INVESTIGATION AND ASSESSMENT OF MIRROR NEURON ACTIVITY FOR REHABILITATION PURPOSES

AYNA NÖRON AKTİVİTELERİNİN REHABİLİTASYON AMAÇLI GÖZLENMESİ VE YORUMLANMASI

GÖZDE BAYER

PROF.DR. TÜLİN KUTSAL

Supervisor

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Prof. Dr. İbrahim VARGEL
Head .....

Prof. Dr. Tülin KUTSAL
Supervisor .....

Prof. Dr. Bülent CENGİZ
Member .....

Assoc.Prof. Dr. Murat ZİNNUROĞLU
Member .....

Asst. Prof. Dr. Ali Emre TURGUT
Member .....

This thesis has been approved as a thesis for the Degree of **DOCTOR OF PHILOSOPHY IN BIOENGINEERING** by Board of Directors of the Institute for Graduate School of Science and Engineering.

Prof.Dr. Menemşe GÜMÜŞDERELİOĞLU
Director of the Institute of Graduate
School of Science and Engineering

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(Bu seçenekle teziniz arama motorlarında indekslenebilecek, daha sonra tezinizin erişim statüsünün değiştirilmesini talep etseniz ve kütüphane bu talebinizi yerine getirse bile, tezinin arama motorlarının önbelleklerinde kalmaya devam edebilecektir.)

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- all cited studies have been fully referenced
- I did not do any distortion in data set
- and any part of this thesis has not been presented as another thesis study at this or any other university.

14 / 09 / 2017

GÖZDE BAYER

ÖZET

AYNA NÖRON AKTİVİTELERİNİN REHABİLİTASYON AMAÇLI GÖZLENMESİ VE YORUMLANMASI

Gözde BAYER

Doktora, Biyomühendislik ABD

Tez Danışmanı: Prof. Dr. Tülin KUTSAL

İkinci Tez Danışmanı: Yrd. Doç.Dr. Kutluk Bilge ARIKAN

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İlk olarak makak maymununun prefrontal korteksinde ve daha sonra da inferior parietal lobülünde keşfedilen ayna nöronlar hem bir eylemin gerçekleştirilmesi hem de aynı eylemin izlenmesi sırasında aktive olan bir grup nöronlardır.Buna benzer bir nöral sistem insanlarda da bulunmaktadır.Bu gözlem-eylem eşlenim sistemi, hareketin anlaşılması ve motor imgelemi gibi oynadığı birçok role dayanarak, inme sonrası üst uzuvlarında hareket kaybı olan hastaların rehabilitasyonu için yeni bir yaklaşım yöntemi olarak önerilmiştir.

Bu tez çalışması ayna nöron sistemi (ANS)'nin Elektroensefalografi (EEG)'de bir göstergeci olan mu ve/veya beta frekans bandındaki güç baskılanmasını incelemektedir. Bu çalışmada uygulanan deney tasarımları ve kontrol düzeneklerinde temel hedef, inmeli hastaların üst

uzuvlarının motor rehabilitasyonuna faydalı olabilecek bilgiler elde edebilmektir.

İlk deneyde, deneye katılan gönüllüler objeye yönelik bir elin hareketini içeren videolar izlemişlerdir. Bu görsel stimulasyonlardan hangisi veya hangilerinin ANS üzerinde nispeten etkili olduğu araştırılmıştır. Bu amaçla C3, C4, P3, P4, F7 ve F8 elektrot lokasyonlarında dört farklı video stimulasyonu için EEG ölçülmüştür. Sonuçlar, dört farklı hareket videosunun, duyumotor korteks üzerinde, mu (8-12 Hz) frekans bandında anlamlı derecede baskılanmaya sebep olduğunu göstermiştir. Görsel stimulasyonların ANS üzerindeki etkisinin detaylı incelenmesinde yumuşak ve sert yayların gösterildiği video stimulasyonlarının beynin alt premotor korteksine karşılık gelen beyin bölgesinde ana etkiye sebep olduğu bulunmuştur. Ayna nöronların premotor kortekste hareketin gözlenmesi sırasındaki aktivasyonu gözlemsel öğrenmede önemli bir rol oynamaktadır. Bu sonuçlara dayanarak, belirli görsel stimulasyonların, eylemin gözlemi içerikli rehabilitasyon protokollerine uygulanabilirliği önerisinde bulunulmuştur.

Motor imgelemin inme sonrası motor fonksiyonların geri kazanılmasında yararlı olabileceği önerilmektedir. İmgelem tabanlı rehabilitasyona uygulanan yöntemsel yaklaşım, imgelemin etkinliğini en uygun hale getirebilir. Bu kapsamda, imgelemin eylemden sonra yapılmasının imgelem performansı üzerinde etkisi olup olmadığı araştırılmıştır. İmgelemi yapılacak hareket sembolik bir görsel (ipucu) ile bağdaştırılmış ve bu koşul altında çalışma yapılmıştır. Deneye katılan 10 kişi, iki gruba ayrılarak bir grup önce eylemi sonra imgelemi yapmış (GEF grubu), diğer grup ise deneye imgelem ile başlamıştır (GIM grubu). Olaya Bağlı Spektral Pertürbasyon (OBSP) değerleri, mu (8-12 Hz) ve beta (15-25 Hz) frekans bandında eylem ve imgelem koulları için merkezi (orta), parietal (arka) ve frontal (ön) beyin bölgeleri için çıkarılmıştır. Sonuçlar, hem eylemin yapılması hem de imgelemi koşulları için anlamlı derecede ($p<0.05$) mu ve beta band baskılanması göstermiştir. 10 kişiden alınan verilerin analizi, imgelem koşulu altındaki baskılanmada, frekansın tüm elektrot bölgelerinde ana etkiye sahip olduğunu göstermektedir. Bu sonuç, mu ve beta ritimlerinin imgelem sırasında farklı fonksiyonel özeliklerinin olduğu görüşünü desteklemektedir. Deney sırasında ayrılan iki gruptan alınan imgelem koşulu OBSP değerleri göstermiştir ki, baskılanma miktarı GEF grubunda biraz daha fazladır. İki grup arasında anlamlı fark kontralateral parietal ve iki taraflı ön beyin bölgelerinde bulunmuştur. Bir ipucu ile bağdaştırılan basit bir motor hareket için eylemin öncelikle yapılmasının sonra gelen imgelemin yapılmasını kolaylaştırdığı ve ön beyin bölgelerinin imgelem performansını yansıttığı sonucuna varılmıştır. Sonuçlar, inmeli hastaların imgelem tabanlı rehabilitasyonunda ilave içerik oluşturacaktır.

Son deneyde, tam tahrikli harici iskelet yapısına sahip *ExoPinch* parmak robotu kullanılarak hareket beklentisinin gözlem üzerindeki etkisi araştırılmıştır. Sonuçlar göstermiştir ki duyu-motor korteks civarındaki merkezi kanallarda gözlemsel koşul (beklenti var veya yok) beyin yarıküresi etkileşimi anlamlıdır. Ek olarak, ayna nöron sisteminin görsel stimulasyonların kinetik özelliklerine göre verdiği cevaplar da incelenmiştir. Sonuçlar, yaklaşık ventralpremotor korteks'e karşılık gelen ön kanallarda kinetik özellikler ile beyin yarıküresi arasında anlamlı bir etkileşim göstermiştir. Bu alandaki ayna nöron aktivitesi gözlemsel öğrenmede önemli bir rol oynamaktadır. Bu sonuçlara dayanarak, belirli görsel stimulasyonlar ve ayna nöronların fonksiyonel becerileri birleştirilerek, inmeli hastalarda el motor fonksiyon kaybının iyileştirilmesinde olumlu motor cevaplar alınabileceği önerisi getirilmiştir.

Anahtar Kelimeler: ayna nöronlar, eylemin gözlemi, imgelem, elektroensefalografi (EEG), olaya bağlı spektral pertürbasyon (OBSP), mu/beta baskılanması (desenkronizasyonu), inme, rehabilitasyon

ABSTRACT

INVESTIGATION AND ASSESSMENT OF MIRROR NEURON ACTIVITY FOR REHABILITATION PURPOSES

Gözde BAYER

Doctor of Philosophy, Department of Bioengineering

Supervisor: Prof. Dr. Tülin KUTSAL

Co-Supervisor: Asst. Prof. Dr. Kutluk Bilge ARIKAN

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Mirror neurons, discovered on prefrontal cortex and subsequently on inferior parietal lobule of macaque monkey, are a class of neurons that become activated with both performing an action and observing the same action. A similar system of neurons also exists in humans. On the basis of features of the putative mirror neuron system (MNS) and its role in action understanding and internal rehearsal (motor imagery) of actions, this action observation-execution matching system has been proposed as a new approach for training in the rehabilitation of patients with motor impairment of the upper limb after stroke.

This thesis investigates the mu and/or beta frequency band suppression as an index of the human mirror neuron system (MNS) in Electroencephalography (EEG). Several experimental design and control procedures were applied with the primary objective that the study might be beneficial to motor rehabilitation programs of upper extremities for stroke patients.

In the first experiment, subjects observed different types of object-directed hand actions in order to explore whether observation of any of these actions may have a relatively strong effect on MNS activity. Here, EEG was recorded at electrode locations C3, C4, P3, P4, F7 and F8. The results showed that all conditions were associated with a significant mu band (8-12 Hz) desynchronization over the somatosensory cortex. Further investigation of the effect of the visual stimuli on MNS revealed the main effect of video stimuli of hand squeezing soft and hard springs, at the frontal channels nearly corresponding to ventral premotor cortex (vPMC) area of the brain. The activation of mirror neurons in this area during action observation plays a crucial role in observational learning. Based on these results, it was proposed that specific type of visual stimuli may be implemented in the action observation-based treatment of stroke patients to have a positive additional impact.

Recent evidence suggests that motor imagery might be beneficial to recovery of motor functions after stroke. The implemented strategy in imagery-based rehabilitation may have a crucial role to optimize the imagery performance. In the second experiment, it has been explored if prior execution facilitates the subsequent imagery performance when the motor task to be imagined was associated with a symbolic cue. 10 healthy participants were divided into two groups and performed the execution and imagery of a sequential pinch grip task: one group started the experiment by execution of the task (group named GEF) and the other group performed the imagery session at first stage (group named GIM). Event Related Spectral Perturbations (ERSPs) at mu (8-12 Hz) and beta (15-25 Hz) frequency bands from EEG data were extracted for imagery and execution conditions of 10 subjects over central, parietal and frontal brain regions. The results showed that both simple execution and imagery conditions were associated with a significant ($p<0.05$) mu and beta band desynchronization over the somatosensory cortex. A significant main effect of frequency was found during imagery condition of 10 subjects and over all relevant channels. This supplies evidence that mu and beta rhythms might have different functional properties for mental rehearsal of actions. ERSP data from two experimentally manipulated groups showed that brain activity (desynchronization) for imagery condition was slightly higher for group GEF. Significant differences between two groups were found at contralateral parietal and bilateral frontal sides. It was concluded that for a cue-based simple motor task, a prior execution of the motor task might facilitate the subsequent imagery task and frontal regions appears to reflect the motor imagery performance. The results will have further implications in imagery-based rehabilitation of patients with stroke.

In the last experimental study of this thesis, a fully actuated finger exoskeloton robot *ExoPinch* was utilized to investigate the anticipatory

effect of execution on observation. The results showed that the observational condition (with or without anticipation) interacted with hemisphere at central channels near somatosensory cortex. Additionally, the response of MNS was explored on the kinetics features of visual stimuli. The results revealed an interaction effect of kinetics features and hemisphere at frontal channels corresponding nearly to the ventral premotor cortex area of the brain. The activation of mirror neurons in this area plays a crucial role in observational learning. Based on the results, it was proposed that specific type of visual stimuli can be combined with the functional abilities of the MNS in the action observation based treatment of hand motor dysfunction of stroke patients to have positive functional motor responses.

Keywords: mirror neurons, action observation, motor imagery, electroencephalography (EEG), event related spectral perturbation (ERSP), mu/beta suppression (desynchronization), stroke, rehabilitation

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TABLE OF CONTENTS

Page

LIST OF TABLES

Page

LIST OF FIGURES

Page

NOMENCLATURE AND ABBREVIATIONS

Nomenclature

dB	Decibel
Hz	Hertz
μ	Mu
$F_k(f,t)$	Spectral estimate of trial *k* at time *t* and frequency *f*

Abbreviations

ANOVA	Analysis of Variance
AO	Action Observation
AOT	Action Observation Treatment
AIP	Anterior Intraparietal Lobule
BCI	Brain Computer Interface
BA	Brodmann Area
BOLD	Blood Oxygen Level Dependent
CAR	Common Average Reference
DIP	Distal Interphalangeal
DOF	Degrees of Freedom
dPMC	Dorsal Premotor Cortex
EEG	Electroencephalography
EP	Evoked Potential
ERD	Event Related Desynchronization
ERP	Event Related Potential
ERS	Event Related Synchronization

ERSP	Event Related Spectral Perturbation
FIR	Finite Impulse Response
fMRI	Functional Magnetic Resonance Imaging
GEF	Group Execution First
GIM	Group Imagery
GUI	Graphical User Interface
hs	Hard Spring
ICA	Independent Component Analysis
IPL	Inferior Parietal Lobule
LP	Long Pinch
M1	Primary Motor Cortex
MI	Motor Imagery
MBC	Metallic Binder Clip
MEG	Magnetoencephalography
MEP	Motor Evoked Potential
MCP	Metacarpophalangeal
MNS	Mirror Neuron System
MT	Mirror Therapy
MTG	Middle Temporal Gyrus
PFG	Prefrontal Gyrus
PIP	Proximal Interphalangeal
PL	Parietal Lobule
RA	Right Arrow
ROM	Range of Motion (Movement)
SI	Somatosensory Cortex

SMA	Supplementary Motor Area
SP	Short Pinch
SS	Soft Spring
STS	Superior Temporal Sulcus
TMS	Transcranial Magnetic Stimulation
vPMC	Ventral Premotor Cortex

1. INTRODUCTION

Since their discovery in monkeys in 1992, mirror neurons, which fire in response both to the performance and to the observation of specific actions, have been the focus of an extensive debate in cognitive neuroscience [1, 2, 3]. Multiple brain imaging techniques have shown that humans also possess a homologous neural structure, the putative *mirror neuron system* (MNS). Over the past 25 years, a broad range of functions have been ascribed to this neural system. It is thought to be involved in action understanding, imitation, empathy, language processing, social interaction and certain types of learning [4]. MNS is probably essential for learning actions and goals from others by direct and automatic linking of observed actions and corresponding motor areas [5]. It should be emphasized, however, that MNS is not the only system responsible for any type of learning. It integrates information from other brain areas and these areas in turn are engaged in regulating MNS.

Based on the features of the MNS and its role in action understanding and imitation, a systematic activation of this observation–execution matching system has been proposed as a novel approach for training in the rehabilitation of patients with motor impairment of the upper limb following stroke [6, 7]. It is the plasticity of brain that might be induced by coupling action observation and execution. Hand motor skill is heavily represented in mirror neuron regions, and there is significant reason to believe that good recovery from stroke might also depend on use of this system.

Intervention of robotic assistive devices has been useful tools in the treatment of hemiparesis due to stroke since 1990’s. Many of these efforts have been primarily focused and restricted on restoring hand motor function given the central role that hand movements play a vital role in human existence. Specifically, the tips of the thumb and the index

finger allow humans to pinch and manipulate small objects in a very precise way. Therefore, the focus of this thesis study has been the pinching motion (precise grip) and for this purpose an exoskeleton type robotic system *ExoPinch* was developed and used primarily for hand rehabilitation.

It was postulated that by matching observation with execution in the therapy tasks, functional outcome of stroke patients can be well improved. In addition, the degree of recovery will depend on changes to the ventral/dorsal premotor cortices, one of the core regions of the MNS. The activation of mirror neurons in premotor cortex during action observation plays a crucial role in observational learning.

This thesis study was designed to investigate the activity of the MNS using Electroencephalography (EEG) technique in the presence of different visual stimuli of hand motions with precision grip. Event related desynchronization (ERD) of mu (8-12 Hz) and beta (15-25 Hz) frequency band rhythms were studied in association with execution and imagery of hand movements and also with the observation of different types of object-directed hand actions. The stimulus generation and experimental control were prepared using PsychoPy2 software. EEG data were collected using 16 channel OpenBCI and Ultra Headset dry electrode system. Data were preprocessed and analyzed using EEGLAB, a signal processing toolbox under MATLAB.

In this thesis, a fully actuated (with 2 DOF) finger exoskeleton robot *ExoPinch* was utilized to evaluate the MNS in healthy subjects.

EEG studies of MNS have mostly considered the effect of observation (or imagery) of visual stimuli on somatosensory cortex. Here, the research has been extended to the core areas of this system. Based on the results, it was proposed that specific type of visual stimuli can be combined with

the functional abilities of the MNS in the action observation based treatment of stroke patients to have a positive additional impact.

In Chapter 3, each experimental setup was detailed with the relevant/specific literature survey. Much of the emphasis has been placed on hand motor deficits after stroke. More specifically, the activity of the MNS has been assessed for the precise grip (pinching) motion of index finger and the thumb.

This thesis study was supported by the Scientific and Technical Research Council of Turkey (TÜBİTAK) under Grant 114E621.

2. GENERAL INFORMATION

People suffering from stroke typically exhibit loss of control and weaknesses in their affected side (face, arm or leg). In stroke rehabilitation, treatment has mainly been on restroring the upper limb motor deficits given the vital role that the re-use of the upper limbs (especially hands) play a central role for patients daily lifes.

In neurophysiology, there is increasing experimental evidence that the mere observation of actions performed by others recruits the same motor areas that are also recruited when actions are actually executed [1]. The underlying mechanism of this action observation-execution matching system has been the neurons that *mirror* or reflect the observed actions into their motor representations. Brain areas that are endowed with this matching mechanism are defined as the mirror neuron system (MNS) [2, 4].

Facilitation of this neural substructue for functional recovery has been proposed as a novel approach for the recovery of motor functions after stroke [6,7].

2.1. Discovery of the MNS

2.1.1. Evidence from Non-human Primates

In 1992, a particular class of neurons was discovered by single cell recordings in the rostral part of inferior area 6 (F5) of the monkey (Macaca nemestrina) premotor cortex during observation of object-oriented hand actions such as grasping, manipulating and placing [1]. The most effective visual stimuli in triggering these neurons were the actions in which hand or mouth interacted with an object. Further investigation by the same research group revealed a subset of these F5 neurons that discharge both when the monkey observes an individual (human or monkey) performing a specific action and when it does that same action [2, 3]. In cognitive

neuroscience literature, neurons with this capacity of responding to the visual stimulus and coding the corresponding motor response have been referred to as the “mirror” neurons.

In macaque monkey, mirror neurons have also been described in detail in the prefrontal gyrus (PFG) of inferior parietal lobule (IPL) and anterior intraparietal (AIP) area [8]. As in area F5, most mirror neurons in these areas were found mainly to show a correspondence between the observed and executed motor acts and they are heavily connected with two sectors of F5: PFG mostly with F5c and AIP with F5a [9]. Another cortical area in which neurons responding to the observation of actions per- formed by others is the superior temporal sulcus (STS) [10]. The neurons in this region contribute to the visual recognition of action but they do not a ear to be endowed with motor properties that are defining features of mirror neurons and cannot be part of the MNS [4]. Instead, PFG of IPL receives higher-order visual input from STS and sends the output to the ventral premotor cortex including area F5 [11]. The parieto-frontal network of PFG, AIP and F5 forms the core of the monkey mirror neuron circuitry [12].

2.1.2. MNS Structure in Human Brain

Similarities between a monkey and human brain have led some researchers to question the existence of the mirror neuron system in humans. However, the activity of these neurons in humans cannot be recorded directly in the same way except under special circumstances [13]. In this study, a significant portion of neurons in su lementary motor area (SMA) responded during both execution and observation of hand grasping actions and facial emotional expressions.

A first evidence of action observation-execution matching system was provided in 1950s by an Electroencephalography (EEG) study [14]. The decrease in EEG spectral power recorded over central scalp locations

occurred not only when the subjects observed actions performed by others but also during active movements of the subjects.

A more direct evidence is based on the Transcranial Magnetic Stimulation (TMS) of the motor cortex of healthy human subjects [15]. In this study, subjects were required to observe an experimenter grasping objects or performing meaningless arm gestures during which the motor-evoked potentials (MEPs) were measured from hand muscles. It was demonstrated that MEPs increased significantly during observation of experimenter grasping an object or making arm movements. The MEP pattern was very similar to the pattern of muscle activity recorded when the subjects performed those movements. These findings suggest that, in humans, there is a neural system matching action observation and execution.

Most authors generally agree that area F5 is the monkey homolog of Broca's area (Brodmann area (BA) 44) in the human brain [16]. One notable functional difference between these two areas is that the Broca's area (left inferior frontal gyrus-IFG; BA 44 and 45 in IFG overlap at least in part, with the ventral premotor cortex) in humans is most commonly thought of as an area for speech, while F5 is often considered as an area for mouth and hand representations. The earliest experiments on the neural substrate during action observation of grasping actions identified areas of increased blood flow activity in Broca's area but this area did not find to be involved during the execution of grasping actions [17]. This result led researchers to assume that Broca's area could not be considered a potential neural area with "mirror" property. However, a positron emission tomography (PET) study [18], which follows oxygen consumption in the brain, showed that during the execution of a hand movement sequence, the blood flow in correspondence with Broca's area was highly significant.

Besides the acquisition of grammatical rules and speech production (production of words) functions, Broca's area seems to be involved in action understanding, action planning and imitation [19].

In humans, MNS is considered to be composed of two main cortical regions: the inferior parietal lobule (IPL) and the inferior section of the precentral gyrus plus the posterior part of the inferior frontal gyrus (IFG) forming a parieto-frontal circuitry [11]. The regions, such as the superior temporal sulcus, that do not contain neurons with mirror properties are anatomically connected to the "core" mirror neuron system. The level of the transformed data through these regions to the core MNS makes them critical to any of the processes attributed to the core MNS and their inclusion would define the extended mirror neuron circuit [11]. Another critical component from both an anatomical and functional perspectives of this extended MNS is sensorimotor cortex (primary motor (MI) and somatosensory (SI) cortices) which is responsible for action representation in the brain during the observation and execution of motor tasks [21, 22]. Such representations are most likely involved in understanding and performing actions via simulation of observed behavior (e.g., hand-object interactions) [2].

The sequence of cortical activation for healthy subjects was studied by a whole-head magnetoencephalography (MEG) study [20]. The results of this study demonstrated that after the observation of still pictures of implied motions, cortical activation progressed in steps from the occipital cortex to the superior temporal region (STS), the inferior parietal lobule (IPL), and the inferior frontal lobe (Broca's area), and finally, 50–140 ms later, to the primary motor cortices (fronto-central areas) of each hemisphere. This study revealed that strong magnetic fields were evoked in IFG (BA 44/45) involving Broca's area during imitation than other

conditions, therefore emphasizing the role of this brain region on imitation of action.

2.2. Functional Significance of Mirror Neurons: What Do Mirror Neurons Code?

Since the discovery of the mirror neurons in monkeys, considerable effort has been devoted to investigating their functional roles in the human brain. The observed action done by another individual can be interpreted in two distinct ways: *what* the actor is doing (e.g. hand grasping of a cup) and *why* the actor is doing it (e.g. hand grasping of a cup in order to drink it)? The term "intention" can be used in this specific sense, to indicate the "why" of an action [5].

In order to recognize another individual's action, one has to put the observed action into a semantic motor network. If mirror neurons are involved in action understanding, they should also respond to conditions in which the action occurred is not seen but there are still sufficient clues to create the motor representation of that action. This functional favor of the mirror neuron system was observed in an experimental paradigm where monkey MNS was tested from single unit recordings in two conditions: one was action presentation (full vision condition) and the other one was when the final part of the action was hidden (hidden condition) and could therefore only be inferred [23]. In the hidden condition, more than half of the F5 mirror neurons discharged meaning that the monkey *knows* the outcome without actually seeing the hand-object interaction. Furthermore, when the action effective in triggering the F5 mirror neurons was performed without an object behind the occlude, there was no response, although the monkey saw the same hand motion of the experimenter in two conditions. These findings suggest that a population of mirror neurons is endowed with a visual property and they are able to code the observed actions without full vision of them. Indeed,

mirror neurons do not respond or respond only very weakly to mere presentation of an object and to mimicking of motor acts without a target object [8].

As in the monkey, parieto-frontal network of MNS in humans mostly code for the goal of the motor act [24]. The results of this study showed that the various hand actions, be they simple or complex, human or robotic, activated the dorsal/ventral premotor (dPM/vPM), middle temporal gyrus (MTG) and parietal areas, typically considered to compose the MNS. These results further suggest that the mirror neuron system might respond to movements with different kinematics than those of humans. The main goal of the observed action rather than how it is performed might be more effective in triggering the human MNS.

Another evidence in favor of goal coding is provided by a functional magnetic resonance imaging (fMRI) [25]. Nineteen healthy subjects observed the residual limb of a woman amputee as a novel effector and a familiar effector (e.g., hand) as control. Participants initially demonstrated activity in the bilateral inferior and superior parietal cortices when observing actions made by the novel effector compared to the control indicating that the kinematics of a novel effector is matched to one's own existing sensorimotor system. Participants then received extended visual exposure to both effectors, after which they showed little difference between activation in response to familiar biological effector (hand) compared to novel effector (hand actions of the residual limb). It can therefore be argued that when observing others' actions, the muscle activation underlying the movement is not seen but rather the external consequences of that action [26].

Several research on goal-directed actions suggest a functional gradient of cognition-motor function in the frontal region of the brain such that the premotor cortex (PMC) functionally plays a critical role in motor control

and learning of goal directed actions in humans [27]. The neural activity in PMC while reaching and grasping has been shown to be independent of the recording side (dorsal or ventral) suggesting a cluster of PM neurons encode reaching and grasping [28]. Being densely interconnected with the hand area of the primary motor cortex (M1), makes the ventral premotor cortex (vPM) that is known to be a part of the MNS, a critical node in the neural circuit that is important for sensorimotor processing of grasping.

In general, premotor cortices together with sensorimotor regions are associated with motor preparation, sequencing, and response selection during motor learning [29].

2.3. Cortical Distribution of MNS

The functional role of the MNS depends on the anatomical and physiological properties of the brain areas in which these neurons are located, they do not have a specific functional property *per se*. Many studies have shown that mere observation of actions recruits the precentral gyrus (BA 4, 6 including the SMA), the middle frontal gyrus (BA 9, 46), the inferior frontal gyrus (BA 44, 45) and the inferior parietal lobule (BA 40) [30, 31]. A Meta-analysis of brain imaging techniques supports a consistent pattern of cortical network recruited during the observation of others' actions, overlapping with the cortical activity evoked by the action execution [31]. Data in these studies show that the executed and observed goal-directed grasping movements are encoded in a fronto-parietal circuit formed by vPMC, the IPL and by the caudal part of the IFG. In an fMRI study, observation of grasping hand actions containing objects activated the vPMC and BA 44 indicating that the mirror neurons are involved in understanding of others' *intention* [5]. A functional MRI experiment in monkeys studied the active brain regions while observing a hand grasping objects [32]. It was found that rostral part of F5, areas 45A, 45B, and 46 were activated for the observation of hand grasping an

object. Specifically, observation of objects with shapes activated the BA 45. This finding converges to the evidence that area 45 may be important for full comprehension of actions.

By means of non-invasive brain imaging techniques, it has been possible to show that action observation activates the premotor and parietal cortices in a somatotopic manner [33]. Observation of hand actions activates the precentral gyrus and the pars opercularis of IFG in a medial-to-lateral direction. Hand and arm motor acts are also represented caudally in inferior parietal lobule (IPL). It was further postulated that the inferior parietal lobule in the monkey brain may furnish area F5 with visual properties of the object (e.g., size) for selecting the appropriate motor schema related to the seen object. Thus, MNS organization first starts in the IPL region and then expands to area F5. The mirror neurons in the IPL brain region mainly respond to the mere observation of hand-object interaction [8]. It was found that the neural activities in motor regions were observed in association with the main goal of the motor act (e.g., grasping an object) rather than the detailed representation of that movement (arm extension or finger flexion). It then appears to be valid that the mirror neurons in IPL allow one to recognize the goal of the action (action understanding) rather than the detailed visual description of that action. A series of control experiments further supported that the selectivity of the mirror neurons in IPL is not dependent on force, movement kinematics, or type of grasped stimulus [34].

2.4. Relationship to Mirroring: Mu and Beta Rhythms

Since the discovery of "mirror neurons" in monkey brain, researchers have investigated whether these neurons also exist in human brain. Human "mu rhythm" was first described by the French scientist Henri Gastaut [14] in 1950s and was also termed "rolandic rhyhtm" since these waves seemed to arise from the rolandic regions, at a rate of around 8-13 Hz. They

observed that the rhythm recorded from central derivations occurs not only during active movements of studied subjects, but also when the subjects observed actions performed by others.

The mu rhythm occurring within the standard "alpha" band (i.e., 8–13 Hz (oscillations per second) was first thought to be considered indicative of psychopathology. A link between mu and epilepsy was suggested as a reminiscent of recent work linking autism spectrum disorders to mu abnormalities [35]. However, the use of standardized EEG caps and new advanced techniques / softwares for analyzing EEG established that mu occurred more commonly than previously thought. One prominent theory is that when an individual is at rest, the neural cells in the SI cortex fire in synchrony. Similarly, when he or she performs or observes a motor act, these neural groups fire in a desynchronized way (reflecting cortical activity) so the power in mu band is reduced, compared to when the individual is at rest [36]. Therefore, mu suppression is taken as an indicator of the engagement of the mirror neuron system in humans [37]. These mu rhythms are usually associated with 15-25 Hz beta rhythms, another candidate index of MNS engagement. Similar to mu suppression, spectral power at beta band also decreases by executing an action, MI and by merely observing an action. While some beta rhythms are harmonics of mu rhythms with a typical peak frequency of around 20 Hz, some are separable from them by topography and/or timing, and thus are considered to be independent EEG features [38, 39, 40]. Mu and beta rhythms might provide independent control signals for an EEG-based Brain Computer Interface (BCI) system [38].

When evaluating studies on mu suppression and the MNS, it was found that all papers studied a lower frequency band (around 8–13 Hz), with some additionally considering the beta frequency band (15-25 Hz) [41]. Studies have shown that sources underlying mu rhythm recorded with EEG are

mainly concentrated over the central and parietal cortical areas of human brain [37]. These brain regions have similar to the areas that fMRI research has shown activate during both execution and observation of an action [31]. Specifically, these clusters showing mirror properties were located in the inferior parietal lobule, inferior frontal gyrus and the adjacent ventral premotor cortex.

2.5. Methodological Moderators and Stimulus Characteristics

The parameters (e.g., used effector, muscle involvement) in the observed movement have been shown to modulate the activity patterns of the cortical areas matched to the observer's motor system, even at the level of single muscles [15, 42]. Moreover, the corticospinal excitability in the hand area of M1 while subjects observed the lifting of objects of different weight increased considerably higher when observing heavy object lifting compared with light object lifting [43]. Data in this study convincingly indicate that the observer's M1 is facilitated by the muscular requirement of the observed movement in terms of the force that is produced in the particular muscle.

It was shown by a TMS study that when the intrinsic characteristics (size and shape) of the to-be-grasped object was congruent with the hand movement kinematics, motor evoked potentials (MEPs) were statistically significant greater during observation of congruent (or suitable) videos than during observation of object videos without a suitable grasping movement [44].

2.6. Stroke and Rehabilitation: The MNS Approach

2.6.1. Background

Stroke is the most common cause of long-term disability in many countries [45]. Stroke is either caused by the local bleeding (hemorrhagic stroke) or by obstruction of a blood vessel inside the brain (ischemic stroke). If these

conditions are prolonged, brain cells are deprived of oxygen and glucose and begin to die causing loss of abilities controlled by that area of the brain such as muscle control. Depending on which region of the brain is damaged, different motor deficits and cognitive impairments can arise: upper limb paresis, attention and memory deficits and language disorders are the most common manifestations of stroke [46]. The most commonly observed hand impairment after stroke is weakness in finger extension/flexion [159]. Since all these limitations can dramatically affect the performance of daily life activities of the patient and family, the physical therapy is of utmost importance [47].

Traditional physiotherapy is based on physical practice and much of the emphasis has been placed on motor abilities such as coordination and muscular strength relegating sensory and cognitive aspects to a secondary role [48]. Increasing evidence exists on the effectiveness of newer methods of intervention. Motor imagery (MI) and action observation (AO) treatment have been recently gained attention as a promising rehabilitation tool for patients with neurological disorders [6, 49]. Neurophysiological basis of these innovative tools are represented by the activation of the MNS in humans [7].

2.6.2. Brain Repair after Stroke

As neural networks are developed and shaped by intensive experience in years of practice [50, 51], the neural cortical connections can be remodeled by similar level of experience. It is the cerebral *plasticity* that depends not only on the anatomical and biological (endogenous) factors but also on exogenous inputs such as a triggering stimulus (afferent information) in both healthy subjects and stroke patients [51, 52].

The successful treatment of upper limb motor dysfunction after stroke requires the neural reorganization that theoretically includes the wiring of the dynamic neural network through stimulus-dependent plasticity [53,

6]. A large body of literature has focused on a neurological model in which the motor therapy of a patient with stroke is understood in terms of physical repair (remediation) of the neural circuits that underlie the relevant impaired functions. For example, therapy for chronic aphasia patients could be devised for repairing or rebuilding of the damaged neural circuits by a short-term intensive language training [54].

It is possible that the plasticity of brain might be induced in motor cortex by coupling action observation and execution. In an fMRI study, observation of daily actions with concomitant physical training of the observed actions has been shown to reinforce a network of areas consisting of bilateral ventral premotor and inferior parietal areas (core regions of the MNS) in chronic stroke patients [7]. It is most likely that the neural populations that are normally interconnected with the damaged area are involved in the reorganization process. Since ventral premotor cortex has reciprocal connections with primary motor cortex [27], it is important to identify these network related changes for a better understanding of neuroplastic mechanisms that underlie recovery after stroke [52].

2.6.3. Action Observation Treatment (AOT): A Novel Rehabilitation Approach

The stimulus dependent property of brain plasticity requires a carefully tailored behavioral intervention to produce relevant desired modulation of the neural circuits in the treatment of upper limb motor functions. Over the past several decades, one of the remarkable neurophysiological findings has been the discovery of the mirror neuron system that links the action observation with execution [1]. Based on principles of motor physiology and MNS, it has been suggested that observation of meaningful (goal-directed actions) followed by their execution (*action observation treatment*-AOT) could be an effective strategy in the treatment of patients with neurological disorders [53].

Several studies have demonstrated that AOT exploits the action observation-execution matching mechanism to recover the performance of a specific motor skill. In a study, observation of thumb movements induced lasting specific changes in motor representations that resembled that elicited by physical training [55]. The results of a TMS study have shown that observation of a simple intransitive movement (abduction of right index and middle fingers) increased the finger abduction force of both hands when compared with an untrained group [56]. In an AOT, patients with chronic ischemic stroke showed a significant improvement of the motor function compared with the control group [7].

On the basis of these findings, AOT has been thought to have a positive impact on recovery of motor functions after stroke by reactivation of cortical motor areas that are involved in the performance of the observed actions, the putative MNS.

