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FACULTY OF HEALTH SCIENCES

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An investigation into cortical activity associated with robotic upper limb rehabilitation after stroke

by

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Thesis for the degree of Doctor of Philosophy

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ABSTRACT

FACULTY OF HEALTH SCIENCES

Thesis for the degree of Doctor of Philosophy

AN INVESTIGATION INTO CORTICAL ACTIVITY ASSOCIATED WITH ROBOTIC UPPER LIMB REHABILITATION AFTER STROKE

Sebastien Pollet

Background: Many stroke survivors are left with upper limb impairments that affect their ability to carry out functional tasks. Using neuroimaging and electrophysiological technology, advances have been made in understanding brain function and reorganisation after stroke. These findings provide valuable insights and may provide the key to more effective rehabilitation practices.
Objectives: This research aimed to improve understanding of cortical function recovery after stroke, as measured by electroencephalography (EEG) during a reaching movement, before and following robotic upper limb rehabilitation. In particular, the study looked for event-related changes in EEG waves commonly referred to as event-related desynchronisation (ERD) and event-related synchronisation (ERS), which are measured in the frequency domain.
Methods: EEG was recorded over the sensorimotor cortex during a reaching movement with all participants using a customised experimental setup developed for this study. Four studies were carried out: 1) a feasibility study tested data collection methods with four participants, 2) test-retest variability of ERD/ERS measures over three sessions was determined with five healthy participants, 3) averaged ERD/ERS measures were examined in a group of ten healthy participants, 4) ERD/ERS measures of six stroke participants who underwent ten sessions of robotic upper limb rehabilitation over two weeks were examined, and changes following rehabilitation were compared to changes in measures of upper limb impairment (Fugl-Meyer Assessment) and function (Action Research Arm Test).
Results: Results from the stroke participant study show that 1) two participants presented with reduced alpha ERD over the ipsilateral hemisphere, three participants had a predominant alpha and/or beta ERD over the ipsilateral hemisphere, and beta ERS following movement was predominantly found to occur over the ipsilateral hemisphere for four participants, and 2) two participants showed changes in ERD/ERS measures that could be attributed to the effects of rehabilitation, with associations made with measures of upper limb impairment and function. These changes related to hemispheric lateralisation of alpha ERD, as demonstrated by a decrease of excessive contralateral predominance (when compared to healthy participants) as well as to a hypothesised normalisation of interhemispheric inhibitory mechanisms demonstrated by a decrease in abnormal alpha and beta ERS during movement.
Conclusions: Abnormal ERD/ERS measures of hemispheric laterality were a recurrent feature of stroke participants, with some changes that could be attributed to the effects of rehabilitation, indicating that measures of ERD/ERS during reaching using this experimental setup could be used to assess and monitor cortical activity recovery after stroke. Further work is however proposed to determine the responsiveness of the methods used, as improved motor function was not always accompanied by changes in measures of ERD/ERS.

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Data supporting this study are openly available from the University of Southampton repository at https://doi.org/10.5258/SOTON/D0594.

DECLARATION OF AUTHORSHIP

I, Sebastien Pollet

declare that this thesis and the work presented in it are my own and has been generated by me as the result of my own original research.

An investigation into cortical activity associated with robotic upper limb rehabilitation after stroke.

I confirm that:

1. This work was done wholly or mainly while in candidature for a research degree at this University;
2. Where any part of this thesis has previously been submitted for a degree or any other qualification at this University or any other institution, this has been clearly stated;
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7. Parts of this work have been published/presented as:

Pollet S, Burridge, J, and Conway, B (2012) Cortical activity changes among stroke patients following robotic upper limb rehabilitation as measured by EEG during reaching movements. In: 7th World Congress for NeuroRehabilitation (WCNR 2012), 16-19 May 2012, Melbourne, Australia. The abstract for this poster presentation was published in the *Journal of NeuroRehabilitation and Neural Repair* June 2012; 26 (5) issue.

Pollet S, Burridge, J, and Conway, B (2013) Development of a method to measure cortical activity changes associated with robotic upper limb rehabilitation after stroke. In: The Society for Research Rehabilitation (SRR) Winter Meeting, 5 February 2013, Bath, United Kingdom.

Signed: ....

Date: ....

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Definitions and Abbreviations

ACA	Anterior cerebral artery
ADL	Activities of daily living
ARAT	Action Research Arm Test
BCI	Brain-computer interface
BOLD	Blood oxygen level-dependent
BP	Bereitschaftspotential
CIMT	Constraint-induced movement therapy
CNS	Central nervous system
CVA	Cerebrovascular accident
DTI	Diffusion tensor imaging
EEG	Electroencephalography
EMG	Electromyography
EPSP	Excitatory postsynaptic potential
ERD	Event-related desynchronisation
ERP	Event-related potential
ERS	Event-related synchronisation
ERSP	Event-related spectral perturbation
FES	Functional electrical stimulation
FMA	Fugl-Meyer Assessment
fMRI	Functional magnetic resonance imaging
ICA	Independent Component Analysis
ICF	International Classification of Functioning, Disability and Health

IPSP	Inhibitory postsynaptic potential
LTP	Long-term potentiation
MCA	Middle cerebral artery
MEG	Magnetoencephalography
MEP	Motor evoked potential
MP	Motor potential
MRCP	Movement-related cortical potential
MRP	Motor Relearning Programme
NDT	Neuro-developmental Treatment
NIBS	Non-invasive brain stimulation
NIRS	Near-infrared spectroscopy
NS’	Negative slope
PET	Positron emission tomography
PNF	Proprioceptive Neuromuscular Facilitation
RD	Readiness potential
RT	Robotic therapy
SENIAM	Surface Electromyography for the Non-Invasive Assessment of Muscles
sMRI	Structural magnetic resonance imaging
TBS	Theta-burst stimulation
tDCS	Transcranial direct current stimulation
TMS	Transcranial magnetic stimulation
VR	Virtual reality
WHO	World Health Organisation

Chapter 1: Introduction

This chapter presents an overview of the context of this study and its rationale. Chapter 2 provides background information about stroke, motor recovery, rehabilitation approaches, clinical outcome measures, cortical recovery, and electroencephalography. Following this, Chapter 3 expands on Chapter 2 by exploring current literature findings on movement-related ERD/ERS. Chapters 4 to 8 present study development considerations, as well as results from four studies: a feasibility study, a test-retest variability study, a study with healthy volunteers, and another with stroke participants. Chapter 9 ends the thesis with a summary of findings and concluding statements.

1.1 Stroke research in context

In England, approximately 110 000 people experience a stroke every year, and around half of those who survive become dependent on others for everyday activities (National Audit Office and Dept. of Health 2010). Stroke has become a valued area of research in the UK, with research spending increasing over recent times, from £23 million in 2008 to £56 million in 2012 (Luengo-Fernandez et al. 2015).

Of the several impairments associated with stroke, upper limb motor deficits play a large role in the development of occupational performance issues (Broeks et al. 1999). Difficulties with functional reaching, which include grasping and simultaneous shoulder and elbow movements, often contribute to these issues. Improvements obtained through rehabilitation vary and as many of these individuals do not fully recover their previous abilities, the need for more effective rehabilitation practices remains. An important development in recent years has been the increasing use of technology to optimise stroke recovery.

1.2 Research problem

Traditionally, evidence for effective upper limb rehabilitation has arisen from studies investigating outcomes using impairment and function-based assessments. Improvements in motor behaviour can be observed in many individuals, however little is known about what changes take place in the brain itself, where the injury occurred (Boyd et al. 2007). The greatest improvements take place in the first few months following stroke, and subsequent progress slows down in intensity (Hendricks et al. 2002). The term ‘neuroplasticity’ is used to refer to the brain’s ability to adapt to external stimuli, learning new skills, or neurological injury (Johansson 2000). However, neuroplasticity after stroke remains only partially understood (Boyd et al. 2007). More research is required to clarify the nature, sequence, and timing of spontaneous and rehabilitation-induced neuroplastic changes that occur following stroke, and to explore how these changes relate to improvements in motor function.

1.3 Rationale for the project

In recent years, scientists from the fields of rehabilitation and neuroscience have increased our understanding of neuroplasticity by using technologically-based investigative methods such as neuroimaging and electrophysiology. These two methods are currently the only available to monitor brain function during voluntary movement (Boyd et al. 2007). Within the field of neuroimaging, the use of fMRI (functional magnetic resonance imaging) is being included in current and planned stroke research efforts. However, due to the lack of space within the magnetic resonance imaging equipment, upper limb movements are limited to hand and finger joints (Kimberley and Lewis 2007), although new ‘open’ models may possibly remove this restriction in the future. Electrophysiological techniques, such as electroencephalography (EEG) and, to a lesser extent, magnetoencephalography (MEG), have also been used to explore neuroplasticity. Unlike fMRI, upper limb movements performed during EEG measurement sessions are not restricted. This allows for testing to occur in a more natural setting and body posture, and for movements performed during EEG recording to be more representative of movements performed during clinical assessments. It is therefore a more suitable tool to use than fMRI when brain activity related to complex movement and possible links between cortical activity changes and functional changes are investigated. As EEG has better temporal resolution than fMRI, it also has the advantage of allowing researchers to differentiate cortical activity according to whether it occurs during movement preparation, execution, or recovery, which is not possible with fMRI (Pfurtscheller et al. 1999). EEG systems are also more accessible than fMRI (mostly due to costs) and therefore have a better potential of being used routinely by clinicians of the future to monitor cortical activity changes after stroke.

EEG studies have considered movement-related ERD (event-related desynchronisation) and ERS (event-related synchronisation) to understand healthy peoples’ brain function during voluntary movement of the upper limbs. Movement-related ERD and ERS are signal characteristics that reflect the degree of activation and deactivation of neurons involved with the production of movement. However, only a small number of studies have examined how this signal is affected by stroke, and whether it can be associated with changes in motor function.

This study aimed to 1) develop a method to record and investigate cortical activation, as characterised by movement-related ERD/ERS during a reaching movement, 2) examine variability of ERD/ERS measures in healthy volunteers, 3) characterise ERD/ERS measures in a group of healthy volunteers, and 4) investigate whether people who have had a stroke present with different ERD/ERS measures, whether any changes can be observed following a period of upper limb rehabilitation, and to compare potential changes, if any, with findings from measures of upper limb impairment and function.

Chapter 2: Background

2.1 Introduction

This chapter provides fundamental background information about stroke, motor recovery, rehabilitation approaches, clinical outcome measures, cortical recovery, and electroencephalography.

2.2 Stroke

2.2.1 Pathology

Stroke, also known as cerebrovascular accident (CVA), is often being cited as having been defined some time ago by the World Health Organisation (WHO) as

> “Rapidly developing clinical signs of focal (or global) disturbance of cerebral function, with symptoms lasting 24 hours or longer, or leading to death, with no apparent cause other than vascular origin.”
>
> (Aho et al. 1980)

An additional explanation provided by the WHO describes the mechanisms of stroke in more detail:

> “A stroke is caused by the interruption of the blood supply to the brain, usually because a blood vessel bursts or is blocked by a clot. This cuts off the supply of oxygen and nutrients, causing damage to the brain tissue.”
>
> (World Health Organization 2010)

Depriving cells from oxygen and glucose eventually causes them to die, compromising the function(s) associated with the area in which they are situated (Longstaff 2005). The particular function(s) that will be affected depend on the artery that is occluded (or from which haemorrhage has occurred), as different arteries supply different areas of the central nervous system (CNS) (Markus et al. 2010).

For strokes occurring in the brain, a first simple distinction relates to whether the anterior or posterior circulatory system is affected. The anterior system is of particular interest as the anterior and middle cerebral arteries (ACA and MCA, respectively) supply the motor areas (see Figure 1) (Markus et al. 2010).

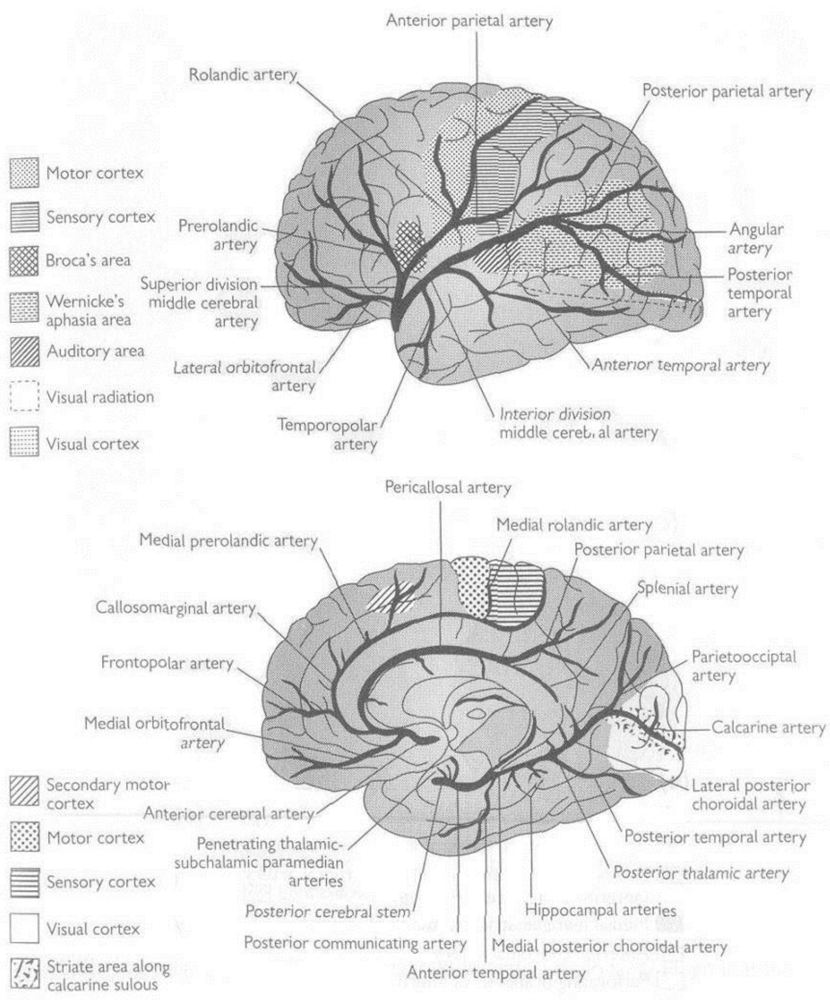

Figure 1 Areas supplied by the middle (top) and anterior (bottom) cerebral arteries (areas supplied by the posterior cerebral artery are also shown) (Markus et al. 2010). Copyright of Oxford University Press reproduced with permission.

2.2.2 Clinical consequences

Strokes which occur in the cerebrum may affect survivors in a number of ways. They may result in difficulties with motor control, movement disorders, sensory disturbances, visual impairment, emotional lability, communication deficits, behavioural changes, as well as perceptual and cognitive dysfunction (Markus et al. 2010). These impairments may occur from involvement not only of cortical areas but also of ascending and descending connections serving these areas (Markus et al. 2010). Fatigue is also present in approximately 30% to 60% of stroke survivors (De Groot et al. 2003).

2.2.3 Motor deficits of the upper limb

Involvement of the middle cerebral artery often results in difficulties with contralateral upper limb motor control. This is due to the fact that regions of the motor cortex which control upper limb movement are supplied by this artery, as opposed to the anterior cerebral artery, which lies more medially, closer to lower limb and trunk regions of the motor homunculus (see left half of Figure 2) (Markus et al. 2010).

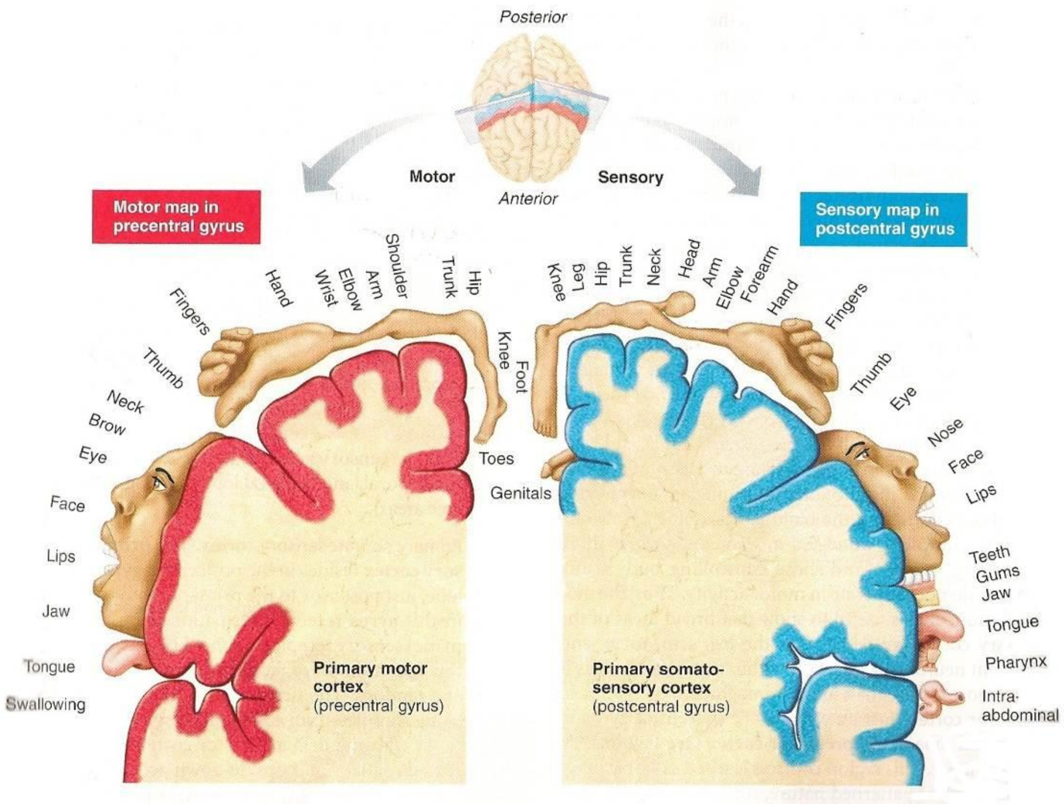

Figure 2 Motor and somatosensory homunculi (Marieb and Hoehn 2010). MARIEB, ELAINE N.; HOEHN, KATJA, HUMAN ANATOMY & PHYSIOLOGY, 8th Edition, © 2010 Reprinted by permission of Pearson Education, Inc., Upper Saddle River, NJ.

The most important resulting upper limb impairments are weakness and loss of dexterity (Carr and Shepherd 2003). When considered in isolation or in combination, these deficits are often referred to as either hemiparesis, where partial movement and strength remain, or to its more severe counterpart, hemiplegia, where total paralysis occurs.

Weakness, or lack of ability of muscles to generate appropriate force, is caused not only from the damage to the brain’s motor areas, but also from decreased use and immobility, which causes further muscle weakness (Farmer et al. 1993).

Loss of dexterity, also known as lack of motor control, refers to a decreased ability to control coordination between muscles as required for a specific task, a phenomena that is thought to occur independently from muscle weakness (Canning et al. 2000).

Spasticity, a velocity-dependent hyperexcitability of the stretch reflex (Lance 1980), may also be present, but there is a lack of evidence to show an association with degree of disability (Pierrot-Deseilligny 1990; Fellows et al. 1994).

2.3 Motor recovery of the upper limb

2.3.1 Degree of recovery

Recovery of upper limb function after stroke is known to vary from person to person (Hendricks et al. 2002), and long term deficits often remain. It was also found, from a sample of 680 stroke participants, that recovery from hemiparesis (as measured with the motor section of the Scandinavian Neurological Stroke Scale) generally varies according to severity (see Table 1), with chances of complete recovery decreasing as the severity of hemiparesis increases (Bonita and Beaglehole 1988). A study reported that presence of finger extension and shoulder abduction at 72 hours after stroke predicts a more favourable functional outcome (Nijland et al. 2010).

	Complete recovery	**Partial recovery**	**No improvement**	**Died**
Severe	7%	31%	21%	41%
Moderate	22%	38%	17%	23%
Mild	46%	N/A	38%	16%

Table 1 Degree of recovery from hemiparesis at 6 months after stroke onset, according to severity of stroke (Bonita and Beaglehole 1988).

2.3.2 Time course

As for the timing of recovery, a study carried out with 1197 stroke participants suggests that temporal variability also depends on the severity of the stroke. Individuals with mild deficits (as measured with the Scandinavian Neurological Stroke Scale) reach their best recovery level faster than those with more severe ones (see Table 2), with mean best recovery times ranging from 6.5 weeks to 15 weeks (Jorgensen et al. 1995).

Severity of stroke	Best recovery time
Very severe	13 weeks
Severe	15 weeks
Moderate	10.5 weeks
Mild	6.5 weeks

Table 2 Mean best recovery time according to severity of stroke (in 95% of participants from each category) (Jorgensen et al. 1995).

Other studies report that later recovery may occur several months after stroke in some individuals, but evidence for this remains limited (Hendricks et al. 2002).

By convention, phases of post stroke recovery are defined as: hyperacute (stroke onset to 6 hours), acute (6 hours to approximately seven days, and ends when physiological processes related to ischemia have resolved and the patient is considered medically stable), subacute (one week to 3-4 months, when rapid potential neurological and functional recovery occurs), and chronic (beyond 3-4 months) (Sullivan 2007).

2.4 Rehabilitation approaches

2.4.1 Recovery vs. compensation

A first distinction between rehabilitation interventions relates to whether they promote neurological recovery or whether their goal is to compensate for impairments with a view to improve functional abilities. Approaches from the first category, also known as remedial or restorative approaches, aim to stimulate nervous system recovery and reorganisation, whilst other approaches, also known as adaptive or compensatory approaches, are intended to improve independence in occupational performance areas such as self-care, productivity, and leisure. The latter make use of problem-solving processes to generate different ways of carrying out activities, and typically involve the unaffected limb to a greater extent and the use of adaptive equipment. In practice, both approaches are used simultaneously during the recovery process.

2.4.2 Remedial/restorative approaches

Several approaches have been developed in the last one hundred years. These have been based on models and theories of central nervous system function and recovery. Both traditional and more recent neurophysiological approaches, including neurodevelopmental and task-related approaches, are summarised in Table 3. Newer task-related approaches have emerged as an alternative to neurodevelopmental approaches, whose assumptions are increasingly questioned as technology provides new insights into brain function (Radomski and Latham 2008). They are based on a systems model of motor control and development, and on motor learning theories (Radomski and Latham 2008). In addition to these, a number of therapies have emerged in recent times, whether technology-assisted, such as robot-assisted therapy (RT), functional electrical stimulation (FES), and virtual reality (VR) training, or based on other rationales such as constraint-induced movement therapy (CIMT), mental imagery/practice, and bilateral training. Robot-assisted therapy, the therapeutic modality used in this study, is discussed in the next section.

Prior to neurophysiological approaches, a combined orthopaedic and compensatory approach was used, including stretching, bracing, strengthening, and teaching the individual to compensate using the unaffected side (Kollen et al. 2009).

Neurodevelopmental approaches	
Sensorimotor approach (Rood, 1950s)	• Static and dynamic stability and limb mobility are key to motor function. • Components of loss of normal movement: abnormal tone, loss of sensory input, loss of voluntary control. • Early reflexes are considered in relearning of motor control. • Uses sensory input (tactile, thermal, proprioceptive, auditory, visual, and olfactory stimuli) for muscle facilitation and inhibition techniques to influence motor responses via reflex arcs. • Values repetition of purposeful activities.
Brunnstrom Movement Therapy (Brunnstrom, 1950-70s)	• Assumes that spinal cord and brain stem reflexes and whole-limb movement patterns after stroke are alike those seen during normal development, and that they are modified into purposeful movements by higher brain centres. • Uses reflexes and primitive movement patterns to elicit normal movement. • Uses proprioceptive (resistance, muscle and tendon tapping) and tactile stimulation to facilitate motion and tonal changes. • Six stages of recovery: from flaccidity to nearly normal movement, working through flexion and extension synergies.
Bobath/Neuro-Developmental Treatment (NDT) (Bobath & Bobath, 1960-70s)	• Focus is on eliminating abnormal movements and restoring normal movements using principles of kinesiology. • A decrease of reflex activity and tone improves posture and movement. • Rejects approaches that encourage reflex activity and abnormal movements. • Involves the use of inhibition and facilitation manual techniques to eliminate abnormal tone. These are intended to provide tactile, proprioceptive, and kinaesthetic messages at 'key points of control' to help organise movements. • Compensation with unaffected side is discouraged.
Proprioceptive Neuromuscular Facilitation (PNF) (Kabat, and modified by many others, including Knot & Voss, 1960-70s)	• Similarly to Rood's approach, sensory stimulation is used to elicit motor responses via reflex arcs. Expands proprioceptive input to include inner ear receptors and also emphasises visual input. • Based on the unique concept that muscles are configured to function in diagonal and spiral patterns rather than in cardinal plane movements such as flexion/extension, abduction/adduction, and internal/external rotation. Involves passive and active-assisted movements. • Breathing is considered in all PNF treatment by using specific positions which increase chest and diaphragm movement. Other vital functions are also considered (facial and tongue motions, swallowing, bowel and bladder control).
Task-related approaches	
Motor Relearning Programme (MRP) (Carr & Shepherd, 1980-90s)	• Rejects hierarchical organisation of the CNS. • Assumes that regaining motor control is a learning process which requires practice, feedback, and goal-setting. • Motor tasks should be practiced in their environmental contexts. • Sensory input from specific motor tasks influence performance. • Intervention is organised around four categories of activities: reach and manipulation, balance, standing up and sitting down, and walking. • Provides specific guidelines for assessment and treatment of motor deficits, but does not discuss guidelines for enhancing participation in life roles.
Occupational Therapy task-oriented approach (Horak, Mathiowetz & Bass-Haugen, 1990s)	• Change results from interaction of person and environment. • Focus is on occupations and required movement patterns. • Identifies personal and environmental factors which affect performance. • Considers types of practice and feedback. • Aims to develop problem-solving skills that can be applied to other activities.

