CORTICO-MUSCULAR FUNCTIONAL INTERACTION BASED ON MOTOR TASK PERFORMANCE

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ABSTRACT

The functional interaction of brain and muscle signals plays an important role in our daily lives. We have to perform various motor tasks using different movements to accomplish our tasks daily. The movements and motor tasks that we use and perform every day finally become a goal. Such goals are the output of motor task performance. The brain and muscles act synchronically during motor task performance to achieve the movement goal. The principles of cortico-muscular interaction play an essential role in the rehabilitation systems of stroke patients, the treatment of motor-impaired people, and the treatment of dyskinesia, Alzheimer's disease, and Parkinson's disease. In order to understand the basic principles of brain and muscle function for future brain-computer interface (BCI) technology, it is important to understand the cortico-muscular functional interaction and its neurophysiological principles.

Although there were well-documented findings of functional interaction with maintained voluntary contraction, executed precision-pinch tasks, static isometric contraction tasks, wrist flexion and extension tasks, and cortico-muscular functional interaction comparison in real movement, the movement intention stage, motor imagery stage, and movement observation condition were lacking in the study. Thus, this study will explore brain-muscle functional interaction and its neurophysiological principles during these tasks as a preliminary study of brain-muscle functional connectivity.

In this study, four different motor performances were applied, such as real hand grasping movement (RM), movement intention (Inten), motor imagery (MI), and only looking at the virtual hand in a three-dimensional head-mounted display (3D-HMD) (OL). This study involved thirteen healthy right-handed participants from Kyushu University. We explored the cortico-muscular functional interaction with the linear coherence method, the nonlinear mutual information method, and the nonlinear mutual information delay time method. The objectives of this study are to investigate the functional interaction of brain-muscle signals and their coupling delay times based on four different motor tasks, to explore the anatomical and neurophysiological principles of brain and muscle function that can lead to cortico-muscular interaction, and to discover consistent and reliable facts about cortico-muscular interaction based on unresolved research issues.

The results proved that brain–muscle functional interaction and delay time change according to motor task performance. Quick synchronization of localized cortical activity and motor unit firing causes good functional interaction, and this can lead to a short delay time between signals. In addition, the motor system inside the human body works hierarchically to accomplish the predefined movements or reach the goals that we set. Those motor systems interact with each other via diverse tracts such as descending motor pathways and ascending motor pathways. Thus, brain and muscle signals can flow with bi-directionality between efferent and afferent pathways. This study will provide consistent and reliable facts about cortico-muscular functional interaction that resulted from our experimental research for rehabilitation systems and a future Brain-Computer Interface (BCI) system.

Keywords : cortico-muscular coherence; delay time; electroencephalogram; electromyogram; functional coupling; mutual information; motor system; motor task performance

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ABBREVIATION

The whole content of the thesis book will use the following abbreviated words.

3D – HMD	Three Dimensional Head Mounted Display
AMI	Auto Mutual Information
ANN	Artificial Neural Network
BCI	Brain Computer Interface
CMC	Cortico-muscular Coherence
CMI	Cross Mutual Information
ECoG	Electrooculography
EEG	Electroencephalogram
EMG	Electromyogram
ERD	Event-Related Desynchronization
ERS	Event-Related Synchronization
f MRI	functional Magnetic Resonance Imaging
ICA	Independence Component Analysis
Inten	Movement Intention
ME	Motor Execution
MEG	Magnetoencephalogram
MI	Motor Imagery
MSC	Magnitude Squared Coherence
OL	Only Looking (Movement Observation)

PET	Positron Emisssion Tomography
PTN	Pyramidal Tract Neuron
RM	Real Movement
TES	Transcranial Electrical Stimulation
TMS	Transcranial Magnetic Stimulation

CHAPTER 1
INTRODUCTION

When brain neurons and muscle fibers' motor neurons synchronize during voluntary movement, functional interaction of brain and muscle signals occurs. The synchronization of numerous neurons inside the spinal cord and motor cortex results in oscillatory activity. In this chapter, the cortico-muscular functional interaction and its neurophysiological principles will be introduced to understand the basic principles of brain and muscle functional interaction during motor task performance.

1.1. Introduction to Cortico-muscular Functional Interaction and Its Neurophysiological Principles

The term "functional" means "of or having a special activity, purpose, or task" and the term "interaction" means "the reciprocal action or influence between the two systems or languages" in the definitions from the Oxford Dictionary. Thus, the meaning of functional interaction comes from the fusion of two words, "functional" and "interaction." It means the reciprocal action between the two systems of having a particular task. Cortico-muscular functional interaction usually appears when the two signals interact within one task or movement performance. In this study, in order to investigate the neurophysiological principles and anatomical nature of brain and muscle signals, we explored cortico-muscular functional interaction during different motor task performances.

Cortico-muscular functional interactions involve transmitting action potentials to the muscles to generate muscle contractions and afferent nerve fibers that transmit somatosensory information back to the central nervous system [1]. The brain connects to muscles with single nerve cells in the spinal cord called "motor neurons." The firing of a motor neuron inside the spinal cord collapses impulses to the muscles along a single cell called an axon. When this impulse travels down the axon to the muscle, a chemical is discharged at its end. The hits of the chemical impulse from the motor neuron to the muscle cause muscle fibers to ratchet past each other, overlapping each other more so that the muscle gets shorter and fatter. The muscle fibers slide back to their original positions when the impulses from the nerves stop. In this way, the muscle contractions happen and the muscles start the interaction with the brain. The concept of brain and muscle signal interaction is important for brain-computer interface (BCI) technology and the rehabilitation of stroke patients [2]. To clearly understand the basic principles of cortico-muscular interaction, the linear coherence method and the nonlinear mutual information method were applied in this research.

The brain and muscle functional interaction can be regarded as a functional coupling in numerous publications [3], [4]. The functional coupling of brain and muscle signals is usually calculated using cortico-muscular coherence (CMC). CMC has been proposed as a biomarker for stroke [3], [4], [5], and [6]. It is a linear technique for measuring the correlation strength between two signals in the frequency domain [7]. There are many studies on the interaction of brain and muscle signals. These studies used positron emission tomography (PET), transcranial magnetic stimulation (TMS), functional magnetic resonance imaging (fMRI), an electroencephalogram (EEG), magnetoencephalography-electromyogram (MEG-EMG), and electrooculography-electromyogram (ECoG-EMG) to investigate the coherence mechanisms of two signals [8], [9], [10], and [11]. EEG-EMG correlation analysis with and without neuro-feedback was performed in some studies [12], [13]. EEG-EMG coherence was calculated with three types of hand movement tasks, namely, hand fisting, wrist flexion, and wrist extension, by using magnitude squared coherence (MSC) and wavelet coherence [14]. The researchers constructed the cortical-muscular functional network and classified the accuracy of movements with Fisher and the artificial neural network (ANN) [15].

One of the major concerns for brain-muscle interaction is the band frequencies that occur during the synchronization of brain and muscle signals. Studies point out that cognitive brain signals produce alpha (8–12 Hz) and beta (13–30 Hz) waves while muscle activities produce beta (13–30 Hz) and piper (30–60 Hz) rhythms [16], [17]. Coherence occurs in the beta band ranges of both low (13–21 Hz) and high (21–31 Hz) beta in flexor and extensor muscles regardless of contraction [18]. The study concluded that alpha-band coherence shows an EMG reflecting ascending or feedback interactions, and gamma-band coherence shows an EMG reflecting descending or feedforward interactions [19]. Coherence values of 4–6 Hz and 8–12 Hz are observed when Parkinson’s disease and essential tremor subjects are subjected to the experiment [20], [21], [22]. Conversely, the coherence value was found to be in the higher beta/low gamma range (30–45 Hz) during dynamic motor tasks [23], [24]. Moreover, the effects of attention and precision of exerted force can cause beta-band EEG-EMG synchronization [25]. There was also a controversial issue of whether EEG-EMG coherence was detected in the motor imagery or not [26], [27], and [28]. Many questions about functional coupling in motor imagery tasks remain unanswered. EMG rectification is also one of the problems in coherence analysis. Rectification can cause significant distortion of the frequency content of an EMG signal [29]. Thus, the functional interaction of two signals depends on the specific band frequency ranges, force level, age correlation, and use of the rectification process for EMG signals [30], [31].

From the perspective of nonlinear correlation analysis, mutual information was used to measure the nonlinear dependency between two signals [32]. Previous studies used mutual information to investigate information transmission between EEG and EEG, delay time, and directionality inference between EEG and EMG, EEG-EMG [28], [35], [33], and [34]. However, there was a lack of research into the comparison of coupled information across different motor tasks with mutual information and delay time estimation methods. The estimation of delay time between two signals can facilitate an understanding of the physiology of a given system and provide information on conduction velocity. Many literacies have expressed that there will be a time lag for descending oscillation (from the brain to muscle) and ascending oscillation (from muscle to brain) between the sensorimotor cortex and the peripheral muscles [5], [36]. The functional interaction of two signals with a delay time usually represents those signals' propagation time [37], [38], and [39]. More research is needed to investigate cortico-muscular synchronization from the standpoint of delay time with directionality inference [40], [41]. Most of the previous studies used the cross-correlation method and phase-based methods to find the delay time between two signals [28], [35], and [42]. However, a lack of directionality inference was the negative aspect of these methods.

To summarize, the various conclusions regarding the occurrence of synchronized frequencies in different bands, the functional interaction amount in different motor tasks, muscle contraction types, motor imagery conditions versus EMG, and the characteristics of rectified and non-rectified EMG signals in the study of CMC remained controversial issues and became the motivation for this research. Moreover, the delay time for information transmission and unclear information flow directions between efferent and afferent pathways were the major problems in carrying out the current study. Nowadays, it is essential to make a study of brain and muscle interaction with a clear explanation of neurophysiological principles that can be fruitful in biomedical engineering and neuroscience fields. For the above reasons, this research will explore cortico-muscular functional interaction and its neurophysiological principles with four different motor task performances as a preliminary study based on the state of the art as listed in **APPENDIX A**.

1.2. Study Aims and Objectives

Based on the controversial issues and problems to be solved, the aims and objectives of the study are as follows.

- To investigate the functional interaction of brain-muscle signals and their coupling delay time based on four different motor tasks,
- To explore the anatomical and neurophysiological principles of brain and muscle function that can lead to cortico-muscular interaction,
- To discover consistent and reliable facts about the cortico-muscular interaction based on unresolved research issues.

1.3. Scope of the Functional Interaction of Brain and Muscle Signals

The human brain and nervous system play an essential role in generating movement. They are assigned to the processing of sensory input for constructing detailed representations of the external environment. In reality, the motor system generates movements. Those movements are adaptive to accomplish the goals of the organisms. These goals are evaluated and set by the high-order of the brain [43]. Thus, the function of the motor system is to transform the goals into the appropriate muscle activations to achieve the desired movement. To evaluate the interaction amount of brain and muscle signals, we focused on the cortico-muscular interaction with linear coherence and nonlinear mutual information methods in four different motor task performances. They are hand grasping real movement (RM), movement intention (Inten), motor imagery (MI), and movement observation in a three-dimensional head-mounted display (3D-HMD) environment (OL).

This study accounted for the motor imagery (MI) and OL tasks together with RM and Inten motor tasks for comparison of functional coupling and delay time as a new experimental task-related perspective based on state-of-the-art as listed in **Appendix A**. In addition, this study considered the efferent descending and afferent ascending pathways' directions by taking into consideration the delay time with the use of lagged power correlation in the specified coupling frequency bands. As this academic research was based on the previous researchers' controversial issues, the problems that remained to be solved were mainly tackled and found out for the cortico-muscular functional interaction.

The research facts of this study were aimed at being applied in the future rehabilitation systems of stroke patients in clinical applications. This study's evidence can also be used in the design of movement intention detectors with various classifiers prosthetic devices for amputee people, and biomedical robotics. Thus, the scope of this study will clearly explain the main root causes of interaction between the brain and muscle with clear anatomical and neurophysiological principles. The abbreviated words RM, Inten, MI, and OL for each task were used for the whole discussion of the thesis book.

1.4. Implementation Program

Matlab is the core software for the analysis of the whole dataset in this research. We wrote the Matlab code and analyzed the brain and muscle recording data. All statistical comparisons were made using IBM SPSS 20 (SPSS Inc., Chicago, IL, USA). To design a place that mimics a real experimental room in a three-dimensional head-mounted display (3D-HMD), Unity (2019.2.9f1) software was used. The MakeHuman software and Blender software were applied to create the hand models for the task instructions in 3D-HMD.

1.5. Outlines of the Thesis

Overview outlines of the study are presented in six chapters. Chapter 1 describes the introduction to cortico-muscular functional interaction. The aims and objectives of the study, the scope of brain-muscle functional interaction, and the implemented program of research are discussed in this chapter. Chapter 2 discusses the functional interaction of brain and muscle signals with the linear coherence method. In chapter 3, the functional interaction of brain and muscle signals with a nonlinear mutual information analysis framework is explained. Chapter 4 explains the delay time of signal propagation between brain and muscle signals. Chapter 5 is the discussion section of the whole study. The last chapter expresses general discussions and conclusions with limitations and future works of study as in Chapter 6.

CHAPTER 2
FUNCTIONAL INTERACTION OF BRAIN AND MUSCLE SIGNALS WITH LINEAR COHERENCE METHOD

The functional interaction of brain and muscle signals has been regarded as functional coupling. The coupling of two signals can be evaluated by using the linear coherence method. This chapter explains the linear coherence method, its application to the cortico-muscular interaction, and the linear coherence results with regard to the anatomical and neurophysiological nature of brain and muscle signals.

2.1. Abstract

The functional interaction of brain and muscle signals was explored with a linear coherence method based on the theory of Pearson correlation. Based on literature reviews and previous research, the application of the linear coherence method and its neurophysiological mechanisms were specifically discussed. In addition, the experimental design, data collection, and results of this study were explained clearly in each section. According to the results, the cortico-muscular functional interaction amount can change based on the motor task performance.

2.2. Introduction to Linear Coherence Method

The linear coherence method is used as an indicator of the linear connection between two signals [3], [30], and [44]. It is the principal measure of the Pearson correlation coefficient between two signals in the frequency domain [45]. The range of coherence exists between zero and one, where one indicates a perfect linear relationship and zero indicates the two signals are not linearly correlated at that frequency [17]. Coherence was calculated from the normalization of the cross-spectrum. When the coherence was greater than >95% confidence limit, it was considered significant [8].

In this study, EEG-EMG coherence was calculated between brain and muscle signals during the motor task performance of RM, Inten, MI, and OL in all participants to predict the amount of cortico-muscular functional interaction. The coherence values within the frequencies of interest are used to estimate the functional interaction between brain signal (x) and muscle signal (y) [13], [28]. To calculate the coherence, the auto-power-spectral density of brain signal (x) and muscle signal (y) is first calculated as Equation (1) and Equation (2).

$$S_{xx}(f) = \frac{1}{n}\sum_{i=1}^{n} X_i(f)\, X_i^*(f) \quad (1)$$

$$S_{yy}(f) = \frac{1}{n}\sum_{i=1}^{n} Y_i(f)\, Y_i^*(f) \quad (2)$$

After calculating the auto-power-spectral density of each signal, the cross power spectral density of the brain signal (x) and muscle signal (y) was calculated as in Equation (3).

$$S_{xy}(f) = \frac{1}{n}\sum_{i=1}^{n} X_i(f)\, Y_i^*(f) \quad (3)$$

The magnitude squared coherence value between brain signal (x) and muscle signal (y) at frequency, *f* can be calculated by the following standard formulation as shown in Equation (4) [44], [45], and [46].

$$Coh_{xy}(f) = \frac{|S_{xy}(f)|^2}{S_{xx}(f)\ x\ S_{yy}(f)} \quad (4)$$

The coherence value significance level was determined based on the confidence limit, CL, as in Equation (5).

$$\text{Confident limit} = 1 - (1 - \alpha)^{\frac{1}{(L-1)}} \quad (5)$$

where L represents the number of data segments used in the coherence calculation and α is a confidence interval and is typically 95%. For statistical comparison, the coherence areas for each frequency band range were calculated by using the formula as in Equation (6), where Δf represents frequency resolution, f is the frequency of the calculated band, and $Coh_{xy}(f)$ is the coherence value [14].

$$A_{coh} = \sum_f \Delta f\,(\,Coh_{xy}(f)\ - CL) \quad (6)$$

To resolve the controversial issues of coherence occurrence in-band frequencies, the magnitude squared coherence values were calculated in all five frequency bands, delta (0.5–3.5 Hz), theta (4–7.5 Hz), alpha (8–12 Hz), beta (13–30 Hz) and gamma (31–50 Hz) ranges for all motor tasks.

2.2.1. Application of the Linear Coherence Method to Cortico-muscular Interaction

The first coherence study in macaque monkeys was done by researchers in the early 1990s. In this study, the researchers recorded local field potential (slow waves) and pyramidal tract neuron (PTN) discharge from pairs of sites in the primary motor cortex with a precision grip task. The coherence was modulated by the movement that occurred in the monkeys [47]. Then, studies were initiated in humans with transcranial electrical stimulation (TES) together with a brain-computer interface (BCI) [8]. BCI with TES is gaining attention as a rehabilitation approach in which motor recovery can be promoted by neuro-feedback based on the recordings of direct manipulation of brain electrical activity [9], [10]. After the revolution of coherence studies with various kinds of noninvasive methods, cortico-muscular coherence became an indicator in the rehabilitation systems of stroke patients [9], [48]. It is an effective method for evaluating how different brain areas are involved in motor recovery after suffering a stroke. Thus, cortico-muscular coherence has been widely applied as a potential biomarker for post-stroke motor deficits, reflecting the recovery of motor function by quantifying interactions between activities from the motor cortex and controlled muscles [3], [8]. As the linear coherence method calculation was based on the frequency domain, the frequencies of these activities may reflect both the intrinsic membrane properties of single neurons and the organization and interconnectivity of neural networks. The beta and gamma-band oscillations of CMC have been used since the early 1990s to investigate and show as a feature of good functional interaction [4], [16], [23], and [28]. Thus, beta band (18–30 Hz) synchronization is a feature of the sensorimotor cortex during motor execution (ME). The high value of CMC has been interpreted by researchers as evidence of the involvement of cortical neurons in motor unit synchronization [4].

In addition, EEG and EMG events are coherent but do not occur simultaneously. This coherence happens with a delay, which reflects signal propagation time between the brain and muscle signals, possible information processing and more detailed information about the temporal structure of interactions. Knowing the delay time can provide not only important information about communication between cortex and muscle but also the direction in which the oscillations propagate and/or by differentiating the corticospinal pathways via which the activity is transmitted [5]. Thus, this study focused on determining coherence in different frequency bands, comparing coherence based on motor task performance, and calculating delay times based on beta and gamma bands to infer the directionality of information flow between brain and muscle pathways.

The real-world applications of CMC have been found in the invention of biomedical robotics, prosthetic and hand orthosis devices for people with disabilities and amputees, in the construction of cortical-muscular functional networks, and in EEG/EMG controllers with different kinds of classifiers, etc. [13], [14]. Moreover, CMC can be widely applied in the study of human motion and movement for behavioral science, such as sports activities, root causes of fatigue, treatment of tremors, Parkinson's disease, dyskinesia, and Alzheimer's disease, and recognition of human motion intention for movement intention detectors with various classifiers, etc. [15], [20], and [21]. Our study is the updated study of functional interaction with delay time in beta and gamma bands that can be advantageous in judging the response time of brain–muscle signals in patients and in the construction of motion intention detectors in real applications of cortico-muscular functional interaction systems [14], [15].

2.2.2. Neurophysiological Brain and Muscle Mechanisms Using the Cortico-muscular Coherence (CMC) Method

Horak's motion control theory, 1991, emphasized that "normal motion control refers to the central nervous system by using existing and past information to transform neural energy into kinetic energy and enable it to perform effectively functional activities" [49]. In this process, the interaction between two systems of motor muscle tissue and the central nervous system is included. When a person utilizes or performs a hand-grasping motor task, the command that is generated by the motor cortex will be transmitted along the motor conduction pathway and can dominate the peripheral nerves and muscles of the upper body. The sense of proprioception is simultaneously passed along the sensory conduction pathway to the spinal cord, the cerebellum, the brain stem, and partly to the cerebral hemisphere. Proprioceptive information is sent to the brain's sensory regions for the regulation of motion commands [50].

The study of cortico-muscular functional interaction can reflect the interaction between the cerebral cortex and muscle tissue, which depicts the transmission of information flow within two systems. The information flow of that system can be associated with the cerebral cortex, which sends commands to the muscle tissue and the afferent feedback of muscle contraction. It needs to understand the neurophysiological root causes of brain-muscle functional interaction in terms of how the brain controls muscle tissue and the effects of peripheral muscle movement on brain function. The researchers and scientists recognized that the CMC reflects both cortical efferent descending passes from the brain to muscles as well as ascending cortical afferent passes from muscles to the brain in producing the CMC [30].

