

Neurobehavioral Strategies of Skill Acquisition in Left and Right Hand Dominant Individuals
by
Jessica Lynn McDonnell
August 2020

Director of Dissertation: J.C. Mizelle
Major Department: Kinesiology

The brain consists of vast networks of connected pathways communicating through synchronized electrochemical activity propagated along fiber tracts. The current understanding is that the brain has a modular organization where regions of specialized processes are dynamically coupled through long-range projections of dense axonal networks connecting spatially distinct regions enabling signal transfer necessary for all complex thought and behavior, including regulation of movement. The central objective of the dissertation was to understand how sensorimotor information is integrated, allowing for adaptable motor behavior and skill acquisition in the left- and right-hand dominant populations. To this end participants, of both left- and right-hand dominance, repeatedly completed a visually guided, force matching task while neurobiological and neurobehavioral outcome measurements were continuously recorded via EEG and EMG. Functional connectivity and graph theoretical measurements were derived from EEG. Cortico-cortical coherence patterns were used to infer neurostrategic discrepancies employed in the execution of a motor task for each population. EEG activity was also correlated with neuromuscular activity from EMG to calculate cortico-muscular connectivity. Neurological patterns and corresponding behavioral changes were used to express how hand dominance influenced the developing motor plan, thereby increasing understanding of the sensorimotor integration process.

The cumulative findings indicated fundamental differences in how left- and right-hand dominant populations interact with the world. The right-hand dominant group was found to rely on visual information to inform motor behavior where the left-hand dominant group used visual information to update motor behavior. The left-hand group was found to have a more versatile motor plan, adaptable to both dominant, nondominant, and bimanual tasks. Compared to the right-hand group it might be said that they were more successful in encoding the task, however behaviorally they performed the same. The implications of the findings are relevant to both clinical and performance applications providing insight as to potential alternative methods of information integration. The inclusion of the left-hand dominant population in the growing conceptualization of the brain will generate a more complete, stable, and accurate understanding of our complex biology.

Neurobehavioral Strategies of Skill Acquisition in Left and Right Hand Dominant Individuals

A Dissertation

Presented To the Faculty of the Department of Kinesiology

East Carolina University

In Partial Fulfillment of the Requirements for the Degree

Doctor of Philosophy in Bioenergetics and Exercise Science

by

Jessica Lynn McDonnell

August 2020

© Jessica Lynn McDonnell, 2020

NEUROBEHAVIORAL STRATEGIES OF SKILL ACQUISITION
IN LEFT- AND RIGHT- HAND DOMINANT INDIVIDUALS

by

Jessica Lynn McDonnell

APPROVED BY:
DIRECTOR OF
DISSERTATION:

_____ J.C. Mizelle, PhD

COMMITTEE MEMBER:

Nicholas Murray, PhD

COMMITTEE MEMBER:

Stefan Clemens, PhD

COMMITTEE MEMBER:

Erik Everhart, PhD

COMMITTEE MEMBER:

Sunghan Kim, PhD

DEPARTMENT
CHAIRPERSON

Joonkoo Yun, PhD

DEAN OF THE
GRADUATE SCHOOL:

Paul Gemperline, PhD

ACKNOWLEDGMENTS

I extend the most sincere gratitude and appreciation to the McDV for the tremendous advantages they have given me in life. Without you all, I would be a fraction of the person I am today. I would like to acknowledge my grandmothers Elinor and Peggy who have both separately and differently served as invaluable role models. From them I learned what I meant properly be a lady. Long live to matriarchy. To my ride or die Hobie Cat, thanks for keeping me company and reminding me to take breaks. *Semper Et Ubique*

LIST OF TABLES	vii
LIST OF FIGURES	viii
LIST OF SYMBOLS AND ABBREVIATIONS	ix
CHAPTER 1. Introduction.....	1
Neuroanatomy.....	3
Occipital Lobe.....	4
Temporal Lobe.....	4
Parietal Lobe	5
Frontal Lobe.....	5
Hemispheric Lateralization.....	7
Purpose	10
Experimental Paradigm.....	10
Electroencephalography.....	12
Signal Oscillation Properties.....	13
Cortico-Cortical Connectivity.....	16
Theta Band Frequency	17
Alpha Band Frequency	18
Mu Band Frequency.....	19
Beta Band Frequency	19
Electromyography.....	21
Cortico-Muscular Connectivity	22
Behavior	23
Quantifying & Interpreting	23
Conclusion	25
CHAPTER 2. Aim One: Neurobiological Indicators of Hand Dominance	26
Introduction	26
Methodology	31
Subjects & Experimental Design.....	31
Data Analysis	33
Statistics	35
Results	36
Theta [4-7 Hz].....	37
Mu [10-12 Hz]	39
Beta [12-30 Hz].....	41
Discussion	43
LH prove to be more adept at using non-dominant hand and skill encoding	44
LH & RH use different strategies to execute the visually guided motor task	45
Hand dominance influences sensorimotor integration strategies	47
Differentially adaptable motor programs are detectable on a 10-trial time scale	48
Conclusion	49
CHAPTER 3. Aim Two: Neurobehavioral Indicators of Hand Dominance	50
Introduction	50
Methodology	54
Subjects & Experimental Design.....	54
Data Analysis	56
Statistics	58

Results	59
Cortico-Cortical Connectivity	60
Theta [4-7 Hz].....	60
Mu [10-12 Hz]	61
Beta [12-30 Hz].....	62
Cortico-Muscular Connectivity	63
Initial Beta [12-30 Hz].....	63
Final Beta [12-30 Hz]	65
Behavior.....	65
Discussion	66
Cortico-Cortical Connectivity	67
Cortico-Muscular Connectivity	69
Conclusion	72
CHAPTER 4. Combined Discussion	74
Populations rely on visual information to a different extent	76
Theta band highlights degree of skill transfer and dual oscillation function	78
Sensorimotor integration reveal hand dominance influence.....	80
Hand dominance reveals uncontrolled manifold properties	81
Concluding Conclusion.....	82
Limitations and Future Work	83
REFERENCES	85
APPENDIX. Aggregate Figures	103

LIST OF TABLES

1. Table 2.1: Handedness score of participants	32
2. Table 2.2: Theta band unimanual graph network metrics	39
3. Table 2.3: Mu band unimanual graph network metrics	41
4. Table 2.4: Beta band unimanual graph network metrics.....	43
5. Table 3.1: Handedness score of participants	55
6. Table 3.2: Theta band bimanual graph network metrics	61
7. Table 3.3: Mu band bimanual graph network metrics	62
8. Table 3.4: Beta band bimanual graph network metrics.	63
9. Table 3.5: Average group by condition error values	66
10. Table A.1: Theta band graph network metrics across conditions	104
11. Table A.2: Mu band graph network metrics across conditions.....	106
12. Table A.3: Beta band graph network metrics across conditions	108

LIST OF FIGURES

1. Figure 2.1: Target force trajectory	32
2. Figure 2.2: Theta band unimanual cortico-cortical coherence	39
3. Figure 2.3: Mu band unimanual cortico-cortical coherence	41
4. Figure 2.4: Beta band unimanual cortico-cortical coherence	43
5. Figure 3.1: Target force trajectory	55
6. Figure 3.2: Theta band bimanual cortico-cortical coherence	61
7. Figure 3.3: Mu band bimanual cortico-cortical coherence	62
8. Figure 3.4: Beta band bimanual cortico-cortical coherence	63
9. Figure 3.5: Early trials beta band bimanual cortico-muscular coherence	64
10. Figure 3.6: Late trials beta band bimanual cortico-muscular coherence	64
11. Figure 3.7: Left- and right- hand dominant error early and late trials	66
12. Figure 3.8: Left- and right- hand dominant error as made by each individual hand	66
13. Figure A.1: Left hand group theta cortico-cortical coherence across conditions	103
14. Figure A.2: Right hand group theta cortico-cortical coherence across conditions ...	103
15. Figure A.3: Left hand group mu cortico-cortical coherence across conditions	105
16. Figure A.4: Right hand group mu cortico-cortical coherence across conditions	5
17. Figure A.5: Left hand group beta cortico-cortical coherence across conditions	7
18. Figure A.6: Right hand group beta cortico-cortical coherence across conditions	107

LIST OF SYMBOLS OR ABBREVIATIONS

CNS	central nervous system.....	3
PNS	peripheral nervous system.....	3
AIP	anterior intraparietal region.....	5
M1	primary motor cortex	5
PMC	premotor cortex.....	6
SMA	supplementary motor area.....	6
EEG	electroencephalogram	10
EMG	electromyography	11
ERP	event related potential.....	12
ERD	event related desynchronization.....	15
ERS	event related synchronization	15
MUAPs	motor unit action potentials synchronization.....	21
CMC	cortico-muscular coherence	22
LH	left-hand dominant.....	27
RH	right- hand dominant.....	27
Ω	impedance	33
rCOH	real coherence	34
iCOH	imaginary coherence	34
ciCOH	corrected imaginary coherence	34
LHd	left hand individual using dominant hand.....	36
LHn	left hand individual using non-dominant hand	36
RHd	right hand individual using dominant hand	36
RHn	right hand individual using non-dominant	36
br	brachioradialis.....	56
fcu	flexor carpi ulnaris	56
d ^{BR}	dominant brachioradialis.....	57
n ^{BR}	non-dominant brachioradialis	57
d ^{FCU}	dominant flexor carpi ulnaris.....	57
n ^{FCU}	non-dominant flexor carpi ulnaris.....	57
msCOH	magnitude squared coherence.....	57

CHAPTER 1. Introduction

The human brain is composed of structurally segregated, functionally distinct regions connected by dense axonal networks (Hagmann et al 2008). These networks form the communication pathways necessary for the signal transfer responsible for facilitating all complex thought and behavior, including the regulation of movement. The functional roles of regions distributed throughout the brain are defined by their inputs and outputs (Sporns et al 2004). Complex circuitry connecting brain regions is a critically important aspect of brain function, enabling the coordination of distinctly different brain areas. The developmental and operational cost of such circuitry is extensive requiring the use of space, materials, and energy. Many aspects of the organization of the brain networks can be explained to be a function of optimizing resource cost, but not all. It is generally hypothesized that neural organization is shaped by a compromise between resource economics, minimizing cost, while permitting the spontaneous emergence of adaptively valuable patterns of communication between multiple neuronal populations (Bullmore & Sporns 2012). The ongoing internally negotiated balance between resource expenditure and network function is variable, with changes occurring on a short and long time scales that span from milliseconds to decades.

Brain functions support adaptable and complex movements, with movement being the predominant way of interacting with the world. The expression or suppression of movement is weighted by cognitive and sensory processes that can be mathematically simplified and represented as a Bayesian inference, or an outcome weighted by two sources of information: the current sensory state and memories of previous sensory states. Think of a weather forecast; based on records of prior conditions an estimate of what the current weather conditions will produce can be calculated. Theoretical neuroscientists often include this Bayesian decision theory in their

conceptualization of an internal model that governs motor behavior; and have shown these mechanisms to be critical for learning new movements and skills (Miall & Wolpert 1996, Wolpert 1997, Wolpert & Ghahramani 2000, Wolpert et al 1995). When intention exists (the origin of consciousness and formation of intention is beyond the scope of this dissertation), past and present sensory inputs are considered and a motor command is dictated. The motor command results in a sequela of electrochemical signals, with the consequence of the summation of the signals being movement, subjected to physics of the environment. We have all experienced a miss calculation, for instance if the weight of a cup was overestimated when lifting a glass of water to sip, some of the water can slosh out and spill, we do not proceed to then spill the entirety of the contents. Sensory feedback informing the state of the body and environment is provided continuously allowing for the motor commands to evolve. Memory of the movement is encoded within the neurons based on the success of the outcome and continued use of the movement pattern.

The study of this, motor control, is the study of the processes by which the brain coordinates the muscles and limbs involved in the execution of a motor skill. It requires cooperative interaction between the central nervous and musculoskeletal systems. Movement, achieved via muscle recruitment, is selectively determined based on various sensory inputs and assigned weights. Information is transmitted with a series of signals, electrochemical impulses propagated along networks that translate intent into action. The continuous integration of sensory information, from the environment and the current state of the body, informs motor commands and their subsequent actions. Ongoing behavioral adjustments, queued by sensory information and subsequent neural processing and organization, reveal the complex nature of the underlying dynamic interactions. The process of sensorimotor integration fundamentally acts to translates

neural signatures into motor commands and is evident in behavioral changes, termed voluntary movements.

Voluntary movements can be described in three phases: planning, execution, and recovery. Each phase exhibits measurable neurological signatures indicative of sensorimotor integration. The adaptation that occurs with repetition embodies the integral process of learning. Reliably successful execution, marking the acquisition of a motor skill, is facilitated by the rapidly changing, widely distributed neural activation patterns involving numerous cortical and subcortical regions activated in different combinations and contexts. Level of proficiency exists on a spectrum with obvious, observable differences between a novice as compared to an expert. Skill acquisition can be represented with neurological and behavioral measures. Dynamic patterns of communication within the brain (cortico-cortical) and between the brain and the body (cortico-muscular) are influenced by experience, drive adaptation, and shape the neural architecture.

NEUROANATOMY

The execution of any voluntary action relies on more than just the primary motor cortex to transmit a signal via the spinal cord to motor neurons enabling muscle activation. Action requires intention and planning which occurs in the parietal lobe and frontal brain areas including premotor and supplementary motor cortices (Horn & Leigh 2011). Higher and lower order processes converge for continuous communication between the central nervous system (CNS) and peripheral nervous system (PNS). This section will discuss major brain areas in the context of voluntary motor control, specifically related to a visually guided dynamic grip force matching task.

OCCIPITAL LOBE

The occipital lobe is specialized for visual processing. For sighted individuals, the information supplied by the retina initiates interactions among multiple subdivisions of the brain resulting in conscious perception of the environment and enabling voluntary movement. Stimulation of the primary visual pathway from the retina to the dorsal lateral geniculate nucleus in the thalamus and on to the primary visual cortex prompts parallel processing that extends beyond the primary visual cortex. Dense projections can be broadly organized into two dichotomous pathways (Goodale & Milner 1992, Haxby et al 1991). The ventral pathway, extending into the temporal lobe, is widely found to transmit information regarding object recognition. Neurons involved in this pathway preferentially activate to signal object shape, color, and texture with higher order processing related to more conceptual properties of objects occurring along the anterior portion of the pathway. The dorsal stream extending into the parietal lobes is active in the decoding of spatial properties, such as positional relations, motion direction, and speed of movement. While visual input is initially segregated for processing, subsequent outputs consecutively converge to integrate derived information.

TEMPORAL LOBE

Within the temporal lobe, the recognition and identification of highly processed sensory information is evaluated for interpretation. The ventral pathway traverses the temporal lobe and terminates at the anterior portion where abstract properties, such as face and object recognition are decoded. This pathway, stemming from the occipital lobe, underlies conscious visual awareness, perceiving visual stimuli (Tresilian 2012). Temporal lobe neurons are highly selective for representing the visual input of a particular action (Keysers et al 2003, Kohler et al 2002). Additionally, language centers are localized along the superior border of the posterior temporal lobe, with a predominantly left-

hemisphere lateralization (Davidson & Hugdahl 1996). The temporal lobe serves a general function of high level information processing and integration (Smallwood et al 2016). It also contains neurons involved in tasks involving grasping and manipulating an object, possessing dense projections to the hand motor areas (Murata et al 1997, Rizzolatti & Arbib 1998, Rizzolatti et al 1998).

PARIETAL LOBE

The parietal cortex has proven to be integral to focusing attention and awareness of the body and to pertinent sensory stimuli. The posterior parietal cortex is comprised of the superior lobule and the angular and supramarginal gyri making up the inferior parietal lobule. Both of which are involved in the formation of motor plans (Johnson et al 2002). Here, a particular ability to direct and control hand, eye, head, and arm movements comes to exist (Rizzolatti et al 1997a, Rizzolatti et al 1997b). From this, planning, monitoring and controlling limb movement, notably including reaching and touching, as well as mimicking or imagining, is facilitated (Grafton et al 1997, Murata et al 1997, Rizzolatti et al 1997a, Rizzolatti et al 1997b, Sheliga et al 1997). The anterior intraparietal region (AIP) is involved in hand manipulation and grasping movements containing neurons related to the processing of visual input and motion recognition in addition to the critical function of processing motor commands (Andersen et al 1997, Rozzi & Coudé 2015, Sakata et al 1995). It has been proposed that within the parietal cortex, information is converged to disseminate what an object is, and how it is to be used.

FRONTAL LOBE

The frontal lobe contains circuitry responsible for the abstract formation of complex behaviors, matching such behaviors to the demands of a situation. Anterior to the parietal lobes, located along the precentral gyrus, exists the primary motor cortex (M1). Here, the posterior aspect of the frontal lobe contains highly interconnected upper motor neurons receiving regular

input from the basal ganglia, cerebellum, and parietal lobe. The pyramidal tract, a large and direct pathway, extends to the lower motor neurons of the brainstem and spinal cord. Just anterior to M1 is the premotor cortex (PMC), responsible for selecting a strategy to execute the task, indicative of a critical role in motor programming. The premotor regions are active when planning a movement to an intended target. Visual information regarding a target and somatosensory information of the hand are assembled in the premotor cortex for execution (Hoshi & Tanji 2000). Lateral divisions of the premotor cortex (PMC) are influential in movement selection and planning, as well as the actual limb movements (Boussaoud 2001, Toni et al 2001). In primates, this lateral premotor region possesses neurons sensitive to object manipulation, as well as when viewing actions such as grasping and manipulation, or visual and auditory representations of particular actions (Keysers et al 2003, Kohler et al 2002, Murata et al 1997, Rizzolatti & Arbib 1998). In humans, these areas (pars opercularis and pars triangularis) are near Broca's area and are active during action recognition and imitation of object use in humans (Hamzei et al 2003, Heiser et al 2003). The supplementary motor area (SMA) is also anterior to M1 and centrally located. The supplementary motor area sharing connections to the primary motor area and spinal cord possesses a direct motor function role with particularly dense anatomical connections to the hand areas of the primary motor cortex (M1) (Arai et al 2012, Luppino et al 1993) . The neurons within the SMA show a correlative function with movement onset as well as specific sequences of movements requiring multiple joints (Rizzolatti et al 1998). The supplementary motor area is responsible for the preparation and execution of complex sequences of voluntary movements requiring coordination of different segments (Carter et al 2000, MacDonald et al 2000, Picard & Strick 1996, Picard & Strick 2001). The summation

of input, beyond just the frontal lobe, influences the planning and initiation of complex temporal sequences of voluntary movements implemented within the motor regions of the frontal lobe.

There is also a large portion of converging, aggregating, and directing information, high level processes occurring in the deeper structures. In essence sensorimotor integration, sorting, and weighting information into something cohesive and singular. Though there is an agreed upon functional segregation within the brain, and networks are said to serve a high- or low-level function, nothing occurs in isolation. Through particular combinations of receptor bindings, blockings, activation, or deactivations, the cumulative responses unite various brain regions. In order for a visual stimulus to invoke a motor response, extrinsic information relating to the state of the world must coalesce with intrinsic information regarding internal states of the body. The task of generating a goal directed movement is often broken down into a series of sequential steps which implies a linear progression advancing toward the motor output. However, there are multiple ways in which an action can be executed successfully, the rate at which it can be done infers a more complex processing design than a simple linear advancement. The brain operates as a whole, with groups of neurons tuned to particular information represented by impulses. Networks are reliably active during specific processing demands, and their combined involvement results in characteristic neural responses and motor behaviors.

HEMISPHERIC LATERALIZATION

Structurally, the left and right cerebral hemispheres look broadly similar; functionally, specialized function has emerged. Morphological asymmetry is common in nature presenting as more of a rule than an exception (Good et al 2001). Our organs for example are distributed asymmetrically, and hemispheric allocation of function appears to exist within our brain to some extent. The most notable example is the language localization to the left hemisphere in 97% of

humans. Individuals with right hemispheric dominance for language predominantly, but not exclusively, identify as left hand dominant (Davidson & Hugdahl 1996). The dominant hemisphere is defined as the hemisphere contralateral to the dominant hand (Purves et al 2004).

Functional asymmetries such as lateralized hand preferences are expected to correlate with brain structure asymmetries, although findings are inconsistent (Amunts et al 2000, Amunts et al 1996, Good et al 2001, Melsbach et al 1996, Moffat et al 1998, White et al 1994). This can at least be partially credited to the nature of the findings and inherent assumptions made in cytoarchitecture studies. Large amounts of classical mapping experiments were performed on anesthetized animals, indicating stable conditions with no context or goal directed behavior. Interpretation of results is limited and experiments on awake species have cast doubt onto the rigid structure presented by models such as Penfield's homunculus and Brodmann's cortical parcellation (Earland et al 2014, Nazarova & Blagovechtchenski 2015). The current understanding is that the brain has a modular organization in which segregated networks supporting specialized processing are linked through a few long-range connections, ensuring high-level integration of information arising from low-level structures (Bortoletto et al 2015, Bullmore & Sporns 2012, Nolte & Marzetti 2014, Zilles & Amunts 2010).

Historically, two opposing paradigms existed to explain brain function: holism and localism. Generally, holism postulated that the entire cerebral cortex was involved in the execution of any brain function while those in favor of the localization paradigm believe that individual functions were localizable to specific cortical areas. Korbinian Brodmann began his work in this era with the goal "to produce a comparative, organic theory of the cerebral cortex based on anatomical features". He studied the cellular composition of neural tissue and compared human and non-human mammals, generating a structural map of the brain depicting 43 cortical

areas (Brodmann 1909). Through this process, the concept of phylogenetically old and more recent neocortical subdivisions of the cerebral cortex was developed. His pioneering work, being the basis for the ongoing analysis of the relations between cortical structure and function, continues to have a tremendous impact on neuroscience and clinical brain research (Zilles & Amunts 2010). Recently the field has moved toward a concept of connectionism, with cortical regions being dynamically coupled forming functional networks associated with tasks and actions (Honey et al 2007, Nazarova & Blagovechtchenski 2015). The human cerebral cortex consists of approximately 10^{10} neurons organized into complex networks of local circuits and long range fiber pathways of which we know to be dynamic (Hagmann et al 2008). While much has been learned regarding the organization and function of the brain, much remains unknown.

Functional brain states emerge from the underlying structural substrates and can result in observable consequences. Hand dominance is among the most obvious and overtly asymmetrical attributes, both behaviorally and in the population distribution (Jäncke 2002). Left-hand dominant individuals make up an estimated 14% of the Western population (Perelle & Ehrman 1994). It was previously assumed that the brain of a left-hand dominant individual was the mirror opposite of a right-hand dominant individual. Despite the idea of chirality being proved inaccurate, the left-handed demographic remains underrepresented in the motor neuroscience literature. Further, whether hand dominance is affecting neurological difference or neural difference effect hand dominance remains unclear.

Hand dominance implies a distinctive, asymmetrical preference for the use of one hand over the other. Anatomically, hand dominance corresponds with a comparatively larger volume of the hand motor area contralateral to the dominant hand. With structure governing function, and hand dominance imposing structural discrepancies, it can be hypothesized that innate hand

preference will influence neurological organization and that the populations will possess fundamental differences in how they interact with the environment.

PURPOSE

The central objective of the dissertation was to understand how sensorimotor information is integrated, thereby allowing for adaptable motor behavior and skill acquisition. Left and right-hand dominant individuals were recruited for the purposes of examining differences in neural communication strategies based on hand dominance. Neurological and behavioral metrics were analyzed and compared between the two populations for the purpose of increasing understanding, and generating a more complete, stable, and accurate understanding of the sensorimotor integration processes. The emerging strategic patterns, termed neurostrategies, were used to infer how the progression of a skill is navigated, as seen with repeated execution of a motor task.

EXPERIMENTAL PARADIGM

The novel motor task described in this work uses visual input to guide dynamic handgrip force output. A visual target was displayed on a monitor and moved at a constant rate along a repeating trajectory. Handheld force scales were used to modulate the position of a cursor simultaneously displayed on the screen, thus providing real time visual feedback. The participants' goal during the task was to modulate hand force output to keep the cursor in constant contact with the target. The overall purpose of the task was to determine neurological strategies for encoding kinetic, kinematic, and dynamic transformations.

Electroencephalogram (EEG) data were collected and analyzed in an effort to understand the underlying nature of the human brain and how hand dominance influences skill acquisition.

The high temporal resolution afforded by EEG provides the opportunity to study the brain as an evolving system. The dynamic, continuous nature of the experimental paradigm prevented both voltage-based and event related analyses. Instead the direct and continuous collection of neuronal activations was used to dynamically represent the function of the brain. Interpreting signals transmitted between regions and populations of neurons informs how information is integrated in the brain. (Nolte & Marzetti 2014). Electromyography (EMG) can capture the electrical impulses transmitted to the muscles, providing a recorded pattern of muscle recruitment directed by the cortically developed motor plan.