Several studies demonstrated that the recruitment of the fronto-parietal MNS during action observation depends on how familiar are the observed actions to observer further suggesting to display daily actions in AOT [6, 57]. Indeed, the human MNS can match an observed action on the neural structures involved in its execution only if the observed action belongs to the perceiver's motor repertoire [58]. Using fMRI technique, demonstrated that participants having a prior physical practice of one type of dance sequence showed an increased level of BOLD activity in vPMC during observation of the dance sequence but not during the observation of an unfamiliar dance sequence. This suggests of an overlapping neural substrates of observation and execution.

What remains to be defined is the treatment effects of action observation therapy, for example, the dosage of AOT for stroke patients is not clear and should be assessed by further studies with large sample sizes [59].

2.6.4. The Neurophysiological Basis of Action Observation in Stroke Rehabilitation: The Role of Mirror Neurons

The neurophysiological basis for AOT relies on the recruitment of motor areas of action observation-execution matching system, the putative human MNS [2, 6]. Recruitment of this neural system to re-enact stored motor representations has been proposed as a potential tool in neurorehabilitation. Cognition becomes the instrument to influence patient recovery by generating afferent information that flows without motor activity [60].

In the observation phase of AOT, the observed actions restore the neural structures normally recruited during the execution of those actions. Observed actions are decomposed into simple motor acts that activate the corresponding motor representations in premotor cortex and in inferior parietal lobule [61]. These regions then recombine to fit the observed motor act. In particular, during the observation of non-practiced hand actions, inferior parietal and ventral premotor areas have been shown to be more strongly activated than for the practiced actions [61]. Similarly, an fMRI study using a treatment task containing manual exploration of objects revealed an increase in a network of areas which overlaps with the mirror neuron system [7]. These findings indicate that MNS can be involved in reactivation of motor areas that might have a positive additional impact on recovery of motor functions following stroke.

In the course of a successful rehabilitation treatment, the functional reorganization of the brain may change in correlation with the behavioral improvements. There is growing evidence that these rehabilitation-related changes are associated with altered activity in motor cortical regions [62]. In an fMRI study, the improvements in the hand motor functions of stroke patients were found to be correlated with BOLD activity in contralateral (to the affected hand) parietal and premotor brain regions [63]. This study

suggested an altered recruitment of sensorimotor cortices after a hand flexion–extension movement therapy and changes in the neural oscillations in these central areas are suggested to be the indication of a successful motor rehabilitation. The mirror neuron system (MNS) in the parietal and premotor areas might therefore constitute a powerful mechanism in the course of rehabilitation treatment of motor functions after stroke.

2.6.5. Motor Learning Principles and Mirror Neurons

Motor learning is defined as a series of processing a practice through which an individual acquires a new motor skill [64]. Most often learning from others involves observation of an action (observational learning) and simultaneously or after a certain delay, execution of that action. While learning a new motor act, the observed model (for example, reaching for a cup of coffee) is decomposed into its elementary acts. Rearranging of these elementary motor acts is performed to fit the given (observed) model and these cognitive operations seem to occur within the putative mirror neuron system [65]. This direct matching system of the observed actions with their correspondent motor representations in the observer's brain can enable individuals to *understand* the action [4]. Therefore, it has been suggested that understanding an action is a prerequisite for learning [66].

Neurophysiological studies have demonstrated that humans can learn novel and complex motor patterns by imitation which combines action observation, imagery and execution [67]. The results showed that an important role in imitation learning is played by the prefrontal lobe and area 46, in particular, appears to play a major role in learning through imitation. An fMRI study demonstrated that the MNS is involved in imitative learning through neural interactions with motor preparation areas and dorsolateral

prefrontal cortex [57]. These studies suggest that the mirror neuron system forms the basis for learning through imitation.

Mirror neuron system could be shaped by a similar process to that of *Hebbian learning*, a type of associative learning, which states that ”any two cells or systems of cells that are repeatedly active at the same time will tend to become ‘associated’ so that activity in one facilitates activity in the other” [68]. This could make gradually better associations of neural circuits through experience; experience can induce regeneration or changes in dendritic sprouting [69]. Once a new motor act has been learnt by experience, the MNS can subsequently cause a faster recognition of that action when observed. This finding has been shown by an fMRI experiment [58] that used experienced dancers and non-dancers. It seemed that the subjects in the group of dancers had higher activity in some brain areas (including parts of the MNS) when watching performances of their dance styles, while for the non-dancers, activity was relatively low while watching dance performances. It has also been shown that previous experience can modulate action perception that might have important implications for observational learning [70]. These findings support the idea that MNS is sensitive to the amount of the prior experience the observer has with the observed action. This can be seen as a contribution of MNS to learning.

In the case of stroke patients, there are damaged neural circuits in the brain. Hebbian learning provides a model for how neural circuits that are partially disconnected by a lesion may regain the original pattern of connections: if they are activated at the same time they may become reconnected and hence the cortical functions that they sub-serve may be regained [71]. With several repetitions of this simultaneous neural activity, these disconnected neurons may become reconnected. This synaptic sprouting is to some extent experience dependent. It has been argued that

the mechanisms underlying learning may be fundamental to the mechanisms involved in recovery of function following brain damage [69].

2.6.6. Robotic Mirror Therapy

People suffering from stroke typically exhibit loss of control and weaknesses in their affected side (face, arm or leg). These patients need timely and persistent rehabilitation to regain their daily life activities. So far, the focus of stroke rehabilitation has been to restore the motor functions of the proximal and distal segments of the upper limbs (arm, hand and fingers) [175].

Intervention of robotic assistive devices has been useful tools in the treatment of hemiparesis due to stroke since 1990's [72]. Many of these efforts have been primarily focused and restricted on the proximal arm through a repetitive and intense training in a specifically designed task [73, 74] to improve the functionality of the upper limb [75, 76, 77]. Such systems utilize a target endpoint to which the patient is asked to move their arm, shoulder or hand.

Rehabilitation robots can be considered of two different types in general [78]: exoskeleton and end-effector. Indeed, for both types, the characteristics of the robotic system (e.g. its degree of freedom (DOF), control strategy etc.) are set according to the goal-directed end point. Exoskeleton robotic systems are designed side-by-side with the upper limb. The distal and the proximal segments are interfaced to the upper limb phalanges and joints. However, a precise matching of the kinematics of the upper limb and that of the robotic mechanism is required for a rehabilitation robot to be feasible [79]. Misalignment between the human limb and the exoskeleton can cause many problems such as injury of the hand and inaccurate sensor measurements. This requires that the joint configuration of the anatomic system/nature of the movement in terms of kinematic parameters should be transformed to the system's functional

frame for a proper and safe movement quality [78]. Most upper limb exoskeletons cover movements from shoulder to wrist. One of such available systems is the ARMin III robot that provides three actuated DOF for the shoulder and one for the elbow joint [80].

Design of a robotic system for hand rehabilitation becomes more difficult since fingers of the hand have many DOFs within a significantly reduced space [81]. Beside, stroke alters a broad array of features of hand movement [82]. Several systems with different characteristics of their mechanism architectures, working principles and control systems have been proposed for the finger rehabilitation [83]. A commercially available Cyberglove (Immersion Corp., San Jose, CA) and a Rutgers Master II-ND haptic glove was used for the rehabilitation of hand function of post-stroke patients in the chronic phase [84]. A hand-wrist robot HWARD showed improvements in hand motor functions of stroke patients [74].

End-effector robotic devices on the contrary, hold the patient's hand or forearm at specific points and forces are generated at the interface to assist the movement of the limb. In an end-effector type mechanism, the control of the torque for a specific joint is not possible and this limits the set of exercises in rehabilitation protocols. Robots such as MIME [84], GENTLE/s [85] and MIT-MANUS [86] are of end-effector type. The Mirror Image Motion Enabler (MIME) system has a passive mode that moves the patient's arm along a predefined trajectory [87]. The system also incorporates a force feedback to either resist or assist to the patient.

Recently, mirror therapy (MT) has been proposed as an alternative treatment for stroke of upper and lower limbs. In MT, the patient places the intact limb on the reflective side of a mirror and the non-intact limb on the non-reflective side of the mirror. Reflection of the unaffected limb in the mirror gives patient the illusion that the affected limb is moving as instructed [88]. The

underlying mechanism of the MT has mainly been related to the activation of the neurons with mirror-like properties [1].

One of the advantages of the MT is that it is a low cost option for an extensive period of time with substantially low to no risk of adverse effects. However, the effectiveness of MT may depend on factors such as stage and the duration of the paralysis post stroke [88]. MT together with robotic assistive devices in the field of rehabilitation has led researchers to the robotics neuro-rehabilitation [89] and robots are particularly suitable for the application of motor learning principles to neurorehabilitation [90].

3. EXPERIMENTAL METHODS

This chapter presents the main experimental hardware and software components used for the assessment of the MNS activity. Existing literature on MNS and the compiled requirements for the methodological approach to investigate this neural structure forms the basic setup integration. The activity of the MNS was monitored by Electroencephalography (EEG). The raw data were first acquired and then analyzed off-line for further evaluation. The visual stimuli that would lead to the activation of the putative MNS were videotaped and processed, with an emphasis on those that are critically relevant for rehabilitation of patients with stroke. An exoskeleton type finger robot was fabricated and utilized for rehabilitation purposes with a main focus on providing a precise grip (pinching) motion of hand. All the subjects recruited in the experiments were adult volunteers with no history of neurological disorders.

3.1. Electroencephalography (EEG)

The existence of the electrical activity of the brain was discovered in 1875 by an English physician Richard Caton. In 1924 Hans Berger, a German neurologist, demonstrated that this electrical activity could be recorded from the human scalp. He used the word electroencephalogram (EEG) as the first for describing brain's electrical activity and suggested that this electrical activity changes according to the functional status of the brain, as from alertness to relaxation.

EEG is a completely non-invasive recording technique from the surface of the scalp generated by many bio potentials in the cerebrum of the brain [91]. When the brain cells (neurons) in the cerebral cortex are activated by the synaptic excitations of the dendrites, local current flows are produced generating recordable electrical activity on the head surface. The

neural contributions of the electrical activity in EEG are the pyramidal neurons in the cortex. These pyramidal neurons with their long apical dendrites are arranged parallel to each other and oriented perpendicular to the cortical surface. Pyramidal neurons, when activated, generate coherent electrical fields by synaptic currents [92] and these currents are recorded by means of electrodes at long distances from the scalp (the EEG) or from the cortical surface (the electrocorticogram or ECoG).

EEG has been found to be a powerful tool in the field of neuropsychology due to its capability to reflect the normal and abnormal brain signals with good temporal resolution. The basic patterns of brain waves are commonly sinusoidal with characteristic amplitudes ranging from 0.5 to 100 μV (peak-peak) [93]. The primary components of EEG can be broken down into 5 frequency ranges: delta (0.5-4 Hz), theta (4-8 Hz), alpha (8-13 Hz), beta (15-20 Hz) and gamma (35-40 Hz) waves.

This thesis study is primarily based on the EEG analysis of the mu (8-12 Hz) and/or beta (15-25 Hz) band rhythms for the existence of the putative MNS.

3.2. EEG Acquisition: Hardware and Software

3.2.1. EEG Acquisition Device: OpenBCI

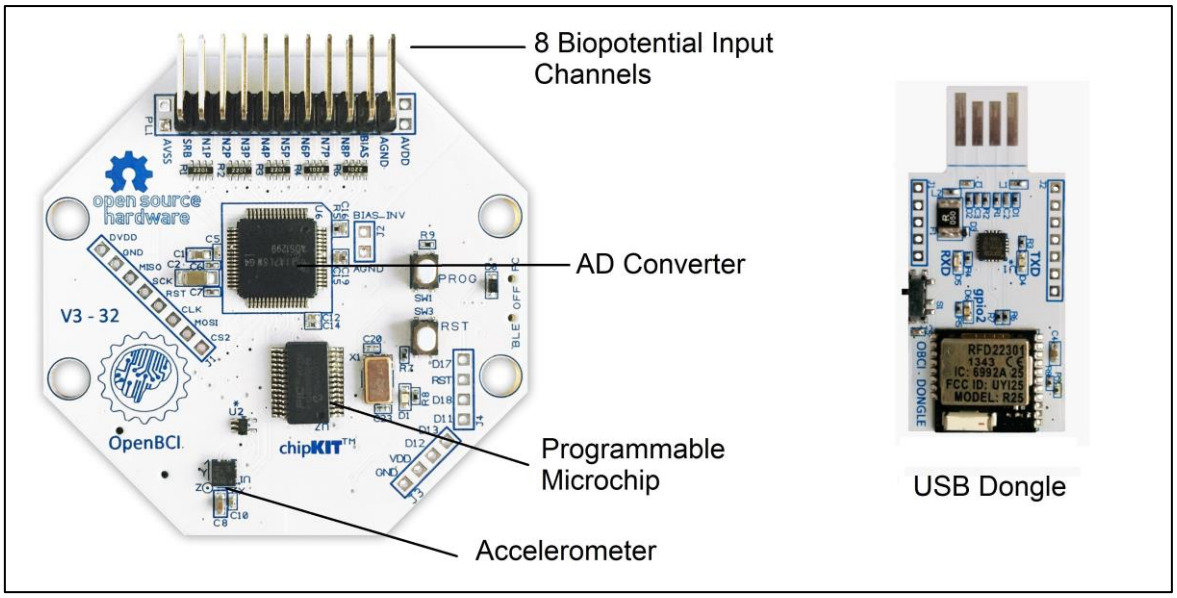
OpenBCI V3 32-bit board was selected as EEG data acquisition device throughout this thesis work (Figure 3.1). OpenBCI is a chipKIT-compatible, 16-channel (8 channel main board and 8 channel Daisy module) neural interface with a 32-bit processor which implements the Microchip PIC32 microcontroller. The board communicates with a computer via wireless network using a USB dongle, which is based on the RFDuino radio module. The RFDuino USB dongle is configured to a ear to the computer as if it is a standard serial (COM) port running at a rate of 115200 baud using the typical 8-N-1 serial setup.

The reference electrode on OpenBCI corresponds to SRB2 pin with a white colour code while the ground electrode is AGND with black colour code. The remaining (active) signal electrodes (Figure 3.2) with their colour code were set constant throughout this study for convenience (Table 3.1).

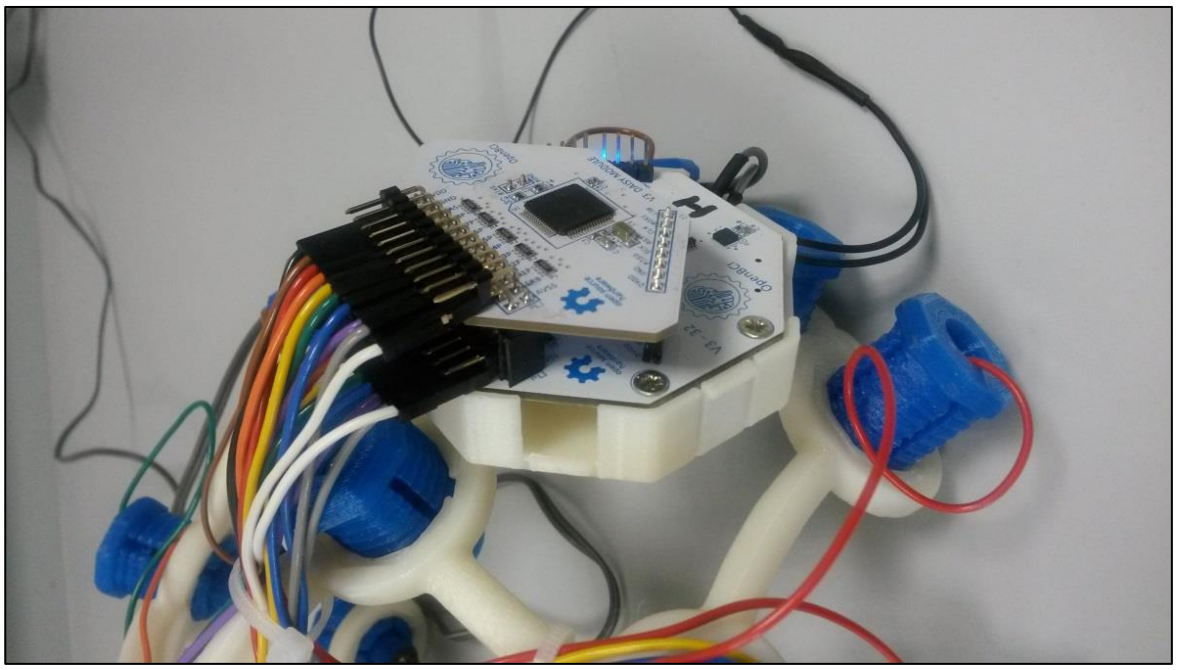
There are two critical pieces of information for interpreting the raw EEG data flow from OpenBCI: the sample rate and the scale factor. The default sample rate of OpenBCI is 250 Hz set mainly by the ADS1299 analog to digital converter. The scale factor, on the other hand, is the multiplier that is used to convert the raw data from *counts* into *volts*. Setting the gain of ADS1299 chip its maximum gain (24x) results in a scale factor of 0.02235 microvolts per count.

Table 3.1. OpenBCI channel configuration with colour codes used in this study.

Channel Number	Channel Name (see Figure 3.2(a)	Colour Code
1	Fp1	Grey
2	Fp2	Purple
3	C3	Blue
4	C4	Green
5	T5	Yellow
6	T6	Orange
7	O1	Red
8	O2	Brown
9	F7	Grey
10	F8	Purple
11	F3	Blue
12	F4	Green
13	T3	Yellow
14	T4	Orange
15	P3	Red
16	P4	Brown
SRB2	Reference	White
AGND	Ground	Black



(a)



(b)

Figure 3.1. Schematic view of openBCI main board (8 channels) and USB dongle (a) and general view of OpenBCI with Daisy module (16 channels) (b).

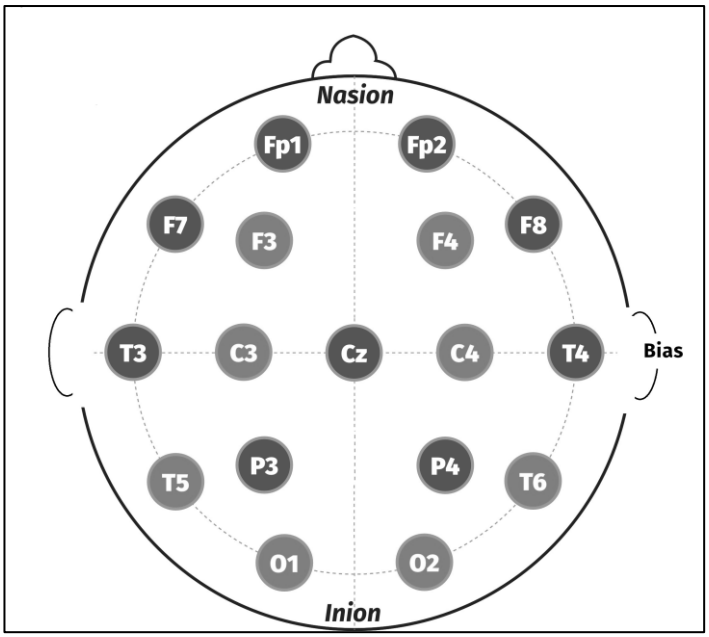
3.2.2. Electrodes

Two types of EEG electrodes were used in this study: (a) wet gold cup and (b) dry electrodes mounted on OpenBCI headset. For both electrode types, international 10-20 system has been used for placement of electrodes on the scalp during EEG recordings [94]. In this setting, each electrode position is uniquely identified by up to two letters representing the sagittal and coronal location (Figure 3.2).

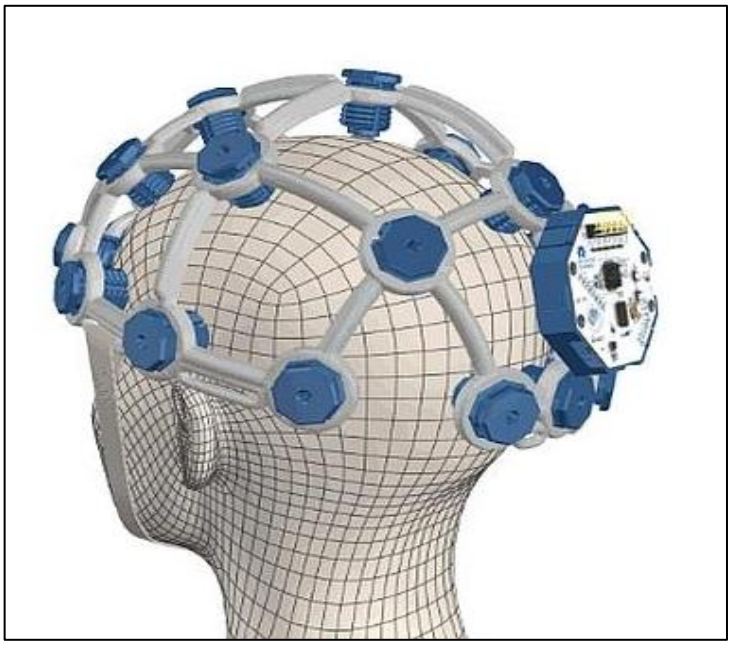
The 10-20 in the name of the montage refers to the placement of the electrodes on the scalp: the electrodes are located 10% or 20 % (of the size of the head) from each other. The electrode locations used in the international 10-20 system are represented by letters and numbers (even or odd). The letters F, C, T, P and O correspond to frontal, central, temporal, parietal and occipital regions of the brain, respectively.

3.2.3. EEG Acquisition Software

The raw EEG data were acquired on-line using Processing 2.2.1 software. The Processing software is an open source and runs on the Windows, Mac and Linux platforms. The OpenBCI's graphical user interface (GUI) was built using Processing, a Java-based coding framework. Data streaming is performed through RS-232 (Serial) port. Several libraries (e.g., controlP5, gwoptics) are to be downloaded additionally to launch the OpenBCI GUI properly.



(a)



(b)

Figure 3.2. (a) International 10-20 electrode setting (montage) for 16 electrodes. The reference was set at vertex (Cz) and the ground electrode was placed at right ear lobe.

(b) General view of OpenBCI Ultracortex Headset

3.2.4. Analysis of EEG Data: EEGLAB

A major problem in electroencephalography (EEG) signal processing is the contamination of the signals by various physiological and non-biological artifacts such as line noise, eye blinks, lateral eye movements, heartbeat, muscle activity and high electrode impedances. The electrical activity of the eyes or muscles causes more disturbances as they have large amplitude when compared to EEG signal. The existing investigations about EEG signals have shown that artifact rejection is one of the central issues in the preprocessing of EEG recordings.

In this thesis study, raw data from EEG acquisition device was preprocessed and analyzed off-line using an open source EEGLAB v13.4.4b [95], a signal processing toolbox running under cross platform MATLAB (The Mathworks, Inc.). There are several favoring features of EEGLAB for using in this thesis work. Some available functions in EEGLAB include scrolling of continuous data, data filtering, artifact rejection, baseline removal, epoching of data and extraction of data epochs time locked to a specified experimental event. Furthermore, electrophysiological data from several subjects can be combined and analyzed in time-frequency domain. This thesis study combined the graphical user interface of EEGLAB, interactive functions from the command window and custom MATLAB scripts for analysis. Many of signal preprocessing steps used in EEGLAB toolbox are common to other EEG analysis environments.

3.2.5. EEGLAB Workflow

The preprocessing steps mainly involve the following operations in this order:

- Raw data file (in .txt format) and channel locations are imported into EEGLAB. For 16 recorded EEG channels, data are saved in one file per task and per person.
- EEG dataset is high-pass filtered and there after low-pass filtered using Finite Impulse Response (FIR) filter. The main reason for this step is to remove DC and very low frequency (<0.1Hz) drifts due to capacitance coupling. High-pass filtered data at 1-2 Hz are recommended for further analysis [96].
- Text files containing event and epoch information are imported via the EEGLAB menu and by using the workspace variables. Event data file contains both the latency at which the event occurred and the name of the event. The data epochs time locked to events of interest are extracted in order to study the event related EEG dynamics of continuously recorded data.
- The epochs that contain atypical behavior of neural activity should be excluded either by careful visual inspection or by automated methods that examine the data with statistical procedures (e.g. kurtosis or probability based procedures).
- The EEG data contain several artifacts with unknown sources. Independent Component Analysis (ICA) [97] algorithms can isolate both neural and artifactual sources in EEG analysis such that these sources are maximally independent of one another with a less-gaussian distribution [98]. Among the several ICA and blind source algorithms, Infomax [99] ICA algorithm was used as a more efficient method at processing EEG data in this study [100].

The core mathematical concept of Independent Componenet Analysis (ICA) also called Blind Source Separation is to minimize the mutual information among the data projections and maximize non-gaussianity (Central Limit

Theorem by kurtosis). When ICA is applied to a matrix of EEG data, an 'unmixing' matrix of weights (w) is found. Multiplying the unmixing matrix by the observed scalp data matrix (channels by time points) returns a matrix of independent component (IC) activations. Therefore, data become maximally temporally independent of one another. The temporal independence assumption of ICA is the basis for separating sources of artifact (e.g., eye blink, line noise), since their activities will ordinarily not be reliably phase-locked to one another.

To summarize, ICA is highly effective where, (a) the time courses of the sources are independent, (b) the mixing medium is linear and the propagation delays are negligible (c) the number of independent sources is the same as the the number of sensors (EEG channels).

After these preprocessing steps have been performed, data can be analysed off-line in the time-frequency domain.

3.2.6. Time-Frequency Analysis

In EEG signal processing of biological sources, the amplitude and latency measures of signal peaks in the average trials are either called sensory evoked potentials (EPs) or sensory/cognitive event-related potentials (ERPs) [101]. ERP method relies on the averaging methods thereby enhances the signal-to-noise ratio. These event-related changes represent the ongoing neural activity in the frequency window and may consist either of increases (ERS) or of decreases (ERD) in the spectral power. The former case may be considered to be due to increase in synchrony (Event Related Synchronization-ERS) while the latter case may be considered to be due to decrease in synchrony (Event Related Desynchronization-ERD) of the underlying neural populations [101].

The non-stationary nature of EEG signals causes transient changes in the power or peak frequency of EEG waves. EEGLAB's custom spectral decomposition techniques are able to quantify the spectral content of the

signals as a function of time [95]. EEGLAB software successfully employs the custom spectral decomposition techniques, such as Event-related spectral perturbation (ERSP) method. The mean spectral power changes (ERS, ERD) for a specific channel (or component) are calculated [95]. ERSP power spectral values are over a sliding latency window. The data are then averaged across all trials. Typically, for *n* number of trials, if, $F_k(f,t)$ is the spectral estimate of trial *k* at time *t* and frequency *f*, then *ERSP* is given by:

$$ERSP\ (f,t) = \frac{1}{n}\sum_{k=1}^{n} F_k(f,t)^2 \qquad (3.1)$$

To compute $F_k(f,t)$, sinusoidal Morlet wavelets are used for which the number of cycles is increased slowly with frequency. Morlet wavelets give better frequency resolutions for higher frequencies than the classical wavelet methods that use constant cycle length. By extracting the mean baseline spectral power from the each spectral power, the ERSP values are produced. This method better visualizes the power changes across the frequency axis. The power (in dB) at a given frequency and latency relative to the time locking event (e.g., visual stimulus onset) at each image pixel is represented by a specific color code. Specifically, in an ERSP time-frequency plot, blue and red colors represents desynchronization and synchronization respectively [95].

3.3. Stimulus Presentation Software: PsychoPy2

Among other software programs for stimulus presentation (e.g., Presentatiton, Psychtoolbox, EPrime), PsychoPy2 v1.83.04 [102] has been used to present the visual and/or audio stimuli and for the control of the experimental setup in this thesis study. As an application, this open-source software package is a platform-free experimental control system

that has two main choices of interface: the *builder* view and the *coder* view. PsychoPy2 is built almost entirely on Python code and it has Application Programming Interface (API) from which experiments can be easily developed in Python. Applying functions in PsychoPy2 may require several sub-modules.

PsychoPy2 is capable of interfacing with external hardware devices via parallel (or serial) ports. This provides precise synchronization with the stimuli and an external device via an 8-bit fast TTL pulse. PsychoPy2 is able to gather and record the responses via keyboard press or mouse click.

Neuroscience and psychology experiments typically need to present visual or audio stimuli with precise timing. When precise timing is needed, it is not very accurate to measure the duration of a stimulus in seconds (or milliseconds) since an LCD screen for a visual stimulus may not have a constant refresh rate [103]. In this case, stimulus onset/duration can be determined by the frame number (or frame rate). Therefore, PsychoPy requires a computer with a graphics card that supports OpenGL drivers (version 2.0 or higher) and multi-texturing. In this case, certain visual functions run faster and stimuli can be updated very rapidly which is critical for stimulus timing especially for experiments that need to draw a large number of stimuli. In general, a powerful graphics card, a fast CPU (Intel i5 or i7), and plenty of memory (8 GB of RAM or more) can result in performance gains on all platforms (Windows 7 +, OS X 10.7.5 +, or Linux Kernel 2.6 +) [102].

3.4. Finger Rehabilitation Robot: ExoPinch

Designing a robot to actuate the finger of the hand is a significant challenge since human finger motions are subject to several constraints that limit the range of the natural movements [155]. The range of movement (ROM), on the other hand, is somewhat ambiguous because

the range depends on various factors involving human hand anthropometry.

In order to design a proper exoskeleton type mechanism for the finger motion, limits of the joint angles and the relative relations among the joints must be analyzed for the specific type of motion. Such an analysis can be exploited as a preliminary step towards the development of an exoskeleton hand device imitating the human hand shape and functionality. For the design of a "wearable" hand robot for the rehabilitation of the impaired hand, primary approach is to ensure that the movement ability should be in the physiological range.

In this thesis study, an exoskeleton type rehabilitation system, *ExoPinch* has been designed specifically for assisting in rehabilitation of the index finger of human left hand. It was preliminary developed to assist stroke patients in moving their index finger individually in a naturalistic pinching motion (precise grip). ExoPinch was primarily designed to study the brain's recovery process during the rehabilitation of stroke patients by monitoring the MNS activities but it also serves as a passive finger rehabilitation training tool after stroke. Overall, the integration of the ExoPinch system to the external stimulus paradigms (e.g., action observation) might serve as a comprehensive approach to stroke rehabilitation.

3.4.1. Basics of Mechanism Design

The mechanism synthesis was based on motion capture of index finger during flexion/extension movement. For this purpose, index finger of the left hand was kinematically simplified; it was modeled as a 4 linkages and 3 revolute joints mechanism as shown in Figure 3.3. Motion captures were recorded with a single camera (Logitech HD Pro webcam C 920). The camera and hand are positioned such that the motion is perpendicular to the camera. The initial resting position of the index finger was aligned along the x-axis as shown in Figure 3.4 and Tema Track Eye Motion 3.5

Analysis program was employed to extract the relevant joint angles (DIP, PIP and MCP) [156].

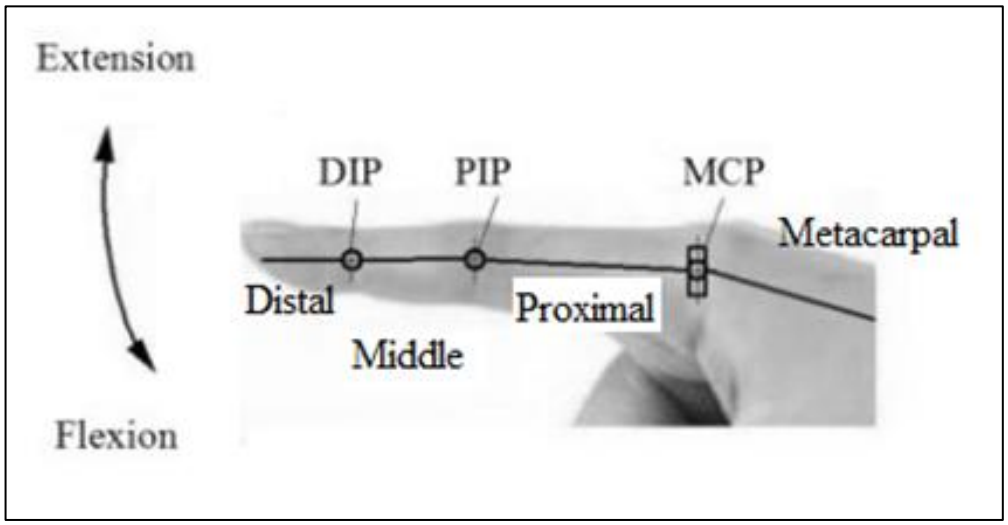
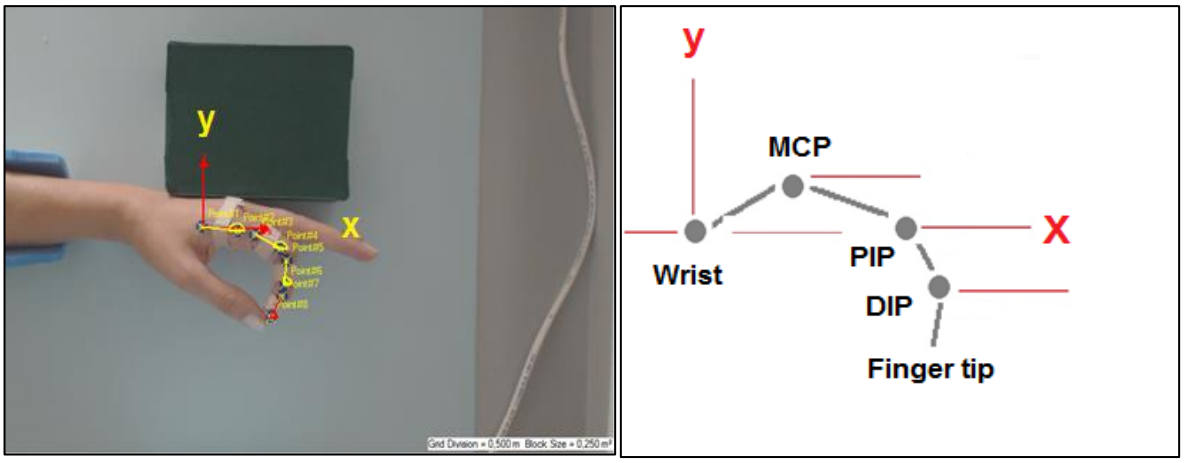


Figure 3.3. Joints and phalanges of the index finger for extension/flexion. DIP: distal interphalangeal, PIP: proximal interphalangeal and MCP: metacarpophalangeal joints.



(a) (b)

Figure 3.4. A general view from motion analysis software (a) and angle notations corresponding to the joint angles of the index finger (b).

10 healthy and right handed volunteers (4 females and 6 males) first watched a video with the desired pinching movement context and told to perform the same movement as natural as possible for approximately 2 seconds for 1 pinching period. For the analysis of the joint angles, linear Plexiglas bars with markers at the terminal points are placed on the index finger corresponding to the proximal, middle and distal phalanges (Figure 3.4, above).