The high coherence values indicate that there is a strong physiological underpinning as an indicator of neural binding across the tasks [51]. From a physiological perspective, RM, Inten, MI, and OL tasks require different patterns of coordination among cortical and motor neurons to produce the necessary motions and forces. For these reasons, the four tasks were chosen as they are distinct from the perspective of mechanical requirements such as force and motion.

2.3. Materials and Methods

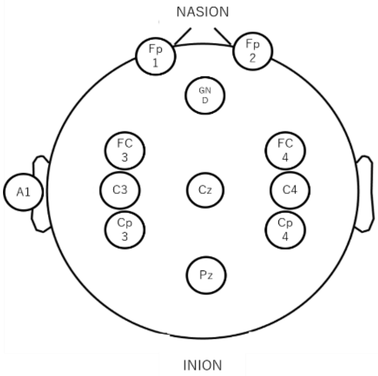
This section will describe the participants who were involved in the experiment, the experimental condition, what type of software was used, and how the apparatus was set up in the experimental room for recording the brain and muscle signals.

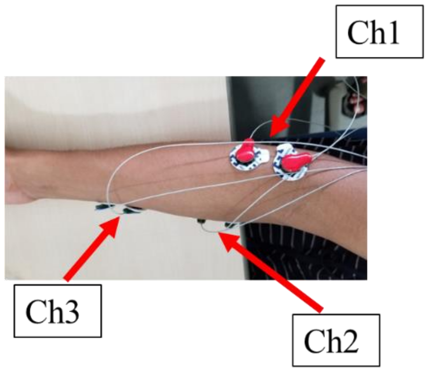
2.3.1. Participants

This experiment involved a total of 13 participants who were right-handed. All participants were from Kyushu University and ranged in age from 21 to 28 years (23.92 ± 1.754 years, mean ± SD). Among the 13 participants, two were females, and the other eleven were males. None of the participants had had a physical disorder or brain damage in the past. The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Institutional Review Board of the Faculty of Information Science and Electrical Engineering, Kyushu University (H 26-3, June 23, 2014). The participants provided written informed consent before the experiment. The consent form is attached in **APPENDIX B**.

2.3.2. Software and Apparatus

We used g.USBamp from g.Tec medical engineering company to record the brain and muscle signals. Ten EEG channels and three surface EMG (sEMG) channels were used. EEG electrodes were Fp1, Fp2, Cz, FC3, C3, CP3, FC4, C4, CP4, and Pz. As shown in Figure 2.1, bipolar EMG electrodes were put on the brachioradialis muscle, flexor carpi ulnaris muscle, and flexor carpi radialis muscle, respectively. We recorded both EEG and EMG signals at a 1200 Hz sampling rate. All the electrodes' impedance values were under 1 kΩ. To suppress the power line noise interference, the notch filter at 60 Hz was used. The A1 electrode was set as a reference, and AFz was set as a ground. In this experiment, we used the Oculus Rift head-mounted display HMD from the Oculus company to create a virtual reality environment. We created the virtual reality environment by using Unity (2019.2.9f1) software and designing a place mimicking a real experimental room in a three-dimensional head-mounted display (3D-HMD). We created hand models with MakeHuman software and Blender software for task instructions. After making a file of the recorded movement, we used this file as an input to Unity, which played this file by using a trigger. We used two computers in this experiment. One computer was used for signal recording and the other one was used for making a virtual reality environment.





(a) (b)

Figure 2.1: Electrode placements for brain-muscle signals data recording (a) EEG electrodes (b) EMG electrodes.

2.3.3. Experiment Design

We used a head-mounted display (HMD) to display the created hand models in virtual reality for motor task instructions and motor learning of hand grasping tasks. We asked the participants to put both hands on the table in the same position as in a virtual reality environment. We placed the towel under the participant's hand in order not to include force. To reduce physiological artifacts, we asked the participant not to blink, clench their jaw, or make unnecessary movements during recording. Firstly, we demonstrated the motor tasks presented in the work before data acquisition to acclimatize participants with the setup. Then, the instructions for the tasks were shown on the monitor screen via a head-mounted display (HMD) in a virtual reality environment. Figure 2.2 shows the experimental design.

We used four different motor tasks. An RM is a task in which a participant moves his or her dominant hand in a real-hand grasping movement. An inten is a kind of isometric contraction that involves the static contraction of a muscle without any visible movement at the angle of the joint. An MI is a task in which participants carry out a mental process by rehearsing or simulating a given motor action. OL is a task in which participants just look at a virtual hand's movement without any brain imaging. To ensure the absence of bias, we designed the motor task with four patterns: Inten→OL→RM→MI, OL→RM→MI→Inten, RM→MI→Inten→OL, and MI→Inten→OL→RM. The participants performed one pattern randomly selected from these four patterns.

Figure 2.2: Experimental design for motor task performance using the 3D-HMD condition in the VR environment.

Figure 2.3 shows the task flow of the experiment. There was a 2 minute rest period as a baseline. Then, there were 8 s of rest, 2 s of being ready, and 5 s of the task in 1 trial. We designed a total of 40 trials with 4 sets in each motor task. During rest, a fixation cross appeared on the virtual palm, but it vanished during the 2 s ready stage. The virtual hand grasping appeared on the monitor in the HMD during the 5 s task. The time to break between each motor task was 5 minutes. Then RM, Inten, MI, and OL tasks were performed, respectively. Figure 2.4 shows the first ten trials of one subject in each task for both EEG and EMG data.

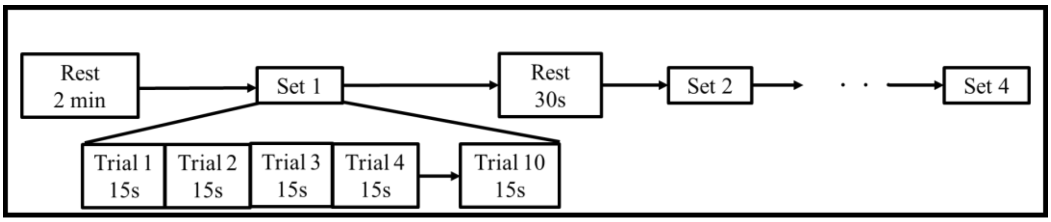
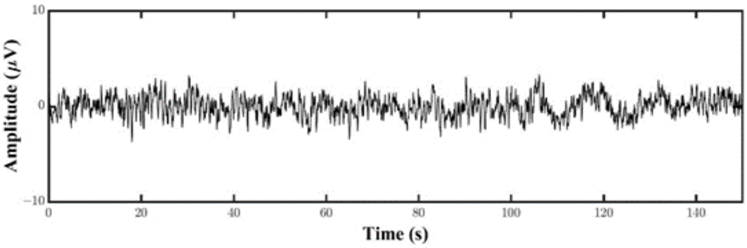
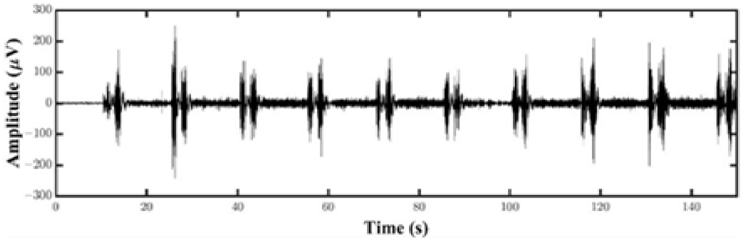


Figure 2.3: Experimental task flow.


Amplitude (μV)
Time (s)

(a)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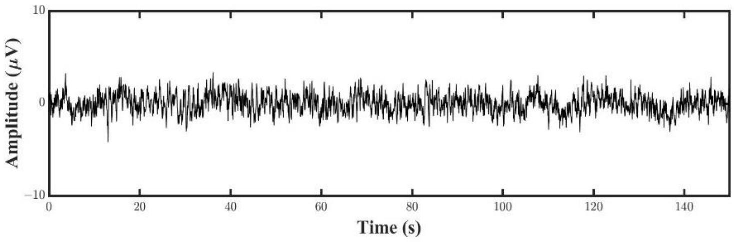
(b)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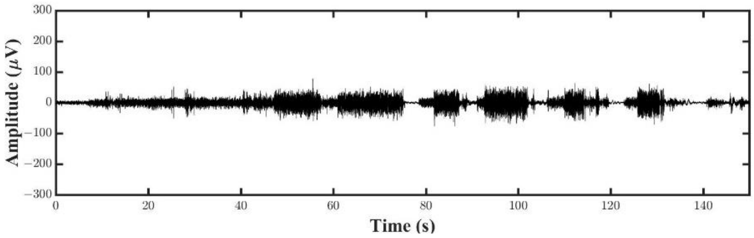
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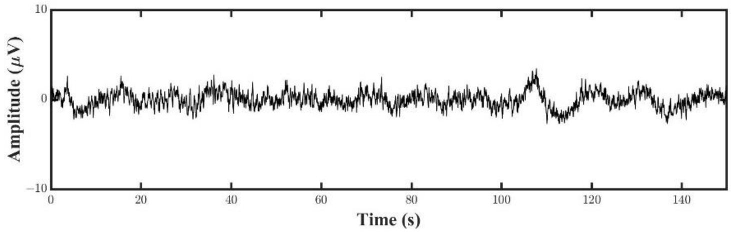
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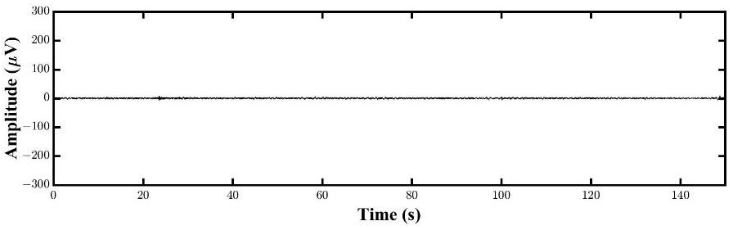
Time (s)

(e)


Amplitude (μV)
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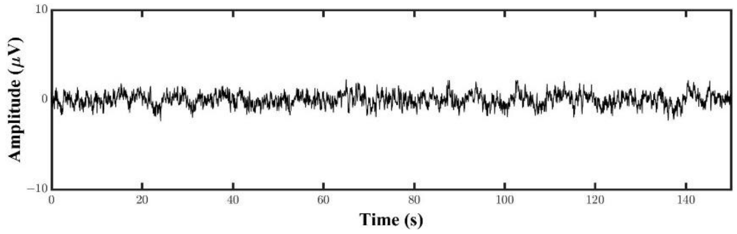
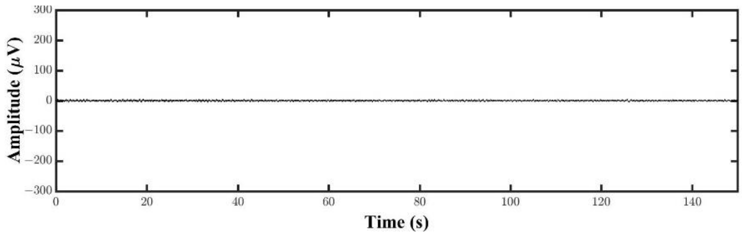


(g)



(h)

Figure 2.4: Ten trials of one subject's EEG and EMG data: (a) EEG data from the RM task; (b) EMG data from the RM task; (c) EEG data from the Inten task; (d) EMG data from the Inten task; (e) EEG data from the MI task; (f) EMG data from the MI task; (g) EEG data from the OL task; and (h) EMG data from the OL task.

2.4. Data analysis

According to the experimental data, there were 40 trials in four sets of each motor task performance, but some data that contained too many noises to analyze was excluded from the analysis. Among 10 channels of EEG data, we chose only the contralateral brain motor cortex C3 and ipsilateral cortex C4 as they were mainly concerned with body movement in the brain [14]. Among three EMG channels, we used only the flexor carpi ulnaris muscle since this muscle was directly involved in hand grasping movement.

In data preprocessing, we resampled both signals to 256 Hz to reduce computation speed and time. We chose the bandpass filter range of 1 to 100 Hz for both signals. The EEG data that contained artifacts was determined by visual inspection with the use of EEGLAB. We used Independent Component Analysis (ICA) as it is an effective tool for rejecting several types of non-brain artifacts. Data above the limit of ±100 μV was excluded to remove eye-blinking and muscle noise. We rejected at most one or two ICA components that apparently affect the EEG channel data. Then, we extracted the EEG data. For EMG signals, the non-rectified EMG signals were filtered with a selected bandpass filter and then exported for further analysis [3], [10], and [29].

After preprocessing the data, we recorded only 0–5 s of EEG and non-rectified EMG data during participants performing the hand grasping movement. We calculated the auto-power spectral analysis and cross power spectral analysis of two signals over all trials by averaging over disjointed sections of Hanning tapered data using an FFT of 128 points. The 128 ms window was moved across the 5 s data with non-overlapping to access the changes in coherence by using Equation 1 to Equation 3. Coherence was normalized with the use of Equation 4. The frequency range of 0.5 to 50 Hz, covering most of the scalp-recorded EEG power spectra and EMG power spectra, was used for coherence analysis.

For statistical analysis, first, we used the Shapiro–Wilk normality test to verify the normality of the data ($p > 0.05$). We used bootstrap estimation for each ANOVA test as it is an effective method for creating non-normal data to normality. We further applied the generalized linear model together with one-way ANOVA to achieve more specific information between different variables. The one-way ANOVA was performed based on frequency bands and designed tasks to know the main effects of brain-muscle functional interaction. We used the LSD and Bonferroni correction methods for all pairwise comparisons with ($p < 0.05$). All statistical comparisons were made using IBM SPSS 20 (SPSS Inc., Chicago, IL, USA).

2.5. Results

This section will describe the results of cortico-muscular functional interaction that were calculated by the linear coherence method. Firstly, we compared the cortico-muscular coherence for C3-EMG and C4-EMG to check whether high coherence occurs or not on the opposite or same side of the brain's motor cortex versus EMG during hand grasping movement. Then, cortico-muscular coherence in each motor task was compared based on bands to clearly examine the occurrence of functional interaction in five different frequency bands. Based on the band frequency comparison results, the functional interaction of brain and muscle signals was compared again based on the motor tasks. This comparison was done in only the highest number of frequency bands.

2.5.1. Comparison of Cortico-muscular Coherence in Contralateral Motor Cortex versus EMG and Ipsilateral Motor Cortex versus EMG

Firstly, we investigated the cortico-muscular coherence to check the synchrony of brain and muscle signals. We checked the coherence of both contralateral and ipsilateral motor cortex versus flexor carpi ulnaris muscle, EMG. A higher amount of coherence occurred in RM and Inten tasks rather than MI and OL tasks in C3-EMG as in Figure 2.5. The coherence values were high in the beta band (13–30 Hz) and gamma band (31–50 Hz) in those tasks, with no coherence in MI and OL tasks. On the other hand, there were very low coherence values in RM and Inten tasks but with no coherence in MI and OL tasks of C4-EMG as in Figure 2.6. The results showed that the higher cortico-muscular coherences occurred in C3-EMG rather than in C4-EMG. The findings proved that the functional interaction could be different across motor task conditions. The results also pointed out that there might not be coherence between two signals if the brain and muscle signals did not couple during motor tasks.

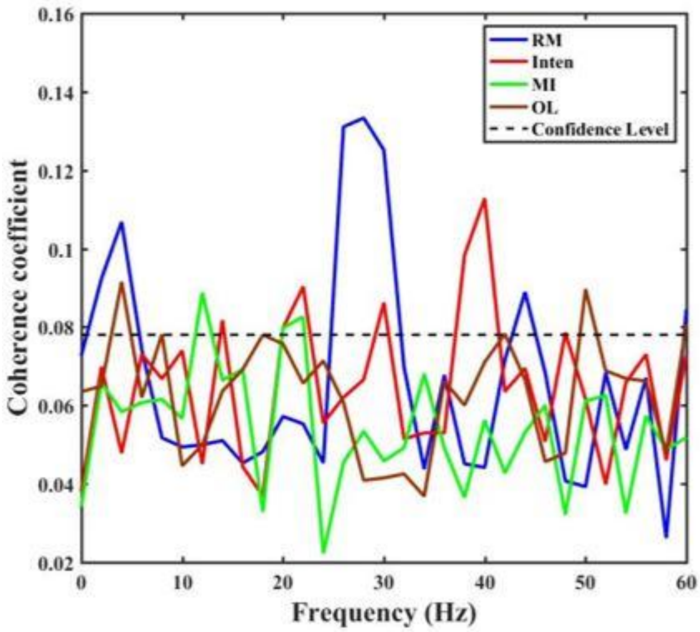


Figure 2.5: Comparison of coherence in one subject’s data across all motor tasks in C3-EMG.

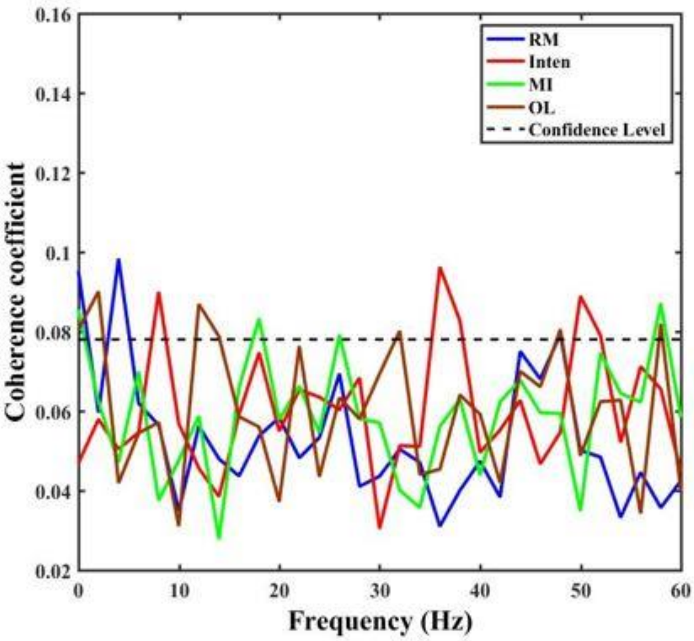


Figure 2.6: Comparison of coherence in one subject's data across all motor tasks in C4-EMG.

2.5.2. Band-based Comparison of Cortico-muscular Coherence in Each Motor Task

As the higher amount of coherence occurred in the C3-EMG rather than the C4-EMG as shown in the above section, we selected only the C3-EMG for further data analysis. To predict the pattern of cortico-muscular coherence clearly, the coherence of one subject's data of C3-EMG in the RM task was shown in Figure 2.7. The highest coherence appeared at 38 Hz during the task. As we have already mentioned above, the functional interaction can happen in different specified frequency bands within different muscle contraction types. Thus, we first checked the averaged values of coherence during coupling in the delta (0.5–3.5 Hz), theta (4–7.5 Hz), alpha (8–12 Hz), beta (13–30 Hz), and gamma (31–50 Hz) ranges for all motor tasks. The hypothesis was that the functional coupling of brain and muscle signals in five different bands was not significantly different in each of the RM, Inten, MI, and OL tasks.

We used the Shapiro–Wilk normality test to check the normality distribution in the statistical analysis. All motor tasks showed normality with $p > 0.05$ in all bands. Then, we performed a one-way ANOVA test with bootstrap estimation and a generalized linear model for the comparison of cortico-muscular coherence based on bands in each motor task. The results rejected the null hypothesis and showed the main effect of functional interaction among all frequency band groups with one-way ANOVA ($F(4, 60) = 3.159$, $p = 0.02$, $\eta_p^2 = 0.174$) in the RM task. The LSD post hoc test showed a significant difference in the coherence (mean ± SE) between the alpha band (0.0503 ± 0.0029, $p = 0.018$) and the beta band (0.0618 ± 0.0018). There was also a significant difference between the delta band (0.0549 ± 0.0050, $p = 0.047$), theta band (0.0534 ± 0.0043, $p = 0.022$) and the alpha band (0.0503 ± 0.0029, $p = 0.004$) compared to the gamma band (0.0645 ± 0.0012). The coherences in the Inten task also rejected the null hypothesis with the main effect of functional interaction in one-way ANOVA ($F(4, 60) = 4.578$, $p = 0.003$, $\eta_p^2 = 0.234$). The LSD post-hoc test resulted in a significant difference in the coherence (mean ± SE) between the delta band (0.0540 ± 0.0030, $p = 0.029$), theta band (0.0543 ± 0.0018, $p = 0.036$), and the alpha band (0.0522 ± 0.0023, $p = 0.007$) compared to the beta band (0.61162 ± 0.0018). There was also a significant difference between the delta band (0.0540 ± 0.0030, $p = 0.006$), theta band (0.0543 ± 0.0018, $p = 0.008$), and alpha band (0.0522 ± 0.0023, $p = 0.001$) compared to the gamma band (0.0631 ± 0.0019). However, there was no significant main effect of brain-muscle functional interaction among the five different bands with one-way ANOVA ($F(4, 60) = 0.140$, $p = 0.967$, $\eta_p^2 = 0.009$) in the MI task and ($F(4, 60) = 0.926$, $p = 0.455$, $\eta_p^2 = 0.058$) in the OL task, as shown in Figure 2.8. Thus, Bonferroni correction post hoc tests were used for multiple comparisons of MI and OL tasks. According to the results, we could say that the cortico-muscular functional interaction can occur in all types of bands but with different interaction amounts. The highest coherences appeared in the beta and gamma bands of RM and Inten tasks, while all five bands had low coherence in MI and OL tasks.