Table 3 Overview of rehabilitation approaches (Radomski and Latham 2008).

2.4.3 Robot-assisted therapy

A number of robotic devices that aim to assist and optimise upper limb rehabilitation have been developed over the last 20 years. Most of these have focused on the proximal part (shoulder and elbow) of the upper limb (Timmermans et al. 2009). Systematic reviews have found that they can significantly improve shoulder and elbow motor function in subacute and chronic stroke participants (Prange et al. 2006; Kwakkel et al. 2008; Mehrholz et al. 2015).

Robotic devices function by providing passive movement, assisting active movement (either by moving the arm or by de-weighting it to remove the force required to counteract gravity), with some allowing for both limbs to be moved simultaneously. They typically involve an orthosis in which the arm is placed and from where the device interacts with the user's limb. An overview of the most well-known devices is presented in Table 4.

Device	Characteristics
MIT-Manus (commercial name: InMotion2)	• Two degrees of freedom (horizontal plane) • Movements: shoulder, elbow and wrist • Passive, active and interactive (reacts to user's actions) modes • Feedback: visual, tactile, auditory • Activities: moving to targets, tracing figures and virtual reality task-oriented training
Mirror-Image Motion Enabler Robots (MIME)	• Six degrees of freedom (3D workspace) • Movements: shoulder, elbow, forearm • Passive, active-assisted, active-constrained and bimanual (mirror movement of unaffected arm) modes • No feedback • Activities: pre-programmed trajectories
Assisted Rehabilitation and Measurement (ARM) Guide	• Four degrees of freedom • Assists reaching in a straight-line trajectory only • Feedback: visual
Bi-Manu-Track	• One degree of freedom • Movements: bilateral forearm pronation/supination and wrist flexion and extension • Passive and active movement modes • No feedback
Neuro-Rehabilitation-Robot (NeReBot)	• Three degrees of freedom (3D workspace) • Movements: shoulder and elbow • Simulates hand-over-hand therapy • Active, active-assisted, and passive modes • Feedback: visual (3D virtual upper limb) and auditory (signals start/end of movement, not performance)
GENTLE/S	• Three degrees of freedom (3D workspace) • Movements: shoulder, elbow, wrist, and gross prehension movements • Affected arm is de-weighted • Feedback: visual • Activities: virtual reality task-oriented training
T/WREX (commercial name: Armeo Spring/Power)	• Three degrees of freedom (3D workspace) • Movements: shoulder, elbow, forearm, wrist, and gross prehension movements • Affected arm is de-weighted • Feedback: visual and auditory, position, speed, and grip force • Activities: virtual reality task-oriented training
MEMOS	• Two degrees of freedom • Movements: shoulder and elbow on a horizontal plane • Passive and active-assisted modes • Feedback: audiovisual • Activities: virtual reality task-oriented training

Table 4 Robotic devices (Timmermans et al. 2009; Basteris et al. 2014; Maciejasz et al. 2014).

Many of these devices are compatible with neurorehabilitation principles that have been shown to induce neuroplastic change (see 'Implications of findings on neuroplasticity for rehabilitation', paragraph 2.6.7), notably by allowing the repetition of skilled goal-orientated movements in highly gradable and reproducible environments.

Further developments are emerging as new or enhanced devices are designed, which include more joints (incorporating hand and finger movements, such as the Amadeo hand rehabilitation system), as well as additional feedback.

2.5 Clinical outcome measures

When assessing upper limb motor function, clinicians may choose from a wide range of assessments, depending on what they decide to measure. A useful starting point is to consider the World Health Organization's International Classification of Functioning, Disability and Health (WHO ICF). This classification provides a framework which his helpful to distinguish between types of disability and to indicate how they may affect individuals. Three broad categories have been defined: body functions and structure, activity, and participation (see Figure 3).

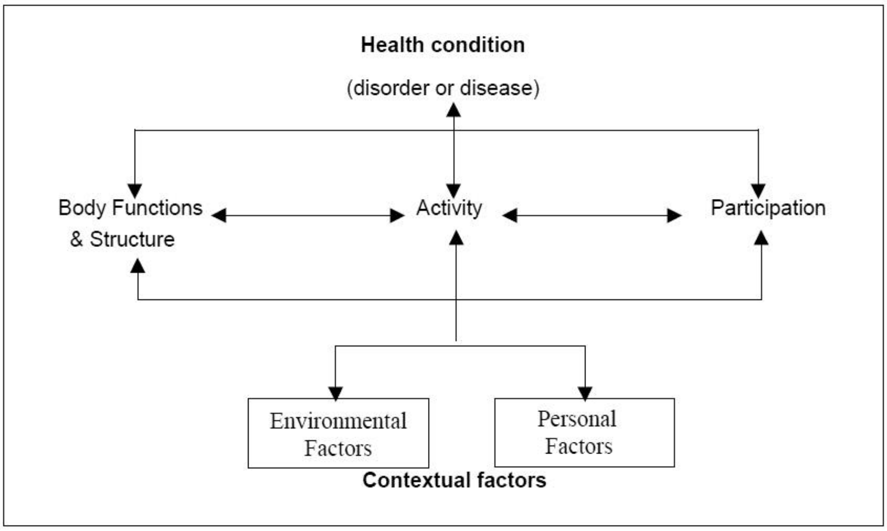

Figure 3 International Classification of Functioning, Disability and Health (ICF) (World Health Organization 2002). Copyright of World Health Organization – no permission required for non-commercial purposes.

Assessments which consider impairments (such as muscle strength or joint range of motion) would be interpreted by the ICF as measurement tools that investigate problems in body function and/or structures. Functional assessments (which typically measure an individual's ability to carry out a purposeful task, such as writing) would be categorized by the ICF as evaluating activity limitations. A third group of assessments which look at life roles (such as being a parent, a worker, a student), would fall under the ICF's category of investigating one's participation restriction.

2.6 Cortical recovery

2.6.1 Review of neuroanatomy and neurophysiology

In order to understand concepts of cortical recovery following stroke, a review of neuroanatomy and neurophysiology is essential. This section presents fundamental information about neuronal physiology, the motor cortex, as well as the activation sequence of brain structures involved in movement.

2.6.1.1 Neuronal physiology

Most neurons function by exciting or inhibiting activity between each other through chemical signals at the synapse, where neurons' axon terminals and dendrites interact (Marieb and Hoehn 2010). To achieve this they create electrical signals, known as action potentials, which consist of cell membrane potentials that are generated at the axon hillock (the membrane potential being the difference in voltage between the interior and exterior of the cell, caused by a difference in concentration of positively and negatively charged ions) and propagated down the length of the axon towards its axon terminals (see Figure 4) (Longstaff 2005).

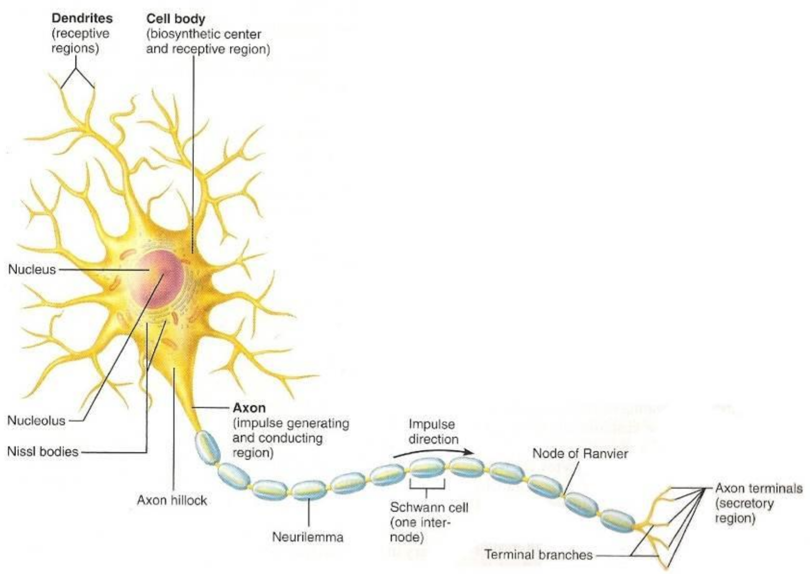

Figure 4 Structure and functioning of a neuron (Marieb and Hoehn 2010). MARIEB, ELAINE N.; HOEHN, KATJA, HUMAN ANATOMY & PHYSIOLOGY, 8th Edition, © 2010. Reprinted by permission of Pearson Education, Inc., Upper Saddle River, NJ.

When these action potentials reach the axon terminals, they cause a release of chemicals, neurotransmitters, which may either excite or inhibit connecting neurons by creating either depolarising or polarising postsynaptic potentials, respectively known as excitatory postsynaptic potentials (EPSPs), and inhibitory postsynaptic potentials (IPSPs) (Kandel et al. 2000). These potentials are graded potentials, meaning that they are proportional to the intensity of the stimulation from neurotransmitters (Stern et al. 2001). Whether an action potential is generated from these depends on whether the combined resulting summation of depolarisation and polarisation influences exceed the minimum threshold required to produce an action potential (Stern et al. 2001). If triggered, in contrast with postsynaptic potentials, action potentials activate the axon at the same voltage intensity, independently from the amplitude of the stimuli at the synapse (Stern et al. 2001).

2.6.1.2 The motor cortex

Figure 5 shows the main areas of the cortex involved in limb movement. Brain area mapping based on anatomical and histological observations by Brodmann (a German anatomist) introduced, in the early 1900s, a numbering system to identify cortical regions (Marieb and Hoehn 2010).

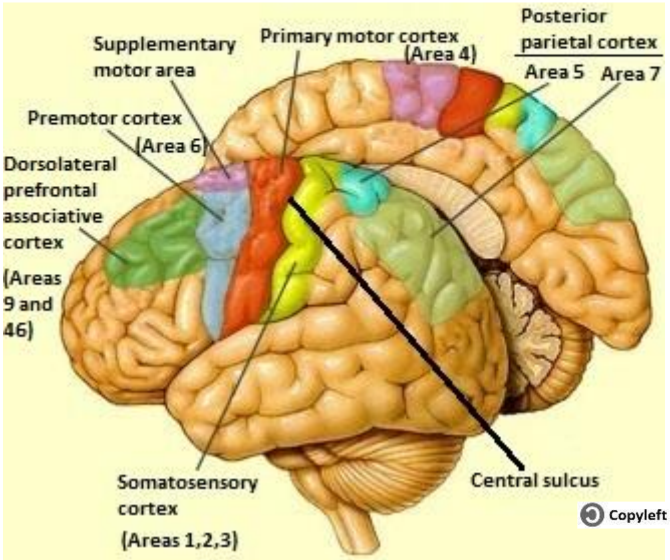

Figure 5 The motor cortex, adapted from (Dubuc 2004).
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The primary motor cortex (area 4), also known as M1, is located in the precentral gyrus (a gyrus can be conceptualised as an anatomical ‘ridge’) in the frontal lobe, anteriorly to the central sulcus (which can be conceptualised as an anatomical ‘valley’). It is organised somatotopically (see Figure 2) according to body part, and is from where axons in the corticospinal tract project towards the spinal cord to synapse with motor neurons (Marieb and Hoehn 2010). The corticospinal tract is also known as the direct pyramidal tract, due to its triangular shape when viewed on a cross-section of the medulla (in the brainstem), where most of the axons cross to the contralateral side of the body via the lateral corticospinal tract (Marieb and Hoehn 2010). A small proportion of axons do not cross at this level and descend via the ventral corticospinal tract, to then synapse with ipsilateral interneurons that in turn cross to the opposite side to make contact with contralateral motor neurons (Marieb and Hoehn 2010). A small number of them however make contact with motor neurons on the ipsilateral side (Marieb and Hoehn 2010). Corticospinal axons do not synapse until they reach the spinal cord and are used to perform skilled movements (Marieb and Hoehn 2010). In contrast with the direct pathways, there are indirect (extrapyramidal) pathways that participate in motor function, such as the tectospinal, vestibulospinal, rubrospinal, and reticulospinal tracts, which are involved with regulating postural muscle activation, muscle tone, coordinated head and eye movements, and some unskilled movements (Marieb and Hoehn 2010).

Also in the frontal lobe, the premotor and supplementary motor areas (which together form area 6) lie anteriorly to the primary motor cortex. The premotor cortex is thought to help regulate posture by supplying the primary motor cortex with information about optimal positions for a specific movement (Dubuc 2004). The supplementary motor area is believed to inform the planning and initiation of movement from knowledge gained from past experience (Dubuc 2004). The dorsolateral prefrontal associative cortex (areas 9 and 46) can be found anteriorly to area 6. This area is thought to be where decisions are made about the general objectives of the movement and what behaviours are required, for example, reaching with the arm to grasp an object with the hand (Dubuc 2004).

Posteriorly to the central sulcus, in the parietal lobe, are the somatosensory cortex (in the postcentral gyrus) and posterior parietal cortex, which consist of areas 1 to 3, and areas 5 and 7, respectively. The somatosensory cortex is where sensory information (from somatic skin sensory receptors and position sense receptors in muscles, joints and tendons) is registered (Marieb and Hoehn 2010). The posterior parietal cortex analyses data from the somatosensory cortex (processed by area 5), as well as visual inputs (processed by area 7), to contribute to the planning of movement in terms of the context in which the movement is to be performed (Dubuc 2004).

2.6.1.3 Activation sequence of brain structures involved in movement

Voluntary movement is the result of a joint effort between areas of the motor cortex, described above, and other brain structures that also contribute, such as the basal ganglia and the cerebellum (Dubuc 2004).

Firstly, the dorsolateral prefrontal associative cortex is activated to prepare and send a plan of action to the premotor and supplementary motor areas by determining what actions, in general terms, are required to achieve a task (Dubuc 2004). The somatosensory cortex and posterior parietal cortex, with help from the basal ganglia, which acts as a relay and filter, send information to the premotor and supplementary motor areas regarding position of the body in space as well as the environmental context in which the movement is to be performed (Dubuc 2004).

Secondly, the premotor and supplementary motor areas then work with the cerebellum to establish the characteristics of the movement and the sequence of muscle contractions required to achieve the movement (Dubuc 2004).

Finally, the primary motor cortex determines the degree of muscle contraction required by each muscle group and instructs them to contract via the brainstem and spinal cord (Dubuc 2004). Throughout the movement, sensory information is fed back to a closed loop system to allow for constant correction of the movement (Dubuc 2004).

2.6.2 Non-invasive methods to examine brain activity

A number of technologies can be used to investigate brain activity by recording various physiological phenomena associated with activation of neuronal networks.

2.6.2.1 Functional magnetic resonance imaging

Functional magnetic resonance imaging (fMRI) has been useful to uncover patterns of neuronal activation during various tasks. The blood oxygen level-dependent (BOLD) signal is used to track blood oxygen levels in the brain and as a result has the ability to measure blood flow, which is linked with neuronal firing, in order to identify which regions of the brain are activated, and to what degree, during a task (Stern et al. 2001).

2.6.2.2 Positron emission tomography

Positron emission tomography (PET) is also used to study brain activity during performance of a task. Like fMRI, it measures blood flow changes, but does so in a different manner. A radioactive tracer substance is injected in an individual and monitored with a PET camera. Its distribution during movement is related to blood flow, indicating activated brain areas (Schaechter 2004).

2.6.2.3 Electrophysiological techniques

Electroencephalography (EEG) and magnetoencephalography (MEG) are also used to measure neuronal activity during specific tasks, by recording electrical signals and electromagnetic fields, respectively, from the surface of the scalp. These methods can also be used to assess the somatosensory system by measuring somatosensory evoked potentials (SEPs). EEG is discussed in further detail in the next section.

Transcranial magnetic stimulation (TMS) is a technique used to evaluate cortex excitability and to create somatotopic brain maps linking areas of the motor cortex to specific body parts. By stimulating the cortex with a magnetic field, an induced current is created, causing a motor evoked potential (MEP), which can be measured by electromyography (EMG) on muscles of interest (Kleim and Schwerin 2010). After stroke, it is particularly useful to evaluate the integrity of the corticospinal system. The presence or absence of MEPs can be used, in conjunction with other measures (shoulder abduction and finger extension strength as well as National Institutes of Health Stroke Scale (NIHSS) scores) to predict upper limb motor function at three months after stroke using the Predict Recovery Potential (PREP2) algorithm. PREP2 can accurately predict upper limb functional outcome in 75 % or people who have had a stroke within 1 to 7 days post stroke onset (Stinear et al. 2017).

2.6.2.4 Diffusion tensor imaging

Diffusion tensor imaging (DTI), an MRI technique developed in the nineties, is being increasingly used to examine brain organisation. DTI provides information about the brain's white matter by measuring how water diffuses in space, as it has a tendency to diffuse more rapidly in the direction of the axons. This method reveals axonal organisation and structural connectivity of the brain (Mori and Zhang 2006).

2.6.2.5 Near-infrared spectroscopy

Near-infrared spectroscopy (NIRS) is a technology that uses measures of near-infrared light absorption by haemoglobin to quantify changes in oxygenated haemoglobin and deoxyhaemoglobin blood concentrations, which in turn indicate neuronal activity (Schaechter 2004).

2.6.3 Neuroplasticity

The human brain is able to adapt and modify its functioning in reaction to experience and learning (Johansson 2000). 'Neuroplasticity' is the term that is used to refer to the brain's ability to continuously remodel neuronal connections (described above) and motor map organisation (see Figure 2). This phenomena has been shown to occur in response to sensory input, experience, learning, and brain lesions (Johansson 2000).

Neuroplasticity has been conceptualised in the past as ‘neuronal learning’ and was thought to occur by changes in the strength of synapses (Longstaff 2005). This was theorised by Hebb in 1949, who suggested that synapses ‘strengthen’ if connected neurons are activated repeatedly, and at the same time (Longstaff 2005). In other words, the presynaptic neuron’s ability to excite the postsynaptic neuron is increased. This theory, called ‘Hebbian Learning’, has evolved to what is now known as long-term potentiation (LTP), one of several mechanisms that have been associated with synaptic modifications, including changes in sensitivity to neurotransmitters (Longstaff 2005).

Other phenomena, in addition to LTP, such as changes in number of synapses, axonal sprouting, increased dendritic arborisation, have also been associated with mechanisms of neuroplasticity (Kleim 2009).

Neuroplasticity is not only observed at the level of the interaction between two neurons, but also occurs over larger populations of neurons, as observed in changes in regional brain activity and reorganisation of sensory and motor representations (Kleim 2009).

2.6.4 Neuroplasticity and motor learning

Neuroplasticity has been shown to support the concept of motor learning, which refers to the enduring changes that can be observed in motor behaviour following motor skill training through the use of practice, feedback, and goal-setting (Kleim 2009). Evidence has demonstrated the link between motor learning and neuroplasticity in the intact brain, by showing that acquisition and refinement of skilled movements, such as reaching and grasping, results in motor cortex changes, including synaptogenesis (formation of synapses), synaptic potentiation (strengthening of synapses) and increased movement representation in the cortex (Adkins et al. 2006). These findings are contrasted to the effects of strength training, which alters motor neuron excitability and causes synaptogenesis in the spinal cord, but does not alter cortical motor map organisation, and to the effects of endurance training, which causes angiogenesis (the formation of new blood vessels) in the motor cortex, but no cortical motor map reorganisation or changes in synapse numbers (Adkins et al. 2006). Motor learning following injury is often referred to as motor re-learning.

2.6.5 Mechanisms of motor-related neuroplasticity following injury

A number of animal and human studies have shown that changes in the injured brain can be initiated or enhanced through rehabilitation by mechanisms of neuroplasticity described above, at the level of synapses as well as at the level of motor maps, similarly to the effects of motor learning on undamaged brains (Kleim 2009).

Three strategies for neuroplastic change have been identified to explain cortical reorganisation following focal injury. These are:

- restoration of function in the compromised residual cortical tissue,
- reorganisation of function in the residual tissue to compensate for lost function, and
- recruitment of function within the undamaged hemisphere. This is discussed further in the next section.

(Kleim 2009)

Reorganisation of function in residual tissue is thought to be possible as a result of three characteristics of motor map organisation:

- individual movement are encoded several times in the cortex, allowing for backups to be used in case of injury,
- neurons in the cortex are heavily interconnected, allowing for compensation by undamaged motor neurons,
- motor maps can rapidly change in response to demand.

(Kleim and Schwerin 2010)

2.6.6 Characteristics of motor-related neuroplastic changes after stroke

Several PET and fMRI studies have shown that well-recovered subcortical stroke participants' secondary motor-related cortical areas, such as premotor, supplementary, and prefrontal and parietal motor areas, are activated at a higher degree than in healthy counterparts during finger movement, and that this greater activation is often bilateral (Ward 2010). This reorganisation is thought to occur as a result of an increased contribution from motor cortex areas that are thought to already play a role in directly contributing to the generation of motor outputs in descending pathways, although it is not clear which are utilised to achieve this (Ward 2010). Additional evidence shows a pattern of increased activation of the immediate areas around the lesion (Ward 2010). There is also evidence from data collected from various neuroimaging and electrophysiological techniques that the location of body part representation in the motor cortex (especially the hand) can change after stroke, but that there is no consistency in the direction of change (Ward 2010). TMS studies have shown that motor recovery of the paretic hand is associated with an increase in motor map size and ipsilesional motor cortex excitability (Schaechter 2004).

Other fMRI studies that have examined stroke participants with greater impairments have shown that there is a correlation between the degree of increased activation of bilateral secondary motor-related cortical areas and level of impairment, as well as with the degree of damage to the corticospinal system (as measured with TMS and EMG) (Ward 2010).

A similar correlation between recruitment of the contralesional primary motor cortex and degree of damage to the corticospinal system has also been observed (Ward 2010). In other words, the contralesional primary motor cortex of those with more severely damaged corticospinal tracts plays a larger role in generating movement on the ipsilateral side of the body.

Cumulatively, these findings suggest that after stroke, reorganisation and recruitment of other areas of the motor cortex and associated parallel descending motor pathways can occur within the motor system, and that this phenomenon tends to depend on severity of stroke, particularly on the degree of damage to the corticospinal tract.

Another aspect to consider is how these neuroplastic changes evolve with time. Data from fMRI studies show that increased activation of bilateral secondary motor cortex areas tend to decrease with time as motor function gains are made, towards a more ipsilesional lateralised activation, suggesting that rehabilitation should focus on reducing contralesional activation (Ward 2010). This increase in lateralised activation over time is however not always observed as some studies show that in some individuals, bilateral activity persists, suggesting that not all individuals recover this way, and that reorganisation may be lesion-specific (Ward 2010). Some evidence indicates that those whose lesion includes primary motor cortex and corticospinal tract tend to continue to exhibit bilateral activation, whilst those with a spared primary motor cortex tend to return to a more lateralised ipsilesional activation (Schaechter 2004).

Altered interhemispheric inhibitory mechanisms may explain hemispheric lateralisation activity changes after stroke. In non-lesioned brains, both hemispheres are functionally coupled and hemispheric lateralisation of neural activity during movement is regulated through mutual inhibition mechanisms that occur between motor cortices via trancallosal connections (Butefisch et al. 2008). An interhemispheric inhibitory system compromised by stroke may result in imbalanced hemispheric mutual inhibition, causing an increased inhibitory drive from the contralesional hemisphere onto the ipsilesional hemisphere (Murase et al. 2004).

It is not clear whether contralesional primary motor cortex compensation helps or hinders recovery, as some findings have shown that temporary suppression of the contralesional primary motor cortex (by using TMS on the contralesional hemisphere to decrease inter-hemispheric inhibition) results in transient improvements in motor function (Ward 2010). A possible hypothesis regarding whether contralesional increased activity is an adaptive or maladaptive strategy relates to the severity of the stroke in terms of lesion size. When a stroke affects a small area of the ipsilesional hemisphere, contralesional hemisphere activity would have a detrimental impact on recovery, whereas when a large lesion occurs, the contralesional hemisphere could play an important compensatory role to drive movement (Di Pino et al. 2014). Consequently, suppressing the contralesional motor cortex with TMS or any other non-invasive brain stimulation (NIBS) technique may not be beneficial in all cases, particularly with those with large lesions.