EEG has been used previously to expose differences between left- and right-hand dominant populations. Handedness has been shown to have an impact on underlying differences in the neural networks of left- and right-hand dominant individuals (Kelly et al 2015). In this study, left- and right-handed participants observed an image of a task being executed by an actor using the left and right hand. It was found that the right-hand dominant population had lateralized activations to the hemisphere opposite of the observed hand, where the left-hand dominant group had a bilateral, dual hemisphere activation pattern when observing either hand execute the task. Additionally, when left- and right-hand participants were asked to determine whether observed hands (in different postures) were either left or right hands, left and right populations had anterior/posterior differences in signal strength and timing (Whittier et al 2017). There is adequate evidence indicating an underlying difference in the neural networks of left- as compared to right-hand dominant individuals. Yet, it remains unknown why there exists such a disproportionate preference for one hand over the other.

ELECTROENCEPHALOGRAPH

Much of neuroscience's understanding regarding brain function has been gleaned via experimentally induced lesions in animals, or naturally occurring damage in human clinical populations (Hillary & DeLuca 2007). The advancement of functional neuroimaging technology affords innovative approaches to new and old questions regarding cognitive, sensory, and motor neuroscience.

The brain operates using electrical impulses signaling for excitation or inhibition. An electrical potential travels down an axon toward the axon terminal/presynaptic terminal, prompting the potential release of neurotransmitters. If an action potential is generated, a postsynaptic current is generated and the electrical impulse, given an appropriate spatial and temporal organization, can be measured at a distance to provide the electrical current comprising an EEG signal. The signal detected by EEG reflects the averaged excitatory or inhibitory postsynaptic activity of a large number of spatially aligned, synchronously active neurons (Arnett & Cooper 1965, Delucchi et al 1962, Ebersole 1997, Harmony 2013, Nunez & Srinivasan 2006), . Scalp EEG represents a spatially smoothed local field potentials possessing a high temporal resolution and spatial orientation (Niedermeyer & da Silva 2005).

Two types of measurable changes in electrical activity of the cortex are known to occur upon a sensory stimulation: evoked and induced responses. The evoked response is time and phase locked to a stimulus. Task-related neural processing results in a reorganization of ongoing signal phases, thereby causing a detectable change in recorded signal amplitude. These event related potential (ERP) changes can be used to inform a variety of cortical organization hypotheses relating to timing and amplitude of event related responses. Conversely, an induced response is elicited by a change in the dynamical state of neural networks and is not phase locked

to any event. Frequency analysis is able to detect changes in both evoked and induced neuronal activity and determine, with proper analysis, changes in oscillatory patterns resulting from local and remote neuronal activity.

SIGNAL OSCILLATION PROPERTIES

Within a particular EEG signal, all frequencies from DC to the Nyquist frequency are represented, accentuating the complexity of information processing accomplished in the human brain. Oscillatory activity within discrete frequency bands are linked to a variety of perceptual, sensorimotor and cognitive operations (Aoki et al 1999, Başar et al 1999, Klimesch 1999, Palva & Palva 2007), and serve to unite assemblies of neurons in either states of activation or inhibition (da Silva 1991). Each oscillatory cycle is a temporal processing window, indicating the initiation and termination of an encoded message with the wavelength of the cycle determining the temporal windows (da Silva 1991, Harmony 2013). Generally, fast oscillators can operate in short time windows and are able to facilitate local integration simply due to limitations of axon conduction delays. Conversely, slower oscillations with larger cycle lengths will serve to transfer information to more remote locations and often serve as global integrators. Using EEG, signal information in the frequency domain can be interpreted in terms of biological and behavioral significance (Wu et al 2014).

The transformation of a signal from the time domain into the frequency domain using a Fourier analysis preserves the information contained within a signal while highlighting specific frequency content embedded within. Rather than monitoring how a signal changes over time, the classic time voltage EEG analysis, a Fourier transformed signal can be used to show how much of the signal lies within frequency band or range. However, this technique masks information regarding signal phase. Alternately, a wavelet transform preserves the time order of the signal

maintaining phase information by decomposing the signal into a set of basic functions (Najarian & Splinter 2005).

The dynamic states of the brain are influenced by the frequency of the signals propagated. The modulation of brain activity can be, in part, illustrated using the power spectrum, a quantification of the distribution of frequency components within a signal derived with a spectral decomposition. EEG data represent the properties of electrical impulses recorded in voltage at discrete time points. The spacing between two points is directly related to the sampling frequency, being the reciprocal of the sampling frequency. In order to interpret the energy ($\cos(2\pi f t)$) contained within the signal, the power spectrum is computed as the squared magnitude of the Fourier transform. A longer segment of data provides a better frequency resolution at the cost of temporal precision. Frequency resolution of Fourier transformed data is defined by the number of points in the times series, thus the larger the time segment the more frequencies can be extracted resulting in the increased frequency resolution. Within a signal, all frequency components exist simultaneously and can be represented in terms of magnitude (power) and phase. The power spectrum illustrates the amplitude of rhythical activity in the data as a function of frequency, describing the distribution of power and when compared against a baseline will reveal frequency modulation as a function of the task (Kramer 2013).

The presentation of a stimulus will result in a pre- to post-stimulus change visible in the power spectrum. Characteristic changes of power, or signal magnitude, have been found within discrete frequency bands and have been associated with particular brain states since the inaugural finding of the alpha band by Hans Berger in 1924. The conventionally defined bands; delta [0.5-4 Hz], theta [4-7 Hz], alpha [8-12 Hz], beta [12-30 Hz], gamma [30-100⁺ Hz] are simultaneously present within a signal and will behave in a predictable fashion under certain known conditions.

A signal desynchronization within a band is accompanied by a decrease in power. The desynchronization is associated with active processing signifying that the underlying neural network or neuronal circuitry, small patches of neurons, or neuronal assemblies are working in a relatively independent or desynchronized manner. Event related desynchronization (ERD) reflects less random oscillations, suggestive of increased non-random information processing. Conversely, large amplitudes of synchronized EEG activity, accompanied by an increase in power was originally believed to be reflective of an idling state. The term ‘idling’ was introduced by Adrian and Matthews (1934) to describe large amplitude oscillations over cortical areas. In this respect, the enhancement of event related synchronized (ERS) activity can be seen as a correlate of a deactivated or inhibited cortical network. For instance, alpha band power will most notably increase with the removal of visual stimuli (closing eyes) and will immediately be diminished upon the return (eyes open). In terms of information theory, a desynchronized system represents a state of maximal readiness and a maximum of information capacity while a synchronized system suggests an increase in random oscillations and decreased information capacity. (Thatcher et al 1983).

The neural activity of the human brain constitutes an exceedingly complex, nonlinear, and dynamic biological system (Wang et al 2010). Neural oscillations are thought to serve as a means of controlling the timing of neuronal firing, temporally coordinating information transfer across brain regions (Engel & Fries 2010). Synchronized activity in the synaptic transmission appears to be preferentially optimized (Singer 1999). Signal synchronization within a frequency band can create temporal windows for segregating cortical populations (Nadasdy 2010), which can separate information intake and transfer processes (Buzsaki 2006). Active neuronal populations within a given frequency form functional assemblies bound together by

synchronization of their action potentials, becoming more likely to interact, exchange information, and modulate synaptic plasticity (Bullmore & Sporns 2012). Rhythmic excitability is thought to form the basis for transient functional networks between spatially distinct sites (Cavanagh & Frank 2014, Fries 2005). The repeated patterns of engagement support spike timing dependent plasticity, a process modulating the strength of neuronal connections (Snyder & Smith 2015) and suggest that cortical regions will dynamically couple for different purposes (Honey et al 2007).

CORTIO-CORTICAL CONNECTIVITY

One benefit of EEG over other neuroimaging techniques is that the EEG signal captures changes in coupling at the millisecond timescale. Neural activation patterns are guided by the underlying architecture of the dense network of fiber pathways connecting distinct regions. Functional roles of brain areas are determined by their inputs and outputs (Sporns et al 2004). An understanding of the topography of the brain can provide context for the intercepted messages transmitted between distinct regions. Frequency measures can be applied to evaluate communication between distinct brain areas and determine functional connectivity. In the context of EEG distinct brain areas can be represented by spatially-normalized electrodes. Coherence determines the statistical dependency between signals recorded from spatially independent electrodes (Nolte et al 2004). The spatial independence is crucial, due to the nature of EEG being a recorded average signal and inherently including noise, the corrected imaginary coherence imposes a time lag (Nolte et al 2004). This addresses the volume conductance associated with EEG signal, removing artifactual ‘self-interaction’ (Ewald et al 2012).

Each of the different frequency bands are not necessarily independent, and the same cognitive process may be associated with changes of EEG signal power at different frequencies

(Canolty & Knight 2010). It is nearly impossible to assign specific cognitive functions to a specific oscillatory pattern, and it is unlikely that each defined frequency range serves a single function in the brain. However, there are characteristic functional associations that will be described for theta, alpha, and beta frequency bands below.

THETA BAND FREQUENCY

Theta activity oscillating within the range of 4 – 7 Hz is stereotypically associated with the frontal lobe and is a characteristic attribute of high-level processes. For example, stimuli requiring increased cognitive control evokes a response in the theta band, and cognitive effort can be seen in the theta phase and power responses to situations involving uncertainty about actions and outcomes (Cavanagh & Frank 2014). When localized over the frontal midline, behavior appears to shift from a habitual response to a goal directed process. Additionally, theta is an important attribute of successful spatial learning, memory maintenance, and drives goal seeking behavior (Caplan et al 2003, Mizelle et al 2010), . Event related changes in the theta band are seemingly related to encoding and retrieval processes of general working memory systems (Niedermeyer & da Silva 2005). Further, there is a documented relationship between theta band activity and sensory and motor events, particularly regarding spatial orientations (Caplan et al 2003). The associations between sensory stimuli and motor behavior that are essential for the performance of spatial navigation tasks implies a memory function (Raghavachari et al 2001, Raghavachari et al 2006). The transfer of information from frontal to posterior regions (frontoparietal areas) supports the association between theta rhythm and spatial encoding, and it has been concluded that theta oscillations mediate the organization of working memory, incorporating multiple items of information, and updating memory (Cavanagh & Frank 2014).

ALPHA BAND FREQUENCY

Alpha band rhythm oscillating within 8 – 12 Hz, was the first identified human electrophysiological brain oscillation (Berger 1929). Despite being overtly present in many contexts, there is little consensus on the functional role of alpha band activity, and many factors confound global interpretation. Three independent alpha rhythms have been localized to distinct regions: the occipitoparietal alpha associated with the visual system, the central alpha, also termed mu rhythm, associated with sensorimotor functions and the temporal alpha, termed the tau rhythm of which not much is known to be difficult to detect (Niedermeyer & da Silva 2005). While there is no unique and homogenous alpha rhythm, it does follow specific trends.

Alpha band activity develops in newly born children within the first three months of life, increases in frequency during childhood maturation, and declines in the elderly , (Niedermeyer 1997, Nunez et al 1978, Nunez & Srinivasan 2006). In healthy, mature individuals, alpha is most generally associated with cortical operations during the awake resting state. Alpha is observed to increase peak frequency with cognitive demand and task engagement (Haegens et al 2014). This is observed with the suppression of amplitude, a signal desynchronization, in response to visual input via opening the eyes (Pfurtscheller & Da Silva 1999). The decrease in power is additionally detected when engaging in tasks requiring perception or attention (Adrian & Matthews 1934, Niedermeyer & da Silva 2005). Further, alpha band activity has been associated with the inhibition of task-irrelevant brain areas as well as memory function and retention (Jensen et al 2002, Sauseng et al 2009, Tuladhar et al 2007). Modulation of alpha has been proposed to serve a gating function for the flow of relevant and irrelevant information (Klimesch 1996), and others have suggested that it supports integrative functions (Halgren et al 2019).

MU BAND FREQUENCY

Mu rhythms, a subset of the alpha band, are often described to oscillate between 10-12 Hz (Pfurtscheller et al 2000) and are most often associated with the sensorimotor cortex and function,(Buser & Rougeul-Buser 1995, da Silva 1991, Niedermeyer 1997). Mu rhythms have a more anterior focus, as compared to the posterior alpha focus (Pineda 2005). Unlike alpha, Mu is not modulated by visual input, but rather experiences desynchronization with actual movement or the motor imagery of movement (Muthukumaraswamy & Johnson 2004, Muthukumaraswamy et al 2004) (Pineda et al 2000). Mu is also thought to integrate different processes involved in the transformation of sensory input into motor output (Pfurtscheller & Andrew 1999).

BETA BAND FREQUENCY

The beta band, defined by oscillations within the range of 12-30 Hz, is a higher frequency band classically associated with voluntary movement and sensorimotor functions. It is a distinguishing feature of the motor system, particularly the primary motor and premotor aspects of the cortex, basal ganglia, cerebellum, and peripheral motor units (Baker 2007, Brown 2007). Beta band activity is most prominent during periods surrounding movements, dampened by voluntary movements (ERD), and inhibited by motor imagery (De Lange et al 2008, Koelewijn et al 2008). Evidence suggests beta activation to be influential in higher order processes. Beta band activity has been detected and interpreted as signaling an ‘active-akinetic process’ (Swann et al 2009). This pattern has been suggested as a signature of an active process that promotes existing motor commands at the cost of incorporating neuronal processes of new movements. Synchronization of beta (ERS) has been suggested to be involved in the suppression of movement related processing (Androulidakis et al 2006, Brown & Williams 2005). This is explicitly observed with elevated oscillatory synchrony in conjunction with measurable

impairments in movement performance (Gilbertson et al 2005). Cumulative findings support beta band activity to be instrumental in motor planning and to exhibit a preference for existing motor plans at the expense of planning new movements. In conjunction with this, beta has been observed to respond in a manner associated with detecting error, actively inhibiting ongoing motor processes (Koelewijn et al 2008, Ridderinkhof et al 2004). Patterns of enhanced beta band rebound following motor errors have been cited as a signature of increased response inhibition (Koelewijn et al 2008). Signal resynchronization following the observation of error is thought to be reflective of an active inhibition of ongoing motor processes. Building evidence suggests that beta oscillations are used to process sensory feedback and directly influence the sensorimotor system in both anticipatory and reactionary contexts. The somatosensory cortex has strong beta band oscillations synchronized with those in the motor cortex, providing a means for sensory reafference to be interpreted in the context of the motor command which produces it (Baker 2007, Engel & Fries 2010). Beta modulation denotes a state of enhanced arousal, distinguished by specific and spatially fine-grained interaction patterns. The increased excitability that occurs with increased frequency allows for increased information integration opportunities and enables rapid system recalibration (Marsden et al 2000, Omlor et al 2007).

Self-paced, voluntary movements can be described in three phases: 1) planning, which begins ~2 seconds prior to movement onset with neural activations localized over the contralateral hemisphere, and exhibit desynchronization of mu and beta rhythms (Chatrian et al 1959, Derambure et al 1993, Pfurtscheller & Berghold 1989); 2) execution, best monitored via EMG, but typified neurologically by a bilateral symmetrical desynchronization in the beta band (Pfurtscheller et al 1996); and 3) a recovery period, marked by the termination of the movement, and followed by rapid beta band recovery synchronizing within a second, not only returning to

baseline but exhibiting a contralateral post-movement power increase or synchronization (Pfurtscheller & Berghold 1989). Mu rhythm recovers at a slightly slower rate, 2-3 seconds post movement termination and occurs slightly more posterior to the site of beta modulation, and suggests the mu rhythm operates as more of a somatosensory signal and beta acts in more of a motor function (Pfurtscheller & Aranibar 1977, Pfurtscheller et al 1996, Stancák & Pfurtscheller 1996). The post movement beta synchronization, contralaterally located, has been assigned to represent a shift from active motor areas during the initial two phases of movement to a resting state upon movement completion (Mulholland 1995).

ELECTROMYOGRAPHY

The Electromyograph (EMG) signal is based upon action potentials at the muscle fiber membrane resulting from a depolarization and repolarization processes. EMG provides a representation of the rate of muscle activity comprising the number of active cells and the frequencies of their discharges (Vredenburg & Rau 1973). The precise control of the muscular contraction is reliant on recruitment pattern specifications and subsequent firing frequency. Surface EMG records superimposed motor unit action potentials (MUAPs). The magnitude and density of the recorded signal is a reflection of the firing characteristics of the measured muscle (Konrad 2005). The relationship between cortical activity and muscular force can be unpacked by examining how the brain communicates movement objective and how behavior is subsequently regulated.

CORTICO-MUSCULAR CONNECTIVITY

Activity does not simply propagate from cortex to muscle to create movement. Rather, afferent information is required to implement, initiate, control, and complete a motor action (Baker & Baker 2003). The continuous processing that facilitates sensorimotor integration

involves the motor system and sensory afferents enabling the preparation, execution, and control of motor actions, both gross and fine. The process is a net result of the central nervous system integrating information coming from multiple sensory modalities, allowing for the performance of specific goal directed tasks (Lattari et al 2010). Continuous, precise communication is necessary for successful movement. The motor cortex regulates muscle activity, transmitting impulses along the corticospinal tract. The corticospinal pathway is a collection of axons predominately extending from the cortical motor areas to alpha motor neurons in the spinal cord, which in turn innervate a muscle. The corticospinal pathway is responsible for initiating and modulating outflow for voluntary control of the body, and damage can result in severe motor impairments such as paralysis (Vanderah & Gould 2015).

The relationship between cortical activity and muscular force can be represented by the oscillatory activity of brain regions coupled with neuromuscular activation. Oscillatory activities at the cortical level are mechanistically involved in determining motor behavior, and can even improve performance (Joundi et al 2012). The cortico-muscular coherence (CMC) denotes the temporal correlation between spatially distinct neural networks and muscle activation, within distinct frequency bands. EMG exhibits coherence with contralateral EEG (Riddle & Baker 2005), and movement and task demands have been shown to modulate cortico-muscular coherence. Mathematically, CMC can be used provide an estimate of information transfer between the brain and a muscular target within specific frequency bands (Farmer et al 1993, Farmer et al 1997, Halliday et al 1998) thus, providing context to the behavioral outcomes and enabling speculation as to signal intention and meaning (Andrykiewicz et al 2007, Patino et al 2008).

BEHAVIOR

Humans excel at rapidly adapting to variable dynamics necessary for environmental interaction (Shadmehr & Mussa-Ivaldi 1994). Experiences shape the nervous system and bring about changed behavior, and such processes exist on a continuum. Level of skill proficiency progresses with practice and time, making the difference between a novice and expert on the learning spectrum obvious, although precise identification of where an individual may be located on the continuum is unclear (Ericsson et al 1993). There are many factors that can influence the progression of learning, potentially confounding accurate distinctions of the learning stages.

Behaviorally, motor learning is measured with performance values. The initial adoption of a behavior results in an idiosyncratic pattern that, with practice, converges to nearly identical patterns of execution (Haith & Krakauer 2013, Nagengast et al 2009). Error measures tend to decline exponentially across trials, consistent with the idea that learning between trials is proportional to error reduction. Behavioral measures represent the outcome of the cortical signals and can aid in translating neural intention. Tracking behavior though time is helpful in monitoring change and provides metrics of the current state of performance and learning.

QUANTIFYING & INTERPRETING

With the intent of studying the brain as a dynamic system, the whole brain was evaluated as a large scale complex network. Graph theory represents a system of interacting elements as a network, and the complex neural circuitry of the brain can be traced using nodes and edges. In the context of EEG, nodes are defined as the electrodes and their underlying brain regions, or in the case of source level reconstruction, dipole sources. The edges are obtained as measures of statistical association between the nodes (Shamas et al 2015). Applications of graph theory

algorithms have identified characteristic patterns of normal and pathological brain activities (Fornito et al 2015, Tononi et al 1994).

Weighing the connections a specific node has with the rest of the network is a fundamental network question representing how a node is embedded in the system. Degree indicates the number of links connected to a particular node and describes the level of interaction between that node with other nodes in the network. In random networks, all connections are equally probable resulting in a Gaussian profile and symmetrically centered degree distribution. Complex networks generally have non-gaussian degree distributions, often with a long tail toward high degrees (Barabási & Albert 1999). The degree distribution of scale free networks, such as the brain, follows an exponentially bounded power law, in which similarly connected areas tend to communicate with each other (Mijalkov et al 2017). Nodes with high degrees are more likely to receive more connections, a tendency also known as preferential attachment. Scale-free networks suggest how a hub may come about (Finotellia & Dulioa 2015). Hubs represent brain regions that commonly interact with many other regions. Degree indicates network density, development and resilience, and wiring cost indirectly. Hubs facilitate integration, thereby increasing network resilience (Finotellia & Dulioa 2015, van den Heuvel & Sporns 2013).

Communication characteristics, how directly a signal is passed from one region to another, distinguishes network efficacies. Clusters within a network form when the nearest neighbors of a node are also directly connected to each other. Random networks have a low average clustering coefficient, whereas complex networks have high coefficients of clustering. The formation of clusters demonstrates an ability for specialized processing to occur within densely interconnected groups of brain regions (Rubinov & Sporns 2010). Global efficiency

denotes functional integration by measuring path length between one node and all other nodes. Longer axonal path projections connecting distributed brain regions are more costly in terms of both material and energy. The long paths between network nodes enable global connectedness and integration of specialized information. Shorter paths imply a greater potential for integration. The clustering coefficient calculates local interconnectedness indicative of local efficiency, stability, and a network's ability to resist perturbation. (Bullmore & Sporns 2012, Finotellia & Dulioa 2015).

CONCLUSION

The nervous system is shaped by experiences, driving learning, and yielding changed behavior. The continuous integration of sensory information, both about the environment and the current state of the body, is presumably used to determine the appropriate set of muscle forces needed to generate a desired movement or action. As a movement is repeated and practiced, movements become faster and increasingly coordinated, and error is reduced at a rate proportional to learning (Haith & Krakauer 2013). The continuous cooperation between the nervous system and the musculoskeletal system enables the sensorimotor plasticity that fosters adaptability. Sensorimotor integration is a multifaceted fusion of incoming signals condensed into one outgoing motor message. Differences in how information is processed and used to control movements could explain differences between the left- and right-hand dominant populations (Riddle & Baker 2005), and may offer a more direct understanding of how skill acquisition strategies differ between left- and right-hand dominance populations.

CHAPTER 2. Aim One: Neurobiological Indicators of Hand Dominance

INTRODUCTION

In nature, left-right asymmetry presents a rule rather than the exception, the universe itself has been found to exert a left-handed bias on particles (Cowan et al 2017, Good et al 2001). Humans exhibit lateralized behavior as soon as ten weeks post conception, our organs are distributed asymmetrically, and hemispheric allocation of function appears to exist within our brain to some extent, with the most notable example being the left lateral language localization for 97% of the population (Davidson & Hugdahl 1996, Hepper et al 1998). Functional asymmetries such as lateralized hand preferences are expected to correlate with brain structure asymmetries, although findings are inconsistent (Amunts et al 2000, Amunts et al 1996, Good et al 2001, Melsbach et al 1996, Moffat et al 1998, White et al 1994). The small percentage of individuals with right hemispheric dominance for language predominantly identifying as left hand dominant. However, not all left-hand dominant individuals have right hemisphere language localization, nor are all of the people with right hemisphere language centers left hand dominant (Davidson & Hugdahl 1996, Ocklenburg et al 2014, Szaflarski et al 2012).

The majority of the population identifies as right-hand dominant, with a minority 12-16% of the population identifying as left-hand dominant (Perelle & Ehrman 1994). The distribution may be partially skewed due to social factors (Jäncke 2002), but it remains that left-hand dominant individuals make up approximately 40 million people in the United States alone (Perelle & Ehrman 1994). This demographic is underrepresented in the scientific literature related to motor control, as it was historically believed that left-hand dominant individuals were the mirror opposites of right-hand dominant individuals. More recent research has revealed both

behavioral and neurological differences between the populations, therein overturning the previous assumptions of a simple hemispheric flip in motor-related activations.

Behaviorally, left-hand dominant (LH) individuals tend to present as more bilateral compared to right-hand dominant (RH) individuals (Knecht et al 2000, Przybyla et al 2012, Walker & Perreault 2015). A study observing grip strength found RH participants to have a distinct strength discrepancy between dominant and non-dominant hands, a discrepancy not found in LH participants (Petersen et al 1989). Neurologically, a study examining twins with different limb dominance found that bilateral occipital and frontal resting state electroencephalographic (EEG) spectral power was a covariate of hand dominance (Zietsch et al 2007). Another study with left and right-hand dominant participants observing images of left and right hands executing a motor task found clear differences in neural activation patterns (Kelly et al 2015). In this work, RH observing right- and left-handed task execution had connectivity patterns distinctly lateralized to the hemisphere opposite to the hand observed, whereas left-handed observers presented with a more bilateral distribution of neural connectivity regardless of the hand observed (Kelly et al 2015). Further work has shown that when left- and right-handed participants were asked to determine whether observed hands (in different postures) were either left or right hands, left- and right-handed groups had anterior/posterior differences in signal strength and timing (Whittier et al 2017). Thus, there is adequate evidence to support the hypothesis of an underlying difference in the neural networks of left as compared to right-hand dominant individuals. However, the exact nature of how the populations differ, and especially how hand dominance influences, or is influenced by, neurological organization in the context of overt motor control and sensorimotor integration, is largely unknown and mostly ignored.