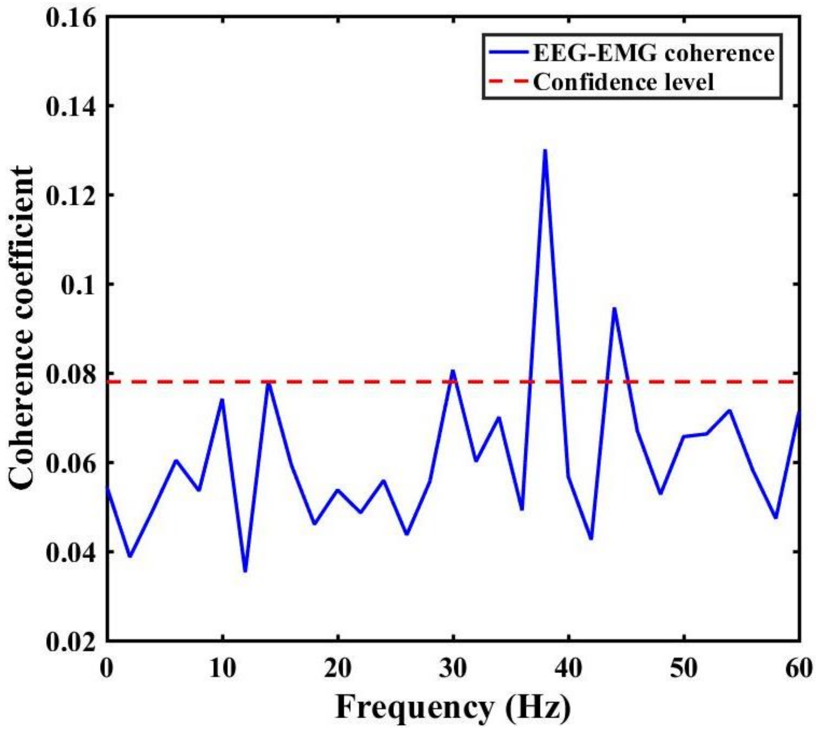


Figure 2.7: EEG-EMG coherence of one subject's data in the RM task.

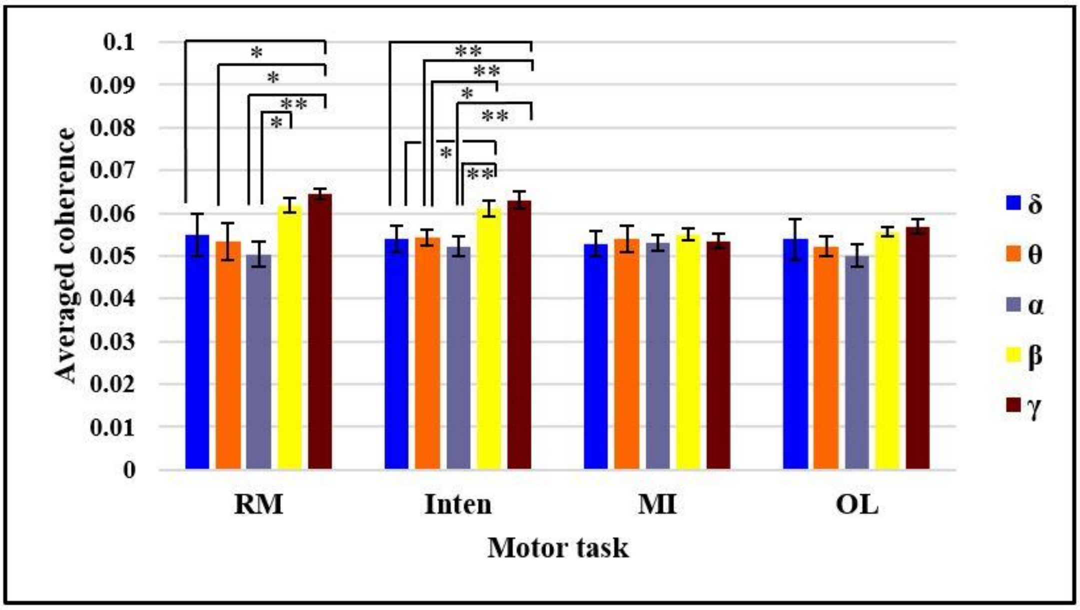


Figure 2.8: Comparison of the averaged coherence based on the frequency band in four motor tasks. Error bars show the standard error of the mean. * $p < 0.05$ ** $p < 0.01$.

2.5.3. Comparison of Cortico-muscular Coherence in Beta and Gamma Bands Based on Motor Tasks

As the higher coherences were detected in the beta and gamma bands, we selected these two bands among five bands and then compared the averaged coherence again based on the tasks in all subjects. Thus, we hypothesized again that functional coupling coherence between cortex and muscle in beta and gamma bands was not statistically significantly different across four types of motor tasks. However, the results also rejected the null hypothesis. As shown in Figure 2.9, the higher coherence occurred in only RM and Inten tasks in both band ranges.

In the beta band, we could clearly observe the averaged coherence amount of RM, Inten, MI, and OL tasks with a significant main effect of functional interaction [task × coherence] value of ($F(3, 48) = 5.145$, $p = 0.004$, $\eta_p^2 = 0.243$) in the ANOVA test. The LSD post hoc test showed a significant difference in coherence (mean ± SE) between the MI task (0.0550 ± 0.0015, $p = 0.004$) and the OL task (0.0557 ± 0.0011, $p = 0.008$) compared to the RM task (0.0618 ± 0.0017), and between the MI task (0.0550 ± 0.0015, $p = 0.008$) and the OL task (0.0557 ± 0.0011, $p = 0.017$) compared to the Inten task (0.0611 ± 0.0018). There was no statistically significant difference between the RM task and the Inten task ($p = 0.762$).

In the gamma band, the results also showed high coherence in the RM and Inten tasks rather than MI and OL tasks, with a significant main effect of functional interaction [task × coherence] value of one-way ANOVA ($F(3, 48) = 9.812$, $p = 0.001$, $\eta_p^2 = 0.380$). Then, the LSD post hoc test showed a significant difference between the MI task (0.0535 ± 0.0117, $p < 0.001$) and OL task (0.0568 ± 0.0016, $p = 0.002$) compared to the RM task (0.06455 ± 0.0011) and the MI task (0.0535 ± 0.0117, $p < 0.001$) and the OL task (0.0568 ± 0.0016, $p = 0.011$) compared to the Inten task (0.0631 ± 0.0199). As with the beta band, there was no statistically significant difference between the RM task and the Inten task in the gamma band ($p = 0.530$).

To be able to check the individual level of the independent variables and to look at the confidence interval in terms of true mean values for coherence, we also performed the 95% CI of the within-subject standard error estimation of coherence across the tasks in both beta and gamma bands as shown in Figure 2.10. Finally, to evaluate the magnitude and variability of coherence across tasks, we further constructed box and whisker plots which depicted the mean coherence obtained within two frequency bands of beta and gamma, as shown in Figure 2.11. The changed cortico-muscular coherence in all subjects was compared across each task. The results confirmed that the functional interaction between brain and muscle signals can be greater in the RM and Inten tasks than in the other MI and OL tasks if the signals are synchronized well during the motor tasks' execution. These results confirmed that the cortico-muscular functional coupling changed based on motor task performance.

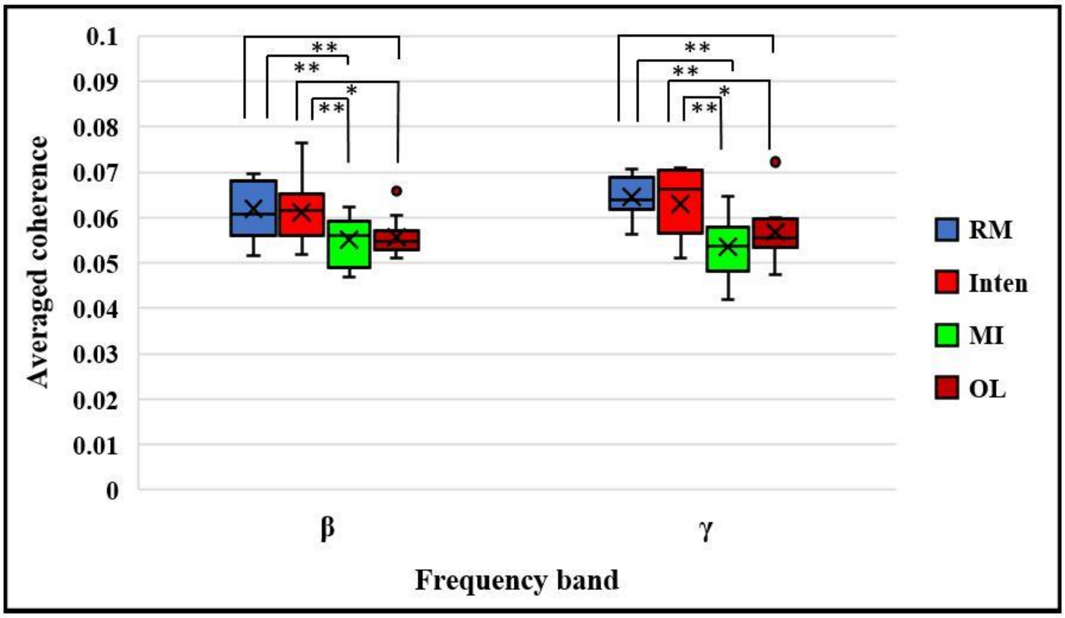


Figure 2.9: Comparison of the average coherence in the beta band and gamma-band based on motor tasks: The top and bottom of each box represent the 25th and 75th percentiles, respectively. The cross sign inside each box represents the mean value. The horizontal black line represents the median. The whiskers are drawn from the ends of the interquartile ranges to the minimum and maximum values. *p < 0.05 **p < 0.01.

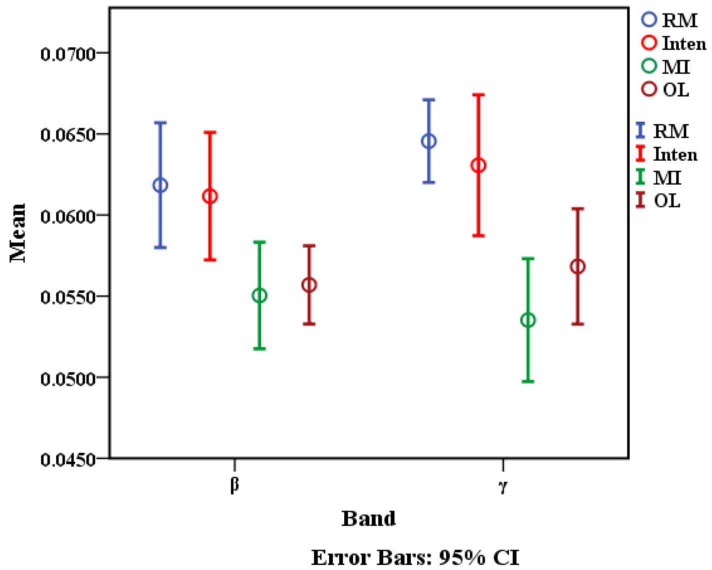


Figure 2.10: The 95% CI of the within-subject standard error estimation of coherence across the tasks in both beta and gamma bands. Circle-marked points represent the means, and bars around these points represent the 95% CI of the within-subject standard error.

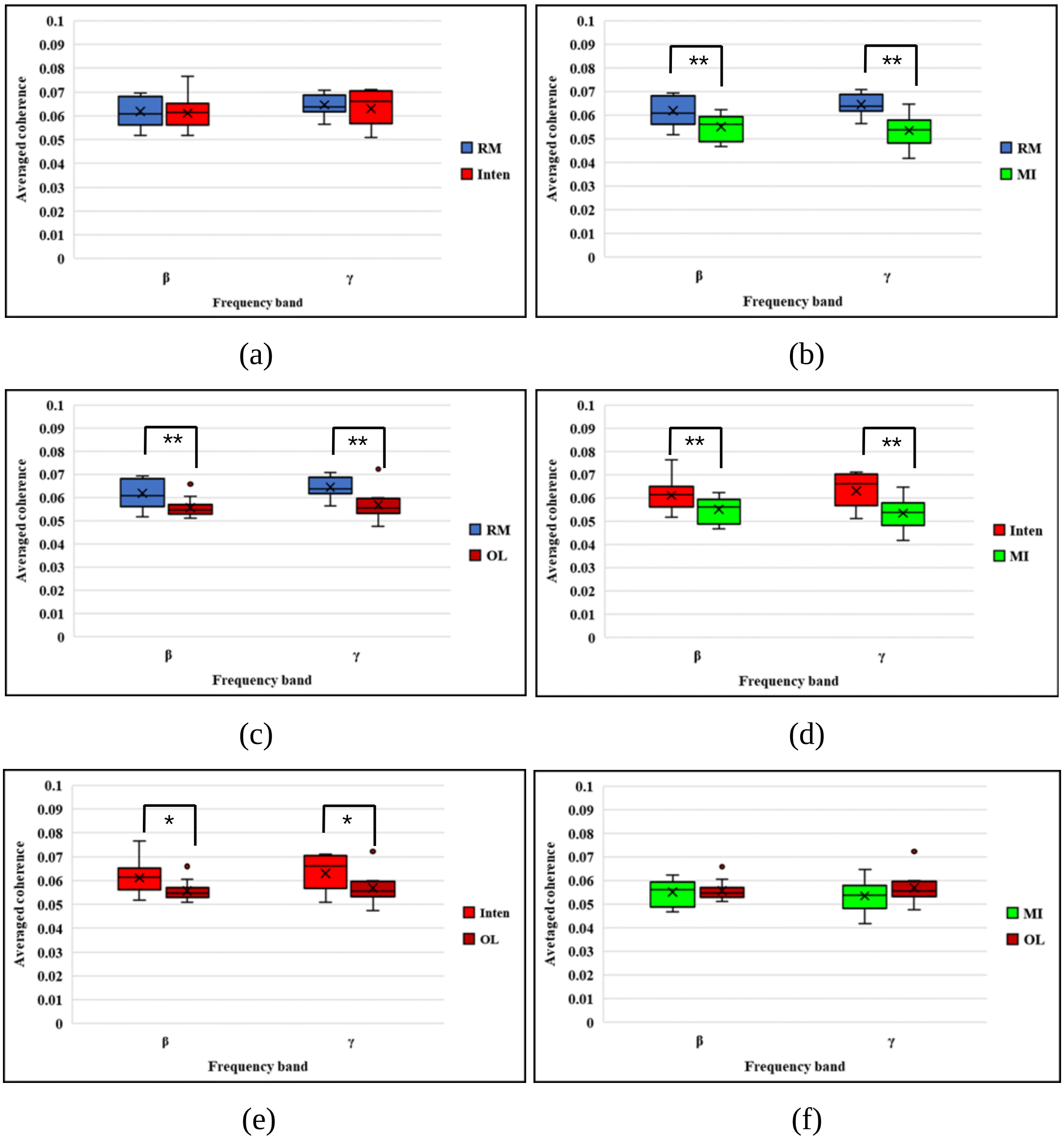


Figure 2.11: EEG-EMG coherence comparison across all subjects in the beta band and gamma band: (a) RM task vs. Inten task; (b) RM task vs. MI task; (c) RM task vs. OL task; (d) Inten task vs. MI task; (e) Inten task vs. OL task; and (f) MI task vs. OL task. * $p < 0.05$ ** $p < 0.01$.

2.6. Discussion

Based on the previous studies' controversial issues on cortical-muscular coherence, this study hypothesized that EEG-EMG functional coupling changes based on different motor task performance [4], [14], [15], and [50]. The results proved that the functional interaction between brain and muscle signals varies depending on the motor tasks that subjects execute. In this study, coupling amounts were greater in the RM and Inten tasks than in the other MI and OL tasks in all subjects. Cortico-muscular functional interaction was systematically decreased and enhanced at specific frequencies of interest from 0.5 Hz to 50 Hz across the four motor tasks. Our results satisfied the remaining controversial issues concerned with band-specific problems, namely whether the highest coherences can appear only in the beta band and gamma band or not. Both beta and gamma bands can appear in RM and Inten tasks, while all five bands had low coherence in MI and OL tasks.

The high coherence values indicate that there is a strong physiological underpinning as an indicator of neural binding across the tasks [51]. From a physiological perspective, RM, Inten, MI, and OL tasks require different patterns of coordination among cortical and motor neurons to produce the necessary motions and forces. Thus, this study motivated the four tasks since they are distinct from the perspective of mechanical requirements such as force and motion. These fundamental mechanical differences are also one of the phenomena associated with task-related changes in brain and muscle activity coordination.

Based on the occurrence of the highest coherence in beta and gamma bands during clenched fist, wrist flexion, and extension tasks, the study extracted features and applied an SVM classifier for reclassifying a motor task among three different motor tasks [14]. Next, the study constructed the cortical-muscular functional network and classified hand movements with Fisher and artificial neural networks for exploration of more effective methods in human behavior perception. The researchers applied theta, alpha, beta, and gamma frequency bands to their constructed model [15]. The presence of beta and gamma-band coherence during motor task execution was confirmed in our study, as it had been in previous studies [14], [15].

There were low coherences in delta, theta, and alpha bands and high coherence in beta and gamma bands. The results of alpha-band coherence are typically thought to reflect the afferent feedback through the stretch reflex loop [51]. There was very low coherence in the alpha band across all tasks in the study. The coherences were more apparent in the efferent pathways than in afferent feedback. Higher band coherences are thought to represent a cortical drive to muscles. Beta band coherence is thought to be very sensitive to movement. It usually happens while holding static and isometric force [11], [16], and [23].In addition, the occurrence of coherence in the beta band could be related to the ERD / ERS phenomenon as an interactive effect of it [52]. The firing behaviors of spinal motor neurons and cortical activity are correlated as a functional coupling within the beta ranges [10]. The study concluded that the amount of significant beta range synchronization decreases below the confidence level when attention is divided between motor tasks and other simultaneously performed tasks. The cortical-muscular network works in good synchronization when the attentive resources are directed towards the motor tasks. Beta range EEG-EMG synchronization was the effect of attention and precision of exerted force during a maintained motor contraction task [25].

The integration of visual and somatosensory information increment could shift cortico-muscular coherence to the gamma range [23]. The 40 Hz rhythms could have occurred during motor preparation and control of finger movement performance [53]. Neuronal gamma-band (40–70 Hz) coherence has been found along the visuomotor pathways and is concerned with visuomotor interactions [22], [54]. In this study, we applied 3D-HMD for the motor task commands and stimulation for the subjects. This process could lead to focused attention from the participants and produce sensory-motor integration of brain signals, which then resulted in the gamma range (31–50 Hz) coherences [25]. During very strong tonic contractions and dynamic forces, cortical gamma-band oscillations may reflect the efferent drive to the muscle [16], [23], and [55].

In addition, as we used the 19 ms Hanning windowing in coherence analysis, this would effectively create a 50 Hz high pass of the original signal. However, this high-pass filter effect of this derivation can remove activity with low spatial frequencies, including volume conducting activity. Thus, coherent values in high-frequency beta and gamma bands cannot be due to volume conduction, and the resulting coherence values are purely a consequence of the execution of different motor tasks. The functional coupling of the higher bands' results was consistent with the results reported in [24], [56]. This coherence could occur in both bands without the use of special dynamic forces in our experiment.

During the fictitious neuromuscular activities, there were coherence similarities between cortical activities [4], [26], and [27]. Nevertheless, there was very low coherence in the MI and OL tasks, except for some subjects in the OL task. In summary, our results showed that the coupling ranges totally changed based on the motor task performance as we had already discussed. During motor tasks, the expression and gating of coherent discrete cortical and spinal networks may be a mechanism that appears to provide good functional coupling between two signals.