2.6.7 Implications of findings on neuroplasticity for rehabilitation

When selecting which type of rehabilitation to use with people who have had a stroke, an approach that would consider neuroplastic changes could include a decision process which outcome would determine whether the goal of therapy is to normalise ipsilesional motor cortex activity or to encourage contralesional hemisphere activity (Schaechter 2004). Several variables could be considered, such as the neural status of the individual (as determined for example by the integrity of the corticospinal tract as indicated by MEP assessments, as measured by TMS and EMG), time post-stroke, and known effects of rehabilitation approaches on the motor system (Schaechter 2004). Several neurological biomarkers, such as DTI, fMRI, structural magnetic resonance imaging (sMRI), and TMS have been investigated in terms of their ability to predict functional outcomes after stroke, with sMRI and a combination of these biomarkers currently providing the highest quality of evidence for predictions purposes (Kim and Winstein 2017). An example of an accessible algorithm for use in a clinical setting is the PREP2 algorithm (mentioned earlier), which can accurately predict upper limb functional outcome in 75 % of stroke patients using motor function assessments and the presence or absence of an MEP (Stinear et al. 2017).

In parallel to these considerations, research from the last twenty years on motor learning and neuroplasticity has provided therapists with a number of general principles that support positive neuroplastic changes in the damaged brain, targeting stimulation of the reorganised motor cortex. These include:

- The “use it or lose it” principle (non-active neural circuits degrade).
- The “use it and improve it” principle (through specific skills training tasks).
- The importance of specificity (greater gains are acquired through task-related motor skill practice, as opposed to simple motor activity training).
- The importance of repetition of re-learned specific movement sequences (required to induce permanent changes and to allow further gains).
- The importance of intensity (neuroplastic changes require sufficient training).
- The importance of time (rehabilitation should occur early rather than late).

- The importance of salience (training tasks that are relevant and that require attention to the individual induce plasticity to a greater extent).
- The significance of age (younger brains respond better to rehabilitation, as opposed to aged brains).
- The importance of transference (neuroplastic changes gained through a particular training experience can enhance acquisition of similar motor tasks).
- The importance of considering interference (training which incorporates compensatory movements interferes with restoring movement).

(Kleim 2009)

2.6.8 Neuroplastic changes associated with specific rehabilitation therapies

Various upper limb rehabilitation interventions have started to be investigated with regards to their effect on neural reorganisation after stroke. Whilst it is currently difficult to synthesise some of the results as there is a large variability in methodology (target population, intensity of therapy, imaging technique used) and tasks used during testing across studies, as well as ongoing debates about what measures are most appropriate to answer specific questions, a recurrent finding after upper limb rehabilitation is an improved, increased engagement of the ipsilesional hemisphere (Richards et al. 2008). The following is a brief overview of some examples of relevant findings.

2.6.8.1 Neurofacilitation techniques

These techniques are usually associated with the Bobath/Neuro-Developmental Treatment (NDT) and Proprioceptive Neuromuscular Facilitation (PNF) approaches, and include various techniques, including cutaneous/proprioceptive stimulation and weight-bearing through the affected limb. It was shown that some of these techniques can instantly improve motor-evoked potentials (MEP) characteristics (increased frequency and amplitude, decreased latency), as measured with TMS and EMG before and after each technique (in subacute/chronic participants with strokes of various severity), but it is unknown whether this improvement is due to changes in excitability levels in the cortex or in the spinal cord (Hummelsheim et al. 1995).

2.6.8.2 Mental imagery/practice

Mental imagery consists of repetitive, imagined movements, without any actual movement being performed. There is some fMRI evidence that suggests that mental imagery, when combined with repetitive task practice, has a significant effect on the activation of motor cortex areas as measured during wrist movements (in chronic stroke participants with strokes of mild/moderate severity; intervention: 30 minute therapy sessions of task practice, three days a week for 10 weeks, followed by 20-30 minutes of mental practice), and that this improvement correlates with functional recovery (Page et al. 2009).

2.6.8.3 Task-oriented training

A small number of studies investigated the effects of task-oriented training, which consists of repetitive practice of skilled functional tasks. Cumulatively, these studies, which have used various imaging techniques (TMS, fMRI, PET) with various training protocols and participants show that this approach can increase ipsilesional cortex representation of the hand and shift activity from the contralesional hemisphere towards the ipsilesional hemisphere (Liepert et al. 2000; Nelles et al. 2001; Jang et al. 2003).

2.6.8.4 Constraint-induced movement therapy (CIMT)

This therapy approach consists of wearing a constraint mitten over the unaffected hand and practicing tasks with the affected side. Cumulative fMRI findings on CIMT and its effects on neural reorganisation (in a variety of subacute/chronic stroke participants, with varying intervention protocols) suggest that it causes an increased activation within the ipsilesional primary, premotor and supplementary motor cortices (Hodics et al. 2006). One study recruited chronic stroke participants with more severe deficits and its findings showed an increased activation over the contralesional motor areas after therapy (10 four-hour training sessions over two weeks), which is consistent with the theory that individuals with greater deficits tend to recruit the contralesional hemisphere as a means for neural reorganisation (Schaechter et al. 2002).

2.6.8.5 Robot-assisted therapy

One fMRI study investigated the neural effects of the Hand Wrist Assistive Rehabilitation Device (HWARD) in chronic stroke participants with moderate weakness and found significant increases in ipsilesional motor cortex activation after therapy (15 ninety-minute training sessions over three weeks) (Takahashi et al. 2008).

2.6.8.6 Virtual reality (VR) training

This type of training typically involves real-time simulation of an activity within an environment presented to the user through immersive (e.g. large screen projection, VR goggles) and non-immersive (e.g. computer screen) systems. One study used an immersive system, the IREX, for providing therapy (20 sixty-minute sessions over four weeks) to chronic stroke participants with mild to moderate hemiparesis, and found a significant shift from bilateral motor cortex activation towards a more predominant ipsilesional activation (Jang et al. 2005), as measured by fMRI.

2.6.8.7 Bilateral arm training

This approach is usually used with individuals with more severe deficits, and makes use of the interlimb coupling concept. It consists of repetitive bilateral movements with a view to stimulate interhemispheric facilitation of limb movement. A study showed that cortical activity (as measured by fMRI) after therapy (18 one-hour sessions over six weeks) in chronic stroke participants was increased over the contralesional hemisphere, which is consistent with the theory that individuals with more severe baseline deficits tend to utilise the contralesional hemisphere as a compensatory mechanism (Luft et al. 2004a).

2.7 Electroencephalography

This section introduces electroencephalography, the method used in this study.

In 1929, Hans Berger, a German psychiatrist, was the first to report the possibility of recording human brain electrical activity (in the form of voltage variations over time) by placing an electrode on the scalp (Luck 2005). Following this discovery, EEG became a recognized scientific tool and a multitude of studies and applications were developed in the following decades.

2.7.1 Definition

Electroencephalography (EEG) is a technique used to record electrical activity generated by the cortex, on the surface of the scalp (Stern et al. 2001).

2.7.2 Neurophysiological basis of EEG

Electroencephalography records the intensity of the net postsynaptic potentials of synchronous activity of populations of cortical cells, as voltage variation over time (Stern et al. 2001). Action potentials do not significantly contribute to EEG signals, and there are several reasons for this. Firstly, the surface of the cortex is largely made up of grey matter, which mainly contains neural cell bodies and dendrites, where synapses are situated, in contrast with white matter, situated further away from the surface of the scalp, which contains axons, where action potentials travel (Marieb and Hoehn 2010). Secondly, the area of membrane that is depolarised by a single action potential is small, compared to the relatively larger area (comprised of dendrites, cell body and axon hillock) where numerous postsynaptic potentials occur (Niedermeyer and Lopes da Silva 1999). Thirdly, action potentials have a short duration (1-2ms), compared to postsynaptic potentials (10-250ms), which as a result overlap much less than do postsynaptic potentials (Niedermeyer and Lopes da Silva 1999).

2.7.3 Recording procedure

Typical recording procedures involve the use of an array of ‘active’ electrodes, which location follows the standardised International 10-20 electrode system (sites at 10 or 20 % from four anatomical landmarks: nasion, inion, preauricular points) or the Modified Combinatorial Nomenclature, which builds on the 10-20 system by adding additional electrodes (see Figure 6) (Niedermeyer and Lopes da Silva 1999; Stern et al. 2001).

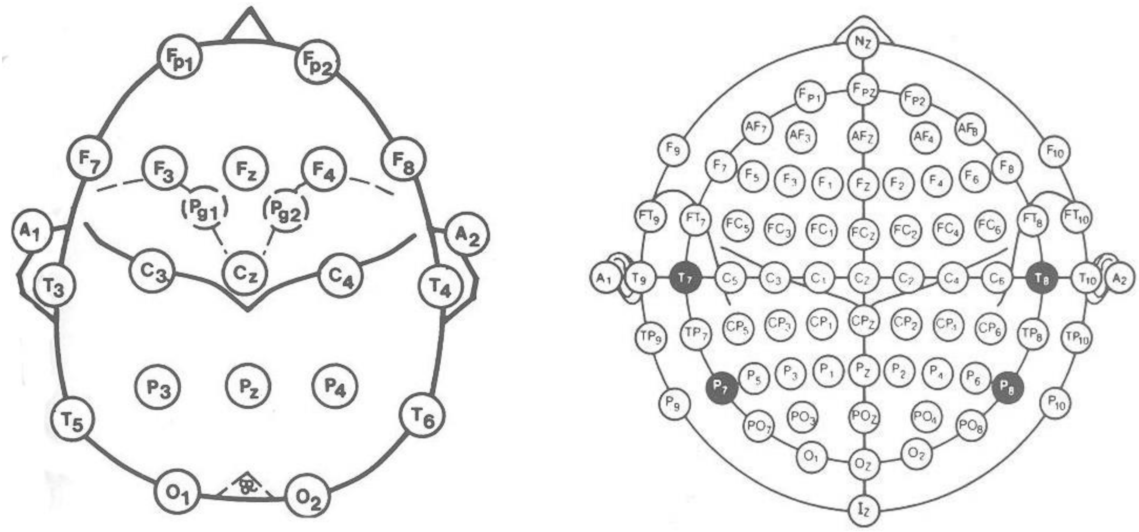


Figure 6 10-20 system (left) and Modified Combinatorial Nomenclature (right) (Niedermeyer and Lopes da Silva 1999). Copyright of Williams & Wilkins reproduced with permission.

A reference electrode also needs to be applied to a site that is away from the active electrodes, such as the ears, mastoids or nose, in order to provide a reference potential with which measurements from all active electrodes can be measured up to. A ground electrode is placed elsewhere on the scalp or body in order to calculate the difference between the active-ground voltage and the reference-ground voltage, which is then amplified by differential amplifiers (Niedermeyer and Lopes da Silva 1999; Stern et al. 2001; Luck 2005). These analogue signals are converted to digital signals and relayed to a computer which records them using specialised software. In order for the recording to be accurate, an impedance (resistance) of less than 5-10 kΩ needs to be achieved for each active electrode, in order to minimise noise and prevent signals from being attenuated whilst crossing the skin (Stern et al. 2001). This is attained with the use of abrasive and conductive gels, which are applied between each electrode and the scalp surface underneath. The abrasive elements of these gels also remove dead skin cells, oil, and dirt, which is helpful to reduce impedance.

2.7.4 Limitations/problems

The main difficulties with EEG come from the fact that it is a sensitive recording instrument and as such, its data can be easily corrupted by nearby unwanted electrical noise artefacts generated by the person or environmental sources. This can be from heartbeat, respiratory, sweat, or pulse artefacts as well as from muscle contractions from nearby body parts involved in facial expressions, talking, eye blinking, eye movements, tongue movements, or from 50 Hz (60 Hz in the Americas) interference from electrical equipment such as electrical power supplies or fluorescent light fixtures (Stern et al. 2001; Tatum et al. 2011). It is thus important to improve the signal-to-noise ratio by considering the physical environment in which the recordings are made, by instructing the participant to be muscularly relaxed and to fix their gaze during recordings (Stern et al. 2001), by inspecting the data to determine the nature and location of such artefacts, and by considering the validity of the data in light of these. In addition to this, the signal-to-noise ratio can be improved by using spatial filtering methods such as the common average reference and Laplacian filtering (Wolpaw et al. 2002).

Study protocols often present the participant with a particular stimulus: a sound, a film, or a cue to perform a cognitive task or movement. It is therefore important that the stimulus and associated task(s), if applicable, remain identical for each recording, as variations could produce different signals. To increase the reliability of the data, tasks are repeated several times (between 50 and 150 times for movement-related EEG), and signals are averaged to reduce the effects of variability.

Whilst it offers good temporal resolution, EEG has inferior spatial resolution than fMRI. Conversely, fMRI has better spatial resolution but lacks high temporal resolution (Stern et al. 2001).

2.7.5 EEG data

EEG data reflects the summation of the synchronised activity of large populations of neurons at varying frequencies, and depends on the state of brain functioning, such as sleep, wakefulness, cognitive processing, and motor function (Stern et al. 2001).

Three basic parameters characterise EEG signals: amplitude (the peak-to-peak size of the wave, in voltage variation), frequency (the number of cycles per second, in Hertz), and location (Stern et al. 2001). Human scalp EEG signals vary in amplitude between 10 and 100 µV, and in frequency from 0.3 to 30 Hz and above (Niedermeyer and Lopes da Silva 1999).

2.7.5.1 Spontaneous EEG

Cortical activity can be recorded in resting participants, at any time, in a continuous fashion. In this case signals are referred to as 'spontaneous EEG' (Stern et al. 2001). Several EEG bands, characterised by their frequency range, are recognisable: delta, theta, alpha, beta, and gamma (Stern et al. 2001). Table 5 presents different types of spontaneous EEG bands, their frequencies, amplitudes, and what type of brain activity they have been said to be associated with.

EEG band	Frequency range	Amplitude	Brain activity/phenomena
Delta (δ)	0.3-4 Hz	High	deep sleep may be indicative of brain tumours predominant during two first years of life
Theta (θ)	4-8 Hz	Variable	drowsiness, hypnagogic (sleep inducing) imagery, REM, hypnosis, sleep problem solving, attention (there may be two different types of theta activity: 1) low levels of alertness, and 2) active processing of cognitive/perceptual tasks)
Alpha (α)	8-12 Hz	Variable: mostly < 50 µV	relaxed wakefulness eyes closed lack of active cognitive processes
Beta (β)	12-30 Hz	Mostly < 30 µV	occurs when one is alert
Gamma (γ)	30-70 Hz	Low	associated with the brain's ability to amalgamate a number of stimuli into a coherent whole

Table 5 Spontaneous EEG frequency ranges and associated brain activity (Niedermeyer and Lopes da Silva 1999; Cacioppo et al. 2000; Stern et al. 2001).

Alpha frequencies are predominant in individuals who are awake, relaxed, with eyes closed, and not engaged in any physical or cognitive activity (Stern et al. 2001). When this state is disturbed, alpha activity decreases. This is sometimes referred to as 'alpha blocking' (Stern et al. 2001).

2.7.5.2 Movement-related cortical potentials

Cortical activity can also be recorded before, during and after a specific event. This could be for example during exposure to a visual stimulus (causing a visual evoked response), a sound (causing an auditory evoked response), stimulation of the skin (causing in this case a somatic evoked response), or movement of a limb (Stern et al. 2001). This cortical activity is referred to as induced activity, and if it is phased locked to the event with every repetition of the event, it is referred to as evoked activity (Stern et al. 2001). Evoked responses are also referred to as event-related potentials (ERPs), and consist of a recognisable sequence of voltage variations (Stern et al. 2001). These are useful to obtain information about brain functioning under different conditions.

ERPs are smaller in voltage (1-10 µV) than the ongoing EEG signals described above and require that the individual repeat a task or be exposed to a stimulus several times in order for the ERPs to be extracted (using coherent averaging) from the ongoing spontaneous EEG signals (Stern et al. 2001).

ERPs that are associated with voluntary movement are referred to as movement-related cortical potentials (MRCPs). A visual representation of an MRCP is shown on Figure 7. The first part of the pre-movement segment of the potential (prior to the ‘0’ value on the x axis, which is when movement starts) is known as the ‘Bereitschaftspotential’ (BP) (also known as the ‘readiness potential’ (RP)), and is thought to result from supplementary motor area activity, whereas the second part (referred to as the ‘negative slope’ (NS’)) is thought to represent both supplementary motor area and contralateral motor cortex activity (Neshige et al. 1988) involved in planning and preparing movement (see Figure 7). The BP segment begins up to one second or longer before movement onset, and is maximal symmetrically over the midline centro-parietal area (Shibasaki and Hallett 2006; Colebatch 2007). The NS’ segment begins 500 ms before movement onset and occurs predominantly over the contralateral precentral cortex (Colebatch 2007).

Another component of the MRCP, associated with movement execution, is the motor potential (MP), which occurs on the contralateral hemisphere 10 ms prior to movement and peaks shortly after, and most likely represents activity in the primary motor cortex (Shibasaki and Hallett 2006).

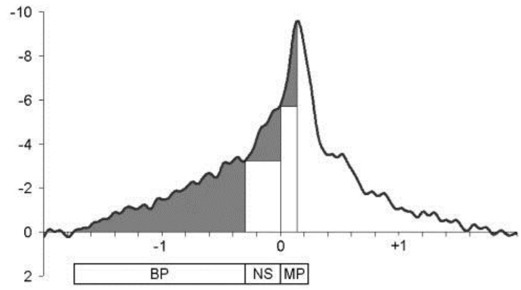


Figure 7 MRCP components: pre-movement segments BP and NS', and movement execution segment MP (x axis: time in seconds relative to movement onset at '0'; y axis: voltage in µV, negative up) (Wiese et al. 2005). Note that in the usual convention for EEG the vertical axis is inverted. Copyright of Wolters Kluwer Health reproduced with permission.

2.7.5.3 Movement-related ERD/ERS

A different way of analysing EEG data generated by a specific event is by examining EEG frequency power variations during perceptual, judgement, memory, and movement tasks (Pfurtscheller and Lopes da Silva 1999). This is done by analysing increases or decreases of power in specific frequency bands (Pfurtscheller and Lopes da Silva 1999).

As mentioned earlier, when an individual is in a state of relaxed wakefulness, not engaged in any significant physical or cognitive activity, alpha band frequencies are predominant. In other words, a large number of neurons are synchronously active (they fire simultaneously) at a frequency between 8 and 12 Hz in the alpha band. If this same individual moves a limb, this alpha frequency predominance will decrease over the areas of the motor cortex that are involved with production of movement. When referring to the alpha band, specific rhythms within the alpha frequency range, called mu rhythms, have been observed to have their own pattern of power attenuation (including topography) as a result of active, passive, and imagined movements (Pfurtscheller and Lopes da Silva 1999). This power attenuation is called event-related desynchronisation (ERD), in this case alpha desynchronisation (or alpha ERD), as networks of neurons that were previously synchronously active in the alpha band become less synchronised in the alpha band, causing their activity to cancel out when averaged, resulting in a reduced alpha activity. The term 'desynchronisation' should not be confused with the concept of 'de-activation of neurons' as in this case desynchronisation relates to the activation of neurons to produce movement. In addition to ERD in the alpha band, ERD also occurs in the beta band.

Conversely, when networks of neurons become progressively synchronised in a given frequency range, this is referred to as event-related synchronisation (ERS). ERS occurs, for example, after the end of a movement, in the beta band. Again, the term 'synchronisation' should not be confused with the concept of 'activation of neurons' as in this case synchronisation relates to the deactivation of neurons involved in the production of movement. Immediately after the end of the movement, neurons increasingly fire synchronously in the beta band for a period of time. ERS also takes place in the alpha band after movement, but this occurs more slowly, as it returns to its pre-movement state.

For movement tasks, a predictable sequence of frequency power changes occurs. ERD and ERS have been observed to occur before, during, and following voluntary movement, in the alpha, beta, and gamma bands. Figure 8 illustrates the time course of movement-related ERD/ERS.

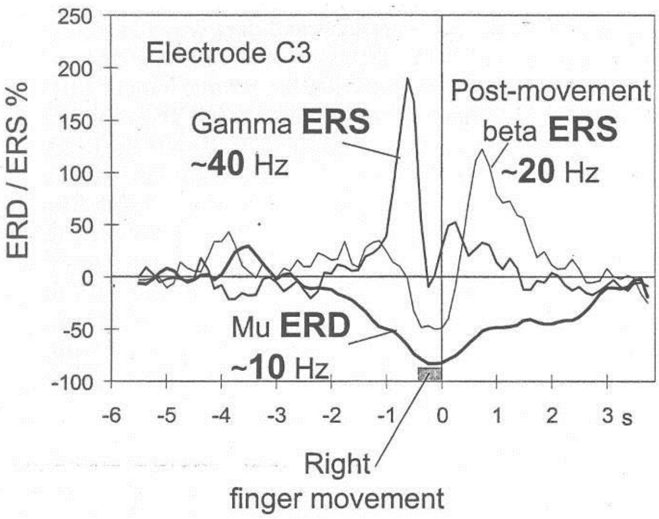


Figure 8 Band power changes for right finger movement for electrode C3 (x axis: time in seconds relative to end of movement at '0'; y axis: ERD/ERS% (upward slope= synchronisation and downward slope= desynchronisation)). Mu ERD and beta ERD occur before and during movement, gamma ERS occurs just before and during movement, and beta ERS occurs after movement (Niedermeyer and Lopes da Silva 1999). Copyright of Williams & Wilkins reproduced with permission.

Alpha/beta ERD starts about two seconds before self-paced movement onset and beta ERS at approximately 500 ms after termination of the movement, and reaches its peak at around one second (Pfurtscheller and Lopes da Silva 1999).

Maximum alpha/beta ERD and beta ERS can be observed over areas of the motor homunculus, according to the part of the body that is moved (Pfurtscheller and Lopes da Silva 1999). ERD starts over the contralateral hemisphere and becomes bilateral immediately before movement onset, whilst beta ERS is dominant over the contralateral hemisphere (Pfurtscheller and Lopes da Silva 1999). When several joints are moved simultaneously, such as in whole-arm movements, ERD is not as spatially focused and occurs over large cortical areas, including precentral, central, and posterior areas (see Figure 9). Post-movement ERS however remains localised to the motor cortex (Pfurtscheller et al. 1999).

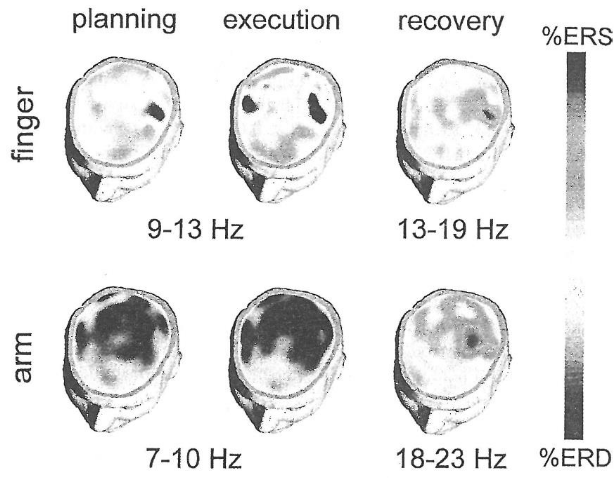


Figure 9 ERD/ERS scalp maps showing areas over which ERD/ERS occurs for finger and arm movements during movement planning and execution, and recovery (Pfurtscheller et al. 1999). Copyright of Elsevier reproduced with permission.

Pre-movement ERD and MRCPs are thought to possibly be generated by non-identical neuronal mechanisms, as their spatial activations over time differ: MRCPs start bilaterally and become larger over the contralateral hemisphere as movement onset approaches, whilst ERD starts over the contralateral hemisphere and spreads bilaterally just before movement onset (Shibasaki and Hallett 2006). The reasons for differing pre-movement MRCP and ERD spatiotemporal patterns are unknown (Shibasaki and Hallett 2006).

Table 6 details frequencies for each EEG band involved in movement-related ERD/ERS.

EEG band	Frequency range	ERD/ERS and movement
Alpha (α)	8-12 Hz	Pre-/during movement alpha ERD
Beta (β)	12-30 Hz	Pre-/during movement beta ERD Post-movement beta ERS
Gamma (γ)	> 30 Hz	Gamma ERS just before and during movement

Table 6 EEG bands, frequency ranges, and ERD/ERS during voluntary movement (Pfurtscheller and Lopes da Silva 1999; Cacioppo et al. 2000; Stern et al. 2001).

Frequencies at which ERD and ERS occur vary from person to person, and depend on the type of movement that is performed (Pfurtscheller et al. 1999).

For alpha and beta frequencies, ERD is interpreted as a correlate of increased activation of a cortical area and ERS as a correlate of deactivation (Pfurtscheller 2001). This is due to two reasons.