The arrangement of cortical networks enabling signal transfer and the propagation of information is an area of high topical interest in neuroscience research. The nervous system is shaped by experiences, driving adaptation through neural coordination and organization. Neural activity is constrained by connectivity, information cannot be transmitted between populations of neurons if there is no anatomical connection between them. These anatomical connections between brain areas provide the structural framework enabling all conscious thought and behavior. Neural networks are metabolically expensive, expendable, and above all, dynamic. The construction and maintenance of the networks are costly; synapses are believed to be pruned when deemed to be extraneous due to redundancy or disuse (Biewener & Gillis 1999, Yamahachi et al 2009). It has been proposed that networks are selectively optimized based on minimizing resource consumption of connections while maximizing adaptive value (Bullmore & Sporns 2012, Poldrack 2000, Yamahachi et al 2009). However, if communication networks were formed exclusively to minimize cost, global integration of information processing would not be possible as each neuronal population would exclusively communicate with their nearest neighbors. Alternately, a purely random organization is unlikely as meaningful information could not be transferred from one region to another with fidelity. A compromise is internally negotiated between strict order and randomness (Honey et al 2007, Sporns et al 2004, Tononi et al 1994). Mapping these neural networks for the purpose of understanding brain function can provide information related to interregional information processing.

The study presented here was designed to examine the nature of the underlying functional, neurobiological differences driving the asymmetric limb preference in the context of motor performance. A dynamic, visually based force matching task involving the unimanual dominant and non-dominant hands was selected due to previous findings showing the two

populations to have behavioral differences (Petersen et al 1989). Visual feedback was provided in real time as movement errors in the visual domain have been shown to influence motor cortical areas and shape neural activity in motor and premotor regions (Adamovich et al 2009, Hadipour-Niktarash et al 2007, Muellbacher et al 2001, Wise et al 1998). Continuous electroencephalography (EEG) was used to capture coherent neurological activations, allowing for the analysis of network activation patterns that are known to undergo reconfiguration on multiple time scales, thus enabling observation of how communication patterns change and develop with task repetition.

The brain is a large scale complex network, a system of interacting elements that combines statistical randomness with regularity (Tononi et al 1994). Neural activation patterns are shaped by the underlying structural connections that form the dense network of fiber pathways. Given that the functional roles of brain areas are specified by their inputs and outputs (Sporns et al 2004), understanding of the topography of the brain can provide context for the messages transmitted between distinct regions. Neural oscillations are presumed to function as a means of controlling the timing of neural firing, temporally coordinating information transfer across brain regions (Engel & Fries 2010). Functional connectivity is related to the temporally dependent activation of distinct brain regions, representing transient relationships between distinct neuronal populations. Cortical regions dynamically couple to form functional networks that can be extracted with the determination of statistical dependencies between discrete neuronal populations or regions.

The execution of any action relies on more than just the primary motor cortex to transmit a signal via the spinal cord to the motor neurons enabling muscle activation. Voluntary movement requires planning which occurs in the parietal lobe and frontal lobe regions, including

premotor and supplementary motor cortices (Horn & Leigh 2011), and visual stimuli will engage the occipital lobe. Higher and lower order processes converge to enable the integration of information. Information encoded within oscillation patterns serves to unite assemblies of neurons in either state of activation or inhibition (da Silva 1991). Each oscillatory cycle is a temporal processing window, indicating the initiation and termination of an encoded message with the wavelength determining the temporal windows (da Silva 1991, Harmony 2013). Generally, fast oscillations can operate in short time windows and often facilitate local integration simply due to limitations of axon conduction delays. Conversely, slower oscillations with longer cycle lengths (periods) can transfer information to more remote locations, and often serve as global integrators. We will thus examine beta, a higher frequency oscillation with a known strategic role in voluntary movement (Baker 2007, Brown 2007). Theta will represent the slow rhythms, and due to the novelty of the task is expected to be modulated with practice and skill acquisition (Cavanagh & Frank 2014). The mu band will be included in the analysis specifically for its higher order function as an integrator of information (Pfurtscheller & Andrew 1999).

In order to understand the brain as a dynamic system, the whole brain must be taken into consideration and evaluated as a network. We will employ a branch of mathematics, graph theory, which focuses on the properties and behaviors of networks defined as systems consisting of a set of nodes (electrodes) linked by edges (connections or interactions) (Shamas et al 2015). We will first determine connectivity profiles associated with the different groups (left- and right-hand dominant) and conditions (dominant hand vs use non-dominant hand) to generate a profile of statistical dependency between brain regions (nodes). This enables the evaluation of how elements of a network interact (Rubinov & Sporns 2010). From these networks, we will calculate

several graph theory measurements. Degree, a node parameter indicative of the number of links connected to a particular node, and suggests a level of interaction for that node with other nodes in the network. This will allow for indirect quantification of network density (Mijalkov et al 2017). The clustering coefficient metric determines the local interconnectedness and has been associated with high local efficiency of information transfer and stability (Bullmore & Sporns 2012). Contrarily, global efficiency will be calculated to determine the connectedness of spatially distant regions that are necessary for the integration of specialized information but may be costly in terms of energy and material (Finotellia & Dulioa 2015).

Based on the experimental paradigm and the current state of the literature, our central hypothesis is that the two populations (LH and RH) will present with different neural activation patterns. Specifically, for all analyzed frequency bands, we expect the network dispersion will present as more bilateral with greater cross hemisphere communication for the left-hand dominant group using both dominant and non-dominant hands, which we expect to be reflected by a comparatively a greater global efficiency, while the right-hand dominant group will have more lateralized patterns expressed along the dominant hemisphere. The more constrained lateralized activity will present with decreased global efficiency. We further speculate that theta band connectivity will decrease with the progression of trials, denoted by a diminished degree, for both groups. We speculate that in the non-dominant conditions, the left-handed group will show a higher clustering coefficient as a function of the group being subjected to operate within a right-handed world and thus likely more adept at adapting to the use of their non-dominant hand.

METHODOLOGY

SUBJECTS & EXPERIMENTAL DESIGN

Fifteen left-hand dominant (5 female 10 male) and fifteen right-hand dominant (10 female 5 male) individuals aged 18-35 participated in the study [tbl. 2.1]. Handedness was determined by the Edinburgh Handedness Inventory (Oldfield 1971), and potential participants with a recorded handedness score between -40 and +40 were considered ambidextrous and excluded from the study. Participants self-reported as healthy, and had normal or corrected-to-normal vision. Experimental procedures were approved by the East Carolina University IRB (UMCIRB 17-002599) and informed consent was obtained from all participants before participation.

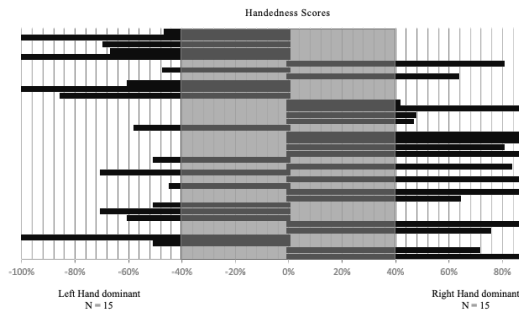


Table 2.1: Handedness score for participants based on Edinburg Handedness Survey. Scores between ± 40 were considered ambidextrous and excluded from analysis.

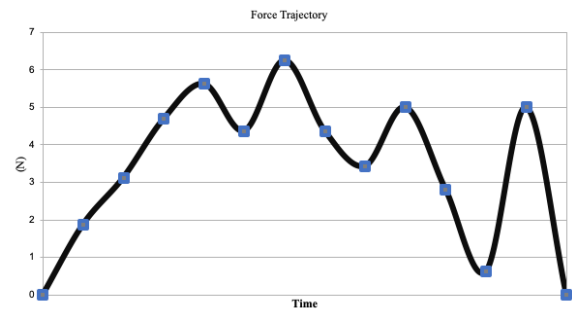


Figure 2.1: Target force trajectory with points of mandatory cursor contact marked with squares.

EEG was collected during two conditions of a visually guided, unimanual handgrip force modulation tasks. A 5' x 3' monitor displayed a target moving linearly along a repeating trajectory [fig. 2.1]. Subjects were instructed to use hand force scales (Innovative Sports Training, Chicago, IL, USA) to control a cursor, also displayed in real time, and attempt to keep the cursor within the target. Magnitude of force output correlated with the distance from the

origin, as the target moved further away from the origin, more force was required to keep the cursor within the target. Target forces fell between the range of 0-6.25 N. Each force trajectory pattern duration was approximately twenty-two seconds, with the target moving at a pseudo constant rate. To ensure that the participants were vigilant in completing the task, target movement along the trajectory occasionally paused until the cursor made contact with the target. Participants completed ten consecutive trials with their dominant hand, followed by ten consecutive trials with their non-dominant hand. Between each trial, a six second rest period was collected for baseline data and there was a two-minute break between dominant and non-dominant hand conditions.

The non-randomized order of conditions was an effort to best mimic general strategies for learning; dividing a complex task into simpler subtasks to be learned independently (Ghahramani & Wolpert 1997). The dominant unimanual condition served as a period for structural learning in which subjects explore how to maximize information and assign errors. Maintaining the structure of the task applies the skills acquired in structural learning to initiate parametric learning. This technique has been used as a method to ‘speed up learning’ (Braun et al 2009, Sailer et al 2005a, Sailer et al 2005b, Wolpert & Flanagan 2010).

DATA ANALYSIS

EEG data were collected at 1 kHz using a 64-channel cap (Compumedics Neuroscan, Charlotte, NC, USA) placed on the scalp in accordance to the international 10 – 20 system with impedance kept below 10 k Ω . Continuous EEG data were exported from the acquisition software (CURRY 7; Compumedics Neuroscan, Charlotte, NC, USA), preprocessed with functions from the EEGLAB toolbox (Delorme & Makeig 2004), and then analyzed with custom Matlab software (The Mathworks, Natick MA, USA). Data were cleaned using high (1 Hz) and

low (55 Hz) pass filters, a linear detrend, and then referenced to the average of the montage. Artifact subspace reconstruction (Mullen et al 2013a) was used for the removal of ocular and muscular artifacts. A Laplacian transform was applied as a spatial filter (Kayser & Tenke 2015) to remove the potential for volume conduction artifact. Data were downsampled to 250 Hz. Throughout recording, events were marked using an outgoing voltage pulse that was triggered with a conditional force and target threshold (if <3 V & target \neq 0), marking the beginning and end of each trial. A time-frequency wavelet decomposition was performed on each trial of 21.875 seconds with the following parameters: cycle range 3 12; minimum and maximum frequencies were set at 1 and 40 Hz, respectively. The complex cross-spectrum was then calculated for each of the 62 channels yielding a symmetrical matrix describing the correlation between all electrodes at each time point at each frequency from 1 through 40Hz. The first three trials for each condition (dominant and non-dominant) and group (left hand dominant [LH] and right hand dominant [RH]) were averaged to represent the early phase, while the final three trials (8:10) were averaged to represent the late phase. The real coherence [Eq. 1] and imaginary coherence [Eq. 2] between all channel pairs were calculated from the complex cross-spectrum for each of the trial bins (early, late, and baseline) and conditions (Nolte et al 2004). A corrective factor was applied to the imaginary coherence to account for artificial suppression of connectivity values near true sources [Eq. 3] (Ewald et al 2012). For each equation below, S_{xy} represents the complex valued cross-spectrum of signals x and y , S_{xx} and S_{yy} represent the complex valued autospectrum of signals x and y , respectively and \otimes represents the complex conjugation.

$$Eq. 1 \quad r_{COH} = \frac{\Sigma[S_{xy}]}{\sqrt{(\Sigma[S_{xx}] \otimes \Sigma[S_{yy}])}}$$

$$Eq. 2 \quad iCOH = \frac{\text{Im}(\Sigma[S_{xy}])}{\sqrt{(\Sigma[S_{xx}] \otimes \Sigma[S_{yy}])}}$$

$$Eq. 3 \quad ciCOH = \frac{iCOH(xy)}{\sqrt{(1 - rCOH(xy)^2)}}$$

The absolute value of the corrected imaginary coherence was taken and individual frequency bands of interest were extracted for the Theta [4-7 Hz], Mu [10-12 Hz], and Beta [12-30 Hz] ranges. Baseline data within each frequency band were used for frequency-specific normalization.

STATISTICS

No assumption could have been made about the underlying distribution of the data, thus a nonparametric permutation statistical approach, based on the FieldTrip toolbox (Maris & Oostenveld 2007), was taken. At the individual participant level, corrected imaginary coherence data were used to create a null statistical distribution or a distribution that would be true if there was no dependence on specific channel pairs in the actual distribution of connectivity estimates. This was accomplished by randomly permuting electrode labels through 1000 permutations. A Fisher's Z-statistic map was then calculated [Eq.4]. A critical value ($t = 1.6449$ for $p < 0.05$) was then used to threshold the Zmap, therein removing values falling below the critical value. The Zmap was then used to mask the true connectivity matrix, leaving only connectivity values that were statistically reliable according to the permutation test.

$$Eq. 4 \quad Zmap = \frac{(true\ connectivity - permuted\ connectivity\ mean)}{std(permuted\ connectivity)}$$

A similar statistical permutation process occurred at the group level for comparisons of interest. First, all thresholded individual adjacency matrices were made symmetrical and then concatenated for two conditions (i.e., LHd and RHd). The true connectivity difference was calculated as the difference of the means of the subject-specific connectivity matrices across conditions. The null distribution was then calculated as above, but both group and electrodes labels were shuffled through 1000 permutations. A similar process was used to calculate a Zmap of the condition differences, and the true difference matrix was thresholded to leave only connectivity values that were statistically reliable according to the permutation test. Each comparison yielded two difference matrices depending on the sign of the differences in the true difference matrix (e.g., Condition A > Condition B and Condition B > Condition A).

Graph theory network metrics were then calculated on these difference matrices to help describe patterns in the observed differences. Degree was calculated by determining how many connections each of the electrodes made with each other. Hubs were defined as possessing a degree of four or greater. Clustering coefficient was calculated as the fraction of closed triangles among three nodes. Global efficiency was determined by finding the distance between each of the connected nodes. For each of the metrics, an average was taken for each of the groups, conditions, time, and frequency bins.

RESULTS

Left- and right-hand dominant individuals were observed while repeatedly executing unimanual force matching tasks with their dominant and non-dominant hands (LHd, LHn, RHd, RHn). EEG was used to capture and evaluate the brain as a dynamic system. By using the frequency content of the signal and the subsequent complex cross-spectrum, connectivity was calculated and used to assess and compare the organizational behavior of the brain between

groups, across conditions and time. Network measures of degree, clustering coefficient, and global efficiency were used to quantify the properties and behaviors of the networks. Skill acquisition was evaluated across the blocks of the trials, early and late, between all groups and conditions.

The overall purpose of this study was to identify different patterns of cortical activation in left-hand dominant and right-hand dominant individuals when performing a dynamic force regulation task with high levels of visuomotor integration. Differences between LH and RH groups executing a motor task are clear when looking within theta [fig. 2.2, tbl. 2.2], mu [fig. 2.3, tbl. 2.2], and beta [fig. 2.4, tbl. 2.4] frequency bands. Generally, the LH group tended to rely on lateral networks to execute the task while the RH group had differentially increased connectivity in midline networks. Frequency band-specific results are discussed below. Conditions were separately evaluated in two phases, an initial phase (first three trials) and a final phase (last three trials). Graph theory network metrics were used to quantify and highlight the strategic differences between the groups by condition.

THETA [4-7 HZ]

LHd showed an initial connectivity pattern along the lateral left aspect with hub locations in posterior-lateral parietal and temporal regions. There is also anterior connectivity with a subnetwork located in midline premotor and frontal regions. Initial RHd, however, shows right posterior connectivity extending anteriorly along the midline. Frontal lobe connectivity is seen anteriorly and centrally. Between the two initial dominant hand conditions, LHd had the higher degree (2.1), greater global efficiency (0.17), and diminished clustering coefficient (0.05) as compared to the RHd degree (1.87), global efficiency (0.09), clustering coefficient (0.07).

For the final dominant hand conditions, LHd shows a general consolidation of connectivity, with regions of left lateral activation remaining and having a clear anterior-posterior divide. The midline frontal connectivity persisted with an anterior and left lateral shift in hub location. Final RHd showed consistent posterior connectivity that became more bilateral with hubs crossing the midline. More defined motor strip connectivity emerged, while the frontal activation shifted posterior and dispersed. Network metrics between final dominant hand conditions were similar between groups and within the RHd early and late trials. The LH group, however, had a decrease in degree (1.81), global efficiency (0.07), and an increase in the clustering coefficient (0.11) between early and late dominant hand conditions. The RH group metrics had small decreases in degree (1.84) and global efficiency (0.08), and a similarly slight increase in clustering coefficient (0.09).

LHn demonstrates early left lateral connectivity similar to the pattern seen in the initial LHd, but with more pronounced midline projections and diminished and diffuse frontal activation. The early RHn trials show dense patterns of connectivity along the right parietooccipital regions with some anterior projections into the right premotor and motor regions. The network metrics showed an increase in degree between initial dominant hand and initial non-dominant hand for both groups, with LHn (2.13) having a greater degree than RHn (2.03). Clustering coefficients followed a similar trend, with increases between both groups from dominant to non-dominant conditions, and the LHn group (0.16) having a greater clustering coefficient than the RHn group (0.09). Global efficiency, however, decreased in the left-hand dominant group from LHd to LHn, while increasing in the right-hand dominant group with RHd group (0.03) having markedly greater global efficiency than RHn (0.3).

Final non-dominant conditions showed LHn to have very sparse connectivity and no nodes defined as hubs. Posterior and left lateral parietal occipital connections remained with some dispersed frontal lobe activation. RHn, however, had an increase in connectivity between bilateral occipital regions as well as bilateral frontocentral and motor regions. This diminished and amplified connectivity for LH and RH, respectively, is reinforced with the network metrics showing the final LHn degree (0.74), clustering coefficient (0.03) and global efficiency (0.02) to be the lowest, while the final RHn condition showed the greatest degree (3.23), clustering coefficient (0.30), and global efficiency (0.2).

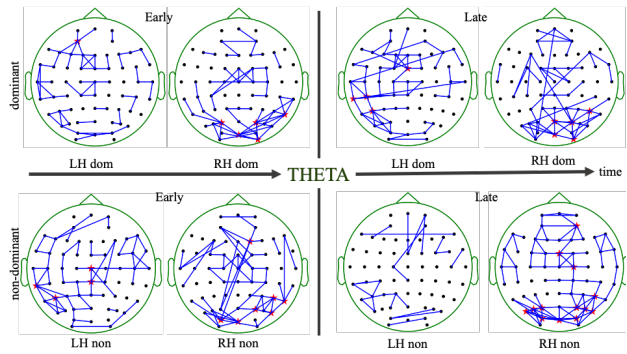


Figure 2.2: Theta band cortico-cortical coherence left- and right-hand dominant difference maps for early and late trials within dominant and non-dominant hand conditions.

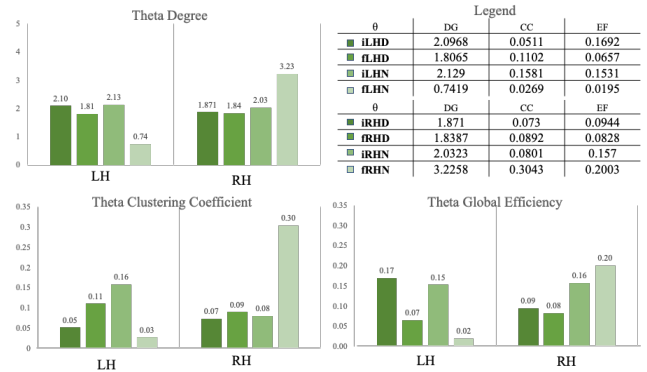


Table 2.2: Theta band graph network metrics.

MU [10-12 HZ]

LHd early trials had a disperse bilateral pattern with a distinct left lateral network as well as a midline projection to right hemisphere premotor and parietal areas. The final condition showed an activation shift centrally with hubs located over the midline somatosensory and premotor regions. RHd early trials show dominant hemisphere activation localized over the left temporal, motor, and premotor regions with ample cross hemisphere projection to the right

premotor regions and right temporal and parietal. The late trials have a consolidated left hemisphere lateral motor and premotor activation with increased projections to the frontal regions in addition to lateral posterior parietal. More distinct right hemisphere anterior-posterior projections emerge with hubs located over the right lateral parietal occipital regions in addition to inline hubs located in the anterior frontal and premotor region. Early dominant hand conditions showed the RH group to display a comparatively greater degree (2.52), clustering coefficient (0.10), and global efficiency (0.23) than the LH group degree (2.81), clustering coefficient (0.12), and global efficiency (0.25). This pattern was present in the final dominant hand conditions as well, with the LH group having a decreased degree between early (2.52) and late (2.32), while the RH group showed an increase from early (3.32) to late (0.13). This trend held for the global efficiency LH (0.21) RH (0.27), while the clustering coefficient increased in both LHd (0.13) and RHd (0.14) with the progression of trials.

The LHn early condition had a generally dispersed pattern of connectivity with a trend toward midline and right hemisphere premotor and parietal areas. The RH group initially had predominantly anterior connectivity, with a focus over the left hemisphere motor regions but also including the right hemisphere, with little cross hemisphere connections. In the final conditions, the LH had a very concentrated right-lateralized inferior lateral frontal concentration of connectivity, extending both medially and posteriorly with a small hub localized over the left lateral posterior parietal region. The RH group showed predominately posterior parietal occipital activation extending laterally, bilaterally through the parietal lobe with some connectivity crossing hemispheres at the motor regions. There was consistency in degree between early LHn (2.65) and RHn (3.68) and late LHn (2.52) RHn (3.58). Global efficiency decreased within groups while remaining higher in the RH population: LHn (0.23) and RHn early (0.32) to LHn

(0.18) and RHn (0.30) late. The clustering coefficient, however, was greater initially for LHN (0.13) than RHn (0.10), and increased for both LHN (0.14) and RHn (0.26), with RHn experiencing the greatest increase.

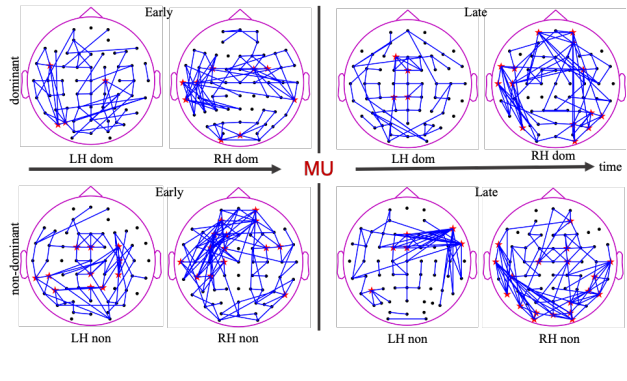


Figure 2.3: Mu band cortico-cortical coherence left- and right- hand dominant difference maps for early and late trials within dominant and non-dominant hand conditions.

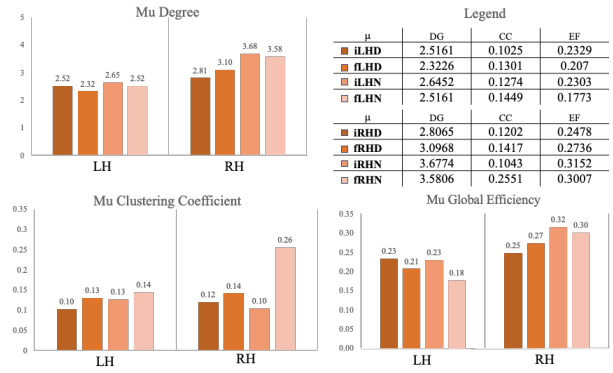


Table 2.3: Mu band graph network metrics.

BETA [12-30 HZ]

The dominant hand conditions showed fairly disperse coherence differences. Early LH had some lateral temporal-parietal connectivity with midline parietal, motor, and premotor connectivity with a hub over electrode Cz. RH had distinct anterior and posterior coherence patterns with a bilateral posterior pattern predominately extending anteriorly along the right hemisphere. The anterior coherence is distributed bilaterally across the motor, premotor, and frontal regions. LHd showed decreased degree (1.58) in the early trials as well as the late trials (1.61) compared to the RHd early (1.77) and late (1.71) degree values. LH group slightly increased degree from the dominant to non-dominant condition while RH decreased. The clustering coefficient behaved in the opposite manner, increasing in both groups from early LHd (0.10), RHd (0.10) to LHd (0.11), and RHd (0.22) late trials, with the final RHd trials exhibiting

the greatest clustering coefficient. LHd late trials had a slight posterior and medial shift with a left parietal hub, and midline to left-of-midline pre-motor coherence extending posteriorly along the midline. The RHd shifts coherence posteriorly, losing some of the anterior frontal connectivity while maintaining the bilateral frontal, premotor, and motor coherence networks. The global efficiency was consistent between LH (0.07) and RH (0.07) groups, and increased between trial bin for the LHd (0.09) but stayed the same for RHd (0.07).