CHAPTER 3
FUNCTIONAL INTERACTION OF BRAIN AND MUSCLE SIGNALS WITH NONLINEAR MUTUAL INFORMATION METHOD

The coupling of two signals can also be evaluated by using a nonlinear mutual information method. This chapter explains the nonlinear mutual information method, its application to the cortico-muscular interaction, and the interpretation of the mutual information results with regard to the anatomical and neurophysiological nature of brain and muscle signals.

3.1. Abstract

The mutual information method is one of the flexible methods in the field of brain informatics and mathematics. After the introduction of information theory by Shannon in 1949, this method has become popular in the analysis of functional connectivity. Thus, this study applied the mutual information method to investigate the brain and muscle functional interaction. The results explain the root causes of higher functional interaction along with neurophysiological mechanisms. The results of nonlinear mutual information are consistent with the results of the linear coherence method.

3.2. Introduction to the Nonlinear Mutual Information Method

The coherence method is a linear method, and it cannot be used for the study of complex and nonlinear brain dynamics. Mutual information is a flexible analysis framework that can be applied to identify the patterns of connectivity regardless of the distributions of the data, for example, linear, non-linear, and circular. Mutual information employs the entropy of higher-order statistics to estimate uncertainty. It is a statistical measure of linear and nonlinear relationships between two-time sequences [28], [37].

To calculate the mutual information, the entropy of the signals must be computed. Thus, we first bin the data to create a histogram with the Matlab function *hist* by using Equation 7 and Equation 8. Next, we compute the probability that a value in the data will fall into each bin.

$$\text{Number of bins for EEG} \ = \left[\frac{max(x)-min(x)}{2.\,s(x).n^{\frac{-1}{3}}} \right] \tag{7}$$

$$\text{Number of bins for EMG } = [\ \frac{max(y)-min(y)}{2.\,s(y).n^{\frac{-1}{3}}}\ ] \tag{8}$$

Where s(x) is the standard deviation, n is the number of samples, max(x) and max(y) are the maximum values of each EEG and EMG signal, respectively, and min(x) and min(y) are the minimum values of each EEG and EMG signal. After calculating the bin value of each signal, we calculated the entropy in time series for each signal to identify the information between EEG and EMG signals as per Equation 9 and Equation 10. Then, we multiply the probability value by the logarithm-base-2 of that probability value and sum all probability values for entropy [37].

$$\mathrm{H}(X) = -\sum_{i=1}^{n} p(x_i)\log_2 p(x_i) \tag{9}$$

$$\mathrm{H}(Y) = -\sum_{j=1}^{n} p(y_j)\log_2 p(y_j) \tag{10}$$

We calculated the joint entropies of both signals by using Equation 11.

$$\mathrm{H}(X, Y) = -\sum_{j=1}^{m}\sum_{i=1}^{n} p(x_i, y_j)\log_2 p(x_i, y_j) \tag{11}$$

After that, we calculated the mutual information of brain and muscle signals. We compared the amount of mutual information across all motor tasks by using Equation 12.

$$\begin{aligned}\mathrm{MI}(X,Y) &= H(X) + H(Y) - H(X,Y)\\ &= \sum_{j=1}^{m}\sum_{i=1}^{n} p(x_i, y_j)\log_2[p(x_i, y_j)/p(x_i)p(y_j)]\end{aligned} \tag{12}$$

3.2.1. Application of Nonlinear Mutual Information to Cortico-muscular Interaction

Since the information theory’s introduction by Shannon in 1949, mutual information has been used in many diverse fields as a measure of coupling or information transmission between two systems [57]. Mutual information is a probability and information theory that is a measure of mutual dependence between two variables. It quantifies the amount of information in terms of units such as Shannons (bits), Nats, or Hartleys. Mutual information has been obtained for one random variable by observing the other random variable [58]. Mutual information can be categorized into two: one is cross-mutual information (CMI) and the other is auto-mutual information (AMI). Cross-mutual information (CMI) quantifies the information transmitted from one-time series to another, whereas auto-mutual information (AMI) in a time series depicts how much the time series' value can be predicted on average from previous points [32], [33], [34], and [35].

Mutual information and its related concepts, including entropy, joint entropy, and conditional entropy, form a set of mathematical techniques that have many uses in science, engineering, and information communication [37]. It is a robust system that can be used to quantify the amount of shared information between two systems. In the neuroscience field, it was mainly used in the case of EEG analyses, in which the two variables could be from two different electrodes or from the same electrodes. Thus, it is a flexible analysis framework that can be applied to identify the pattern of connectivity or interaction regardless of the distribution of the data.

The former applications of mutual information have been found in telecommunication systems, feature selection and transformations in machine learning systems, medical imaging for image registration, detection of phase synchronization in time series analysis, average mutual information in delay embedding theorem, and other application areas [42], [58], and [59]. Although mutual information has many applications, cross-mutual information (CMI) research within the brain and muscle signals is uncommon [28]. Thus, this study was aimed at estimating the amount of cortico-muscular functional interaction with mutual information.

As discussed in the previous Chapter, cortico-muscular coherence can depict information flow within the motor system. This coherence, however, might be related to either cortical command of the muscle or afferent feedback from the contracting muscle [50]. To better understand its generator mechanism and functional connection, it is important to know the direction of information flow between brain and muscle signals. In addition, ordinary coherence only describes the normalized covariance in the frequency domain. It cannot account for the temporal relationship between the two systems [60]. Thus, to reliably measure the temporal relationship between brain and muscle signals, phase information across multiple frequencies or power information across multiple frequencies is required with stability. In this study, cross-mutual information (CMI) was used to analyze the EEG and EMG signals for measuring the dynamical coupling and transmissions of information between brain and muscle areas during different motor task performances. As in the linear coherence method, if one system is completely independent of another, the mutual information between two-time series generated from the brain and muscle signals can be said to be zero.

3.2.2. Nonlinear Mutual Information Method for Neurophysiological Mechanisms of Brain and Muscle

In order to clearly understand the neurophysiological mechanisms of the brain and muscle, mutual information analysis, in contrast to coherence, is taken into account as it can apply to both the linear and nonlinear dependencies of information transmission among brain-muscle regions [32], [33]. In this study, mutual information was calculated with the information produced by the muscles and brain cortex during the hand grasping movement. During the active movement motor task, the activation of brain and muscle signals increased with the appearance of the event-related desynchronization (ERD) pattern. During the movement of motor tasks, the innervation of muscle fibers inside the skeletal muscle and the transmission of neurons inside the motor cortex is strengthened as a consequence of the motor neurons' firing of both signals [28]. The reduced information transmission between pairs of brain-muscle electrodes is the result of the low innervation of brain and muscle neurons.

3.3. Data analysis

To investigate cortico-muscular functional interaction with a nonlinear mutual information analysis framework, we computed the mutual information of C3-EMG and C4-EMG signals during four different motor task types. Data from two electrodes were computed with a sliding 100 ms segment and a step size of 50 ms for all trials in the data range of 2 s to 5 s time series. Then we calculated the amount of mutual information between two signals in each subject for all motor task conditions. We set the mean value of data between 2 s and 0 s as the baseline, and then these baseline values were subtracted from the total interval. We compared the amount of mutual information in all motor tasks of RM, Inten, MI, and OL to check the cortico-muscular interaction between brain and muscle signals. For statistical data analysis, the Shapiro-Wilk normality test was first used to confirm that the data had a non-normality distribution. According to the Shapiro-Wilk test data, the data do not follow normality distribution with ($p < 0.05$). Thus, the independent-sample Kruskal–Wallis test was used to compare more than two groups with the nonparametric method.

3.4. Results

This section explains the results of cortico-muscular functional interaction with nonlinear mutual information methods. Firstly, we calculated the mutual information of brain and muscle signals in both ipsilateral motor cortex, C4-EMG, and contralateral motor cortex, C3-EMG across all motor tasks to check whether there was high or low mutual information in ipsilateral motor cortex versus EMG muscle signals. Then, the average cortico-muscular mutual information was calculated across all motor tasks in all subjects.

3.4.1. Investigation of Cortico-muscular Mutual Information in Contralateral Motor Cortex versus EMG and Ipsilateral Motor Cortex versus EMG

We investigated the amount of correlation between brain and muscle signals in both contralateral and ipsilateral cortices versus EMG. Figure 3.1 shows the result of the mutual information amount on one subject, C3-EMG. The amount of information in the RM task increased during the 5 s task after instructions began. The Inten task also showed higher amount of mutual information during the 5 s motor task nearly the same result as RM. However, the amount of mutual information was low during the MI and OL tasks.

The amount of cortico-muscular mutual information in the ipsilateral cortex, C4-EMG, was shown in Figure 3.2. The information transmission was low across four tasks of RM, Inten, MI, and OL tasks as the results were from the ipsilateral cortex, the same side of the brain as the hand. In all conditions of C3-EMG and C4-EMG, there were small fluctuations concerned with the subjects' motor task preparation and motor task learning before the onset time point for task instructions.

The results confirmed that high functional interaction occurred in C3-EMG rather than in C4-EMG. In addition, the two signals correlate well when motor unit firing and cortical neurons have good coupling. The results proved that there was a very low functional coupling between brain and muscle signals if there was no actual movement and no intention to move. To summarize, the nonlinear mutual information method proved that cortico-muscular functional interaction amounts vary across the types of motor tasks.

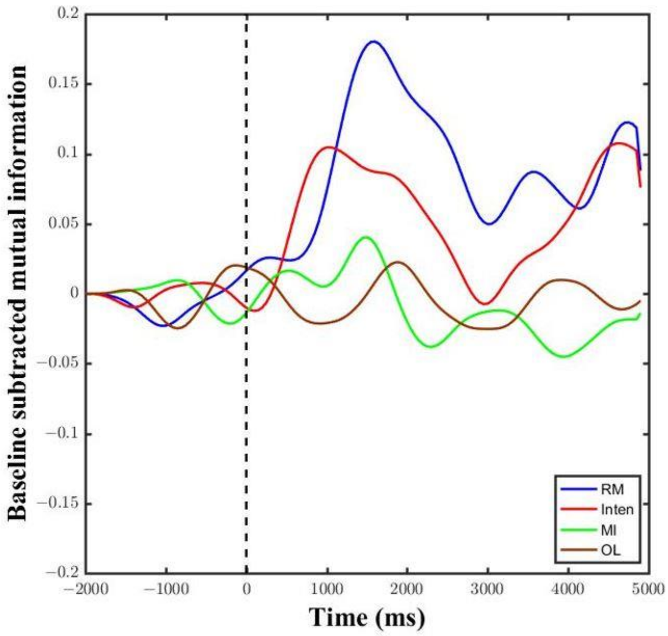


Figure 3.1: Comparison of mutual information in time series of data from one subject across all motor task conditions, C3-EMG. The black vertical dotted line represents the point at which the participant was given the motor task instructions.

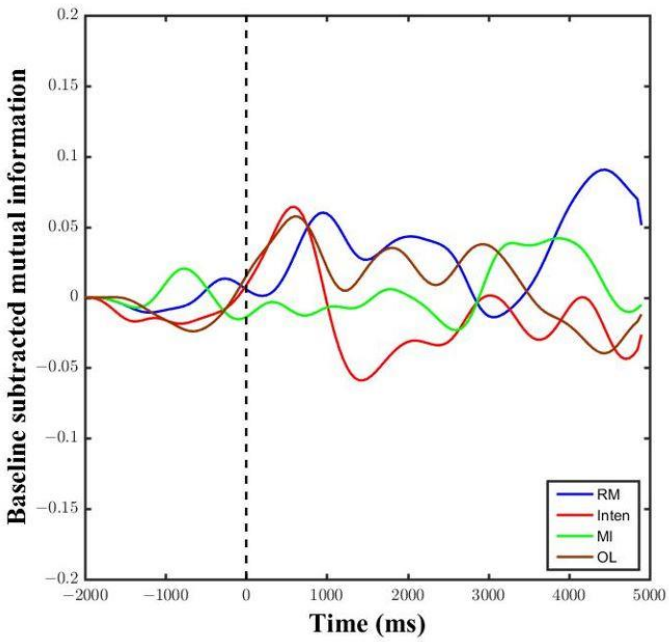


Figure 3.2: Comparison of mutual information in time series of data from one subject across all motor task conditions, C4-EMG. The black vertical dotted line represents the point at which the participant was given the motor task instructions.

3.4.2. Comparison of Cortico-muscular Averaged Mutual Information Across All Subjects

According to the results, there was low cortico-muscular mutual information in the ipsilateral motor cortex versus muscle signals. Thus, we chose only C3-EMG for further analysis. We calculated the average mutual information across all subjects. In the results, the RM showed the highest amount of mutual information during the 5 s motor task, followed by the Inten task, with the second-highest amount of information between brain and muscle signals. Then, the MI and OL tasks showed a slight increase in mutual information in averaged data, and this might concern the subjects' achieving focused attention and sensory-motor integration after some period of stimulus, as shown in Figure 3.3. In addition, there were some fluctuations in movement preparation before the subjects performed the tasks.

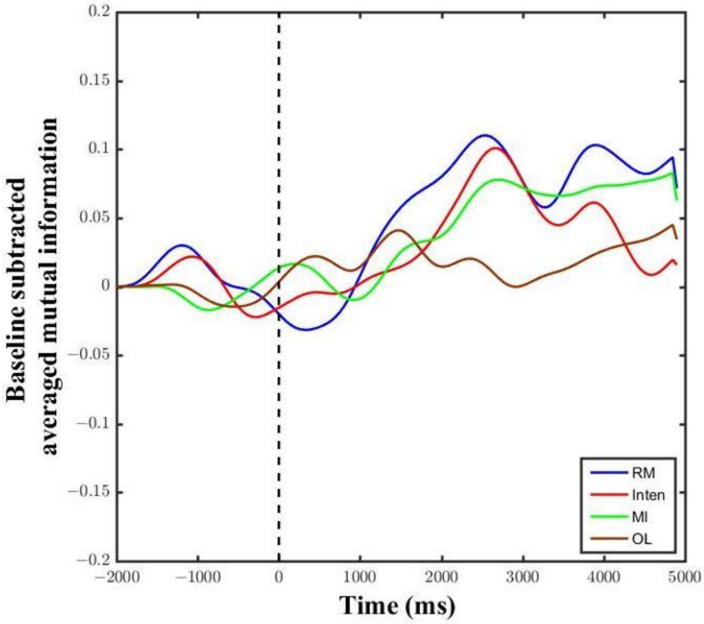


Figure 3.3: Comparison of mutual information in time series of data from all subjects across all motor task conditions. The black vertical dotted line represents the point at which the participants were given the motor task instructions.

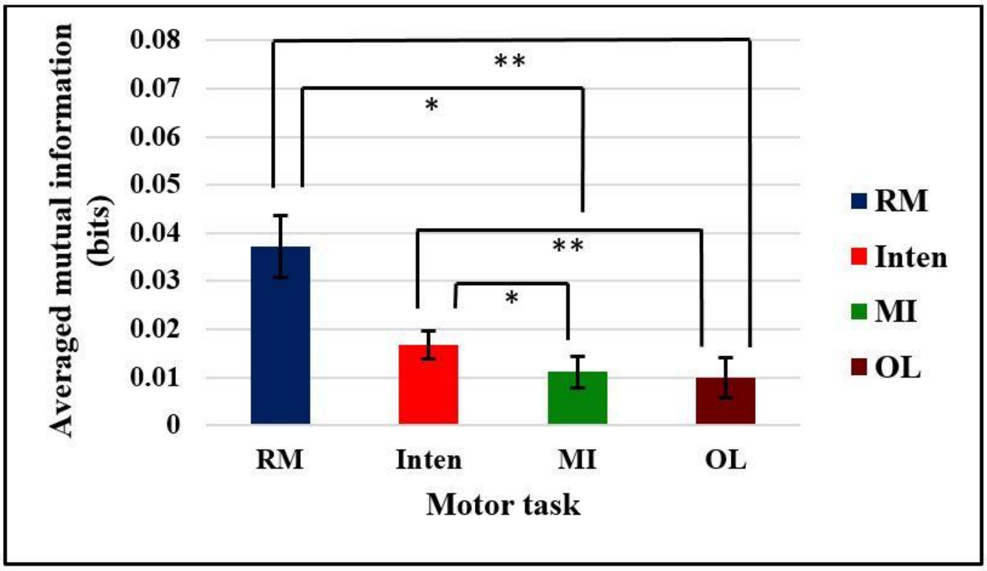


Figure 3.4: Averaged mutual information comparison across all motor tasks. The asymptotic significance (two-sided tests) is displayed with a standard error bar. * $p < 0.05$ ** $p < 0.01$.

3.5. Discussion

This study was the initial study with nonlinear mutual information flow calculation across different task conditions. One of the essential state-of-the-art requirements in brain–muscle correlation, as shown in **Appendix A**, was the comparison of mutual information across different motor tasks. Thus, we extended our study to fill the gap of functional coupling with different motor tasks. When the averaged mutual information was investigated in accordance with the different motor tasks, a greater amount of mutual information was found during the RM and Inten tasks than during the MI and OL tasks. The information increased starting from the baseline onset zero point, as shown in Figure 3.1 and Figure 3.3. Using a 100 ms sliding window in analysis can create an effective high-pass filter, and this can lead to achieving the pure task data mutual information. Increased mutual information between RM and Inten tasks revealed that there were good coupled signals between the brain and muscle signals during motor task execution. The absence of good synchronization between the two signals could lead to a small amount of mutual information. The nonlinear mutual information results were also consistent with the linear coherence method in this study.

In addition, we observed that the MI and OL tasks showed a slight increment after the task instructions point in averaged mutual information results. This transient increase of mutual information during motor imagery and movement observation might be the influence and consequence of the subjects' attention and the impulse responses to visual stimulation [22], [54]. This occurrence was the same coincidence as the occurrence of higher gamma-band coherence, caused by visual effects in the linear analysis [26]. Thus, the mutual information results could determine whether there is a good relationship or not in the form of functional coupling across motor tasks.

During hand grasping tasks, motor unit firing and cortical neurons burst inside the cell, causing synchronization and finally appearing as an action, which we had already proven. In [34], the authors used schizophrenic patients and then checked information transmission between different cortical areas by estimating the average cross-mutual information (ACMI), but they only used brain signals. The authors used DTF based on the MVAR and AR models, but there were still limitations for linear dependencies [60], [61], and [62]. Thus, this study applied both EEG and EMG signals to further explore the relationships between brain and muscle signals by applying the nonlinear information gain method. In summary, this nonlinear correlation method also proved that the cortico-muscular functional interaction of the brain and muscle signals changes based on motor task performance.

CHAPTER 4
INVESTIGATION DELAY TIME OF SIGNAL PROPAGATION BETWEEN BRAIN AND MUSCLE SIGNALS

This chapter explains the nonlinear mutual information delay time method, neurophysiological mechanisms, and its interpretation for inferring the direction of information flow from the motor cortex to muscles and from the peripheral muscles to the motor cortex based on the polarity of delay time across tasks.

4.1. Abstract

A basic understanding of the delay time can provide information on the signal transmission rate. There were controversial issues concerned with the delay time amount within the functional interaction of the brain-muscle system. Previous research works relied on phase-based methods, which are ineffective for determining the directionality of information flow. Thus, this study explored the delay time analysis of nonlinear mutual information flow with lagged power correlation in specific frequency bands. The results showed that the time to transmit the signals between the brain and peripheral muscles could take nearly ± 20 ms, which is an acceptable range according to the neurophysiological facts and is consistent with the previous different methods of delay time results.

4.2. Introduction to Delay Time Signal Propagation with a Nonlinear Method

Investigating the delay time contains important information for the cortico-muscular functional interaction. The delay time of mutual information can be used to infer the directionality of information flow between two signals [37] (p. 404). Every coherence and mutual information of two signals appear with a slight delay, which can tell us about the possible information processing of motor tasks and flow directionality of two signals. In previous studies, delay time during functional coupling was investigated with the phase-based method, the Hilbert transform method, and cross-correlation analysis [28], [42]. However, these methods are only applicable to narrowband coherence and the presence of a minimal phase relation between two signals, and they cannot infer the directionality of information flow. Thus, we investigated the delay time with lagged power correlation in specific frequency bands to infer the direction of information flow between efferent and afferent pathways.