Firstly, it has been observed that the number of synchronous neurons is inversely proportional to frequency (Pfurtscheller and Lopes da Silva 1999). The diagram in Figure 10 illustrates this by showing that larger numbers of synchronous neurons (top of diagram, represented by a large encircled area of neurons) oscillate at lower frequencies (in this example, 10Hz), whilst smaller numbers of synchronous neurons (bottom of diagram) oscillate at higher frequencies (in this example, 12Hz).

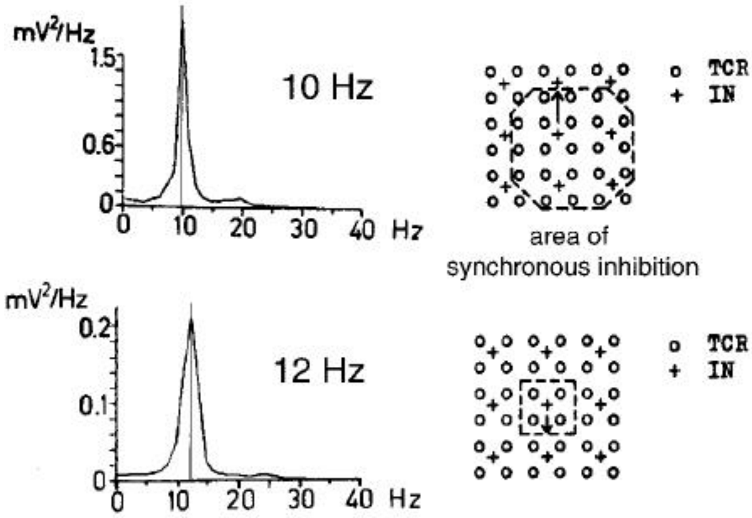


Figure 10 The relationship between frequency and number of synchronous neurons. Larger number of synchronous neurons (top) oscillate at a lower frequency (10 Hz vs. 12 Hz) than smaller number of synchronous neurons (bottom). In this example, TCR: thalamic relay cells and IN: interneurons (Pfurtscheller and Lopes da Silva 1999). Copyright of Elsevier reproduced with permission.

Secondly, neural networks require that they work in a relatively independent manner as smaller populations of neurons need to be able to fire at different rates independently to carry out specific tasks (Pfurtscheller 2001). In other words, the overall number of synchronised neurons decreases as neurons involved in a task (for example neurons involved with movement of a specific limb) are activated and fire at a different frequency from all the others.

It follows that as these smaller populations of neurons activate in a discrete fashion, their firing frequency increases (see Figure 10 for an explanation of the relationship between number of synchronous neurons and frequency), hence the reason why lower frequencies desynchronise, as the number of neurons oscillating at lower frequencies decreases. Following movement, synchronisation of these lower frequencies re-occurs as cortical networks de-activate and more neurons fire at the same (lower) frequencies.

In healthy participants, the intensity of alpha and beta ERD has been found to correlate with levels of cortical excitability (Matsumoto et al. 2010; Kasuga et al. 2015; Daly et al. 2018).

Gamma ERS functions differently and is said to be related to higher-level sensorimotor integration, as it is thought that faster oscillations are required to link spatially separated groups of cells (Pfurtscheller and Lopes da Silva 1999). Its maximum is reached shortly before movement onset and during movement execution (Pfurtscheller and Lopes da Silva 1999).

Data processing

ERD and ERS are quantified in percentage of power decrease (ERD%) or increase (ERS%) at a given frequency or frequency range at a specific electrode site (Pfurtscheller and Lopes da Silva 1999). Power, the square of amplitude (in μV^2), rather than amplitude itself, is used to quantify the magnitude of the signal (Handy 2005). This allows for values to never be negative.

Power is proportional to the square of voltage (Handy 2005). This comes from the following relationships:

$$\text{voltage} = \text{current} * \text{resistance (Ohm's law)}$$

and

$$\text{power} = \text{voltage} * \text{current}.$$

As a result, $\text{power} = \dfrac{\text{voltage} * \text{voltage}}{\text{resistance}}$.

When considering this relationship, it is common practice to implicitly set the resistance to 1.0, so that power equals the square of voltage (Handy 2005).

To compute ERD/ERS power changes over time, raw EEG signals are processed in the following manner:

- bandpass filtering of each repetition of the event/task at the desired frequency,
- squaring of the amplitude to obtain power samples, and
- averaging of all power samples (Pfurtscheller 2001).

ERD% and ERS% values are then determined by computing the difference between the power (in a given frequency band) during the period of interest and a resting reference period:

$$\text{ERD\% or ERS\%} = \frac{(A - R)}{R} \times 100$$

R is given by the power (in a given frequency band) during the resting reference period and A is given by the power (in the same given frequency band) either before, during, or after the performed movement (Pfurtscheller 2001). By using this equation, positive values are obtained for ERS%, and negative values are obtained for ERD%. Figure 11 displays data processing steps and an example of time-varying ERD and ERS values throughout an experimental period.

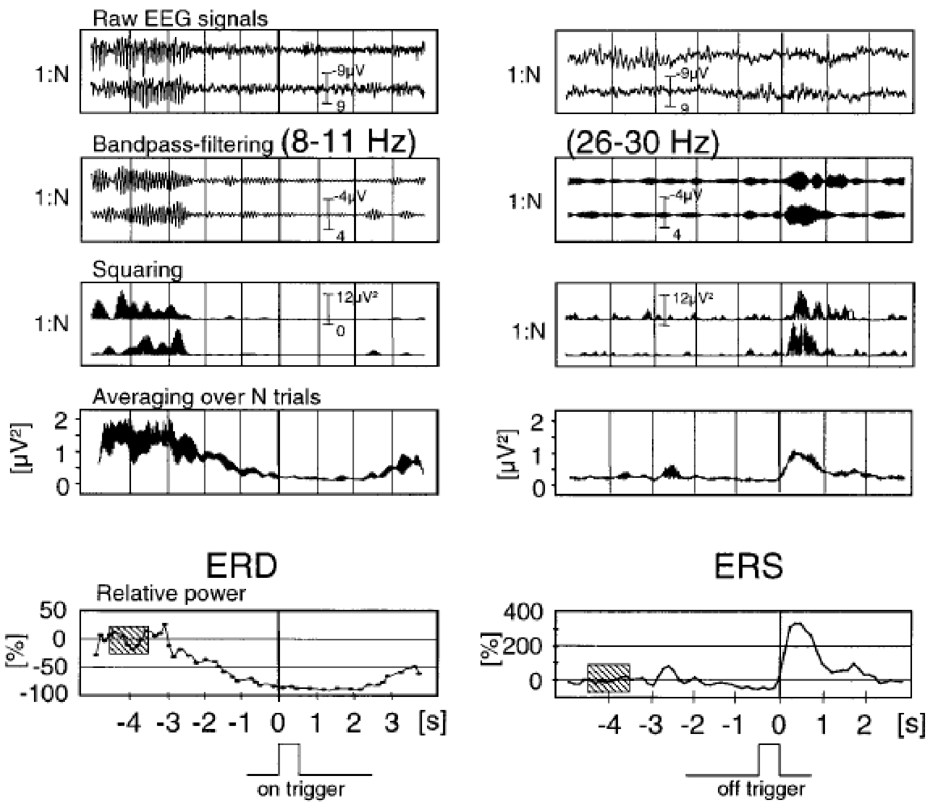


Figure 11 ERD (left panel) and ERS (right panel) data processing and time course (Pfurtscheller and Lopes da Silva 1999). Copyright of Elsevier reproduced with permission.

Data analysis

ERD/ERS data can be analysed according to intensity, location, and time course (Pfurtscheller and Lopes da Silva 1999). The intensity of ERD/ERS can be compared, in percentage values, by considering peak relative power changes. Location and hemispheric lateralisation (predominance or bilaterality of cortical activation over hemispheres) of ERD/ERS may be investigated according to the spatial mapping of the signals, as they can be traced back to specific electrodes. The time course of ERD/ERS can also be examined by contrasting the timing of ERD/ERS peak values.

Chapter 3: Literature review

3.1 Introduction

This chapter presents an overview of relevant findings regarding movement-related ERD/ERS (focusing on the upper limb) among healthy individuals and stroke participants. Gaps in knowledge and the need for further research are discussed.

3.2 Method

A literature search was carried out using the MEDLINE, EMBASE and CINAHL databases. The following keywords were used in combination: "Stroke", "Electroencephalography", "Neuronal plasticity", "Cortical Synchronization", "Event-related desynchronisation", "Event-related synchronisation", "ERD", "ERS". Search results were evaluated for relevant content to the study. The ISI Web of Knowledge was also used to set up citation alerts in order to identify newly-published journal articles that cited pertinent articles.

3.3 Movement-related ERD/ERS findings

The term ERD was introduced by Pfurtscheller and Aranibar in 1977 when they reported, for the first time, data on movement-related ERD during hand movement (Pfurtscheller and Aranibar 1977). Key publications which describe ERD and ERS in further detail include a review in the Clinical Neurophysiology journal (Pfurtscheller and Lopes da Silva 1999), as well as Chapter 16 of the Handbook of Electroencephalography and Clinical Neurophysiology (Pfurtscheller et al. 1999). Best practice principles included in these publications have been considered in the design of this study.

The term 'contralateral' refers to the hemisphere opposite to the side of the arm that was used to perform the movement, and 'ipsilateral' refers to the hemisphere on the same side of the arm used to perform the movement. The term 'ipsilesional' refers to the hemisphere lesioned by stroke and 'contralesional' refers to the hemisphere opposite to the ipsilesional hemisphere.

3.3.1.1 ERD/ERS among healthy participants

In healthy participants, the time course of movement-related alpha ERD has been found to be almost identical for fast and slow finger movements, despite the fact that fast movements are pre-programmed and that slow movements require additional sensory processing from kinaesthetic feedback (Stancak and Pfurtscheller 1996b). Alpha ERD characteristics are also similar for index finger, thumb, and hand movements (Pfurtscheller et al. 1998). An interpretation of these findings is that alpha desynchronisation represents an unspecific pre-activation of neurons, independently from speed and type of movement (Pfurtscheller and Lopes da Silva 1999).

The topography of ERD has been found to vary according to frequency. Beta ERD occurs more anteriorly than alpha ERD (Pfurtscheller and Lopes da Silva 1999). It is postulated that this is due to the fact that alpha rhythms are mainly generated in the sensory cortex whilst beta rhythms are predominant in the motor cortex (Pfurtscheller and Lopes da Silva 1999; Shibasaki and Hallett 2006).

ERD has also been observed during motor imagery (imagination) of movement (Neuper and Pfurtscheller 1999).

The amplitude of alpha ERD has been observed to increase with learning of a movement sequence, and to decrease once the sequence is learned (Zhuang et al. 1997). Another study reported an increase in beta ERD amplitude during movement preparation and execution after a single session of motor training of a highly skilled hand motor task (laparoscopic surgery simulation) with the non-dominant hand (Jochumsen et al. 2017).

Handedness has been identified as a factor that has an effect on alpha ERD. Right-handed participants exhibit larger lateralisation prior to movements on the right side than on the left side, whereas left-handed participants show approximately equal contralateral predominance for movements on both sides (Stancak and Pfurtscheller 1996a). Beta ERD is also affected when right-handed participants perform finger movements with their left hand. In this case, beta ERD starts bilaterally and remains bilateral for the rest of the movement (Bai et al. 2005).

Age also has an influence on ERD. Evidence shows that older adults exhibit a longer, greater, and more spatially diffused alpha ERD over frontal and parietal areas, as opposed to more defined central regions for younger individuals (Derambure et al. 1993). Age is also a factor when imagined movements are performed, where older adults, when compared to younger adults, present with a reduced lateralisation of alpha ERD, due to a stronger ipsilateral alpha ERD (Zich et al. 2015).

It has been shown that alpha and beta ERD for movement of a certain body part can be accompanied by beta ERS for another. For example, it has been observed that a foot area ERS occurs during hand ERD when it is moved, and when the foot is moved, the opposite pattern occurs (Pfurtscheller and Neuper 1994). This antagonistic phenomenon, labelled as ‘focal ERD/surround ERS’ is thought to be gated by thalamic structures and likely represents a mechanism of activation and deactivation of cortical areas (Pfurtscheller and Lopes da Silva 1999). It was also observed that a contralateral beta ERD can be accompanied by an ipsilateral beta ERS during an imagined hand movement (Pfurtscheller and Lopes da Silva 1999).

As for post-movement beta ERS, it has been found to be greater for wrist movements, when compared to finger movements (Pfurtscheller et al. 1998), and is exhibited during imagined movements (Neuper and Pfurtscheller 1999). It has similar amplitudes with slow and brisk finger movements (Pfurtscheller et al. 1997).

Gamma band activity during movement has been investigated in more detail using MEG technology (which essentially measures the same electrical activity by recording associated magnetic fields, but differs from EEG in that it is only sensitive to tangential cortical activity found in the brain's cortical folds (Stern et al. 2001)). As gamma activity is reported to be difficult to accurately measure using EEG as these frequencies can potentially be contaminated by muscle activity, MEG is preferable as its sensors are not in contact with the head (Stern et al. 2001; Cheyne et al. 2008). In addition to 40 Hz gamma ERS described in Chapter 2, a MEG study reported consistent (19 out of 20 healthy participants) contralateral high gamma ERS (70-150 Hz) during unilateral finger movement, with 15 of them displaying ipsilateral gamma ERD and contralateral gamma ERS within broad gamma band (30-150 Hz) (Huo et al. 2010). These findings are consistent with two previous MEG studies that also evidenced high gamma ERS in the contralateral motor cortex (Cheyne et al. 2008; Dalal et al. 2008).

A summary of findings is presented in Table 7. Methodological weaknesses and important omissions are included in the 'Comments' column of this table.

Author(s)	**Participants**	**Movement(s)**	**Results**	**Comments**
Stancak & Pfurtscheller (1996b)	10 healthy volunteers, all right-handed except one	self-paced brisk and slow right index finger extensions/flexions (100 trials per condition)	time course of alpha ERD identical for brisk and slow movements (at electrode locations over the left sensorimotor area)	

Author(s)	Participants	Movement(s)	Results	Comments
Pfurtscheller et al. (1998)	11 right-handed healthy volunteers	3 self-paced brisk movements: right index extension and flexion; pressing button with right thumb; right wrist flexion and extension (70-80 trials per condition)	pre-movement alpha ERD similar for all movements (at electrode location C3)	-same results for movement of larger joints in combination?
Zhuang et al. (1997)	17 right-handed healthy volunteers	cued button pressing with right hand fingers in repeated series (13x100 trials)	maximal alpha ERD was observed during initial learning, and diminished subsequently (at electrode location C3)	
Jochumsen et al. (2017)	47 healthy volunteers (42 right-handed and 5 left-handed); 16 had a single 45 minute session training, nine had six 45 minute sessions (+ nine in a control group without training), and 13 were in a separate control group involving a different type of training (single session)	cued palmar hand grasps (90 trials) with non-dominant hand before and after one or six sessions	increase in beta ERD amplitude during movement preparation and execution after a single session of motor training (laparoscopic surgery simulation); hypothesised that (as per previous literature findings) ERD amplitude increases until task becomes easier (at electrode locations FCz, Cz, and contralateral electrode (C3 or C4))	-handedness not specified within groups
Stancak & Pfurtscheller (1996a)	12 right-handed and 11 left-handed healthy volunteers	randomised self-paced brisk and slow left or right index finger (75-80 trials per condition)	right-handed participants show significantly larger lateralisation of alpha ERD on the right side; left-handed participants show equal contralateral preponderance for both sides (average of 2 electrode locations on each hemisphere showing largest ERD)	

Author(s)	Participants	Movement(s)	Results	Comments
Bai et al. (2005)	9 right-handed healthy volunteers	3 self-paced, pseudo-random key strokes with either hand (with index, middle and ring fingers) (250 trials per hand)	lateralisation of beta ERD observed during preparation of right hand movements, and bilateral beta ERD observed during preparation of left hand movements (at electrode locations C3, C4, P3, P4, and electrodes between C3 and P3, and between C4 and P4)	
Derambure et al. (1993)	9 young (age range 21-26) and 9 older (65-79) right-handed healthy volunteers	self-paced button pressing with left and right thumbs (90 trials)	older adults have a longer, higher-amplitude, more spatially diffused alpha ERD than young individuals (at electrode locations over the sensorimotor area)	
Zich et al. (20015)	39 young (mean age 23.6, SD 2.7 years) and 36 older (62.7, SD 5.7 years) right-handed healthy volunteers	(no movement) Cued imagined left and right thumb abduction (3x40 trials (20 left and 20 right trials in random order))	older adults present with a reduced lateralisation of alpha ERD when compared to younger adults, due to a stronger ipsilateral alpha ERD (over sensorimotor cortex)	
Pfurtscheller & Neuper (1994)	3 right-handed healthy volunteers	cued 1) button pressing with left or right index finger, 2) tongue movement, and 3) right foot toe upwards movement (98 trials per condition)	when alpha ERD occurs when one body is part is moved, a power increase in the alpha band is observed over other body parts' cortical areas (at electrode location over hand area near C3)	-small number of participants

Author(s)	**Participants**	**Movement(s)**	**Results**	**Comments**
Pfurtscheller et al. (1998)	11 right-handed healthy volunteers	self-paced 1) brisk extension/flexion of index finger, 2) brisk pressing of a button on a joystick with thumb, and 3) brisk flexion and extension of wrist (all on right side) (70-80 trials per condition)	post-movement beta ERS larger for wrist movements than for finger and thumb movements (at electrode location C3)	
Neuper & Pfurtscheller (1999)	18 right-handed healthy volunteers	(no movement) cued imagination of lifting movement with left or right hand (4x40 trials (20 left and 20 right trials))	ERD and ERS observed during motor imagery (imagination) of movement; different laterality features than for actual executed movements (at electrode locations C3, Cz, and C4)	
Pfurtscheller et al. (1997)	12 right-handed healthy volunteers	self-paced brisk and slow right index finger extension/flexion (75-80 trials per condition)	similar post-movement beta ERS amplitude for brisk and slow finger movements) (at electrode position over sensorimotor area with largest beta ERS)	-no statistical test reported
Huo et al. (2010)	20 right-handed healthy volunteers	cued brisk left or right index finger tapping (200 trials)	(MEG study) contralateral high gamma band ERS was observed consistently during movement, whilst ipsilateral gamma ERD and contralateral gamma ERS in broad gamma band were observed inconsistently (over primary motor cortex)	-also observable with EEG?

Author(s)	Participants	Movement(s)	Results	Comments
Cheyne et al. (2008)	9 right-handed healthy volunteers	self-paced left or right 1) index finger abduction, 2) elbow flexion, and 3) foot dorsiflexion (100-130 trials per condition)	(MEG study) contralateral high gamma band (65-80 Hz) ERS observed during movement (over primary motor cortex)	-also observable with EEG?
Dalal et al. (2008)	12 right-handed healthy volunteers	self-paced button pressing with right or left index finger (100 trials)	(MEG study) contralateral high gamma ERS observed during movement (over sensorimotor cortex)	-also observable with EEG?

Table 7 Summary of findings for ERD/ERS among healthy participants.

In healthy volunteers, learning was found to have an effect on alpha ERD, which creates an association between the effects of learning and cortical activation levels. As handedness and age have a significant effect on alpha ERD, it follows that these characteristics must be considered in order to minimise variability. As right-handers who perform movements on the right side show a more lateralised alpha ERD prior to movement than when performing left sided movements, this must be taken into consideration when analysing hemispheric lateralisation. Post-movement beta ERS seems to be more sensitive to the type of movement performed, but not to its speed.

No obvious conclusions can be made from gamma band activity studies as they only describe observed activity. More research is required in this area to identify what factors cause this measure to vary.

Again, it is difficult to generalise these findings to other joints or movements, as these results were obtained in varying experimental conditions.

3.3.1.2 ERD/ERS among people who have had a stroke

The effects of stroke on ERD and ERS have also been examined by a small number of studies in different contexts.

In a MEG study, contralateral hemisphere beta ERD was found to be reduced in stroke participants compared with healthy volunteers, with stroke participants with greater motor impairments having more reduced beta ERD (Rossiter et al. 2014).

The magnitude of both alpha and beta ERD has also been found to vary according to the type of lesion in severely paralysed chronic stroke participants. It was found to be tendentially (not statistically) less pronounced in participants whose lesion involved the primary motor cortex, when compared to those with lesions where it was spared (Ray et al. 2017).

ERD was found to be less over the affected hemisphere during movement of the affected hand than over the unaffected hemisphere (Pfurtscheller et al. 1980). Similar results were found in another study where alpha ERD was stronger in the unaffected hemisphere than in the affected hemisphere when the affected hand was moved (Stepien et al. 2011).

The duration and intensity of beta ERD and ERS were found to correlate with motor function in a MEG study. A longer beta ERD was observed in individuals with poor motor function, whereas a longer beta ERS was observed in high-functioning individuals (Shiner et al. 2015). The same study showed that a stronger beta ERD and ERS and a greater relative activity over the ipsilesional hemisphere correlated with greater upper limb function.

ERD and ERS have been found to vary according to types of deficits associated with motor function in subacute stroke participants i.e. hemiparesis vs. somatosensory deficits vs. ideomotor apraxia combined with mild hemiparesis (Platz et al. 2000). During a triangular trajectory performed with the index finger, individuals with mild/moderate hemiparesis showed increased alpha ERD in frontolateral areas (possibly reflecting heightened activation associated with attention to performance) and increased beta ERS in occipital areas (interpreted as potentially reflecting an idling state in visual areas) (Platz et al. 2000). Participants with somatosensory deficits exhibited reduced alpha and beta ERD during movement preparation and execution, reflecting a potential role for somatosensory input in contributing to ERD, whereas participants with ideomotor apraxia had reduced beta ERD during movement preparation, possibly reflecting deficits in areas that are thought to be involved with ideomotor praxis, these being the more anterior regions of the motor cortex involved in movement planning (Platz et al. 2000).

A subsequent study, using the same movement task as above, examined whether MRCPs and ERS/ERD could be used to predict levels of motor recovery among subacute/chronic stroke participants undergoing a specific rehabilitation approach, the Arm Ability Training (Platz et al. 2002). It was found that pre-movement EEG data collected before a three week period of rehabilitation could in fact predict functional measure scores, as measured by the TEMPA upper limb assessment. However, EEG data was not collected following rehabilitation. This result nevertheless creates a link between EEG measures and predicted motor recovery.

Another study aimed to determine whether pre-movement ERD during reaching movements could be used as a signal for brain-computer interfaces (BCIs), in order to guide robot-assisted rehabilitation. Its results show that pre-movement alpha ERD was found to be significantly lower in chronic stroke participants (when compared to healthy volunteers), and that pre-movement alpha ERD was significantly higher when the non-dominant hand was used, across both stroke and control groups (Fu et al. 2006). Problems with data corruption in the beta frequency band prevented a complete analysis of pre-movement ERD.

The relationship between ERD/ERS laterality measures and severity of motor impairment and spasticity after stroke has also been examined during imagined and performed grasping and finger extension movements. Findings show that greater motor impairment is related to an increased ERD in the unaffected hemisphere (during imagined movements), and that greater spasticity is related to an increased ERD in the affected hemisphere (in imagined movements). An increased ERS in the affected hemisphere was found to be related to both greater impairment and spasticity, during both imagined and performed movements of the affected limb (Kaiser et al. 2012).

Post-movement beta ERS was also investigated among acute stroke participants with mild to moderate hemiparesis. Results showed that interhemispheric beta ERS laterality tended to return towards normal values for three participants following a 22 week time period (Eder et al. 2006). This study however does not mention whether rehabilitation (and what type) was provided between measurements. As the number of stroke participants tested was small, additional research is required to confirm these findings.

Another study examined the evolution of ERD in stroke participants over time, starting from the acute phase (Tangwiriyasakul et al. 2014). Results showed that six out of the eight participants who took part had a significant increase in ipsilesional ERD, accompanied by a decreasing trend in contralesional ERD. One participant who did not show any motor recovery had an increase in ERD over time over the contralesional hemisphere.