The beta band showed slightly more concise hemisphere differences for the non-dominant conditions. Initial LH using the right hand had left lateral posterior parietal-occipital hub extending anteromedially into the midline motor and frontal areas. RH using the left hand initially had a right posterior-lateral concentration of connectivity with some bilateral premotor and frontal coherence. In the final conditions, the LH group showed an anterior shift with a lot of connectivity over the midline motor, premotor and frontal regions projecting into the right hemisphere. RH experienced more of a posterior shift with an increased concentration in the right posterior parietal and occipital regions with the frontal activity shifting more into the premotor and motor regions. LH had a fairly stable degree distribution between conditions with the final RHn condition having the greatest. The clustering coefficient had a notable increase in the final RH conditions, both RHd and RHn. LH had an increase from LHd initial to LHd final, and then progressively declined with the final LHn condition showing the smallest.

The two groups executed the force matching task in fundamentally different ways as exhibited by the resulting maps of connectivity differences between the groups. In each of the frequency bands of interest, these findings were supported by the network metrics used to assess individual network properties. The clustering coefficient was interpreted as a measure of local stability, while global efficiency reflected the need for global integration. For the dominant hand

conditions (LHd and RHd) the clustering coefficient increased with trial progression from early to late in the theta, mu, and beta bands. In the non-dominant conditions (LHn and RHn) clustering coefficient decreased in the theta and mu band for LHn but increased from early to late in all bands for RHn and LHn mu. The adaptation between early and late trials suggest progressive skill acquisition, highlighting the impact of hand dominance on fundamental neurological patterns.

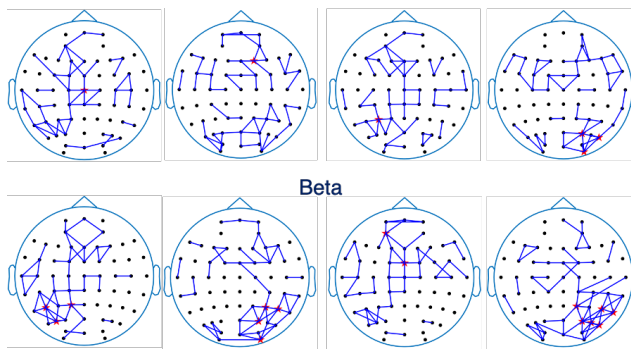


Figure 2.4: Beta band cortico-cortical coherence left- and right- hand dominant difference maps for early and late trials within dominant and non-dominant hand conditions.

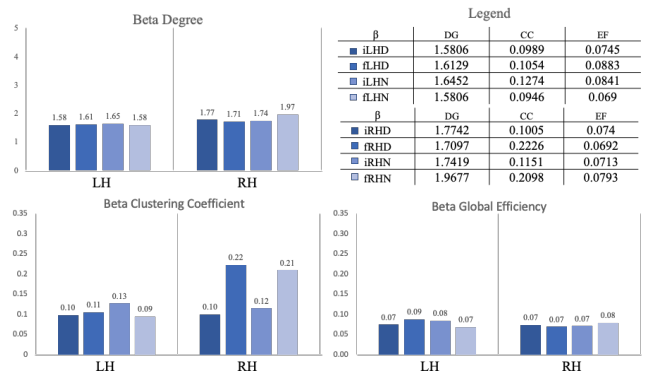


Table 2.4: Beta band graph network metrics.

DISCUSSION

In the present study, the developing communication strategies between left- and right- hand dominant individuals executing a dynamic force tracking task guided by visual input were examined and compared. Subjects completed 10 trials, using first their dominant hand to modulate a cursor via dynamic force output, and then their non-dominant hand. The organization of the trials was intended to promote learning (Wolpert & Flanagan 2010). The first three trials were averaged as an early representation of motor strategy, and the last three trials were averaged to represent their developed strategy after skill acquisition. Communication pathways were

determined using corrected imaginary coherence, and results are displayed as neural connectivity maps that highlighting statistical differences found between groups, trials, and conditions.

Previous work has shown left- and right-hand dominant individuals to exhibit differences in activation patterns when observing a task, as well as when making an action response to images regarding hand orientation. Those differences could be simplified into hemispheric or anterior-posterior differences, respectively. The findings presented in this study found the population differences in a dynamic motor execution task to did not follow those found in the observation based studies. The data suggest that the initial strategies between hand dominant groups differed and that as the trials progressed and cortical reorganization occurred, the groups' strategies remained distinct. The hypothesized increased clustering coefficient for LH was not as straight forward nor was the hemispheric signal segregation that would enable a general statement regarding cross hemispheric activity and global efficiency. With the exception of beta, which remained stable, LH did experience decreased degree with the progression of trials within condition seemingly indicating a progressively optimized strategy. RH did not mirror that trend.

LH PROVE TO BE MORE ADEPT AT USING NON-DOMINANT HAND AND SKILL ENCODING

Both groups showed evidence of attending to the task with frontal midline theta activation in the early trials (Caplan et al 2003). Localized theta activity in this area extending into the lateral prefrontal regions has been associated with error detection and general action monitoring (Devinsky et al 1995). The LH early trials general dispersion over the frontal lobe regions consolidating with task repetition indicate either decreased error or increased monitoring efficacy. While present throughout, the late LHD conditions had particularly concise activation over the medial frontal cortex indicating a shift out of working memory, evidence of positive skill progression. There is a slightly more anterior frontal focalization for RH, particularly in the

early RHd and late RHn trials indicative of ongoing goal directed behavior and memory maintenance.

We hypothesized that theta band connectivity would decrease with the progression of the trials, which would be marked by a decreased degree. This was true for the LH group across the conditions as well as RHd, but not so for the RHn condition. From this we can say that the LH group was able to acquire the necessary motor plan needed to successfully complete and encode the motor task. The diminished degree supports this, as does the decreased global efficiency values between the initial and final trials across conditions. The slow oscillation of theta allows for the long range integration of information, and it appears that the information was able to be applied regardless of the condition. The decrease in the global efficiency between the early dominant and non-dominant conditions suggests the LH group shared a motor plan between the two hands. This pattern is repeated in the opposite direction for the clustering coefficient, with a progressive increase suggesting an increasingly refined, stable pattern requiring less effort until the behavior becomes habitual and the theta band degree, global efficiency and clustering coefficient reach a minimum. This was not seen for RH, in fact they reach maximum measures of degree, clustering coefficient, and global efficiency by the final trials. The network metrics and connectivity patterns reflect a cognitively demanding task with enduring error monitoring, memory maintenance, and global and local integration. The rate of skill acquisition appears to be different between the two groups with the RH group unable to adapt to the use of their non-dominant hand as effectively as their LH counterpart.

LH & RH USE DIFFERENT STRATEGIES TO EXECUTE THE VISUALLY GUIDED MOTOR TASK

The visual nature of the motor task was expected to elicit parietooccipital projections, a pathway with known visual-spatial function. The parietal cortex has a particular role in sensory

control of action coupled with activation of the occipital lobe, indicates an ongoing visual guided action (Goodale & Milner 1992). Both groups were expected to present with the pattern, with a more bilateral involvement for the LH and a lateralized connectivity pattern in RH. None of the bands presented as forthright as this, the two groups appeared to utilize completely different pathways to encode and execute the task.

The nearly consistently expressed hub at the temporal-parietal junction for the RH group, highlighted a region responsible for integrating sensory information and relating that to where the body is in space, or in this case how force output modulates the cursor (Blanke & Arzy 2005). The frontoparietal extension seen in the theta and mu bands for the RH group suggests the transfer and integration of spatial information mediating the organization and maintenance of working and episodic memory (Cavanagh & Frank 2014). The RH group exhibited the classic activation patterns with known goal directed spatial encoding functions (Hutchinson et al 2009).

Alternately, the LH group strategy can be simplified to preferential use of the ventral stream with some additional support of the dorsal stream showing left lateral to left midline activity within all bands. This pattern is typically associated with transmitting visual information to the temporal lobe, often relaying highly processed descriptive information. This is indicative of a strategy that heavily relied on the visual information of the location or route of the target on the screen to dictate the motor action (Nolte et al 2004). With repeated task execution, the visual information became less influential, as seen by the decreased projections from the occipital lobe and a shift toward the midline. This likely reflects utilization of the dorsal stream, responsible for the decoding of spatial properties related to positional relations, motion direction, and speed of movement.

These findings provide evidence that hand dominance influences strategies used to encode visual information necessary for hand motor output. The RH group utilized a right lateral pathway, a strategy that mediating the organization of working memory incorporating multiple items of information and memory maintenance while LH group relied on visual information to develop a strategy fit to the task. While both groups showed a preference for distinct visual pathways, they were not the sole networks used.

HAND DOMINANCE INFLUENCES SENSORIMOTOR INTEGRATION STRATEGIES

The mu band, encompassing sensorimotor communications exhibited diverging coherence patterns between, as well as within groups and conditions. LHn presented with very distinct frontal lobe connectivity patterns. The frontal lobe is characterized by robust hemispheric specialization beyond the classic distinction between linguistic and nonlinguistic processes. The right hemisphere is critical for dealing with novel cognitive situations, while the left hemisphere is engaged for processes mediated by well routinized representations and strategies (Goldberg et al 1994). Therefore, the early LHn strategy appears to have called upon the strategies developed in the dominant hand conditions but adopted a unique strategy in the later trials. A hub located over the right inferior frontal projecting to the medial motor areas and lateral parietal lobe suggests the task was evoking cognitive effort regarding the planning of hand actions (Dippel & Beste 2015, Hartwigsen et al 2019). This region has also been found to encode response inhibition during motor execution, acting as a brake for actions (Aron et al 2014). This is interesting as the motor task required gradient increases and decreases of force. The controlled force output was not an on-or-off task, thus requiring constant control.

The mu band pattern for RH was the most bilateral pattern we had hypothesized to see for LH. Early RHd had strong motor strip connectivity, spanning its length. In the late trials the

communication extended anterior and posteriorly. The purpose of the strategy progression is unclear. The use of non-dominant left-hand evoked bilateral anterior strategy when executing the early trials with a left hemisphere slant while late trial had a very lateralized occipital-temporal bilateral pattern.

Neurons able to recognize actions have been recorded in primates in area F5 (area PMv) (Murata et al 1997, Rizzolatti & Arbib 1998, Rizzolatti et al 1998). These mirror neurons are highly active when a monkey manipulates an object and when viewing grasping and manipulation. Additional evidence has revealed that these neurons are highly selective for representing sounds and visual input of particular actions (Keysers et al 2003, Kohler et al 2002). The LH final non-dominant pattern, showing almost exclusive connectivity from the inferior lateral temporal lobe extending posteriorly and medially to the motor regions, suggests the use of this pathway. The grasping and manipulation task used visual information to represent an action suggests LH group developed some sort of mimicking strategy for the use of the non-dominant hand.

DIFFERENTIALLY ADAPTABLE MOTOR PROGRAMS ARE DETECTABLE ON A 10-TRIAL TIME SCALE

The beta band did not show the ipsilateral hemisphere activity that was expected for the unimanual motor task, although it is important to reiterate that the results highlight statistical differences of neural activation patterns between the groups within a condition, trial, and band. That is to say if, for instance, one group showed uni-hemisphere activation while the other group showed a similar bilateral-hemisphere pattern, the active hemisphere for both groups would show nothing, as they presented similarly. That being said, the beta band activity did reveal premotor and motor strip exhibited activation, as would be expected. Beta band activity is most influential during the times before and after the motor task, synchronizing throughout the task

execution providing a stable representation of state (De Lange et al 2008, Koelewijn et al 2008), . This indicates that the change in communication patterns between the trials and conditions within the beta band are significant indicators of a flexible motor plan. We suspect that the beta band activity during the period between the trials would show significantly different patterns as the motor plan is updated based on the errors detected thought the trial.

CONCLUSION

Many studies have examined functional regions of the brain in motor tasks, however, few have included left-hand dominant individuals. While the study does shed some light on how the two populations differ, it more so highlights the unknown and validates the inclusion of this population thereby warranting further study.

RH group does appear to rely on a strategy that enforces local stability, seen in the increased clustering coefficient for all final trials across all bands. This strategy appears to be adopted with practice and was not transferable across conditions. LH group appears to have greater success in skill transfer showing a progressive increase in clustering coefficient that continues after the shift from dominant to the non-dominant condition with the final condition having a marked minimum, in the theta and beta bands. This was interpreted as an expression of the successful acquisition of the skill, no longer requiring ongoing error monitoring or requiring the stability afforded by local interconnectedness. This pattern was not present for the mu band activity and, in conjunction with the temporal lobe connectivity profiles, suggests that LH relies heavily on high level sensory integration, potentially drawing from internal representations and past motor plans to inform current strategy's motor output pattern.

CHAPTER 3. Aim Two: Neurobehavioral Indicators of Hand Dominance

INTRODUCTION

The process by which the brain coordinates the muscles and limbs involved in the execution of a motor skill requires continuous, cooperative interaction between the central nervous system and the musculoskeletal system. The descending efferent and ascending afferent signal exchange form the sensorimotor loop which can be modeled using electroencephalograph (EEG) and electromyography (EMG) data. From the two signals, cortico-muscular coherence can be calculated and used to inform interpretations of the information exchange, representative of sensorimotor transformations.

Activity does not simply propagate from cortex to muscle, afferent information is required to implement, initiate, and complete a motor action (Baker & Baker 2003). The neural commands that are surmised to embody motor output are derived from sensory inputs. Sensory inputs include information regarding the environment and our body in it. Voluntary movements require progressive sensorimotor transformations arranged in a hierarchal manner. Higher processing levels formulate action goals, where the method of implementations falls to lower levels (Kandel et al 2000). The motor cortex regulates muscle activity, transmitting impulses along the corticospinal pyramidal tract. The corticospinal pathway is a collection of axons predominately extending from the cortical motor areas to alpha motor neurons, which in turn innervate a muscle. As such, the corticospinal pathway is responsible for initiating and modulating outflow for voluntary control of the body (Vanderah & Gould 2015). Continuous, direct, and precise brain-muscle communication is necessary for successful movement. The relationship between cortical activity and muscular activations can be represented by the oscillatory properties of the brain signals (EEG) coupled with muscle activations (EMG).

Cortico-muscular coherence (CMC) denotes the temporal correlation between spatially distinct neural networks and muscle activation, within distinct frequency bands. Physiologically, CMC provides insight into the mechanisms of cerebral control of muscle activity (Sheng et al 2019).

Movement and task demands have been shown to modulate CMC. Functionally, EMG can be used to capture the signals transmitted between the cortex and the muscles to provide an estimate of the magnitude of the correlation between specific frequency components in the two signals (Farmer et al 1993, Farmer et al 1997, Halliday et al 1998). The continuous processing that facilitates sensorimotor integration involves the motor system and sensory afferents, enabling the preparation, execution, and improvement of motor actions, both gross and fine. The process is a net result of the central nervous system integrating information coming from multiple sensory modalities, allowing for the performance of specific goal directed tasks (Lattari et al 2010). Interpreting cortico-cortical and cortico-muscular patterns of coherence provide context to the behavioral outcomes, enabling inferences related to signal intention and meaning (Andrykiewicz et al 2007, Patino et al 2008).

The following study used a dynamic grip force task guided by visual input to elucidate strategy development in left- and right-hand dominant individuals, as determined by the Edinburg Handedness Survey (Oldfield 1971). The left-hand dominant demographic is underrepresented in the scientific literature related to motor control. It was historically believed that left-hand dominant individuals would neurologically present as mirror opposites of right-hand dominant individuals. More recent research has revealed neurological differences between the populations, therein overturning the previous assumptions of hemispheric chirality. If neural activation patterns do not present similarly, then is it fair to assume behavior will? During the

bimanual force matching task, cortico-cortical and cortico-muscular patterns were recorded in addition to monitoring the behavior through error magnitude of force output.

Previous work has shown left-hand dominant individuals to respond with bilateral activation when observing images of left and right hands executing an action compared to right-hand dominant individuals, who showed lateralized coherence pattern when observing the same motor action (Kelly et al 2015). Additional work has shown event related potential (ERP) differences between the two populations when asked to make a motor response identifying an image of a left or right hand (Whitter 2017). The left-hand dominant group presented with greater signal amplitude in the premotor and sensorimotor areas of both hemispheres, whereas the right-hand dominant group had a more rapid and stronger response in the anterior parietal lobe, bilaterally. The groups exhibited no differences in motor response time which has been used as an index of perceptual processing and motor preparation (Buckingham et al 2010). However, behavioral differences have been found between the two populations, beyond innate hand preference. A study recording grip strength found right-hand dominant participants to have a distinct strength discrepancy between dominant and nondominant hands, a discrepancy not found in the left-hand dominant participants (Petersen et al 1989). More intricate analysis has found right-hand dominant groups to express differences between hands but as mentioned previously, left-hand dominance is usually cited as an exclusion factor for research participation. It remains unknown if right-hand population findings regarding motor control programs are transferable to left-hand dominant individuals (Buckingham et al 2010, Sherwood 2014, Walker & Perreault 2015).

This study was part of a larger investigation into differences between left- and right-hand dominant motor control strategies. As described above, an examination of the data from Aim 1

found unimanual differences in connectivity patterns (McDonnell & Mizelle 2019). Those patterns, as described by graph theory metrics, found the right-hand dominant group relied on a strategy that enforces local stability, seen in the increased clustering coefficient for all final trials across all bands. The right-hand strategy was mostly focused on visual input and appeared to be refined with practice but did not transfer from dominant to nondominant hands. The left-hand dominant group appeared to have more success in skill transfer between hemispheres, with a progressive increase in clustering coefficients that continued after the shift from dominant to non-dominant conditions. It was further observed that final trials had a marked minimum in the clustering coefficient in the theta and band bands, expressing successful acquisition of the skill. Thus, the left-hand dominant group no longer required ongoing error monitoring and took advantage of the stability afforded by local interconnectedness. This pattern was not present for the mu band activity, however, this band in conjunction with the temporal lobe activity seen in the left-hand dominant group, indicated a reliance on high level sensory integration potentially drawing from internal representations and past motor plans to inform the current motor output pattern. Looking within the same frequency bins (theta, mu, and beta) we hypothesize that these trends will continue with the bilateral task of Aim 2. We hypothesize the right-hand dominant group would rely on visual input and local interconnectedness seen with an increased clustering coefficient between trials. We further hypothesize the left-hand dominant group would rely on the ventral and dorsal streams and will employ a global integration strategy reflected by global efficiency values that would decrease with skill progression and decreased error magnitude.

The performance of a goal driven dynamic force task is generally accepted to require direct spinal projections from the primary motor cortex (M1), with additional corticospinal projection stemming from the premotor (PMC) and supplementary motor areas (SMA) (Chen et

al 2013). This is supported by the characteristically prominent beta band activity present during tonic contractions that are attenuated just prior to, and throughout voluntary movement (Engel & Fries 2010). It has been suggested that during movement, beta activity promotes postural and tonic contractions at the cost of the generation of new movements,(Gilbertson et al 2005, Pogosyan et al 2009). Oscillatory activities at the cortical level are mechanistically involved in determining motor behavior; thus beta will be evaluated throughout a dynamic, goal directed grip force task (Joundi et al 2012). This study specifically focused on differences between groups using coherence between EEG and EMG. Resulting cortico-muscular coherence maps were used to highlight hemispheric discrepancies as well as anterior-posterior activations rather than showing motor strip activations which would be present in both groups (Chen et al 2013). Based on previous work, we hypothesize that the left-hand dominant group will present with more anterior motor region connectivity and the right-hand dominant group would show a more posterior pattern in general, specifically in parietal and occipital regions. Error is hypothesized to decrease with the progression of trials in both groups. However, based on the results from Aim 1 showing the left-hand dominant group to have decreased theta activity in the later trials, we hypothesize that this group will show a greater decline in error. For the decline in error between trial bins we expected to see concurrent CMC adjustment reflective of improved tactics.

Methodology

Subjects & Experimental Design

Eighteen left-hand dominant (8 female 10 male) and eighteen right-hand dominant (13 female 5 male) individuals aged 18-35, scored based on the Edinburgh Handedness Inventory (Oldfield 1971), participated in the study (table 3.1). Those with a recorded handedness score between ± 40 were considered ambidextrous and excluded from the analysis. Participants self-

reported as healthy and had, normal or corrected-to-normal, vision. Experimental procedures were approved by the East Carolina University IRB (UMCIRB 17-002599). Informed consent was obtained from all participants before participation.

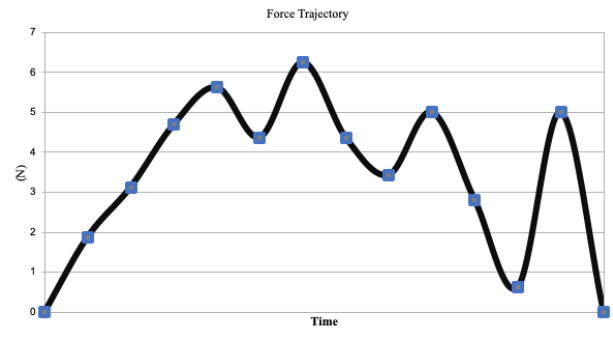
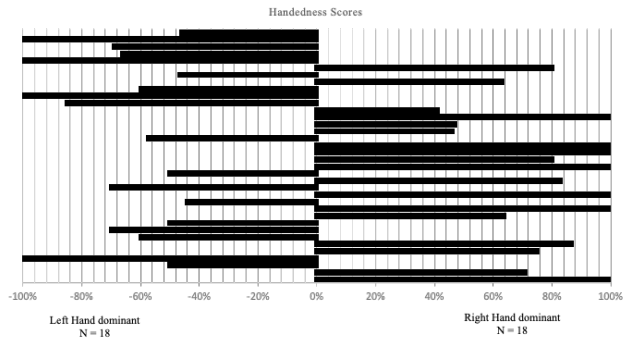


Figure 3.1: Target force trajectory with points of mandatory cursor contact marked with squares.

Table 3.1: Handedness score for participants based on Edinburgh Handedness Survey. Scores between ± 40 were considered ambidextrous and excluded from analysis.

EEG was collected during a visually guided, bimanual handgrip force modulations tasks. A 5' x 3' monitor displayed a target moving along a repeating trajectory. Subjects were instructed to use handheld force scales (Innovative Sports Training, Chicago, IL, USA) to control a cursor, also displayed in real time, and attempt to keep the cursor within the target. The magnitude of force output correlated with the distance from the origin, as the target moved further away from the origin more force was required to keep the cursor within the target. Each hand was responsible for either the horizontal or vertical trajectory of the cursor, with equal input required to maintain contact with the target. Half of each population used the dominant hand to control horizontal motion while the other half control vertical motion with the dominant hand. Target force range fell between the range of 0-6.25 N moving at a constant rate [fig. 3.1]. The force trajectory pattern duration was approximately 21 seconds, with the target moving at a pseudo constant rate, meaning that along the trajectory the cursor needed to obtain contact with

the target (marked on fig. 3.1 with squares). This was to ensure that the participants were in fact completing the task. Subjects completed 10 trials with a six second rest period between each trial. These data were collected following the completion of unimanual trials as reported previously in Aim 1 (McDonnell & Mizelle 2019). EMG was collected from bilateral brachioradialis (br) and flexor carpi ulnaris (fcu) throughout the task.

DATA ANALYSIS

EEG data were collected at 1 kHz using a 64-channel cap (Compumedics Neuroscan, Charlotte, NC, USA) placed on the scalp in accordance to the international 10 – 20 system with impedance kept below 10 k Ω . Continuous EEG data were exported from the acquisition software (CURRY 7; Compumedics Neuroscan, Charlotte, NC, USA) and preprocessed with the EEGLAB toolbox (Delorme & Makeig 2004) and then analyzed with proprietary Matlab software (The Mathworks, Natick MA, USA). Data were cleaned using high (1 Hz) and low (40 Hz) pass filters for the cortico-cortical and cortico-muscular analyses. Data were linear detrend and referenced to the average of the montage. Automatic subspace reconstruction was used for the removal of ocular and muscular artifacts (Mullen et al 2013b). A Laplacian transform was applied as a spatial filter (Kayser & Tenke 2015) to reduce the potential of artifacts related to volume conduction. During recording, events were marked using an outgoing voltage pulse that was triggered with a conditional force and target threshold (if <3 V & target $\neq 0$) marking the beginning and end of each trial.

The cortico-cortical data was further processed using a time-frequency wavelet decomposition performed on each trial of 21.875 seconds, downsampled to 250 Hz. The wavelet parameters were as follows: cycle range 3-12; minimum and maximum frequencies were set at 1 and 40Hz, respectively. The complex cross-spectrum were then calculated for each of the 62

channels yielding a symmetrical adjacency matrix describing the correlation between all electrodes at each time point at each frequency from 1 through 40Hz. The first three trials for each group (left hand dominant [LH] and right hand dominant [RH]) were averaged to represent the early condition while the final three trials (8:10) were averaged to represent the late condition. The corrected imaginary coherence between all channel pairs was then calculated from the complex cross-spectrum for each of the trial bins (early, late, and baseline) and conditions (Nolte et al 2004). A corrective factor was applied to the imaginary coherence to account for artificial suppression of connectivity values near true sources (Ewald et al 2012). The absolute value of the corrected imaginary coherence was taken and individual frequency bands of interest were extracted for the theta [4-7 Hz], mu [10-12Hz], and beta [12-30] ranges. Baseline data within each frequency band were used for frequency-specific normalization.