We consider the two time series X(t) and Y(t) (t = 1 ... T) at T discrete points. The mutual information of signals at each discrete time point can be written in terms of a probability density function as per Equation 13 [59].

$$\mathrm{MI}(X(t), Y(t)) = \mathrm{H}(X(t)) + H(Y(t)) - H(X(t),Y(t))$$
$$= \sum_{j=1}^{m} \sum_{i=1}^{n} p(x_i(t), y_j(t)) \log_2\left(\frac{p(x_i(t), y_j(t))}{p(x_i(t))\, p(y_j(t))}\right) \quad (13)$$

Since the highest coherence values occurred in the range of beta (13–30 Hz) and gamma (31–50 Hz) in the results, we calculated the delay time of EEG and EMG signals in those bands by making power fluctuations time series using Morlet wavelet transformation. First, we constructed the time-frequency representation of beta and gamma bands based on the Morlet wavelet decomposition, which provides an optimal concentration in time and frequency [35]. In the Morlet wavelet, (*t, f*) in terms of time and frequency representation is given as in Equation 14.

$$\omega(t, f) = A\, exp\left(\frac{-t^2}{2\sigma_t^2}\right) exp\,(2i\pi ft) \quad (14)$$

Where, $\sigma f = 1/(2\,\pi\sigma\, t)$, $A = (\sigma\, t\sqrt{\pi}\,)^{\frac{-1}{2}}$

We calculated the convolution of the wavelet with the signal from the epoch at every time instant, *t*, and every frequency, *f.* The square norm of the convolution was the time-varying energy of EEG and EMG signals at a specific frequency, as in Equation 15 and Equation 16.

For EEG signal, $|E_x(t,f)| = |\, \omega(t,f) * x_q(t)\,|^2$ (15)

For EMG signal, $|E_y(t,f)| = |\, \omega(t,f) * y_q(t)\,|^2$ (16)

In this analysis, we calculated the power of beta and gamma bands to check the time delay mutual information of all motor task performances. We computed mutual information repeatedly for the multiple time lags by shifting one signal with respect to another. Then, it was graphed by calculating mutual information between two signals by fixing EEG signals and measuring the information according to the delayed time in EMG signals [37] (p. 404). We used Equation 17 for the calculation of time delay mutual information between EEG and EMG signals.

$$TDMI\big(X(t), Y(t+\tau)\big) = H\big(X(t)\big) + H\big(Y(t+\tau)\big) - H\big(X(t), Y(t+\tau)\big)$$
$$= \sum_n p\,\big(x(t), y(t+\tau)\big) \times \log_2[p(x(t), y(t+\tau))/p(x(t), y(t+\tau))] (17)$$

If the information present at the location EEG is transmitted to the location EMG, there will be a peak in the curve TDMI$(X(t), Y(t+\tau))$ at $\tau > 0$ and if the information present at the location EMG is transmitted to the location EEG with a delay time TDMI$(X(t), Y(t+\tau))$ at $\tau < 0$. A peak that occurs at $T = 0$ implies that a zero delay for the EMG and EEG may be due to the nullification of two strong counteracting forces driven from EEG to EMG and the opposing drive from EMG to EEG [38].

4.3. Brain and Muscle Neurophysiological Mechanisms with Delay Time

As it has been shown in Figure 4.1, the neurophysiological mechanisms of the brain and muscle are complex and compact in their interactions during motor task performance [36], [37]. The signals transmitted from the motor cortex to muscle are called "*descending motor pathways*," and those from the peripheral muscles to the brain's motor cortex are called "*ascending motor pathways*." As has been already stated, the hierarchical organization of the motor system works bi-directionally during the movements to achieve the goals. However, the direction of information transmission and its flow along muscle fibers may be difficult to judge with normal eyes. Thus, it is required to check the delay time of information flow between two systems of brain and muscle signals to infer the directionality of information flow. In this study, the mutual information delay time analysis framework was used to analyze the flow of information in terms of directionality and to explore the facts of neurophysiological mechanisms of brain and muscle signals.

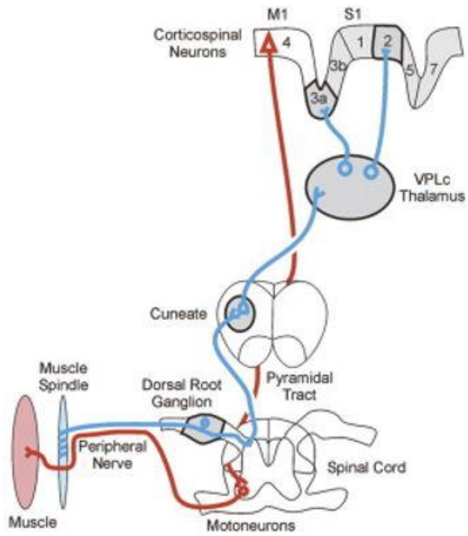


Figure 4.1: The descending (red) and ascending (blue) pathways which could mediate the information flow of the brain's motor cortex and peripheral muscles [36].

4.4. Data Analysis

For the analysis of delay time values in beta and gamma bands, time lag was calculated for each motor task across all subjects according to Equation 17. Based on the polarity of delay time results, in which mutual information is shown with the maximal value, the direction of information flow can be inferred. The positive delay time results indicate the information flow from the brain motor cortex to muscle with some extended amount of lagged time, and the negative delay time results indicate the information transmission travels from the peripheral muscle to the brain motor cortex. If the delay time result were zero, the information transmission would be nulled inside the two systems. For statistical comparison among four motor tasks, the Shapiro-Wilk test was first used to check the normality distribution. After that, a one-way ANOVA was performed to check the main effect of delay time across the tasks in the results. The LSD post hoc test was used for all multiple group comparisons.

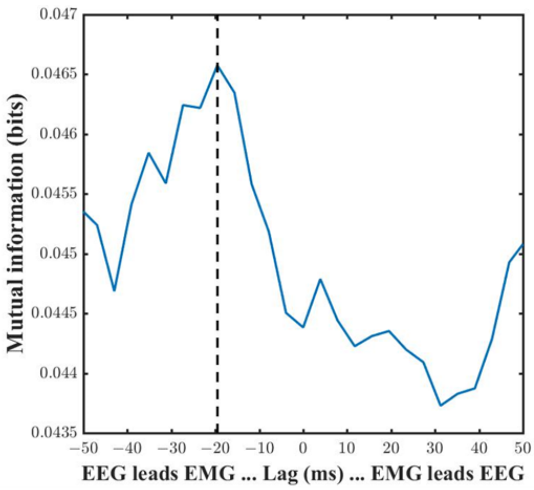
4.5. Results

This section emphasizes the results of calculated delay time during brain motor cortex and muscle functional interaction across four motor tasks of RM, Inten, MI, and OL in both beta and gamma bands. The averaged delay time results were statistically compared in both beta and gamma bands.

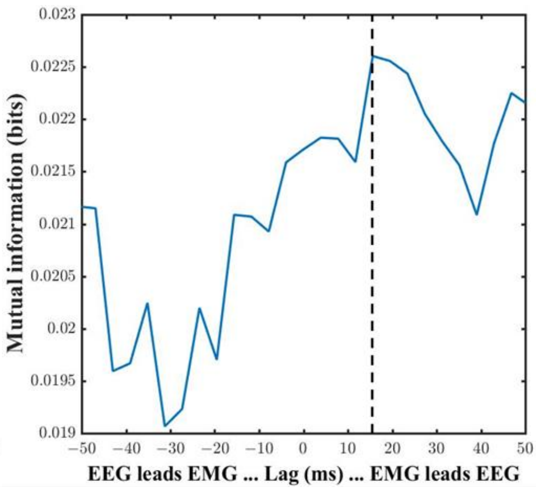
4.5.1. Delay Time Calculation Between the Brain's Motor Cortex and Peripheral Muscle

We finally investigated whether a good correlation of two signals would require a smaller delay time in signal transmission from one to another or not. Based on the occurrence of high coherence within the frequency ranges of beta (13–30 Hz) and gamma (31–50 Hz), the delay time values were calculated to determine the signal propagation and interaction time from the motor cortex to the muscle periphery or the muscle periphery to the motor cortex. In the calculation, a positive value of delay indicates that the time series of EMG is in advance; a negative value of delay indicates that the time series of EEG is in advance [37], [39]. The results of delay time mutual information in one subject's data for the beta and gamma bands of the RM task were shown in Figure 4.2. Based on the results, we could infer that information flow direction with (–) 20 ms of lagged time from peripheral muscle to motor cortex in the beta band and (+) 15 ms of lagged time from cortex to muscle in the gamma band.

In Table 4.1, we reported the delay time values of each subject across all motor tasks in both beta and gamma ranges. According to the results, the average delay time in the RM and Inten tasks was in the range of 15–25 ms, in agreement with [5]. Conversely, the delay time in the no-movement tasks, such as the MI and OL conditions, was higher than those in the RM task and Inten task in both beta and gamma bands. The amount of delay time in the gamma band also occurred with a smaller amount of mutual information if we compared it with the beta band. It is noteworthy that the higher the frequency ranges we investigated, the lower the delay time, with a lower amount of mutual information. This might have occurred in the gamma band ranges of averaged results for all subjects. Some subjects showed zero delay time. A zero-delay might be due to the nullification of strong counteracting forces driven from the motor cortex to the muscle and the opposing drive from the muscle to the motor cortex. This result indicates that the amount of time to transmit the signals from one area to another could be high if they were not coherent or even if they had a low correlation. In summary, good functional interaction between brain and muscle would require a smaller delay time for signal transmission in both efferent and afferent pathways.



(a)



(b)

Figure 4.2: Delay time mutual information of one subject in the RM task: (a) in the beta band; (b) in the gamma band. The black vertical dotted line represents the delay time at the maximum value of mutual information.

Delay Time (ms) Obtained by Maximizing Mutual Information [1]								
Subject	**RM**		**Inten**		**MI**		**OL**	
	β	**γ**	**β**	**γ**	**β**	**γ**	**β**	**γ**
1	−20	+15	+20	−20	−40	−15	−45	−30
2	−20	+15	+20	−20	−30	−20	−45	−39
3	−25	+20	+25	−20	+25	−45	−35	+35
4	+30	+23	−25	+25	+30	−28	+35	−40
5	+25	−30	0	−30	−35	−30	+20	−39
6	−20	+30	−35	−15	−25	−30	−43	−25
7	−25	−20	−35	−20	−40	+20	−43	+20
8	−30	0	−25	−20	−30	+30	−35	−25
9	−15	−15	+30	−25	−40	−28	−35	−20
10	−25	−30	+15	−30	−35	−35	−25	+25
11	−16	+23	−35	−28	−39	−43	−43	−39
12	−20	−15	−30	+30	+35	−40	+25	−20
13	+25	−15	−30	0	−30	−45	−30	−15
Mean	22.76	19.31	25.00	21.76	33.38	31.46	35.31	28.61
SD	4.83	8.35	9.78	8.16	5.45	9.78	8.37	8.86

[1] Delay time values were calculated by maximizing the mutual information for the thirteen subjects. Positive and negative signs were introduced to infer the directionality of information flow and these polarities were not taken into account in the calculation.

Table 4.1: Summary of delay time in the beta band and gamma-band across all motor tasks.

4.5.2. Delay Time Statistical Analysis Across All Subjects

We also performed a statistical analysis of the averaged delay time to check multiple comparisons across all subjects in four kinds of motor tasks. First, we checked the normality distribution of the data with the Shapiro–Wilk test. The data of each task for all individuals together follow the normality with $p > 0.05$. Then, we used the parametric test ANOVA with the task × delay time value for statistical analysis. A significant main effect of delay time was found among four different motor tasks in the beta band delay time with one-way ANOVA ($F(3, 48) = 8.479$, $p = 0.001$). The LSD post hoc test showed a significant difference between the MI task (33.38 ± 1.5129 ms, $p < 0.001$) and OL task (35.31 ± 2.32 ms, $p < 0.001$) compared with the RM task (22.77 ± 1.31 ms), and between the MI task (33.38 ± 1.5129 ms, $p = 0.011$) and the OL task (35.31 ± 2.32 ms, $p < 0.001$) compared with the Inten task (25 ± 2.71 ms). There was no statistically significant difference between the RM task and the Inten task beta band delay time ($p = 0.445$).

In the gamma band delay time, the results also showed a significant difference with (F (3, 48) = 4.053, p = 0.012). The LSD post-hoc test resulted in the MI task (31.46 ± 2.71 ms, p = 0.003) and OL task (28.61 ± 2.46 ms, p = 0.012) compared with the RM task, and the MI task (31.46 ± 2.71 ms, p = 0.044) compared with the Inten task (21.77 ± 2.262 ms), as shown in Figure 4.3. We could prove that cortico-muscular functional interaction delay time values in both the beta band and the gamma band are also significantly different and variable based on the motor task performance.

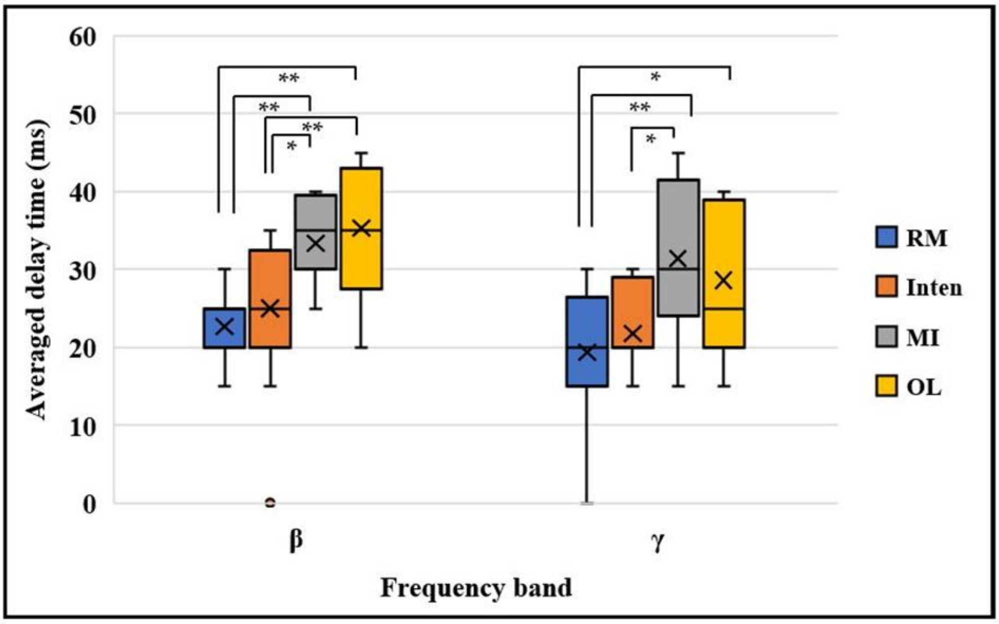


Figure 4.3: Averaged delay time mutual information comparison across all motor tasks in the beta band and gamma band. The top and bottom of each box represent the 25th and 75th percentiles, respectively. The cross sign inside each box represents the mean value. The horizontal black line represents the median. The whiskers are drawn from the ends of the interquartile ranges to the minimum and maximum values. * $p < 0.05$ ** $p < 0.01$.

4.6. Discussion

Delay time calculation is fundamentally important for brain-muscle interaction, especially in the design of prosthetic devices and movement intention detectors. The previous studies used only classifiers and then classified the movement types and they did not calculate the amount of the time lag between brain and muscle signals [15], [63]. Thus, we finally emphasized the calculation of the cortico-muscular functional interaction delay time based on the motor task performance. It is well-known that the direction of information flow cannot be calculated by the functional coupling of coherence. Because it is symmetrical, conventional mutual information is also limited in that it cannot be used to determine the direction of information flow. To overcome this limitation, we used delayed time mutual information by defining a time series in one of the variables to calculate mutual information, which can lead to an asymmetric measure. The delay time between EEG and EMG data was 11–27 ms between the tremor correlated parts (cortex) of the brain EEG and the trembling hand EMG. The coherence delay time was calculated based on the highest coherence frequency bands as a function of time lag, but the authors could not infer the directionality of information flow [39].

Based on the nerve fibers' conduction velocity of 50–65 m/s in the arms and the distance between the scalp and the hand of approximately 1.2 m, most delay times are in the range of 18–24 ms [64]. We chose the beta (13–30 Hz) and gamma (31–50 Hz) ranges since there has been a lack of delay time analysis based on these bands. Our results indicate that the average delay time values were within the range of 15–25 ms for RM and Inten tasks. These ranges were consistent with physiological facts, as we discussed above [5], [64]. Moreover, there was a longer delay time in the no-movement task condition of the MI and OL tasks. These results showed that the time will take longer or higher for the transmission of signals from one point to another if there is no high coupling or greater mutual information. The gamma-band delay time-averaged values showed a smaller amount of delay time than the beta-band delay time-averaged values.

The advantage of mutual information time lag was that we could infer the direction of information flow based on the polarity of the time value rather than the linear method of coherence. Thus, we could clearly see the signal propagation or transmission time from the brain to muscle (descending) or muscle to brain (ascending) oscillation in terms of the lag time, as in Table 4.1. Some subjects demonstrated information flow from the brain to the peripheral muscle, while others demonstrated information flow from the peripheral muscle to the brain [36], [49]. In our research, investigation of the delay time with the nonlinear method based on the beta and gamma bands represented a new approach to directionality inference. However, future studies still need to be undertaken in order to obtain more exact results with more subjects of different ages. In summary, cortico-muscular functional interaction values are also significantly different and they change based on the motor tasks in both beta and gamma bands, according to the results.

CHAPTER 5
DISCUSSION

This chapter is the discussion section of the research. We mainly emphasized the reasons for using the four tasks to calculate the functional interaction of brain and muscle signals. In addition, we discuss how these four motor tasks relate to each other and how they can take part in judging the level of interaction between two signals from the brain's motor cortex and an EMG muscle based on the occurrences of the results. Based on the hypothesized questions and previous remaining problems, this session will discuss the issues surrounding them.

5.1. Abstract

First, we discussed the differences in neurophysiology and relationships between the four tasks: how they can relate to each other and how these tasks are essential for research work. Then, we discussed point-by-point findings regarding controversial issues in the functional interaction of brain and muscle signals. We discussed anatomical and neurophysiological principles, factors that influence CMC, and real-world applications of this research. Based on the study results, we concluded with consistent and reliable facts about brain-muscle signals' functional interaction.

5.2. Differences in Neurophysiology and Relationships Across RM, Inten, MI, and OL Tasks

The four motor tasks are principally related as forms of movement activity in our daily lives. However, they are physiologically different in terms of internal motor dynamic structures. Thus, it needs to understand how these four tasks relate to each other, how much they differ, and how they play an essential role in neuroscience fields, especially in biomedical engineering. Studies need to be analyzed to explore the task-related functional interaction and explore the rehabilitation techniques or means for stroke patients. As it was already depicted in section 2.2.2, the motor tasks of RM, Inten, MI, and OL require different motion and force, and that leads to different patterns of coordination among cortical and motor neurons as a functional interaction. The level of neural binding across the tasks can state the amount of functional interaction. Thus, this study compared these tasks to investigate the level of functional interaction.

The real movement (RM) task is the real hand grasping movement of the participants. Whenever the subjects perform the motor task to achieve the expected goal for the movement (e.g., hand grasping movement), the motor neurons, interneurons, and complex neural circuits inside the spinal cord execute the command to generate the proper forces on individual muscles and muscle groups to enable that movement. The neurophysiological principles state that the excitation of alpha motor neurons innervates the muscle and causes the muscle contractions to generate the movement [43]. Thus, the RM task mainly involves the excitation of alpha motor neurons inside the spinal cord and muscle fibers, and that leads to functional interaction appearance.

In movement intention (Inten), the Inten task involves mental activities of planning and forethought. An intention is a mental state that represents a commitment to carry out an action or actions in the future [65]. In this study, the Inten task applied both mental activities of planning to move like the real movement and forethought of that movement without actually moving the hand. As a consequence of practicing mental activities inside the brain and mind, the motor intention task may involve a slight excitation of motor neurons inside the spinal cord and muscle fibers, which leads to the functional interaction appearance in both linear and nonlinear analysis framework results, as we have already discussed in sections 2.5 and 3.4. The designing Inten task together with the RM task depicted the physiological status of the human motor system from the inside. This study clearly showed the two conditions of real movement status and movement intention condition for the interaction level of brain and muscle signals. As intention can show the connections between mental states and actions carried out by the subject in order to achieve a goal, it includes the causes of psychological and neurophysiological phenomena, as has already been discussed by Astington et al. [66].

Together with the RM and Inten tasks, this study applied the motor imagery (MI) task. As there were many controversial issues regarding the occurrence of EMG signals during motor imagery, we took them into consideration together with other motor tasks [67]. The difference between an Inten task and an Image MI task is that the MI task does not include a commitment to carry out in the future or forethought. However, like the Inten task, motor imagery can involve a purely mental process by which the participant rehearses or simulates a given action or motor task. In our experiment, the subjects were asked to imagine themselves performing the action. There are two types of motor imagery: kinesthetic motor imagery and visuomotor imagery. Visuomotor imagery (VMI) is a visual representation of the corresponding movement [68]. This study used visuomotor imagery, which requires the use of a participant's imagination to simulate the motor task action without any physical movement. In this study, we considered the MI task as a form of mental practice [69]. The MI task might not involve motor neuron excitation inside the spinal cord and muscle fibers as in the RM and Inten tasks. As a result, this leads to very low functional interaction between the brain and muscle signals. The MI task leads to the rare occurrence of EMG signals during data recording and it satisfied the controversial problems in previously published works [67].