Results of a pilot study investigating the effects of upper limb rehabilitation on pre-movement ERD on chronic stroke participants show a reduced ERD and that improvements in ERD were found following a period of four weeks of robot-mediated therapy, and that improvements correlated with movement efficiency, as measured by the Motor Status Score for Shoulder and Elbow (MSS-SE) (Mazzoleni et al. 2009). These findings were however only validated with two hemiparetic stroke participants, which is insufficient to represent the population of people who have had a stroke. Inclusion and exclusion criteria are not mentioned, making it difficult to determine participant characteristics, such as location and severity of stroke. Healthy volunteers were much younger than stroke participants, which may present with significantly different EEG signals from older individuals. Healthy volunteers' handedness is not consistent, which can cause variability in the data. The selection process of participants is not detailed either. A small number of electrodes were used to record EEG signals (16 in total), which limits the ability to carry out spatial analysis. As far as the movement task, it is unclear whether the movement was cued or self-paced, what instructions were given to participants, whether the length of the movement was standardised, and included a low number of repetitions (35 in total), which may have affected the accuracy of findings. It is not mentioned if the EEG recording equipment was calibrated prior to data collection sessions. It is not clear how artefacts have been dealt with as at some point it is mentioned that Independent Component Analysis (ICA) was used to remove eye and muscle artefacts from the data, and later it is stated that trials containing artefacts such as eye blinking were excluded. Qualifications or training of the evaluators who administered the clinical assessments are not mentioned, and whether they were blinded to the timing of the assessments, which could cause a bias towards lower scores before treatment and higher scores after treatment. On a positive note, the age, gender and handedness of participants are well described, as is the rehabilitation intervention, the location of electrodes, the timing of measurements, and the sampling and anti-aliasing frequencies. The data analysis is also well detailed.

Findings are summarised in Table 8. Methodological weaknesses and important omissions are included in the 'Comments' column of this table.

Author(s)	Participants	Movement(s)	Results	Comments
Rossiter et al. (2014)	25 subacute and chronic stroke participants (22 of those were right-handed), and 32 healthy volunteers	visually cued isometric hand grips (60 trials)	(MEG study) contralateral hemisphere beta ERD reduced in stroke participants compared with healthy volunteers; more impaired individuals have more reduced beta ERD than less impaired	-also observable with EEG?
Ray et al.(2017)	30 chronic stroke participants with complete paralysis of the hand (13 of those had lesions that involved the primary motor cortex)	reaching movement attempts (150 trials)	for those with lesions that include the primary motor cortex, alpha and beta ERD is tendentially (not statistically) less pronounced than for those whose lesions where the primary motor cortex is spared (at electrode sites C3/CP3/P3 or C4/CP4/P4 depending on the side of stroke)	-handedness not specified
Pfurtscheller et al. (1980)	2 right hemisphere stroke participants	movement of the affected hand	contralateral ERD less than ipsilateral ERD	-small number of participants
Stepien et al. (2011)	14 stroke participants in the acute phase (2-13 days post stroke), and 10 age-matched healthy volunteers	cued random left or right button pressing with index finger (200 trials)	in stroke participants, alpha ERD was stronger in the ipsilateral hemisphere than in the contralateral hemisphere when the affected hand was moved (at electrodes sites over sensorimotor areas)	-handedness not specified
Shiner et al. (2015)	10 chronic stroke participants	cued finger tapping (80 trials)	(MEG study) longer beta ERD correlated with poor motor function; longer beta ERS correlated with high motor function; strong ERD/ERS and greater relative ipsilesional activity correlated with greater motor function	-handedness not specified -also observable with EEG?

Author(s)	Participants	Movement(s)	Results	Comments
Platz et al. (2000)	13 stroke participants: 8 with mild to moderate arm paresis without somatosensory deficits, 3 with somatosensory deficits without paresis, and 2 with ideomotor apraxia (tested on average 8.8 weeks (SD 7.3 weeks) after stroke onset), and 10 healthy volunteers of comparable age	self-paced triangular trajectory performed with index finger of affected limb (5x30 trials)	during movement, paretic individuals had increased alpha ERD in frontolateral areas and increased beta ERS in occipital areas; participants with somatosensory deficits had reduced alpha and beta ERD during movement preparation and execution (over centroparietal areas); participants with ideomotor apraxia had reduced parietal beta ERD during movement preparation	-handedness not specified -small number of stroke participants in two of the stroke participant groups -unknown how combination of symptoms would interact
Platz et al. (2002)	9 stroke participants with mild to moderate arm paresis receiving the Arm Ability Training for 3 weeks (tested between 3 weeks to 6 months post stroke)	self-paced triangular trajectory performed with index finger of affected limb (5x30 trials)	EEG measures can predict motor recovery as measured by the TEMPA assessment (at electrodes sites over sensorimotor areas)	-handedness not specified -EEG data not collected following rehabilitation
Fu et al. (2006)	12 right-handed stroke participants with chronic (>12 months) arm coordination deficits and 8 right-handed age matched healthy volunteers	cued 14 cm left or right forward reaching movement using the InMotion[2] Shoulder Elbow Robot (50 trials)	pre-movement alpha ERD significantly lower in stroke participants; pre-movement alpha ERD significantly higher when the non-dominant hand is used, for both groups (at electrodes sites over sensorimotor areas)	-location and severity of stroke not specified -incomplete results due to beta ERD data corruption problem

Author(s)	Participants	Movement(s)	Results	Comments
Kaiser et al. (2012)	29 subacute/ chronic stroke participants with varying degrees of motor deficit in the upper limb	cued execution or imagination of grasping and finger extension of affected and unaffected hand (30 trial per run; 1 run for each task and side)	for movements performed with the affected side: no significant correlation found for ERD, however increased ipsilesional post-movement beta ERS was found for participants with decreased strength (as measured with the MRC scale) and increased contralesional ERS for participants with better strength for imagined movements of the affected side: decreased contralesional ERD for less impaired (as measured by the European Stroke Scale) and increased contralesional ERD for more impaired; decreased ipsilesional ERD and increased contralesional ERS for those with low spasticity and increased ipsilesional ERD and increased ipsilesional ERS for high spasticity (at electrode locations C3 and C4)	-handedness not specified
Eder et al. (2006)	8 right-handed acute stroke participants (6 were tested 1 week post-stroke) with mild to moderate paresis and 8 right-handed healthy volunteers; 3 stroke participants tested after 22 weeks	cued left and right hand movement in arbitrary direction with mouse on drawing board (elbow resting on arm support) (60 trials per hand)	significantly decreased post-movement beta ERS laterality observed when the left paretic arm was used; laterality improved after 22 weeks (at electrode locations C3, Cz, and C4)	-unclear if stroke participants received rehabilitation between measurements -small number of participants tested after 22 weeks

Author(s)	Participants	Movement(s)	Results	Comments
Tangwiriyasakul et al. (2014)	8 right-handed acute stroke participants with mild to severe paresis, tested soon after stroke onset, and after 1, 2, and 4 months	cued random left and right hand opening movement (32 trials)	six out of the eight participants had a significant increase in ipsilesional ERD, accompanied by a decreasing trend in contralesional ERD over time; one participant with no motor recovery had an increase in ERD over time over the contralesional hemisphere (ERD was characterised in this study a modulation strength measure representing the area and amplitude of ERD) (at electrode locations C3 and C4)	-unclear if and which participants underwent rehabilitation, and for how long

Author(s)	Participants	Movement(s)	Results	Comments
Mazzoleni et al. (2009)	2 right-handed chronic (>1 year) stroke participants with hemiparesis and 4 healthy volunteers (3 right-handed and 1 left-handed)	simple unassisted forward reaching movement using the InMotion^2 Shoulder Elbow Robot (35 trials)	(includes follow-up data halfway through and at the end of 4 weeks of robot-mediated therapy with the InMotion^2 system (60 mins/day, 5 days/week)) stroke participants' pre-movement alpha ERD was less than for healthy volunteers prior to therapy (no statistical test reported); stroke participants' ERD comparable to healthy volunteers' post-therapy; correlation (for one participant) between increased ERD and improved movement efficiency (as measured by the Motor Status Score for shoulder and elbow (MSS-SE)); correlation (for one participant) between decreased ERD and increased MRCP amplitude; ERD duration not significantly different between groups (at electrode locations C3 and C4)	(see text)

Table 8 Summary of findings for ERD/ERS among people who have had a stroke.

A limited amount of ERD/ERS data after stroke (and even less after a period of rehabilitation) has thus been generated so far in various experimental conditions. Some predictive properties for motor recovery have been attributed to ERD/ERS. The duration and hemispheric laterality of ERD/ERS has also been compared between healthy and stroke participants, and characterised with relation to severity of motor impairment and spasticity. When examining potential changes over time, one study reported improvements towards more normalised lateralisation of ERD. Another study showed that a decrease in pre-movement alpha ERD occurs in motor cortex areas after stroke and that improvements following recovery and rehabilitation are possible, suggesting that changes in ERD/ERS are associated with neuroplastic changes (Mazzoleni et al. 2009). This study however contains a number of methodological weaknesses. Some links have also been made between increased ERD and increased movement efficiency. More research is required in all areas of ERD/ERS after stroke, particularly on the effects of rehabilitation, in order to understand and confirm the findings described above.

3.4 Summary of key findings

When considering all findings from ERD/ERS studies, it is clear that movement-related cortical activity varies according to a number of factors. Researchers examining how these signals vary in a specific population need to carefully control these factors, as much as possible, to optimise the validity of measurements.

In ERD/ERS studies with healthy individuals, motor learning has been found to have an effect on cortical activity, as measured by alpha ERD. Handedness, in combination with side of movement, impacts on the laterality of cortical activation.

In stroke participants, a reduced ERD occurs over the ipsilesional hemisphere as a consequence of stroke, and improvements are possible over time. Links have been made between those changes and measures of motor function. In more severely affected individuals, an increase in ERD can also be observed in the contralesional hemisphere.

3.5 Gaps in knowledge and need for further work

Neuroplasticity after stroke, as measured with movement-related EEG, has not been explored extensively. More research is required to determine what therapies have the maximal effect on cortical recovery (as measured by EEG) and motor recovery, according to level of impairment and time post-stroke.

Many of these studies concentrate on the movement of isolated joints, with a minority examining more complex movements. More research is needed to describe motor cortex activity during more functional movements such as reaching, as these movements are more often than not the focus of rehabilitation approaches. Additional knowledge in this area could contribute to better treatment decision-making based on individual measurements.

Only a small number of studies examined ERD/ERS in stroke participants. Of these, only one investigated ERD/ERS before and after a period of robotic upper limb rehabilitation and its potential relationship with measures of motor function (Mazzoleni et al. 2009). This study however contains a number of weaknesses and thus definitive conclusions cannot be made about the effects of rehabilitation on ERD/ERS. As this study recruited chronic stroke participants, more research is required to determine if similar effects can be found with acute and subacute stroke participants.

These gaps in knowledge have led to the design of the present study, in which an experimental method to record and investigate cortical activity (as measured by movement-related ERD/ERS during reaching movements) was developed. As part of this, the customised experimental setup was tested as part of a feasibility study. Test-retest variability was then examined for a group of healthy volunteers. Next, cortical activity was characterised by averaged data from another group of healthy volunteers. Finally, cortical activity was examined in subacute and chronic stroke participants with mild to moderate hemiparesis, before and following a period of robotic rehabilitation. Stroke participants' measures of ERD/ERS were compared to averaged data from the group of healthy individuals in order to observe any differences, and potential changes following rehabilitation were compared to results of measures of upper limb impairment and function. This study aimed to address methodological weaknesses outlined in Table 7 and Table 8. The study required a significant amount of development work, which is described in the next chapter.

3.6 Analysis method used for this study

This study presents results of the analysis of ERD/ERS measures. MRCP analysis was not carried out as a 2 Hz high-pass filter was applied early on in the data processing procedure (to ensure a stable baseline when examining the data by attenuating gradual voltage shifts caused by skin potentials), preventing MRCP analysis, which requires frequencies below 2 Hz. In order to carry out this analysis, the data would need to be re-processed from the beginning (by applying a lower high pass filter with a value such as 0.01 Hz), which was not possible due to limitations on time.

Chapter 4: Development

4.1 Introduction

This chapter presents research questions as well as development work and study design choices regarding data collection methods, including the profile and provenance of participants to be recruited to the sample groups, the timing of measurements, the movement task during which EEG recordings will be made (including the design of the cueing setup), the design of the reaching device and other pieces of equipment used in the EEG laboratory, the EEG/EMG electrode configuration, EEG data processing and analysis, the therapeutic modality for upper limb rehabilitation, and clinical measures of impairment and function used in this study.

A positivistic approach was used in the design of this study in that the study's aims require that they be achieved using objective measures and that findings should not be subject to participants' personal contexts, or to the researcher's biases or personal interpretation of results. Every aspect of the study was designed with this in mind.

For the stroke participant study, an uncontrolled, repeated measures experimental design was used. It was selected as it lends itself to the proposed research questions. As measurements were taken before and after stroke participants were exposed to the experimental variable (the use of a rehabilitation robot), a repeated measures design was chosen. As data was compared between stroke participants and healthy volunteers, randomisation to groups was not relevant.

References to existing literature that have informed choices were included when appropriate.

This study was designed with a view to answering the following questions:

4.2 Research questions

1. Are recruitment procedures, data collection and data analysis methods developed for this study effective to investigate ERD/ERS measures during reaching?
2. What is the variability over time of ERD/ERS measures during reaching for a small sample of healthy participants?
3. What are the characteristics of ERD/ERS measures during reaching for healthy participants?
4. Do characteristics of ERD/ERS measures during reaching in a small sample of stroke participants differ from those observed in healthy participants?

5. What changes, if any, does a period of robotic rehabilitation cause in ERD/ERS measures during reaching in these stroke participants?
6. For these stroke participants, is there an association between potential changes in ERD/ERS measures and changes in measures of upper limb impairment and function?

To answer these questions, the following objectives were achieved:

4.2.1 Study objectives

- Develop a method to record and investigate cortical activity, as measured by movement-related ERD/ERS during reaching movements.
- Determine whether recruitment procedures, data collection and data analysis methods developed for this study are effective to investigate ERD/ERS measures during reaching.
- Explore the variability over time of ERD/ERS measures during reaching for a small sample of healthy participants.
- Determine characteristics of ERD/ERS measures during reaching for a group of healthy participants.
- Explore characteristics of ERD/ERS measures during reaching for a small sample of stroke participants, before and following a period of robotic rehabilitation. Find out whether there are any differences with healthy participants' ERD/ERS measures, and whether any changes can be observed after rehabilitation. Determine if these potential changes are associated with changes in measures of impairment and function.

To achieve these objectives, the following tasks were carried out:

4.2.2 Study tasks

- Situate the study in perspective of recent findings and inform the research design by reviewing movement-related EEG research literature.
- Define and implement all aspects of the study such as equipment requirements (including the design and construction of a reaching device), cueing setup, EEG/EMG configuration, rehabilitation protocol, and clinical measures of impairment and function to be used.
- Carry out a feasibility study to validate research methods and to determine if changes are required before continuing further.
- Measure ERD/ERS during reaching with a small sample of healthy participants over three sessions to explore variability over time.
- Measure ERD/ERS during reaching in healthy participants and average data to characterise ERD/ERS in healthy participants.

- Measure ERD/ERS during reaching with a small sample of stroke participants before and after a period of rehabilitation. Obtain measures of impairment and functional concurrently. Compare differences between stroke participants and healthy participants' data. Compare potential changes in ERD/ERS measures with changes in measures of impairment and function.

4.3 Participants

In order to achieve the study's objectives, four separate groups of participants were required. In the first instance, two stroke participants and two healthy participants were recruited to complete a feasibility study to ensure that data collection methods were appropriate and to identify any changes that might need to be implemented for further data collection. Following this, recruitment to three groups commenced: the first group consisting of healthy participants to examine the variability of ERD/ERS measures over time, another consisting of healthy participants to characterise averaged ERD/ERS measures in a healthy population, and a third made up of chronic and subacute stroke participants. It had been planned that a minimum of four participants would be recruited to the feasibility study, a minimum of five participants would be recruited to the test-retest variability and stroke participant groups, and a minimum of ten for the averaged ERD/ERS healthy participant group.

4.3.1 Recruitment of healthy participants

Healthy participants were required as literature findings show that EEG measures are experiment-specific and vary according to the movement performed during EEG recording (see Chapter 3). Healthy participants' data from other studies may thus not be used.

Non-probability sampling was used by selecting a convenience sample, as and when suitable participants became available and agreed to be recruited to the study. Participants were recruited from the University of Southampton's School of Psychology research participant register, as well as from the researcher's academic and social networks. Healthy participants' journeys were documented throughout their involvement in the study). Potential participants received an information sheet (see Appendices E and F, for participants participating in the test-retest variability study and the healthy participant study, respectively). If still interested, the participant contacted the researcher, who paid a visit to discuss their participation and to answer any questions. The potential participant was asked to complete a health questionnaire (including a revised version of the Edinburgh Handedness Inventory), which was reviewed by the researcher (see Appendix G). If the study's criteria were met, the researcher sought written consent (see

Appendix H). The researcher and the participant planned all sessions immediately. The researcher provided a copy of the planned timetable to the participant.

4.3.2 Recruitment of stroke participants

This study's population of interest consists of people who have had a stroke with residual upper limb hemiparesis. As the brain's capacity to change is greatest in the first weeks following stroke (Jorgensen et al. 1995), subacute stroke participants were to be identified soon after stroke onset. Non-probability sampling was used by selecting a convenience sample, as and when suitable participants became available and agreed to be recruited to the study. Subacute stroke participants were recruited from the local inpatient stroke ward at the Southampton General Hospital (University Hospital Southampton NHS Foundation Trust), from the Southampton Stroke Early Supported Discharge Service (Solent NHS Trust), as well as from the Winchester Early Supported Discharge Team (Hampshire Hospitals NHS Foundation Trust). Participants were recruited as early as possible in order for the first measurement session to be carried out between two and twelve weeks following stroke onset. Potential chronic stroke participants were screened for eligibility from a variety of sources: from the Work Rehabilitation service (Solent NHS Trust), as well as from non-NHS sites, such as stroke clubs, private rehabilitation clinics, and the University of Southampton's Faculty of Health Sciences research participant register. Participants identified through any other means who expressed a wish to participate in the study were also considered. An assessment session took place to determine participants' eligibility. For subacute stroke participants, this assessment session was not carried out any sooner than one week following discharge to their usual residence. This allowed enough time for participants to settle down at home, whilst benefiting from the period of time offering the greatest neuroplasticity.

Participants' journeys were documented throughout their involvement in the study. Potential subacute stroke participants were identified by nursing, medical, and therapy staff looking after them, and were given a participant information sheet (PIS) explaining the study and recruitment process, including the researcher's contact details (see Appendix I). Once a potential participant contacted the researcher directly or via their relatives, carer, or health professional, expressing an interest in participating in the study, the researcher paid a visit to the individual on the ward or at home (depending on the timing of the visit) to discuss their participation and to answer any questions. If the potential participant renewed interest in participating in the study, the researcher sought written consent (see Appendix J) from the individual to consult medical notes and to speak to staff involved with their care to determine whether they met the study's preliminary requirements. Once medical notes and staff were consulted the researcher met with the potential participant for a second time. The researcher explained whether they met the study's preliminary requirements. If these were met, the researcher waited for a discharge date (if the individual was still in hospital) to be determined in order to seek verbal consent from the individual to arrange an assessment session at the University of Southampton to complete the last part of the eligibility assessment. If they consented, a memo was given to the potential participant outlining the date, time and place of the assessment session, along with a map of the campus which included car parks. Chronic stroke participants were identified through non-NHS sites and also attended an assessment session to determine eligibility.

The assessment session consisted of a review of the study's requirements, and testing the potential participant's abilities to complete the required tasks involved with EEG data collection. Other tests were performed to ensure all eligibility criteria were met. These included: a revised version of the Edinburgh Handedness Inventory (included activities: writing, throwing, using scissors, using a toothbrush, using a knife (without a fork), using a spoon, striking a match, and using a computer mouse), MRC muscle grading (for hemiparesis), Modified Ashworth Scale (for spasticity), Star Cancellation Test (for unilateral spatial neglect), and Mini Mental State Examination Version 2 (a screening test for cognition). Scores were recorded on a scoring sheet (see Appendix K). Official forms were purchased for the Mini Mental State Examination, as this was the only test that required a license/permission. If the potential participant was successful, the researcher and the participant planned all measurement and training sessions immediately, and written consent was sought (see Appendix L). The researcher provided a copy of the planned timetable to the participant. He also sent a letter to the participant's GP, with their consent, to inform them of the individual's participation in the study (see Appendix M).

4.3.3 Inclusion and exclusion criteria

Inclusion and exclusion criteria were developed in accordance with the research question requirements, keeping in mind what is known about movement-related EEG activity and the ArmeoSpring's (the upper limb rehabilitation robot used in this study) contraindications.

<u>Inclusion criteria common to both healthy and stroke participants:</u>

- Upper limb dominance: right-handedness, as defined by a laterality quotient of 71 or more (Schachter 2000) as measured by a revised version of the Edinburgh Handedness Inventory. As EEG data varies with hand dominance (see Chapter 3), right-handedness was chosen to ensure homogeneous data, and also for ease of recruitment, as right-handedness is more prevalent in the general population than left-handedness).
- Ability to perform the movement task for EEG data collection.

<u>Inclusion criteria for stroke participants:</u>

- First unilateral stroke (to avoid effects from previous strokes, particularly when analysing spatial distribution and hemispheric lateralisation of measures of ERD/ERS), as confirmed by a clinical diagnosis of stroke.
- Mild to moderate upper limb hemiparesis (as participants need to be able to carry out the movement task for EEG data collection), as measured by an MRC grade for triceps between 2 and 4, inclusively; for grade 2, participants were required to be able to extend their elbow sufficiently to complete the reaching movement required for EEG data collection. As stroke participants were required to be able to perform a substantial number of reaching movements for EEG data collection, those with severe hemiparesis would not be able to participate, for the reason that they would not have been able to successfully complete the required number of movements necessary for data collection.

<u>Exclusion criteria common to both groups:</u>

- History of epilepsy (as this condition may affect EEG data).
- History of neurological disorder affecting central or peripheral nervous systems (may also affect EEG data).
- History of musculoskeletal condition affecting upper limb movement (may affect movement performance and EEG data).
- History of chronic pain syndrome (may not be appropriate for upper limb training).
- Visual impairments, excluding decreased acuity fully compensated with eyeglasses/contact lenses (as participants need to see the ArmeoSpring's screen).
- Taking medications altering the level of cortical excitability (e.g. antiepileptics, neuroleptics, benzodiazepines, antidepressants) or with a presumed positive or negative effect on brain plasticity (e.g. Dopamine, Fluoxetine, D-Amphetamine).
- Involvement in any other research study involving the upper limbs (as it may affect rehabilitation outcomes and EEG data).

<u>Contraindications to the use of the ArmeoSpring upper limb rehabilitation robot:</u>

(Hocoma AG 2008)

- ArmeoSpring orthosis cannot be fitted to the relevant arm
- Bone instability (nonconsolidated fractures, severe osteoporosis)
- Pronounced, fixed contractures affecting the relevant extremity
- Paraesthesia
- Shoulder joint subluxation or pain in the shoulder joint
- Severe spasticity

- Severe spontaneous movements, e.g. ataxia, dyskinesia, myoclonic jerks
- Non-stable vital functions: Pulmonary or cardio-circulatory contraindications (instability or instrumental support for these functions)
- Need for long-term infusion therapy
- Severe postural instability
- Contraindicated sitting position
- Confused or non-cooperative individuals
- Severe cognitive deficits
- Individuals requiring isolation due to infections
- Severe visual problems (individual would not be able to see displayed elements on the computer screen)

<u>Exclusion criteria for stroke participants:</u>

- Severe spasticity (Modified Ashworth Scale score ≥ 3) (not appropriate for EEG data collection movement task as movement performance would be excessively affected).
- Unilateral spatial neglect (Star Cancellation Test score < 44) (participants needed to attend to all visual stimuli on the ArmeoSpring's screen).
- Cognitive impairment (Mini Mental State Examination (Version 2) score ≤ 23) (minimum requirement to reasonably understand ArmeoSpring's games and researcher's instructions).
- Independent clinical evidence (documented in medical records) of:
    - Severe disorders of execution of movement such as dyspraxia or tremors (not appropriate for EEG data collection movement task).
    - Severe perceptual deficits such as difficulties with spatial relations (participants needed to attend to visual stimuli from the ArmeoSpring's screen).
    - Severe speech and language deficits such as dysphasia affecting communication between participant and investigator (minimum requirement for communication between participant and researcher).

4.4 Timing of measurements

The timings of measurement sessions were different for each group.

4.4.1 Healthy participants

Healthy participants forming the test-retest variability study group attended three EEG recording sessions: (Figure 12) two on consecutive days, and a third two weeks later (± two days to allow for the unavailability of participants on certain days or for unforeseen circumstances). This two week period of time matched stroke participants' time period between the two pre-rehabilitation measures and between the two post-rehabilitation measures.

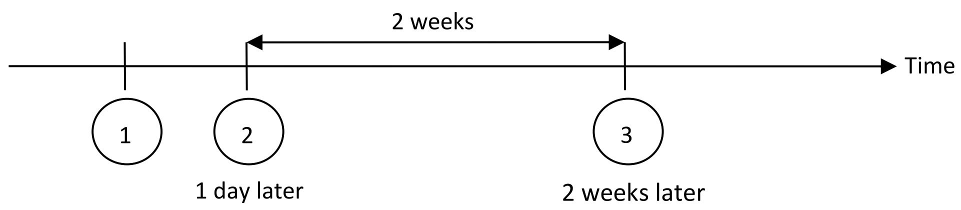


Figure 12 Timeline of sessions for healthy participants in the test-retest variability study.