EMG was collected at 1kHz using Delseys EMG sensors (Delsys Incorporated, Boston, MA, USA). The EMG data subjected to a 4th order Butterworth filter with a high (1) and low (100) pass filter with a notch applied between (50-60Hz). EMG data was not rectified due to the impact rectification has on the power spectrum and subsequent coherence analysis (Neto & Christou 2010, Yao et al 2007). Magnitude squared coherence (Eq. 5) was calculated using the Matlab function mscohere between the four EMG channels (d^{BR} , d^{FCU} , n^{BR} , n^{FCU}) and all 62 EEG channels. For Eq. 5, S_{xy} is the complex valued cross-spectrum of signals x and y, S_{xx} and S_{yy} are the complex valued autospectrum of signals x and y, respectively and \otimes represents the complex conjugation.

$$Eq. 5 \quad msCOH = \frac{|\Sigma(S_{xy})|^2}{\sqrt{(\Sigma(S_{xx}) \otimes (S_{yy}))}}$$

STATISTICS

No assumption could have been made about the underlying distribution of the data, thus a nonparametric permutation approach was taken. At the individual participant level, both corrected imaginary cortico-cortical coherence and magnitude squared cortico-muscular coherence were used to create a null statistical distribution, or a distribution that would be true if there was no dependence on specific channel pairs in the actual distribution of connectivity estimates. This was accomplished by randomly permuting electrode labels through 1000 permutations. A Fisher's Z-statistic map was then calculated (Eq. 4). A critical value ($t = 1.6449$ for $p < 0.05$) was then used to threshold the Zmap, removing values falling below the critical value. The Zmap was then used to mask the true connectivity matrix, leaving only statistically reliable connectivity values.

A similar statistical permutation process occurred at the group level for comparisons of interest. Thresholded individual adjacency matrices were concatenated for two conditions (i.e., LH and RH). The true connectivity difference was calculated as the difference of the means of the subject-specific connectivity matrices across conditions. The null distribution was then calculated as above, but both group and electrodes labels were shuffled through 1000 permutations. A similar process was used to calculate a Zmap of the condition differences, and the true difference matrix was thresholded to leave only connectivity values that were statistically reliable according to the permutation test. Each comparison yielded two difference matrices depending on the sign of the differences in the true difference matrix (e.g., Condition A > Condition B and Condition B > Condition A). The figures depicted can be assumed to reflect nonrandom relationship being twice thresholded against a statistical test.

Graph theory network metrics were calculated on the group cortico-cortical difference matrices for descriptive purposes. Degree was calculated by determining how many connections each of the electrodes made with each other. Hubs were defined as possessing a degree of 4 or greater. Clustering coefficient was calculated as the fraction of closed triangles among 3 nodes. Global efficiency was determined by finding the distance between each of the connected nodes. For each of the metrics, an average was taken for each of the groups, conditions, time, and frequency bins.

RESULTS

Left- and right-hand dominant individuals were observed while repeatedly executing a bimanual force matching task. EEG was used to capture and evaluate the brain as a dynamic system. By using the frequency content of the signal, connectivity was calculated and used to assess and compare the organizational behavior of the brain between groups and across time. Network measures of degree, clustering coefficient, and global efficiency were used to quantify the properties and behaviors of the networks. The addition of EMG data was used to calculate cortico-muscular coherence which was compared between the two groups to further explore the differences between motor plans as a function of hand dominance. Error was determined by the distance between cursor and target, with a bandpass the size of the cursor such that no error was recorded if the cursor was in contact with the target in any capacity. Skill acquisition was evaluated across the blocks of the trials, early and late.

The overall purpose of this study was to identify different patterns of cortical activation in left-hand dominant and right-hand dominant individuals when performing a visually guided dynamic force regulation task. Differences between LH and RH groups executing a motor task are clear when looking within theta [fig. 3.2, tbl. 3.2], mu [fig. 3.3, tbl. 3.3], and beta [fig. 3.4,

tbl. 3.4] frequency bands. Generally, the RH group utilized a much more visually driven strategy, whereas the LH group tended to rely on midline networks in addition to the left hemisphere ventral stream.

CORTICO-CORTICAL CONNECTIVITY

THETA [4-7 HZ]

The LH bilateral cortical coherence difference maps in the theta band showed anterior activation in the early trials, consistent with error monitoring functions. This general connectivity persisted into the later trials, although the pattern became less concise with increased lateral and midline activity which was additionally present in the early trials. The RD group had more posterior theta connectivity in addition to cross hemisphere motor area activity. While no concentrated connectivity over the SMA was seen for the RH early trials, the emergence of anterior midline frontal connectivity was seen in the final trials but extending posteriorly and laterally. The LH group showed strategy refinement with a decrease in degree from early to late trials (1.9, 1.74), and the RH group alternately increased degree both comparatively and between the two time bins (2.32, 2.39). Clustering coefficient increased for both groups from early to late (LH 0.07, 0.08; RH 0.15, 0.16), with RH having less change but a universally greater clustering coefficient. The RH group also had greater global efficiency values with a negligent change between trials while the LH group showed an increase in global efficiency (0.09, 0.11).

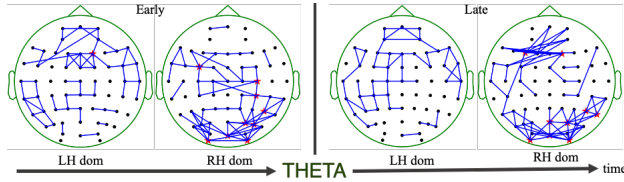


Figure 3.2: Theta band cortico-cortical coherence left- and right- hand dominant difference maps for early and late trials.

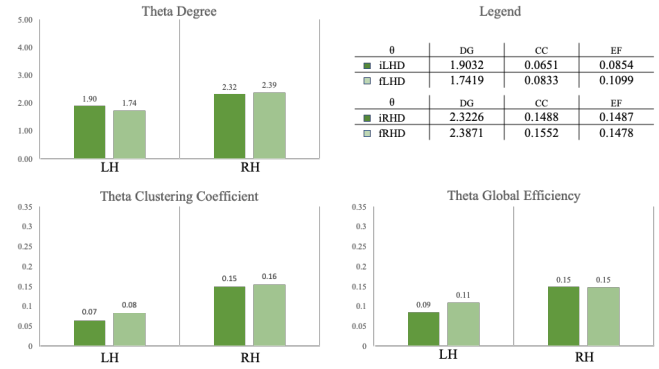


Table 3.2: Theta band graph network metrics depicted between left-and right-hand groups for early and late trials.

MU [10-12 Hz]

The Mu band was highly lateralized to the dominant hemisphere for the RH group, extending across into the right hemisphere. This pattern persisted with the progression of trial, degree decreasing slightly (4.1, 3.35). There was an additional decrease in global efficiency (0.31, 0.28) and an increase in the clustering coefficient (0.14, 0.17). For the LH group, a progressively sparser pattern emerged which was supported by the comparatively decreased degree (2.8, 2.6). The LH connectivity pattern extended along the lateral aspect of the left hemisphere, extending into the posterior parietal lobe with occipital lobe projections in the early trials. Midline connectivity was persistent throughout, but dense right temporal lobe connectivity emerged in the later trials. The LH patterns had an increased clustering coefficient (0.19, 0.23), following the same pattern as the RH group. However, as compared to RH, LH global efficiency decreased (0.14, 0.17).

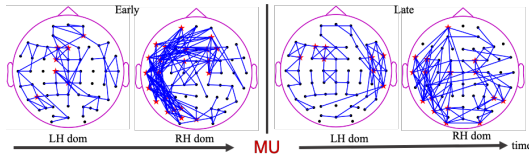


Figure 3.3: Mu band cortico-cortical coherence left- and right- hand dominant difference maps for early and late trials.

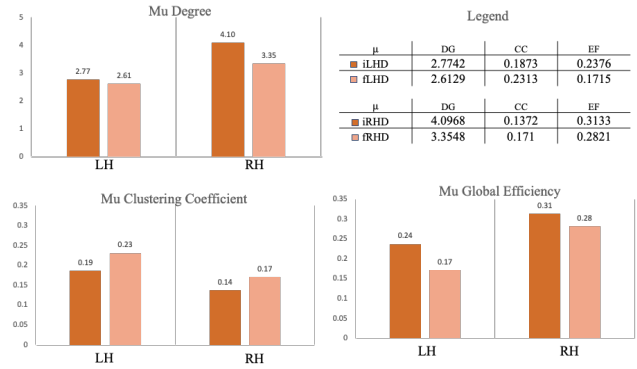


Table 3.3: Mu band graph network metrics depicted between left- and right-hand groups for early and late trials.

BETA [12-30 Hz]

Both LH and RH groups showed beta connectivity laterally along the motor strip. The LH group had a much more central focus for both early and late trials with hubs all aligning anteriorly, centrally, or just left of center. The RH beta pattern was much more focused over the bilateral occipital regions extending anteriorly. This pattern seemed to solidify with practice.

The network metrics all behaved in opposite directions between the groups. The LH group initially showed a comparatively greater degree that decreased with time (1.87, 1.84) and was surpassed by the final RH degree (1.74, 1.9). The LH group maintained a greater clustering coefficient value, which increased across trials (0.18, 0.2), while RH group's clustering coefficient decreased (0.15, 0.09). The opposite was true for the global efficiency with RH expressing a high value and increased (0.1, 0.12) while LH decreased (0.09, 0.08).

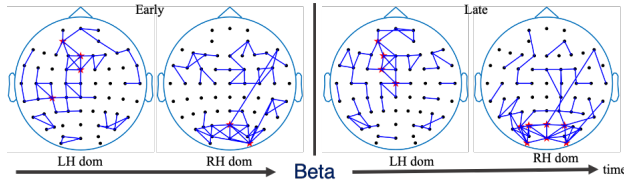


Figure 3.4: Beta band cortico-cortical coherence left- and right- hand dominant difference maps for early and late trials.

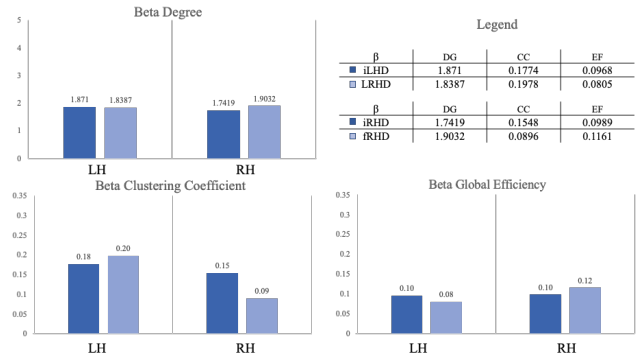


Table 3.4: Beta band graph network metrics depicted between left-and right-hand groups for early and late trials.

CORTICO-MUSCULAR CONNECTIVITY

Cortico-muscular coherence was calculated as magnitude squared coherence between dominant and non-dominant brachioradialis (br) and flexor carpi ulnaris (fcu) and the 62 EEG channels. Results are displayed as differences maps between the groups' dominant and non-dominant CMC (LHd, LHn, RHd, RHn) early [fig. 3.5] and late [fig 3.6] trial bins. The following sections will detail and discuss the findings within the beta band.

INITIAL BETA [12-30 HZ]

The left-hand dominant group exhibited no dominant brachioradialis (LHd^{BR}) CMC differences from the right-hand dominant coherence to dominant brachioradialis (RHd^{BR}). The RHd^{BR} did display differences in location and magnitude of coherence with dominant (left) hemisphere connectivity in addition to the central primary motor and posterior right lateral parietal connectivity that extended centrally but not much beyond the midline. RHd^{FCU} displayed a similar pattern of left lateral connectivity from frontal and occipital as well as midline motor areas. LHd^{FCU} shows a region of differential lateral frontal coherence at F3 over the anterior left frontal cortex. The muscles of the non-dominant limb appear to have more constrained coherence

for RH. RHn^{BR} exhibits left motor strip activation not extending into the parietal lobe in addition to midline motor coherence. LHn^{BR} has some central frontal as well as right frontal coherence as well as midline occipital and just off midline bilateral posterior parietal coherence. RHn^{FCU} again mimicked the brachioradialis, but with no lateral frontal activation, rather, having left lateral premotor (FC3) and midline (Cz) CMC. LHn^{FCU} shows increased right frontal lobe coherence extending beyond the midline with similar occipital lobe and bilateral, generally midline, parietal CMC.

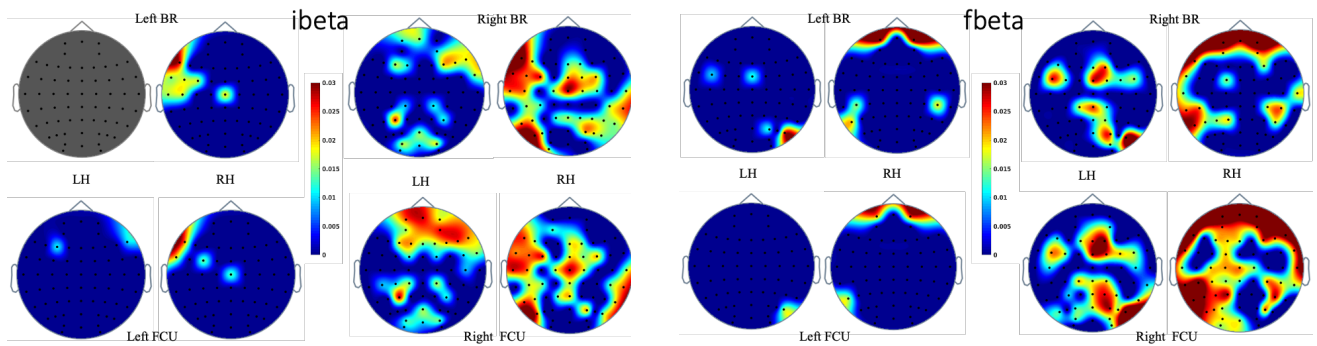


Figure 3.5: Early trials beta band cortico-muscular coherence left- and right- hand dominant difference maps between left arm brachioradialis and flexor carpi ulnaris (left) and right arm brachioradialis and flexor carpi ulnaris (right).

Table 3.6: Late trials beta band cortico-muscular coherence left- and right- hand dominant difference maps between left arm brachioradialis and flexor carpi ulnaris (left) and right arm brachioradialis and flexor carpi ulnaris (right.)

FINAL BETA [12-30 HZ]

LHd^{BR} expressed CMC with the frontal midline (FCz) and left (FC5) motor strip, and a region of the right parietal-occipital cortex showed coherence with LHd^{FCU}. Again, the RH group showed more cortical involvement with both RHd^{BR} and RHd^{FCU} CMC at anterior frontal regions, with connectivity extending laterally along the dominant hemisphere to the lateral parietal lobe as well as left premotor (FC1) for BR modulation. FCU showed bilateral connectivity extending into the parietal lobe with a left hemisphere extension to the occipital lobe extending back to the frontal lobe left of midline. LHn^{BR} and LHn^{FCU} showed a pattern of left lateral, a midline to right premotor CMC, as well as central parietal connectivity extending posteriorly to the right lateral occipital lobe. RHn^{FCU} and RHn^{BR} showed left lateral parietal occipital coherence.

BEHAVIOR

Error was significantly diminished with the progression of trials [fig 3.7] for both groups, with the LH group having less error in the initial and final trials compared to the RH group (median mean and integral values displayed in [tbl. 3.5]. When error was assigned to a hand based on target horizontal or vertical position, it was observed that both LH and RH groups produced less error with the left hand, with the right hand generating altogether more error regardless of dominant or non-dominant hand status.

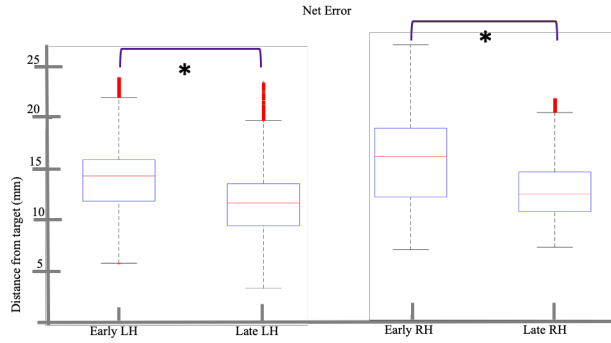


Figure 3.7: Left- and right- hand dominant error early and late trials.

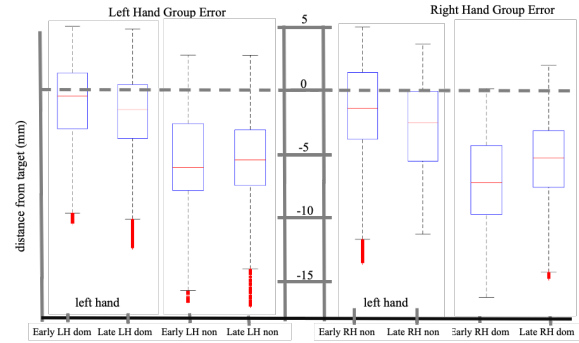


Figure 3.8: Left- and right- hand dominant error as assigned per hand, significant comparisons marked on table 3.8 for visual clarity.

			median	mean	integral
	*	i LH dom	-0.46	-0.4646	5.61E+04
	*	f LH dom	-1.60	-1.5980	6.65E+04
		i LH non	-6.70	-6.7003	5.61E+04
		f LH non	-6.38	-6.3846	6.65E+04
*	*	i LH	14.31	14.3144	5.61E+04
*	*	f LH	12.41	12.4091	6.65E+04
*					
		i RH dom	-6.82	-6.8158	1.56E+05
	*	f RH dom	-4.96	-4.9643	1.20E+05
	*	i RH non	-0.83	-0.8265	1.56E+05
		f RH non	-2.14	-2.1393	1.20E+05
	*	i RH	15.33	15.3284	1.56E+05
		f RH	12.21	12.2089	1.20E+05

Table 3.5: Average group by condition error values with significant comparisons denoted with '*'.

In sum, the two groups expressed different patterns of neural communication used to complete the goal driven motor task. Cortico-cortical and cortico-muscular coherence patterns were additionally modulated with task repetition. These modulations were additionally reflected in the task performance, with error magnitude diminishing with task repetition.

DISCUSSION

In the present study, cortico-cortical and cortico-muscular communication strategies in left- and right-hand dominant individuals developed while executing a dynamic force tracking

task guided by visual input were examined. Performance was assessed by error magnitude measured by the distance between a cursor and a target. It was hypothesized that the left-hand dominant group would present with greater cortico-cortical coherence throughout anterior motor regions as opposed to a more posterior parietal-occipital pattern in the right-hand dominant group. These hypotheses were generally supported, although connectivity patterns are more intricate than that. Error was expected to decrease with the progression of trials, which was found to be true. Theta connectivity was hypothesized to decline as error magnitude declined, which was not found to be the case. Cortico-muscular patterns were found to be different across groups and reflected strategy development by way of altered coherence between early and late trial bins.

CORTICO-CORTICAL CONNECTIVITY

Theta band activity is typically thought to be of cingulate gyrus origins with a midline, anterior frontal distribution, and a role of error monitoring and memory encoding which is present for the LH group. The pattern is particularly concise in the early trials, emphasized with the presence of a hub. The connectivity was not confined to the frontal lobe but bilaterally extended posteriorly along the lateral temporal cortex. This pattern persisted with continued task repetition. The later trials showed an increase of global efficiency and clustering coefficient, reflective of increased global and local interconnectedness. This pattern is not consistent with our prior work examining unimanual task execution in Aim 1. It is possible that the bimanual task requires more practice, but based on the decrease in degree and the general posterior signal shift, a unique strategy does appear to be developing. This is supported by a decrease in error across the trials. The dual increase in clustering coefficient and global efficiency, as well as the error variability (fig. 3.7, 3.8), suggests that more trials would have resulted in further strategy

development which would have resulted in a decrease in theta band clustering coefficient and global efficiency.

Theta band pattern in the RH group does not initially present with a typical error monitoring distribution but has a more posterior presence. The slow oscillation of theta enables long range integration, which is supported by global efficiency values, both early and late. The RH strategy did evolve as the late trials showed anterior, midline frontal connectivity consistent with the error monitoring necessary for task improvement, which was evident with a decline in error. However, the posterior occipital, occipital parietal focus, and density, as seen by the multiple hub locations suggest that the strategy was reliant on visual integration and long-range communication. Based on theta coherence patterns it appears as though the task continued to be difficult, requiring the involvement of multiple brain regions and continuous cognitive effort to successfully execute the force matching task.

Based on the theta patterns for both groups the task required considerable effort and integration. Mu frequency has been cited as a band with integrative functions (Mullen et al 2013b). The patterns of integration between LH and RH groups are distinctly different, although here they follow similar network trends between early and late trials. The RH group has a strong dominant (left) hemisphere involvement. The bilateral extension occurs predominately anteriorly in early trials. The relative density of the bilateral connectivity implies information redundancy. Later trials had a posterior shift in cross-hemisphere communication and the dispersal of the hubs seems to suggest an improved strategy that is based on using the dominant hemisphere to assign control properties for both limbs. The increased clustering coefficient is consistent with the unimanual findings, suggesting the RH group employs a strategy of local interconnectedness to resist perturbation and increase the stability of signal transfer.

The coherence patterns in the LH group were generally more bilateral. The early trials had a particularly central focus with dual, lateral hemisphere connectivity. The final trials maintained the central involvement with dual lateral activation; however, they did seem to adopt the dominant (right) hemisphere control pattern seen with the increased right lateral frontal / anterior temporal connectivity activity and hub development. Based on degree it would seem the LH group used a comparatively more efficient integration strategy, which was not as strongly based on visual information.

Beta band activity shows the RH group consistently utilized occipital and occipitoparietal connectivity, which appears to increase with task repetition as seen by the bilateral addition of hubs. Motor strip activity decreases, shifting posteriorly. The clustering coefficient decreases while global efficiency increases, suggesting a strategy of visual processing and concise motor involvement was developed by the conclusion of the task. The LH group had much more premotor connectivity in addition to central and posterior involvement. Additionally, the right posterior parietal distribution of coherent beta activity was consistent from early trials to late trials, and with the addition of the cortico-muscular coherence data suggests an integration zone for outgoing motor commands.

CORTICO-MUSCULAR CONNECTIVITY

Cortico-muscular coherence was evaluated from two dominant arm and two non-dominant arm EMG sensors placed on the brachioradialis (BR) and flexor carpi ulnaris (FCU). Coherence was calculated from the onset of each trial as magnitude squared coherence. Over 21-second trials, participants used handheld force scales to modulate a cursor on screen coinciding with force output. The goal of the task was to keep the cursor inside of the target which continuously moved at a constant rate, increasing and decreasing force necessary for successful

tracking. Prior work has found prominent beta band activity to be attenuated during a voluntary tonic contraction with some suggesting that the synchronization during the task prevents real time adaptation (Engel & Fries 2010, Gilbertson et al 2005, Pogosyan et al 2009) ,. Thus, the beta band cortico-muscular coherence patterns potentially represent strategy updates based on prior trial experience. The CMC patterns differ between groups and trials, supporting the cortico-cortical findings of the two groups behaving with neurologically distinct mechanisms.

Cortico-muscular communication strategies to the left-hand were very similar between groups. In fact, the LH group showed no difference in BR CMC and a small F3 and F8 localized FCU coherence. The RH group, however, showed differential left lateral dominant arm BR and FCU CMC connectivity extending along the ventral stream from the occipital to the frontal lobe. Additionally, midline motor regions, including the premotor, primary motor, and somatosensory region, were coherently active with the addition of the right parietooccipital junction for FCU and BR. The strategy is refined in the later trials to predominantly left lateral and bilateral temporal-parietal connectivity extending centrally. The RH group had surprisingly high anterior frontal coherence values in the later trials, which is speculated to reflect frustration rather than neurological activity. Further, a furrowed brow would generate significant noise in the data. The bimanual task proved to be challenging and the RH group, not often asked to include their non-dominant left hand in any activity, and may have experienced greater frustration at the ongoing effort of completing the task.

The LH, right non-dominant arm CMC pattern involves the right inferior temporal and lateral frontal lobe regions previously seen to be utilized in this group in the cortico-cortical connectivity patterns utilizing non-dominant limb in the final trials. It was concluded that this was reflective of a mimicking strategy which would continue to hold true. Additional bilateral

central occipital and bilateral posterior parietal coherence was seen with both BR and FCU. The progression of trials results in BR and FCU distributed premotor coherence and midline somatosensory and posterior parietal coherence, weighted toward the right hemisphere. The posterior parietooccipital junction presents with a high magnitude of coherence in both BR and FCU late trials within the LH group. This activity was present for both left and right limbs, as well as in the beta cortico-cortical measure.

We suspect the LH group utilized the right hemisphere parietooccipital junction to integrate the peripheral information in addition to bilateral motor regions. The RH group appeared to also adopt this dominant hemisphere connectivity at posterior and lateral parietooccipital regions in the late trials. Additionally, the RH group appeared to rely on the ventral stream to encode the outgoing motor commands to the right limb, with some parietal lobe assistance. This brings to light a potentially interesting trend. RH group is consistently able to rely visual information, thus potentially employ efficient high-level integration strategies. Executing the task requires increased sensory integration, hence the involvement of the ventral stream. It is possible that the LH group cannot reliably use visual information to inform and generate actions. Given that left-hand dominant individuals are the heavy minority in the population, most visual information regarding task execution would require increased integration for successful sensorimotor transformation, as instruction would likely be tailored to or given by right-handed individuals. Thus the adaptation of a ventral stream strategy would be more effective for cortical visual processing (Goodale & Milner 1992, Tresilian 2012). Regarding motor output, visual information is a reliable source of feedback as to the success of a movement and is directly utilized for the generation and refinement of motor commands, seen with the LH occipital and parietooccipital CMC.

