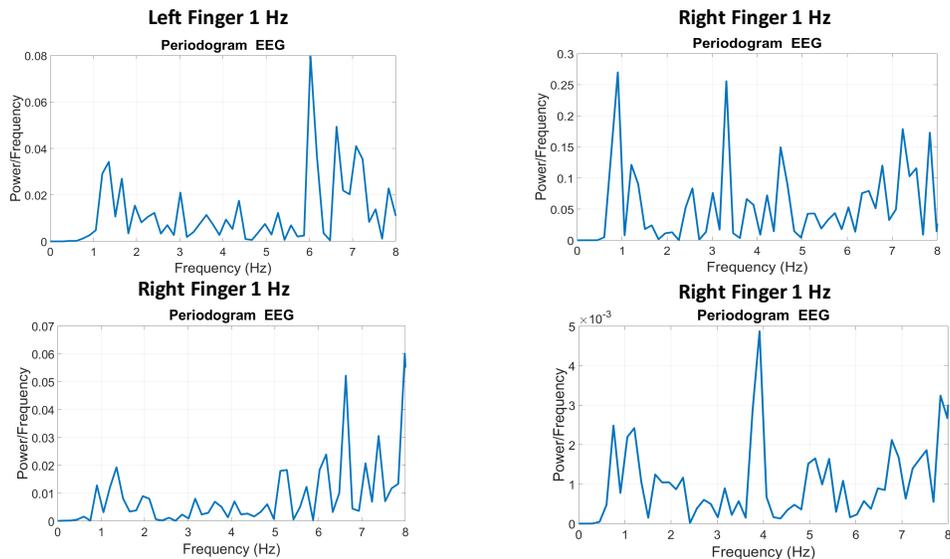


Figure A.13. Power spectrum of EEG signal for right hand and left hand 1Hz finger tapping with metronome for PD subject 4.

Finger Tapping with Metronome PD 4 EEG signal

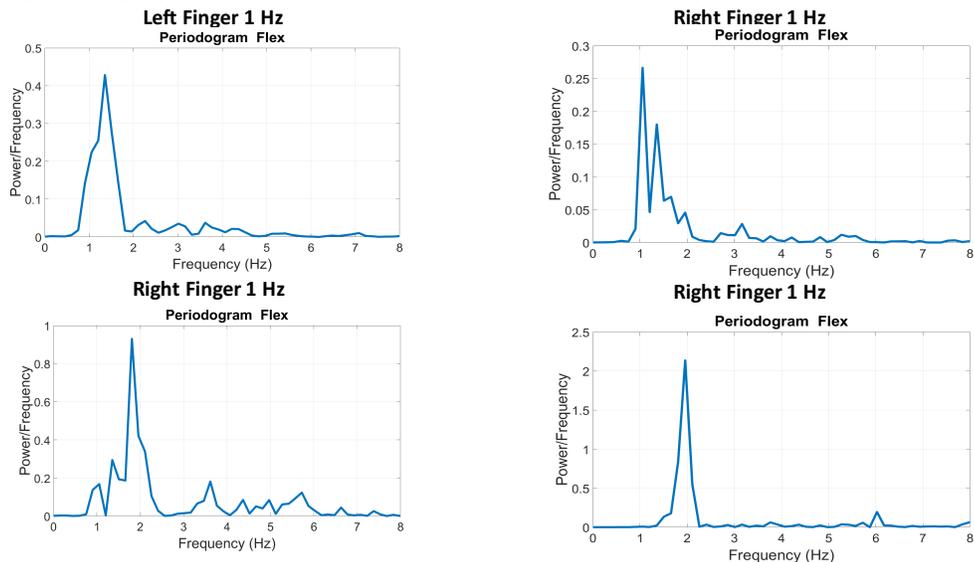


Figure A.14. Power spectrum of Flex signal for right hand and left hand 1Hz finger tapping with metronome for PD subject 4.

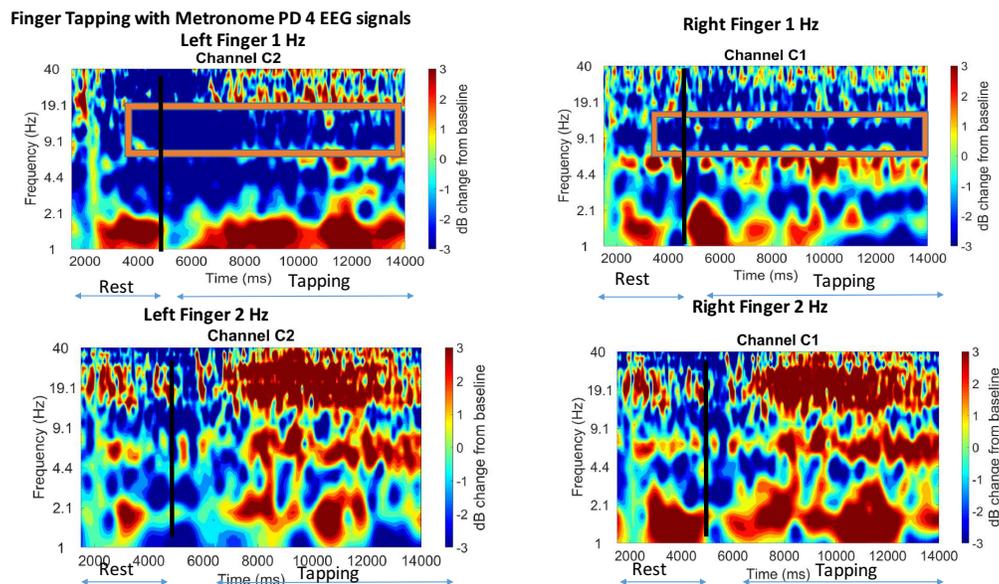


Figure A.15. Time frequency plots for PD subject 4 for both right and left 1 Hz and 2 Hz finger tapping with metronome

2 Hz Tapping right hand vs only metronome

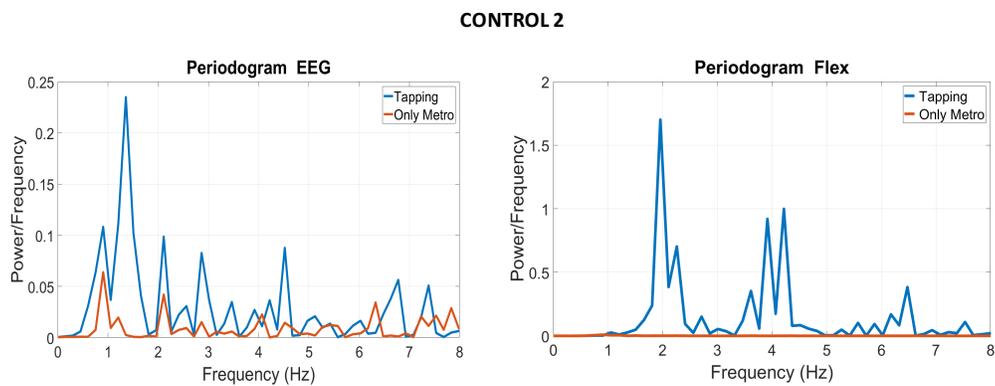


Figure A.16. Power spectrum EEG and Flex signals for right hand 2Hz finger tapping with metronome vs only metronome and no tapping condition.

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