Healthy participants part of the averaged ERD/ERS measures group only attended one EEG recording session.

4.4.2 Stroke participants

Stroke participants attended four EEG recording and upper limb assessment sessions (see Figure 13): two weeks before the first training session, just before the first training session, just after the last training session, and two weeks after the last training session (± three days before and after planned measurement points was permitted to allow for the unavailability of participants on certain days or for unforeseen circumstances). The first two measurement sessions were to observe whether pre-rehabilitation measurements were similar or whether changes could be observed, particularly in the case of participants in the subacute phase of stroke. The third and fourth sessions were to determine whether improvements were made and maintained following a period of rehabilitation using an upper limb rehabilitation robot.

Figure 13 Timeline of sessions for stroke participants.

4.5 Movement task for EEG data collection

4.5.1 Nature of the movement task

As upper limb rehabilitation interventions target improvements in functional movements and activities, investigating cortical activity changes, as measured during a simple forward reaching movement, would better reflect the effects of rehabilitation than a single joint movement. Forward reaching is a common difficulty for people who have had as stroke who have upper limb strength and motor control impairments. EEG recording procedures require that movements be standardised as much as possible in terms of direction and speed to minimise variability between each movement. In order to achieve a standard reach in both direction and length, it became apparent that a 'reaching device' needed to be constructed, as no such apparatus was available commercially. To standardise the speed of movement as much as possible, participants were instructed to perform the movement as quickly as possible, as soon as possible after the cue.

4.5.2 Cueing of movement

To further standardise the recording procedure, movement repetitions were cued. This ensured that participants did not move their arm during pre and post-movement time periods of interest. This was achieved by running the Presentation stimulus delivery program (Neurobehavioral Systems, USA) on a computer screen placed directly in front of the participant. A looped scenario was developed (see Figure 14), which was controlled by the researcher by using a 4-button box in the adjoining room to the one where participants performed the movement task (the researcher used a camera system to monitor participants' movements). The scenario consisted of three different screens: a full black screen with a small red square at the centre, a full black screen with a small green square at the centre, and a full black screen with the word 'Return', in grey (see Figure 15). The small square at the centre of the screen was to help participants fix their gaze, as eye movements produce artefacts in EEG data. The red and green colours were to indicate when the participant was to perform the movement (green) and when to stay still (red). The size of the square was small (2 x 2 cm) in order to avoid generating a significant visual evoked response.

To ensure that sufficient pre and post-movement data was collected, a computer-generated random time interval of seven to eleven seconds of immobility preceded movement, and the researcher ensured that at least four seconds of immobility followed movement. The pre-movement random time interval was to ensure that participants did not anticipate movement cues in advance.

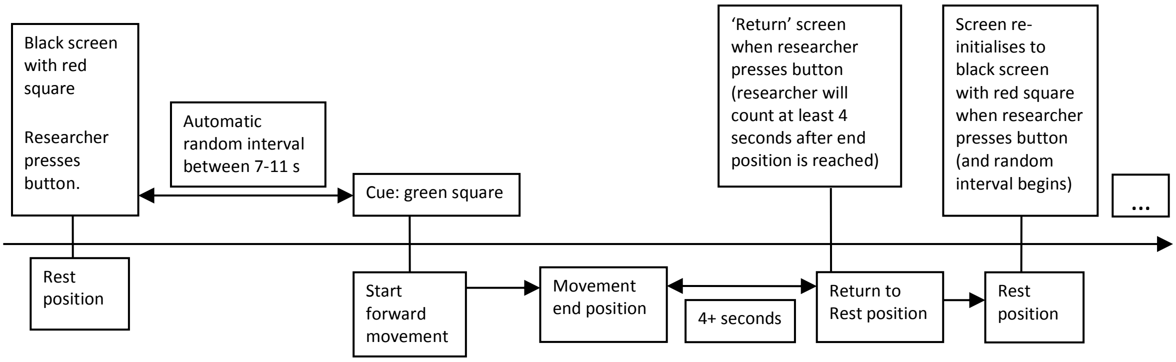


Figure 14 Looped cueing scenario over time.

Figure 15 Cueing screens.

4.5.3 Number of repetitions

For participants taking part in the test-retest variability and stroke participant group studies, 150 reaching movements were performed by each participant at each recording session, in blocks of 25 movements, with two minute pauses between each block. This number of repetitions was selected as it takes in consideration stroke participants' reduced physical abilities (in terms of effort and fatigue) whilst assuring that a sufficient number of trials would be attained to obtain more accurate data. It is also comparable to past movement-related EEG studies with stroke participants. Stroke participants used their affected arm and healthy participants were assigned either left or right arm movements with a view to have an equal number of participants using each side. Participants taking part in the healthy participant study performed 160 movements: 80 movements with each arm (in three blocks of movements for each arm with two minute pauses between each block), in order to characterise cortical activation with both left and right arm movements.

4.6 Design of the reaching device and other equipment

4.6.1 Reaching device

A reaching device was designed and constructed by the researcher (see Figure 16), using an iterative design process which included two earlier prototypes that led to the final design. It consists of a moveable arm trough (with straps to keep the forearm in position) and hand cone that glide along a fixed 15 cm path. The position of the hand cone could be modified to adapt to varying forearm lengths (see Figure 17). The trough and the base of the cone were constructed with thermoplastic splinting material and are lined with synthetic sheepskin (Sherpa lining material). The hand cone was enveloped by fabric, and also has a strap to keep fingers in position, for those with poor hand grip. A linear potentiometer (Celesco SP1 with precision potentiometric output accuracy of ± 0.25 to ± 1.00 %) was fitted underneath the reaching device to record the movements' kinematic characteristics (see Figure 18). As the device made a small amount of sound, participants wore earplugs during recordings in order to avoid producing a significant auditory evoked response.

Figure 16 Reaching device.

Figure 17 Adjustable hand cone.

Figure 18 Linear potentiometer.

4.6.2 Table

To support the reaching device, a height-adjustable table was adapted (see Figure 19) to allow the reaching device to sit at a 10 degree angle towards participants' midline, to facilitate a natural reaching movement. The table was fitted with wooden and metal parts to prevent the reaching device from moving during movement, whilst allowing for the reaching device to be easily removed when switching sides. The table could accommodate for both left and right reaching movements.

Figure 19 Table with reaching device in situ.

4.6.3 Chair

A high-back height-adjustable chair was modified (see Figure 20) by removing its armrests and by adding a chest harness (Poziform Contoured Shoulder Harness, Size 4) to ensure that stroke participants did not compensate for impaired upper limb motor control by moving their chests forward during reaching movements. The chest harness was adjustable and could be either fitted on the left or on the right of the chair to accommodate both left and right reaching movements.

Figure 20 Chair with harness and adjustable positions for harness.

The complete configuration is shown in Figure 21.

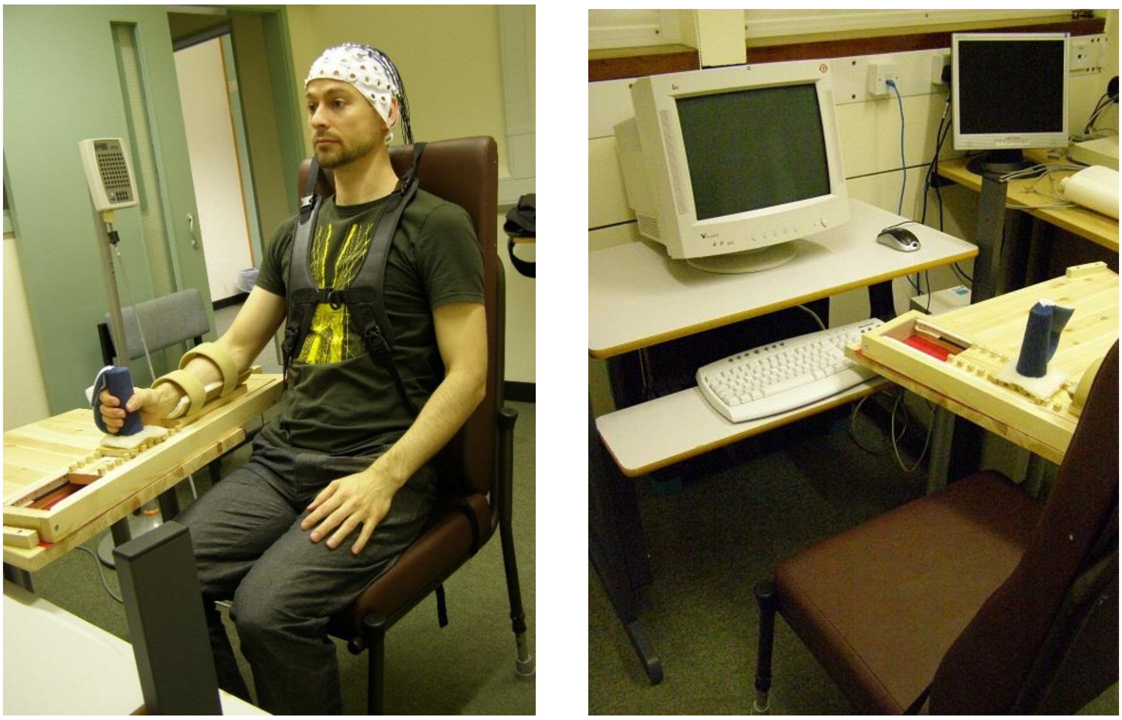


Figure 21   Complete configuration.

4.7 Laboratory equipment configuration

The EEG laboratory equipment configuration that was developed and used for the study is shown on Figure 22. The equipment was spread over two rooms, with the participant separated from the researcher by a wall.

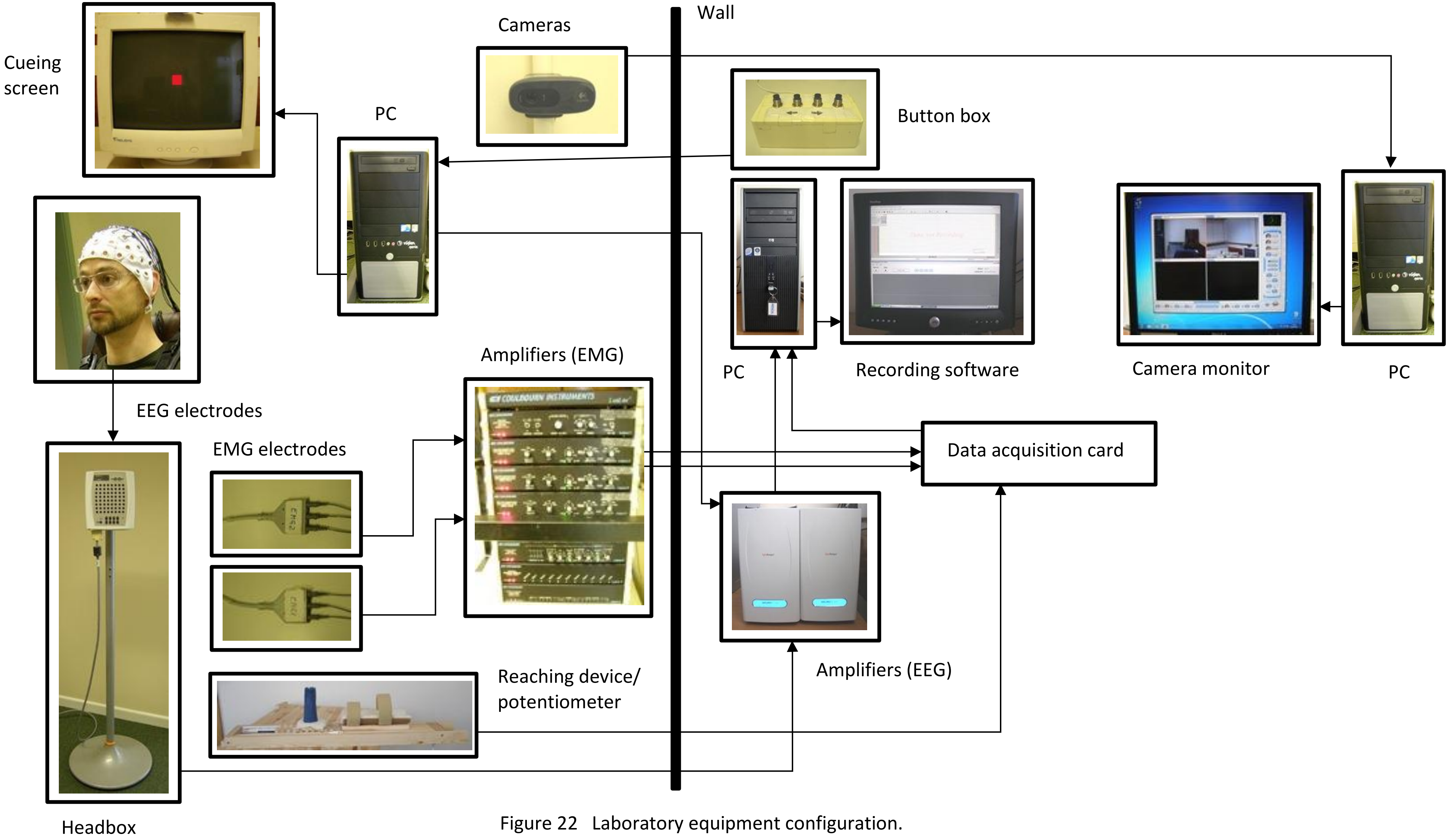


Figure 22 Laboratory equipment configuration.

4.8 EEG and EMG electrode configuration

4.8.1 EEG

The number and configuration of electrodes from previous movement-related ERD/ERS studies were reviewed and a decision was made to include 35 channels in order to cover premotor, supplementary motor, primary motor, and somatosensory cortices. This was a compromise between the need for good resolution and the required time to prepare a large number of electrodes, which would be too demanding on stroke participants in terms of time. The configuration was based on the Modified Combinatorial Nomenclature (see Chapter 2) and includes [F5, F3, F1, Fz, F2, F4, F6], [FC5, FC3, FC1, FCz, FC2, FC4, FC6], [C5, C3, C1, Cz, C2, C4, C6], [CP5, CP3, CP1, CPz, CP2, CP4, CP6], and [P5, P3, P1, Pz, P2, P4, P6] (see Figure 23). Four additional electrodes were placed to record eye blinking (on the right cheek, at FP2, F9, and F10), two additional electrodes on the left and right ears (linked common reference electrodes), and a final electrode at AFz (for the ground electrode). The researcher also adapted a chin strap by sewing Velcro on to it to ensure that the electrode cap would not move during recordings.

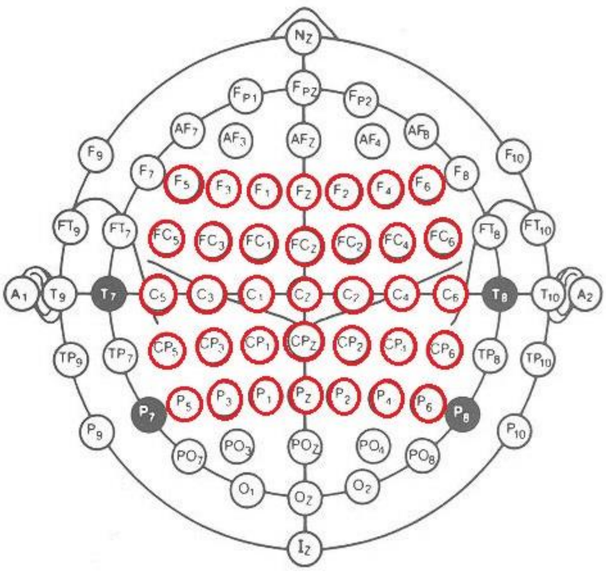


Figure 23 EEG electrode configuration (selected electrodes in red).

4.8.2 EMG

EMG data was also recorded in order to obtain additional information on the execution of the reaching movement. Contractions of two muscles involved in forward reaching were recorded: the anterior deltoid and the triceps brachii (lateral head). Bipolar electrodes were positioned as per the Surface Electromyography for the Non-Invasive Assessment of Muscles (SENIAM) guidelines (Hermens 1999). Reference electrodes were applied on one of the bony prominences of the wrist, the ulnar head.

4.9 EEG data processing and analysis

A number of custom MATLAB scripts were developed to align and combine EEG, EMG, and potentiometer data into single datasets compatible with EEGLAB, a MATLAB toolbox for processing and analysing EEG data. These scripts also created event markers for movement onset and offset, based on movement data, as recorded by the potentiometer. Further scripts were developed to examine and analyse the data.

4.10 Choice of therapeutic modality for the stroke participant group

4.10.1 The ArmeoSpring

The ArmeoSpring upper limb rehabilitation robot is based on the Therapy Wilmington Robotic Exoskeleton (TWREX), developed in the United States, and manufactured by Hocoma A.G., in Switzerland. The ArmeoSpring (see Figure 24), which was designed to rehabilitate hemiparetic individuals, consists of an arm orthosis which counteracts the effect of gravity, allowing them to move their arm more freely. To encourage and motivate individuals to repeat reaching movements, a number of interactive activities and games are presented via a computer screen. The ArmeoSpring is adjustable to match peoples’ abilities in a variety of ways. The amount of upper arm and forearm weight support can be modified. The workspace, which defines the three-dimensional area within which the arm is moved, can be adapted to match participant’s reaching abilities. Each activity can also be configured in terms of level of difficulty.

It was chosen for a number of reasons. Firstly, the ArmeoSpring’s effectiveness in significantly improving upper extremity function after stroke (as measured by the Fugl-Meyer Assessment and active range of movement measures) has been shown in a randomised controlled trial (Housman et al. 2009), with gains maintained at six months post rehabilitation for Fugl-Meyer scores. This trial compared two groups of chronic participants with moderate/severe hemiparesis: one group who used the ArmeoSpring for 24 one-hour sessions over eight to nine weeks, and another group who followed a conventional exercise programme, consisting of 24 sessions of range of motion exercises, active range of motion strengthening exercises, weight bearing exercises, and prescribed activities of daily living practice (with intermittent supervision from a therapist). Secondly, its activities target reaching movements, thus providing a training programme that is consistent with the movement task that was performed during EEG recordings. Thirdly, it satisfies a number of therapeutic principles that have been identified as promoting neuroplastic changes (see Chapter 2), as the ArmeoSpring's training activities consist of motor skill practice (as opposed to simple motor activity practice), allow for repetition, intensity, and require attention from the user. Fourthly, its activities are highly gradable and are adaptable to users' particular abilities. Fifthly, it allows for a standardised, progressive, and reproducible course of therapy. Sixthly, anecdotal evidence suggests that people who have had a stroke find the ArmeoSpring's activities enjoyable and motivating.

Figure 24 ArmeoSpring arm orthosis, screen, and virtual activity (Hocoma AG 2009). Copyright of Hocoma AG reproduced with permission.

4.10.2 Training protocol

A selection of activities from the ArmeoSpring's collection were used to create treatment plans which differed in terms of level of difficulty for each participant. These were constantly reviewed to ensure that levels of difficulty matched participants' increasing abilities. The aim was to complete ten sessions within two weeks, at a frequency of five times per week. Individual sessions lasted two hours (including arrival time and breaks), for a total duration of 20 hours. This timeframe was based on findings from two studies described in Chapter 3 and in this chapter: one study which evidenced significant neuroplastic changes (as observed with EEG) in chronic stroke participants following 20 one-hour sessions of robotic therapy using the InMotion2 system (Mazzoleni et al. 2009), and a study which evidenced significant motor improvements in chronic stroke participants after 24 hours of therapy using the Armeo, at a rate of one hour of therapy per day, three times a week (Housman et al. 2009). To allow for unforeseen circumstances, the maximum permitted total duration was three weeks. The timeline of each session was the following:

- arrival of participant, adjustment of ArmeoSpring: 10 minutes
- 4 X 20 minute work periods = 80 minutes
- 3 X 10 minute interspersed rest periods = 30 minutes

4.11 Choice of clinical measures

Selection criteria were defined to select two assessments that would separately measure upper limb impairment and function. These should be designed to assess either upper limb impairment or function in adults with hemiparesis, assess performance in unilateral tasks only, have evidence of adequate psychometric properties for a stroke population, be used and known by the stroke research community, take a reasonable length of time to administer (15 minutes or less, as EEG data collection already takes a considerable amount of time), and include a variety of reaching and grasping tasks.

Several upper limb assessments were considered (see Table 9): the Action Research Arm Test (ARAT), the Arm Motor Ability Test (AMAT), the Box and Block Test (BBT), the Chedoke Arm and Hand Activity Inventory (CAHAI), the Frenchay Arm Test (FAT), the Fugl-Meyer Assessment (FMA), the Jebsen Hand Function Test, the Southampton Hand Assessment Procedure (SHAP), the Upper Extremity Performance Test for the Elderly (TEMPA), the Upper Limb - Motor Assessment Scale (UL-MAS), and the Wolf Motor Function Test (WMFT).

	ARAT	AMAT	BBT	CAHAI	FAT	FMA	Jebsen Test	SHAP	TEMPA	UL-MAS	WMFT
Designed for the assessment of individuals with hemiplegia	✓	✓	✓ (not exclusively)	✓	✓	✓	✓ (not exclusively)	✓ (not exclusively)	✓ (not exclusively)	✓	✓
Assesses either impairment (I) or function (F)	✓ (F)	✓ (F)	dexterity	✓ (F)	✓ (F)	✓ (I)	dexterity	✓ (F)	✓ (F)	mixed	mixed
Unilateral tasks only	✓		✓			✓	✓	✓			✓
Includes a variety of reaching and simple grasping tasks	✓	✓	one task only	✓	✓	✓	✓	✓	✓	✓	✓
Evidence of adequate psychometric properties for stroke population	✓	✓	✓	✓	✓	✓		✓		✓	✓
Reasonable length of time to administer (≤15 mins)	✓	> 30 mins	✓	25 mins	✓	✓	30-45 mins	20 mins	Information not available	✓	30 mins

Table 9 Considered upper limb assessments (Kopp et al. 1997; Metcalf et al. 2007; Metcalf 2012; StrokEngine 2017c).

Each assessment was examined using the defined criteria, resulting in the upper extremity section of the Fugl-Meyer Assessment (FMA) and the Action Research Arm Test (ARAT) being selected to assess upper limb impairment and function, respectively. These were administered as according to published administration guidelines for the FMA (Platz 2005) and the ARAT (Yozbatiran et al. 2008). In order to standardise the ARAT to these guidelines, the researcher acquired a shelf with correct dimensions and a non-slip mat and marked the mat with standard positions for all the test items.

The researcher filmed these assessments and a blinded assessor with experience of scoring the ARAT and the Fugl-Meyer Assessment viewed the films and independently scored these assessments to ensure results would be unbiased.

4.11.1 Impairment

In this study, the motor score of the upper extremity section of the Fugl-Meyer Assessment (FMA) was used to characterise stroke participants' upper limb impairments. The FMA has been specifically designed for people who have had a stroke (Fugl-Meyer et al. 1975), and is the gold standard against which other assessments have been compared (StrokEngine 2017b). This section of the assessment tests upper limb reflex activity, active movement, and coordination (score range 0-66). Approximate time to administer this section of the test is estimated to be 10-15 minutes. Psychometric properties have been extensively examined with people who have had a stroke and are reported to be excellent (StrokEngine 2017b). The minimal clinically important difference for overall upper limb function (in people with minimal to moderate impairment in the chronic phase of stroke) is 5.25 points (Page et al. 2012). No license or permission was required to administer this assessment.

4.11.2 Function

The Action Research Arm Test (ARAT) was used to generate scores related to upper limb function. The ARAT has been designed for individuals with hemiplegia due to cortical damage (Lyle 1981). It tests functional grasp, grip, pinch, and gross movement (score range 0-57). Approximate time to administer is on average eight minutes (Hsieh et al. 1998). The ARAT has been deemed to be reliable, valid, and responsive when used with people who have had a stroke (StrokEngine 2017a). The minimal clinically important difference for the ARAT has not been rigorously examined, apart from one study that determined it to be (for the purpose of investigating the ARAT's intra- and interrater reliability), based on clinical experience and estimates, 10 % of the maximum score, or 5.7 points (Van der Lee et al. 2001). No license or permission was required to administer this assessment.

4.12 Ethical considerations

Ethical approval by the Southampton & South West Hampshire Research Ethics Committee 'A' was obtained as was R&D approval from NHS trusts (see Appendices A and B). Sponsorship and insurance arrangements were also made (see Appendices C and D).

4.12.1 Gatekeepers

For subacute stroke participants, nursing, medical and therapy staff from recruiting sites acted as gatekeepers, by identifying potential participants and providing information regarding the study.

The initial contact between potential participants and the researcher was consequently always initiated by interested participants.

4.12.2 Sampling and recruitment

The researcher visited gatekeepers prior to recruitment of participants and explained the study in more detail to ensure appropriate individuals were offered information in order to avoid disappointment. Gatekeepers were instructed to simply describe the study, without expressing any opinions they might have about it or encouraging individuals to participate.