The confounding lack of CMC differences with the left limb, seen in both LH and RH groups, was corroborated with the error data. Both groups showed a decrease in error with the trials, but when the error was assigned to the responsible hand, based on the direction of error, both groups were found to have made less error with the left hand. This could potentially be explained with the origin of the experimental paradigm being on the left aspect of the screen and moving right, forcing a rightward bias in attention that extending to limb focus (Buckingham et al 2010). Alternately, it could represent a fundamental difference in strategy, one in which the RH group focused attention on mimicking the right-hand movements to the left-hand movements, yoking the left hand to the right, a strategy demonstrated within the mu band activity (Buckingham et al 2010, Marteniuk et al 1984). This strategy may have yielded a decreased dominant right limb performance but generated an overall satisfactory execution of the bimanual task. Conversely, the LH group, being more adept at skill transfer, focused attention on the control of the right hand in an effort to improve performance. Ultimately the strategy used to control the left limb did not differ between the groups and the performance of this limb between groups was greater.

CONCLUSION

Hand dominance is found again to yield fundamental neurological differences in motor behavior, and the two groups utilized different neural mechanisms to execute the bimanual dynamic force matching task presented in this work. The right-hand group adopted a strategy reliant on visual information and used their dominant hemisphere to canonically control non-dominant actions. The two groups however did exhibit similarities, as both groups utilized the dominant hemisphere lateral parietooccipital junction to integrate information utilized in motor control. Surprisingly, both groups exhibited a greater magnitude of cortico-muscular coherence

with the right limb. Behaviorally, both groups performed better with their right hand, seen with task performance. The findings indicate that either the cause or result, of handedness influences basic motor control strategies. The complex nature of the task likely accounts for the discrepancies found in this study and prior work examining left-and right-hand dominant neurological tendencies. Further work should continue to include left-hand dominant individuals.

CHAPTER 4. Combined Discussion

Structurally, hand dominance corresponds with a comparatively larger volume of the hand motor area contralateral to the dominant hand. Functionally, hand dominance indicates an innate asymmetrical preference for the use of one hand over the other. Neurologically, hand dominance results in organizational tendencies influencing fundamental interactions with the environment. The nervous system is shaped by experiences, driving learning, and yielding changed behavior. The continuous integration of sensory information, both about the environment and the current state of the body, is presumably used to determine the appropriate set of muscle forces needed to generate a desired movement or action. The coordination between the nervous system and the musculoskeletal system enables the sensorimotor plasticity that fosters adaptability. Sensorimotor integration is a multifaceted fusion of incoming signals condensed into one outgoing motor message. Hand dominance has been found to influence sensorimotor integration properties and processes.

Prior work has shown left- and right-hand dominant groups to differ in action observation, overturning a previously held assumptions of hemispheric chirality. The studies conducted for this dissertation built upon previous work, having left- and right-hand dominant individuals perform unimanual and bimanual motor tasks. The tasks were designed in such a way as to elicit learning. Given, however, that the tasks were completed consecutively, and learning implies a period of sleep (Huber et al 2004, Maquet 2001, Walker & Stickgold 2004), findings extrapolated only to strategies of skill acquisition. To this end, left- and right-hand groups (LH & RH) were found to rely on differing neural communication strategies, determined by cortico-cortical and cortico-muscular coherence. Network analysis based on graph theory principles was

applied to further describe the evoked patterns across groups (LH / RH), conditions (unimanual dominant/unimanual non-dominant / bimanual), and trials (early/late).

The progression of trials across conditions, from unimanual dominant to unimanual non-dominant, and then to bimanual hand use, revealed distinctive patterns of connectivity between left- and right-hand dominant groups that were revised with repetition. It would seem, based on the findings of these studies and the current state of the literature, hand dominance influences, or is influenced by, patterns of neural connectivity. Both groups exhibited altered coherence patterns indicative of skill acquisition, which was supported behaviorally through the reduction of error. The initial and final strategies of both populations highlighted the ways in which the variation of sensory information reshapes neurological organization.

While each condition (unimanual dominant and non-dominant, and bimanual tasks) has thus far been treated independently, the non-random organization of trials in this work was intended to provoke learning, mimicking the general strategies for learning. Specifically, here we focused on dividing a complex task into simpler subtasks to be learned independently (Ghahramani & Wolpert 1997). The dominant unimanual condition served as a period for structural learning in which subjects explore how to maximize information and assign error. Maintaining the structure of the task enabled skills acquired in the structural learning phase to initiate parametric learning. This technique has been used as a method to ‘speed up learning’ (Braun et al 2009, Sailer et al 2005a, Sailer et al 2005b, Wolpert & Flanagan 2010). Thus, the concluding section will address the cumulative findings across all conditions [tables and figures located in the appendix], bringing to light the differences in which left- and right-hand dominant groups progressively adapted to the demands of the sensorimotor integration task.

Specifically, neuromotor strategies are demarked using cortico-cortical and cortico-muscular coherence difference maps between left- and right- hand dominant groups (LH, RH). Graph theory based metrics were calculated to assist in describing and quantifying the differences in the observable network patterns between LH and RH groups. Degree was used as an indicator of network density and general cortical involvement. Hubs were defined as a degree with greater than or equal to four connections. The clustering coefficient represented local interconnectedness and global efficiency denoted global integration.

POPULATIONS RELY ON VISUAL INFORMATION TO A DIFFERENT EXTENT

Because the force matching task was guided by visual input, we naturally expected coherent cortico-cortical occipital lobe activity propagating anterolaterally to the parietal lobe, where neurons with known involvement in the processing of visual input and motion recognition, in addition to the critical function of processing motor commands, particularly those involved in hand manipulation and grasping movements (Andersen et al 1997, Rozzi & Coudé 2015, Sakata et al 1995) . In the RH group we observed precisely this, bilateral occipital to right parietal cortical projections. The pattern was consistent across bands, conditions, and trials, and a hub or multiple hubs in most cases were present. The pattern of cortical connectivity suggests the reliance on visual input to inform subsequent processing necessary for the formation and adaptation of an appropriate motor plan. Conversely, the LH group presented with comparatively sparse to absent occipital lobe involvement. Rather, the ventral stream was utilized as the primary mechanism for processing. The ventral stream is classically considered to serve as a site for transmitting highly processed, descriptive visual information (Goodale & Milner 1992). The LH strategy did not rely exclusively on visual input to guide performance of the task, a pattern

potentially adopted due to the generally unreliable nature of raw visual information. Being in the minority population, left-hand dominant individuals observing a task most likely being executed by, or with instruction geared toward, a right-hand dominant individual. Additional sensorimotor processing would be required to transform the visual information into motor cognition and eventually motor output. Over time, this pathway would become habitually utilized for visually guided motor tasks.

The cortico-muscular coherence patterns seemingly support the proposed, varied role of visual information between left- and right-hand dominant groups. LH group cortico-muscular coherence patterns displayed distinct occipital lobe involvement, interestingly, to a greater extent with the non-dominant right arm. Nonetheless, the LH group settled upon a motor strategy in the bilateral condition that involved the right hemisphere parietal-occipital junction. This suggests that visual information was used to monitor and update motor output, being a reliable indicator of movement success. The RH dominant group, however, predominately utilized the ventral stream. This could have been on account of the partial occipital network being occupied, or the use of the left hand required increased sensorimotor processing. In this respect, the two populations do present as opposites, but in unique ways not described by hemispheric equivalence. Rather, RH individuals rely on visual input to generate a motor plan and the ventral stream for sensorimotor transformation, monitoring, and adjusting the descending motor instructions. Conversely, LH individuals utilize the ventral stream for processing of visual information and generation of high level motor plans and use the resulting visual information for task feedback to inform subsequent motor adjustments. An additional similarity was found in the later trials, with cortico-muscular coherence from the lateral parietooccipital region of the

dominant hemisphere present in both groups (RH: PO7; LH: PO8). This is likely a result of the compulsory visual-spatial processing of the task.

THETA BAND HIGHLIGHTS DEGREE OF SKILL TRANSFER & DUAL OSCILLATION FUNCTION

The theta band is stereotypically associated with cognitive processing and error monitoring, as well as spatial and memory encoding. The relatively slow rate of theta band oscillations allows for long range transfer information, allowing theta to act as a global integrator. The role of theta has been partly determined by location, a frontal midline presence is reflective of error monitoring (Caplan et al 2003, Mizelle et al 2010), . The band is thought to originate from the cingulate, a midline structure that sits under the SMA (Niedermeyer & da Silva 2005). Thus, even the slow theta wave can have rapid local influence necessary for error detection and correction. The LH group presented with organized frontal midline activity in the dominant hand conditions. This activity progressively dispersed in the non-dominant hand trials, to focalize again in the early bimanual trials, before dispersing again with practice. The RH group presented with some anterior frontal midline connectivity in the unimanual conditions that decreased in the dominant hand late trials, a pattern not seen in the non-dominant condition. In fact, in the late trials for both non-dominant and bimanual conditions, frontal theta activity appeared to increase, signifying ongoing error monitoring. These patterns are indicative of the state of the task, with the LH group expressing comparatively greater successful task encoding, while the RH group demonstrated a continued reliance on the working memory.

The graph metrics of theta connectivity patterns provide additional insight as to the neural strategy differences. The LH group showed an alternating pattern of increasing and decreasing degree values between early and late trials. A similar trend is seen in the global

efficiency with initial trials having the greatest global efficiency value, decreasing, then increasing again for the initial non-dominant trials but remaining less than the initial dominant hand condition. The final unimanual trials had a minimum degree, global efficiency, and clustering coefficient. A progressive increase in the clustering coefficient occurred from the initial trial and condition to the final unimanual (non-dominant) trials. From this, it would appear that there existed a continued strategy progression from dominant, to non-dominant conditions. The motor plan was able to transfer and rapidly adjust to the non-dominant hand. By the final unimanual trial, theta band activity was neither needed for error monitoring nor global integration, as the task had been successfully encoded. The novel bimanual task elicited increased theta activity, although degree remained below the initial trials and condition as did global efficiency. While the clustering coefficient increased beyond initial trial and conditions but did not surpass the later trials (excluding the final non-dominant trial), suggesting the pattern was not yet stable and required continued local signal coherence to maintain success. It is possible that the more difficult bimanual task required more repetitions to successfully encode the task.

While the RH group in the initial dominant condition did not appear to drastically modulate network characteristics between trial bins, degree and global efficiency decreased slightly and clustering coefficient increased. The initial strategy was modestly refined. The following unimanual non-dominant condition initial trials had an increase in degree from the initial dominant hand trial, and an increase was seen also in the global efficiency. Here we can begin to speculate that the RH group utilized the theta band as a mechanism for sensory and motor integration. The final non-dominant trials showed a further increase in degree and global efficiency and a substantial increase in the clustering coefficient. This suggests, in conjunction

with the coherence patterns, that the strategy adopted by the dominant hand was not transferrable to the nondominant hand and required continuous cognitive effort required to complete the task, again supporting the continued reliance on working memory. In fact, the final non-dominant trials do not reflect any level of skill acquisition, as the RH group required continued local and global interconnectedness as well as ongoing error monitoring. Comparatively, it can be inferred the RH group had greater difficulty with the unimanual non-dominant condition.

SENSORIMOTOR INTEGRATION REVEAL HAND DOMINANCE INFLUENCE

The mu band is believed to serve an integration function in the transformation of sensory input into motor output (Pfurtscheller & Andrew 1999). Coherent activity coordinates high level abstract activity necessary for the organization of information and formation of a discrete motor plan. The differences between the groups reveal a preferential weighting of information. The progressive evolution of neural connectivity with practice again supports strategic progression and skill acquisition.

The RH group, with a generally increased dominant (left) hemisphere activation, suggests a reliance on the dominant hand for instructions. Even in the unimanual non-dominant condition, early trials had dense left hemisphere coherent activity, despite not using their right hand. With practice, a strategy more reliant on visual information was adopted. In the bimanual trials, a strategy of canonically controlling the non-dominant left hand with the dominant right-hand motor network persisted. The strategy was dependent on extensive cross hemisphere connectivity, seen visually as well as numerically with the extensive global integration values. Similar to the theta band activity, activity does not indicate that the task was fully acquired,

although a pattern of visual integration and motor strip activity appears to have been developing, perhaps trending toward a strategy utilizing the ventral stream.

The LH group appears to have a comparatively more economical strategy, requiring less whole brain involvement. The LH degree values all being lower than any RH condition or trial. The strategy appears to stay fairly stable, with ventral stream and central midline connectivity, with the late, non-dominant condition being the exception. In this condition a right anterior inferior frontal hub appears with posterior, lateral projections as well as projections medially to the midline motor and premotor regions. We suggested that this pattern was reflective of evoked effort regarding the planning of hand actions (Dippel & Beste 2015, Hartwigsen et al 2019). This region has also been found to encode response inhibition during motor execution, acting as a brake for actions (Aron et al 2014). This is relatable as the motor task required gradient increases and decreases of force. The controlled force output was not an on-or-off task, thus requiring constant control. While the final bimanual trials have an increased right anterior temporal lobe connectivity, it does not project in the same manner and likely is not reflective of the same strategy developed for the non-dominant hand conditions. The LH group did appear to have more skill acquisition success, with progressively increasing clustering coefficient values, again suggesting a transferable, flexible motor plan.

HAND DOMINANCE REVEALS UNCONTROLLED MANIFOLD PROPERTIES

Despite obvious neurological differences, the two groups behaved statistically similar. Both groups showed improved task performance, as seen by the decrease of error from the early to the late bimanual trials. When the direction of error was used to assign the error to the responsible hand, both left- and right-hand dominant individuals were found to produce greater

error with the right hand. RH group made significantly more error with their dominant right hand in both early and late trials compared to the LH group dominant or non-dominant hands. These data suggest that while neural strategies and individual components of a task may differ, the net effect can be the same. This motor equivalence, or degrees of freedom problem, is a long standing confounding factor in motor control (Bernstein 1966). Different movements, produced by either the same or different parts of the body, under the same or different internal and external conditions, are performed with incredible adaptability and consistency; a capability beyond the scope of human comprehension. We have established that hand dominance results in characteristic cortico-cortical and cortico-muscular differences that influence skill acquisition, and yet the net outcome is consistent behavior across groups. The uncontrolled manifold hypothesis postulates that the central nervous system permits variability as long as an outcome falls within an acceptable range (Latash & Anson 2006, Scholz & Schöner 1999). In this case, the outcome is performance, and individual input components such as neural organization, left or right hand, are flexible. It is interesting to see that performance of a wholly arbitrary task is prioritized over the strict regulation of canonical neuromotor parameters. I think it speaks to the human condition, when presented with a task the drive to succeed is optimized.

CONCLUDING CONCLUSION

With structure governing function and hand dominance imposing structural discrepancies, hand dominance was found to correspond with distinct functional neurological organization. The groups exhibited fundamental differences in how they interact with the environment. The right-hand dominant group was found to rely on visual information to inform and generate a motor plan where the left-hand dominant group used visual information as a

source of feedback to update motor behavior, relying instead on the ventral stream to generate a motor plan. The left-hand dominant group was found to have a more versatile motor plan, adaptable to dominant, nondominant, and bimanual tasks. Compared to the right-hand group it might be said that they were more successful in encoding the task, however behaviorally they performed the same. Further similarities included dominant hemisphere parieto-occipital cortico-muscular coherence and increased cortico-muscular coherences with the right limb potentially corresponding to the generally greater magnitude right hand of error. Although, this may have been a factor of the rightward bias of the task.

LIMITATIONS AND FUTURE WORK

The work contained limitations that should be acknowledged. Chiefly the task had an origin on the left aspect of the screen and moved right with increased force, imposing a rightward bias in attention that may have extended to limb focus. Along this vein, the task was not event related, thus event related dynamics could not be evaluated. Moreover is the groups were dictated by the Edinburgh survey, a crude measure despite it being an acceptable and widely used tool. The groups were also comprised of a relatively uniform population of predominantly students and university employees. More elemental limitations include the inherent limitation of EEG work in terms of spatial accuracy, the unknown influence of deep brain structures activity, and the unknown contribution of the cerebellum.

Although the work contained limitations, findings proved to be compelling and warrant continued research. Implications of these findings took a surprising turn, with the optimization of the neuromotor system preferentially tuned to minimize error. Further research will need to be conducted in order to explore this idea. More definite findings would solidify the two

populations' fundamental neurological differences that nevertheless allow for consistent behavior. One notable area for future work is related to their skill acquisition strategies and how they differ, which directly implies the motor learning process could be improved with a personalized approach based on neurological profiles. Findings have direct clinical and performance applications regarding motor rehabilitation and tuning. Knowledge of neurological tendencies and preferences allow for a productive and perhaps accelerated regime aimed at improving outcomes, be them medical or otherwise.

REFERENCES

- Adamovich SV, Fluet GG, Tunik E, Merians AS. 2009. Sensorimotor training in virtual reality: a review. *NeuroRehabilitation* 25: 29-44
- Adrian ED, Matthews BH. 1934. The interpretation of potential waves in the cortex. *The Journal of Physiology* 81: 440-71
- Amunts K, Jäncke L, Mohlberg H, Steinmetz H, Zilles K. 2000. Interhemispheric asymmetry of the human motor cortex related to handedness and gender. *Neuropsychologia* 38: 304-12
- Amunts K, Schlaug G, Schleicher A, Steinmetz H, Dabringhaus A, et al. 1996. Asymmetry in the human motor cortex and handedness. *Neuroimage* 4: 216-22
- Andersen RA, Snyder LH, Bradley DC, Xing J. 1997. Multimodal representation of space in the posterior parietal cortex and its use in planning movements. *Annual review of neuroscience* 20: 303-30
- Androulidakis AG, Doyle LM, Gilbertson TP, Brown P. 2006. Corrective movements in response to displacements in visual feedback are more effective during periods of 13–35 Hz oscillatory synchrony in the human corticospinal system. *European Journal of Neuroscience* 24: 3299-304
- Andrykiewicz A, Patino L, Naranjo JR, Witte M, Hepp-Reymond M-C, Kristeva R. 2007. Corticomuscular synchronization with small and large dynamic force output. *BMC neuroscience* 8: 101
- Aoki F, Fetz E, Shupe L, Lettich E, Ojemann G. 1999. Increased gamma-range activity in human sensorimotor cortex during performance of visuomotor tasks. *Clinical Neurophysiology* 110: 524-37
- Arai N, Lu M-K, Ugawa Y, Ziemann U. 2012. Effective connectivity between human supplementary motor area and primary motor cortex: a paired-coil TMS study. *Experimental brain research* 220: 79-87
- Arnett C, Cooper J. 1965. Effect of thiamine analogs on the electrical activity of the rabbit vagus nerve. *Experientia* 21: 605-07

- Aron AR, Robbins TW, Poldrack RA. 2014. Inhibition and the right inferior frontal cortex: one decade on. *Trends in cognitive sciences* 18: 177-85
- Baker MR, Baker SN. 2003. The effect of diazepam on motor cortical oscillations and corticomuscular coherence studied in man. *The Journal of physiology* 546: 931-42
- Baker SN. 2007. Oscillatory interactions between sensorimotor cortex and the periphery. *Current opinion in neurobiology* 17: 649-55
- Barabási A-L, Albert R. 1999. Emergence of scaling in random networks. *science* 286: 509-12
- Başar E, Başar-Eroğlu C, Karakaş S, Schürmann M. 1999. Are cognitive processes manifested in event-related gamma, alpha, theta and delta oscillations in the EEG? *Neuroscience Letters* 259: 165-68
- Berger H. 1929. Über das elektroencephalogramm des menschen. *Archiv für psychiatrie und nervenkrankheiten* 87: 527-70
- Bernstein N. 1966. The co-ordination and regulation of movements. *The co-ordination and regulation of movements*
- Biewener AA, Gillis GB. 1999. Dynamics of muscle function during locomotion: accommodating variable conditions. *J Exp Biol* 202 Pt 23: 3387-96.
- Blanke O, Arzy S. 2005. The out-of-body experience: disturbed self-processing at the temporo-parietal junction. *The Neuroscientist* 11: 16-24
- Bortoletto M, Veniero D, Thut G, Miniussi C. 2015. The contribution of TMS–EEG coregistration in the exploration of the human cortical connectome. *Neuroscience & Biobehavioral Reviews* 49: 114-24
- Boussaoud D. 2001. Attention versus intention in the primate premotor cortex. *Neuroimage* 14: S40-S45
- Braun DA, Aertsen A, Wolpert DM, Mehring C. 2009. Motor task variation induces structural learning. *Current Biology* 19: 352-57

- Brodmann K. 1909. *Vergleichende Lokalisationslehre der Grosshirnrinde in ihren Prinzipien dargestellt auf Grund des Zellenbaues*. Barth.
- Brown P. 2007. Abnormal oscillatory synchronisation in the motor system leads to impaired movement. *Current opinion in neurobiology* 17: 656-64
- Brown P, Williams D. 2005. Basal ganglia local field potential activity: character and functional significance in the human. *Clinical neurophysiology* 116: 2510-19
- Buckingham G, Binsted G, Carey DP. 2010. Bimanual reaching across the hemispace: Which hand is yoked to which? *Brain and cognition* 74: 341-46
- Bullmore E, Sporns O. 2012. The economy of brain network organization. *Nature Reviews Neuroscience* 13: 336
- Buser P, Rougeul-Buser A. 1995. Do cortical and thalamic bioelectric oscillations have a functional role? A brief survey and discussion. *Journal of Physiology-Paris* 89: 249-54
- Buzsaki G. 2006. *Rhythms of the Brain*. Oxford University Press.
- Canolty RT, Knight RT. 2010. The functional role of cross-frequency coupling. *Trends in cognitive sciences* 14: 506-15
- Caplan JB, Madsen JR, Schulze-Bonhage A, Aschenbrenner-Scheibe R, Newman EL, Kahana MJ. 2003. Human θ oscillations related to sensorimotor integration and spatial learning. *Journal of Neuroscience* 23: 4726-36
- Carter CS, Macdonald AM, Botvinick M, Ross LL, Stenger VA, et al. 2000. Parsing executive processes: strategic vs. evaluative functions of the anterior cingulate cortex. *Proceedings of the National Academy of Sciences* 97: 1944-48
- Cavanagh JF, Frank MJ. 2014. Frontal theta as a mechanism for cognitive control. *Trends in cognitive sciences* 18: 414-21
- Chatrjian GE, Petersen MC, Lazarte JA. 1959. The blocking of the rolandic wicket rhythm and some central changes related to movement. *Electroencephalography and clinical neurophysiology* 11: 497-510

- Chen S, Entakli J, Bonnard M, Berton E, De Graaf JB. 2013. Functional corticospinal projections from human supplementary motor area revealed by corticomuscular coherence during precise grip force control. *PloS one* 8
- Cowan GA, Craik DC, Needham M. 2017. RapidSim: an application for the fast simulation of heavy-quark hadron decays. *Computer Physics Communications* 214: 239-46
- da Silva FL. 1991. Neural mechanisms underlying brain waves: from neural membranes to networks. *Electroencephalography and clinical neurophysiology* 79: 81-93
- Davidson RJ, Hugdahl K. 1996. *Brain asymmetry*. Mit Press.
- De Lange FP, Jensen O, Bauer M, Toni I. 2008. Interactions between posterior gamma and frontal alpha/beta oscillations during imagined actions. *Frontiers in human neuroscience* 2: 7
- Delorme A, Makeig S. 2004. EEGLAB: an open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. *Journal of neuroscience methods* 134: 9-21
- Delucchi M, Garoutte B, Aird RB. 1962. The scalp as an electroencephalographic averager. *Electroencephalography & Clinical Neurophysiology*
- Derambure P, Defebvre L, Dujardin K, Bourriez J, Jacquesson J, et al. 1993. Effect of aging on the spatio-temporal pattern of event-related desynchronization during a voluntary movement. *Electroencephalography and Clinical Neurophysiology/Evoked Potentials Section* 89: 197-203
- Devinsky O, Morrell MJ, Vogt BA. 1995. Contributions of anterior cingulate cortex to behaviour. *Brain* 118: 279-306
- Dippel G, Beste C. 2015. A causal role of the right inferior frontal cortex in implementing strategies for multi-component behaviour. *Nature communications* 6: 6587
- Earland K, Lee M, Shaw P, Law J. 2014. Overlapping structures in sensory-motor mappings. *PloS one* 9