The movement observation (OL) task was considered together with the other three tasks in the study. Mirror neurons can occur during movement observation of motor tasks, so movement observation can also be considered as mirroring. In our study, we explored the effect of movement observation with a three-dimensional 3D-HMD in a virtual reality environment for motor task observation, called the OL task. According to the results, some subjects showed higher functional interaction in the gamma band during the OL task, as shown in Figure 2.8 as a result of mirror neurons. Mirror neurons are neurons that show similar responses to action observation and action execution for meaningful goal-directed action [70], [71]. As a consequence of attention in 3D-HMD, firing motor neurons inside the spinal cord and the output of mirror neurons, the OL task generates some high coherences at higher frequencies. However, the neurophysiological facts behind the concept of movement observation are still complex.

Because each motor task was unique, we considered investigating the relationship between brain and muscle signals. To conclude, these four motor tasks differ from each other based on the level of neural binding across the task and generate different aspects of results for the interaction of brain and muscle signals. The main difference between each motor task can rely on the inside neurophysiological factors and components which depend on the performance of each participant.

5.3. Functional Interaction of Brain and Muscle Signals Discovered Using the Linear Coherence Method's Controversial Issues

There remains the controversial issues of the linear coherence method in previous studies. Thus, this study discusses the major findings and occurrences based on the results of our own experimental data.

5.3.1. Noise Level Detection and Its Effect on Brain-muscle Functional Interaction Analysis

In this study, the influence of noise on EEG data led to misleading results. To remove the eye-blinking noise and non-brain artifacts in the EEG signals, we used Independent Component Analysis (ICA) in EEGLAB. We kept a maximum of eight to nine IC's and excluded one or two components that apparently affect the EEG channel across all tasks in all subjects. In the original recorded EEG raw data, each row of the channel data activation matrix represents the time course summed in voltage differences in each channel, as shown in Figure 5.1.

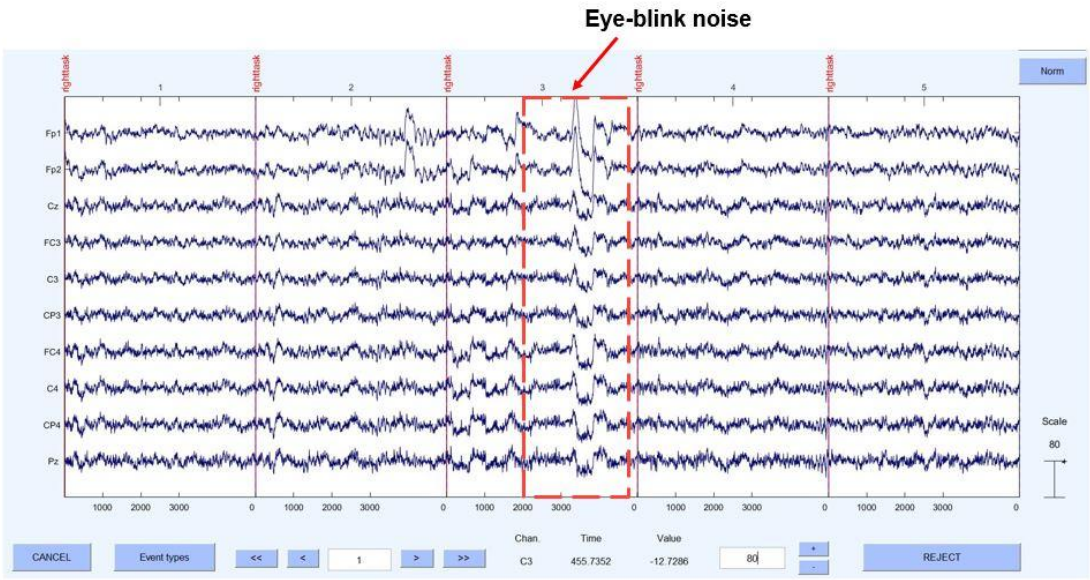


Figure 5.1: EEG data with eye-blink noise.

EEG data that contained artifacts was determined by EEGLAB's automated artifact rejection with a set threshold voltage of (±)100 µV. The independent component filters were chosen to get maximally temporally independent signals available in each EEG channel data set in ICA decomposition. After ICA decomposition, results from each row of the data activation matrix are the time course of the activity of one component process spatially filtered from channel data. By removing redundancies in the data, ICA allows keeping most of the information for functional interaction analysis, as shown in Figure 5.2.

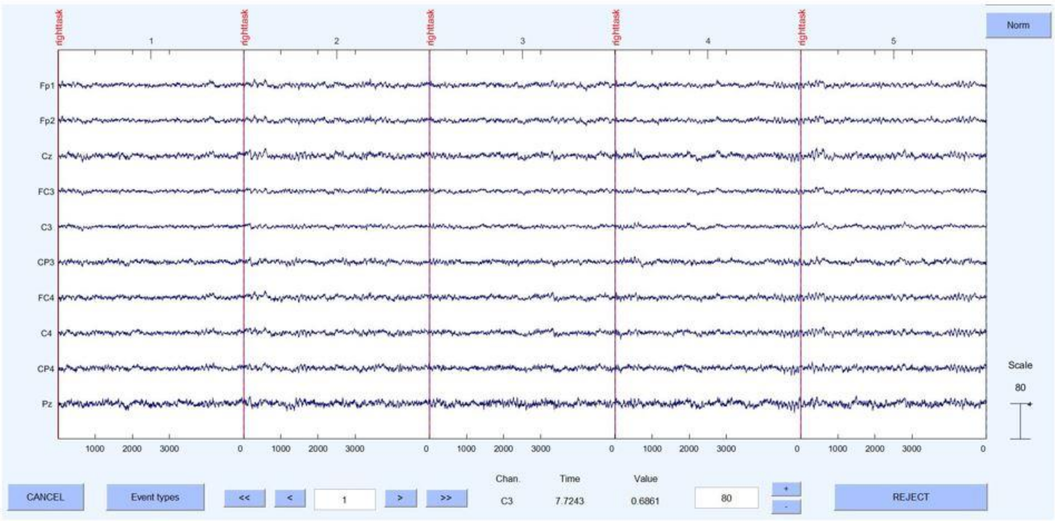
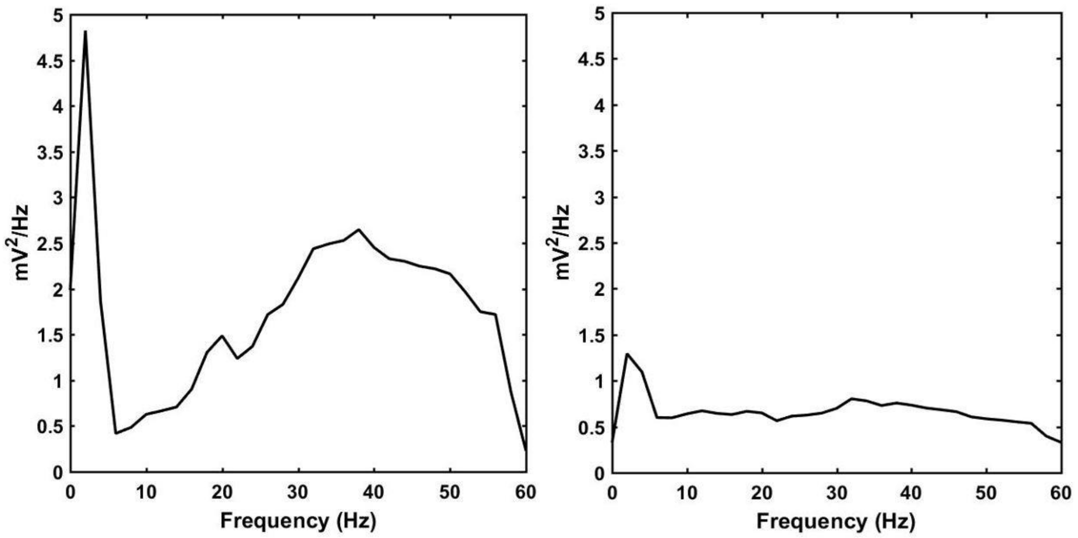


Figure 5.2: EEG data after using Independent Component Analysis (ICA).

5.3.2. Investigating the Effects of Rectified and Non-rectified EMG Signals

EMG rectification is one of the ongoing debates in finding the functional interaction of brain and muscle signals. The rectified EMG signal was used in the majority of previous studies [3], [4], and [28]. On the other hand, EMG rectification is a nonlinear operator and should therefore not be applied in the coherence analysis that detects linear coupling [29], [31]. Thus, we explored the difference between rectification and non-rectification for the purposes of coherence and mutual information analysis. According to our results, EMG rectification leads to a shift of the EMG power spectrum to the lower frequency, which corresponds to the MU firing rate, and it diminishes the important power spectral components for coherence analysis. We discussed and proved that rectification can distort the frequency content of the signal and power spectral values as shown in Figure 5.3.



(a) (b)

Figure 5.3: Auto spectral EMG of a participant during one motor task (a) unrectified EMG signal (b) rectified EMG signal.

5.3.3. Calculation of EEG-EMG Spectral Power and Related Coherence Across RM, Inten, MI, and OL Tasks

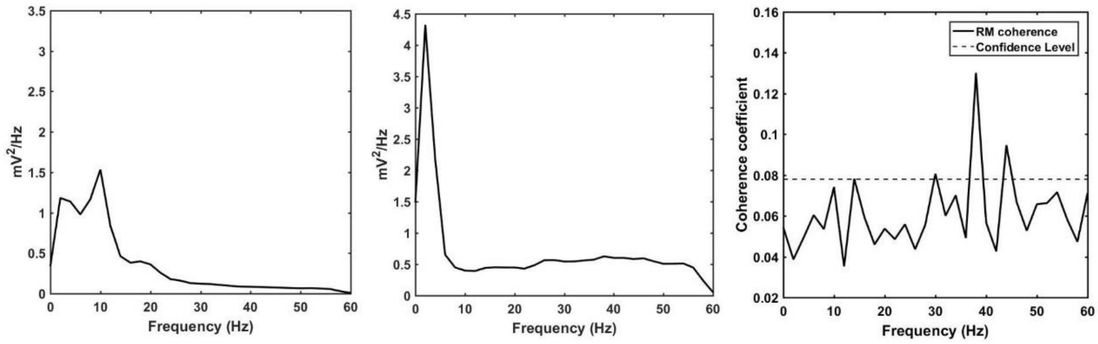
To check experimental data results, we first discuss the spectral power and their auto spectral power across all tasks. The auto spectral values depict the power related to each frequency. The calculation of auto spectral power and cross-spectral power was needed in the calculation of coherence. From the experimental results, the auto spectra values showed the different amounts of spectral content in each RM, Inten, MI, and OL task. In the RM task, the spectral value of the EEG showed cortical oscillatory activity, which is closely coupled to the synchronized motor unit and can reflect the rhythmic discharges of the spinal motoneuronal pool. Figure 5.4 shows the auto spectra power of EEG and EMG and their related coherence coefficient in each task for one subject data set.

The distinct peaks of EEG-EMG auto spectra power were detected at about 3 Hz, 10 Hz, and less than 10 Hz in the RM task. The peak centered around 10 Hz is reduced in the EEG signal while the peak in the 20–50 Hz range was enhanced in the non-rectified EMG signal during the task performance. In spite of the similarity of both EEG and EMG auto spectra, both of them showed a distinct peak centered about 40 Hz in terms of coherence between two signals. This high coherence shows the significant correlations of brain-muscle signals in the RM task. The distinct peaks of auto spectra are also at about 2 Hz and 10 Hz in the EEG signal of the Inten task. The non-rectified auto spectra values increased until 35 Hz during the intention. The coherence was also detected in the Inten task within the beta band. Our experimental results proved that the intention force generates the beta-band coherence.

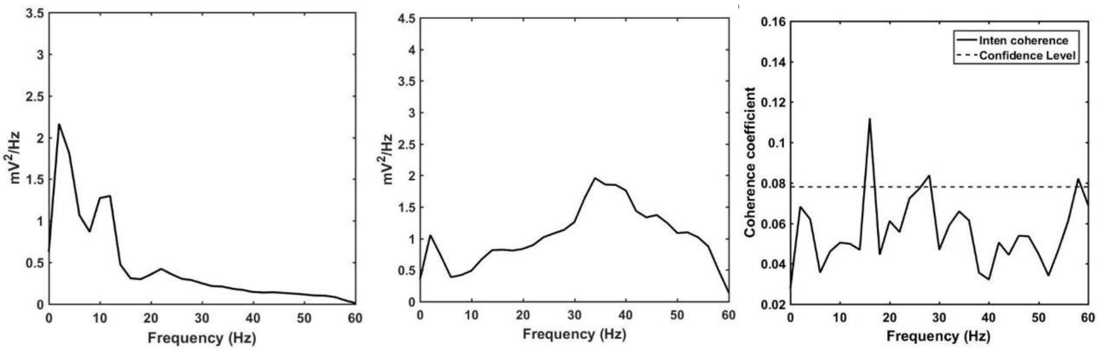
Previous studies have stated that the coherence frequency values can greatly change based on the tasks and force levels of muscle contraction. The static force generates the beta-band coherence and the dynamic motor task outputs the gamma-band coherence [16], [23]. According to our study, it has been shown that the coherence frequency values in beta (13–30 Hz) and gamma bands (31–50 Hz) can be seen in RM and Inten tasks with statistically significant differences across four types of motor tasks, as shown in Figure 2.8 and Figure 2.9, respectively.

The auto spectra values of EEG spectral values have occurred at 10 Hz in both the MI and OL tasks. As it has been described in previous studies, conscious motor imagery and unconscious motor preparation share common mechanisms and they are functionally equivalent [26], [27], [67], [68], and [69]. Thus, the auto spectral values of MI and OL tasks showed a spectral pattern that looked like the experimental results of RM. During the resting stage of the motor task, the auto spectral value of EMG signals leads to an increase during the whole period of the task. There was no coherence in MI tasks while some subjects generated the coherence values as an effect of attention in the OL task [26].

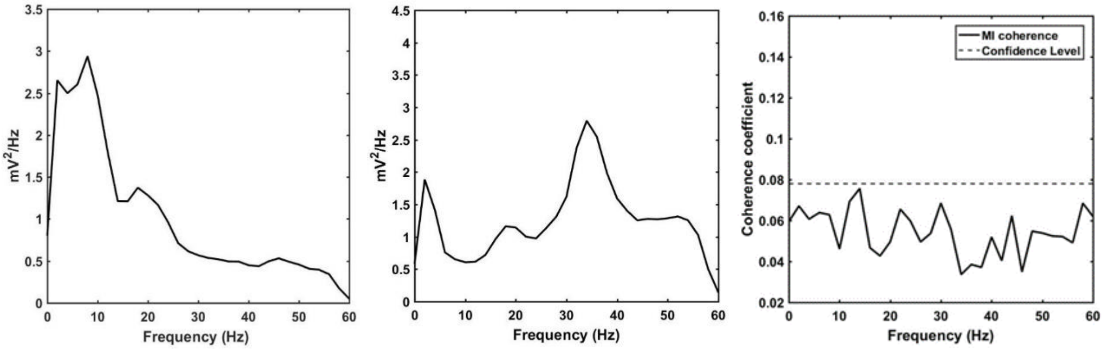
This study proved that as the estimated auto spectral power amount changes based on motor task performance, this study provided more validated results for the coherence analysis. We concluded that during RM and Inten tasks, the auto spectra values of brain and muscle signals tend to decrease within the designated frequency bands and then lead to the higher coherence output, whereas the spectra power tends to increase, especially in EMG frequency bands, with very low coherence levels in both MI and OL tasks. All subjects showed similar frequency components in the EEG and EMG auto spectra for each kind of motor task, although there was considerable variation in the amplitudes between subjects and between tasks.


mV^2/Hz
Frequency (Hz)
mV^2/Hz
Frequency (Hz)
RM coherence
Confidence Level
Coherence coefficient
Frequency (Hz)

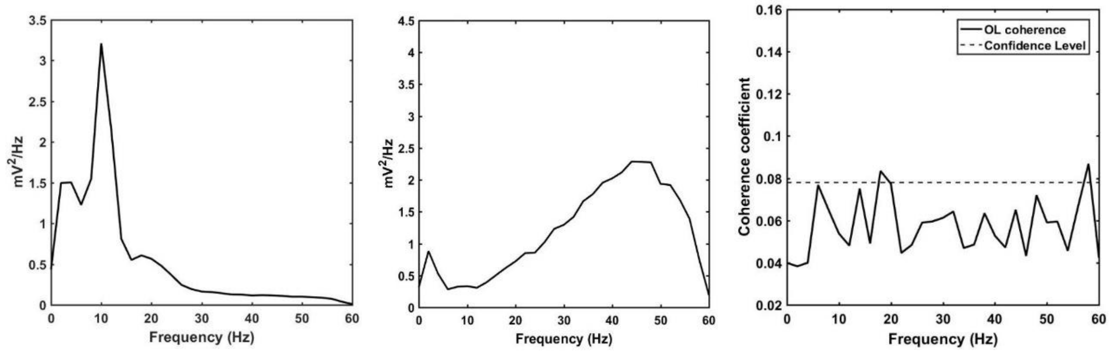
(a)


mV^2/Hz
Frequency (Hz)
mV^2/Hz
Frequency (Hz)
Inten coherence
Confidence Level
Coherence coefficient
Frequency (Hz)

(b)


mV^2/Hz
Frequency (Hz)
mV^2/Hz
Frequency (Hz)
MI coherence
Confidence Level
Coherence coefficient
Frequency (Hz)

(c)


mV^2/Hz
Frequency (Hz)
mV^2/Hz
Frequency (Hz)
OL coherence
Confidence Level
Coherence coefficient
Frequency (Hz)

(d)

Figure 5.4: EEG-EMG spectral power and related coherence results across tasks: estimated EEG auto spectrum (left panel), estimated EMG auto spectrum (middle panel), EEG-EMG coherence (right panel) in (a) the RM task, (b) the Inten task, (c) the MI task, and (d) the OL task

5.3.4. Band Frequencies in Cortico-muscular Coherence

According to the ongoing oscillations of brain signals, our study was designed to investigate the brain and muscle signals within five frequency bands to check the coherence of subjects across tasks. We checked the EEG-EMG coherence amount in delta (0.5-3.5 Hz), theta (4-7.5 Hz), alpha (8-12 Hz), beta (13-30 Hz), and gamma (31-50 Hz) across all tasks. The results showed that brain-muscle functional interaction is highly variable across motor tasks, with an absence of significant coherence in MI and OL tasks.

From the experimental results, the coherence values were mainly detected in the beta (13–30 Hz) and gamma bands (31–50 Hz) of RM and Inten tasks, while low coherence values occurred in MI and OL tasks. However, as an exception, very few subjects diminish coherence in these band frequency ranges even when they perform the RM and Inten tasks. Furthermore, some subjects show coherence values in the alpha band (8–12 Hz), in the delta band (0.5–3.5 Hz), and in the theta band (4–7.5 Hz) according to the experimental results. Thus, functional interaction coherence of brain and muscle signals can be detected in all five frequency bands but with different amounts, as already discussed in section 2.5. Oscillatory activities in these five different frequency bands have distinct physiological roles, and each can be assigned to specific perceptual, sensorimotor, or cognitive operations.

In addition, the different parameters of physiological features in internal motor dynamic structure across tasks are the main causes of coherence occurrence [49]. We could say that the occurrence of coherence in beta and gamma bands was not because of the task and force differences; there will be some neurophysiological matter inside the brain and muscle signals. From this experimental design and results, we could say the most critical point is that the between-subject variabilities greatly influence the amount of coherence.

5.3.5. Muscle Contraction Force-related Changes in Cotrico-muscular Coherence

The experimental results demonstrated that cortico-muscular coherence in beta and gamma bands was muscle contraction force-related changes. According to our experimental results [25], [55], and [72], the highest amount of coherence was detected in RM and Inten tasks across all subjects, and this meant that the amount of coherence depends on the level of muscle contraction force. Beta bands occurred in some subjects, and gamma bands were detected in some subjects during RM and Inten tasks. The decrease in beta band (13–30 Hz) coherence during the tasks may also be related to the event-related desynchronization (ERD) of EEG activity.