Cultural and religious issues that could have arisen would have been accommodated for as much as possible, as long as they did not affect the training programme or the accuracy of measurements. For example, a participant wearing something over their head would not be suitable for EEG data collection. These issues would have been dealt with on a case-by-case basis, when applicable.

4.12.3 Informed consent

The researcher aimed to ensure participants understood all training and measurement procedures and that they had an opportunity to voice their concerns, ask questions, before consent was given at the assessment session. Consenting participants were reminded that they could pull out of the study at any time. Potential risks and benefits associated with participation in the study were included in the participant information sheets given to potential participants, and were also discussed at the assessment session. Participants were asked for consent for video recordings to be used for analysis and optionally for teaching and research presentations. If used for teaching and research presentations, the video footage would be masked to maintain anonymity.

4.12.4 Confidentiality

To ensure confidentiality, data was kept in locked filing cabinets, in a locked office. Anonymisation was achieved by physically separating participants' data into two separate folders. Personal data and eligibility assessment data were stored in a filing cabinet and the rest of the data in another. A number was assigned to each participant, which was used to link both sets of data. The researcher ensured that EEG data and video footage were stored on password-protected electronic media. Guidelines from the University of Southampton Data Protection Policy were followed.

4.12.5 Risks and benefits for participants

There are no known physical or psychological risks associated with the use of the ArmeoSpring rehabilitation robot. The ArmeoSpring is a CE-marked commercially available system and is used clinically worldwide. As fatigue may result from prolonged use, the researcher monitored this at intervals during training sessions. There is a small risk of skin irritation or allergy to skin preparation and conductive gels used for EEG data collection. These were tested on participants' hands to ensure they did not negatively react to them.

Direct benefits associated with participation in the study were primarily related to the opportunity for stroke participants to receive additional rehabilitation following discharge.

4.12.6 Monetary compensation for travel expenses

The researcher offered each participant up to GBP 5 per visit to cover their travel expenses.

4.12.7 Sharing of results with participants

Participants were offered to receive a brief summary describing the study's results in lay terms. At the end of the study, a letter thanking the participant was sent (see Appendix N).

4.13 Conclusion

Recruitment procedures and design choices regarding data collection methods developed for this study have been discussed in this chapter. In order to test these, a feasibility study was carried out with a small number of participants. Its results are presented in the next chapter.

Chapter 5: Feasibility study

5.1 Introduction

In order to answer the first research question, ‘Are recruitment procedures, data collection and data analysis methods developed for this study effective to investigate ERD/ERS measures during reaching’, a feasibility study was carried out to try out recruitment of both healthy participants and stroke participants, test data collection methods, to confirm that ERD was elicited in the expected cortical areas and bandwidths, and to identify issues and improvements for subsequent studies. A small number of participants were recruited and a preliminary analysis of the data was carried out. Issues were identified and solutions were proposed for following studies.

5.2 Methods

5.2.1 Participants

Two right-handed chronic stroke participants with moderate hemiparesis were recruited and gave consent to participate in the study. Figure 25 provides details on recruitment. Table 10 presents characteristics of the two stroke participants who participated.

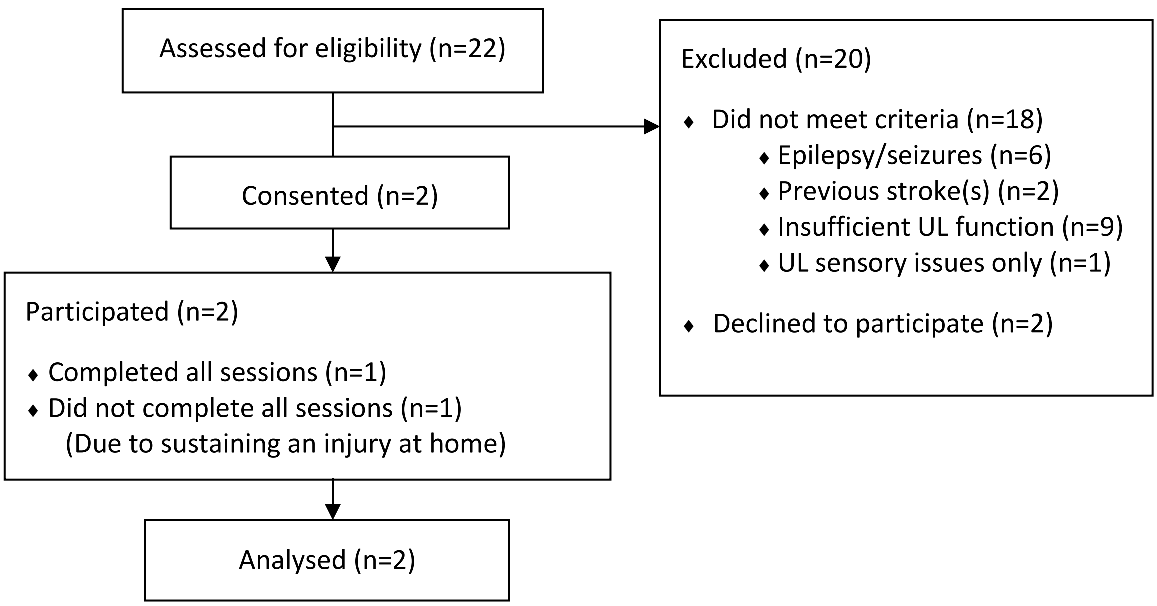


Figure 25 Recruitment of stroke participants.

Participant	Age (years)	Gender	Time since stroke (months)	Side affected	Stroke type	Baseline Fugl-Meyer score	Baseline ARAT score
P1	69	M	48	Right	Left haemorrhagic stroke	48	45
P2	67	F	43	Left	Right ischaemic stroke	37	11

Table 10 Stroke participants' characteristics.

Three right-handed healthy participants were recruited and gave consent to participate in the study. Data from one participant (H3) could not be used due to excessive artefacts. Figure 26 provides details on recruitment. Table 11 presents characteristics of the healthy participants who participated.

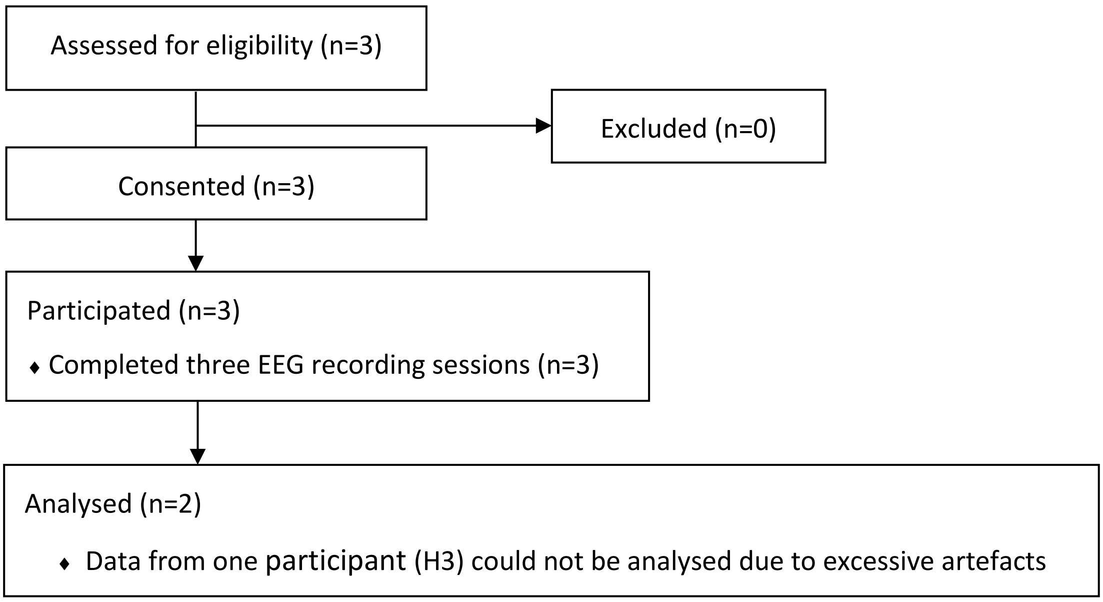


Figure 26 Recruitment of healthy participants.

Healthy participant	Age (years)	Gender	Arm moved for EEG recordings
H3	67	F	Left
H5	70	M	Right
H7	68	M	Left

Table 11 Healthy participants' characteristics.

5.2.2 Data recording

Data was collected as per the measurement schedule described in Chapter 4. One of the stroke participants (P2) only completed two measurement sessions as they injured themselves at home after two pre-rehabilitation measurement sessions and five rehabilitation sessions. A total of 15 EEG datasets were obtained (two for one stroke participant, four for the other and three for each of the three healthy participants).

5.2.2.1 Motor task

All participants performed 150 cued reaching movements at each session, reaching forward as quickly as possible using the experimental setup described in Chapter 4. Stroke participants used their affected side and healthy participants were either assigned left or right arm movements (see Table 11). Participants were asked to relax their arm muscles, as much as possible, after reaching the end of the movement. As potential difficulties associated with EEG equipment are related to the production of signal artefacts caused by unwanted muscle contractions (frowning, swallowing, and jaw or neck/shoulder tension), participants were therefore carefully briefed about these before recording began.

5.2.2.2 EEG recording

The researcher carried out all recording sessions and collected data using the 35 channel EEG electrode configuration described in Chapter 4. All participants were instructed to wash their hair before the recordings, and to avoid using any hair conditioning or styling product. Participants' head circumference and distance between nasion and inion were measured to determine the size of cap to be used. When applying the cap to participants' heads, the location of the Cz electrode was verified to ensure it was located halfway between the nasion and inion.

The EEG lab at the School of Psychology at the University of Southampton was used for all participants. The lab is equipped with SynAmps2 amplifiers (24 bit analogue to digital (AD) conversion) and the NeuroScan Acquire 4.4 software package for EEG signal acquisition. SynAmps2 amplifiers are factory calibrated and do not require any further calibration

(Compumedics Neuroscan USA Ltd. 2007). Recordings were carried out in AC mode. Data was sampled at 1000 Hz with an anti-alias bandpass filter of 0.05 – 100 Hz. This complies with the sampling theorem which states that the sampling rate should be at least twice the maximum frequency in a signal. Ag/AgCl ring electrodes (12 mm in diameter) were used, as was Abralyt HiCl (EasyCap GmbH, Germany) abrasive electrolyte gel, to prepare participants' scalps and to ensure impedance was less than 10 KΩ for all electrodes. The following consumable items were also used: iso-propyl alcohol (to prepare the skin prior to the application of electrolyte gel), 10 ml and 30 ml syringes (to apply the electrolyte gel), adhesive pads for the face electrode, and SNR 35dB earplugs (Moldex, USA). Angie Barks, research technician, assisted the researcher with preparing participants' scalps by applying the iso-propyl alcohol and electrolyte gel.

5.2.2.3 EMG and potentiometer data recording

Surface EMG signals were recorded from the anterior deltoid and the triceps brachii (lateral head) muscles using setup described in Chapter 4. The BioReader program (Dr Matt Jones, Neuroscience Training and Development Lead, School of Psychology, University of Southampton) was used to record EMG and potentiometer data (from the reaching device described in Chapter 4), along with Isolated BioAmplifiers with Bandpass Filter (Model V75-04, Coulbourn Instruments LabLinc). EMG and potentiometer data was sampled at 10000 Hz, with an 8 Hz to 1 kHz filter and a gain of 1000. Participants' skin was prepared with iso-propyl alcohol. EMG self-adhesive Ag/AgCl electrodes (3M, USA) were used in a bipolar setup.

5.2.2.4 Clinical assessments of impairment and function

The researcher filmed stroke participants as the Fugl-Meyer and ARAT assessments were administered. A blinded assessor (Seng Kwee Wee, physiotherapist experienced in using the assessments) viewed the films in random order and independently scored these assessments to ensure results were unbiased. Scores were recorded on scoring sheets (see Appendices O and P).

5.2.3 Rehabilitation with the ArmeoSpring

Only participant P1 completed a programme of rehabilitation using the ArmeoSpring, situated at the University of Southampton, as per the protocol described in Chapter 4. The other participant, P2, only completed five sessions, due to an injury.

5.2.4 Data processing and analysis

A number of steps were required to process the data before it could be examined. MATLAB version R2012a (MathWorks Inc, USA) and EEGLAB version v10.2.5.8b (Delorme and Makeig 2004), a MATLAB toolbox for processing EEG data, were used to prepare the data for analysis.

5.2.4.1 Data processing

Synchronising data and creating movement onset/offset event markers

A custom-made MATLAB script was developed by Dr Matt Jones (University of Southampton) to prepare EEG, EMG, and potentiometer data. This script resamples the EMG and potentiometer data (to match the sampling rate of the EEG data), synchronises and combines data into an EEGLAB format file, and creates movement onset and offset event markers, based on potentiometer data.

Editing of EEG channel locations

EEGLAB was used for adding channel location coordinates, using the BESA spherical coordinate system.

Inspection of movement performance and event markers

Potentiometer data for every movement was visually inspected with EEGLAB to ensure there was no more than one second between the cue and the movement onset event marker (as this would signify a missed cue due to inattention), that movement onset and offset event markers were located in the correct position along the potentiometer data curve, and that there was at least four seconds of immobility following the movement offset marker. Movement data that did not satisfy these criteria was removed.

EEG artefact rejection

The iterative method suggested by the creators of EEGLAB was used to reject eye artefacts (Delorme 2011), based on Independent Component Analysis (ICA):

1) Visual inspection and rejection of continuous EEG data

All six data files (one file for each block of 25 movements) for each recording session were combined into one before visual inspection of the data. Unsuitable portions of the data containing large paroxysmal artefacts not related to eye activity were removed with EEGLAB.

2) Extraction of epochs

Epochs were then extracted from the EEG data with EEGLAB, using the movement onset marker to time-lock data, retaining four seconds before and four seconds after movement onset.

3) First ICA

EEGLAB's 'runica' routine was performed a first time to derive independent components.

4) Rejection of epochs based on visual inspection of components

Independent components were visually inspected and epochs containing significant artefacts that were present in several components were removed with EEGLAB.

5) Second ICA

EEGLAB's 'runica' ICA routine was performed a second time on the pruned collection of epochs.

6) Rejection of components

A cautious approach for removal of artefact components was taken, only removing clear, well-defined eye-related components associated with blinking or movement of the eyes. This approach was used to avoid removing components that may include movement-related activity. This was achieved by using EEGLAB to visually inspect components characteristics, as well as by inspecting their spatial localisation to confirm they were eye-related.

7) Additional removal of epochs

A final visual inspection of epochs was performed with EEGLAB, and when appropriate, additional epochs with remaining significant artefacts were removed.

Alternative EEG artefact rejection procedure

When eye artefacts were not well defined following ICA decomposition for a specific dataset (due to an insufficient number of blinks in epoched data), an alternative approach was used. In this case, ICA was performed before data was epoched. Eye blink components were removed at this point, and data epoched afterwards. A second ICA was performed to identify further epochs to be removed.

5.2.4.2 Movement characteristics

A custom MATLAB script was developed by the researcher to compute mean reaction times (and standard deviations) for every dataset, by calculating the time elapsed between the timing of the movement cue event marker and the movement onset event marker. A similar script was developed and used to compute mean movement times (and standard deviations), by calculating the time difference between the movement onset and movement offset markers.

5.2.4.3 ERD/ERS time frequency maps

In order to determine whether ERD was elicited in the expected cortical areas and bandwidths, EEGLAB's 'newtimef' routine (Makeig 1993) was used to develop a custom-made MATLAB script (Dr Ulrich Hoffmann, Tecnalia, Spain) to plot ERD/ERS time frequency maps for all channels arranged topographically, showing ERD/ERS in the 2-60 Hz range, using a one second reference period between -3500 and -2500 ms before movement onset, a bootstrap significance of 0.05 (based on random data shuffling), and colour scale limits of -7 to 7 dB for all datasets. Morlet wavelets were used for frequency decomposition. The width of the windows required for frequency decomposition was calculated, with results for the 2 to 30 Hz frequency range presented by Table 12. Every outputted time point as part of the frequency decomposition was at the centre of the wavelet window. It can be observed that lower frequencies require a larger window than higher frequencies. This is an important observation as when considering the timing of ERD/ERS, for example, at 12 Hz, ERD/ERS at a specific time point represents summed activity taking place 34 ms before and after that time point (as the window's length is 68 ms at 12 Hz and time points are at the centre of this window).

Frequency (Hz)	Wavelet window width (ms)
2	477
3	314
4	232
5	183
6	150
7	127
8	109
9	95
10	85
11	76
12	68
13	62
14	56
15	52
16	48
17	44
18	41
19	38
20	35
21	33
22	31
23	29
24	27
25	26
26	24
27	23
28	21
29	20
30	19

Table 12 Wavelet window widths for the 2-30 Hz frequency range.

EEGLAB's 'newtimef' routine calculates event-related spectral perturbation (ERSP), described by its author (Makeig 1993) as being a generalisation of the narrow-band ERD. For ease of reading, the terms ERD and ERS will be used instead of ERSP as they are useful to distinguish between desynchronisation and synchronisation. This data was also used to produce plots of ERD/ERS% over time for select channels. As the 'newtimef' function outputs values in decibels (dB), these were converted to ERD/ERS% using the following equation:

$$\text{ERD/ERS\%} = (10^{(\text{ERSP}/10)} - 1) * 100 \qquad \text{(ERSP value in dB)}$$

ERD/ERS% quantifies the percentage decrease (ERD%) or increase (ERS%) in power relative to the resting reference period.

5.2.4.4 Maximum ERD% values

The MATLAB script developed for calculating and plotting ERD/ERS was modified by Professor David Simpson (Institute of Sound and Vibration Research, University of Southampton) to also create data matrices that only reflect significant ERD/ERS, as this significance is stored separately from the 'raw' ERD/ERS data produced by EEGLAB's 'newtimef' function. These matrices were used by a custom MATLAB scripts written by the researcher to extract maximum ERD% values (by first converting values from ERSP (in dB) to ERD% as described above) in the alpha frequency range (8-12 Hz) for electrodes C3 and C4, as well as the time at which it occurs. For the purpose of this feasibility study, electrodes C3 and C4 were chosen as they are centrally located over the motor cortex and are often used to characterise its activity. The electrode within the FC, C, and CP rows of electrodes at which the maximal ERD% occurs was also identified, along with its associated timing. This process was repeated for the beta frequency range (13-30 Hz).

5.2.4.5 Clinical assessments scores

Total scores were calculated for the Fugl-Meyer (motor score of the upper extremity section only) and ARAT outcome measures, by adding up individual scores from every subtest.

5.3 Results

5.3.1 Clinical assessment scores

Table 13 and Table 14 present clinical assessment scores for participants P1 and P2. The maximum scores (reflecting the best performance possible) for the Fugl-Meyer and ARAT assessments are 66 and 57, respectively.

For participant P1, slight changes were observed between pre- and post-therapy assessments, with Fugl-Meyer scores being lower post therapy (with a lowest score of 44 for the assessment carried out three days after the end of the therapy programme), and ARAT scores being slighter higher after the therapy programme. The Fugl-Meyer score of 44 at session 3 was mainly due to a small amount of compensatory trunk movements and slightly incomplete movements over a number of subtests, as opposed to drastic changes in certain test items. Improvements for ARAT scores were found in the grasp and pinch subtests, indicating slight improvements in hand function. Participant P2's scores decreased by one point from session 1 to session 2.

Session	Fugl-Meyer	ARAT
1	48	45
2	49	43
3	44	46
4	47	47

Table 13 Clinical assessment scores for participant P1.

Session	Fugl-Meyer	ARAT
1	37	11
2	36	10

Table 14 Clinical assessment scores for participant P2.

5.3.2 Movement characteristics

Table 15 presents the number of movements retained for analysis, as well as mean reaction times and movement times for all datasets. It was observed that for some sessions, the number of movements retained for analysis was low (participant H5, session 1: 51 movements; participant P1, session 1: 61 movements), due to a high occurrence of muscle artefacts in the data. Mean movement times were generally higher for stroke participants than they were for their healthy counterparts. Most standard deviations varied between 20 and 50 ms, indicating that movements from each recording session were mostly similar in terms of speed. Variation of mean movement times was relatively low, except for participant P1, where the difference between the smallest and greatest mean movement times was 120 ms. The mean reaction time for participant H5's first session, just above the 200 ms mark, was deemed to be questionably small. Further examination was carried out by examining the frequency distribution histograms of reaction times (see Figure 27). They revealed that many occurrences from datasets 1 and 3 were unrealistic (some being below 200 ms), as mean reaction times following a visual stimulus have been found to be at around the 295 ms mark for the 61 to 80 year old age group (Deary et al. 2011).

Participant	Session	Number of movements	Mean reaction time	± SD	Mean movement time	± SD
H5	1	51	202	71	250	40
	2	144	337	91	288	33
	3	138	327	99	233	28
H7	1	101	512	192	256	74
	2	91	695	147	242	22
	3	110	586	157	220	30
P1	1	61	585	135	272	31
	2	69	442	117	292	50
	3	93	408	125	333	47
	4	96	497	170	393	59
P2	1	97	318	133	328	35
	2	91	498	147	377	31

Table 15 Number of movements retained for analysis, mean reaction times (in ms), and mean movement times for all participants (in ms).

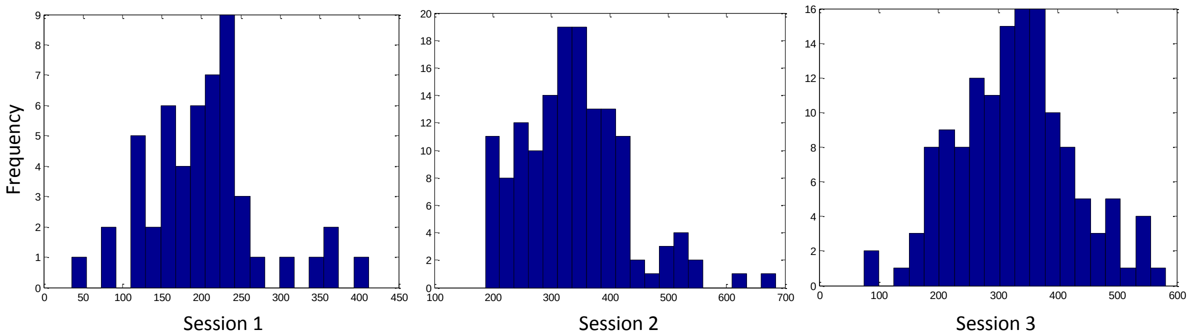


Figure 27 Frequency distribution of reaction times (in ms) for participant H5.

Further investigation revealed that there were software and hardware problems with the data acquisition card that relays data from the reaching device's potentiometer and from EMG amplifiers to the BioReader recording software. Dr Matt Jones (University of Southampton) reported that "There were a number of reasons why the old approach was giving errors. Firstly, the polling method was missing some events, due to timing inaccuracies brought about by the operating system not keeping up with the high resolution demands made upon it. Secondly, the time associated with the event was obtained from the recording buffer, which was not guaranteed to be synchronised to real (world) time, since the buffer was filled only when the system had time to process the incoming data, which happened frequently but in spurts – i.e. not regularly as would be used for accurate timing. The new setup, which uses a new data acquisition card and new software has very good accuracy. This is because rather than polling the digital inputs to see if anything has changed, it records the digital data alongside the analogue data. This guarantees synchronisation between the two data streams." This problem with synchronisation resulted in EMG and potentiometer data, as well as the cueing event markers, to be misaligned with EEG data, as synchronisation was achieved by aligning the timing of the event markers. As this misalignment was not systematic and varied over time, it was not possible to correct this problem. Reaction times presented in Table 15 are thus inaccurate. Movement times are however accurate as they are simply derived from the potentiometer data.

The researcher subsequently tested the accuracy of the new revised setup, by recording 90 minutes with one EEG channel and one EMG channel, and producing event markers (by going through the cueing loop) every five minutes. It was found that data was accurately synchronised throughout the dataset, with the application of a small scale factor of 1.0000559946 applied to the time-scale of the EEG data. This was because NeuroScan and BioReader's sample rates differ by a small, constant factor. Analysis of adjusted timings from the test showed that the error margin was at most 2 ms over the first ten minutes of recording, which is the approximate length of the six recording blocks for each recording session. Such as small error would not greatly affect the temporal analysis of the signals.

5.3.3 ERD/ERS time frequency maps

ERD/ERS time frequency maps were produced for all datasets. A number of maps showed widespread ERS during the execution of the movement in the 25 to 60 Hz range. A Hjorth style (Hjorth 1975) Laplacian filter was applied (using up to eight neighbouring channels) using a bespoke MATLAB script developed with Professor David Simpson (University of Southampton), which successfully attenuated the widespread ERS and enhanced localised activity.