- Ebersole JS. 1997. Defining epileptogenic foci: past, present, future. *Journal of clinical neurophysiology* 14: 470-83
- Engel AK, Fries P. 2010. Beta-band oscillations—signalling the status quo? *Current opinion in neurobiology* 20: 156-65
- Ericsson KA, Krampe RT, Tesch-Römer C. 1993. The role of deliberate practice in the acquisition of expert performance. *Psychological Review* 100: 363
- Ewald A, Aristei S, Nolte G, Rahman RA. 2012. Brain oscillations and functional connectivity during overt language production. *Frontiers in psychology* 3: 166
- Farmer S, Bremner F, Halliday D, Rosenberg J, Stephens J. 1993. The frequency content of common synaptic inputs to motoneurons studied during voluntary isometric contraction in man. *The Journal of physiology* 470: 127-55
- Farmer S, Halliday D, Conway B, Stephens J, Rosenberg J. 1997. A review of recent applications of cross-correlation methodologies to human motor unit recording. *Journal of neuroscience methods* 74: 175-87
- Finotellia P, Dulioa P. 2015. Graph Theoretical Analysis of the Brain. An Overview. *Scienze e Ricerche* 9: 89-96
- Fornito A, Zalesky A, Breakspear M. 2015. The connectomics of brain disorders. *Nature Reviews Neuroscience* 16: 159
- Fries P. 2005. A mechanism for cognitive dynamics: neuronal communication through neuronal coherence. *Trends in cognitive sciences* 9: 474-80
- Ghahramani Z, Wolpert DM. 1997. Modular decomposition in visuomotor learning. *Nature* 386: 392
- Gilbertson T, Lalo E, Doyle L, Di Lazzaro V, Cioni B, Brown P. 2005. Existing motor state is favored at the expense of new movement during 13-35 Hz oscillatory synchrony in the human corticospinal system. *Journal of Neuroscience* 25: 7771-79
- Goldberg E, Podell K, Lovell M. 1994. Laterlization of Frontal Lobe Functions and Cognitive Novelty. *Neurosciences* 6: 371-78

- Good CD, Johnsrude I, Ashburner J, Henson RN, Friston KJ, Frackowiak RS. 2001. Cerebral asymmetry and the effects of sex and handedness on brain structure: a voxel-based morphometric analysis of 465 normal adult human brains. *Neuroimage* 14: 685-700
- Goodale MA, Milner AD. 1992. Separate visual pathways for perception and action.
- Grafton ST, Fadiga L, Arbib MA, Rizzolatti G. 1997. Premotor cortex activation during observation and naming of familiar tools. *Neuroimage* 6: 231-36
- Hadipour-Niktarash A, Lee CK, Desmond JE, Shadmehr R. 2007. Impairment of retention but not acquisition of a visuomotor skill through time-dependent disruption of primary motor cortex. *Journal of Neuroscience* 27: 13413-19
- Haegens S, Cousijn H, Wallis G, Harrison PJ, Nobre AC. 2014. Inter-and intra-individual variability in alpha peak frequency. *Neuroimage* 92: 46-55
- Hagmann P, Cammoun L, Gigandet X, Meuli R, Honey CJ, et al. 2008. Mapping the structural core of human cerebral cortex. *PLoS biology* 6: e159
- Haith AM, Krakauer JW. 2013. Theoretical models of motor control and motor learning. *Routledge handbook of motor control and motor learning*. London: Routledge: 7-28
- Halgren M, Ulbert I, Bastuji H, Fabó D, Erőss L, et al. 2019. The generation and propagation of the human alpha rhythm. *Proceedings of the National Academy of Sciences* 116: 23772-82
- Halliday DM, Conway BA, Farmer SF, Rosenberg JR. 1998. Using electroencephalography to study functional coupling between cortical activity and electromyograms during voluntary contractions in humans. *Neuroscience Letters* 241: 5-8
- Hamzei F, Rijntjes M, Dettmers C, Glauche V, Weiller C, Büchel C. 2003. The human action recognition system and its relationship to Broca's area: an fMRI study. *Neuroimage* 19: 637-44
- Harmony T. 2013. The functional significance of delta oscillations in cognitive processing. *Frontiers in integrative neuroscience* 7: 83

- Hartwigsen G, Neef NE, Camilleri JA, Margulies DS, Eickhoff SB. 2019. Functional segregation of the right inferior frontal gyrus: evidence from coactivation-based parcellation. *Cerebral Cortex* 29: 1532-46
- Haxby JV, Grady CL, Horwitz B, Ungerleider LG, Mishkin M, et al. 1991. Dissociation of object and spatial visual processing pathways in human extrastriate cortex. *Proceedings of the National Academy of Sciences* 88: 1621-25
- Heiser M, Iacoboni M, Maeda F, Marcus J, Mazziotta JC. 2003. The essential role of Broca's area in imitation. *European Journal of Neuroscience* 17: 1123-28
- Hepper PG, McCartney GR, Shannon EA. 1998. Lateralised behaviour in first trimester human fetuses. *Neuropsychologia* 36: 531-34
- Hillary FG, DeLuca J. 2007. *Functional neuroimaging in clinical populations*. Guilford Press.
- Honey CJ, Kötter R, Breakspear M, Sporns O. 2007. Network structure of cerebral cortex shapes functional connectivity on multiple time scales. *Proceedings of the National Academy of Sciences* 104: 10240-45
- Horn AK, Leigh RJ. 2011. The anatomy and physiology of the ocular motor system In *Handbook of clinical neurology*, pp. 21-69: Elsevier
- Hoshi E, Tanji J. 2000. Integration of target and body-part information in the premotor cortex when planning action. *Nature* 408: 466-70
- Huber R, Ghilardi MF, Massimini M, Tononi G. 2004. Local sleep and learning. *Nature* 430: 78-81
- Hutchinson JB, Uncapher MR, Wagner AD. 2009. Posterior parietal cortex and episodic retrieval: convergent and divergent effects of attention and memory. *Learning & memory* 16: 343-56
- Jäncke L. 2002. The case of a left-handed pianist playing a reversed keyboard: a challenge for the neuroscience of music. *Neuroreport* 13: 1579-83

- Jensen O, Gelfand J, Kounios J, Lisman JE. 2002. Oscillations in the alpha band (9–12 Hz) increase with memory load during retention in a short-term memory task. *Cerebral cortex* 12: 877-82
- Johnson S, Rotte M, Grafton S, Hinrichs H, Gazzaniga M, Heinze H. 2002. Selective activation of a parietofrontal circuit during implicitly imagined prehension. *Neuroimage* 17: 1693-704
- Joundi RA, Jenkinson N, Brittain J-S, Aziz TZ, Brown P. 2012. Driving oscillatory activity in the human cortex enhances motor performance. *Current Biology* 22: 403-07
- Kandel ER, Schwartz JH, Jessell TM, Biochemistry Do, Jessell MBT, et al. 2000. *Principles of neural science*. McGraw-hill New York.
- Kayser J, Tenke CE. 2015. On the benefits of using surface Laplacian (current source density) methodology in electrophysiology. *International journal of psychophysiology: official journal of the International Organization of Psychophysiology* 97: 171
- Kelly R, Mizelle J, Wheaton LA. 2015. Distinctive laterality of neural networks supporting action understanding in left-and right-handed individuals: an EEG coherence study. *Neuropsychologia* 75: 20-29
- Keysers C, Kohler E, Umiltà MA, Nanetti L, Fogassi L, Gallese V. 2003. Audiovisual mirror neurons and action recognition. *Experimental brain research* 153: 628-36
- Klimesch W. 1996. Memory processes, brain oscillations and EEG synchronization. *International journal of psychophysiology* 24: 61-100
- Klimesch W. 1999. EEG alpha and theta oscillations reflect cognitive and memory performance: a review and analysis. *Brain research reviews* 29: 169-95
- Knecht S, Dräger B, Deppe M, Bobe L, Lohmann H, et al. 2000. Handedness and hemispheric language dominance in healthy humans. *Brain* 123: 2512-18
- Koelewijn T, van Schie HT, Bekkering H, Oostenveld R, Jensen O. 2008. Motor-cortical beta oscillations are modulated by correctness of observed action. *Neuroimage* 40: 767-75

- Kohler E, Keysers C, Umiltà MA, Fogassi L, Gallese V, Rizzolatti G. 2002. Hearing sounds, understanding actions: action representation in mirror neurons. *Science* 297: 846-48
- Konrad P. 2005. The abc of emg. *A practical introduction to kinesiological electromyography* 1: 30-5
- Kramer MA. 2013. An introduction to field analysis techniques: The power spectrum and coherence. *The Science of Large Data Sets: Spikes, Fields, and Voxels. Short Course by the Society for Neuroscience.* <https://www.sfn.org/~media/SfN/Documents/Short%20Courses/2013%20Short%20Course%20II/Short%20Course%202>
- Latash ML, Anson JG. 2006. Synergies in health and disease: relations to adaptive changes in motor coordination. *Physical therapy* 86: 1151-60
- Lattari E, Velasques B, Paes F, Cunha M, Budde H, et al. 2010. Corticomuscular coherence behavior in fine motor control of force: a critical review. *Rev Neurol* 51: 610-23
- Luppino G, Matelli M, Camarda R, Rizzolatti G. 1993. Corticocortical connections of area F3 (SMA-proper) and area F6 (pre-SMA) in the macaque monkey. *Journal of Comparative Neurology* 338: 114-40
- MacDonald AW, Cohen JD, Stenger VA, Carter CS. 2000. Dissociating the role of the dorsolateral prefrontal and anterior cingulate cortex in cognitive control. *Science* 288: 1835-38
- Maquet P. 2001. The role of sleep in learning and memory. *science* 294: 1048-52
- Maris E, Oostenveld R. 2007. Nonparametric statistical testing of EEG-and MEG-data. *Journal of neuroscience methods* 164: 177-90
- Marsden J, Werhahn K, Ashby P, Rothwell J, Noachtar S, Brown P. 2000. Organization of cortical activities related to movement in humans. *Journal of Neuroscience* 20: 2307-14
- Marteniuk R, MacKenzie C, Baba D. 1984. Bimanual movement control: Information processing and interaction effects. *The Quarterly Journal of Experimental Psychology Section A* 36: 335-65

- McDonnell J, Mizelle J. *JOURNAL OF SPORT & EXERCISE PSYCHOLOGY* 2019, 41: S42-S42. HUMAN KINETICS PUBL INC 1607 N MARKET ST, PO BOX 5076, CHAMPAIGN, IL 61820
- Melsbach G, Wohlschläger A, Spieß M, Güntürkün O. 1996. Morphological asymmetries of motoneurons innervating upper extremities: clues to the anatomical foundations of handedness? *International journal of neuroscience* 86: 217-24
- Miall RC, Wolpert DM. 1996. Forward models for physiological motor control. *Neural networks* 9: 1265-79
- Mijalkov M, Kakaei E, Pereira JB, Westman E, Volpe G, Initiative AsDN. 2017. BRAPH: a graph theory software for the analysis of brain connectivity. *PloS one* 12
- Mizelle J, Forrester L, Hallett M, Wheaton LA. 2010. Theta frequency band activity and attentional mechanisms in visual and proprioceptive demand. *Experimental brain research* 204: 189-97
- Moffat SD, Hampson E, Lee DH. 1998. Morphology of the planum temporale and corpus callosum in left handers with evidence of left and right hemisphere speech representation. *Brain: a journal of neurology* 121: 2369-79
- Muellbacher W, Ziemann U, Boroojerdi B, Cohen L, Hallett M. 2001. Role of the human motor cortex in rapid motor learning. *Experimental Brain Research* 136: 431-38
- Mulholland T. 1995. Human EEG, behavioral stillness and biofeedback. *International journal of psychophysiology* 19: 263-79
- Mullen T, Kothe C, Chi YM, Ojeda A, Kerth T, et al. *Engineering in Medicine and Biology Society (EMBC), 2013 35th Annual International Conference of the IEEE 2013a*: 2184-87. IEEE.
- Mullen T, Kothe C, Chi YM, Ojeda A, Kerth T, et al. *2013 35th annual international conference of the IEEE engineering in medicine and biology society (EMBC) 2013b*: 2184-87. IEEE.
- Murata A, Fadiga L, Fogassi L, Gallese V, Raos V, Rizzolatti G. 1997. Object representation in the ventral premotor cortex (area F5) of the monkey. *Journal of Neurophysiology* 78: 2226-30

- Muthukumaraswamy SD, Johnson B. 2004. Changes in rolandic mu rhythm during observation of a precision grip. *Psychophysiology* 41: 152-56
- Muthukumaraswamy SD, Johnson BW, McNair NA. 2004. Mu rhythm modulation during observation of an object-directed grasp. *Cognitive brain research* 19: 195-201
- Nadasdy Z. 2010. Binding by asynchrony: the neuronal phase code. *Frontiers in Neuroscience* 4: 51
- Nagengast AJ, Braun DA, Wolpert DM. 2009. Optimal control predicts human performance on objects with internal degrees of freedom. *PLoS Comput Biol* 5: e1000419
- Najarian K, Splinter R. 2005. *Biomedical signal and image processing*. CRC press.
- Nazarova M, Blagovechtchenski E. 2015. Modern Brain Mapping—What Do We Map Nowadays? *Frontiers in psychiatry* 6: 89
- Neto OP, Christou EA. 2010. Rectification of the EMG signal impairs the identification of oscillatory input to the muscle. *Journal of Neurophysiology* 103: 1093-103
- Niedermeyer E. 1997. Alpha rhythms as physiological and abnormal phenomena. *International Journal of Psychophysiology* 26: 31-49
- Niedermeyer E, da Silva FL. 2005. *Electroencephalography: basic principles, clinical applications, and related fields*. Lippincott Williams & Wilkins.
- Nolte G, Bai O, Wheaton L, Mari Z, Vorbach S, Hallett M. 2004. Identifying true brain interaction from EEG data using the imaginary part of coherency. *Clinical neurophysiology* 115: 2292-307
- Nolte G, Marzetti L. 2014. Methods to estimate functional and effective brain connectivity from MEG data robust to artifacts of volume conduction In *Magnetoencephalography*, pp. 477-501: Springer
- Nunez PL, Reid L, Bickford RG. 1978. The relationship of head size to alpha frequency with implications to a brain wave model. *Electroencephalography and clinical neurophysiology* 44: 344-52

- Nunez PL, Srinivasan R. 2006. *Electric fields of the brain: the neurophysics of EEG*. Oxford University Press, USA.
- Ocklenburg S, Beste C, Arning L, Peterburs J, Güntürkün O. 2014. The ontogenesis of language lateralization and its relation to handedness. *Neuroscience & Biobehavioral Reviews* 43: 191-98
- Oldfield RC. 1971. The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia* 9: 97-113
- Omlor W, Patino L, Hepp-Reymond M-C, Kristeva R. 2007. Gamma-range corticomuscular coherence during dynamic force output. *Neuroimage* 34: 1191-98
- Palva S, Palva JM. 2007. New vistas for α -frequency band oscillations. *Trends in neurosciences* 30: 150-58
- Patino L, Omlor W, Chakarov V, Hepp-Reymond M-C, Kristeva R. 2008. Absence of gamma-range corticomuscular coherence during dynamic force in a deafferented patient. *Journal of Neurophysiology* 99: 1906-16
- Perelle IB, Ehrman L. 1994. An international study of human handedness: The data. *Behavior genetics* 24: 217-27
- Petersen P, Petrick M, Connor H, Conklin D. 1989. Grip strength and hand dominance: challenging the 10% rule. *American Journal of Occupational Therapy* 43: 444-47
- Pfurtscheller G, Andrew C. 1999. Event-related changes of band power and coherence: methodology and interpretation. *Journal of clinical neurophysiology* 16: 512
- Pfurtscheller G, Aranibar A. 1977. Event-related cortical desynchronization detected by power measurements of scalp EEG. *Electroencephalography and clinical neurophysiology* 42: 817-26
- Pfurtscheller G, Berghold A. 1989. Patterns of cortical activation during planning of voluntary movement. *Electroencephalography and clinical neurophysiology* 72: 250-58
- Pfurtscheller G, Da Silva FL. 1999. Event-related EEG/MEG synchronization and desynchronization: basic principles. *Clinical neurophysiology* 110: 1842-57

- Pfurtscheller G, Neuper C, Krausz G. 2000. Functional dissociation of lower and upper frequency mu rhythms in relation to voluntary limb movement. *Clinical neurophysiology* 111: 1873-79
- Pfurtscheller G, Stancak A, Neuper C. 1996. Event-related synchronization (ERS) in the alpha band—an electrophysiological correlate of cortical idling: a review. *International journal of psychophysiology* 24: 39-46
- Picard N, Strick PL. 1996. Motor areas of the medial wall: a review of their location and functional activation. *Cerebral cortex* 6: 342-53
- Picard N, Strick PL. 2001. Imaging the premotor areas. *Current opinion in neurobiology* 11: 663-72
- Pineda JA. 2005. The functional significance of mu rhythms: translating “seeing” and “hearing” into “doing”. *Brain research reviews* 50: 57-68
- Pineda JA, Allison B, Vankov A. 2000. The effects of self-movement, observation, and imagination on/spl mu/rhythms and readiness potentials (RP's): toward a brain-computer interface (BCI). *IEEE Transactions on Rehabilitation Engineering* 8: 219-22
- Pogosyan A, Gaynor LD, Eusebio A, Brown P. 2009. Boosting cortical activity at beta-band frequencies slows movement in humans. *Current biology* 19: 1637-41
- Poldrack RA. 2000. Imaging brain plasticity: conceptual and methodological issues—a theoretical review. *Neuroimage* 12: 1-13
- Przybyla A, Good DC, Sainburg RL. 2012. Dynamic dominance varies with handedness: reduced interlimb asymmetries in left-handers. *Experimental brain research* 216: 419-31
- Purves D, Augustine GJ, Fitzpatrick D, Hall WC, LaMantia A-S, et al. 2004. *Neuroscience*. Sunderland, MA: Sinauer Associates 773
- Raghavachari S, Kahana MJ, Rizzuto DS, Caplan JB, Kirschen MP, et al. 2001. Gating of human theta oscillations by a working memory task. *Journal of Neuroscience* 21: 3175-83

- Raghavachari S, Lisman JE, Tully M, Madsen JR, Bromfield E, Kahana MJ. 2006. Theta oscillations in human cortex during a working-memory task: evidence for local generators. *Journal of Neurophysiology* 95: 1630-38
- Ridderinkhof KR, Ullsperger M, Crone EA, Nieuwenhuis S. 2004. The role of the medial frontal cortex in cognitive control. *science* 306: 443-47
- Riddle CN, Baker SN. 2005. Manipulation of peripheral neural feedback loops alters human corticomuscular coherence. *The Journal of physiology* 566: 625-39
- Rizzolatti G, Arbib MA. 1998. Language within our grasp. *Trends in neurosciences* 21: 188-94
- Rizzolatti G, Fadiga L, Fogassi L, Gallese V. 1997a. The space around us. *Science* 277: 190-91
- Rizzolatti G, Fogassi L, Gallese V. 1997b. Parietal cortex: from sight to action. *Current opinion in neurobiology* 7: 562-67
- Rizzolatti G, Luppino G, Matelli M. 1998. The organization of the cortical motor system: new concepts. *Electroencephalography and clinical neurophysiology* 106: 283-96
- Rozzi S, Coudé G. 2015. Grasping actions and social interaction: neural bases and anatomical circuitry in the monkey. *Frontiers in psychology* 6: 973
- Rubinov M, Sporns O. 2010. Complex network measures of brain connectivity: uses and interpretations. *Neuroimage* 52: 1059-69
- Sailer J, Scharitzer M, Peloschek P, Giurea A, Imhof H, Grampp S. 2005a. Quantification of axial alignment of the lower extremity on conventional and digital total leg radiographs. *Eur Radiol* 15: 170-73
- Sailer U, Flanagan JR, Johansson RS. 2005b. Eye–hand coordination during learning of a novel visuomotor task. *Journal of Neuroscience* 25: 8833-42
- Sakata H, Taira M, Murata A, Mine S. 1995. Neural mechanisms of visual guidance of hand action in the parietal cortex of the monkey. *Cerebral Cortex* 5: 429-38

- Sauseng P, Klimesch W, Gerloff C, Hummel FC. 2009. Spontaneous locally restricted EEG alpha activity determines cortical excitability in the motor cortex. *Neuropsychologia* 47: 284-88
- Scholz JP, Schönner G. 1999. The uncontrolled manifold concept: identifying control variables for a functional task. *Experimental brain research* 126: 289-306
- Shadmehr R, Mussa-Ivaldi FA. 1994. Adaptive representation of dynamics during learning of a motor task. *Journal of Neuroscience* 14: 3208-24
- Shamas M, Wendling F, El Falou W, Hassan M. 2015 7th International IEEE/EMBS Conference on Neural Engineering (NER)2015: 1064-67. IEEE.
- Sheliga B, Craighero L, Riggio L, Rizzolatti G. 1997. Effects of spatial attention on directional manual and ocular responses. *Experimental brain research* 114: 339-51
- Sheng Y, Liu J, Liu H. 2019. Corticomuscular coherence and its applications: A review. *Frontiers in Human Neuroscience* 13: 100
- Sherwood DE. 2014. Aiming accuracy in preferred and non-preferred limbs: implications for programming models of motor control. *Frontiers in psychology* 5: 1236
- Singer W. 1999. Neuronal synchrony: a versatile code for the definition of relations? *Neuron* 24: 49-65
- Smallwood J, Karapanagiotidis T, Ruby F, Medea B, De Caso I, et al. 2016. Representing representation: Integration between the temporal lobe and the posterior cingulate influences the content and form of spontaneous thought. *PloS one* 11
- Snyder AC, Smith MA. 2015. Stimulus-dependent spiking relationships with the EEG. *Journal of Neurophysiology* 114: 1468-82
- Sporns O, Chialvo DR, Kaiser M, Hilgetag CC. 2004. Organization, development and function of complex brain networks. *Trends in cognitive sciences* 8: 418-25
- Stancák A, Pfurtscheller G. 1996. The effects of handedness and type of movement on the contralateral preponderance of μ -rhythm desynchronisation. *Electroencephalography and clinical Neurophysiology* 99: 174-82

- Swann N, Tandon N, Canolty R, Ellmore TM, McEvoy LK, et al. 2009. Intracranial EEG reveals a time-and frequency-specific role for the right inferior frontal gyrus and primary motor cortex in stopping initiated responses. *Journal of Neuroscience* 29: 12675-85
- Szaflarski JP, Rajagopal A, Altaye M, Byars AW, Jacola L, et al. 2012. Left-handedness and language lateralization in children. *Brain Research* 1433: 85-97
- Thatcher R, McAlaster R, Lester M, Horst R, Cantor D. 1983. Hemispheric EEG asymmetries related to cognitive functioning in children In *Cognitive processing in the right hemisphere*, pp. 125-46: Elsevier
- Toni I, Thoenissen D, Zilles K. 2001. Movement preparation and motor intention. *Neuroimage* 14: S110-S117
- Tononi G, Sporns O, Edelman GM. 1994. A measure for brain complexity: relating functional segregation and integration in the nervous system. *Proceedings of the National Academy of Sciences* 91: 5033-37
- Tresilian J. 2012. *Sensorimotor control and learning: An introduction to the behavioral neuroscience of action*. Palgrave Macmillan.
- Tuladhar AM, Huurne Nt, Schoffelen JM, Maris E, Oostenveld R, Jensen O. 2007. Parieto-occipital sources account for the increase in alpha activity with working memory load. *Human brain mapping* 28: 785-92
- van den Heuvel MP, Sporns O. 2013. Network hubs in the human brain. *Trends in cognitive sciences* 17: 683-96
- Vanderah T, Gould DJ. 2015. *Nolte's The Human Brain E-Book: An Introduction to its Functional Anatomy*. Elsevier Health Sciences.
- Vredenburg J, Rau G. 1973. Surface electromyography in relation to force, muscle length and endurance In *New Concepts of the Motor Unit, Neuromuscular Disorders, Electromyographic Kinesiology*, pp. 607-22: Karger Publishers
- Walker EH, Perreault EJ. 2015. Arm dominance affects feedforward strategy more than feedback sensitivity during a postural task. *Experimental brain research* 233: 2001-11

- Walker MP, Stickgold R. 2004. Sleep-dependent learning and memory consolidation. *Neuron* 44: 121-33
- Wang X, Meng J, Tan G, Zou L. 2010. Research on the relation of EEG signal chaos characteristics with high-level intelligence activity of human brain. *Nonlinear biomedical physics* 4: 2
- White LE, Lucas G, Richards A, Purves D. 1994. Cerebral asymmetry and handedness. *Nature*
- Whittier, T.T., Murray, N., Mizelle, J.C. Differing neural strategies in left and right-handed individuals during motor imagery. Program No. 085.20/SS48. 2017 Neuroscience Meeting Planner. Washington, DC: Society for Neuroscience, 2017. Online
- Wise S, Moody S, Blomstrom K, Mitz A. 1998. Changes in motor cortical activity during visuomotor adaptation. *Experimental Brain Research* 121: 285-99
- Wolpert DM. 1997. Computational approaches to motor control. *Trends in cognitive sciences* 1: 209-16
- Wolpert DM, Flanagan JR. 2010. Motor learning. *Current biology* 20: R467-R72
- Wolpert DM, Ghahramani Z. 2000. Computational principles of movement neuroscience. *nature neuroscience* 3: 1212-17
- Wolpert DM, Ghahramani Z, Jordan MI. 1995. An internal model for sensorimotor integration. *Science* 269: 1880-82
- Wu J, Srinivasan R, Kaur A, Cramer SC. 2014. Resting-state cortical connectivity predicts motor skill acquisition. *Neuroimage* 91: 84-90
- Yamahachi H, Marik SA, McManus JN, Denk W, Gilbert CD. 2009. Rapid axonal sprouting and pruning accompany functional reorganization in primary visual cortex. *Neuron* 64: 719-29
- Yao B, Salenius S, Yue GH, Brown RW, Liu JZ. 2007. Effects of surface EMG rectification on power and coherence analyses: an EEG and MEG study. *Journal of neuroscience methods* 159: 215-23

Zietsch BP, Hansen JL, Hansell NK, Geffen GM, Martin NG, Wright MJ. 2007. Common and specific genetic influences on EEG power bands delta, theta, alpha, and beta. *Biological psychology* 75: 154-64

Zilles K, Amunts K. 2010. Centenary of Brodmann's map—conception and fate. *Nature Reviews Neuroscience* 11: 139-45

APPENDIX. Aggregate Figures

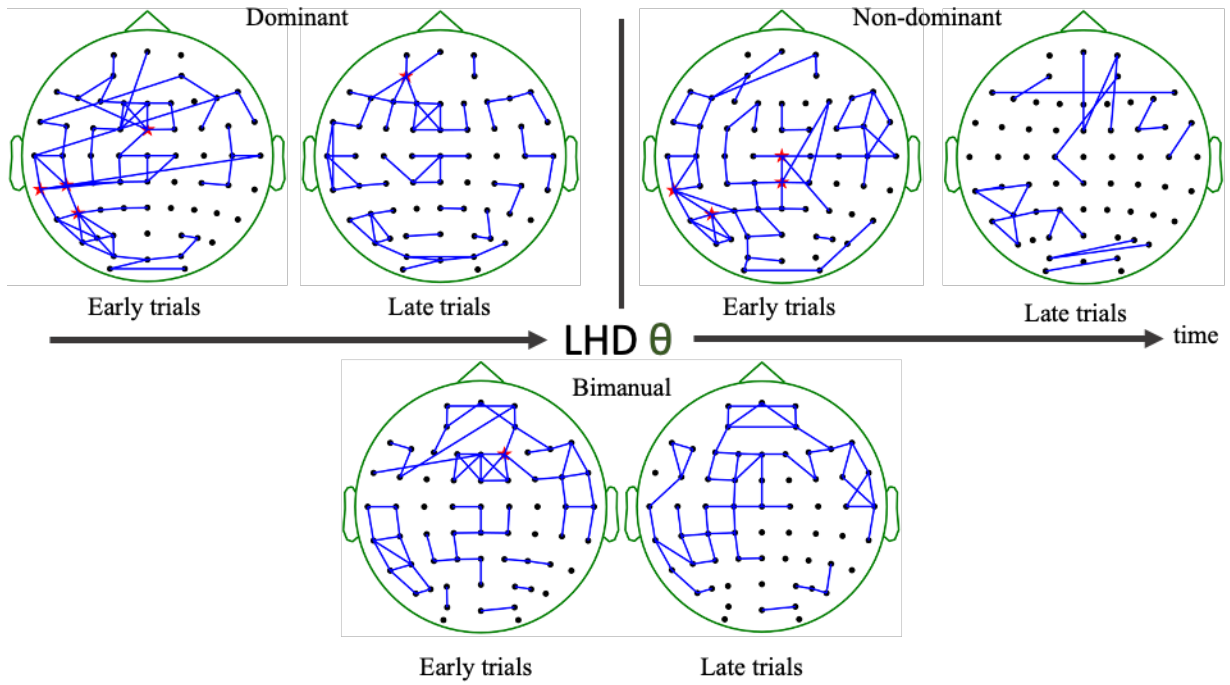


Figure A.1: Left-hand group theta cortico-cortical coherence trial progression from unimanual dominant unimanual nondominant and bimanual trials.