In order to define the finger motion during pinching, the angular relations between PIP-DIP (Figure 3.5a) and MCP-PIP (Figure3.5b) were calculated. The equations used to fit the data shown in Figure 3.5a and 3.5b are:

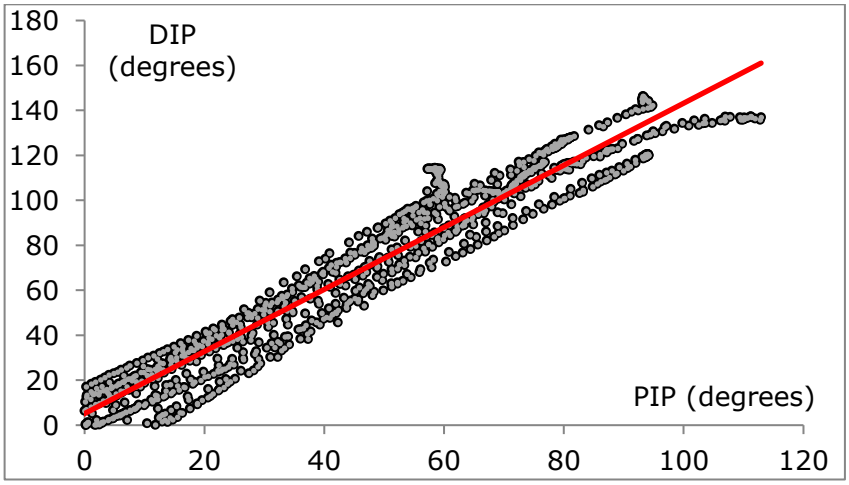
$$\mathrm{DIP} = 1.38\mathrm{PIP} + 5.17,\ \mathrm{R}^2 = 0.95 \qquad (3.2)$$

$$\mathrm{PIP} = -0.0000002\ \mathrm{MCP}^5 + 0.0002\ \mathrm{MCP}^4 - 0.0067\ \mathrm{MCP}^3 + 0.07\ \mathrm{MCP}^2 + 2.6376\ \mathrm{MCP} + 5.93,\ \mathrm{R}^2 = 0.70 \qquad (3.3)$$

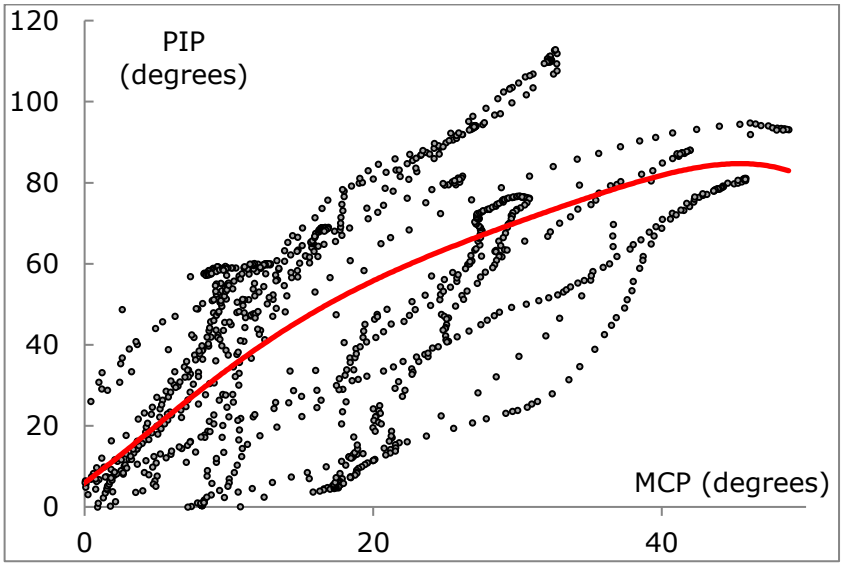
The ExoPinch mechanism consisted of four *4-bar mechanism* to maintain a flexible use for patients with different hand sizes while keeping computational complexity of the design reasonable. Equations 3.2 and 3.3 were adapted to the kinematic synthesis of ExoPinch. In kinematic synthesis, the objective is to calculate the mechanism dimensions required to achieve prescribed mechanism output parameters. While the prescribed mechanism output parameters include link positions, path points, and displacement angles, calculated mechanism dimensions include link lengths, link positions, and joint coordinates [157].

The exoskeletal mechanism was synthesized using genetic Levenberg–Marquardt algorithm and dynamical models were built in MATLAB and Simmechanics toolbox. The final link lengths and structure of the proposed mechanism were emerged as a result of kinematics based optimization

criteria by considering displacement angles with an optimized transmission angle for each 4-bar mechanism (Figure 3.6a, 3.6b).



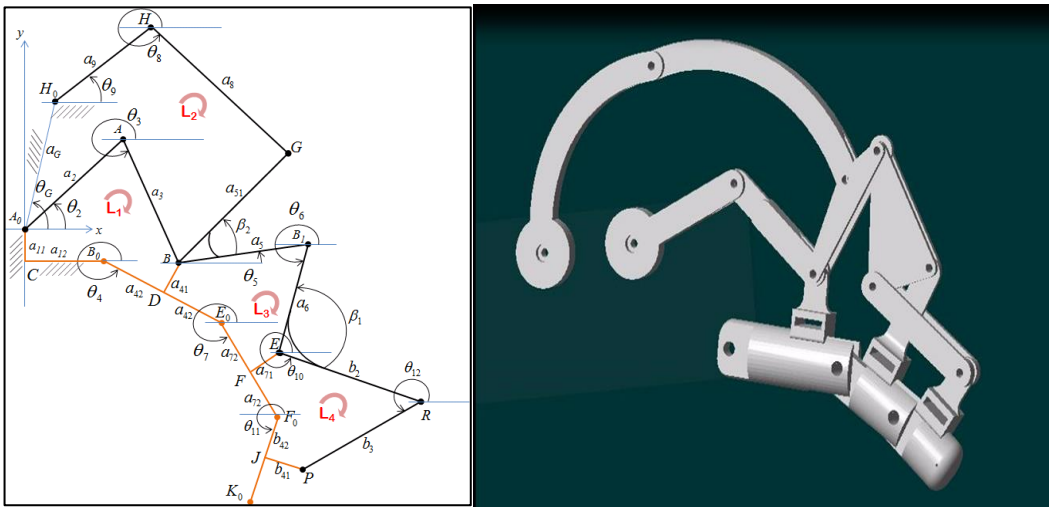
(a)



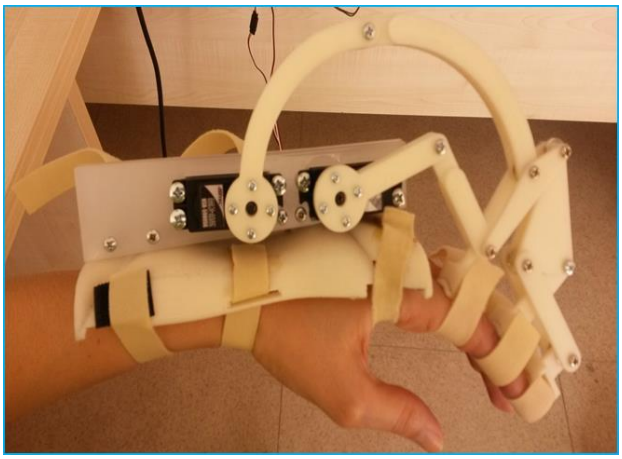
(b)

Figure 3.5. The relation between PIP and DIP (a); MCP and PIP joints (b). The black points were data collected from motion capture, and the red line is the curve-fit.

To meet the requirements above, a fully actuated 2 DOF mechanism was designed in a way that two actuators (Hitec HSR 5980SG, steel gear) drive the MP and PIP directly and DIP is driven indirectly with PIP (Figure 3.6c). To this end, maximum torque outputs with minimum bearing forces were obtained.



(a) (b)



(c)

Figure 3.6. Fully actuated 2 DOF exoskeleton mechanism: Structural dimensions and configuration angles of the 4-bar mechanism (a); Dynamical model in MATLAB/Simmechanics (b) and general view of ExoPinch assembly with two actuators (c).

4. EXPERIMENTAL STUDIES

The experiments reported in this chapter are designed to investigate the activity of the mirror neuron system for rehabilitation purposes. Although an extended survey of literature on MNS and rehabilitation was provided in Chapter 2, the relevant literature was compiled specific to the each experimental design and its contribution to rehabilitation was emphasized.

Experiment 4.1 establishes a paradigm to assess the effects of sensorimotor characterictis of observed actions on the MNS. Experiment 4.2 addresses the effect of prior execution on subsequent imagery of a simple motor act. Finally, Chapter 4.3 explores whether an anticipatory effect of execution controlled by an exoskeleton type robot modulates the mirror neuron activity while observing hand actions.

4.1. Response of Mirror Neurons during Observation of Actions with Different Sensorimotor Characteristics

The current study investigates the mu suppression as an index of the human MNS while subjects observed different types of object-directed hand actions: squeezing a hard and a soft spring; grasping a long and a short stick. It was explored whether observation of any of these actions might have a relatively strong effect on MNS activity. Here, EEG was recorded at electrode locations C3, C4, P3, P4, F7 and F8 for four different visual stimuli.

4.1.1. Theoretical Background on the Experiment

Mirror neurons that were initially discovered [1] in ventral premotor and subsequently in parietal cortex of macaque monkey are particular class of neurons that discharge both when an agent (human or monkey) itself performs a particular action, and when it sees another agent performing a similar action [2, 3]. Given its astonishing properties, this observation-execution matching system, now commonly referred to as the mirror

neuron system (MNS), has been proposed to subserve as a key neural basis for action understanding [5, 24, 104] social communication and motor learning [55, 65].

The functional involvement of MNS in motor learning has been supported by evidence demonstrating that mere observation of hand grasping actions leads to the formation of neural structures normally recruited during the execution of that action [30, 31, 105]. Moreover, there is strong evidence that human MNS is activated in a somatotopic manner [33] during observation of object-directed actions (such as pinching) but not during observation of a grasping movement without an object [1, 2, 105]. Functional neuroimaging studies have implicated the activity of premotor cortex (PMC), BA 44 and IPL, typically considered to compose the MNS in humans, during observation of object directed grasping actions [11, 30, 31].

One of the critical brain areas involved in learning of a goal-directed action is the PMC [27]. The mirror neurons in PMC mostly respond to the perception of specific hand-object interactions, or more specifically goal of the observed action [2]. It has been further suggested that vPMC neurons involve in observation-induced plasticity, the reorganization of the neural cortical connections [27]. Action observation exploits this neurophysiological mechanism for the recovery of motor impairment after stroke, thus it is a powerful tool for the improvement of upper limb motor functions of patients with stroke [6, 7, 55]. Since the mirror neurons in vPMC are known to be a part of the action observation-execution matching network and primary motor (M1) neurons are facilitated after PMC activation via dense premotor M1 connections, vPMC is thought to play a significant role in reorganization following injury to M1 [27, 106].

In action observation treatment, the presence of an object is known to recruit automatically the corresponding motor program [6]. The parameters (e.g.,used effector, muscle involvement) in the observed

movement have been shown to modulate the activity patterns of these cortical areas matched to the observer's motor system, even at the level of single muscles [15, 42]. Corticospinal excitability in the hand area of M1 while subjects observed the lifting of objects of different weight increased considerably when observing heavy object lifting in comparison to light object lifting [43]. Data in this study convincingly indicate that the observer's M1 is facilitated by the muscular requirement of the observed movement in terms of the force that is produced in that particular muscle. It was shown by a TMS study that when the intrinsic characteristics (size and shape) of the to-be-grasped object was congruent with the hand movement kinematics, motor evoked potentials (MEPs) were significantly greater during observation of congruent (or suitable) videos than during observation of object videos without a suitable grasping movement [44].

There is a growing body of literature that is revealing the functional properties of sensorimotor mu band (8-12 Hz) suppression (desynchronization) as an index of human MNS [37, 105, 107,]. It has been suggested that the power of alpha (mu) band is sensitive to sensorimotor characteristics (e.g., the required force) of the action [70].

The aim of this experiment is to shed new light on the functional significance of this dependent measure, if any, in relation to observation of different grasping actions. The purpose was to elucidate a particular action observation video clip that might have a possible capacity of modulating cortical oscillations relevant to the mirror neuron system. Electroencephalography (EEG) studies of mirror neuron system have mostly considered the effect of observation of visual stimuli on somatosensory cortex. Here, the research was extended to the core areas of this system. For this purpose, human EEG cortical oscillatory activity in the alpha/mu (8-12 Hz) band was measured at electrode locations that nearly correspond to the core areas of MNS, while participants watched

object-directed grasping movements. In particular, it was investigated whether mu oscillations are modulated by the type of the precision grip that is a ropriate for the objects' intrinsic attributes (e.g., size or stiffness). The methodological approach in this study allows exploring the MNS from a wider point of view.

4.1.2. Experimental Setup

4.1.2.1. Subjects

7 right-handed volunteers (one female, mean age=31.6, SD=11.2) without a neurological disorder participated in this study. The participants had a normal or a corrected-to-normal vision. Subjects were informed about the procedure before the experiment. They were presented with the objects and asked to grasp the object with a similar grasp type as appeared in subsequent video stimuli. The experimental procedure was approved by the local Ethics Committee in accordance with the ethical standards of the Declaration of Helsinki.

4.1.2.2. Stimuli and Procedure

Subjects sat on a comfortable chair 1 meter away from a computer screen (18" LCD screen with 60 Hz refresh rate). Stimuli were video clips of actions performed by the right hand of the experimenter. Video recordings were converted to gray-scale and clipped such that the motion of the agent began at the first frame of each video. Subjects were instructed to watch the stimuli carefully. They were told that there might be questions about the stimuli after the end of the session to maintain attention.

The stimulus generation and experimental control were prepared using PsychoPy2 software [102]. EEG data were collected during four conditions (Figure 4.1): (1) watching the video of the hand squeezing a soft spring (condition: *ss*) (2) watching the video of the hand squeezing a hard spring (condition: *hs*) (3) watching the video of the hand reaching and grasping a

short stick (condition *sp*) (4) watching the video of the hand reaching and grasping a long stick (condition *lp*). All video sequences of object grasping consisted of alignment of right hand with the main axis of the object, while shaping hand by the opposition of the index finger and thumb. A unique randomization of the 48 trials was created for each participant (12 repetition of each video) to obtain a reasonable experimental run time and enough EEG data for off-line analysis. The random sequences of video presentations were recorded by PsychoPy2 software for each subject and events were labeled in EEG data stream. Videos were between 4 and 6 s in length and a baseline of 4 s black screen was presented prior to the onset of each trial.

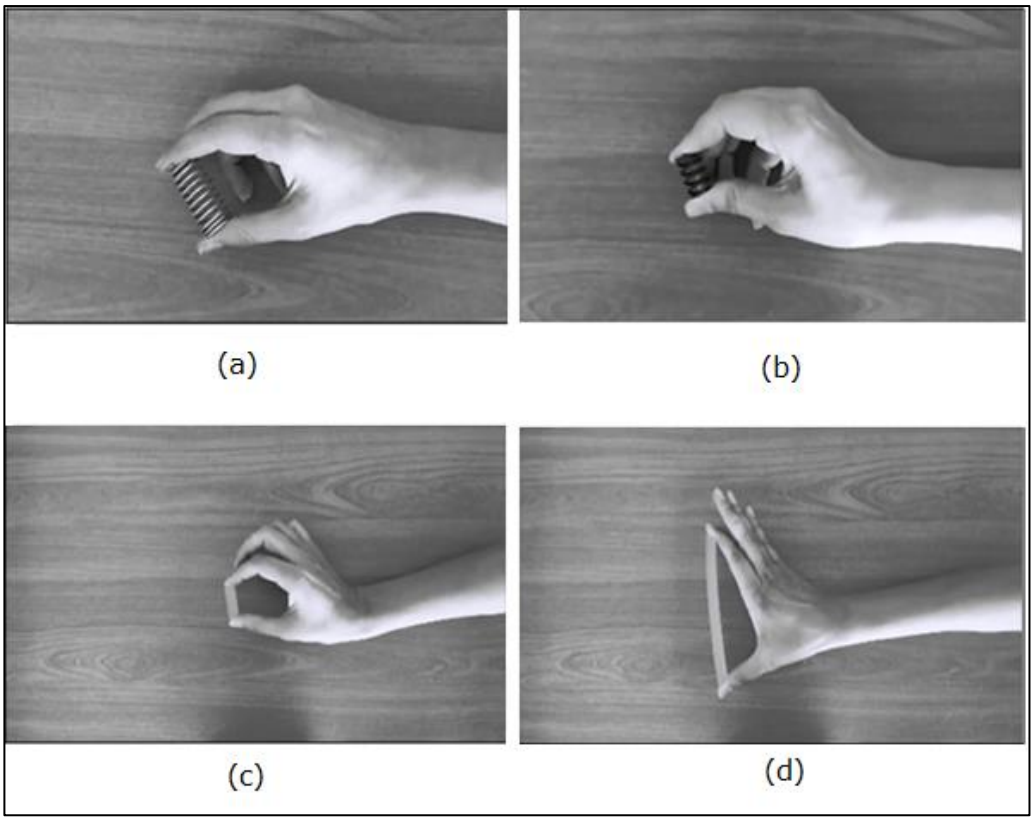


Figure 4.1. Still frames from the videos for condition ss: hand-soft spring interaction (a); hs: hand-hard spring interaction (b); sp: hand-short stick interaction (c) and lp: hand-long stick interaction (d).

4.1.2.3. EEG Data Acquisition

The EEG data were recorded continuously (bandpass, 0.1-100 Hz; sampling rate, 250 Hz) with the 16 channel 32-bit A/D converter using OpenBCI with Daisy module. UltraCortex Mark 4 dry electrode headset was used conforming international 10-20 electrode placement: Fp1, Fp2, C3, C4, F3, F4, F7, F8, T3, T4, T5, T6, P3, P4, O1, and O2. The reference electrode was set at vertex (Cz). Electrode impedances were confirmed to be less than 5 kΩ using real time electrode impedance measurements provided by the open source Processing software.

In order to synchronize the visual stimuli with continuous EEG recording, an additional Pyhton code was added to the existing stimulus code in PsychoPy2 software. The code enabled the data pins of parallel port (LPT) of the data acquisition computer (8 GB RAM, 64-bit Windows 7) to reach a low or a high logic level. A trigger code was uploaded to the Ardunio IDE (1.6.5) compatible OpenBCI board to enable the external trigger pin (D17) of the EEG device (Figure 4.2).

A Schmidtt trigger (74HC14) was added to the experimental circuit to speed up the signal and to step up the signal to +5V. By default, the last three auxiliary channels of the OpenBCI 32 bit board record the trigger inputs at 250 Hz sampling rate. A Matlab (Mathworks, Inc.) code was generated to process and sort out the raw EEG data.

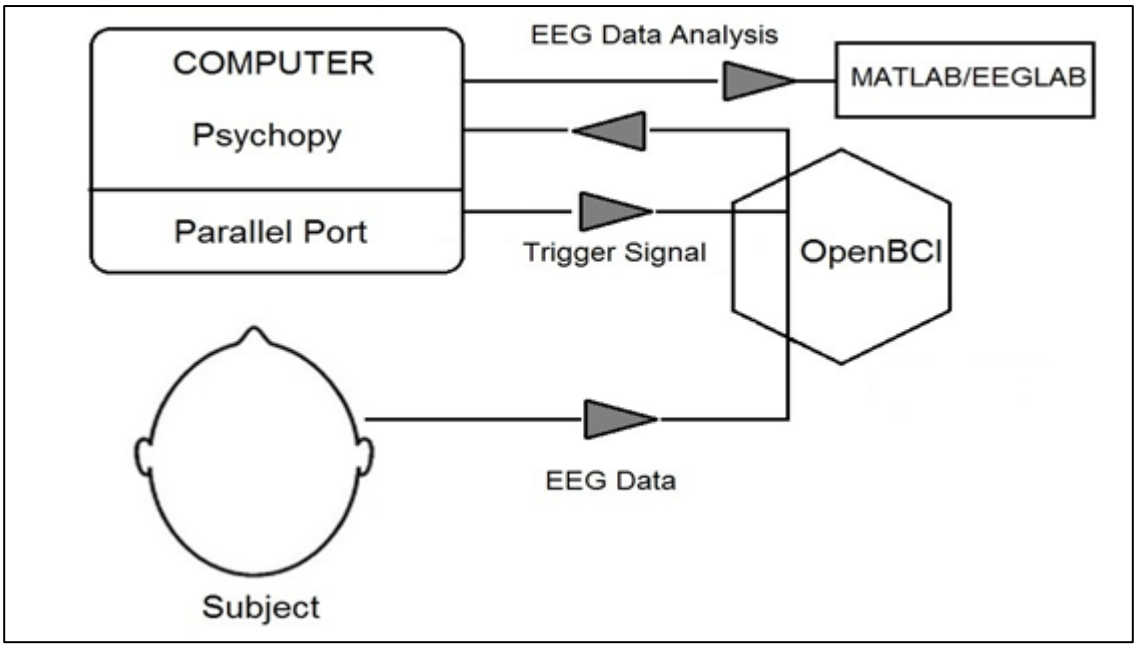


Figure 4.2. Schematic diagram illustrating the experimental setup. Stimulus presentation software sets the parallel port of the computer from "off" to "on" mode informing the EEG recording device of the time of the stimulus onset in continuous EEG data. The raw data from OpenBCI were preprocessed with MATLAB and the EEGLAB toolbox.

4.1.2.4. Electrophysiological Recording and Data Analysis

EEG data were preprocessed using EEGLAB 13.4.4b MATLAB (Mathworks, Inc) tool- box [95]. A linear finite impulse response (FIR) filter from 1 Hz to 20 Hz was applied to eliminate the baseline drifts and the 50 Hz line noise. A common average reference (CAR) was performed on all 16 electrodes in order to produce the reference free EEG data. The CAR method provides a better signal-to-noise ratio for the mu or beta-rhythm than does the any standard (e.g.ear-reference) method [108]. Data were epoched ranging from 1000 ms preceding stimulus onset (appearance of hand object interaction on the screen) to 2000 ms after stimulus onset and were time locked to the onset. In each epoch, baseline was considered

as the period starting 1000 ms before the onset of stimulus and ending at the stimulus onset. Atypical epochs were removed from further analysis by applying improbability test with standard deviation ≥ 6. Independent Component Analysis (ICA) method with extended Infomax algorithm [100] was used to remove eye blink, cardio graphic, electrical and muscle related artifacts. The components with typical artifact characteristics were removed from the data.

After preprocessing, data for each subject and condition were analyzed in the time frequency domain at all channels. EEG spectra were decomposed using a 3-cycle wavelet with the baseline corrected Event Related Spectral Perturbation (ERSP) method [95]. For each trial, the mean spectral power of the baseline (before onset) period was removed from the power at each time point.

Both the spectral and the time windows of mu oscillations for statistical analysis were determined from ERSP data plotted in EEGLAB/MATLAB environment. The mean mu band power values (in dB) were extracted at a number of frontal (F7, F8), central (C3, C4) and parietal (P3, P4) channels since these regions almost exclusively included regions that have been associated with the MNS in the literature: d/vPMC, Brodmann area 44/2 and IPL [4, 24, 109].

A two-way (object by hemisphere) repeated measures analysis of variance (ANOVA) was performed on data for *(a)* spring (soft, hard) × hemisphere (left, right) and *(b)* stick (short, long) × hemisphere (left, right) as within-subjects factors. The significance level was set at $p < 0.05$. A Mauchly's test showed that the sphericity assumption was not violated.

4.1.3. Results

In the channels of interest, C3, C4, P3, P4, F7 and F8, action observation led to attenuation in alpha band (8-12 Hz) power starting around 400 ms after stimulus onset (Figure 4.3). Plots for the other electrode locations (C4, P3, P4, F7, and F8) and for conditions hs and ss were similar and are not shown.

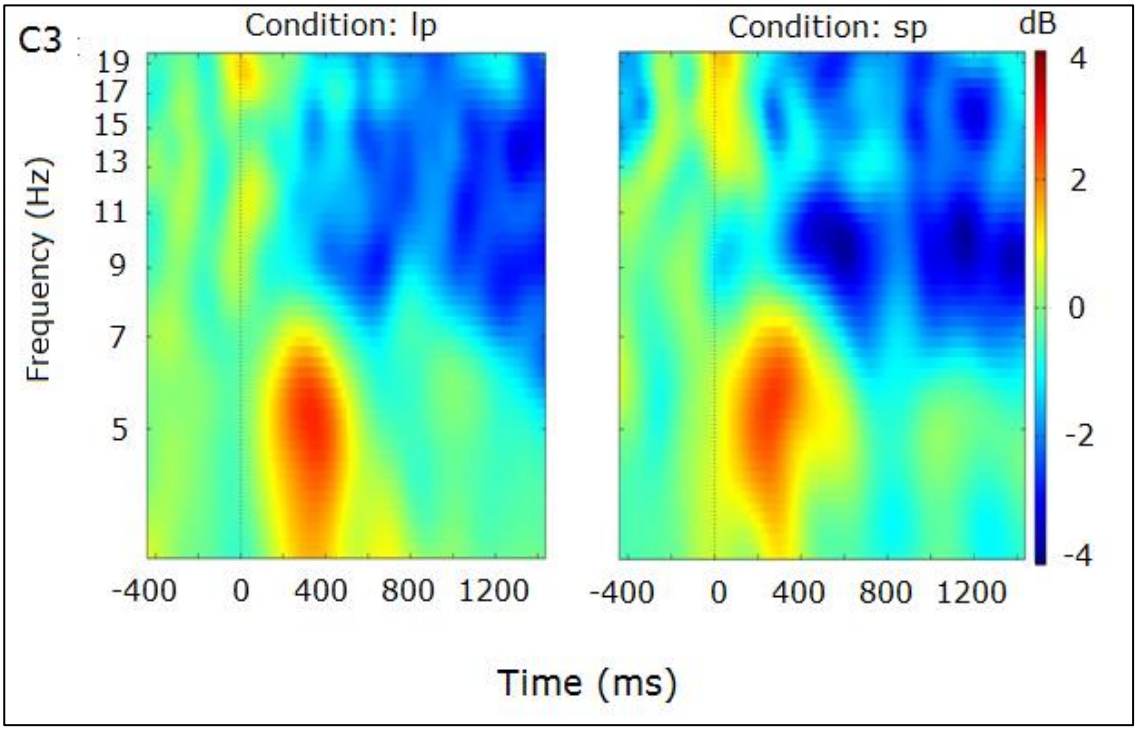


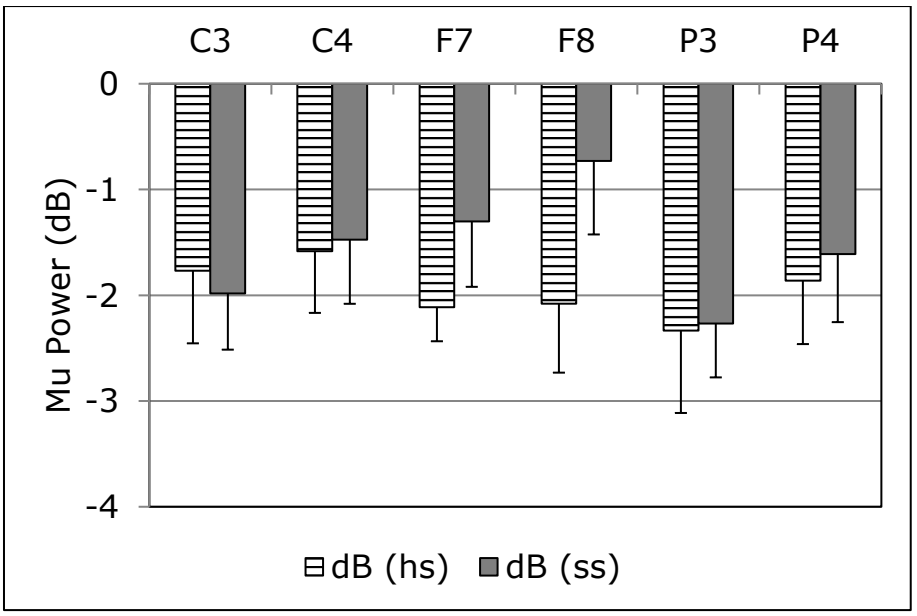
Figure 4.3. Event Related Spectral Perturbation (ERSP) plots for the two conditions (lp: grasping of long stick (*left*), sp: grasping of short stick (*right*)) at channel C3. The frequency axis is log scaled and the zero point on the time axis indicates the onset of the stimulus. A log ratio in dB less than zero indicates suppression.

Electrophysiological responses for mu frequency band (8-12 Hz) were extracted from ERSP analysis for 500-1500 ms time range at all

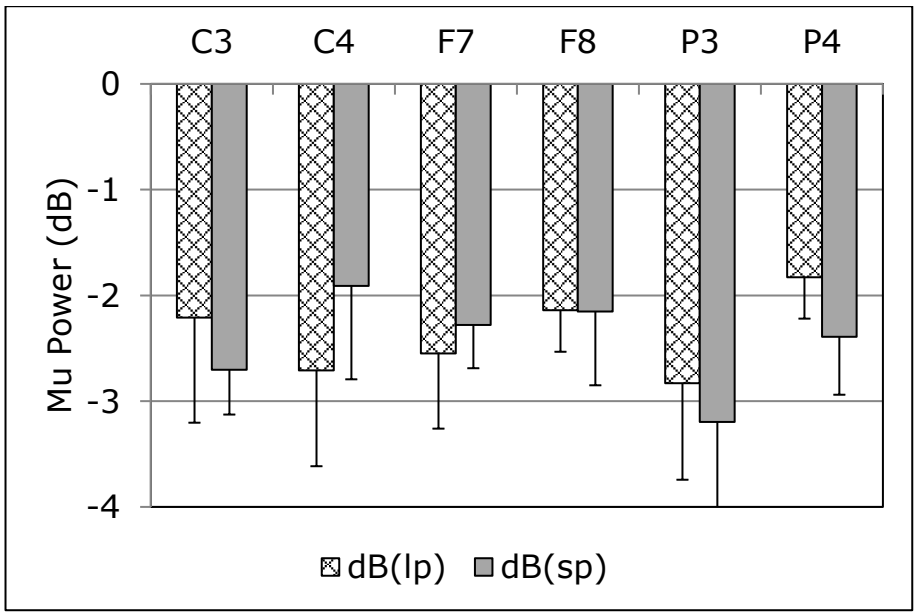
electrode sides and were detailed in Figure 4.4 only for the relevant channels. For observation of all video conditions (ss, hs, sp and lp), Wilcoxon signed rank test revealed that attenuation of mu oscillations from baseline were robust and significant ($p < 0.05$) over the somatosensory cortex (Figure 4.4; C3: ss (Mean= -1.98, SD= 1.64); hs (Mean= -1.77, SD= 0.85); sp (Mean= -2.70, SD= 1.08); lp (Mean= -2.70, SD= 1.08), and C4 : ss (Mean= -1.47, SD= 1.84); hs (Mean= -1.58, SD= 1.73); sp (Mean= -1.91, SD= 1.84); lp (Mean= -2.71, SD= 1.04). Mu suppression was also observed in the parietal and frontal channels of interest over the scalp with greater suppression at parietal channels (Figure 4.4a, 4.4b).

The primary comparison of interest, the 2 (spring type) × 2 (hemisphere) repeated measures ANOVA at channels C3 and C4 revealed no significant main effects of spring type ($F(1,6)=0.019$, $p=0.93$) nor hemisphere ($F(1,6)=0.547$, $p=0.49$), nor a significant presence of spring type by hemisphere interaction ($F(1,6)=0.18$, $p=0.64$). Similar 2 (spring type) × 2 (hemisphere) repeated measures ANOVA at parietal channels revealed no main effects or interactions (spring type: $F(1,6)=0.143$, $p=0.72$; hemisphere: $F(1,6)=1.252$, $p=0.31$; spring type × hemisphere: $F(1,6)=0.075$, $p=0.8$). Further statistical analysis at frontal channels (F7, F8) revealed a main effect of spring type ($F(1,6)=9.526$, $p=0.021$) but there was no spring type× hemisphere interaction ($F(1,6)=0.698$, $p=0.44$).

It was then examined whether grasping of a stick (long or short) rather than squeezing a spring had a significant effect on mu suppression over the electrode channel locations that have been associated with the MNS. It was again utilized the two way repeated measures ANOVA for this purpose. The effect of stick, hemisphere and interaction were not significant for frontal, central and parietal



(a)



(b)

Figure 4.4. Attenuation in the power (in dB) of the mu band (8-12 Hz) oscillations for conditions hs and ss (a); lp and sp (b) plotted at channels of interest: C3, C4, P3, P4, F7, F8. Error bars indicate the standard error of the mean.

channels (central channels; stick: $F(1,6)=0.409$, $p=0.55$; hemisphere:$F(1,6)=0.089$,$p=0.78$;stick × hemisphere:$F(1,6)=1.907$, $p=0.22$. Parietal channels; stick: $F(1,6)=0.314$, $p=0.60$; hemisphere: $F(1,6)=1.708$, $p=0.24$; stick × hemisphere: $F(1,6)=0.031$, $p=0.87$. Frontal channels; stick:$F(1,6)=0.091$, $p=0.77$; hemisphere: $F(1,6)=0.264$, $p=0.63$; stick × hemisphere: $F(1,6)=0.317$, $p=0.60$).

4.2. Monitoring the Mu and Beta Rhythm Modulations in a Cue-Based Paradigm: an EEG Study for Imagery-Based Rehabilitation

Motor imagery (mental rehearsal of an action) is a novel rehabilitation approach for patients with upper extremity disabilities. Instead of forcing a patient to move their extremities, motor imagery causes neural reorganizations in order to re-obtain motor functions learned before the stroke damage. The implemented strategy in imagery-based rehabilitation may have a crucial role to optimize the imagery performance. Here it was examined whether prior execution facilitates the subsequent imagery performance when the motor task to be imagined was associated with a symbolic cue. 10 healthy participants were divided into two groups and performed the execution and imagery of a sequential pinch grip task: one group started the experiment by execution of the task (group named GEF) and the other group performed the imagery session at first stage (group named GIM). Event Related Spectral Perturbations (ERSPs) at mu (8-12 Hz) and beta (15-25 Hz) frequency bands from EEG data were extracted for imagery and execution conditions of 10 subjects over central, parietal and frontal brain regions.

4.2.1. Theoretical Background on the Experiment

Motor imagery (MI) is a cognitive process in which a particular action is imagined without actually doing it [30]. Therefore, it has been suggested as a novel tool in rehabilitation of patients with neurological disorders [49, 110]. One important reason for the interest in imaginary movements is their application to brain computer interfaces (BCIs) for stroke rehabilitation [111]. Control of remote devices can be achieved non-invasively by utilizing electrophysiological changes during motor imagery [101]. The basis for the effectiveness of motor imagery is that a common neural substrate is partially shared between execution of an action and mental rehearsal (MI) of that action [112, 113]. In an electroencephalogram (EEG) study, neural activity patterns of motor imagery and actual movement have been found to be similar [38]. The functional magnetic resonance imaging (fMRI) techniques showed significant activities at supplementary motor area, premotor cortex and primary motor cortex areas during both motor imagery and execution [114]. The pattern of EEG desynchronization related to imagination of a movement is similar to the pattern during planning of a voluntary movement [115]. There is also a temporal congruence between real and imagined movements: duration of mentally simulated actions usually correlates with the duration of real movements [116]. These operations seem to be performed by a class of neurons with *mirror* properties [4, 107, 117].