The new evidence for controversial issues from this study is that the occurrence of coherence frequencies in these beta and gamma bands may not require to have dynamic forces. We strongly confirmed these facts since the highest coherence appeared even during the Inten task. Only performing the real contraction and just the intention to do tasks can generate both beta and gamma bands, and these results contradicted the previous studies in which coherence in gamma bands was an effect of dynamic forces [23], [47]. Muscle contraction force and motor task performance-related changes in cortico-muscular coherence were widely expressed in Chapter 2, section 2.5 of this study.

5.3.6. Cortico-muscular Functional Interaction Based on Motor Task Performance

Motor task performance with the use of 3D-HMD influences the frequency content of the neural drive to muscle and the gain of efferent and afferent pathways. The high cortico-muscular interaction was associated with the normal force output of muscles, especially in the RM and Inten tasks. The beta (13–30 Hz) and gamma (31–50 Hz) ranges were related to the output of strong force muscle contractions, which is directly correlated with the activation of motor neurons in descending pathways. The alteration of visual stimulation influences nearly the entire coherency frequency of common input to motor neurons, as well as the gain of the proprioceptive (afferent). This research proved that task-related modulation of cortical muscular activity can generate afferent feedback and efferent feedforward functional interaction. Thus, the cortico-muscular functional interaction greatly changes based on the motor task performance with bi-directional information flow.

5.3.7. Event-related Coherence, Synchronization, and Desynchronization

The presence of alpha band (8-12 Hz), beta band (13-30 Hz), and gamma band (31-50 Hz) coherence in our study is related to event-related desynchronization (ERD) and event-related synchronization (ERS) [6], [52], and [73]. During the motor tasks of RM, Inten, and MI, the power reduction of these frequencies is the result of cortical activation and muscle innervation. During motor task preparation and execution, the amount of functional interaction coherence increases when ERD is prominent in the sensorimotor area. Furthermore, after movement execution, the ERS is prominent and the level of coherence tends to decrease.

5.3.8. The Influence of Attention and the Virtual Reality Environment on Cortico-muscular Functional Interaction

The effect of attention during experimental performance influences the results of coherence [25], [56]. In some subjects, in the OL task, there were higher coherence frequencies during functional interaction. These are the effects of the 3D- HMD on a virtual environment. The 3D-HMD display for motor task instruction acts as sensory input and sensory information to the brain for designated motor tasks. When a participant receives a sight sense or perceives things through their eyes via the 3D-HMD instructions for the RM, Inten, MI, and OL tasks, the motor neurons and receptors inside the brain and muscle synchronously oscillate, and these oscillations lead to the participant’s motor task goal and finally to a higher output of cortico-muscular functional interaction.

5.3.9. Cortico-muscular Functional Interaction in Motor Imagery

We investigated the effect of motor imagery as a task condition in this experiment because there were many controversial issues regarding the detection of EMG signal in motor imagery conditions [26], [27], [67], [68], and [69]. On the physiological basis, the execution of movement and its imagery show the same and parallel results, and there was a relationship between motor execution and the imaging of that movement. Thus, it occurred that the power spectra value of motor imagery is nearly the same as the curve of real movement in the experimental results, and it had already been depicted in Figure 5.4. However, there was no occurrence of significant EMG signals during motor imagery, and very low coherence values occurred in all subjects’ coherence results, as shown in Figure 2.4. Thus, this study’s designed experiment solved the remaining unclear problems of EMG versus motor imagery [67], [68], and [69].

5.4. Cortico-muscular Mutual Information Across RM, Inten, MI, and OL Tasks

Analysis of the mutual information of the brain and muscle signals demonstrated that the mutual information of the RM task and Inten task generally showed more synchronized information than the MI task and OL task, as shown in Figure 3.3. As shown in Figure 3.2, the reduced mutual information and distant transmission information were more apparent for the ipsilateral motor cortex, C4 versus EMG muscle. This made the results strong that the information flow from brain to muscle and muscle to brain follows the neurophysiological principles.

As the same results in the linear method, the two signals have the most shared information in the RM task. Although generally, most of the subjects tend to increase the shared information within the whole 5-second motor task, some subjects show mutual information just in the first 2 s after onset, and some subjects show no significant information even in the RM task. For example, subjects 09 and 12 have atypical profiles of shared information, while subject 01 has the correct amount of information synchronization between brain and muscle signals, as shown in Figure 5.5.

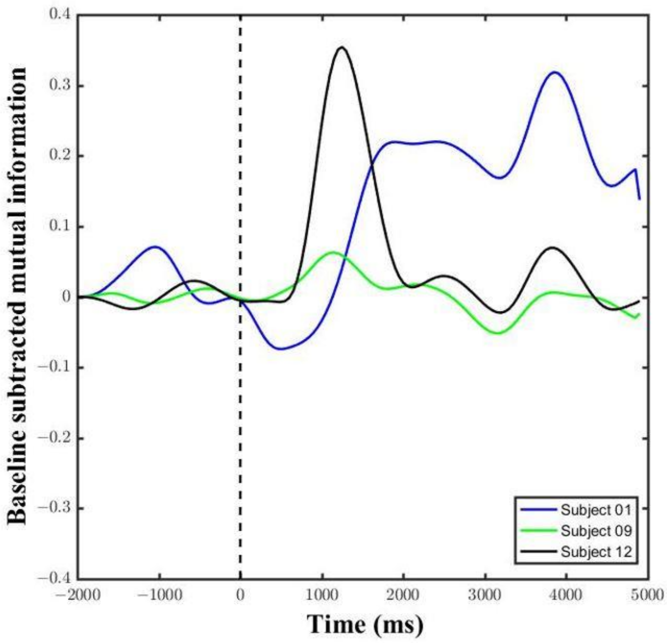


Figure 5.5: Comparison of typical and atypical mutual information profiles in the RM task.

In the calculation of mutual information, bin number selection is a critical matter to achieve the correct shared information. As the calculation of mutual information depends on the estimation of entropy values within two signals, we need to choose suitable bin numbers. In our study, we applied the *Freedman-Diaconis* rule to calculate the required probability value that falls into each bin [37]. The amount of information can be lost if the selected number of bins and calculated data do not fit. Otherwise, there will be little sensitivity to the distribution of the data. There was a relationship between bins and the influence of noise from the calculated data.

In addition, from the experimental results of mutual information, the effect of movement preparation occurred with a slight fluctuation within the first 2 s before the task onset point in all tasks across all subjects. In this study, the experiment was designed with a total of 15 s for each trial, in which the first 8 s is the resting stage, the next 2 s is the ready stage, and the last 5 s is the only task stage. During a 2-second ready stage, the participants had to prepare for the instructed motor task. The findings suggest that during the course of determining a task goal or making a decision for a task, the prepared state is updated as the desired motor task changes in light of views and beliefs. The motor system can generate an appropriate movement as rapidly as possible when necessary. The patterns of muscle activation to achieve even simple goals are subject to the occurrence of cortico-muscular functional interaction. Thus, our findings from the mutual information proved that there was a relationship between decision-making, movement preparation, and movement execution.

According to studies [32], [34], and [37], mutual information does not work in parametric statistical methods. Our study has already proved non-normality distributed data to be widespread. Thus, we applied the non-parametric method, the Kruskal-Wallis test, and the independent-sample Kruskal-Wallis test to analyze the statistical output of the mutual information as in Figure 3.4. To summarize, the functional interaction between brain and muscle signals differed significantly across motor tasks with nonlinear mutual information.

5.5. Cortico-muscular Mutual Information Delay Time Across RM, Inten, MI, and OL Tasks

Functional interactions of brain and muscle signals do not occur simultaneously, but with a slight time lag to allow information to flow from brain to muscle and from muscle to brain. This lag time can be interpreted as a delay time for the information flow between two systems. Coherence results showed the highest coupling frequencies occurred within the range of beta and gamma bands during different motor task performances. Based on the highest number of coupling frequencies, we calculated the delay time values in the beta and gamma band ranges with power fluctuations time series using Morlet wavelet transformation.

In the experimental results as in Table 4.1, the delay time values in beta bands were greater than gamma bands in all tasks. The RM task and Inten tasks took a smaller amount of delay time than MI and OL tasks in both beta and gamma bands. All subjects had polarities of both positive and negative signs, indicating that information in the brain and muscles flows in both directions. In addition, some of the subjects showed no delay time. This will be the effect of the lack of mutual information between two signals and the fitted bin number in the calculation of the mutual information. Although we can infer the information direction flow, the main limitation of delay time mutual information is that specific directional information cannot be separated from common inputs of brain and muscle signals. Transfer entropy, Granger Causality, and DTF may be the extensions of mutual information.

In calculating the delay time, choosing a suitable time window is important to achieve reliable delay time results. The results revealed that low-functional interactions, such as MI and OL tasks, may require a longer time delay, whereas good functional interactions, such as RM and Inten tasks, may require a short delay time in both beta and gamma rhythms across four different motor tasks. Cortico-muscular mutual information flows from the brain to the peripheral muscles (efferent pathways) and from the peripheral muscles to the brain's motor cortex (afferent pathways) [74], [75]. However, in some cases, there might be a nullification of counteracting forces in the interaction of two systems with zero delay time. The findings of delay time calculation claim that information can flow with bi-directionality during functional interaction across tasks. The advantage of delay time mutual information is that it can infer the direction of information flow, whereas the phase-based mutual information method cannot.

5.6. Anatomical and Neurophysiological Principles of Brain-muscle Signals During Cortico-muscular Functional Interaction

The main causes of such a higher functional interaction are the excitation of motor neurons inside the spinal cord. This excitation of alpha motor neurons, many interneurons, and complex neural circuits causes an action potential to propagate along with the muscle fiber and finally generate the proper forces on individual muscles and muscle groups to enable adaptive movements and muscle contraction [36], [37], and [50]. In the motor system hierarchy, alpha and gamma motor neurons are included. The alpha motor neurons innervate extrafusal fibers, which can cause highly contacting fibers that supply the muscle with its power. The gamma motor neurons innervate the intrafusal fibers, which contract slightly [43]. The motor tasks of RM and Inten for hand grasping movement involve the innervation of alpha motor neurons, while the other two tasks, MI and OL, mainly involve the innervation of gamma motor neurons in this study. Very low cortico-muscular coherence in the MI task and OL task can be detected in some subjects as a consequence of this gamma neurons innervation inside the spinal cord. The high coupling of brain and muscle signals can lead to shorter delay times for signal transmission, and that can lead to descending oscillations. In addition, high-stimulated visuomotor instructions can influence the different parameters of motor control, including synchrony among motor units [72]. The appearance of afferent feedback's magnitude and gain are also highly tasked dependent and can influence the drive to motor neurons at low frequencies delta (0.5–3.5 Hz), theta (4–7.5 Hz), and as well as high-frequency beta (13–30 Hz) and gamma (31–50 Hz) bands.

5.7. Factors Affecting the Cortico-muscular Functional Interaction System

The factors affecting cortico-muscular functional systems include experimental designs, muscle contraction force, motor task types, and muscle fatigue. The band frequencies and age correlation are the major factors that can influence the brain-muscle functional system. In addition, the age difference of subjects relates to neuromuscular changes that can impair cortico-muscular communication. Healthy participants and stroke patients may affect the amount of cortico-muscular functional interaction system [30].

5.8. Cortico-muscular Functional Interaction in Real-world Applications

From the perspective of real-world situations, the results from this study are aimed at being able to be applied in the rehabilitation systems for training stroke patients. Based on the functional coupling level of the brain and muscles during the training period, we can decide the physiological and anatomical changes of patients [3], [13]. However, it needs to be examined with a more optimized experimental model. In addition to stroke rehabilitation systems, this research can be applied to the study of human motion and movements for behavioral science purposes, such as sports activities, root causes of fatigue, cortical-muscular functional network studies, treatment of dyskinesia and Alzheimer's disease, and recognition of human motion intention for movement intention detectors with various classifiers, etc. [15]. This study is an updated study of functional coupling with delay time in beta and gamma bands that can be helpful in judging the response time of brain–muscle signals in patients and in the construction of motion intention detectors [14], [15]. The results of the current study provide stronger arguments for both previous studies and current studies of cortical-muscular coupling in the neuroscience fields.

5.9. Consistent and Reliable Facts of Brain-muscle Signals Functional Interaction Based on the Study Results

To conclude, the findings and results reached the main objectives of the study. We discussed the main occurrences and findings that remained unclear in the previously published works. Finally, we could make a consistent deduction based on the reliable facts of our experimental results as follows:

- EMG rectification could lead to distort the frequency content of the signal and power spectral values.
- There was no occurrence of EMG signal during motor imagery.
- The functional interaction of brain and muscle signals in five bands (delta, theta, alpha, beta, and gamma) was significantly different in each RM, Inten, MI, and OL task.
- Functional interaction in the beta (13–30 Hz) and gamma (31–50 Hz) bands was statistically significantly different across four types of motor tasks.
- The mutual information delay time method can be used to calculate bi-directional information.
- Cortico-muscular mutual information flows from the brain to the peripheral muscles (efferent pathways) and from the peripheral muscles to the brain's motor cortex (afferent pathways). Thus, functional interaction of the brain and muscles can appear with bi-directionality.

- The four motor tasks: RM, Inten, MI, and OL were basically different and required different synchronization levels of neurons' firing and excitation inside the brain and muscle fibers to appear as a functional interaction.
- Finally, the amount of functional interaction differs across the task conditions of RM, Inten, MI, and OL with both linear and nonlinear methods.

CHAPTER 6
CONCLUSION AND FUTURE WORK

This chapter discusses the conclusion and future work of the study. The limitations of both linear and nonlinear correlation methods are also discussed in this section.

6.1. Conclusion

This study fulfilled the requirement of a functional interaction study with different motor task conditions that have been lacking in much of the existing literature. Depending on the motor tasks executed by the participants, the cortico-muscular functional interaction amount and delay time varied. The results proved that the cortical muscle coupling levels were high only in the beta and gamma bands, and not in the other three bands during the tasks. According to the results, the beta and gamma-band frequencies do not highly depend on force levels. The higher frequencies of CMC depend on all possible neurophysiological factors that lie inside the motor system. In addition, this research demonstrates that a high correlation and association between two signals occurred when the participants performed the motor tasks of RM and Inten. The results of the Inten task coupling level were almost the same as those of the RM task, and it was a peculiar and innovative result for almost all subjects. The new consideration of the MI and OL motor tasks together with the RM and Inten tasks confirmed that the unclear controversial issues were clear since low signal correlations occurred in those two tasks. No cortico-muscular interaction occurred in motor imagery conditions with non-rectified EMG. However, as an exception, some subjects showed a slightly higher correlation in the OL task. Thus, the new interesting evidence to study in the future will be whether the attention caused by the OL task will lead to the high coupling of brain and muscle signals or not, and how it benefits the coupling system. Finally, this study explored the signal propagation delay time with directionality inference. Information can flow with an exact amount of delay time from efferent to afferent (descending oscillations) and afferent to efferent pathways (ascending pathways) when coupling exists. The strength of this study is that it points out that the mutual information delay time values can be used to infer the direction of information flow between two signals rather than the traditional linear method. In conclusion, this study demonstrated that the functional interaction between motor cortex and muscle differed statistically across all delta, theta, alpha, beta, and gamma bands depending on the task. Our results complemented the existing studies in which functional coupling of brain and muscle signals and delay time changes were not performed across motor tasks.

6.2. Limitations and Future Work

In the calculation of the linear coherence method, there are some important notes and limitations. The output results of coherence depend on the windowing and selected filter design. Thus, suitable window and filter ranges must be chosen in order to achieve the correct results. Next, the analyzed data needs to be free of artifacts as much as possible. In some cases, EMG signals may become noise for EEG. Thus, we need to choose the suitable ICA components during preprocessing. For the calculation of nonlinear correlation, the selection of the bin number is also somewhat complex to obtain the optimized values for entropy. If the number of bins is too large but the number of data points is too small, it can lead to spurious information. In such a case, the amount of information we calculated may be wrong or may be biased. Mutual information calculation can be quite difficult if the data is non-stationary. Thus, data needs to be stationary for the calculation of the correlation between two signals. It is necessary to make sure that the data is roughly equally noisy across all conditions, electrode pairs, and subject groups. Using surface EMG (sEMG) signals may impact the calculation of signal correlation. Contamination of signals from the neighboring muscles can cause cross-talk in data recording. Thus, surface EMG (sEMG) has some limitations in comparison to using fine wire EMG electrodes [76].

According to our study, as there were occurrences of both beta and gamma-band coherence based on tasks across subjects, it may be necessary to investigate further experiments that can provide stronger evidence of these occurrences. In addition, this new experimental paradigm might lead to future investigations, such as a hypothesis regarding whether the gamma band in the OL task might relate to visual stimulation, visuomotor pathways, and attention or not. The number of subjects participating in this study was also small, and we needed to test with more participants of different ages, real stroke patients, control subjects, and control tasks to obtain an absence of bias. Different types of visual stimulation and feedback paradigms still need to be investigated in order to explore the effect of attention and visualization on information processing during functional coupling [25]. Additionally, finding out the effect of motor imagery with different experiments in kinesthetic and visual EEG-EMG coupling is also required. Functional coupling research involving various types of movement features and classifiers is critical for real-world movement detectors, prosthetic devices, and controllers [14], [15] and [63]. The construction of a brain-muscle functional network in terms of nonlinear and delay time methods is one of the problems to be explored in the future. To establish the directionality of information flow precisely, it still needs to be investigated with transfer entropy, DTF, Granger causality, and other directionality inference methods.

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BIBLIOGRAPHY

[1] Wikipedia contributors. Brain-body interaction — Wikipedia, the free encyclopedia, 2022. [Online; accessed 16-January-2022].

[2] Valery L Feigin, Bo Norrving, and George A Mensah. Global burden of stroke. Circulation research, 120(3):439–448, 2017.

[3] Richard Krauth, Johanna Schwertner, Susanne Vogt, Sabine Lindquist, Michael Sailer, Almut Sickert, Juliane Lamprecht, Serafeim Perdikis, Tiffany Corbet, José del R Millán, et al. Cortico-muscular coherence is reduced acutely post-stroke and increases bilaterally during motor recovery: a pi- lot study. Frontiers in neurology, 10:126, 2019.

[4] Yasunari Hashimoto, Junichi Ushiba, Akio Kimura, Meigen Liu, and Yutaka Tomita. Correlation between eeg-emg coherence during isometric contraction and its imaginary execution. Acta Neurobiol Exp (Wars), 70(1):76–85, 2010.

[5] Yuhang Xu, Verity M McClelland, Zoran Cvetković, and Kerry R Mills. Corticomuscular coherence with time lag with application to delay estimation. IEEE Transactions on Biomedical Engineering, 64(3):588–600, 2016.

[6] BA Conway, DM Halliday, SF Farmer, U Shahani, P Maas, AI Weir, and JR Rosenberg. Synchronization between motor cortex and spinal motoneuronal pool during the performance of a maintained motor task in man. The Journal of physiology, 489(3):917–924, 1995.

[7] JR Rosenberg, AM Amjad, P Breeze, DR Brillinger, and DM Halliday. The fourier approach to the identification of functional coupling between neuronal spike trains. Progress in biophysics and molecular biology, 53(1):1–31, 1989.

[8] Tatsuya Mima, Keiichiro Toma, Benjamin Koshy, and Mark Hallett. Coherence between cortical and muscular activities after subcortical stroke. Stroke, 32(11):2597–2601, 2001.

[9] Yang Zheng, Yu Peng, Guanghua Xu, Long Li, and Jue Wang. Using corticomuscular coherence to reflect function recovery of paretic upper limb after stroke: a case study. Frontiers in neurology, 8:728, 2018.

[10] James M Kilner, Stuart N Baker, Stephan Salenius, Riitta Hari, and Roger N Lemon. Human cortical muscle coherence is directly related to specific motor parameters. Journal of Neuroscience, 20(23):8838–8845, 2000.

[11] Shinji Ohara, Takashi Nagamine, Akio Ikeda, Takeharu Kunieda, Riki Matsumoto, Waro Taki, Nobuo Hashimoto, Koichi Baba, Tadahiro Mihara, Stephan Salenius, et al. Electrocorticogram–electromyogram coherence during isometric contraction of hand muscle in human. Clinical Neurophysiology, 111(11):2014–2024, 2000.

[12] K von Carlowitz-Ghori, Z Bayraktaroglu, G Waterstraat, G Curio, and Vadim V Nikulin. Voluntary control of corticomuscular coherence through neurofeedback: a proof-of-principle study in healthy subjects. Neuroscience, 290:243–254, 2015.

[13] Anirban Chowdhury, Haider Raza, Yogesh Kumar Meena, Ashish Dutta, and Girijesh Prasad. An eeg-emg correlation-based brain-computer interface for hand orthosis supported neuro-rehabilitation. Journal of neuroscience methods, 312:1–11, 2019.