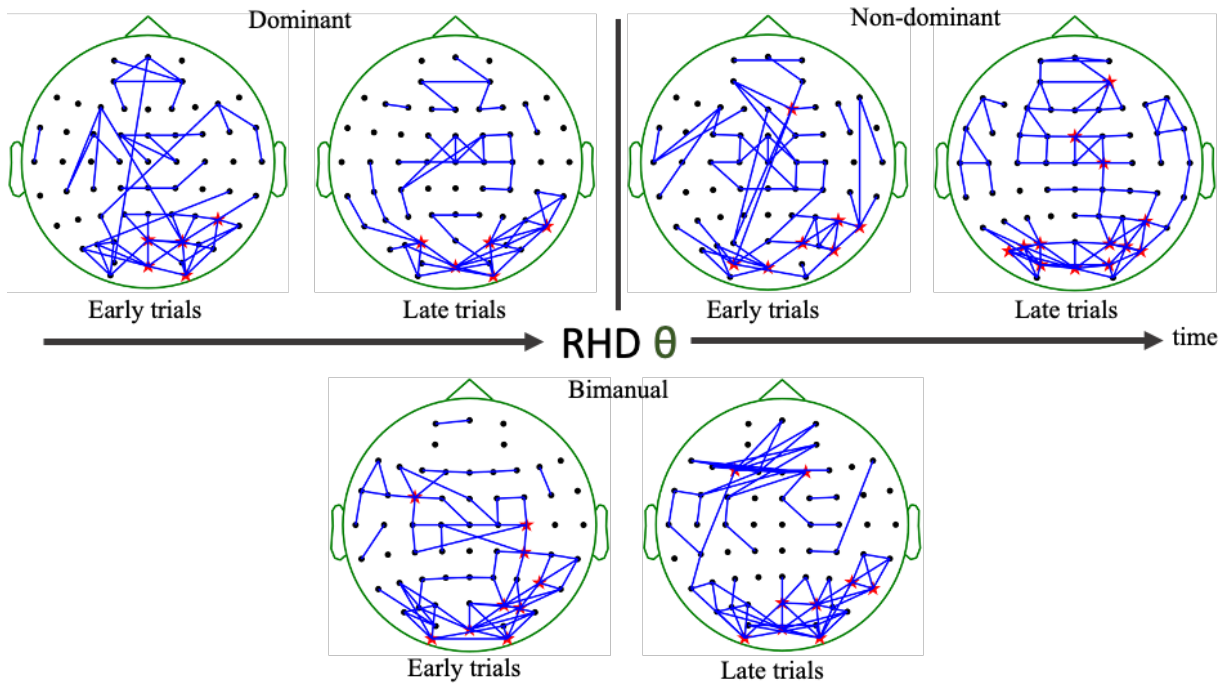
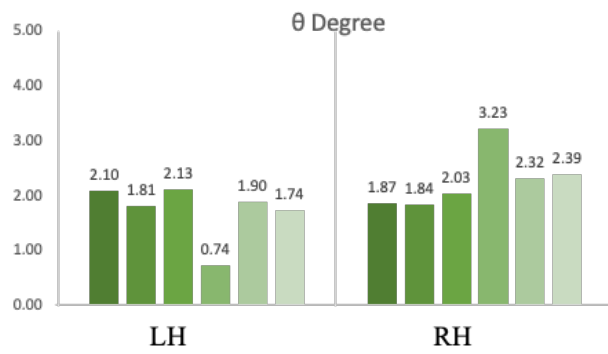


Figure A.2: Right-hand group theta cortico-cortical coherence trial progression from unimanual dominant unimanual nondominant and bimanual trials.



θ	DG	CC	EF
iLHD	2.0968	0.0511	0.1692
fLHD	1.8065	0.1102	0.0657
iLHN	2.129	0.1581	0.1531
fLHN	0.7419	0.0269	0.0195
iLHD	1.9032	0.0651	0.0854
fLHD	1.7419	0.0833	0.1099
θ	DG	CC	EF
iRHD	1.871	0.073	0.0944
fRHD	1.8387	0.0892	0.0828
iRHN	2.0323	0.0801	0.157
fRHN	3.2258	0.3043	0.2003
iRHD	2.3226	0.1488	0.1487
fRHD	2.3871	0.1552	0.1478

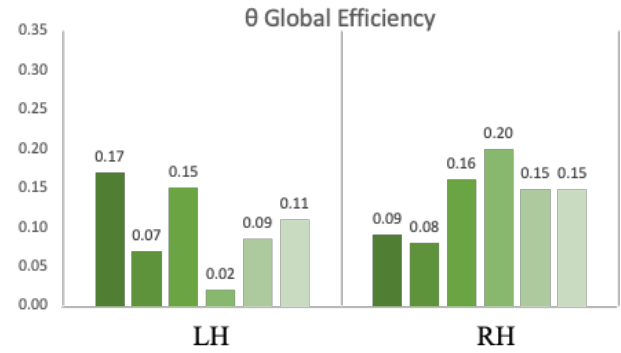


Table A.1: Left- and right-hand theta cortico-cortical coherence network metric from all conditions and trials.

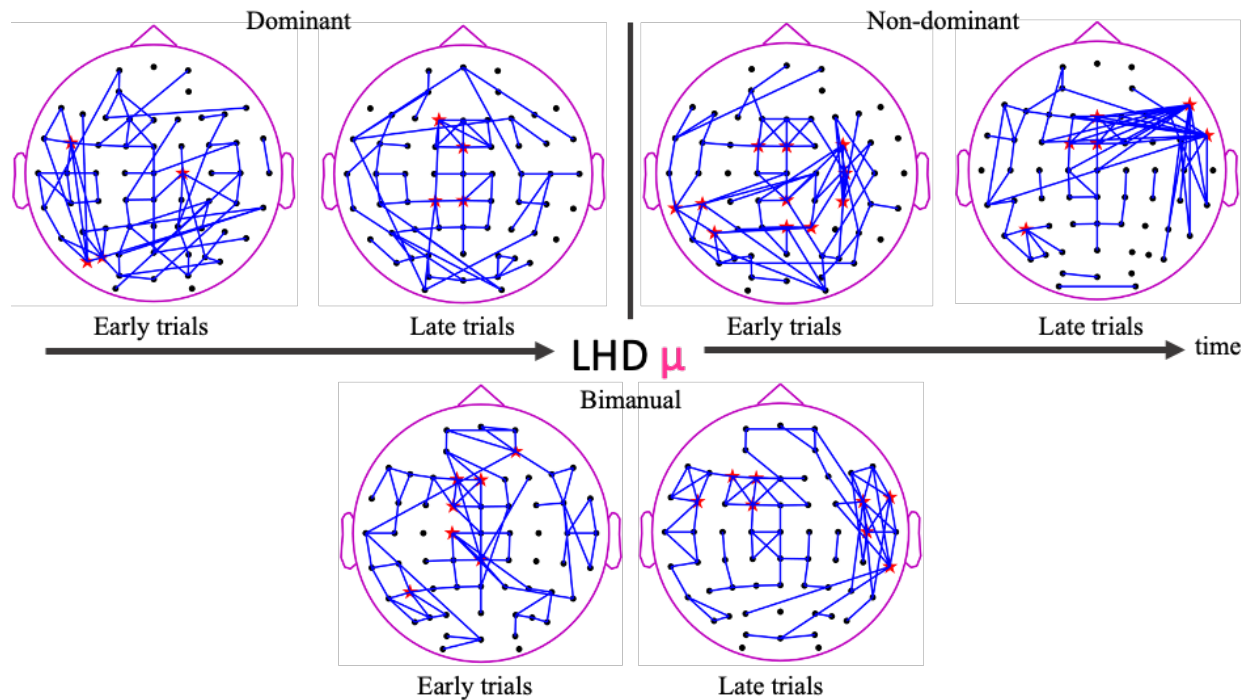


Figure A.3: Left-hand group mu cortico-cortical coherence trial progression from unimanual dominant unimanual nondominant and bimanual trials.

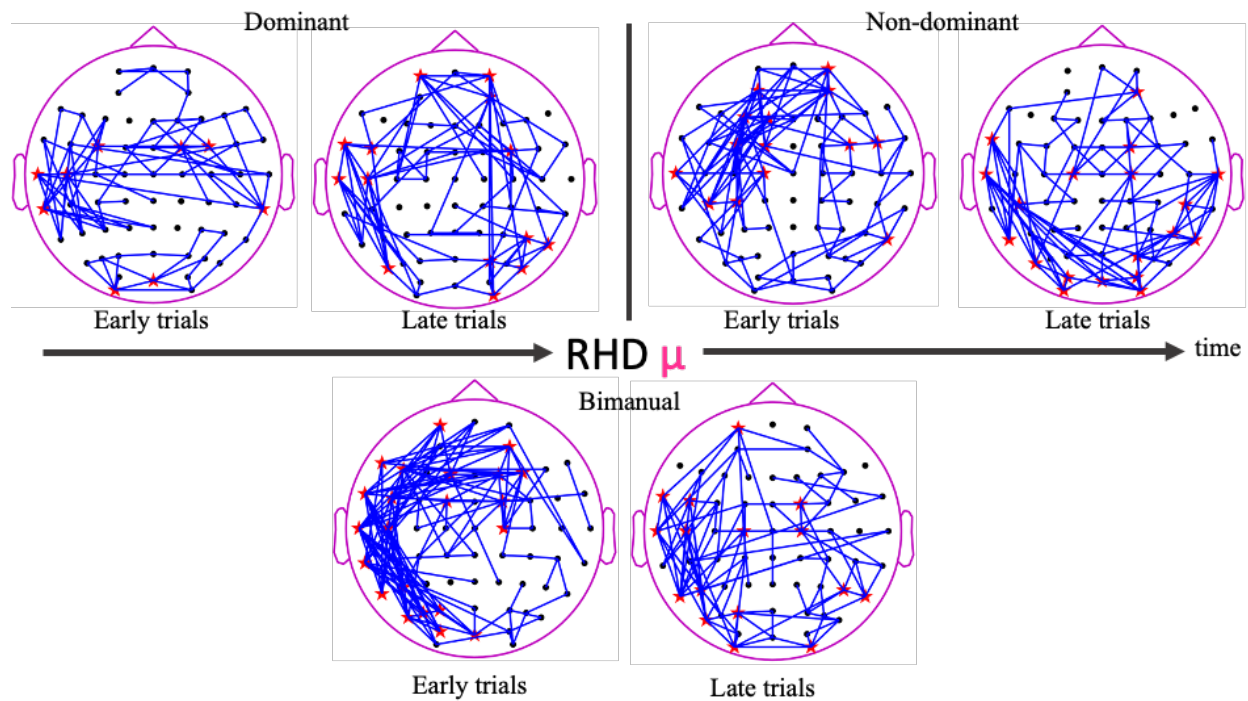
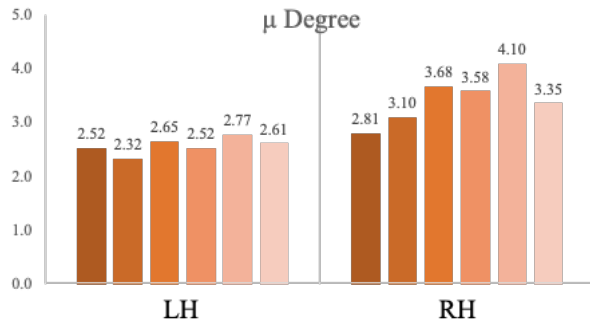


Figure A.4: Right-hand group mu cortico-cortical coherence trial progression from unimanual dominant unimanual nondominant and bimanual trials.



μ	DG	CC	EF
iLHD	2.5161	0.1025	0.2329
fLHD	2.3226	0.1301	0.207
iLHN	2.6452	0.1274	0.2303
fLHN	2.5161	0.1449	0.1773
iLHD	2.7742	0.1873	0.2376
fLHD	2.6129	0.2313	0.1715
iRHD	2.8065	0.1202	0.2478
fRHD	3.0968	0.1417	0.2736
iRHN	3.6774	0.1043	0.3152
fRHN	3.5806	0.2551	0.3007
iRHD	4.0968	0.1372	0.3133
fRHD	3.3548	0.171	0.2821

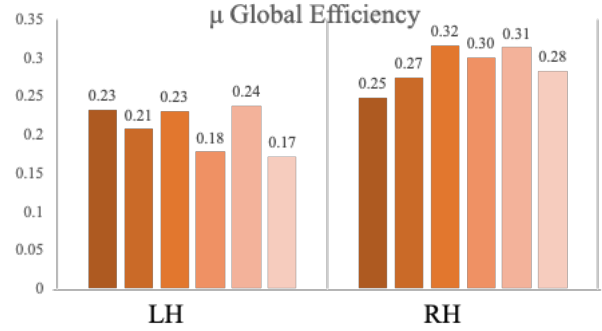


Table A.2: Left- and right-hand mu cortico-cortical coherence network metric from all conditions and trials.

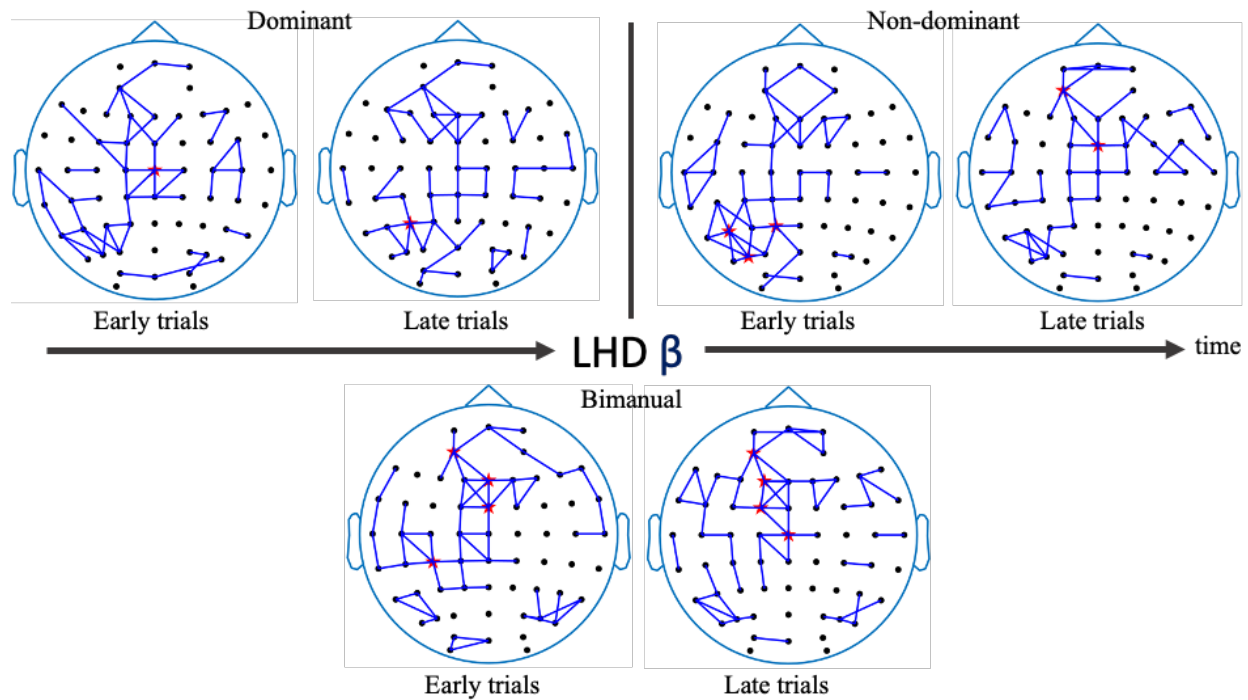


Figure A.5: Left-hand group beta cortico-cortical coherence trial progression from unimanual dominant unimanual nondominant and bimanual trials.

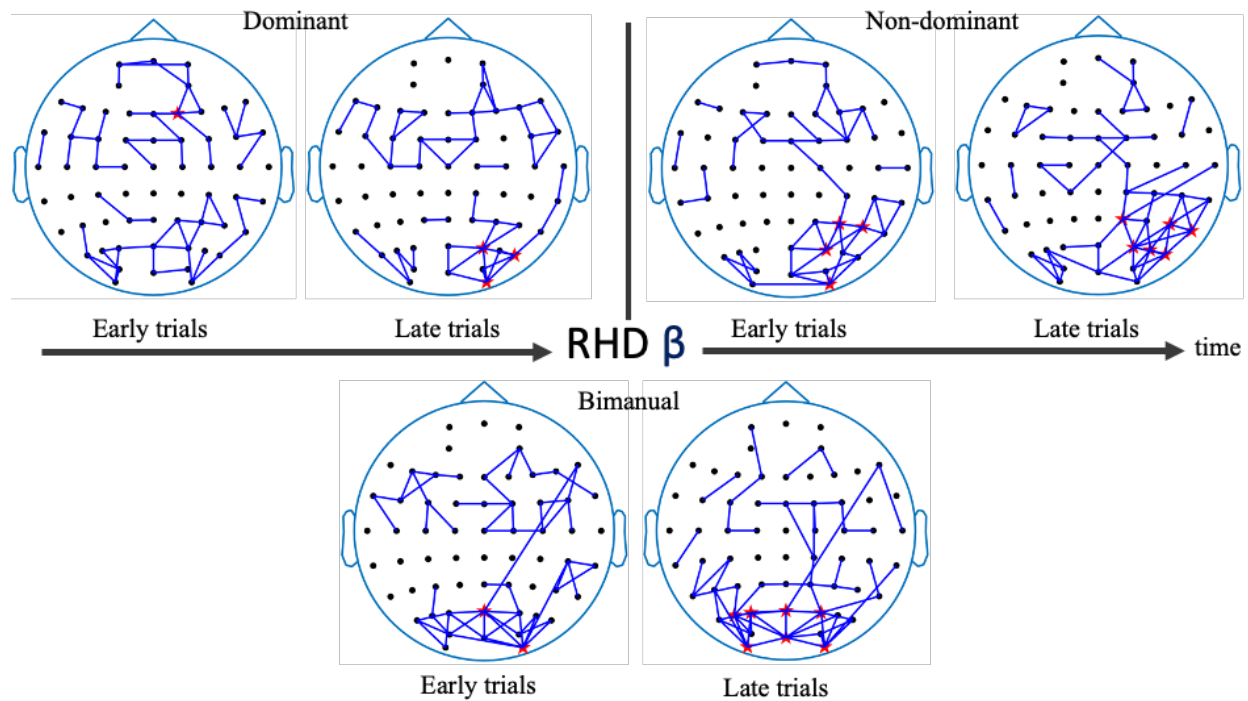
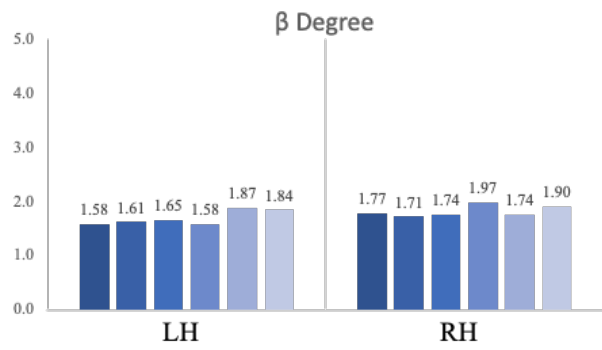


Figure: A.6: Right-hand group beta cortico-cortical coherence trial progression from unimanual dominant unimanual nondominant and bimanual trials.



β	DG	CC	EF
iLHD	1.5806	0.0989	0.0745
fLHD	1.6129	0.1054	0.0883
iLHN	1.6452	0.1274	0.0841
fLHN	1.5806	0.0946	0.069
iLHD	1.871	0.1774	0.0968
fLHD	1.8387	0.1978	0.0805
β	DG	CC	EF
iRHD	1.7742	0.1005	0.074
fRHD	1.7097	0.2226	0.0692
iRHN	1.7419	0.1151	0.0713
fRHN	1.9677	0.2098	0.0793
iRHD	1.7419	0.1548	0.0989
fRHD	1.9032	0.0896	0.1161

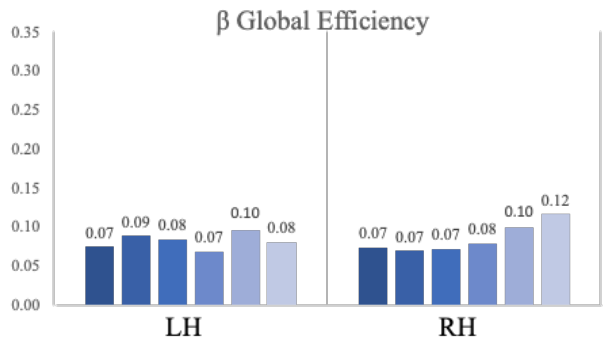
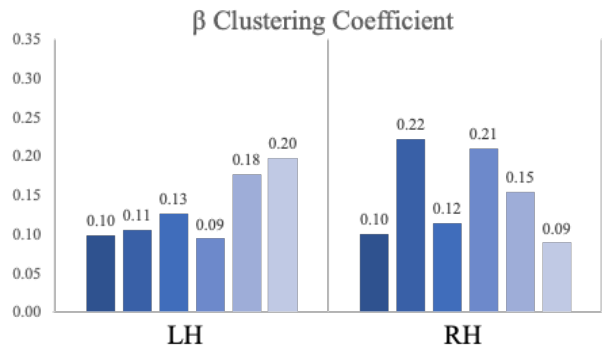


Table A.3: Left- and right-hand beta cortico-cortical coherence network metric from all conditions and trials.