Variety of neurorehabilitation studies has highlighted the positive effects of motor imagery for improving upper limb movements in stroke patients [118, 119]. However, common biomechanical structure of actual movement and imagery presents the challenge that effectiveness of MI might depend on the presence of a prior physical practice. This ordering may be a prerequisite for the generation of an initial motor

representation that is subsequently reinforced via MI [120]. Although motor imagery has been shown to be most effective when combined with physical practice [121], MI-based practice alone may also be able to generate the required motor representations that may have useful applications in rehabilitation [49, 122].

The implemented MI strategy may have a crucial role to optimize MI performance both in healthy adults and stroke patients. For example, external cuing (visual, auditory or combined) of an imagined finger movement significantly enhanced MI accuracy, speed, and vividness in a healthy and neurorehabilitation population [123]. Indeed, in human cognitive system, there is a close link between visual stimuli and motor responses [124]. The observed action is processed in the visual system and then directly mapped on to the observer's own motor representation of that action [2]. It is now well established that in humans, this observation-execution matching system is activated by mere observation of others actions [117, 13, 107] and by viewing of static actions or implied body actions [125], or by the observation of tools of common use [126]. Sensorimotor pathways have been shown to be facilitated when a colored fixation cross (cue) was associated with a finger movement [127]. A cue-based (visual or audio) training has been shown to improve the imagery vividness of healthy subjects [128] and motor performance of patients with neurological conditions [129]. However, instructions for an accurate motor imagery performance differed considerably across studies. In fact, patients must be able to develop accurate imaging characteristics of the actual movement to gain the most from motor imagery training [130, 131].

In EEG, rhythms in the alpha/mu (8-12 Hz) and beta (15-25 Hz) frequency ranges are typically accompanied by a power decrease in response to both execution and mental rehearsal of an action [38, 107, 109, 115,

132]. This reduction has been labeled ‘event-related desynchronization’ (ERD) [133, 134]. So far, the activity of the mirror neurons has been linked to mu and beta frequency oscillations in EEG over the sensorimotor areas [41]. Here, the research was extended to the core areas of this system. For this purpose, human EEG cortical oscillatory activities were measured at electrode locations that nearly correspond to areas of the putative MNS [11]: ventral premotor cortex and inferior frontal gyrus (combined region) and inferior parietal lobule. In particular, it was investigated whether mu/beta oscillations are modulated by prior execution for a cue-based imagery task. It was hypothesized that prior execution of the motor task would result in greater activity in the subsequent imagery task.

Although several previous studies have highlighted the effectiveness of MI in neurorehabilitation [110, 111, 118, 119, 121, 135], for patients with neurological disorders, mental representation of an action may not be performed accurately. For example, patients with unilateral parietal cortex damage showed impairments in MI [131]. Furthermore, this impairment increased with increasing finger movement complexity suggesting that ability in mental rehearsal of an action might depend on generating mental movement representations clearly. Implementing a cue-based strategy for mental rehearsal of an action might resolve this problem and the efficacy of imagined motor actions might increase significantly. It was suggested that patients should practice the imagery task with a clear beginning and end, as opposed to open tasks that are characterized by highly variable or more complex movement patterns.

The aforementioned studies involved MI tasks mostly with visual inputs from, for example, action observation or objects used in the action to conceptualize the movement whereas in this study a symbolic cue-based imagery task with a prior execution were combined which may provide

participants with a clear mental representation of the movement to be imagined. The motivation behind the present study was to determine the degree to which imagery effectiveness might achieve. In particular, it was tested whether imagery effectiveness might depend on a prior execution for a stimulus that associates a symbolic cue with a motor task with which the subjects are already familiar. The results will produce further support for use of MI as an adjunct to prior physical practice in facilitating upper limb motor functions of patients with neurological disorders. This study explores the recruitment of MNS from a wider point of view and the results might provide useful pieces of information for MI-based treatment of stroke patients to have a positive additional impact.

4.2.2. Experimental Setup

4.2.2.1. Subjects

10 right-handed volunteers (two females, mean age=36.9, SD=6.9) without a neurological illness or a history of upper limb injury participated in this study. The participants had normal or corrected-to-normal vision. Subjects were informed about the procedure before the experiment. The experimental procedure was approved by the local Ethics Committee.

4.2.2.2. Stimuli and Procedure

Subjects sat on a comfortable chair 1 meter away from a computer screen. They placed their right hand on a table and a soft, thin pad was positioned under their hand for comfort. The stimulus generation and experimental control were presented using PsychoPy2 (v1.83.04) software [102]. The stimuli were displayed on an 18” LCD monitor with 60 Hz refresh rate. The stimuli were presented in two sessions, execution and imagery using the following paradigm: each trial started with the presentation of a black screen of random duration ranging between 3 and

7 seconds. Then a green fixation cross was presented for 1 s at the center of the monitor with a short warning tone (“beep”). Starting from the visual fixation task, subjects were asked to withhold any movement as much as possible. Next, an arrow pointing to the right (“cue”) was presented for 4s (Figure 4.5). Cueing was used to facilitate initiation and continuation of the movement [136]. The subject was instructed to execute or imagine the movement of squeezing of a metallic binder clip (MBC) with his/her right hand continuously until the right arrow disappeared. The execution (or imagery) was ended till the offset of the visual stimulus (Arrow pointing to right: RA). This way, a cue was associated with a simple motor task with an unpredictable timing. The experiment consisted of two experimental runs of 35 trials (35 execution and 35 imagery trials) to obtain a reasonable experimental run time and enough EEG data for off-line analysis.

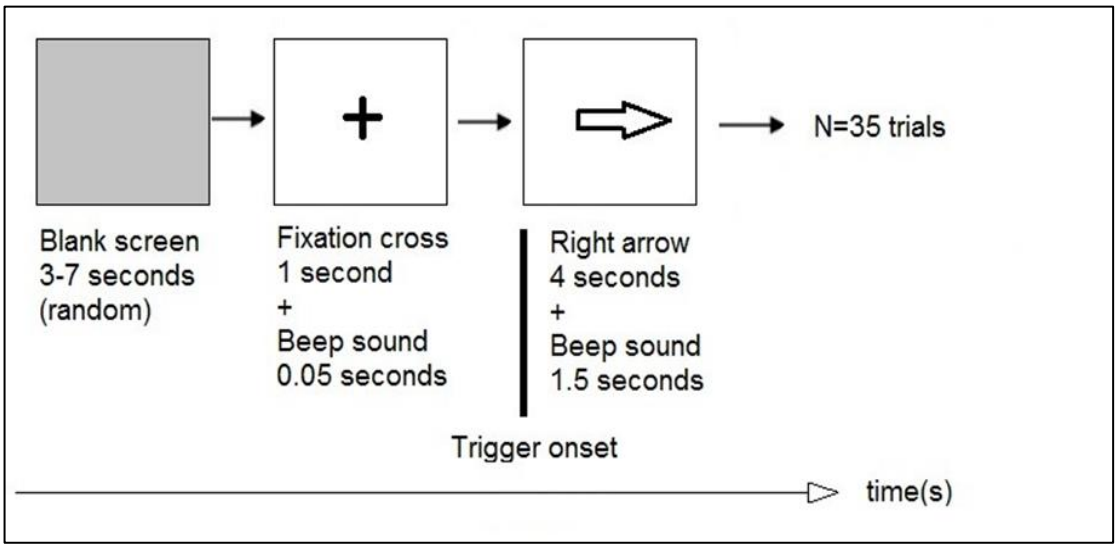


Figure 4.5. Experimental paradigm: schematic diagram illustrating the time course of stimulus presentation. In each trial, trigger is sent to EEG acquisition device (OpenBCI) starting from the right arrow (RA) appearance.

Prior to the experiment, each subject was given the opportunity to practice the actual movements according to the arrow display onset on the monitor. No EEG data were recorded during this training session. A short break was provided to the subjects between execution and imagery sessions. During the imagination task the subjects were instructed to keep their arms and hands fixed while holding the MBC. After the training session of each subject, participants were divided into two groups each having 5 subjects. One of the groups (GEF) started the experimental sessions with the execution according to the stimuli and after a few minutes break they performed the imagery session. The subjects in the other group (GIM) were asked to perform the imagery task first and then in a similar fashion they continued with the execution task. Subjects were kept blind to the goal of this experimental manipulation.

An additional Pyhton code was added to the existing stimulus code in PsychoPy2 software to synchronize the visual appearance of RA (together with warning tone) with continuous EEG recording. The code enabled the data pins of parallel port of the computer (8 GB RAM, 64 bit) to reach a low or a high logic level of 0 V or +5V respectively (Figure 4.6). A trigger code was uploaded to the Ardunio IDE (1.6.5) compatible OpenBCI to enable the external trigger pin (D17) of the EEG device. A Schmidtt trigger (74HC14) was added to the experimental circuit to accelerate the signal and to step up the signal to +5V. A Matlab (Mathworks, Inc.) code is generated to process and sort out the raw EEG data. By default, the last three auxiliary channels of the OpenBCI 32 bit board record the trigger inputs at 250 Hz sampling rate.

A video set up was used to monitor the course of the experimental trials to ensure that the participants were performing the sessions correctly as instructed. All sessions were started after the examination of continuous

EEG data reception and all the electrodes were placed by expert EEG technicians.

4.2.2.3. Electrophysiological Recording and Data Analysis

The electroencephalogram (EEG) was recorded continuously (bandpass, 0.1-100 Hz; sampling rate, 250 Hz) with the 32 bit board OpenBCI including the Daisy module with a 16 channel system. International 10-20 electrode placement (Fp1, Fp2, C3, C4, F3, F4, F7, F8, T3, T4, T5, T6, P3, P4, O1, and O2) was used with the reference electrode at vertex (Cz). Electrolytic paste was applied at each electrode site and the skin surface at these locations was lightly abraded to reduce the impedance of the electrode-skin contact. Electrode contact resistances were confirmed to be less than 5 kΩ using real time electrode impedance measurements provided by an open project Processing 2.2.1.

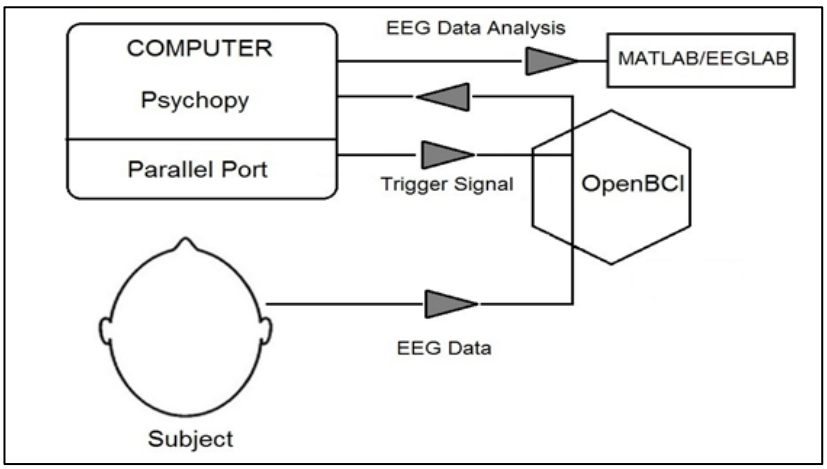


Figure 4.6. Schematic diagram illustrating the experimental setup. Stimulus presentation software sets the parallel port of the computer from "off" to "on" mode informing the EEG recording device of the time of the stimulus onset in continuous EEG data. The raw data from OpenBCI were preprocessed with MATLAB and the EEGLAB toolbox.

EEG data were analyzed using EEGLAB 13.4.4b [95], running under the cross platform MATLAB environment (Mathworks, Inc).

A band pass filter (finite impulse response-FIR) from 1 Hz to 40 Hz was applied to eliminate the baseline drifts and the 50 Hz line noise. A common average reference (CAR) was performed on all 16 electrodes in order to produce the reference free EEG data. The CAR method provides a better signal-to-noise ratio for the mu or beta-rhythm than does the any standard (e.g. ear-reference) method [108]. Data were epoched ranging from 1000 ms preceding stimulus onset (appearance of RA on the screen) to 2000 ms after stimulus onset and were time locked to the a appearance of RA displayed on the screen. In each epoch, baseline was considered as the period starting 1000 ms before the onset of stimulus and ending at the stimulus onset. Atypical epochs were removed from further analysis by applying improbability test with standard deviation ≥ 6. To remove eye blink, cardiographic, electrical and muscle related artifacts, the data were decomposed by Independent Component Analysis (ICA) using extended infomax algorithm [100] and components that showed typical artifact characteristics were removed from the data.

The time-frequency analysis of neural activity was performed at central (C3, C4), parietal (P3, P4) and frontal (F7, F8) channels. Analysis consisted of two main steps: (1) time-frequency decomposition of the EEG signal of the relevant channel(s). In this step, event related dynamics of the EEG spectrum were analyzed using a 3-cycle wavelet with the baseline corrected Event Related Spectral Perturbation (ERSP) method [137]. The mean power of the baseline period was removed from the power at each time point of the experimental trials. In step (2) mu and beta band power values in the relevant time window (from 0 to 1400 ms) were extracted and analyzed for each condition (execution and imagery)

at channels C3, C4, P3, P4, F7 and F8 corresponding nearly to the brain regions of the MNS. First, sensorimotor mu and beta suppression were analyzed at channels C3 and C4. Non-parametric t-test was applied with p-values set at 0.05 for the comparisons of mu and beta power against zero. It was also reported the graphical representation from other channels for completeness while reporting the suppression over sensorimotor cortex. Second, for the main comparison of interest, effect of frequency and hemisphere on imagery was analyzed with 2 (hemisphere) × 2 (frequency) repeated measures ANOVA at central, frontal and parietal channels separately. Levene's test was performed for homogeneity of variances and data were shown to be normally distributed by Shapiro-Wilk test. Finally, the attenuation at mu and beta frequency bands for imagery condition were compared between two experimentally manipulated groups at each electrode side independently by using Mann-Whitney U-test to reveal whether prior execution has a significant effect on imagery.

4.2.3. Results

4.2.3.1. Behavioral Performance

All subjects performed the experiment with 100% accuracy during both conditions and no subjects were excluded from the study. It can therefore be inferred that any differences found in mu and beta suppression are not due to differences in attending to the stimuli.

4.2.3.2. Spectral Analysis of Mu and Beta Suppression

The EEGLAB *timef* function returns 69 frequency values ranging from 3.0 Hz to 39 Hz and 200 time points ranging from -440 ms to 1436 ms from timelock throughout the analysis. EEG mu rhythm (8-12 Hz) over sensorimotor cortex contralateral to the right hand led to a decrease, starting around the stimulus onset and became stronger at nearly 500

ms (Figure 4.7). The ERSP analysis of C3 and C4 showed comparable patterns of power spectrum decrease (ERD) centered at around 10 Hz frequency level. The foci of desynchronization over C3 electrode, starting from the stimulus onset of 10 subjects was observed at a mean frequency of 10,01±0,83 Hz with a mean time latency at 508,80∓135,79 ms. (Figure 4.7). Time-frequency analyses over the other electrode sides of interest (C4, P3, P4, F7 and F8) resulted in similar patterns and were not shown.

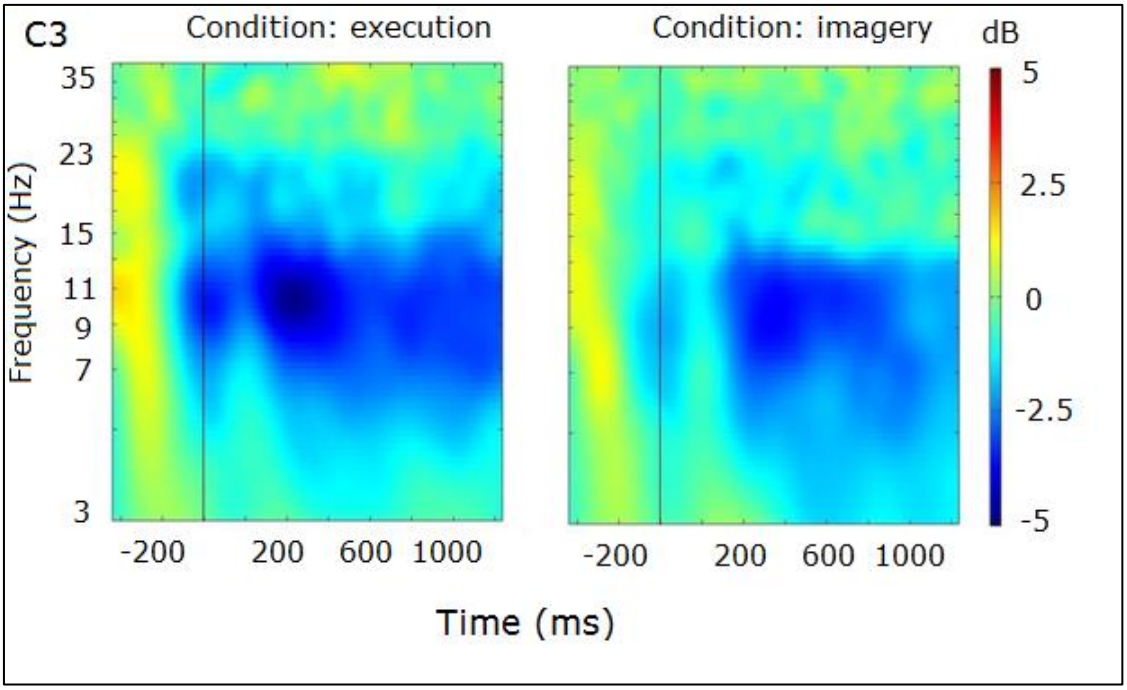


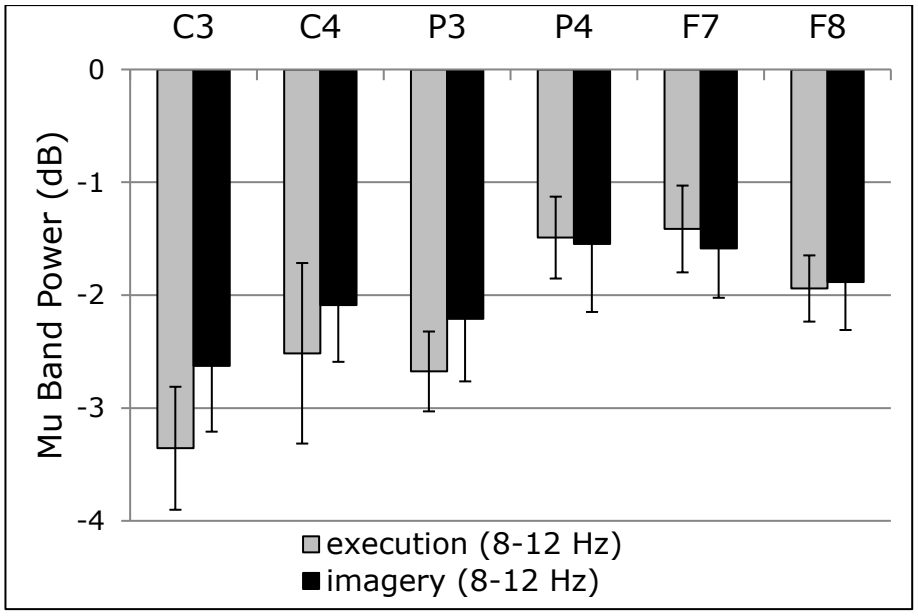
Figure 4.7. Time-frequency ERSP plots for two conditions: execution (*left*) and imagery (*right*) at channel C3. Plots for electrode side C4 were similar and are not shown. The frequency axis is log scaled. The vertical line on time axis indicates the onset of the RA appearance on the screen (t=0). A log ratio of less than zero indicates suppression (desynchronization).

4.2.3.3. Significance of Mu and Beta Band Suppression over Sensorimotor Cortex

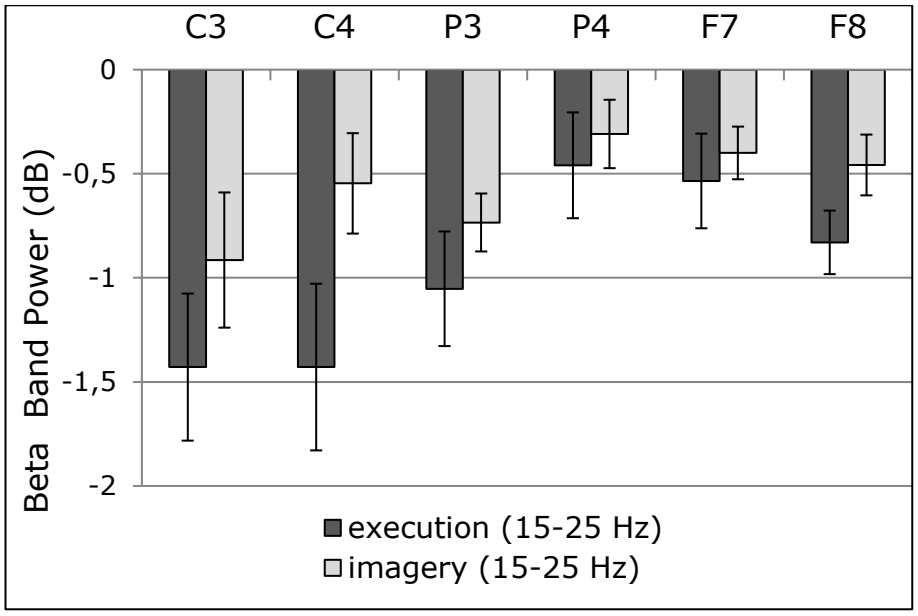
Electrophysiological responses were extracted from grand average (10 subjects) ERSPs (in dB) for two conditions and frequency bands at 0-1400 ms latency range over the electrode locations C3, C4, P3, P4, F7 and F8 (Figure 4.8a and 4.8b). This specific time window was determined from the ERSP plots of the relevant channels across all subjects.

Over the sensorimotor cortex, both execution and imagery are associated with bilateral desynchronization in the mu band that is greater on the contralateral side (Figure 4.8a). In beta frequency band, however, desynchronization is rather bilateral for the execution condition (Figure 4.8b).

For execution and imagery conditions, attenuation of the beta oscillations were robust and significant over the contralateral hemisphere (Figure 4.8b; C3: execution: mean= - 1.43, SD= 1.12; imagery: mean= -0.91, SD= 1.03; Wilcoxon signed-rank test; $p<0.05$). Statistical analysis for the ipsilateral side revealed that beta band suppression is significant for execution of the motor task condition but not for the imagery of the same task (Figure 4.8b; C4: execution: mean= -1.32, SD= 1.27; Wilcoxon signed-rank test; $p<0.05$ imagery: mean= -0.55, SD= 0.76; Wilcoxon signed-rank test; $p>0.05$).



(a)



(b)

Figure 4.8. Attenuation in the power (in dB) of the mu (a) and beta (b) band oscillations for two conditions (execution, imagery) plotted at channels C3, C4, P3, P4, F7 and F8. A log ratio (in dB) less than zero indicates mu (or beta) suppression. Error bars represent the standard error of the mean.

The effect of frequency and hemisphere on imagery were analyzed with 2 (hemisphere) × 2 (frequency) repeated measures ANOVA. At central channels, there was a significant main effect of frequency [$F(1,9)=23.923$, $p<0.05$] but no main effect of hemisphere [$F(1,9)=3.066$, $p>0.05$] or frequency × hemisphere interaction [$F(1,9)=0.558$, $p>0.05$]. A similar 2 way repeated measures ANOVA for frontal channels revealed a significant main effect of frequency [$F(1,9)=9.674$, $p<0.05$] but no main effect of hemisphere [$F(1,9)=3.535$, $p>0.05$] or frequency×hemisphere interaction [$F(1,9)=0.660$, $p>0.05$].

At parietal channels a significant main effect of frequency was found [$F(1,9)=9.879$, $p<0.05$] but there was no main effect of hemisphere [$F(1,9)=2.619$, $p>0.05$] or frequency×hemisphere interaction [$F(1,9)=0.311$, $p>0.05$].

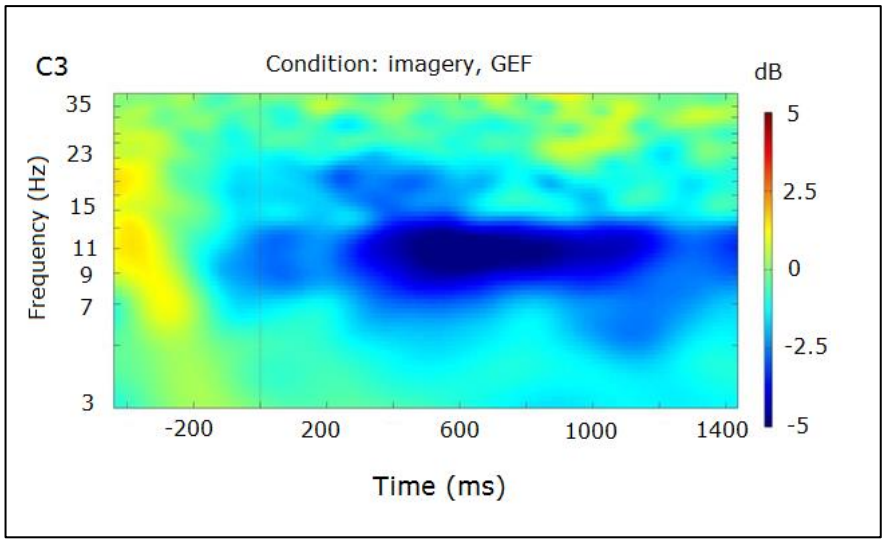
4.2.3.4. The Effect of Execution on Imagery

The 5-subject groups (GEF and GIM) were compared for imagery condition to reveal the effect of a prior execution of the task on subsequent imagery task. For each group, ERSP plots at electrode side C3 is shown in Figure 4.9a and 4.9b. ERSP analysis of group GEF displayed a more sustained attenuation around 8-12 and 15-25 Hz (see Figure 4.9a).

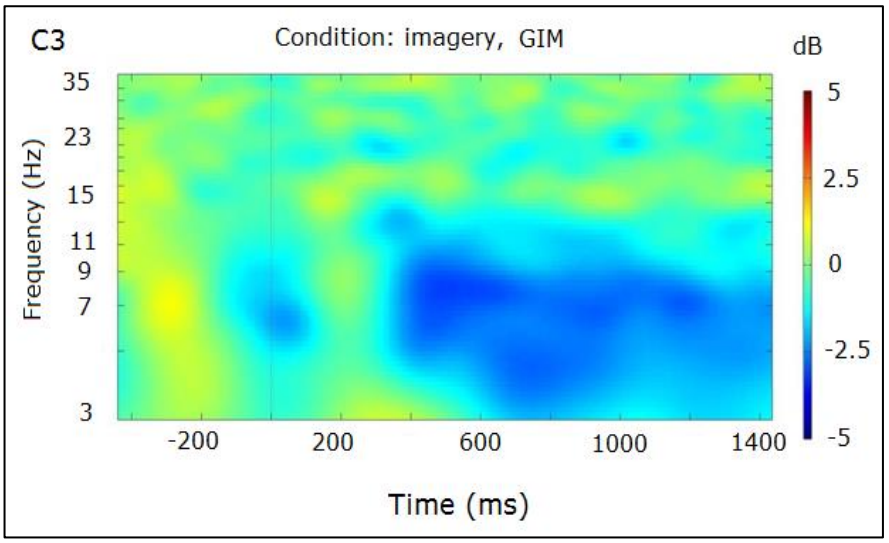
ERSP values were extracted (in dB) for two groups (GEF, GIM; 5 subjects in each group) for imagery condition for the same 0-1400 ms latency range. Over the channels of interest and for both frequency bands, group GEF showed slightly larger band power desynchronization than group GIM (Figure 4.10).

Mann-Whitney U-test revealed that the attenuation at mu and beta frequency bands were not significant between two groups (GEF, GIM)

over the somatosensory cortex (mu frequency, C3: U=4, p=0.076 and C4: U=5, p=0.117 and beta frequency, C3: U=5,p=0.117 and C4: U=9, p=0.465). At parietal channels, only the attenuation in mu band power was at the cusp of significance (mu frequency, P3: U=3,p=0.047 and P4: U=9, p=0.465 and beta frequency, P3: U=7,p=0.251 and P4: U=7, p=0.251). Suppression at frontal channels were significantly different between two groups only for mu frequency band (mu frequency, F7: U=3, p=0.047 and F8: U=2, p=0.028 and beta frequency, F7: U=12, p=0.917 and F8: U=7, p=0.251).

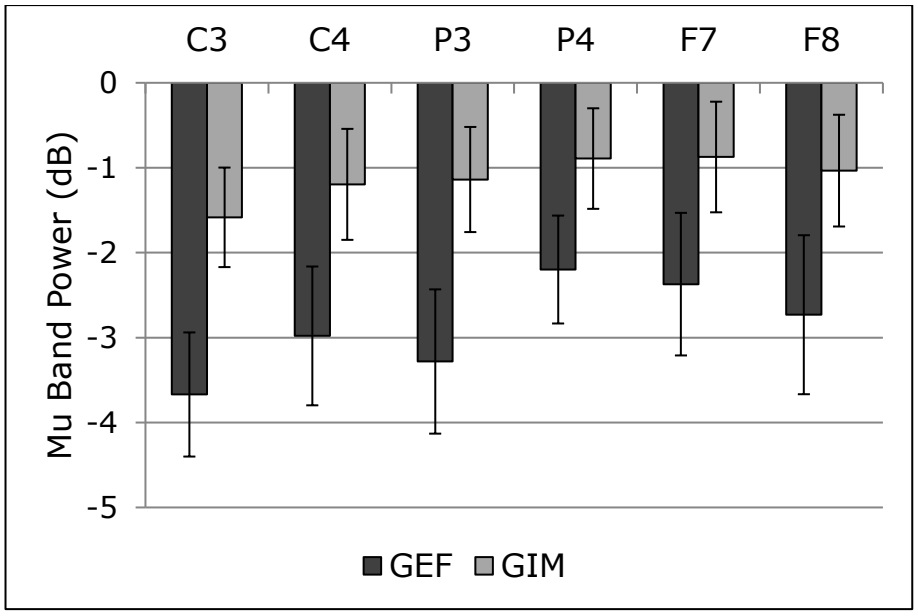


(a)

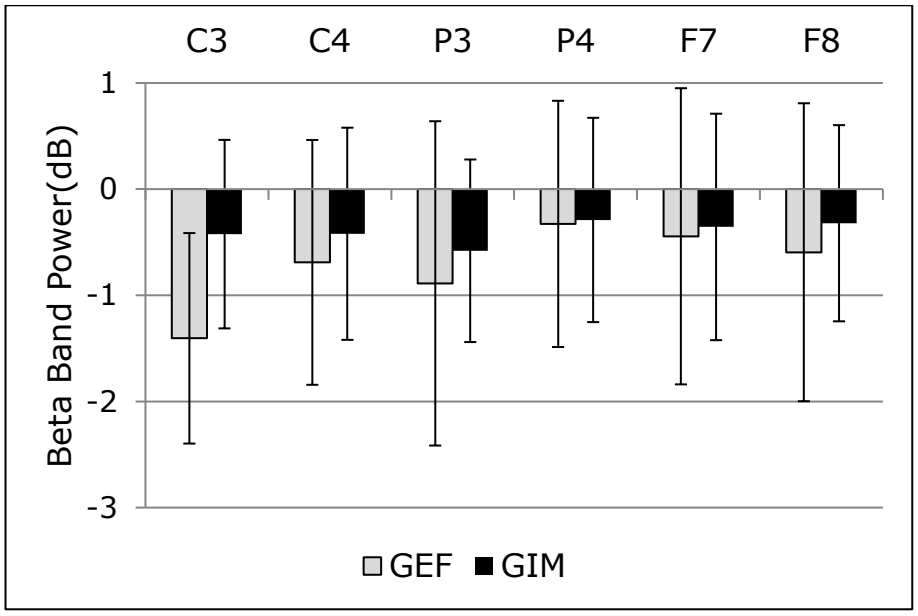


(b)

Figure 4.9. Event related spectral perturbation (ERSP) plots for imagery condition of group GEF (a) and group GIM (b) at channel C3. Group GEF imagines the motor task after execution session; group GIM starts the experiment with imaging the same task. Plots for the right hemisphere (C4) were similar and are not shown. The frequency axis is log scaled. The vertical line on time axis indicates the onset of the RA appearance on the screen (t=0). A log ratio of less than zero indicates suppression (desynchronization).



(a)



(b)

Figure 4.10. Power in mu (a) and beta (b) frequency range (in dB) for imagery condition at central (C3, C4), parietal (P3, P4) and frontal (F7, F8) channels. Group GIM performs the imagery session in the first session. Group GEF performs the imagery in the second (last) session after execution. Error bars indicate the standard error of the mean.

4.3. Anticipatory Effect of Execution on Observation: an Approach using ExoPinch Finger Robot

In cognitive neuroscience, there is increasing evidence that mere observation of actions performed by others recruits the same motor areas that are also recruited when the same actions are actually performed [1]. Areas that are active with this putative matching mechanism are parts of the mirror neuron system (MNS) [2,4]. AO exploits this neural structure and has been successfully applied in rehabilitation of motor dysfunction for the patients with stroke.

This study aims to explore the MNS involvement using mu (8-12 Hz)/beta (15-25 Hz) band suppression in an action observation-execution paradigm. Electrophysiological (EEG) data from 16 electrodes were recorded while 8 participants observed video clips of a hand sequeezing a spring. Specifically, the effect of anticipated execution on observation was studied. For this purpose, a fully actuated finger exoskeloton robot was utilized to synchronize observation and execution and to control the execution condition for the participants. Anticipatory effect was created with a randomized robot accompany session. The results showed that the observational condition (with or without anticipation) interacted with hemisphere at central channels near somatosensory cortex. Additionally, the response of MNS was explored on the kinetics features of visual stimuli (hard or soft spring). The results showed an interaction effect of kinetics features and hemisphere at frontal channels corresponding nearly to the ventral premotor cortex area of the brain. The activation of mirror neurons in this area plays a crucial role in observational learning. Based on the results, it is proposed that specific type of visual stimuli can be combined with the functional abilities of the MNS in the action observation based treatment of hand motor dysfunction of stroke patients to have a positive additional impact.

4.3.1. Theoretical Background on the Experiment

An impaired hand function is often reported to be the most disabling motor deficit after stroke. The functional re-use of the hand is of paramount importance for the patient's physical independence and social integration. Therefore, the focus of stroke rehabilitation has been mainly the treatment of the proximal and distal segments of the upper limb, (hand and arm) [175]. Additionally, several researchers have reported the effects of robot-assisted therapy approach for the recovery of the paretic upper limb [160].

Different rehabilitation approaches for this neurological injury have been proposed; among them action observation (AO) treatment could be a viable strategy to improve motor rehabilitation following stroke [6,7,53]. During a typical session in AO treatment, patients observe a meaningful action performed by an agent and afterwards they perform the observed motor act at the best of their ability [6]. AO-based rehabilitation approach has the potential that the treatment can be tailored to a specific need of a single patient. For example, the type and amount of visually presented actions (stimulations) can be well defined according to the patients' needs.

It is now a well-accepted notion in neurophysiology that in human brain, motor areas are recruited not only when actions are executed but also when they are observed [161]. The neurophysiological basis for this execution-observation matching system relies on the discovery of the mirror neuron system (MNS) [2,3]. The observed or seen action seems to be *reflected* by neurons with *mirror* properties in the motor representation for the same action of the observer. This neural network supporting the action observation and execution processing corresponds to a set of areas in parietal, frontal and sensorimotor cortices [11] and has been proposed to subserve as a key neural basis for action

understanding [5, 24, 104], social communication and motor learning [55, 65].