[14] Xugang Xi, Cunbin Ma, Changmin Yuan, Seyed M Miran, Xian Hua, Yun Bo Zhao, and Zhizeng Luo. Enhanced eeg–emg coherence analysis based on hand movements. Biomedical Signal Processing and Control, 56:101727, 2020.

[15] Xugang Xi, Ziyang Sun, Xian Hua, Changmin Yuan, Yun-Bo Zhao, Seyed M Miran, Zhizeng Luo, and Zhong Lü. Construction and analysis of cortical–muscular functional network based on eeg-emg coherence using wavelet coherence. Neurocomputing, 438:248–258, 2021.

[16] Joseph T Gwin and Daniel P Ferris. Beta-and gamma-range human lower limb corticomuscular coherence. Frontiers in human neuroscience, 6:258, 2012.

[17] Pascal Grosse and Peter Brown. Corticomuscular and intermuscular frequency analysis. Supplements to Clinical neurophysiology, 57:570–576, 2004.

[18] Fabien Dal Maso, Marieke Longcamp, Sylvain Cremoux, and David Amarantini. Effect of training status on beta-range corticomuscular coherence in agonist vs. antagonist muscles during isometric knee contractions. Experimental brain research, 235(10):3023–3031, 2017.

[19] Saeid Mehrkanoon, Michael Breakspear, and Tjeerd W Boonstra. The reorganization of corticomuscular coherence during a transition between sensorimotor states. Neuroimage, 100:692–702, 2014.

[20] B Hellwig, S Häussler, M Lauk, B Guschlbauer, B Köster, R Kristeva-Feige, J Timmer, and CH Lücking. Tremor-correlated cortical activity detected by electroencephalography. Clinical neurophysiology, 111(5):806–809, 2000.

[21] Lars Timmermann, Joachim Gross, Martin Dirks, Jens Volkmann, Hans-Joachim Freund, and Alfons Schnitzler. The cerebral oscillatory network of parkinsonian resting tremor. Brain, 126(1):199–212, 2002.

[22] Jan-Mathijs Schoffelen, Robert Oostenveld, and Pascal Fries. Neuronal coherence as a mechanism of effective corticospinal interaction. Science, 308(5718):111–113, 2005.

[23] Wolfgang Omlor, Luis Patino, Marie-Claude Hepp-Reymond, and Rumyana Kristeva. Gamma-range corticomuscular coherence during dynamic force output. Neuroimage, 34(3):1191–1198, 2007.

[24] Tatsuya Mima, Jürg Steger, Andrew E Schulman, Christian Gerloff, and Mark Hallett. Electroencephalographic measurement of motor cortex control of muscle activity in humans. Clinical neurophysiology, 111(2):326–337, 2000.

[25] Rumyana Kristeva-Feige, Christoph Fritsch, Jens Timmer, and Carl-Hermann Lücking. Effects of attention and precision of exerted force on beta range eeg-emg synchronization during a maintained motor contraction task. Clinical Neurophysiology, 113(1):124–131, 2002.

[26] Tianchen Zhai, Anshuang Fu, Rui Xu, Shuang Qiu, Hongzhi Qi, Peng Zhou, Lixin Zhang, Baikun Wan, and Dong Ming. Cortico-muscular coherence analysis under voluntary, stimulated and imaginary neuromuscular activities. Biomedical Engineering/Biomedizinische Technik, 58(SI-1-Track-A), 2013.

[27] Rui Xu, Feng He, Shuang Qiu, Long Chen, Shuang Liu, Xin Zhao, Hongzhi Qi, Lixin Zhang, Baikun Wan, and Dong Ming. Corticomuscular coherence based on wavelet transform during imagination, execution and stimulation tasks. Journal of Medical Imaging and Health Informatics, 5(2):335–341, 2015.

[28] Byeongnam Kim, Laehyun Kim, Yun-Hee Kim, and Sun K Yoo. Cross-association analysis of eeg and emg signals according to movement intention state. Cognitive Systems Research, 44:1–9, 2017.

[29] Verity M McClelland, Zoran Cvetkovic, and Kerry R Mills. Rectification of the emg is an unnecessary and inappropriate step in the calculation of corticomuscular coherence. Journal of neuroscience methods, 205(1):190–201, 2012.

[30] Jinbiao Liu, Yixuan Sheng, and Honghai Liu. Corticomuscular coherence and its applications: a review. Frontiers in human neuroscience, 13:100, 2019.

[31] LJ Myers, M Lowery, M O'malley, CL Vaughan, C Heneghan, A St Clair Gibson, YXR Harley, and R Sreenivasan. Rectification and non-linear pre-processing of emg signals for cortico-muscular analysis. Journal of neuro-science methods, 124(2):157–165, 2003.

[32] Jaeseung Jeong, John C Gore, and Bradley S Peterson. Mutual information analysis of the eeg in patients with alzheimer's disease. Clinical neurophysiology, 112(5):827–835, 2001.

[33] Thomas M Cover and Joy A Thomas. Elements of information theory second edition solutions to problems. Internet Access, pages 19–20, 2006.

[34] Sun Hee Na, Seung-Hyun Jin, Soo Yong Kim, and Byung-Joo Ham. Eeg in schizophrenic patients: mutual information analysis. Clinical Neurophysiology, 113(12):1954–1960, 2002.

[35] Seung-Hyun Jin, Peter Lin, and Mark Hallett. Linear and nonlinear information flow based on time-delayed mutual information method and its application to cortico-muscular interaction. Clinical Neurophysiology, 121(3):392–401, 2010.

[36] Stuart N Baker. Oscillatory interactions between sensorimotor cortex and the periphery. Current opinion in neurobiology, 17(6):649–655, 2007.

[37] Mike X Cohen. Analyzing neural time series data: theory and practice. MIT press, 2014.

[38] JM Nichols, M Seaver, and ST Trickey. A method for detecting damage-induced nonlinearities in structures using information theory. Journal of Sound and Vibration, 297(1-2):1–16, 2006.

[39] RB Govindan, J Raethjen, F Kopper, JC Claussen, and G Deuschl. Estimation of time delay by coherence analysis. Physica A: Statistical Mechanics and its Applications, 350(2-4):277–295, 2005.

[40] Thomas Müller, Michael Lauk, Matthias Reinhard, Andreas Hetzel, Carl H Lücking, and Jens Timmer. Estimation of delay times in biological systems. Annals of biomedical engineering, 31(11):1423–1439, 2003.

[41] C Nicholas Riddle and Stuart N Baker. Manipulation of peripheral neural feedback loops alters human corticomuscular coherence. The Journal of physiology, 566(2):625–639, 2005.

[42] Andreas Wilmer, Marc de Lussanet, and Markus Lappe. Time-delayed mutual information of the phase as a measure of functional connectivity. 2012.

[43] JH Byrne and L Gray. Neuroscience online: An electronic textbook for the neurosciences http://nba. uth. tmc. edu/neuroscience. Department of Neurobiology and Anatomy—The University of Texas Medical School at Houston (UTHealth) r, 2012, 1997.

[44] P Grosse, R Guerrini, L Parmeggiani, P Bonanni, A Pogosyan, and P Brown. Abnormal corticomuscular and intermuscular coupling in high-frequency rhythmic myoclonus. Brain, 126(2):326–342, 2003.

[45] Tatsuya Mima and Mark Hallett. Corticomuscular coherence: a review. Journal of clinical neurophysiology, 16(6):501, 1999.

[46] Yin Fang, Janis J Daly, Jiayang Sun, Ken Hvorat, Eric Fredrickson, Svetlana Pundik, Vinod Sahgal, and Guang H Yue. Functional corticomuscular connection during reaching is weakened following stroke. Clinical neurophysiology, 120(5):994–1002, 2009.

[47] SN Baker, Etienne Olivier, and RN Lemon. Coherent oscillations in monkey motor cortex and hand muscle emg show task-dependent modulation. The Journal of physiology, 501(1):225–241, 1997.

[48] Steven C Cramer, Gereon Nelles, Randall R Benson, Jill D Kaplan, Robert A Parker, Ken K Kwong, David N Kennedy, Seth P Finklestein, and Bruce R Rosen. A functional mri study of subjects recovered from hemiparetic stroke. Stroke, 28(12):2518–2527, 1997.

[49] Fay B Horak. Assumptions underlying motor control for neurologic rehabilitation. In Contemporary management of motor control problems: Proceedings of the II STEP conference, pages 11–28. Foundation for Physical Therapy Alexandria, Va, 1991.

[50] Claire L Witham, C Nicholas Riddle, Mark R Baker, and Stuart N Baker. Contributions of descending and ascending pathways to corticomuscular coherence in humans. The Journal of physiology, 589(15):3789–3800, 2011.

[51] Christopher M Laine and Francisco J Valero-Cuevas. Intermuscular coherence reflects functional coordination. Journal of neurophysiology, 118(3):1775– 1783, 2017.

[52] Gert Pfurtscheller and FH Lopes Da Silva. Event-related eeg/meg synchronization and desynchronization: basic principles. Clinical neurophysiology, 110(11):1842–1857, 1999.

[53] Stephan Salenius, Riitta Salmelin, Christa Neuper, Gert Pfurtscheller, and Riitta Hari. Human cortical 40 hz rhythm is closely related to emg rhythmic- ity. Neuroscience letters, 213(2):75–78, 1996.

[54] Pascal Fries. A mechanism for cognitive dynamics: neuronal communication through neuronal coherence. Trends in cognitive sciences, 9(10):474–480, 2005.

[55] Tatsuya Mima, Nicole Simpkins, Tomi Oluwatimilehin, and Mark Hallett. Force level modulates human cortical oscillatory activities. Neuroscience letters, 275(2):77–80, 1999.

[56] JV Jacobs, G Wu, and KM Kelly. Evidence for beta cortico-muscular coherence during human standing balance: effects of stance width, vision, and support surface. Neuroscience, 298:1–11, 2015.

[57] Wikipedia contributors. A mathematical theory of communicatio— Wikipedia, the free encyclopedia. https://en.wikipedia.org/w/ index.php?title=A_Mathematical_Theory_of_Communication&oldid= 1053554027, 2021. [Online; accessed 14-December-2021].

[58] Wikipedia contributors. Mutual information—Wikipedia, the free encyclopedia, 2021. [Online; accessed 21-October-2021].

[59] Andrew M Fraser and Harry L Swinney. Independent coordinates for strange attractors from mutual information. Physical review A, 33(2):1134, 1986.

[60] Tatsuya Mima, Takahiro Matsuoka, and Mark Hallett. Information flow from the sensorimotor cortex to muscle in humans. Clinical Neurophysiol- ogy, 112(1):122–126, 2001.

[61] David Popivanov and Juliana Dushanova. Non-linear eeg dynamic changes and their probable relation to voluntary movement organization. Neuroreport, 10(7):1397–1401, 1999.

[62] F Panzica, L Canafoglia, S Franceschetti, S Binelli, C Ciano, E Visani, and G Avanzini. Movement-activated myoclonus in genetically defined progressive myoclonic epilepsies: Eeg–emg relationship estimated using autoregressive models. Clinical neurophysiology, 114(6):1041–1052, 2003.

[63] Firas Sabar Miften, Mohammed Diykh, Shahab Abdulla, Siuly Siuly, Jonathan H Green, and Ravinesh C Deo. A new framework for classification of multi-category hand grasps using emg signals. Artificial Intelligence in Medicine, 112:102005, 2021.

[64] Robert Hodes, MG Larrabee, and W German. The human electromyogram in response to nerve stimulation and the conduction velocity of motor axons: studies on normal and on injured peripheral nerves. Archives of Neurology & Psychiatry, 60(4):340–365, 1948.

[65] Wikipedia contributors. Intention — Wikipedia, the free encyclopedia. https://en.wikipedia.org/w/index.php?title=Intention&oldid= 1060995443, 2021. [Online; accessed 4-January-2022].

[66] Janet W Astington. The child's discovery of the mind, volume 31. Harvard University Press, 1993.

[67] Aymeric Guillot, Florent Lebon, and Christian Collet. Electromyographic activity during motor imagery. The neurophysiological foundations of mental and motor imagery, pages 83–93, 2010.

[68] Yu Jin Yang, Eun Jeong Jeon, June Sic Kim, and Chun Kee Chung. Characterization of kinesthetic motor imagery compared with visual motor imageries. Scientific Reports, 11(1):1–11, 2021.

[69] Wikipedia contributors. Motor imagery — Wikipedia, the free encyclopedia. https://en.wikipedia.org/w/index.php?title=Motor_imagery& oldid=1058782958, 2021. [Online; accessed 4-January-2022].

[70] Alexander M Dreyer and Jochem W Rieger. High-gamma mirror activity patterns in the human brain during reach-to-grasp movement observation, retention, and execution—an meg study. Plos one, 16(12):e0260304, 2021.

[71] Giacomo Rizzolatti, Leonardo Fogassi, and Vittorio Gallese. Neurophysiological mechanisms underlying the understanding and imitation of action. Nature reviews neuroscience, 2(9):661–670, 2001.

[72] CM Laine, ŞU Yavuz, and D Farina. Task-related changes in sensorimotor integration influence the common synaptic input to motor neurones. Acta Physiologica, 211(1):229–239, 2014.

[73] L Leocani, C Toro, Paolo Manganotti, P Zhuang, and M Hallett. Event-related coherence and event-related desynchronization/synchronization in the 10 hz and

20 hz eeg during self-paced movements. Electroencephalography and Clinical Neurophysiology/Evoked Potentials Section, 104(3):199–206, 1997.

[74] Robert Neal Stiles and JE Randall. Mechanical factors in human tremor frequency. Journal of applied physiology, 23(3):324–330, 1967.

[75] JH McAuley, JC Rothwell, and CD Marsden. Frequency peaks of tremor, muscle vibration and electromyographic activity at 10 hz, 20 hz and 40 hz during human finger muscle contraction may reflect rhythmicities of central neural firing. Experimental brain research, 114(3):525–541, 1997.

[76] Giovanni Tagliabue, Michael Ji, Jenny V Suneby Jagers, WooSurng Lee, Devin Dean, Dan J Zuege, Eric R Wilde, and Paul A Easton. Limitations of surface emg estimate of parasternal intercostal to infer neural respiratory drive. Respiratory Physiology & Neurobiology, 285:103572, 2021.

[APPENDIX A]

Table A1. Comparison Table for Different Methods of State-of-the-Art in Functional Coupling of EEG and EMG.

No.	Authors	Investigated Area	Method	Strengths and Weakness
1	Yasunari, H., et al., 2010	EEG-EMG coherence during Isometric contraction and its imagery.	Power spectrum. EEG—Cz, FCz, C1, C2, CPz. Rectified EMG—right TA muscle. n = 13	Coherence occurred in motor imagery conditions. Uses linear correlation analysis. Remains controversial issues of EMG during motor imagery.
2	James, M., et al., 2000	Task-dependent modulation in coherence between motor cortex and hand muscles.	Amplitude and phase correlation method. MEG—over the left sensorimotor cortex. EMG—1DI, AbPB, FDS, EDC. n = 13	Tests task-dependent modulation of coherence. Coherence was much lower level during isometric grip of the fixed levers compared to grasp under complaint conditions. Remains to investigate with different motor tasks.
3	Shinji, O., et al., 2000	ECoG-EMG coherence during isometric contraction in hand muscle.	Auto spectra and frequency domain analysis method. Rectified EMG. ECoG—mesial and lateral surfaces of frontoparietal cortices. EMG—ECR muscle. n = 8 (patients with epilepsy)	Coherence occurred only in the 15 ± 3 Hz beta bands. Time lags were calculated with a cross-correlogram method. Time lags range from 10 ms to 22 ms. Lack of directionality inference and nonlinear correlation. Remains to find out the coherence in other bands.
4	Wolfgang, O., et al., 2006	Gamma range Cortico-muscular coherence during dynamic performance in visuo motor tasks.	Cortico motor spectral power method. EEG—52 electrodes. Rectified EMG—flexor digitorum superficialis muscle. n = 8	Beta band coherences occur during static force. Gamma band coherence occurs during dynamic force. Uses only linear correlation method. No include delay time estimation. Remains task-dependent CMC investigation.
5	Seung-Hyun, P., et al., 2010	Linear and nonlinear information flow with time delay mutual information.	Used surrogate data sets and experimental data sets. Investigated CM interaction during a right wrist extension tasks. EEG—29 electrodes. EMG—Extensor digitorum communis. n = 7	Well-distinguished linear and nonlinear information flow. Requires relatively long stationary time series data for the analysis. Needs to improve directionality inferences with stationarity.
6	Andreas, W., et al., 2012	Time delay mutual information of the phase as a measure of functional connectivity.	Phase lag index and weighted phase lag index methods. Making numerical implementation. Synthetic data sets by a mutual amplitude coupled network of Rossler oscillatior.	Limitations and assumptions existed as synthetic data sets were applied. De-correlation step does not respect a background synchronicity. Uses a data-driven approach.

[APPENDIX B] Research Informed Consent Form

九州大学

Consent to Participate in a Research Study
Kyushu Universiy ● Neuroinformatic and Neuroimaging

Title of Study : A Study of Cortico-Muscular Functional Interaction and Its Neurophysiological Principles Based on Motor Task Performance

Researcher:

Name: **Nyi Nyi Tun, Fumiya Sanuki** **Phone:** **080-9392-9429**

Introduction

The brian and muscle acts synchronically at the time of motor task performance to reach the movement goal. In order to understand the basic principles of brain and muscle function in neuroscience or future brain computer interface (BCI) technology, it is basically important to understand the cortico-muscular functional interaction and its neurophysiological principles.

Functional interaction between brain and muscle signal is referred to as functional coupling. The amount of interaction between two signals greatly depends on the motor task performance. In this study, we designed the experimental paradigm with four types of motor tasks such as real hand grasping movement (RM), movement intention (Inten), motor imagery (MI) and only looking at virtual hand in three dimensional head mounted display (OL).

Purpose of Study

- To investigate the functional interaction of brain-muscle signals and its coupling delay time based on four different motor tasks
- To explore the anatomical and neurophysiological principles of brain and muscles function that can lead to cortico-muscular interaction

Description of the Study Procedures

- If you agree to be in this study, you will be asked to do the following things:
    1. Put the 10 EEG electrodes Fp1, Fp2, Cz, FC3, C3, CP3, FC4, C4, CP4, and Pz on your head
    2. Recording three bipolar EMG electrodes on radialis muscle, flexor carpi ulnaris muscle and flexor carpi radialis muscle
    3. Performing the four motor tasks, RM, Inten, MI and OL tasks. There was a 2 min rest period as a baseline. Then, there were 8 s of rest, 2 s of being ready and 5 s of the task in 1 trial. We had designed a total of 40 trials in each motor task. A fixation cross was shown on the virtual palm during rest, which disappeared during the 2 s ready stage. The virtual hand grasping appeared on the monitor in three dimensional head-mounted display (3D-HMD) during 5 s task. The grasping

movement was performed 2 times in 1 trial. The time to break between each motor task was 5 min, then RM, Inten, MI and OL tasks were performed respectively.

Risks/Discomforts of Being in this Study

- There are no reasonable foreseeable (or expected) risks.

Confidentiality

- The records of this study will be kept strictly confidential. Research records will be kept in a locked file, and all electronic information will be coded and secured using a password protected file. We will not include any information in any report we may publish that would make it possible to identify you.

Right to Refuse or Withdraw

- The decision to participate in this study is entirely up to you. You may refuse to take part in the study ***at any time*** without affecting your relationship with the researchers of this study or Kyushu University. Your decision will not result in any loss or benefits to which you are otherwise entitled. You have the right not to answer any single question, as well as to withdraw completely from the interview at any point during the process; additionally, you have the right to request that the interviewer not use any of your interview material.

Right to Ask Questions and Report Concerns

- You have the right to ask questions about this research study and to have those questions answered by me before, during or after the research. If you have any further questions about the study, at any time feel free to contact me, Nyi Nyi Tun at tun.nyi.721@s.kyushu-u.ac.jp or by telephone at 080-9392-9429. If you like, a summary of the results of the study will be sent to you.
- If you have any problems or concerns that occur as a result of your participation, you can report them to Kyushu University.

Consent

- Your signature below indicates that you have decided to volunteer as a research participant for this study, and that you have read and understood the information provided above. You will be given a signed and dated copy of this form to keep, along with any other printed materials deemed necessary by the study researchers.

Subject's Name:

Subject's Signature: Date :

Researcher’s Signature : Date:

Questionnaire for Demographic Data of subject

Participant No. :

Group :

Nationality:

Student ID :

Email:

Age:

Gender : Female Male

Height (cm): Weight (lb):

Hand preference: Right Left

Do you have any physical disorder? No Yes:

(If you answered yes, please describe your disorder)

I understand that my identity will not be linked my data, and that all information I provide will remain confidential.

……………………………..
(Participant's signature)