Observation of action exploits this neural mechanism by activating the physiological network of motor areas where motor representations of observed actions are known to be present. In a study, observation of another person learning a novel reaching task affected the subsequent performance of naive observers [162]. Moreover, observation of a simple intransitive movement of the index and middle fingers increased the excitability of the motor cortex [56]. These and several other studies demonstrate that AO produces an increase in the excitability of the corticospinal pathways within the MNS [15, 21].

The applied therapeutic strategies in AO treatment may have a crucial role to recruit more deeply the related motor representations. Several of these approaches utilize the capacity of MNS to enhance recovery of the upper limb after stroke and assume that MNS actively participate in the process. Along this line, it was demonstrated that showing video clips of daily actions and subsequent imitation of these actions resulted in a significant improvement of motor functions in the experimental group of patients [67]. Indeed, when the observed action belongs to the motor repertoire of the observer, the putative MNS can match the observed action on the neural structures involved in its execution and can activate previously learned movements [57, 58]. Furthermore, the observation of hand-object interactions allows the observer to code the intentions of individuals performing the observed actions [2]. The same mirror neuron mechanism serves the decoding of the immediate scope of that action. Understanding the intention beside the observed action is an important component that allows for the preparation of the action execution system [169]. Overall, these findings suggest the value of

showing actions that are common to the observer in context to ameliorate the therapeutic effects in AO treatment.

Thus far, AO has been combined with subsequent physical practice as a new neurorehabilitative program. When the physical training of actions are accompanied with the observation of those actions, a significant improvement of motor functions is achieved after stroke [7, 163]. Additionally, recent evidence suggest that when action observation and training exercises are performed simultaneously, the effects of action observation may increase, as it is known that corticomotor excitability is stronger when the observed action kinematically (spatially and temporally) matches the direction of the physical training [163, 164, 165]. The corticospinal excitability is also modulated when anticipating to see a movement and there will be a preparation for a possible motor response prior to the onset of the movement subsequently observed [166]. Since the observation of movement and execution of that movement share common neural processes [1, 112], anticipatory changes in motor cortical neural activity also occur for an expected movement [167, 168]. These findings demonstrate that expectancy of an upcoming action automatically activates the motor system.

Among the methods used for inferring human MNS activity are power changes in the electroencephalogram (EEG) alpha (8-12 Hz) and beta (15-25 Hz) bands primarily over the sensorimotor areas [40, 41]. In EEG, rhythms in the alpha and beta frequency ranges are typically accompanied by a power decrease (reflecting cortical activity) in response to both execution and observation of an action [38, 107, 109, 115, 132]. This decrease in alpha band, in reference to a baseline condition is known as *mu desynchronization* [36, 37, 38].

This study model focuses on the core and the extended areas of the putative MNS at both mu and beta frequency bands. For this purpose,

human EEG cortical oscillatory activities were measured at electrode locations that nearly correspond to the areas of this system [11]: somatosensory and ventral premotor cortex plus the inferior parietal lobule.

The major novelty of this study was to assess whether neural activity during action observation can be enhanced by an anticipatory effect of execution when this actual movement is externally generated by a robotic system. The motivation behind the present study was to determine the degree to which the efficiency of action observation might achieve for treatment of stroke. For this purpose, given the significance of robot-induced technology for post-stroke rehabilitation [160], a finger exoskeleton robot was utilized to fully synchronize the action observation with execution in an experimental session. The random robot accompany (i.e., execution of the observed action) to observation in the subsequent session allowed to create a unique scenario in which the execution becomes an anticipatory concurrent factor of the observation. In the current experiment, it was hypothesized that the effect of anticipation would change the functional activation in the areas of the MNS.

This methodology makes use of a robot-guided execution of an action rather than a self-initiated action and the results of this study will have an additional positive effect over an AO-based rehabilitation protocol.

4.3.2. Experimental Setup

4.3.2.1. Subjects

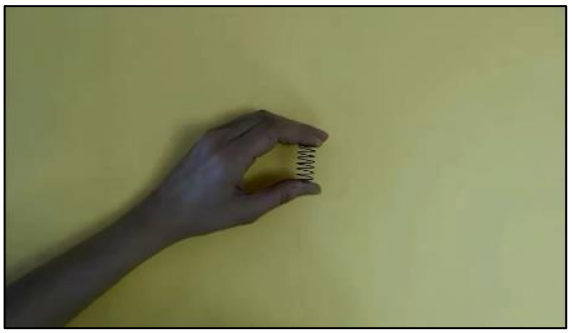
8 right-handed volunteers (all males, mean age=35.8, SD=9.3) without a neurological illness or a history of upper limb injury participated in this study. The participants had normal or corrected-to-normal vision. Subjects were informed about the procedure before the experiment and

were given their informed consent for participation in the study. The experimental procedure was approved by the local Ethics Committee.

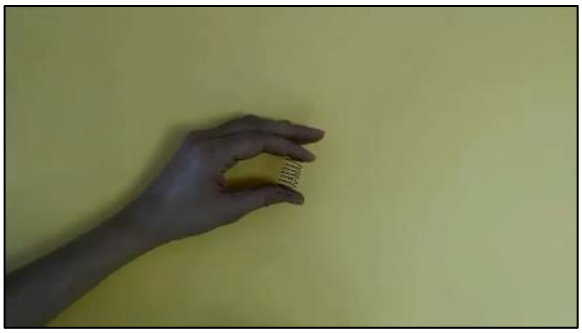
4.3.2.2. Stimuli and Procedure

Subjects sat on a comfortable chair 1 meter away from a computer screen (18" LCD monitor at 60 Hz). Stimuli were video clips of actions performed by the left hand of the experimenter. Video recordings were converted to gray-scale and clipped such that the motion of the hand began at the first frame of each video. A video clip lasted for 2 seconds and one session of the experiment consisted of 40 trials. The stimuli were videotaped with the same background and hand/wrist position on the screen (Figure 4.11). A black screen of 4 s was presented between each video as a baseline condition. A short break was provided to the subjects between the sessions.

Before starting EEG recordings, participants were presented with the objects used in the video stimuli. EEG data were recorded during 3 successive sessions: in the first session (*obs*), subjects merely observed videos of the hand squeezing and releasing a hard or a soft spring (Figure 4.11). These conditions will be referred to as *hs* and *ss*, respectively.



(a)



(b)

Figure 4.11. Still frames from the videos used in the experiment depicting the squeezing the hard spring-hs (a) and soft spring-ss (b).

In the second session (*obs+exe*), the exoskeleton finger robot ExoPinch simultaneously accompanied the left hand's index finger of the subjects with each observed movement presented in the video clip (Figure 4.12). The joints of the robotic system are aligned with the joints of the human index finger such that the enclosed index finger is manipulated by the robot. For the precise synchronization of the robot movement with the observed one, 5 main steps were followed prior to the experiment: (1) each type of video clip (hs, ss) was decomposed into their video frames (Asus 2 GB NVIDIA GTX 128 bit Graphics card) by PsychoPy2 software [102]. (2) Several frames were selected including the initial position, final position and some intermediate positions in between. Care was

taken to ensure that the chosen frames were able to basically define the 2 s movement. (3) Time elapsed for the selected frames were obtained by PsychopPy software [102]. (4) Kinematic motion analysis of the selected frames was performed by Tema Trackeye 3.5 motion analysis software (Image Systems AB).

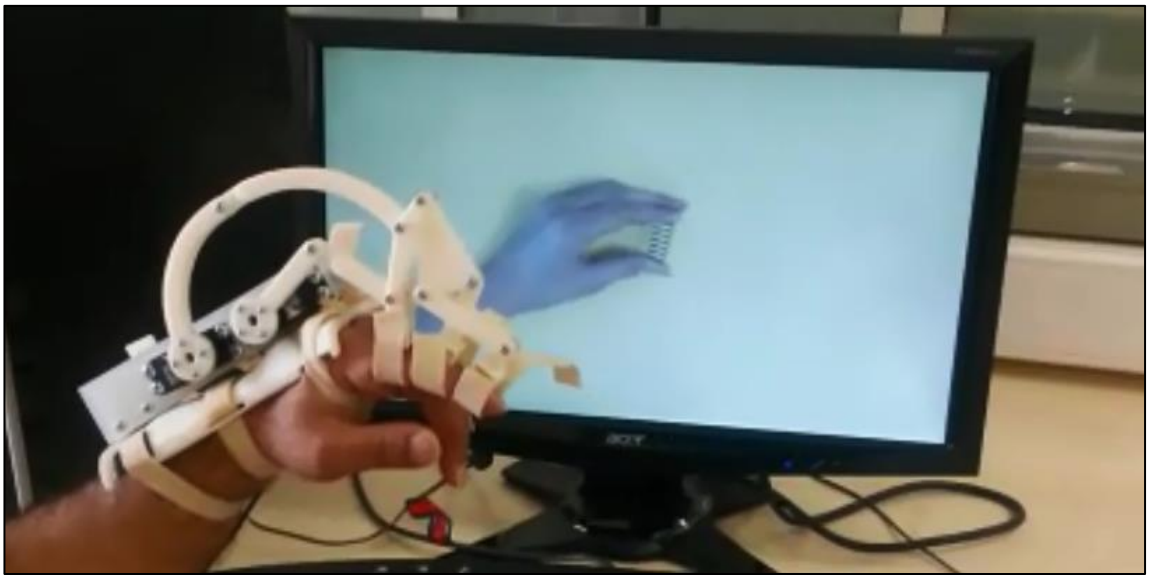


Figure 4.12. A still frame from session 2 (*obs+exe* condition): simultaneous action observation and action execution with exoskeleton robot ExoPinch.

The angles were measured from the distal and proximal interphalangeal joints of the index finger during squeezing of the spring. (5) Both the temporal and angular data -obtained from steps 3 and 4- of the selected frames were adapted to Matlab Simulink (Mathworks, Inc) environment for the precise synchronization of the robot finger ExoPinch with the visual stimuli.

In session 3, ExoPinch accompanied the observed movements but in a randomized paradigm created by a separate code using PsyhcoPy2 software [102]. Neither the subject nor the experimenter knew which trials were mere observations (without robot accompany) or

combination of robot execution with observation. These experimental conditions will be referred to as *no robot* (robot did not accompany) and *robot* (robot accompanied), respectively. The experimental conditions were detailed in Table 4.1.

In session 2 and 3, subjects were told to keep their hand relaxed in order not to interfere with ExoPinch's regular motion execution.

In all sessions, the experimental conditions were chosen to be strictly associated with the observation (with or without execution) of hand-object interaction, given the high responsiveness of the MNS to object directed hand actions [67]. The visual appearance of stimuli and continuous EEG recording were synchronized with PsychoPy2 software [102]. Visual stimuli in each session were presented in a randomized order ensuring that each participant experienced a different randomized sequence of trials.

Table 4.1. Tabular representation of the conditional details in the experiment

Session	Condition	Observation	Execution	Anticipation	Simultaneous
1	*obs*	✓			
2	*obs+exe*	✓	✓		✓
3	*robot*	✓	✓	✓	✓
3	*No robot*	✓		✓	

4.3.2.3. Robot Control, Electrophysiological (EEG) Recording and Data Analysis

The experimental setup utilized two separate computers (3.2 GHz CPU, 8 GB RAM), one for the visual stimuli and EEG acquisition and the other for the finger robot control (Figure 4.13). Computer 1 in Figure 4.12 presented the visual stimuli and recorded the EEG data stream. On the other hand, it served as a trigger signal station; onset of the each visual stimulus was marked in EEG acquisition device by computer 1 via its parallel port utility (Trigger 1 in Figure 4.13). Computer 2 initiated the robot finger upon receiving the signal from the parallel port of Computer 1 (Trigger 2 in Figure 4.13). It has to be emphasized that separate data pins for the trigger signals of the parallel port were enabled to discriminate the task for the robot. The termination of ExoPinch accompany was accomplished by the previously defined (kinematically) movement pattern in Computer 2.

The electroencephalogram (EEG) was recorded continuously (bandpass, 0.1-100 Hz; sampling rate, 250 Hz) with the 32 bit board OpenBCI including the Daisy module with a 16 channel system. UltraCortex Mark 4 dry electrode headset was used conforming international 10-20 electrode placement: Fp1, Fp2, C3, C4, F3, F4, F7, F8, T3, T4, T5, T6, P3, P4, O1, and O2. Electrode contact resistances were confirmed to be less than 5 kΩ using real time electrode impedance measurements provided by an open project Processing 2.2.1. A Matlab (Mathworks, Inc.) code is generated to process and sort out the raw EEG data. EEG data were then preprocessed using EEGLAB 13.4.4b MATLAB (Mathworks, Inc) toolbox [95].

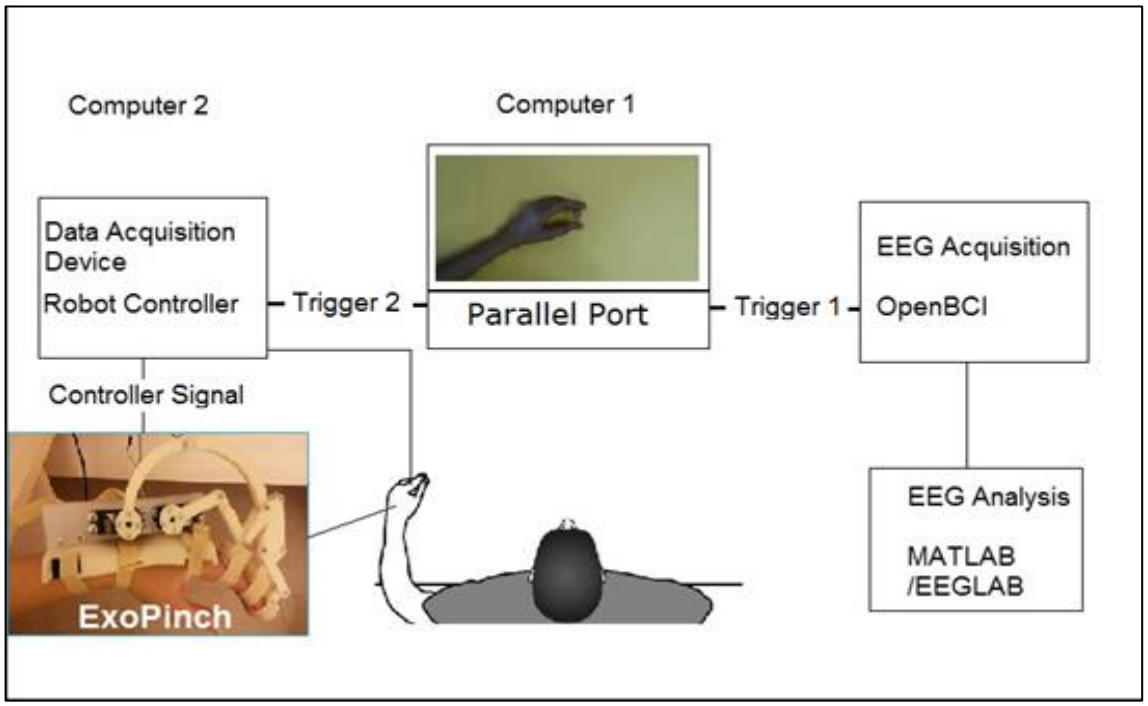


Figure 4.13. Graphic representation of the experimental set up. Computer 1 presents the visual stimuli and records the EEG data; Computer 2 controls the robot movement.

A linear finite impulse response (FIR) filter from 1 Hz to 40 Hz was applied to eliminate the baseline drifts and the 50 Hz line noise. A common average reference (CAR) was performed on all 16 electrodes in order to produce the reference free EEG data. The CAR method provides a better signal-to-noise ratio for the mu or beta-rhythm than does the any standard (e.g. ear-reference) method [108]. Data were epoched ranging from 1000 ms preceding stimulus onset (appearance of hand object interaction on the screen) to 2000 ms after stimulus onset and were time locked to the onset. In each epoch, baseline was considered as the period starting 1000 ms before the onset of stimulus and ending at the stimulus onset. Atypical epochs were removed from further

analysis by applying improbability test with standard deviation ≥ 6. To remove eye blink, cardiographic, electrical and muscle related artifacts, the data were decomposed by Independent Component Analysis (ICA) using extended Infomax algorithm [100] and components that showed typical artifact characteristics were removed from the data.

After preprocessing, averaged data (n=8 subjects) were analyzed for each condition in the time frequency domain at all 16 channels. EEG spectra were decomposed using a 3-cycle wavelet with the baseline corrected Event Related Spectral Perturbation (ERSP) method [95]. The mean power of the baseline period was removed from the power at each time point of the experimental trials. Both the spectral and the time windows of mu/beta oscillations for statistical analysis were determined from ERSP data plotted in EEGLAB/MATLAB environment. The mean mu/beta band power values (in dB) were extracted at a number of frontal (F7, F8), central (C3, C4) and parietal (P3, P4) channels since these regions almost exclusively included regions that have been associated with the MNS in the literature: d/vPMC, Brodmann area 44/2 and IPL [4, 24, 109]. Each channel with the experimental condition was carefully analyzed in ERSP time- frequency plots for the specific time window of desynchronization of mu/beta band power before entering the data into statistical analysis.

Significance of mu/beta band power desynchronization against zero (baseline) for all conditions was analyzed using t-test with p-value set at 0.05. p-values reported below are two-tailed except for the comparisons of mu and beta power against zero, where results are for one-tailed since a decrease in mu/beta power was expected. The Shapiro-Wilk test was applied to assess whether data were likely from a normal distribution. Although data were obtained from 16 electrodes across the scalp, the focus has been on the relevant channels (C3, C4,

F7, F8, P3 and P4) and significance of mu/beta desynchronization was reported over the somatosensory cortex (C3 and C4), given the prior literature.

In statistical analysis of any anticipatory effect, the main comparison of interest was based on two main assumptions: condition *obs* in session 1 was matched to *no robot* condition in session 3 and similarly, condition *obs+exe* in session 2 was matched to *robot* condition in session 3. Indeed, both in *obs* and *no robot* conditions, subjects merely observed the video stimuli, but they knew that there was a possibility of robot accompany in *no robot* condition. Similarly, both condition *obs+exe* in session 2 and *robot* condition in session 3 were observation of action with execution. This methodology with the current experimental paradigm allowed analyzing whether a possible anticipation of execution during observation of an action (*no robot* condition in session 3) facilitates the mirror neuron activity more effectively than the mere observation of that action without any anticipation (*obs* condition in session 1). It is also possible that neural oscillations (mu/beta suppression) during action observation with execution (*obs+exe* condition in session 2) might be modulated when execution was unexpectantly present (*robot* condition in session 3). Therefore, two separate (2 (condition) X 2 (hemisphere)) repeated measures ANOVA were performed for conditions (*obs, no robot; obs+exe, no robot*) and hemisphere (right, left) over central (C3, C4), frontal (F7, F8) and parietal channels (P3, P4). Mauchly's test indicated that the assumption of sphericity was not violated ($p>0.05$).

Although the primary interest was to analyze the anticipatory effect on observation, additionally, EEG oscillatory activity in mu/beta frequency band was analyzed from the ERSP plots for the hand movement with different kinetic (conditions *hs* and *ss*) in session 1, on the frontal areas

to explore any modulation that may be specific to kinetic features of the action [43, 143, 144, 145]. Before starting EEG recordings, subjects were presented with the objects used in the video clips and were asked to practice their stiffness (hard or soft). The response of MNS is stronger to observed actions for which the subject has familiarity or he/she has a prior practice with the visual stimuli [44, 70]. It is therefore plausible to think that the mu suppression is a measure of the resonance between observed kinetics and those of the observer. Taken together, the observed actions were in their personal motor repertoire [58].

For the first session (*obs*) of the experiment, ERSP data (in dB) were extracted for two separate observational conditions (*hs, ss*) at the group level (8 participants). However, for completeness, the results from the parietal and central channels were also reported to cover the putative MNS on the scalp. Otherwise, conditions *hs* and *ss* in session 1 were combined into mere observation condition (*obs*) for the main discussion on the anticipatory effect.

4.3.3. Results

4.3.3.1. Comparison of *obs* and *obs+exe* Conditions

Suppression of mu/beta band power was observed in central (C3, C4) frontal (F7, F8) and parietal (P3, P4) channels with greater suppression at central channels (Figure 4.14). All the relevant channels showed slightly larger desynchronization values (in dB) for *obs+exe* condition.

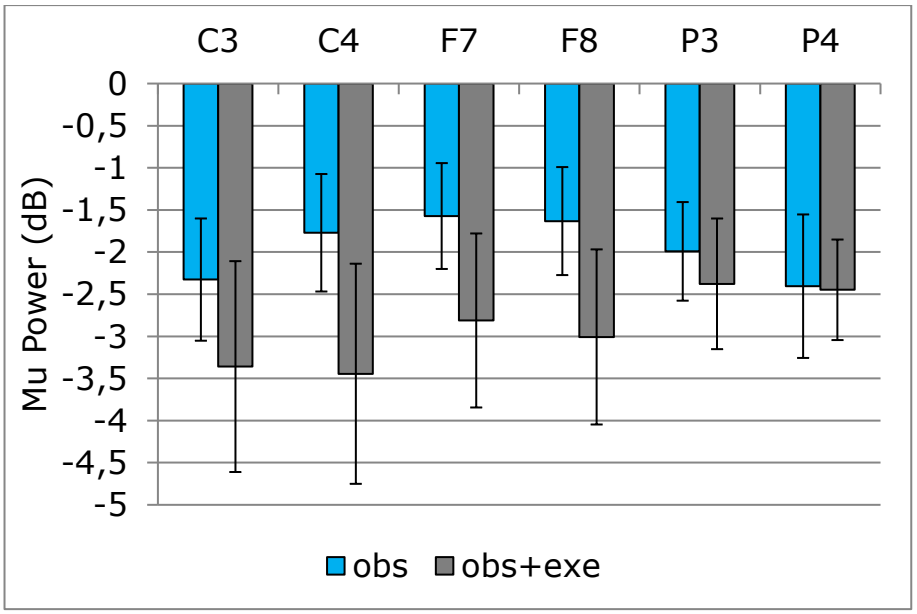
At channels C3 and C4, t-tests comparing mu/beta suppression during each of the experimental conditions (*obs*, *obs+exe*) to zero showed significant suppression from baseline in mu [Condition: *obs*; **C3** t(7)=-3.21, p=0.008; **C4** t(7)=-2.54, p=0.02. Condition: *obs+exe*; **C3** t(7)=-2.68, p=0.016; **C4** t(7)=-2.64, p=0.017] and beta band [Condition: *obs*; **C3** t(7)=-3.96, p=0.003; **C4** t(7)=-3.63, p=0.004 Condition:

obs+exe; **C3** t(7)=-5.92, p=0.0005; **C4** t(7)=-3.96, p=0.003] oscillations (Figure 4.14a,b).

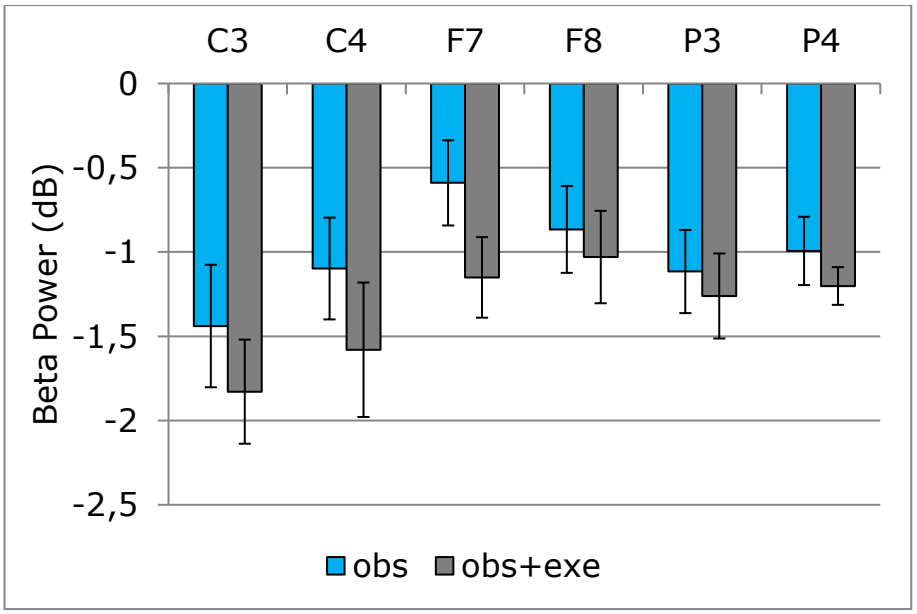
4.3.3.2. Comparison of *no robot* and *robot* Conditions

Suppression of mu/beta band power was observed in central (C3, C4) frontal (F7, F8) and parietal (P3, P4) channels with greater suppression at central channels (Figure 4.15). Desynchronization of mu/beta band (in dB) was slightly larger for *robot* condition over C4, contralateral to the movement (Figure 4.15).

At channels C3 and C4, T-tests comparing mu/beta suppression during each of the experimental conditions (*no robot*, *robot*) to zero showed significant suppression from baseline in mu [Condition: *no robot*; **C3** t(7)=-1.83, p=0.05; **C4** t(7)=-2.61, p=0.02. Condition: *robot*; **C3** t(7)=-2.70, p=0.016; **C4** t(7)=-2.85, p=0.013] and beta band [Condition: *no robot*; **C3** t(7)=-2.35, p=0.03; **C4** t(7)=-2.61, p=0.018 Condition: *robot*; **C3** t(7)=-3.33, p=0.007; **C4** t(7)=-3.15, p=0.008] oscillations (Figure 4.15a,b).

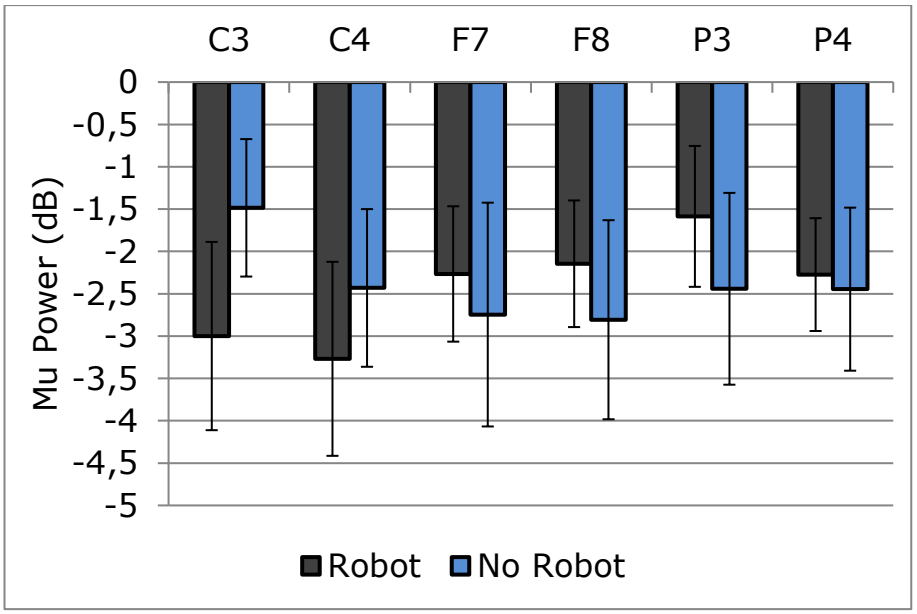


(a)

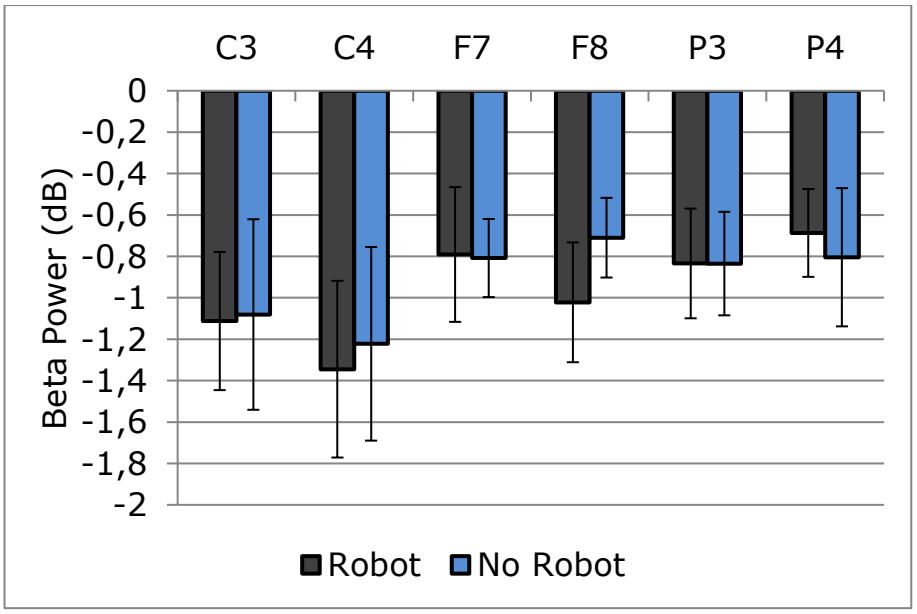


(b)

Figure 4.14. Mu (a) and beta (b) band suppression to experimental conditions. Bars represent the mean log ratio of power in the mu (8-12 Hz) and beta (15-25 Hz) frequency bands during session 1 (*obs*) and session 2 (*obs+exe*). Error bars indicate the standard error of the mean. A log ratio less than zero indicates mu/beta suppression.



(a)



(b)

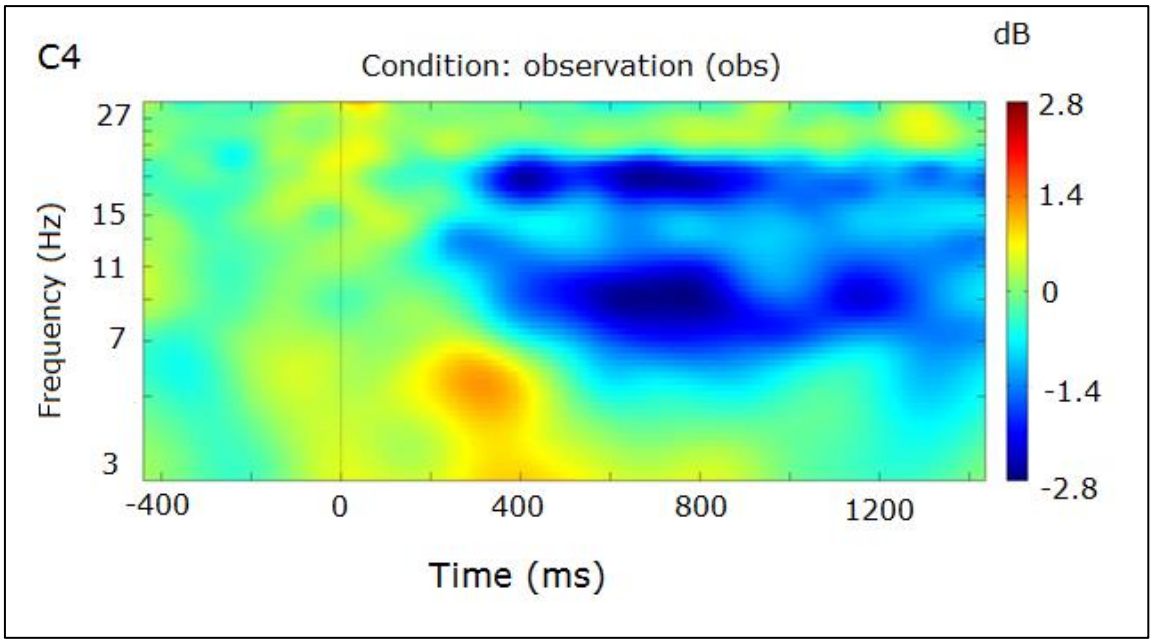
Figure 4.15. Mu (a) and beta (b) band suppression to experimental conditions. Bars represent the mean log ratio of power in the mu (8-12 Hz) and beta (15-25 Hz) frequency bands during session 3 (*robot, no robot*). Error bars indicate the standard error of the mean. A log ratio less than zero indicates mu/beta suppression.

4.3.3.3. Effect of Anticipation on Observation and Execution

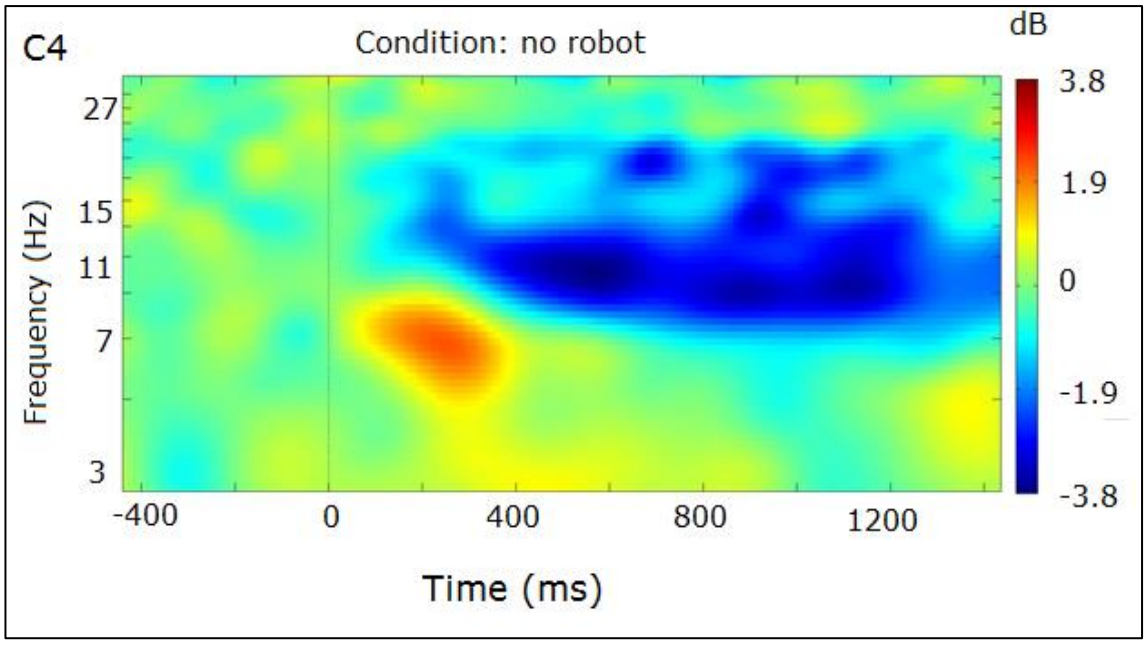
Anticipation and Observation

Over the somatosensory cortex, time-frequency analysis of the relevant channels led to a decrease in mu (8-12 Hz) and beta (15-25 Hz) band power shortly after stimulus onset starting around 300 ms (Figure 4.16).

In mu band, a 2 (observational condition: *obs* vs. *no robot*) by 2 (hemisphere: left vs. right) within subjects analysis of variance over central channels (C3, C4) revealed no significant main effects of observational condition [$F(1,7)=0.015$, $p>0.05$] nor hemisphere [$F(1,7)=0.367$, $p>0.05$], but there was a significant presence of observational condition by hemisphere interaction [$F(1,7)=8.161$, $p<0.05$]. Similar 2 (observational condition) by 2 (hemisphere) repeated measures ANOVAs at frontal (F7, F8) and parietal channels (P3, P4) revealed no main effects or interactions {F7-F8: observational condition [$F(1,7)=1.806$], hemisphere [$F(1,7)=0.089$], observational condition x hemisphere [$F(1,7)=0.001$]; P3-P4: observational condition [$F(1,7)=0.102$], hemisphere [$F(1,7)=0.725$], observational condition x hemisphere [$F(1,7)=0.219$], all $p>0.1$}.



(a)



(b)

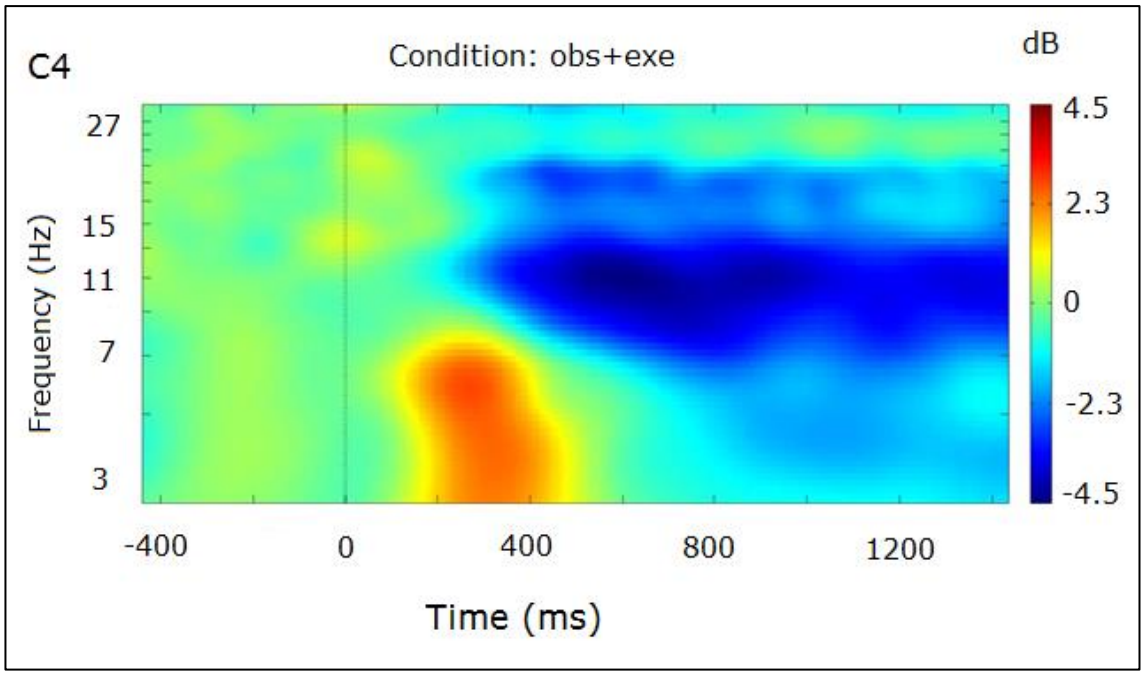
Figure 4.16. Time-frequency plots for conditions (*obs* (a) and *no robot* (b)) at channel C4 (right hemisphere). Plots for the left hemisphere (C3) were similar and are not shown. The frequency axis is log scaled. The zero point on the time axis indicates the onset of the video stimuli.

For beta frequency band, a similar 2 (observational condition: *obs* vs. *no robot*) by 2 (hemisphere: left vs. right) repeated measures ANOVAs were utilized. There were no main effects or interactions { C3-C4: observational condition [F(1,7)=0.095], hemisphere [F(1,7)=1.195], observational condition x hemisphere [F(1,7)=3.048]; F7-F8: observational condition [F(1,7)=0.015], hemisphere [F(1,7)=0.515], observational condition x hemisphere [F(1,7)=3.252]; P3-P4: observational condition [F(1,7)=0.530], hemisphere [F(1,7)=0.007], observational condition x hemisphere [F(1,7)=0.483], all p>0.1}.

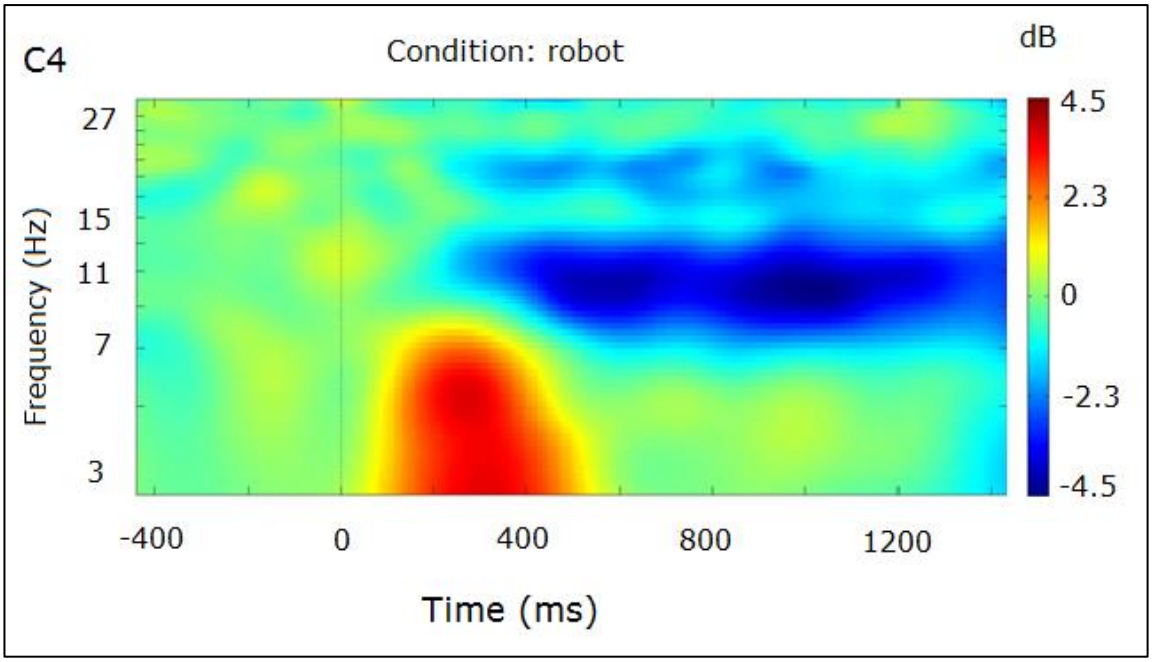
Anticipation and Execution

Over the somatosensory cortex, time-frequency analysis of the relevant channels led to a decrease in mu (8-12 Hz) and beta (15-25 Hz) band power shortly after stimulus onset starting around 300 ms (Figure 4.17).

In mu band, a 2 (executional condition: *obs+exe* vs. *robot*) by 2 (hemisphere: left vs. right) within subjects analysis of variance over central channels (C3, C4) revealed no significant main effects of executional condition [F(1,7)=0.377, p>0.5] nor hemisphere [F(1,7)=0.254, p>0.5], nor a significant presence of executional condition by hemisphere interaction [F(1,7)=0.453, p>0.5]. Similar 2 (executional condition) by 2 (hemisphere) repeated measures ANOVAs at frontal (F7, F8) and parietal channels (P3, P4) revealed no main effects or interactions {F7-F8: executional condition [F(1,7)=1.918], hemisphere [F(1,7)=0.052], executional condition x hemisphere [F(1,7)=0.647]; P3-P4: executional condition [F(1,7)=1.887], hemisphere [F(1,7)=1.176], executional condition x hemisphere [F(1,7)=1.449], all p>0.1}



(a)



(b)

Figure 4.17. Time-frequency plots for conditions (*obs+exe* (a) and *robot* (b)) at channel C4 (right hemisphere). Plots for the left hemisphere (C3) were similar and are not shown.

For beta frequency band, a similar 2 (executional condition: *obs* vs. *no robot*) by 2 (hemisphere: left vs. right) repeated measures ANOVAs were utilized. There were no main effects or interactions { C3-C4: executional condition [F(1,7)=3.532], hemisphere [F(1,7)=0.003], executional condition x hemisphere [F(1,7)=3.836]; F7-F8: executional condition [F(1,7)=0.637], hemisphere [F(1,7)=0.276], executional condition x hemisphere [F(1,7)=0.664]; P3-P4: executional condition [F(1,7)=3.695], hemisphere [F(1,7)=0.316], executional condition x hemisphere [F(1,7)=0.176], all p>0.1}.

4.3.3.4. Effect of Observation of Hand Movement Stimuli with Different Kinetics

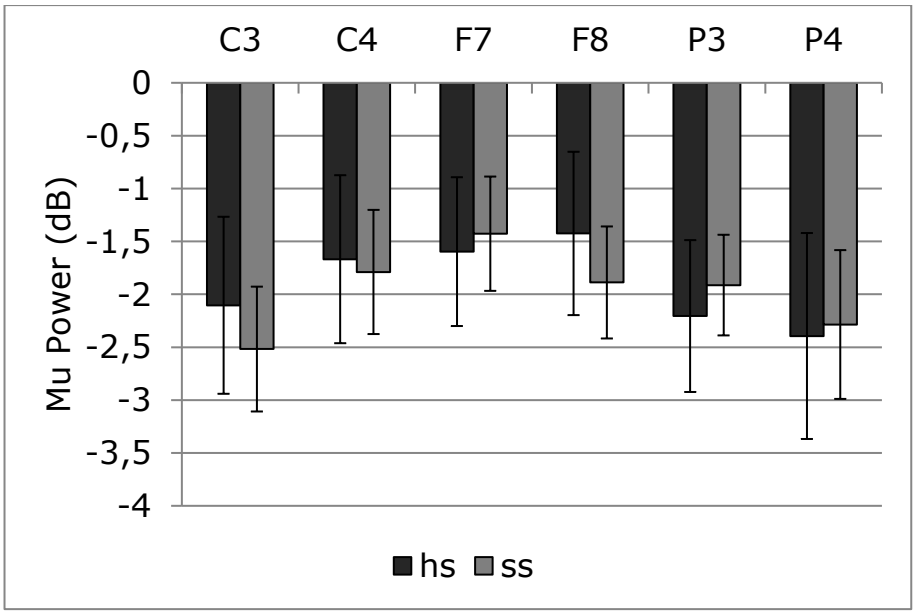
For mu and beta frequencies a 2 way ANOVA [spring type (hard, soft by hemisphere (right, left)] was performed at frontal (F7, F8) channels (Figure 4.18).

Mu suppression

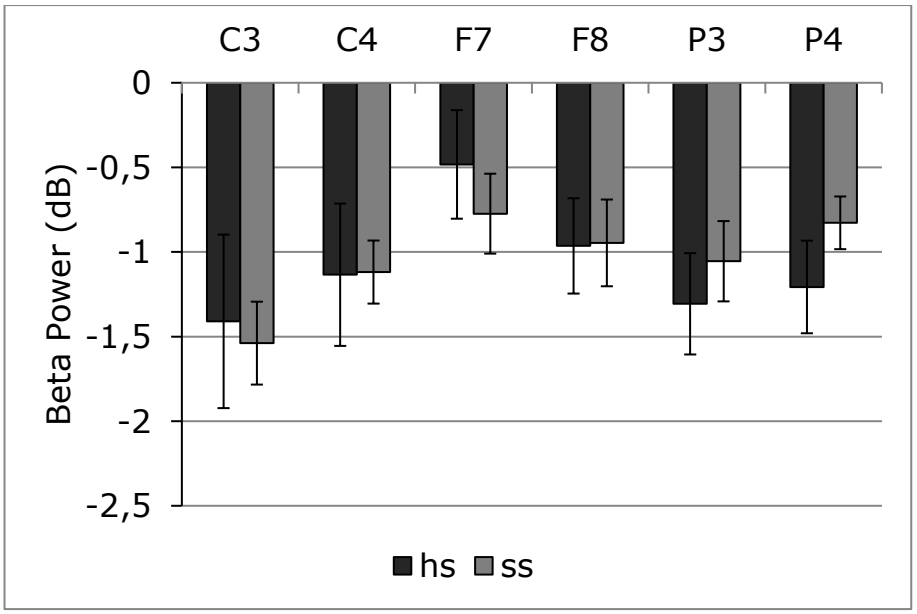
Mu oscillations did not reveal a main effect of spring type [F(1,7)=0.145, p>0.1] or hemisphere [F(1,7)= 0.178, p>0.1] but the spring type x hemisphere interaction was at the cusp of significance [F(1,7)=5.303, p=0.054].

Beta Suppression

Beta oscillations did not reveal significant main effects or interactions {spring type: [F(1,7)=1.012], hemisphere [F(1,7)=2.841], hemisphere X spring type interaction [F(1,7)=1.047] all p>0.1}.



(a)



(b)

Figure 4.18. Mu (a) and beta (b) band suppression to experimental conditions (hs, ss). Bars represent the mean log ratio of power in the mu (8-12 Hz) and beta (15-25 Hz) frequency bands during session 1 (hs*:hard spring, ss: soft spring*). Error bars indicate the standard error of the mean. A log ratio less than zero indicates mu/beta suppression.

5. CONCLUSIONS AND DISCUSSION

Several experimental paradigms with action observation, execution and imagery were designed in this thesis. A novel robotic therapy system, the ExoPinch, was designed and fabricated.

In this last chapter, each experiment was discussed separately based on their results. It was proposed that specific type of visual stimuli with a well-defined experimental paradigm may be implemented in the action observation treatment of stroke patients to have a positive additional impact.

From a clinical standpoint, further research is required to investigate whether the experiments presented here are applicable to patients with stroke. However, it is hoped that the results of this thesis will be beneficial to motor rehabilitation programs of upper extremities, as well as possible future research directions in this area.

5.1. Discussion on Response of Mirror Neurons During Observation of Actions with Different Sensorimotor Characteristics

The aim of this study was to investigate the effect of different types of video stimuli on MNS activity in one experimental run for each subject. This method allows to present sequences of different video clips reducing the possibility of habituation in the MNS [138]. Videos that are not engaging for long periods of time give rise to attentional disengagement and consequently increased alpha activity [139].

5.1.1. Mu Suppression

In this experiment, observation of all conditions (ss, hs, sp and lp) resulted in significant attenuations in the power of mu oscillations over the somatosensory cortex (electrode locations C3 and C4). This finding replicates several previous mu suppression studies [105, 107, 109].

Consistent with the previous work on observations of hand engaged in a precision grip, it was found that mu suppression during observation of object-directed hand actions is bilateral in nature [105].

Data analysis showed greater mu suppressions over parietal channels P3 and P4. These results confirm findings from a previous study reporting greater mu suppression in parietal regions relative to central one during observation of different hand movements [140]. The parietal lobe is a part of the human MNS and most importantly, it is strongly involved in the observation of object-directed actions [141].

5.1.2. Methodological Approach

Although the majority of the studies on human MNS have investigated mu suppression over central scalp locations, a meta-analysis of mu suppression suggests that for action observation, it does not show topographic specificity to central channels [31]. This approach to the EEG study of MNS activity during observation of different object-directed actions is based on several previous studies. Human fMRI studies indicate that the observed goal-directed grasping movements are encoded in a fronto-parietal circuit including vPMC and the IPL (BA 44/45, 6, 39/40 in particular) [30, 31]. In a recent study, simultaneous recording of EEG and fMRI tested the hypothesis that the mu rhythm is associated with the activity of multiple brain regions of the MNS. They found a negative correlation between the mu power in EEG and BOLD activity of fMRI from areas of the putative MNS [142]. In a similar study including the simultaneous recording of EEG and fMRI from 19 subjects suggested that the mu suppression during action observation and execution correlates with some regions including the somatosensory cortex, IPL and dorsal premotor cortex (dPM). This study further suggested that these regions might be directly causing mu suppression or that the functional connectivity within these regions is more likely to do

so [143]. It is theoretically possible that the existence of visuomotor mirror neurons in prefrontal cortex provide a downstream modulation of sensorimotor neurons [109]. These results support the methodological study of mu suppression that has been linked to the activation of the putative MNS not only at channels C3 and C4 but also at P3, P4, F7 and F8.

5.1.3. Effects of Visual Stimuli on Mu Suppression

Over the centro-parietal regions (C3, C4, P3 and P4), observation of hand actions at each channel with different conditions (ss, hs, sp and lp) did not result in significant differences in the mu suppression. Since in all conditions, the hand movement is biological, volitional and object-directed, it is more likely that the MNS equally responds to these actions at the electrode sites corresponding to centro-parietal brain regions [105, 107, 140, 141]. These findings suggest that mu suppression might not be sensitive to the visual appearance and movement kinematics but instead might be more involved in computing goals and intentions [5, 138].

A substantial finding of this study was that for the attenuation of mu suppression, there was a main effect of spring type (soft or hard) at frontal channels. It is likely that the neural activity might be context-dependent in vPMC [144], and that changes in attenuation may occur depending on the required force in the task. Indeed, vPMC is strongly connected to M1 [55] and action upon the object is necessary to trigger the encoding of force requirements in the motor system [43]. Overall, modulation of mu suppression at frontal channels is likely to be associated with the observed force requirement.

Although grasp dimension (the grasp width of the object) is an important determinant of the firing of cells in both PMC and M1 [145], the difference between two grasping types (sp and lp) at frontal channels F7 and F8

was not significant. This result may also suggest that the visual features of the stimuli in conditions sp and lp are similar in nature with the same intentional goal (i.e., reaching and grasping an object) and therefore MNS activity (mu suppression) for both conditions did not result in significant differences. The goal of the observer might be more important to trigger MNS than the way the action is performed [24].

The MNS responds strongly to actions for which the observer has familiarity with the observed stimuli [70]. In this experiment, observers were equally familiar with the goal and the kinematics of the observed movement with a prior practice with the same objects [44]. It is therefore plausible to think that the observed mu suppression is a measure of the resonance between observed kinematics and those of the observer. Taken together, the observed actions were in their personal motor repertoire when they observed kinematically comparable actions [58].

5.1.4. MNS and Rehabilitation

The potential role of MNS in humans has been shown to provide a powerful tool for the improvement of upper limb motor functions of patients with stroke [7]. Reorganization of neural circuits is crucial for functional recovery after brain damage. Given its potential role in reorganization, vPMC is critical for motor control and learning for visually guided actions. Recruitment of MNS and harnessing vPMC in this respect with action observation might provide an effective neurorehabilitative program for patients with stroke. The results of this study may help to better understand critical features necessary for successful development of an action observation rehabilitation program.

Further investigation of the effect of the visual stimuli on MNS revealed the main effect of video stimuli of hand squeezing soft and hard springs, at the frontal channels corresponding nearly to ventral premotor cortex

area of the brain. The activation of mirror neurons in premotor cortex during action observation plays a crucial role in observational learning. Based on the results, it was proposed that specific type of visual stimuli may be implemented in the action observation treatment of stroke patients to have a positive additional impact. However, it should be emphasized that further research is needed to demonstrate its validity and effectiveness.

5.2. Discussion on Monitoring the Mu and Beta Rhythm Modulations in a Cue-Based Paradigm: an EEG Study for Imagery-Based Rehabilitation

The results of this study showed that both execution and imagery of right hand movement resulted in significant attenuations in the power of mu and beta band oscillations over somatosensory cortex. At electrode sides C3 and C4, motor execution condition elicited slightly larger desynchronization than imagery with left focus slightly stronger for mu frequency band. These findings are consistent with several previous studies [38, 146, 147, 148]. Similarly, beta frequency band showed a lateralized activity, with a greater desynchronization in the hemisphere contralateral to the performing hand but this difference becomes less prominent for execution condition. These results suggest that the beta rhythm shows a bilateral symmetrical desynchronization with unilateral voluntary movement [40]. Since motor imagery of an action requires the inhibition of neural oscillations involved in controlling particular features of that action, it is likely that beta band is directly related to this inhibition [39] and desynchronization emerges with a more contralateral dominance at beta frequency band while imaging the right hand movement similar to what has been observed for active movement [115].

In this experiment, a significant main effect of frequency was found for central, parietal and frontal areas on imagery task. This finding is

consistent with previous studies that mu and beta frequency band oscillations might have distinct functions during mental simulations of actions [38, 39] and MI could be used to control mu and/or beta rhythm changes. The functional properties of these bands play an important role in EEG-based robotic rehabilitation devices and BCIs [38].

In general, the ERSP patterns of desynchronization with motor execution were similar to those with imagery [119, 135]. One of the main results revealed in this study is that there were differences in time latencies of attenuations between the motor execution and imagery tasks. Specifically, ERSP pattern of imagery condition showed delayed amplitude in the imagery task with respect to the stimulus onset over the contralateral hemisphere. Although there is an assumption that motor execution and imagery share nearly a common neural substructure, recent evidence shows that during motor imagery, the roles of these areas may be more complex [149]. This could support the different delayed latencies in the present study. In line with the result, a near-infrared spectroscopy (NIRS) study showed a delayed change in concentration of oxygenated hemoglobin in a hand imagery task when compared to real movement execution [150]. In addition, ERSP patterns showed suppression patterns near the stimulus onset that was stronger around mu frequency band both for execution and imagery conditions. This result can be interpreted as a general arousal for the observation of the upcoming stimulus already *known* by the subject. Due to the design of the experimental paradigm, participants were already able to anticipate the upcoming action and mu rhythm suppression was observed just before the onset of hand movement, which supports previous findings such as those of [151]. This anticipatory effect may enhance the related neural pathways and shorten the reaction time and thus should be considered in detail for stimulus-based rehabilitation paradigms.

The 5-subject groups were compared only for imagery condition to reveal the possible effect of a prior execution on imagery. The main difference found in the electrophysiological responses between the two groups was a more sustained pattern in group GEF around mu and beta frequency bands. In addition, for both frequency bands of interest, group GEF exhibited slightly greater desynchronization than group GIM at central, parietal and frontal channels. These findings reinforce the idea that prior execution might result in finer motor representations in imagery session. It is also plausible to think that for group GIM, the participants' active involvement in the imagery might be affected in the absence of a prior execution leading to a less contribution from the mirror neuron system at the group level. Taken together, integration of MI and prior physical practice might be an effective strategy in the treatment of patients with upper limb motor dysfunctions. Nevertheless, the differences in the motor imagery ability of the individuals might also affect the ERSP patterns in this study [152]. Moreover, the performance of motor imagery depends on the subject's attention to the related imagery task. The fact that subjects held the MBC in their hand during the imagery session might serve as kinesthetic MI (rather than visual imagery) which elicits very similar brain activity patterns to that obtained during active movement execution [153].

Analysis of electrophysiological responses around the brain regions that nearly correspond to the MNS allowed us to explore the effect of prior execution on imagery from a wider point of view. One of the major findings of this study was that for mu and beta frequency ranges, imagery ERSP values did not differ significantly between two experimentally manipulated groups over the central channels while contralateral parietal channel (P3) and frontal channels (F7, F8) revealed significant differences between the groups. The difference at frontal

channels may be attributed to the fact that these regions are reflecting the task performance of the imagery mode. Areas F7 and F8 are, in part, possible homologues of area F5 (ventral premotor cortex-vPMC) in non-human primates, which has motor representations of the hand [126]. Since the mirror neurons in vPMC are known to be a part of the MNS network and primary motor (M1) neurons are facilitated after PMC activation via dense premotor-M1 connections, vPMC is thought to play a significant role in reorganization following injury to M1 [27, 106]. Given the significance of these frontal regions in motor imagery [120, 154], more attention should be paid in the recruitment of these areas during imagery-based rehabilitation.

In the present study there is some probability that the participants may have had some minor hand motions during the imagery sessions. The whole experimental run for each subject's right hand position was carefully monitored by a video set up and no overt movement during an imagery session was encountered.

Although this study mainly focuses on alpha (8-12 Hz) and its counterpart beta frequency (15-25 Hz) ranges, studies in the mirror neuron system literature vary in terms of the precise frequency ranges [101]. Several studies further argue that the finer subdivision of these frequency bands (e.g, lower or upper alpha bands) should also be considered in order not to miss the key phonemena of interest. The reproducible differences in these results should be considered.

The functional recovery after stroke may require reorganization of the relevant brain areas. The mirror neuron mechanism could have important implications in understanding this cortical reorganization. This study approaches to imagery-based rehabilitation from mirror neuron system view since this putative network plays an important role in development of motor skills. This study provides several results that

might be beneficial to motor rehabilitation programs of upper extremities based on motor imagery. If motor imagery is to be used as an adjunct to physical practice to facilitate skill acquisition in patients with upper limb disorders, it is suggested that a prior physical execution will have an additional positive impact for a symbolic cue-based movement paradigm. This study emphasizes that neurorehabilitation studies should approach the problem from a wider possible view and progress in this direction will bring new rational treatments to post-stroke rehabilitation.

5.3. Discussion on Anticipatory Effect of Execution on Observation: an Approach using ExoPinch Finger Robot

This study investigated how the EEG Mu/Beta rhythm that is considered to index human MNS activity is modulated by an anticipatory effect of execution. The study model was based on two critical assumptions: that the mere observation condition (*obs*) in session 1 was matched to the *no robot* condition in session 3; and that *obs+exe* condition in session 2 was matched to *robot* condition in session 3. This approach in the experimental design is unique and reveals the possible anticipatory effect of robot accompany on observation and execution.

In the current study, only the conditions *obs+exe* and *robot* include execution of the left hand. This execution was initiated and terminated by ExoPinch finger robot and therefore the action is not a voluntary self-initiated motion of the individual. It was previously suggested that the MNS responds to the observation of both voluntary and involuntary hand actions [107]. Additionally, passive movements (e.g., controlled by a robot) share much of the motor control circuitry used for voluntary movements [170]. It is then plausible to think that neural circuits that are active during a self-initiated execution might also be active during

the passive execution of the finger by the exoskeleton robot. This conclusion emphasizes the advantage of using robot-assistive treatment in post-stroke rehabilitation.

The principal finding in this study was that an anticipatory effect of execution modulated the existing neural activity during action observation over the sensorimotor areas which might further suggest the preparatory processes of cortical motor areas.

5.3.1. Mu/Beta Suppression in Cortical Motor Areas

In the *obs* condition subjects knew that they would merely observe the stimuli without any robot accompany (it was absent in the experiment area) and similary in the *obs+exe* condition, the finger robot ExoPinch would certainly and simultaneously present in each experimental trial and this was again known by the subjects, none of the conditions presented unexpectedly to the subjects in these first two sessions.

All the experimental conditions (*obs, obs+exe, robot, no robot*) resulted in significant attenuations in the power of mu and beta band oscillations over somatosensory cortex indicating more desynchronized neural assemblies. Consistent with several previous work [38, 140], larger suppressions of mu/beta band power have been found over the somatosensory cortex (C3, C4) than other electrode locations for all conditions of the experiment. Additionally, *obs+exe* condition had a larger magnitude of MNS activity over the relevant electrode sides than *obs* condition. In other words, mu and beta band suppressions were larger when execution and observation were performed simultaneously. This finding supports several previous studies that simultaneous action observation and execution has a relatively stronger effect on mu/beta suppression than mere observation [37]. However, for *robot* and *no robot* conditions such evidence of a difference in magnitude were evident

only over sensorimotor cortex. This result supports the conditional (execution, observation) selectivity of central area of the cortex for mu/beta suppression [171].

5.3.2. Effect of Anticipation on Observation and Execution

In this experiment, an interaction effect was found between observational condition (*obs*, *no robot*) and hemisphere (C3, C4) at mu frequency band. In these two conditions, subjects were merely observing the video stimuli without any overt movement. It is likely that an anticipation of the robot accompany in *no robot* condition modulated the neural activity at mu frequency band over somatosensory areas while subjects were merely watching the video clips.

The exact synchronization of the observation and execution session (*obs+exe*) was preceded by the random accompany session (session 3). Therefore subjects experienced the exact motor movement (flexion/extension of the index finger) in the *obs+exe* session while matching or "mirroring" this motor response to the visual stimulus due to the precise synchronization. The same neural mirroring mechanism might be active during the last session of the experiment. The behavioral changes related to anticipation in this session might be correlating with changes in functional activation in cortical motor areas [148]. This anticipatory effect may have prepared the central brain regions in planning of a visually guided finger movement by engaging the mirror neuron mechanism [172, 173].

Although main hypothesis primarily related to the anticipatory effect of execution on observation, *obs+exe* and *robot* conditions were also analyzed over the channels of interest to explore any modulatory effect of anticipation on execution. Neither main nor interaction effects were found in these analyses. Since the anticipated action (flexion/extension

of their left hand's index finger) is already known by the subjects due to the experimental design, the anticipatory effect of execution on its counterpart might not have a remarkable effect.

5.3.3. Effect of Visual Stimuli on MNS

In the current study, analysis of visual stimuli with different kinetical properties (hs, ss) was investigated to better understand whether the contextual features might have a facilitatory effect on observation. It was revealed that the attenuation of mu suppression was significantly modulated by the visual stimuli ss and hs at frontal channels. It is likely that the neural activity might be context-dependent in the corresponding brain area, ventral premotor cortex (vPMC) [144], and that changes in attenuation may occur depending on the required force in the task. Indeed, vMPC is strongly connected to M1 [55] and action upon the object is necessary to trigger the encoding of force requirements in the motor system [43]. Overall, modulation of mu suppression at frontal channels is likely to be associated with the observed force requirement [145].

5.3.4. MNS and Rehabilitation

It is now a well-accepted notion that mere observation of actions activates the corresponding motor representations of those actions in the brain [33]. The neurorehabilitative use of this approach is based on the discovery of the putative *mirror neuron system* and their functional abilities.

The main mechanism of the activation of the MNS is supposed to be an internal simulation of the observed action. Using an internal simulation of an action, an individual can re-activate the action representations previously stored in the brain [15, 158].

The approach in the experimental design serves as a novel framework for an action-observation based treatment of stroke. The observation of action with a concomitant effect of anticipation may initiate the related motor pathways of the observed action by mostly simulating the corresponding motor act. Furthermore, the type of the observed stimuli (e.g., hand-object interaction, kinematical or kinetical parameters) may have a relatively strong effect on MNS activity. In this study, investigation of the effect of the visual stimuli on MNS revealed the main effect of video stimuli of hand squeezing soft and hard springs, at the frontal channels corresponding nearly to ventral premotor cortex area of the brain. The activation of mirror neurons in premotor cortex during action observation plays a crucial role in observational learning [27].

The combination of motor exercise and action observation seems to constitute a powerful approach for neurorehabilitation of motor deficits following stroke [174]. An anticipatory effect of execution may well facilitate the observation session and this would allow a better eventual action execution performance. The common neural network for action observation and execution (mirror neuron system), in this sense, increases the value of the treatment of post-stroke motor disabilities.

Based on the results, it is proposed that specific type of visual stimuli can be combined with the functional abilities of the MNS in the action observation based treatment of hand motor dysfunction of stroke patients to have a positive additional impact.

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APPENDICES

APPENDIX 1

Matlab Code for Importing Raw EEG data into EEGLAB with Event Values/Timings:

```
clear all;      % CLEAR THE WORKSPACE
clc;            % CLEAR THE COMMAND WINDOW
filename=input('enter the file name : ', 's');

A=load(filename);%load(filename)

B=A(:,2:end-3); % removes last three columns so this is raw EEG with
column index

C=A(:,20:end); % matrix for triggers with 3.14
[row,col,v]=find(C==3.14); %get only 3.14s (nonzero)
D=[row,v]; % this is the trigger matrix
rowtime=(row-1)/250; % column index in seconds

E=[rowtime,v];

varname=genvarname(filename); % constructs a variable from string
save(varname,'B'); % save the file as .mat with --starting the original
file name--
save('Event.txt','E','-ascii');
```

APPENDIX 2

Fundamental Matlab Commands used in this Thesis Study:

```
%%%% this script includes main commands for ERSP ANALYSIS%%

STUDY=pop_erspparams(STUDY,'freqrange',[1 40]); % sets the main
ersp parameters, check from STUDY.etc.erspparams

% if topographic plot was done somewhere at the STUDY level,
topotime and topofreq variables must be checked.

STUDY=pop_erspparams(STUDY,'freqrange',[1
40],'topotime',[],'topofreq',[]);

% now check again STUDY erspparams

[STUDY ersp times
freqs]=std_erspplot(STUDY,ALLEEG,'channels',{'C3'},'plotsubjects','on')
;%to plot ERSPs for channels

%this command brings erspdata, ersptimes and erspfreq data to
workspace

% now to consider all channels and a specific frequency band,e.g.mu
(8-12 Hz)
chanlocs=eeg_mergelocs(ALLEEG.chanlocs);
[STUDY ersp times
freqs]=std_erspplot(STUDY,ALLEEG,'channels',{chanlocs.labels},'topoti
me',[100 500],'topofreq',[8 12]);
% now ersp includes only this frequency band(8-12),it is a new
workspace variable to get the ersp data for one subject simply write :
[STUDY ersp times
freqs]=std_erspplot(STUDY,ALLEEG,'channels',{chanlocs.labels},'topoti
me',[100 500],'subject',['GBayer'],'topofreq',[15 25]);

% to change the current design
STUDY = std_selectdesign(STUDY, ALLEEG, 7); % chooses design 7
%t change the condiition
STUDY.condition={'execution'} %or
STUDY.condition={'execution','imagery'}
```

APPENDIX 3

PsychoPy2 Code used in the Experiment in Chapter 4.1:

```
#!/usr/bin/env python2
# -*- coding: utf-8 -*-
"""
This experiment was created using PsychoPy2 Experiment Builder
 (v1.83.04), 2016_11_28_1643
"""
from __future__ import division  # so that 1/3=0.333 instead of 1/3=0
import time
from psychopy import locale_setup, visual, core, data, event, logging,
 sound, gui,parallel
from psychopy.constants import *  # things like STARTED, FINISHED
import numpy as np  # whole numpy lib is available, prepend 'np.'
from numpy import sin, cos, tan, log, log10, pi, average, sqrt, std,
 deg2rad, rad2deg, linspace, asarray
from numpy.random import random, randint, normal, shuffle
import os  # handy system and path functions
import sys # to get file system encoding
from ctypes import windll #for parallel port connection


# Ensure that relative paths start from the same directory as this
 script
_thisDir =
 os.path.dirname(os.path.abspath(__file__)).decode(sys.getfilesystem
 encoding())
os.chdir(_thisDir)


# Store info about the experiment session
expName = 'Experiment1'  # from the Builder filename that created
 this script
expInfo = {'participant':'', 'session':'001'}
dlg = gui.DlgFromDict(dictionary=expInfo, title=expName)
if dlg.OK == False: core.quit()  # user pressed cancel
```

```
expInfo['date'] = data.getDateStr()  # add a simple timestamp
expInfo['expName'] = expName

# Data file name stem = absolute path + name; later add .psyexp,
 .csv, .log, etc
filename = _thisDir + os.sep + u'data/%s_%s_%s'
 %(expInfo['participant'], expName, expInfo['date'])

# An ExperimentHandler isn't essential but helps with data saving
thisExp = data.ExperimentHandler(name=expName, version='',
    extraInfo=expInfo, runtimeInfo=None,
    originPath=None,
    savePickle=True, saveWideText=True,
    dataFileName=filename)
#save a log file for detail verbose info
logFile = logging.LogFile(filename+'.log', level=logging.EXP)
logging.console.setLevel(logging.WARNING)  # this outputs to the
 screen, not a file

endExpNow = False  # flag for 'escape' or other condition => quit the
 exp

# Start Code - component code to be run before the window creation
dev=windll.Inpout32 #initiate the parallel port
value=dev.Out32(0x378,0)

# Setup the Window
win = visual.Window(size=(1366, 768), fullscr=True, screen=0,
 allowGUI=False, allowStencil=False,
    monitor='testMonitor', color=[-1,-1,-1], colorSpace='rgb',
    blendMode='avg', useFBO=True,
    )
# store frame rate of monitor if we can measure it successfully
expInfo['frameRate']=win.getActualFrameRate()
if expInfo['frameRate']!=None:
    frameDur = 1.0/round(expInfo['frameRate'])
```

```
else:
    frameDur = 1.0/60.0 # couldn't get a reliable measure so guess

# Initialize components for Routine "trial"
trialClock = core.Clock()
ISI = core.StaticPeriod(win=win, screenHz=expInfo['frameRate'],
 name='ISI')

# Initialize components for Routine "tools"
toolsClock = core.Clock()
image = visual.ImageStim(win=win, name='image',
    image='C:\\Users\\Adams1\\Desktop\\PSYCHOPY
 DATA\\Rehabilitation_2\\tools.jpg', mask=None,
    ori=0, pos=[0, 0], size=[2, 2],
    color=[1,1,1], colorSpace='rgb', opacity=1,
    flipHoriz=False, flipVert=False,
    texRes=128, interpolate=True, depth=0.0)
ISI_2 = core.StaticPeriod(win=win, screenHz=expInfo['frameRate'],
 name='ISI_2')

# Initialize components for Routine "trial2"
trial2Clock = core.Clock()
ISI_3 = core.StaticPeriod(win=win, screenHz=expInfo['frameRate'],
 name='ISI_3')

# Create some handy timers
globalClock = core.Clock()  # to track the time since experiment
 started
routineTimer = core.CountdownTimer()  # to track time remaining of
 each (non-slip) routine

# set up handler to look after randomisation of conditions etc
trials_1 = data.TrialHandler(nReps=12, method='random',
    extraInfo=expInfo, originPath=-1,
    trialList=data.importConditions('conditions1.xlsx'),
    seed=None, name='trials_1')
thisExp.addLoop(trials_1)  # add the loop to the experiment
```

```
thisTrial_1 = trials_1.trialList[0]  # so we can initialise stimuli with
 some values
# abbreviate parameter names if possible (e.g. rgb=thisTrial_1.rgb)
if thisTrial_1 != None:
    for paramName in thisTrial_1.keys():
        exec(paramName + '= thisTrial_1.' + paramName)

for thisTrial_1 in trials_1:
    currentLoop = trials_1
    # abbreviate parameter names if possible (e.g. rgb =
 thisTrial_1.rgb)
    if thisTrial_1 != None:
        for paramName in thisTrial_1.keys():
            exec(paramName + '= thisTrial_1.' + paramName)

    #------Prepare to start Routine "trial"-------
    t = 0
    trialClock.reset()  # clock
    frameN = -1
    # update component parameters for each repeat
    movie1 = visual.MovieStim2(win=win, name='movie1',
        noAudio = True,
        filename=paramet_1,
        ori=0, pos=[0, 0], opacity=1,
        size=[1366,788],
        depth=-1.0,
        )
    # keep track of which components have finished
    trialComponents = []
    trialComponents.append(ISI)
    trialComponents.append(movie1)
    for thisComponent in trialComponents:
        if hasattr(thisComponent, 'status'):
            thisComponent.status = NOT_STARTED

    #-------Start Routine "trial"-------
```

```
  continueRoutine = True
  while continueRoutine:
      # get current time
      t = trialClock.getTime()
      frameN = frameN + 1  # number of completed frames (so 0 is
the first frame)
      # update/draw components on each frame


      # *movie1* updates
      if t >= 4 and movie1.status == NOT_STARTED:
          # keep track of start time/frame for later
          movie1.tStart = t  # underestimates by a little under one
frame
          movie1.frameNStart = frameN  # exact frame index
          movie1.setAutoDraw(True)


          value2=dev.Out32(0x378,255)######send trigger to
parallel port
          win.flip()
          value3=dev.Out32(0x378,0)


      if movie1.status == FINISHED:  # force-end the routine
          continueRoutine = False
      # *ISI* period
      if t >= 0.0 and ISI.status == NOT_STARTED:
          # keep track of start time/frame for later
          ISI.tStart = t  # underestimates by a little under one frame
          ISI.frameNStart = frameN  # exact frame index
          ISI.start(4)
      elif ISI.status == STARTED: #one frame should pass before
updating params and completing
          ISI.complete() #finish the static period


      # check if all components have finished
      if not continueRoutine:  # a component has requested a forced-
end of Routine
```

```
            break
        continueRoutine = False  # will revert to True if at least one
component still running
        for thisComponent in trialComponents:
            if hasattr(thisComponent, "status") and thisComponent.status
!= FINISHED:
                continueRoutine = True
                break  # at least one component has not yet finished

        # check for quit (the Esc key)
        if endExpNow or event.getKeys(keyList=["escape"]):
            core.quit()

        # refresh the screen
        if continueRoutine:  # don't flip if this routine is over or we'll get
a blank screen
            win.flip()

    #-------Ending Routine "trial"-------
    for thisComponent in trialComponents:
        if hasattr(thisComponent, "setAutoDraw"):
            thisComponent.setAutoDraw(False)
    # the Routine "trial" was not non-slip safe, so reset the non-slip
timer
    routineTimer.reset()
    thisExp.nextEntry()

# completed 12 repeats of 'trials_1'

#------Prepare to start Routine "tools"-------
t = 0
toolsClock.reset()  # clock
frameN = -1
routineTimer.reset()
# update component parameters for each repeat
# keep track of which components have finished
```

```
toolsComponents = []
toolsComponents.append(image)
toolsComponents.append(ISI_2)
for thisComponent in toolsComponents:
    if hasattr(thisComponent, 'status'):
        thisComponent.status = NOT_STARTED

#-------Start Routine "tools"-------
continueRoutine = True
while continueRoutine and routineTimer.getTime() > 0:
    # get current time
    t = toolsClock.getTime()
    frameN = frameN + 1  # number of completed frames (so 0 is the
 first frame)
    # update/draw components on each frame

    # *image* updates
    if t >= 4 and image.status == NOT_STARTED:
        # keep track of start time/frame for later
        image.tStart = t  # underestimates by a little under one frame
        image.frameNStart = frameN  # exact frame index
        image.setAutoDraw(True)
    if image.status == STARTED and t >= (4 + (8-
 win.monitorFramePeriod*0.75)): #most of one frame period left
        image.setAutoDraw(False)
    # *ISI_2* period
    if t >= 0.0 and ISI_2.status == NOT_STARTED:
        # keep track of start time/frame for later
        ISI_2.tStart = t  # underestimates by a little under one frame
        ISI_2.frameNStart = frameN  # exact frame index
        ISI_2.start(4)
    elif ISI_2.status == STARTED: #one frame should pass before
 updating params and completing
        ISI_2.complete() #finish the static period

    # check if all components have finished
```

```
    if not continueRoutine:  # a component has requested a forced-end
of Routine
        break
    continueRoutine = False  # will revert to True if at least one
component still running
    for thisComponent in toolsComponents:
        if hasattr(thisComponent, "status") and thisComponent.status !=
FINISHED:
            continueRoutine = True
            break  # at least one component has not yet finished

    # check for quit (the Esc key)
    if endExpNow or event.getKeys(keyList=["escape"]):
        core.quit()

    # refresh the screen
    if continueRoutine:  # don't flip if this routine is over or we'll get a
blank screen
        win.flip()

#-------Ending Routine "tools"-------
for thisComponent in toolsComponents:
    if hasattr(thisComponent, "setAutoDraw"):
        thisComponent.setAutoDraw(False)

# set up handler to look after randomisation of conditions etc
trials_2 = data.TrialHandler(nReps=12, method='random',
    extraInfo=expInfo, originPath=-1,
    trialList=data.importConditions('conditions2.xlsx'),
    seed=None, name='trials_2')
thisExp.addLoop(trials_2)  # add the loop to the experiment
thisTrial_2 = trials_2.trialList[0]  # so we can initialise stimuli with
 some values
# abbreviate parameter names if possible (e.g. rgb=thisTrial_2.rgb)
if thisTrial_2 != None:
    for paramName in thisTrial_2.keys():
```

```
        exec(paramName + '= thisTrial_2.' + paramName)

for thisTrial_2 in trials_2:
    currentLoop = trials_2
    # abbreviate parameter names if possible (e.g. rgb =
 thisTrial_2.rgb)
    if thisTrial_2 != None:
        for paramName in thisTrial_2.keys():
            exec(paramName + '= thisTrial_2.' + paramName)

    #------Prepare to start Routine "trial2"-------
    t = 0
    trial2Clock.reset()  # clock
    frameN = -1
    # update component parameters for each repeat
    movie2 = visual.MovieStim2(win=win, name='movie2',
        noAudio = False,
        filename=para_2,
        ori=0, pos=[0, 0], opacity=1,
        size=[1366,768],
        depth=-1.0,
        )
    # keep track of which components have finished
    trial2Components = []
    trial2Components.append(ISI_3)
    trial2Components.append(movie2)
    for thisComponent in trial2Components:
        if hasattr(thisComponent, 'status'):
            thisComponent.status = NOT_STARTED

    #-------Start Routine "trial2"-------
    continueRoutine = True
    while continueRoutine:
        # get current time
        t = trial2Clock.getTime()
```

```
    frameN = frameN + 1  # number of completed frames (so 0 is
the first frame)
    # update/draw components on each frame

    # *movie2* updates
    if t >= 4 and movie2.status == NOT_STARTED:
        # keep track of start time/frame for later
        movie2.tStart = t  # underestimates by a little under one
frame
        movie2.frameNStart = frameN  # exact frame index
        movie2.setAutoDraw(True)

        value2=dev.Out32(0x378,255)####parallel port trigger
        win.flip()
        value3=dev.Out32(0x378,0)

    # *ISI_3* period
    if t >= 0.0 and ISI_3.status == NOT_STARTED:
        # keep track of start time/frame for later
        ISI_3.tStart = t  # underestimates by a little under one frame
        ISI_3.frameNStart = frameN  # exact frame index
        ISI_3.start(4)
    elif ISI_3.status == STARTED: #one frame should pass before
updating params and completing
        ISI_3.complete() #finish the static period

    # check if all components have finished
    if not continueRoutine:  # a component has requested a forced-
end of Routine
        break
    continueRoutine = False  # will revert to True if at least one
component still running
    for thisComponent in trial2Components:
        if hasattr(thisComponent, "status") and thisComponent.status
!= FINISHED:
            continueRoutine = True
            break  # at least one component has not yet finished
```

```
        # check for quit (the Esc key)
        if endExpNow or event.getKeys(keyList=["escape"]):
            core.quit()

        # refresh the screen
        if continueRoutine:  # don't flip if this routine is over or we'll get
 a blank screen
            win.flip()

    #-------Ending Routine "trial2"-------
    for thisComponent in trial2Components:
        if hasattr(thisComponent, "setAutoDraw"):
            thisComponent.setAutoDraw(False)
    # the Routine "trial2" was not non-slip safe, so reset the non-slip
 timer
    routineTimer.reset()
    thisExp.nextEntry()

# completed 12 repeats of 'trials_2'

# these shouldn't be strictly necessary (should auto-save)
thisExp.saveAsWideText(filename+'.csv')
thisExp.saveAsPickle(filename)
logging.flush()
# make sure everything is closed down
thisExp.abort() # or data files will save again on exit
win.close()
core.quit()
```

APPENDIX 4

PsychoPy2 Code used in the Experiment in Chapter 4.2:

```
#!/usr/bin/env python2
# -*- coding: utf-8 -*-

from __future__ import division
import psychopy.visual
# so that 1/3=0.333 instead of 1/3=0
from psychopy import locale_setup, visual, core, data, event, logging,
    sound, gui,parallel
from psychopy.constants import *  # things like STARTED, FINISHED
import numpy as np  # whole numpy lib is available, prepend 'np.'
from numpy import sin, cos, tan, log, log10, pi, average, sqrt, std,
    deg2rad, rad2deg, linspace, asarray
from numpy.random import random, randint, normal, shuffle
import os  # handy system and path functions
import sys # to get file system encoding

from ctypes import windll #for parallel port connection

# Ensure that relative paths start from the same directory as this
    script
_thisDir =
    os.path.dirname(os.path.abspath(__file__)).decode(sys.getfilesys
    temencoding())
os.chdir(_thisDir)

# Store info about the experiment session
expName = 'psychopy_work3'  # from the Builder filename that
    created this script
expInfo = {'participant':'', 'session':'001'}
dlg = gui.DlgFromDict(dictionary=expInfo, title=expName)
if dlg.OK == False: core.quit()  # user pressed cancel
expInfo['date'] = data.getDateStr()  # add a simple timestamp
expInfo['expName'] = expName
```

```
# Data file name stem = absolute path + name; later add .psyexp,
      .csv, .log, etc
filename = _thisDir + os.sep + u'data/%s_%s_%s'
      %(expInfo['participant'], expName, expInfo['date'])

# An ExperimentHandler isn't essential but helps with data saving
thisExp = data.ExperimentHandler(name=expName, version='',
   extraInfo=expInfo, runtimeInfo=None,
   originPath=None,
   savePickle=True, saveWideText=True,
   dataFileName=filename)
#save a log file for detail verbose info
logFile = logging.LogFile(filename+'.log', level=logging.EXP)
logging.console.setLevel(logging.WARNING)  # this outputs to the
      screen, not a file

endExpNow = False  # flag for 'escape' or other condition => quit the
      exp

# Start Code - component code to be run before the window creation

dev=windll.Inpout32 #initiate the parallel port
value=dev.Out32(0x378,0)

# Setup the Window
win = visual.Window(size=(1366, 768), fullscr=True, screen=0,
      allowGUI=False, allowStencil=False,
   monitor='testMonitor', color=[-1,-1,-1], colorSpace='rgb',
   blendMode='avg', useFBO=True,
   )
# store frame rate of monitor if we can measure it successfully
expInfo['frameRate']=win.getActualFrameRate()
if expInfo['frameRate']!=None:
   frameDur = 1.0/round(expInfo['frameRate'])
else:
```

```
    frameDur = 1.0/60.0 # couldn't get a reliable measure so guess

# Initialize components for Routine "trial"
trialClock = core.Clock()
ISI = core.StaticPeriod(win=win, screenHz=expInfo['frameRate'],
      name='ISI')
fixation_cross = visual.ImageStim(win=win, name='fixation_cross',
    image='C:\\Users\\Adams1\\Desktop\\Fixation Cross.jpg',
      mask=None,
    ori=0, pos=[0, 0], size=[2, 2],
    color=[1,1,1], colorSpace='rgb', opacity=1,
    flipHoriz=False, flipVert=False,
    texRes=128, interpolate=True, depth=-1.0)

Right_Arrow = visual.ImageStim(win=win, name='Right_Arrow',
    image='C:\\Users\\Adams1\\Desktop\\Right Arrow2.jpg',
      mask=None,
    ori=0, pos=[0, 0], size=[0.4, 0.4],
    color=[1,1,1], colorSpace='rgb', opacity=1,
    flipHoriz=False, flipVert=False,
    texRes=128, interpolate=True, depth=-2.0)

# Create some handy timers
globalClock = core.Clock()  # to track the time since experiment
      started
routineTimer = core.CountdownTimer()  # to track time remaining of
      each (non-slip) routine

# set up handler to look after randomisation of conditions etc
trials = data.TrialHandler(nReps=35, method='sequential',  #
      NUMBER OF TRIALS -CHANGE AFTERWARDS
    extraInfo=expInfo, originPath=-1,
    trialList=[None],
    seed=None, name='trials')
thisExp.addLoop(trials)  # add the loop to the experiment
thisTrial = trials.trialList[0]  # so we can initialise stimuli with some
      values
```

```
# abbreviate parameter names if possible (e.g. rgb=thisTrial.rgb)
if thisTrial != None:
    for paramName in thisTrial.keys():
        exec(paramName + '= thisTrial.' + paramName)

for thisTrial in trials:
    currentLoop = trials
    # abbreviate parameter names if possible (e.g. rgb = thisTrial.rgb)
    if thisTrial != None:
        for paramName in thisTrial.keys():
            exec(paramName + '= thisTrial.' + paramName)

    #------Prepare to start Routine "trial"-------
    t = 0
    trialClock.reset()  # clock
    frameN = -1
    routineTimer.add(9.000000)
    # update component parameters for each repeat
    # keep track of which components have finished
    trialComponents = []
    trialComponents.append(ISI)
    trialComponents.append(fixation_cross)
    trialComponents.append(Right_Arrow)
    for thisComponent in trialComponents:
        if hasattr(thisComponent, 'status'):
            thisComponent.status = NOT_STARTED

    #-------Start Routine "trial"-------
    continueRoutine = True
    while continueRoutine and routineTimer.getTime() > 0:
        # get current time
        t = trialClock.getTime()
        frameN = frameN + 1  # number of completed frames (so 0 is
        the first frame)
        # update/draw components on each frame
```

```
# *fixation_cross* updates
if t >= 4 and fixation_cross.status == NOT_STARTED:
    # keep track of start time/frame for later
    fixation_cross.tStart = t  # underestimates by a little under one frame
    fixation_cross.frameNStart = frameN  # exact frame index
    fixation_cross.setAutoDraw(True)
    s=sound.Sound(value='Bfl', secs=0.05,octave=5)     #sound play
    s.play()



if fixation_cross.status == STARTED and t >= (4 + (1.0-win.monitorFramePeriod*0.75)): #most of one frame period left
# *Right_Arrow* updates

 if t >= 5 and Right_Arrow.status == NOT_STARTED:
    # keep track of start time/frame for later
    Right_Arrow.tStart = t  # underestimates by a little under one frame
    Right_Arrow.frameNStart = frameN  # exact frame index
    Right_Arrow.setAutoDraw(True)
    s=sound.Sound(value='Bfl', secs=1.5,octave=4.6)     #sound play


    #######   sending trigger...write to parallel port in decimal(0-256)
    value2=dev.Out32(0x378,255)
    win.flip()


    s.play()
    #core.wait(0.5)
    value3=dev.Out32(0x378,0)

if Right_Arrow.status == STARTED and t >= (5 + (4-win.monitorFramePeriod*0.75)): #most of one frame period left
    Right_Arrow.setAutoDraw(False)
```

```
    # *ISI* period
    if t >= 0.0 and ISI.status == NOT_STARTED:
        # keep track of start time/frame for later
        ISI.tStart = t  # underestimates by a little under one frame
        ISI.frameNStart = frameN  # exact frame index
        ISI.start(4)
    elif ISI.status == STARTED: #one frame should pass before
    updating params and completing
        ISI.complete() #finish the static period



    # check if all components have finished
    if not continueRoutine:  # a component has requested a forced-
    end of Routine
        break
    continueRoutine = False  # will revert to True if at least one
    component still running
    for thisComponent in trialComponents:
        if hasattr(thisComponent, "status") and thisComponent.status
    != FINISHED:
            continueRoutine = True
            break  # at least one component has not yet finished


    # check for quit (the Esc key)
    if endExpNow or event.getKeys(keyList=["escape"]):
        core.quit()


    # refresh the screen
    if continueRoutine:  # don't flip if this routine is over or we'll get
    a blank screen
        win.flip()

#-------Ending Routine "trial"-------
for thisComponent in trialComponents:
    if hasattr(thisComponent, "setAutoDraw"):
```

```
            thisComponent.setAutoDraw(False)
    thisExp.nextEntry()

# completed 35 repeats of 'trials'

# these shouldn't be strictly necessary (should auto-save)
thisExp.saveAsWideText(filename+'.csv')
thisExp.saveAsPickle(filename)
logging.flush()
# make sure everything is closed down
thisExp.abort() # or data files will save again on exit
win.close()
core.quit()
```

APPENDIX 5

PsychoPy2 Code used in the Experiment in Chapter 4.3:

Condition: Observation and Simultaneous Robot Accompany:

```
#!/usr/bin/env python2
# -*- coding: utf-8 -*-
######THIS CODE IS FOR THE SS AND MS SPRING STIMULATION
        AND SENDS TRIGGERS WHICH ARE SPECIFIC FOR THE VIDEO
        (MS OR SS)
######THIS CODE SENDS TRIGGER TO D0(1) FOR OPENBCI, D1(2)
        FOR SS SPRING AND D2(4) FOR MS SPRING
"""
This experiment was created using PsychoPy2 Experiment Builder
        (v1.83.04), 2016_11_28_1643
"""
from __future__ import division  # so that 1/3=0.333 instead of 1/3=0
import time
from psychopy import locale_setup, visual, core, data, event, logging,
        sound, gui,parallel
from psychopy.constants import *  # things like STARTED, FINISHED
import numpy as np  # whole numpy lib is available, prepend 'np.'
from numpy import sin, cos, tan, log, log10, pi, average, sqrt, std,
        deg2rad, rad2deg, linspace, asarray
from numpy.random import random, randint, normal, shuffle
import os  # handy system and path functions
import sys # to get file system encoding
from ctypes import windll #for parallel port connection
```

```
# Ensure that relative paths start from the same directory as this
        script
_thisDir =
        os.path.dirname(os.path.abspath(__file__)).decode(sys.getfilesy
        stemencoding())
os.chdir(_thisDir)
# Store info about the experiment session
expName = 'Exp'  # from the Builder filename that created this script
expInfo = {'participant':'', 'session':'001'}
dlg = gui.DlgFromDict(dictionary=expInfo, title=expName)
if dlg.OK == False: core.quit()  # user pressed cancel
expInfo['date'] = data.getDateStr()  # add a simple timestamp
expInfo['expName'] = expName

# Data file name stem = absolute path + name; later add .psyexp,
        .csv, .log, etc
filename = _thisDir + os.sep + u'data/%s_%s_%s'
        %(expInfo['participant'], expName, expInfo['date'])

# An ExperimentHandler isn't essential but helps with data saving
thisExp = data.ExperimentHandler(name=expName, version='',
    extraInfo=expInfo, runtimeInfo=None,
    originPath=None,
    savePickle=True, saveWideText=True,
    dataFileName=filename)
```

```
#save a log file for detail verbose info
logFile = logging.LogFile(filename+'.log', level=logging.EXP)
logging.console.setLevel(logging.WARNING)  # this outputs to the
        screen, not a file

endExpNow = False  # flag for 'escape' or other condition => quit the
        exp
########################################################
        ####################START CODE
dev=windll.Inpout32 #initiate the parallel port
value=dev.Out32(0x378,0) # set all data pins to zero

# Setup the Window
win = visual.Window(size=(1366, 768), fullscr=True, screen=0,
        allowGUI=False, allowStencil=False,
    monitor='testMonitor', color=[-1,-1,-1], colorSpace='rgb',
    blendMode='avg', useFBO=True,
    )
# store frame rate of monitor if we can measure it successfully
expInfo['frameRate']=win.getActualFrameRate()
if expInfo['frameRate']!=None:
    frameDur = 1.0/round(expInfo['frameRate'])
else:
    frameDur = 1.0/60.0 # couldn't get a reliable measure so guess

# Initialize components for Routine "trial"
```

```
clock=core.Clock()
trialClock = core.Clock()
ISI = core.StaticPeriod(win=win, screenHz=expInfo['frameRate'],
        name='ISI')
# Initialize components for Routine "trial2"
trial2Clock = core.Clock()
ISI_3 = core.StaticPeriod(win=win, screenHz=expInfo['frameRate'],
        name='ISI_3')

# Create some handy timers
globalClock = core.Clock()  # to track the time since experiment
        started
routineTimer = core.CountdownTimer()  # to track time remaining of
        each (non-slip) routine
# set up handler to look after randomisation of conditions etc
trials_1 = data.TrialHandler(nReps=20, method='random',
    extraInfo=expInfo, originPath=-1,
    trialList=data.importConditions('conditions1.xlsx'),
    seed=None, name='trials_1')
thisExp.addLoop(trials_1)  # add the loop to the experiment
thisTrial_1 = trials_1.trialList[0]  # so we can initialise stimuli with
        some values
# abbreviate parameter names if possible (e.g. rgb=thisTrial_1.rgb)
if thisTrial_1 != None:
    for paramName in thisTrial_1.keys():
        exec(paramName + '= thisTrial_1.' + paramName)
```

```
for thisTrial_1 in trials_1:
    currentLoop = trials_1
    # abbreviate parameter names if possible (e.g. rgb =
        thisTrial_1.rgb)
    if thisTrial_1 != None:
        for paramName in thisTrial_1.keys():
            exec(paramName + '= thisTrial_1.' + paramName)

    #------Prepare to start Routine "trial"-------
    t = 0
    trialClock.reset()  # clock
    frameN = -1
    # update component parameters for each repeat
    movie1 = visual.MovieStim2(win=win, name='movie1',
        noAudio = True,
        filename=paramet_1,
        ori=0, pos=[0, 0], opacity=1,
        size=[1366,768],
        depth=-1.0,
        )
    # keep track of which components have finished
    trialComponents = []
    trialComponents.append(ISI)
    trialComponents.append(movie1)

    for thisComponent in trialComponents:
```

```
    if hasattr(thisComponent, 'status'):
        thisComponent.status = NOT_STARTED

#-------Start Routine "trial"-------

continueRoutine = True
while continueRoutine:
    # get current time
    t = trialClock.getTime()
    frameN = frameN + 1  # number of completed frames (so 0 is
     the first frame)
    # update/draw components on each frame

    # *movie1* updates
    if t >= 4 and movie1.status == NOT_STARTED:
        # keep track of start time/frame for later
        movie1.tStart = t  # underestimates by a little under one
     frame
        movie1.frameNStart = frameN  # exact frame index
        movie1.setAutoDraw(True)
        dev.Out32(0x378,1)
        ##########SEND TRIGGER TO OPENBCI VIA "DO" PIN
        win.flip()
        dev.Out32(0x378,0)
```

```
    if paramet_1=='C:\\Users\\Adams1\\Desktop\\PSYCHOPY
  DATA\\Rehabilitation_3\\Experiment1_1_1
  pinch\\ss_modified_2.mp4':
        for frameN in range(105):###corrected
            if 1<=frameN<2:
                dev.Out32(0x378,2)
            if 103<=frameN<104:
                dev.Out32(0x378,0)
            win.flip()

    if paramet_1=='C:\\Users\\Adams1\\Desktop\\PSYCHOPY
  DATA\\Rehabilitation_3\\Experiment1_1_1
  pinch\\ms_modified_2.mp4':

        for frameN in range(97):###corrected

            if 1<=frameN<2:###corrected
                #print clock.getTime()
             dev.Out32(0x378,4)
            if 95<=frameN<96:
             dev.Out32(0x378,0)
            win.flip()

if movie1.status == FINISHED:  # force-end the routine
    win.flip()
    continueRoutine = False
```

```
    #print "clock2",clock.getTime()


# *ISI* period
if t >= 0.0 and ISI.status == NOT_STARTED:
    # keep track of start time/frame for later
    ISI.tStart = t  # underestimates by a little under one frame
    ISI.frameNStart = frameN  # exact frame index
    ISI.start(4)
elif ISI.status == STARTED: #one frame should pass before
 updating params and completing
    ISI.complete() #finish the static period


# check if all components have finished
if not continueRoutine:  # a component has requested a forced-
 end of Routine
    break
continueRoutine = False  # will revert to True if at least one
 component still running
for thisComponent in trialComponents:
    if hasattr(thisComponent, "status") and thisComponent.status
 != FINISHED:
        continueRoutine = True
        break  # at least one component has not yet finished


# check for quit (the Esc key)
```

```
        if endExpNow or event.getKeys(keyList=["escape"]):
            core.quit()

        # refresh the screen
        if continueRoutine:  # don't flip if this routine is over or we'll get
         a blank screen
            win.flip()

    #-------Ending Routine "trial"-------
    for thisComponent in trialComponents:
        if hasattr(thisComponent, "setAutoDraw"):
            thisComponent.setAutoDraw(False)
    # the Routine "trial" was not non-slip safe, so reset the non-slip
        timer
    routineTimer.reset()
    thisExp.nextEntry()

# completed 12 repeats of 'trials_1'
#------Prepare to start Routine "tools"-------
t = 0
toolsClock.reset()  # clock
frameN = -1
routineTimer.reset()
# update component parameters for each repeat
# keep track of which components have finished
toolsComponents = []
```

```
toolsComponents.append(image)
toolsComponents.append(ISI_2)
for thisComponent in toolsComponents:
    if hasattr(thisComponent, 'status'):
        thisComponent.status = NOT_STARTED


#-------Start Routine "tools"-------
continueRoutine = True
while continueRoutine and routineTimer.getTime() > 0:
    # get current time
    t = toolsClock.getTime()
    frameN = frameN + 1  # number of completed frames (so 0 is the
         first frame)
    # update/draw components on each frame


    # *image* updates
    if t >= 4 and image.status == NOT_STARTED:
        # keep track of start time/frame for later
        image.tStart = t  # underestimates by a little under one frame
        image.frameNStart = frameN  # exact frame index
        image.setAutoDraw(True)
    if image.status == STARTED and t >= (4 + (8-
         win.monitorFramePeriod*0.75)): #most of one frame period left
        image.setAutoDraw(False)
        #win.flip()
    # *ISI_2* period
```

```
if t >= 0.0 and ISI_2.status == NOT_STARTED:
    # keep track of start time/frame for later
    ISI_2.tStart = t  # underestimates by a little under one frame
    ISI_2.frameNStart = frameN  # exact frame index
    ISI_2.start(4)
elif ISI_2.status == STARTED: #one frame should pass before
     updating params and completing
    ISI_2.complete() #finish the static period


# check if all components have finished
if not continueRoutine:  # a component has requested a forced-end
     of Routine
    break
continueRoutine = False  # will revert to True if at least one
     component still running
for thisComponent in toolsComponents:
    if hasattr(thisComponent, "status") and thisComponent.status !=
     FINISHED:
        continueRoutine = True
        break  # at least one component has not yet finished


# check for quit (the Esc key)
if endExpNow or event.getKeys(keyList=["escape"]):
    core.quit()


# refresh the screen
```

```
    if continueRoutine:  # don't flip if this routine is over or we'll get a
        blank screen
        win.flip()

#-------Ending Routine "tools"-------
for thisComponent in toolsComponents:
    if hasattr(thisComponent, "setAutoDraw"):
        thisComponent.setAutoDraw(False)

# set up handler to look after randomisation of conditions etc
trials_2 = data.TrialHandler(nReps=12, method='random',
    extraInfo=expInfo, originPath=-1,
    trialList=data.importConditions('conditions2.xlsx'),
    seed=None, name='trials_2')
thisExp.addLoop(trials_2)  # add the loop to the experiment
thisTrial_2 = trials_2.trialList[0]  # so we can initialise stimuli with
        some values
# abbreviate parameter names if possible (e.g. rgb=thisTrial_2.rgb)
if thisTrial_2 != None:
    for paramName in thisTrial_2.keys():
        exec(paramName + '= thisTrial_2.' + paramName)

for thisTrial_2 in trials_2:
    currentLoop = trials_2
    # abbreviate parameter names if possible (e.g. rgb =
        thisTrial_2.rgb)
```

```
    if thisTrial_2 != None:
        for paramName in thisTrial_2.keys():
            exec(paramName + '= thisTrial_2.' + paramName)

print "final time", clock.getTime
# completed 12 repeats of 'trials_2'

# these shouldn't be strictly necessary (should auto-save)
thisExp.saveAsWideText(filename+'.csv')
thisExp.saveAsPickle(filename)
logging.flush()
# make sure everything is closed down
thisExp.abort() # or data files will save again on exit
win.close()

core.quit()
```

Condition: Random Robot Accompany:

```
##########

##########THIS CODE IS GENERATED FOR THE RANDOM ROBOT
    ACCOMPANY-ACTION OBSERVATION EXPERIMENT

#########

#!/usr/bin/env python2

# -*- coding: utf-8 -*-

"""

This experiment was created using PsychoPy2 Experiment Builder
    (v1.83.04), 2016_11_28_1643

"""

from __future__ import division  # so that 1/3=0.333 instead of 1/3=0

import time

from psychopy import locale_setup, visual, core, data, event, logging,
    sound, gui,parallel

from psychopy.constants import *  # things like STARTED, FINISHED

import numpy as np  # whole numpy lib is available, prepend 'np.'

from numpy import sin, cos, tan, log, log10, pi, average, sqrt, std,
    deg2rad, rad2deg, linspace, asarray

from numpy.random import random, randint, normal, shuffle

import os  # handy system and path functions

import sys # to get file system encoding

from ctypes import windll #for parallel port connection

# Ensure that relative paths start from the same directory as this script

_thisDir                                                          =
    os.path.dirname(os.path.abspath(__file__)).decode(sys.getfilesys
    temencoding())

os.chdir(_thisDir)

# Store info about the experiment session
```

```
expName = 'Experiment1'  # from the Builder filename that created this
    script
expInfo = {'participant':'', 'session':'001'}
dlg = gui.DlgFromDict(dictionary=expInfo, title=expName)
if dlg.OK == False: core.quit()  # user pressed cancel
expInfo['date'] = data.getDateStr()  # add a simple timestamp
expInfo['expName'] = expName


# Data file name stem = absolute path + name; later add .psyexp, .csv,
    .log, etc
filename = _thisDir + os.sep + u'data/%s_%s_%s'
    %(expInfo['participant'], expName, expInfo['date'])


# An ExperimentHandler isn't essential but helps with data saving
thisExp = data.ExperimentHandler(name=expName, version='',
    extraInfo=expInfo, runtimeInfo=None,
    originPath=None,
    savePickle=True, saveWideText=True,
    dataFileName=filename)
#save a log file for detail verbose info
logFile = logging.LogFile(filename+'.log', level=logging.EXP)
logging.console.setLevel(logging.WARNING)  # this outputs to the
    screen, not a file


endExpNow = False  # flag for 'escape' or other condition => quit the
    exp
################################################################
    ##############################START CODE
```

```
dev=windll.Inpout32 #initiate the parallel port
value=dev.Out32(0x378,0) # set all data pins to zero


# Setup the Window
win = visual.Window(size=(1366, 768), fullscr=True, screen=0,
    allowGUI=False, allowStencil=False,
   monitor='testMonitor', color=[-1,-1,-1], colorSpace='rgb',
   blendMode='avg', useFBO=True,
   )
# store frame rate of monitor if we can measure it successfully
expInfo['frameRate']=win.getActualFrameRate()
if expInfo['frameRate']!=None:
   frameDur = 1.0/round(expInfo['frameRate'])
else:
   frameDur = 1.0/60.0 # couldn't get a reliable measure so guess


# Initialize components for Routine "trial"
clock=core.Clock()
trialClock = core.Clock()
ISI = core.StaticPeriod(win=win, screenHz=expInfo['frameRate'],
    name='ISI')
# Initialize components for Routine "trial2"
trial2Clock = core.Clock()
ISI_3 = core.StaticPeriod(win=win, screenHz=expInfo['frameRate'],
    name='ISI_3')


# Create some handy timers
```

```
globalClock = core.Clock()  # to track the time since experiment started
routineTimer = core.CountdownTimer()  # to track time remaining of
    each (non-slip) routine


# set up handler to look after randomisation of conditions etc
trials_1 = data.TrialHandler(nReps=20, method='random',
    extraInfo=expInfo, originPath=-1,
    trialList=data.importConditions('conditions1.xlsx'),
    seed=None, name='trials_1')
thisExp.addLoop(trials_1)  # add the loop to the experiment
thisTrial_1 = trials_1.trialList[0]  # so we can initialise stimuli with some
    values
# abbreviate parameter names if possible (e.g. rgb=thisTrial_1.rgb)
if thisTrial_1 != None:
    for paramName in thisTrial_1.keys():
        exec(paramName + '= thisTrial_1.' + paramName)


for thisTrial_1 in trials_1:
    currentLoop = trials_1
    # abbreviate parameter names if possible (e.g. rgb = thisTrial_1.rgb)
    if thisTrial_1 != None:
        for paramName in thisTrial_1.keys():
            exec(paramName + '= thisTrial_1.' + paramName)


    #------Prepare to start Routine "trial"-------
    t = 0
    trialClock.reset()  # clock
```

```
frameN = -1
# update component parameters for each repeat
movie1 = visual.MovieStim2(win=win, name='movie1',
    noAudio = True,
    filename=paramet_1,
    ori=0, pos=[0, 0], opacity=1,
    size=[1366,768],
    depth=-1.0, flipHoriz=False########mirror image of video
    )
# keep track of which components have finished
trialComponents = []
trialComponents.append(ISI)
trialComponents.append(movie1)

for thisComponent in trialComponents:
    if hasattr(thisComponent, 'status'):
        thisComponent.status = NOT_STARTED

#-------Start Routine "trial"-------
mynumber=np.random.randint(2,4)
continueRoutine = True
while continueRoutine:
    # get current time
    t = trialClock.getTime()
    frameN = frameN + 1  # number of completed frames (so 0 is the
    first frame)
    # update/draw components on each frame
```

```
# *movie1* updates
if t >= 4 and movie1.status == NOT_STARTED:
    # keep track of start time/frame for later
    movie1.tStart = t  # underestimates by a little under one frame

    movie1.frameNStart = frameN  # exact frame index
    movie1.setAutoDraw(True)
    dev.Out32(0x378,1)##########SEND TRIGGER TO OPENBCI VIA "DO" PIN
    win.flip()
    dev.Out32(0x378,0)
    if paramet_1=='C:\\Users\\Adams1\\Desktop\\PSYCHOPY DATA\\Rehabilitation_3\\Experiment1_3\\ss_modified_2.mp4':
        for frameN in range(105):
            if 1<=frameN<2:
                if mynumber==2:
                    print 'robot'
                    dev.Out32(0x378,2)
            if 103<=frameN<104:
                dev.Out32(0x378,0)
                if mynumber==3:
                    print 'no robot'
            win.flip()

    if paramet_1=='C:\\Users\\Adams1\\Desktop\\PSYCHOPY DATA\\Rehabilitation_3\\Experiment1_3\\ms_modified_2.mp4':
```

```
        for frameN in range(97):
            if 1<=frameN<2:

                if mynumber==2:
                    print 'robot'

                    dev.Out32(0x378,4)
            if 95<=frameN<96:
                dev.Out32(0x378,0)
                if mynumber==3:
                    print 'no robot'
            win.flip()

    #print "clock2",clock.getTime()

if movie1.status == FINISHED:  # force-end the routine
    win.flip()

    continueRoutine = False

    #print "clock2",clock.getTime()
# *ISI* period
if t >= 0.0 and ISI.status == NOT_STARTED:
    # keep track of start time/frame for later
    ISI.tStart = t  # underestimates by a little under one frame
```

```
        ISI.frameNStart = frameN  # exact frame index
        ISI.start(4)
    elif ISI.status == STARTED: #one frame should pass before updating params and completing
        ISI.complete() #finish the static period


    # check if all components have finished
    if not continueRoutine:  # a component has requested a forced-end of Routine
        break
    continueRoutine = False  # will revert to True if at least one component still running
    for thisComponent in trialComponents:
        if hasattr(thisComponent, "status") and thisComponent.status != FINISHED:
            continueRoutine = True
            break  # at least one component has not yet finished


    # check for quit (the Esc key)
    if endExpNow or event.getKeys(keyList=["escape"]):
        core.quit()


    # refresh the screen
    if continueRoutine:  # don't flip if this routine is over or we'll get a blank screen
        win.flip()


#-------Ending Routine "trial"-------
```

```
    for thisComponent in trialComponents:
        if hasattr(thisComponent, "setAutoDraw"):
            thisComponent.setAutoDraw(False)
    # the Routine "trial" was not non-slip safe, so reset the non-slip timer
    routineTimer.reset()
    thisExp.nextEntry()

# completed 12 repeats of 'trials_1'
#------Prepare to start Routine "tools"-------
t = 0
toolsClock.reset()  # clock
frameN = -1
routineTimer.reset()
# update component parameters for each repeat
# keep track of which components have finished
toolsComponents = []
toolsComponents.append(image)
toolsComponents.append(ISI_2)
for thisComponent in toolsComponents:
    if hasattr(thisComponent, 'status'):
        thisComponent.status = NOT_STARTED

#-------Start Routine "tools"-------
continueRoutine = True
while continueRoutine and routineTimer.getTime() > 0:
    # get current time
```

```
t = toolsClock.getTime()
frameN = frameN + 1  # number of completed frames (so 0 is the first frame)
# update/draw components on each frame


# *image* updates
if t >= 4 and image.status == NOT_STARTED:
    # keep track of start time/frame for later
    image.tStart = t  # underestimates by a little under one frame
    image.frameNStart = frameN  # exact frame index
    image.setAutoDraw(True)
if image.status == STARTED and t >= (4 + (8-win.monitorFramePeriod*0.75)): #most of one frame period left
    image.setAutoDraw(False)
    #win.flip()
# *ISI_2* period
if t >= 0.0 and ISI_2.status == NOT_STARTED:
    # keep track of start time/frame for later
    ISI_2.tStart = t  # underestimates by a little under one frame
    ISI_2.frameNStart = frameN  # exact frame index
    ISI_2.start(4)
elif ISI_2.status == STARTED: #one frame should pass before updating params and completing
    ISI_2.complete() #finish the static period


# check if all components have finished
if not continueRoutine:  # a component has requested a forced-end of Routine
```

```
        break
    continueRoutine = False  # will revert to True if at least one
        component still running
    for thisComponent in toolsComponents:
        if hasattr(thisComponent, "status") and thisComponent.status !=
        FINISHED:
            continueRoutine = True
            break  # at least one component has not yet finished


    # check for quit (the Esc key)
    if endExpNow or event.getKeys(keyList=["escape"]):
        core.quit()


    # refresh the screen
    if continueRoutine:  # don't flip if this routine is over or we'll get a
        blank screen
        win.flip()


#-------Ending Routine "tools"-------
for thisComponent in toolsComponents:
    if hasattr(thisComponent, "setAutoDraw"):
        thisComponent.setAutoDraw(False)


# set up handler to look after randomisation of conditions etc
trials_2 = data.TrialHandler(nReps=12, method='random',
    extraInfo=expInfo, originPath=-1,
    trialList=data.importConditions('conditions2.xlsx'),
```

```
    seed=None, name='trials_2')
thisExp.addLoop(trials_2)  # add the loop to the experiment
thisTrial_2 = trials_2.trialList[0]  # so we can initialise stimuli with some
        values
# abbreviate parameter names if possible (e.g. rgb=thisTrial_2.rgb)
if thisTrial_2 != None:
    for paramName in thisTrial_2.keys():
        exec(paramName + '= thisTrial_2.' + paramName)
for thisTrial_2 in trials_2:
    currentLoop = trials_2
    # abbreviate parameter names if possible (e.g. rgb = thisTrial_2.rgb)
    if thisTrial_2 != None:
        for paramName in thisTrial_2.keys():
            exec(paramName + '= thisTrial_2.' + paramName)


# completed 12 repeats of 'trials_2'
# these shouldn't be strictly necessary (should auto-save)
thisExp.saveAsWideText(filename+'.csv')
thisExp.saveAsPickle(filename)
logging.flush()
# make sure everything is closed down
thisExp.abort() # or data files will save again on exit
win.close()
core.quit()
```

APPENDIX 6

PsychoPy2 Code used in the Experiment 4.3; Frame Decomposition of a Video File:

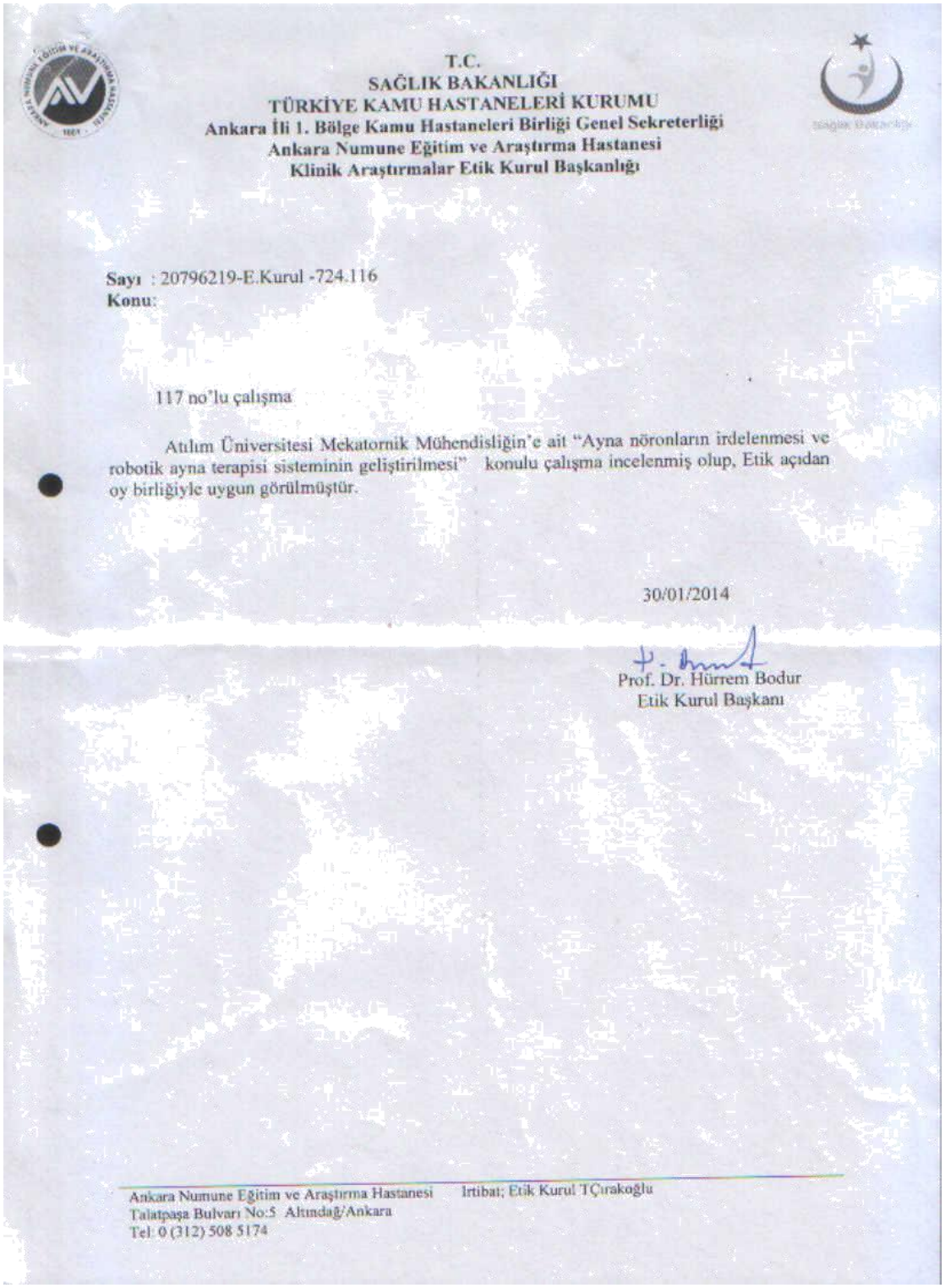
```
##THIS CODE CREATES EACH FRAME AS AN IMAGE FILE
from psychopy import visual, core
from ctypes import windll #for parallel port connection
dev=windll.Inpout32 #initiate the parallel port
value=dev.Out32(0x378,0)
win=visual.Window([500,500])
movie = visual.MovieStim2(win=win, name='movie',units='pix',
    noAudio = False,
########Location of the
Video File to be decomposed should be defined here######

    filename=u'C:\\Users\\Adams1\\Desktop\\PSYCHOPY
        DATA\\Rehabilitation_3\\ms_modified_2.mp4', # video file
    ori=0, pos=[0, 0], opacity=1,
    size=[1366,768],
    depth=0.0,
    )
clock = core.Clock()
print "MOVIE DURATION IS:", (movie.duration)
#let's draw a stimulus for n frames.
for frameN in range(135): ###check for this frame rate
    movie.draw()
    win.getMovieFrame(buffer='back')
```

```
    win.flip()
win.saveMovieFrames('frame.png')#### image file in png format
win.close()
```

APPENDIX 7

Ethical Approval (in Turkish):



T.C.
SAĞLIK BAKANLIĞI
TÜRKİYE KAMU HASTANELERİ KURUMU
Ankara İli 1. Bölge Kamu Hastaneleri Birliği Genel Sekreterliği
Ankara Numune Eğitim ve Araştırma Hastanesi
Klinik Araştırmalar Etik Kurul Başkanlığı

Sayı : 20796219-E.Kurul -724.116
Konu:

117 no'lu çalışma

Atılım Üniversitesi Mekatornik Mühendisliğin'e ait "Ayna nöronların irdelenmesi ve robotik ayna terapisi sisteminin geliştirilmesi" konulu çalışma incelenmiş olup, Etik açıdan oy birliğiyle uygun görülmüştür.

30/01/2014

Prof. Dr. Hürrem Bodur
Etik Kurul Başkanı

Ankara Numune Eğitim ve Araştırma Hastanesi İrtibat; Etik Kurul TÇırakoğlu
Talatpaşa Bulvarı No:5 Altındağ/Ankara
Tel: 0 (312) 508 5174

KLİNİK ARAŞTIRMALAR ETİK KURULU KARAR FORMU

ETİK KURUL BİLGİLERİ		
	ETİK KURULUN ADI	Ankara Numune Eğitim ve Araştırma Hastanesi Klinik Araştırmalar Etik Kurulu
	AÇIK ADRESİ:	Etik Kurul Sekreterliği Eğitim Merkezi Danışma Birimi B Blok -1.Kat Altındağ Ankara
	TELEFON	0 312 5085174
	FAKS	0 312 5084938
	E-POSTA	cirakogluten@hotmail.com

BAŞVURU BİLGİLERİ					
	ARAŞTIRMANIN AÇIK ADI	Ayna nöronların irdelenmesi ve robotik ayna terapisi sisteminin geliştirilmesi			
	ARAŞTIRMA PROTOKOL KODU	-			
	KOORDİNATÖR/SORUMLU ARAŞTIRMACI UNVANI/ADI/SOYADI	Yard. Doç. Dr. Kutluk Bilge Arıkan			
	KOORDİNATÖR/SORUMLU ARAŞTIRMACININ UZMANLIK ALANI	Mühendislik			
	KOORDİNATÖR/SORUMLU ARAŞTIRMACININ BULUNDUĞU MERKEZ	Ankara			
	DESTEKLEYİCİ	-			
	DESTEKLEYİCİNİN YASAL TEMSİLCİSİ	-			
	ARAŞTIRMANIN FAZI VE TÜRÜ	FAZ 1	☐		
		FAZ 2	☐		
		FAZ 3	☐		
		FAZ 4	☐		
		Gözlemsel ilaç çalışması	☐		
		İlaç dışı klinik araştırma	☒		
		Diğer ise belirtiniz :			
	ARAŞTIRMAYA KATILAN MERKEZLER	TEK MERKEZ ☒	ÇOK MERKEZLİ ☐	ULUSAL ☐	ULUSLARARAS I ☐

1

KLİNİK ARAŞTIRMALAR ETİK KURULU KARAR FORMU

DEĞERLENDİRİLEN BELGELER	Belge Adı	Tarihi	Versiyon Numarası	Dili		
	ARAŞTIRMA PROTOKOLÜ			Türkçe ☒	İngilizce ☐	Diğer ☐
	BİLGİLENDİRİLMİŞ GÖNÜLLÜ OLUR FORMU			Türkçe ☒	İngilizce ☐	Diğer ☐
	OLGU RAPOR FORMU			Türkçe ☒	İngilizce ☐	Diğer ☐
	ARAŞTIRMA BROŞÜRÜ			Türkçe ☐	İngilizce ☐	Diğer ☐

DEĞERLENDİRİLEN DİĞER BELGELER	Belge Adı		Açıklama
	SİGORTA	☐	
	ARAŞTIRMA BÜTÇESİ	☒	
	BİYOLOJİK MATERYEL TRANSFER FORMU	☐	
	İLAN	☐	
	YILLIK BİLDİRİM	☐	
	SONUÇ RAPORU	☐	
	GÜVENLİLİK BİLDİRİMLERİ	☐	
	DİĞER:	☐	

KARAR BİLGİLERİ		
	Karar No: 117/2014	**Tarih: 29.01.2014**
	Yukarıda bilgileri verilen Atılım Üniversitesi Mekatronik Mühendisliği Bölümü'nden Yard. Doç. Dr. Kutluk Bilge Arıkan sorumluluğunda yapılması planlanan "Ayna nöronların irdelenmesi ve robotik ayna terapisi sisteminin geliştirilmesi" isimli klinik araştırma başvuru dosyası ile ilgili belgeler araştırmanın/çalışmanın gerekçe, amaç, yaklaşım ve yöntemleri dikkate alınarak incelenmiş ve uygun bulunmuş olup araştırmanın/çalışmanın başvuru dosyasında belirtilen merkezlerde gerçekleştirilmesinde etik ve bilimsel sakınca bulunmadığına toplantıya katılan etik kurul üye tam sayısının salt çoğunluğu ile karar verilmiştir.	

KLİNİK ARAŞTIRMALAR ETİK KURULU	
ETİK KURULUN ÇALIŞMA ESASI	Klinik Araştırmalar Hakkında Yönetmelik, İyi Klinik Uygulamaları Kılavuzu
BAŞKANIN UNVANI / ADI / SOYADI:	**Prof. Dr. Hürrem BODUR**

Unvanı/Adı/Soyadı	Uzmanlık Alanı	Kurumu	Cinsiyet		Araştırma ile ilişki		Katılım *		İmza
Prof. Dr. Hürrem BODUR	Enf. Hast.ve Kl.Mikrobiyoloji	Ankara Numune EAH	E ☒	K ☐	E ☐	H ☒	E ☒	H ☐	
Prof. Dr. Süreyya BARUN	Farmakoloji	Gazi Üniversitesi Tıp Fakültesi	E ☐	K ☒	E ☐	H ☒	E ☒	H ☐	
Prof. Dr. Adil ERYILMAZ	Kulak Burun Boğaz	Ankara Numune EAH	E ☒	K ☐	E ☐	H ☒	E ☒	H ☐	
Prof. Dr. Ahmet Deniz BELEN	Beyin Cerrahi	Ankara Numune EAH	E ☒	K ☐	E ☐	H ☒	E ☒	H ☐	
Doç. Dr. Sezer KULAÇOĞLU	Patoloji	Ankara Numune EAH	E ☐	K ☒	E ☐	H ☒	E ☒	H ☐	
Doç. Dr. Adem ÖZKARA	Aile Hekimliği	Ankara Numune EAH	E ☒	K ☐	E ☐	H ☒	E ☒	H ☐	
Doç. Dr. Altuğ TUNCEL	Üroloji	Ankara Numune EAH	E ☒	K ☐	E ☐	H ☒	E ☒	H ☐	
Doç. Dr. Betül BOZKURT	Genel Cerrahi	Ankara Numune EAH	E ☐	K ☒	E ☐	H ☒	E ☒	H ☐	
Doç. Dr. Doğan UNCU	Tıbbi Onkoloji	Ankara Numune EAH	E ☒	K ☐	E ☐	H ☒	E ☒	H ☐	
Doç. Dr. İsmail KARABULUT	Fizyoloji	Hacettepe Üniversitesi Tıp Fakültesi	E ☒	K ☐	E ☐	H ☒	E ☐	H ☒	
Uzm. Dr. Dilek KANYILMAZ	Halk Sağlığı	Ankara Numune EAH	E ☐	K ☒	E ☐	H ☒	E ☒	H ☐	
Dr. Ecz. Dilek ATABEY	Eczacılık	Ankara Numune EAH	E ☐	K ☒	E ☐	H ☒	E ☒	H ☐	
Avukat Buket ÖZBEK	Hukuk	Ankara Barosu	E ☐	K ☒	E ☐	H ☒	E ☐	H ☐	
Müftü Yard. M. Münip ŞALLIOĞLU	İlahiyat	Ankara İl Müftülüğü	E ☒	K ☐	E ☐	H ☒	E ☒	H ☐	

*:Toplantıda Bulunma

APPENDIX 8

Table: Examples of Hand Rehabilitation Robots:

Robotic System	Reference(s)	Link (August 2017)
Amadeo	Sale, Patrizio, Valentina Lombardi, and Marco Franceschini. "Hand robotics rehabilitation: feasibility and preliminary results of a robotic treatment in patients with hemiparesis." Stroke research and treatment 2012 (2012).	http://tyromotion.com/en/products/amadeo/overview
ExoHand		http://www.festo.com/cms/en_corp/12713.htm
CyberGrasp	Adamovich, Sergei V., et al. "Design of a complex virtual reality simulation to train finger motion for persons with hemiparesis: a proof of concept study." Journal of neuroengineering and rehabilitation 6.1 (2009): 28.	http://www.cybergloves ystems.com/products/cybergrasp/overview
GLOREHA PROFESSIONAL	Polygerinos, Panagiotis, et al. "Towards a soft pneumatic glove for hand rehabilitation." Intelligent Robots and Systems (IROS), 2013 IEEE/RSJ International Conference on. IEEE, 2013.	http://www.gloreha.com/professional/
Hand of Hope	Hu, X. L., et al. "The effects of post-stroke upper-limb training with an electromyography (EMG)-driven hand robot." Journal of Electromyography and Kinesiology 23.5 (2013): 1065-1074.	http://www.rehab-robotics.com/

HAND CARE	IEEE Trans Neural Syst Rehabil Eng. 2008 Dec;16(6):582-91. doi:10.1109/TNSRE.2008.2010347. http://www.ncbi.nlm.nih.gov/pubmed/19144590	
HEXORR	-Am J Phys Med Rehabil. 2013 Nov; 92(11):947-58. doi:10.1097/PHM.0b013e31829e7a07. -Conf Proc IEEE Eng Med Biol Soc. 2010;2010:4485-8. doi:10.1109/IEMBS.2010.5626037. -J.NeuroEngineering and Rehabilitation 2010, 7:36 doi:10.1186/1743-0003-7-36	
InMotion HAND	In Proc. IEEE 10th International Conference on Rehabilitation Robotics (ICORR).Noordwijk, Netherlands; 2007:1085-1089.	http://interactive-motion.com/healthcarereform/upper-extremity-rehabilitiation/inmotion-hand/
Reha-Digit	J Neuroeng Rehabilitation 2008, 5:21. http://dx.doi.org/10.1186/1743-0003-5-21	http://www.reha-stim.de/cms/index.php?id=109
Rutgers Master II	Mechatronics, IEEE/ASME Transactions on 2002 (Volume:7, Issue: 2) doi: 10.1109/TMECH.2002.1011262	https://www.nsf.gov/od/lpa/news/press/00/stim2.htm
FINGER	J.Neuro Eng and Rehabilitation 2014,11:10 doi:10.1186/1743-0003-11-10	https://www.asme.org/engineering-topics/articles/robotics/designing-a-soft-robot

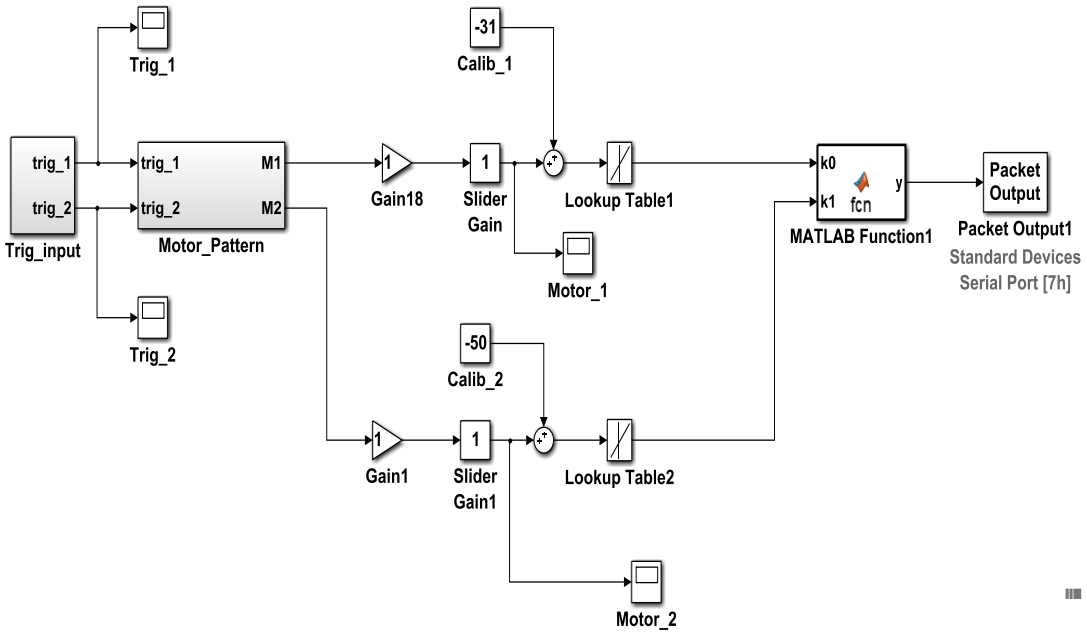
FingerBot	Ann Biomed Eng. 2010 Feb;38(2):259-68. doi: 10.1007/s10439-009-9845-4. Epub 2009 Nov 25.	http://smpp.northwestern.edu/Kamper/projects/researchFingerbot.shtml
ReHapticKnob	Metzger, Jean-Claude, et al. "Design and characterization of the ReHapticKnob, a robot for assessment and therapy of hand function." *Intelligent Robots and Systems (IROS), 2011 IEEE/RSJ International Conference on*. IEEE, 2011.	http://www.relab.ethz.ch/research/current-research-projects/robot-assisted-rehabilitation-and-assessment-of-hand-function.html
HWARD	Rehabilitation Robotics, 2005. ICORR 2005. 9th International Conference on http://dx.doi.org/10.1109/ICORR.2005.1501041	http://www.strokerobot.com/default.aspx
Exo-Glove	Hyunki In, Brian Byunghyun Kang, "Exo-Glove: Soft wearable robot for the hand using soft tendon routing system," IEEE Robotics Automation Magazine, vol. 22, no. 1, pp. 97–105, Mar. 2015.	http://biorobotics.snu.ac.kr/rehabilitation-robot/exo-glove/?ckattempt=1
YouGrabber	Eng, K, Siekierka, E, Pyk, P, Interactive Visuo-Motor Therapy System for Stroke Rehabilitation. Med Bio Eng Comput 2012; 45:901-907.	http://yourehab.com/our-products/yougrabber/
MusicGlove	J Neuroeng Rehabil. 2014; 11: 76. Published online 2014 Apr 30. doi: 10.1186/1743-0003-11-76	https://www.flintrehab.com/product/musicglove-hand-therapy/

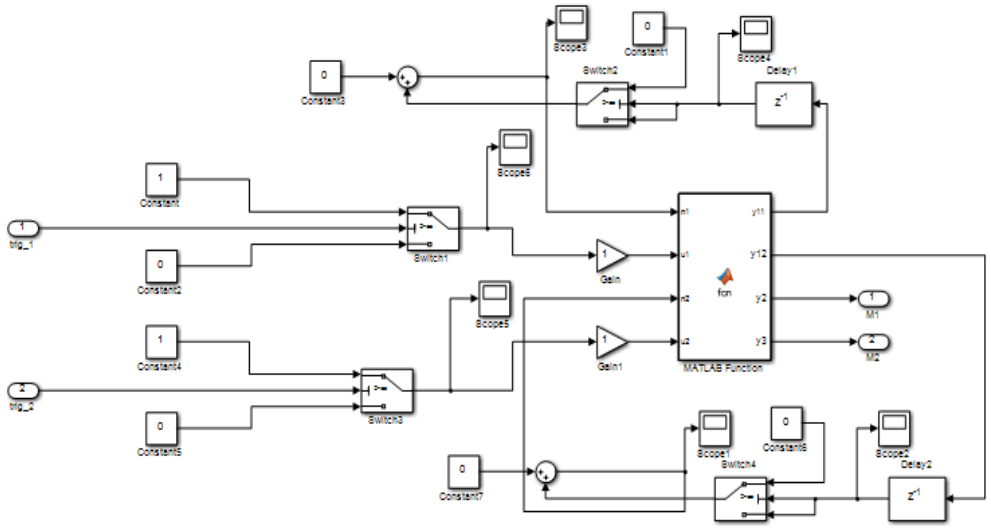
HandSOME	Neural Systems and Rehabilitation Engineering, IEEE Transactions on DOI: 10.1109/TNSRE.2011.2157705 (Volume:19 , Issue: 4)	http://www.elizabethbrokaw.com/portfolio/HandSOME.html
Hexosys I	Conf Proc IEEE Eng Med Biol Soc. 2010;2010:3694-7. doi: 10.1109/IEMBS.2010.5627448.	
WaveFlex		http://www.remingtonmedical.com/product/detail/A1
Maestra Portable	Biomedical Research 2015; 26 (1): 197-201	http://kinetec.fr/en/kinetec-selection/cpm-continuous-passive-motion/attelle-kinetec-maestra-portable-detail.html
HandExos	Intelligent Robots and Systems, 2009. IROS 2009. IEEE/RSJ International Conference on	http://www.percro.org/node/161
AFX	Biomedical Robotics and Biomechatronics (BioRob), 2010 3rd IEEE RAS and EMBS International Conference on	
Hand Mentor	L. Yanlin, J. Murayama, K. Akahane, S. Hasegawa, and M. Sato, "Development of new force feedback interface for two-handed 6dof manipulation-SPIDAR-G and G system," in Int. Conf. Artif. Reality Telexis	http://motusnova.com/products/hand-mentor-pro/ l
Dexmo		http://www.dextarobotics.com/products/Dexmo

REHAB	Robotics and Automation (ICRA), 2013 IEEE International Conference on DOI:10.1109/ICRA.2013.6631126	http://ral.web.nitech.ac.jp/research.html
HandTutor	Physiother Res Int. 2011 Dec;16(4):191-200. doi: 10.1002/pri.485. Epub 2010 Aug 25.	http://meditouch.co.il/products/handtutor/
DLR	C. Castellini, E. Fiorilla and G. Sandini, Multi-subject / Daily-Life Activity EMG-based control of mechanical hands, Journal of Neuroengineering and Rehabilitation 6:41, 2009.	http://www.dlr.de/rm/en/desktopdefault.aspx/tabid-3817/6237_read-9003

APPENDIX 9

Matlab /Simulink Model of Experiment 4.3:





APPENDIX 10

Imported Channel Locations* in 10-20 System for 16 Channel OpenBCI

Channel	theta	radius	X	Y	Z	sph_theta	sph_ph	sph_radius
FP1	-18	0,511	0,95	0,309	-0,0349	18	-2	1
FP2	18	0,511	0,95	-0,309	-0,0349	-18	-2	1
C3	-90	0,256	4,40E-17	0,719	0,695	90	44	1
C4	90	0,256	4,40E-17	-0,719	0,695	-90	44	1
T5	-126	0,341	-0,516	0,71	0,48	126	28,7	1
T6	126	0,341	-0,516	-0,71	0,48	-126	28	1
O1	-162	0,511	-0,95	0,309	-0,0349	162	-2	1
O2	162	0,511	-0,95	-0,309	-0,0349	-162	-2	1
F7	-54	0,511	0,587	0,809	-0,0349	54	-2	1
F8	54	0,511	0,587	-0,809	-0,0349	-54	-2	1
F3	-39	0,333	0,673	0,545	0,5	39	30	1
F4	39	0,333	0,673	-0,545	0,5	-39	30	1
T3	-90	0,341	5,37E-17	0,877	0,48	90	28,7	1
T4	90	0,341	5,37E-17	-0,877	0,48	-90	28,7	1
P3	-141	0,333	-0,673	0,545	0,5	141	30	1
P4	-141	0,333	-0,673	-0,545	0,5	141	30	1

* ftp://sccn.ucsd.edu/pub/locfiles/eeglab contains additional information.

CURRICULUM VITAE

Credentials

Name, Surname : Gözde BAYER
Place of Birth : Ankara
Marital Status : Single
E-mail : gbayer@hacettepe.edu.tr,
gbayer@alumni.bilkent.edu.tr
Address : Bağlıca Mah.1214.sok.No:3, Etimesut/ANKARA

Education

BSc. : Ankara University, Faculty of Science, Department of Space Sciences, 1995

MSc. : (1) Ankara University Graduate School of Natural and Applied Sciences, Department of Space Sciences, 1997;

(2) Bilkent University, Graduate School of Engineering and Science, Department of Physics, 2003

PhD. : Hacettepe University, Graduate School of Science and Engineering, Department of Bioengineering, 2017

Foreign Languages

English (advanced), German (Basic)

Work Experience

- Marmara Research Center of the Scientific and Technical Research Council of Turkey (TÜBİTAK), Researcher, Gebze, 1996-1997
- Abant IB University, Phsycis Department, Research Assistant, Bolu, 1997-1999
- Max-Planck Institute, Researcher, Bonn, Germany,1999-2001
- Bilkent University, Phsycis Department, Research Assistant, Ankara, 2001-2003
- Gazi University, Faculty of Medicine, Biophysics Department, Researcher, Ankara, 2004-2006
- Gazi University, Nanomedicine and Advanced Technologies Research Center, Researcher, Ankara, 2009-2011
- National MR Research Center, Researcher, Ankara, 2012
- Cognitive Robotics Research Laboratory, Atılım University, Researcher, Ankara, 2017

Areas of Experiences

Neuroimaging methods, electrophysiological data analysis, programming languages, experimental control software, scholarly writing

Projects and Budgets

The Scientific and Technical Research Council of Turkey (TÜBİTAK) grant 114E621; 330.000 TL

Publications

Neuroscience Letters, 2017 (submitted), Experimental Brain Research, 2017 (submitted)

Oral and Poster Presentations

- 33th National Clinical Neurophysiology EEG-EMG Congress, Antalya, 12-16 April 2017 (oral)
- 26th National Physical Medicine and Rehabilitation Congress, Antalya, 25-29 April 2017 (poster)

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THESIS/DISSERTATION ORIGINALITY REPORT

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Student No:	N10142690
Department:	Bioengineering
Program:	Bioengineering
Status:	☐ Masters ☒ Ph.D. ☐ Integrated Ph.D.

ADVISOR APPROVAL

APPROVED.

T. Kutsal

(Prof. Dr. Tülin KUTSAL)