Figure 28 and Figure 29 show examples of maps for a healthy volunteer and a stroke participant. For participant H7, bilateral ERD in centroparietal areas was present in a wide frequency range in the alpha and beta bandwidths, before and during movement, with alpha ERD peaks being distinguishable from beta ERD. A lateralised beta ERS following movement could also be seen to occur in centroparietal areas. For participant P1, widespread bilateral ERD was present in all areas in a wide frequency range in the alpha and beta bandwidths, before and during movement, with alpha ERD peaks being distinguishable from beta ERD in some areas. Bilateral beta ERS following movement could also be seen to occur in centroparietal areas.

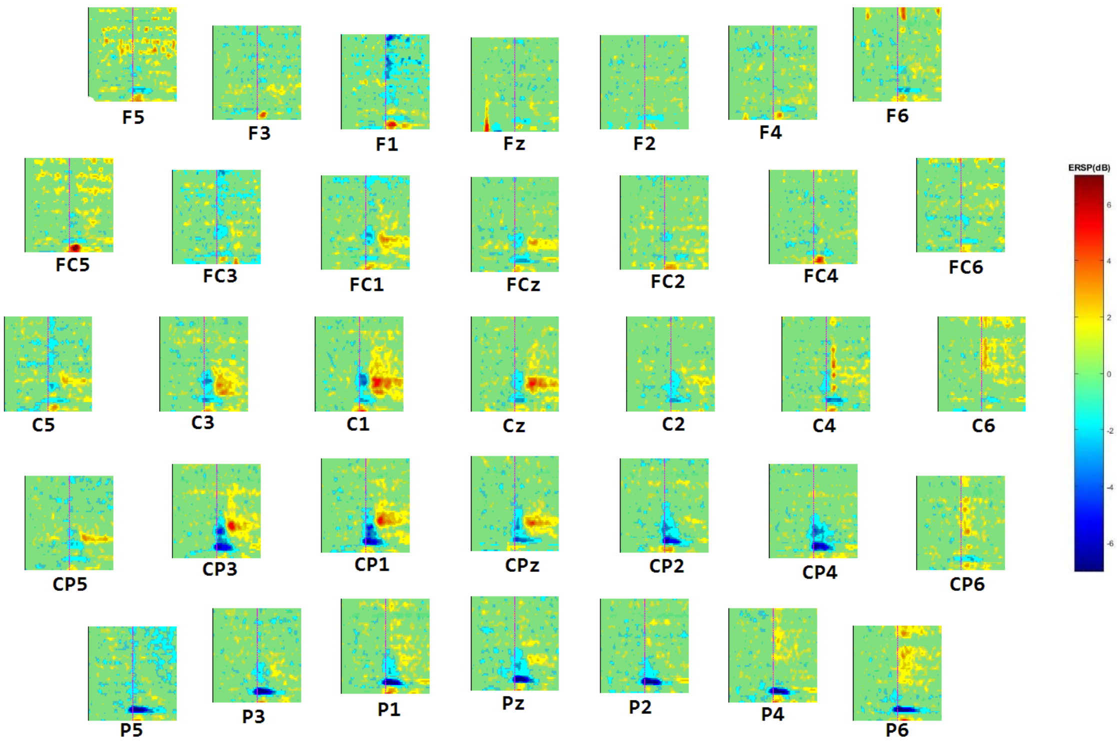


Figure 28 ERD/ERS time frequency maps for participant H7, session 1. X axis: time (-3167 to +3167 ms), movement onset at 0 ms, indicated by a vertical line; y axis: frequency (2-60 Hz); significant ERD displayed on a colour gradient from light blue to dark blue (maximum value of -7 dB); significant ERS displayed on a gradient from yellow to dark red (maximum value of +7 dB). Green indicates non-significant changes (displayed as 0 dB). Left arm movements.

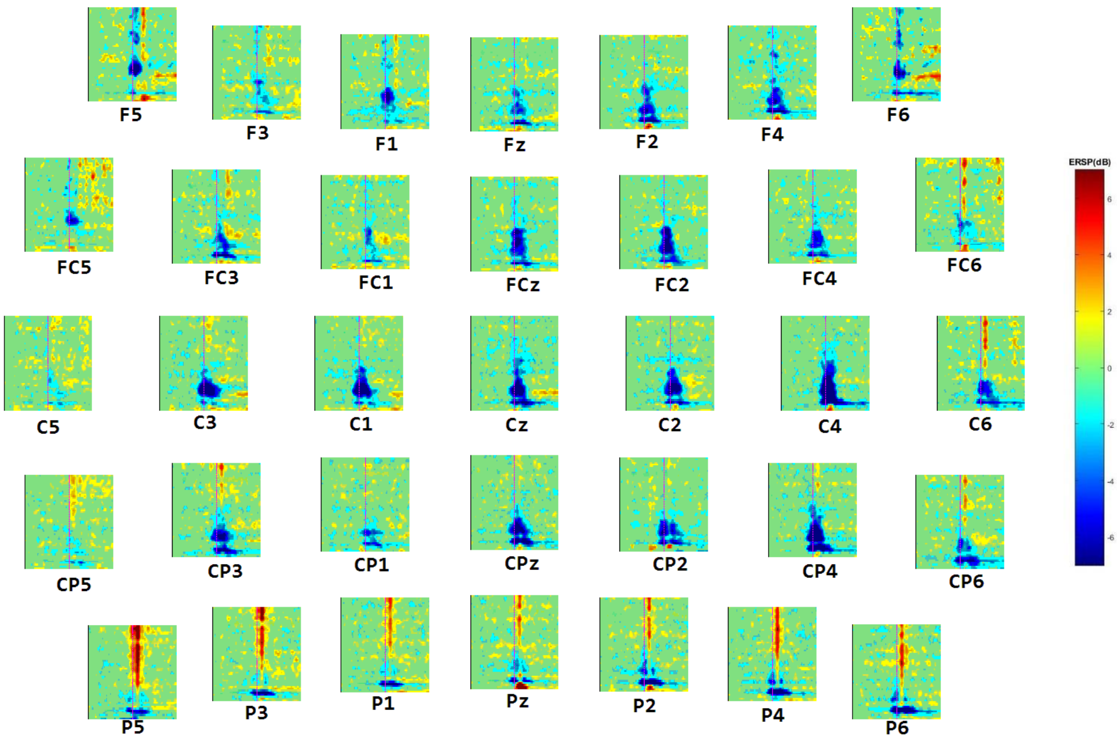


Figure 29 ERD/ERS time frequency maps for participant P1, session 1. X axis: time (-3167 to +3167 ms), movement onset at 0 ms, indicated by a vertical line; y axis: frequency (2-60 Hz); significant ERD displayed on a colour gradient from light blue to dark blue (maximum value of -7 dB); significant ERS displayed on a gradient from yellow to dark red (maximum value of +7 dB). Green indicates non-significant changes (displayed as 0 dB). Right arm movements.

All other participants' maps showed alpha and beta ERD, as well as beta ERS, similarly to the plots above. It was however observed that there is variability between participants.

5.3.4 Maximum ERD%

Table 16 and Table 17 present all maximum ERD% values for all 12 datasets for the alpha and beta ranges, respectively. Times at which maximum values were found are reported, but due to the synchronisation problem discussed earlier, these should be examined with caution as they are inaccurate.

For participant H5, no consistent hemispheric predominance could be observed between electrodes C3 and C4, and maximum values occured along the longitudinal fissure at electrodes C1, C2, Cz, and CPz.

For participant H7, a consistent right hemispheric predominance could be observed for alpha ERD (ERD% at C4 is larger than ERD% at C3), with maximum values occurring on the right hemisphere at electrodes CP2 and CP4. A consistent left hemispheric predominance could be observed for beta ERD (ERD% at C3 is larger than ERD% at C4), with maximum values occurring at various locations on both hemispheres at Cz, CP1 and CP4.

For participant P1, a small but consistent right hemispheric predominance could be observed for both alpha and beta ERD (ERD% at C4 is larger than ERD% at C3), with maximum values occurring consistently on the right hemisphere at electrode C4. Figure 30 shows an example of significant alpha ERD%, plotted over time.

For participant P2, a consistent left hemispheric predominance could be observed for both alpha and beta ERD (ERD% at C3 is larger than ERD% at C4), with maximum values occurring almost exclusively at electrode C3 (dataset 1 shows a maximum alpha ERD% on the right hemisphere at electrode location CP4).

Participant	Arm moved	Session	Mean movement time (ms)	Max ERD% at C3	Time (ms)	Max ERD% at C4	Time (ms)	Max ERD%	Time (ms)	Electrode
H5	Right	1	249.90	-66.1	1092	-78.4	838	-89.0	680	C2
		2	287.75	-75.9	854	-69.6	617	-85.4	506	CPz
		3	233.18	-55.2	980	-55.7	807	-82.3	443	CPz
H7	Left	1	255.92	-58.2	142	-62.6	253	-82.9	221	CP4
		2	242.29	-62.5	0	-65.5	-63	-83.8	-63	CP4
		3	220.30	-58.4	47	-71.3	111	-86.1	127	CP2
P1	Right	1	272.12	-87.7	585	-95.5	142	-95.5	142	C4
		2	292.00	-93.5	744	-93.5	158	-93.5	158	C4
		3	333.33	-87.1	79	-91.1	316	-91.1	316	C4
		4	392.88	-84.8	16	-90.7	206	-90.7	206	C4
P2	Left	1	327.65	-73.8	285	-69.0	759	-81.4	174	CP4
		2	377.05	-74.3	775	-70.7	759	-74.3	775	C3

Table 16 Maximum ERD% in the alpha band (8-12 Hz), with times at which maximums occur, relative to movement onset. Times at which maximums occur are not accurate.

Participant	Arm moved	Session	Mean movement time (ms)	Max ERD% at C3	Time (ms)	Max ERD% at C4	Time (ms)	Max ERD%	Time (ms)	Electrode
H5	Right	1	249.90	-87.2	1044	-84.1	886	-93.6	427	Cz
		2	287.75	-86.2	570	-83.3	206	-95.2	142	C1
		3	233.18	-74.3	1218	-80.9	316	-95.4	221	CPz
H7	Left	1	255.92	-58.0	427	-42.6	63	-67.9	285	CP1
		2	242.29	-60.0	-16	-48.2	79	-69.0	174	Cz
		3	220.30	-63.3	111	-54.9	-32	-69.3	32	CP4
P1	Right	1	272.12	-91.1	111	-96.8	95	-96.8	95	C4
		2	292.00	-92.9	554	-95.2	506	-95.2	506	C4
		3	333.33	-91.2	190	-93.0	206	-93.0	206	C4
		4	392.88	-86.2	48	-94.1	269	-94.1	269	C4
P2	Left	1	327.65	-90.4	237	-70.5	554	-90.4	237	C3
		2	377.05	-87.5	664	-69.5	617	-87.5	664	C3

Table 17 Maximum ERD% in the beta band (13-30 Hz), with times at which maximums occur, relative to movement onset. Times at which maximums occur are not accurate.

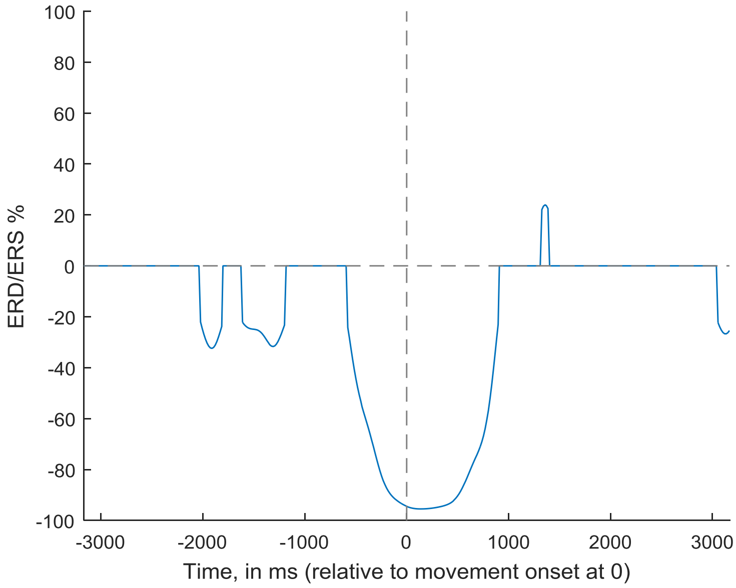


Figure 30   Example of significant alpha ERD% for participant P1 at electrode C4, session 1. Non-significant ERD/ERS% represented with a value of zero; bootstrap significance level of 0.05. Times are not accurate.

5.4 Discussion

This feasibility study's results answered the first research question: 'Are recruitment procedures, data collection and data analysis methods developed for this study effective to investigate ERD/ERS measures during reaching?'. Results demonstrated that the recruitment procedures, data collection and data analysis methods were viable and effective, in that results were reasonable with regards to ERD/ERS being elicited in all participants in the expected cortical areas and bandwidths, as per previous literature findings. Results have highlighted a number of issues that needed to be addressed before recruitment to subsequent studies began.

Recruitment of stroke participants

Recruitment of stroke participants to the feasibility study was a challenge, in that there was a high number individuals who did not meet the criteria to be included in the study. It became evident that more recruitment sites were required to increase the number of potential participants, and that recruitment of individuals in the chronic phase should also be sought, as initially, only people in the subacute phase had been considered. A number of sites were added during the recruitment phase, including the Work Rehabilitation Service (Solent NHS Trust), and non-NHS sites, such as stroke clubs, a private rehabilitation clinic, as well as the University of Southampton's Faculty of Health Sciences research participant register.

For future recruitment, an additional piece of information would be sought from participants during the assessment session. Details regarding the location of stroke (sub-cortical, cortical, or mixed) would be documented, when possible, as cortical activation has been found to vary according to location of the stroke (Luft et al. 2004b).

Recording

Software and hardware problems were found with the data acquisition card that relays data from the reaching device's potentiometer and from EMG amplifiers to the BioReader recording software. These problems were addressed by a replacing the acquisition card and by a software redesign.

The quality of the raw EEG data was also an issue in that several datasets had a high rejection rate of unusable portions of data due to the presence of important artefacts. Data from one participant (H3) was not retained for analysis due to excessive artefacts. The presence of a wide spread ERS in several datasets during the execution of the movement led to the application of a Laplacian filter, as it was assumed that this was due to a widespread artefact. To possibly avoid having to use this filter and improve on the number of epochs retained for analysis, the quality of the data needed to be improved. To achieve this, two measures would be taken with future participants. They would be given a preparation instruction document (see Appendix Q) prior to the first recording session, to ensure that participants have a better understanding of what is required of them in terms of movement performance. Secondly, participants would be trained at the first recording session to increase body awareness. This would be achieved by displaying real-time EEG traces on a computer screen, in order for participants to see the effects of artefact-producing activities such as jaw tension, frowning, eye movements, and swallowing.

Data processing

The time required to prepare each EEG dataset was lengthy, mostly due to the time taken to run the ICA decomposition routine. To improve on this, future EEG datasets were downsampled from 1000 to 250 Hz, and the amount of computer RAM used to run ICA routines was increased from 4 to 8 Gb.

Clinical assessments

The absence of important improvements for the stroke participant who completed all sessions could be explained by their limited potential for neuroplastic change (as they were in the chronic phase), by the possible insufficient responsiveness of the assessments to perceive subtle changes, or by an insufficient amount of therapy. More data was required to examine what cortical activity changes could be observed in individuals in whom substantial motor improvements did occur. As the potential for motor improvement is usually greater in people in the subacute phase of stroke, participants from this group would be sought.

To further track potential subtle improvements in upper limb function, three assessments from the ArmeoSpring system ('A Goal', 'Vertical Catch', and 'Reaction Time') would be administered for future participants from the stroke participant study at the first rehabilitation session, at midpoint, and at the last rehabilitation session. These consist of timed activities where the participant is required to reach for targets, requiring a variety of arm movements. These assessments are described further in Chapter 8.

Movement characteristics

The greater difference in mean movement times for participant P1 (which was not due to changes in arm function) highlighted the need to standardise movement performance as much as possible, in order to be able to compare cortical activity resulting from movements of similar speed. A couple of factors could have contributed to the variability of movement times. The first factor relates to the lengthy, repetitive nature of the movement task and the dark environment in which the EEG recordings are made, which causes sleepiness, as reported by most participants. The second relates to how motivated participants are to perform the movement as quickly as possible. For future recordings, participants would be encouraged before every block of movements to perform them as quickly as they can when they see the cue.

ERD/ERS time frequency maps and maximum ERD%

The analysis of movement-related ERD showed that it occurred bilaterally over large cortical areas (as opposed to being spatially focused, as it is the case for isolated joint movements), as reported previously (Pfurtscheller et al. 1999). Laterality of activation was thus not as marked as it is with isolated joint movements, however general observations can be made about data obtained so far. Both stroke participants consistently presented with an ipsilateral hemisphere maximum ERD% predominance (as measured at electrode sites C3 and C4) in both alpha and beta bands, which could be interpreted as an attempt by the motor cortex to compensate for inadequate contralateral hemisphere function. Healthy participants however did not present with such a constant lateral predominance, with one healthy participant (H5) having inconsistent lateral predominance between sessions in both frequency bands, and the other (H7) showing predominance on the hemisphere contralateral to the arm moved in the alpha band and predominance on the hemisphere ipsilateral to the arm moved in the beta band. More data was required to make conclusions regarding patterns of predominance in both stroke participant and healthy participant groups.

5.5 Conclusion

The preliminary results from this feasibility study showed that movement-related ERD/ERS was elicited in all participants in the expected cortical areas and bandwidths using this experimental setup, in line with previous movement-related EEG literature findings. Issues relating to recruitment, recording of EEG data, and data processing were identified and solutions proposed for the next study, which examined the variability over time of ERD/ERS measures during reaching for a group of healthy participants.

Chapter 6: Test-retest variability study

6.1 Introduction

In order to answer the second research question, ‘What is the variability over time of ERD/ERS measures during reaching for a small sample of healthy participants?’, a test-retest variability study was carried out to determine the degree of variability of ERD/ERS measures among healthy participants. Results of this study were useful when looking at results from the stroke participant study (see Chapter 8), in order to determine whether potential changes were due to natural variability or whether they could be associated to the effects or rehabilitation.

6.2 Methods

6.2.1 Participants

Seven right-handed healthy participants (mean age 54.3 ± 16 years; range 25-71 years; three females and four males) were recruited and gave consent to participate in the study. Data from participant H14 could not be used due to excessive artefacts, preventing the accurate definition of an eye blinking ICA component. Data from participant H18 was not included for analysis due to low intensity ERD/ERS.

Figure 31 provides details on recruitment. Table 18 presents characteristics of the seven individuals who participated.

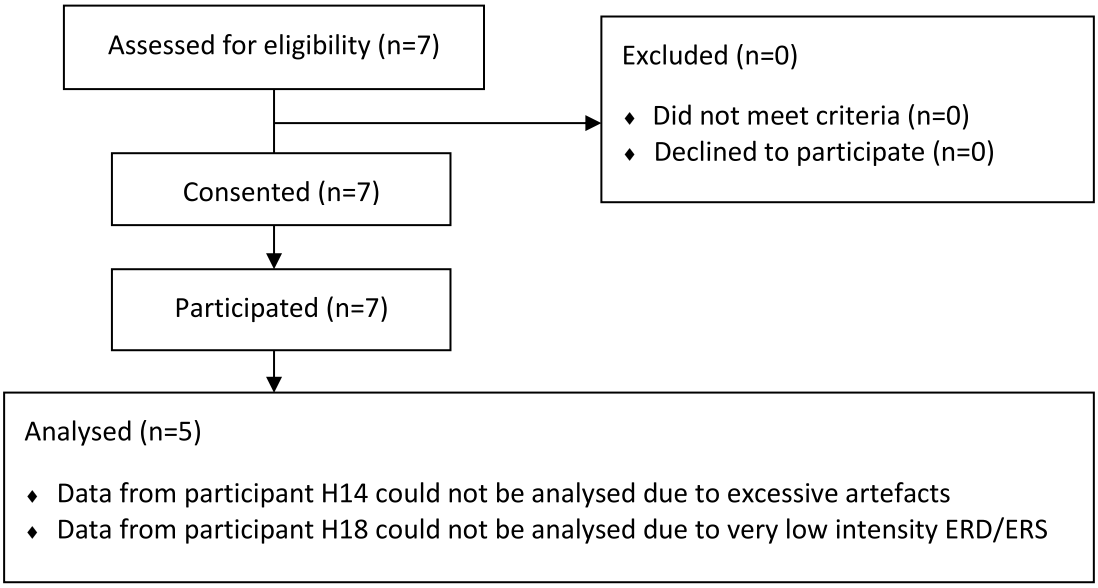


Figure 31 Recruitment of healthy participants.

Participant	**Age (years)**	**Gender**	**Arm moved for EEG recordings**
H14	68	M	Right
H18	71	M	Right
H19	53	F	Right
H16	53	F	Right
H15	25	F	Left
H23	45	M	Left
H26	65	M	Left

Table 18 Healthy participants' characteristics.

6.2.2 Data recording

Each participant attended three recording sessions as per the measurement schedule described in Chapter 4. A total of 21 EEG datasets were obtained (three for each of the seven participants).

6.2.2.1 Motor task

All participants performed 150 cued reaching movements at each session, reaching forward as quickly as possible using the experimental setup described in Chapter 4. Participants were either assigned left or right arm movements (see Table 18). Participants were given preparation instruction sheets prior to attending the recording session. Participants were asked to relax their arm muscles after reaching the end of the movement, and to avoid the production of signal artefacts caused by frowning, swallowing, and jaw or neck/shoulder tension.

6.2.2.2 EEG recording

The researcher carried out all recording sessions and collected data using the 35 channel EEG electrode configuration described in Chapter 4. All aspects of EEG recording were the same as for the feasibility study (see Chapter 5), except for using a more recent version (version 4.5) of the NeuroScan Acquire software package for EEG signal acquisition.

6.2.2.3 EMG and potentiometer data recording

All aspects of EMG and potentiometer data recording were the same as for the feasibility study (see Chapter 5), using the revised software and hardware setup.

6.2.3 Data processing and analysis

6.2.3.1 Data processing

MATLAB version R2016a (MathWorks Inc, USA) and EEGLAB version v13.6.5b (Delorme and Makeig 2004) were used for this study. Synchronisation of data, creation of movement onset/offset event markers, and artefact rejection procedures were the same as the ones described in the feasibility study (see Chapter 5), except for also filtering (50 Hz notch filter, 2 Hz high pass, and 45 Hz low pass) and downsampling EEG data from 1000 to 250 Hz to reduce ICA decomposition processing time. In addition to these, a procedure was added at the end: using EEGLAB, seven channels not part of the electrode sites used for analysis were removed from each dataset. These were the ones used to record eye blinking (right cheek, FP2, F9, and F10), as well as EMG and potentiometer data channels. Average referenced data was then derived using EEGLAB for the remaining 35 channels used for analysis. The rationale behind using an average reference relates to the fact that, if enough evenly-spaced electrodes (at least 32) are used for recording, the average voltage in the head should be approximately zero, due to the sum of variations in voltage and phase across the head (Davidson et al. 2000).

6.2.3.2 Movement characteristics

Mean reaction and movement times (and standard deviations) were calculated using the same method as the one used for the feasibility study (see Chapter 5). To compare each participant's mean movement times over three sessions, a one-way unbalanced analysis of variance (ANOVA) was carried out (using MATLAB's 'anova1' function).

6.2.3.3 ERD/ERS

ERD/ERS time frequency maps were produced for all datasets using the same methods as for the feasibility study. In addition to these, EEGLAB's STUDY functions were used to produce series of scalp maps showing the spatial distribution and intensity of ERD/ERS over time for both alpha (8-12 Hz) and beta (13-30 Hz) frequency ranges. This data was also used to produce plots of ERD/ERS% over time for pairs of symmetrical electrodes C3/C4 or CP3/CP4, as well as to extract peak ERD/ERS% values. Pairs of electrodes were chosen following visual inspection of participants' individual scalp maps, depending on where ERD was greater at the time of movement onset.

Hemispheric lateralisation of ERD

Rather than extracting ERD% values at arbitrarily chosen time points before and after movement onset, which would produce variable laterality indices depending on the chosen time points, a different approach was used that takes into account the general trend of lateralisation of ERD before and after movement onset. A laterality index (LI) measuring the values of relative ERD% present at either symmetrical pairs of electrode C3/C4 or CP3/CP4 was calculated using the following equation:

$$\text{Laterality index} = (A_X - A_Y) / (A_X + A_Y)$$

where A_X and A_Y are the area over the curve of plots of ERD% over time for electrode locations X and Y, respectively. MATLAB's 'trapz' function was used in a MATLAB script developed by the researcher. This function approximates the area over the curve by breaking down the area between each time point into trapezoids. Values for A_X and A_Y were calculated for two time periods of interest: -200 to 0 ms, and 0 to 500 ms (relative to movement onset at 0 ms). This allows examination of pre-movement onset lateralisation as well as of post-movement onset lateralisation. Calculation were made for both alpha (8-12 Hz) and beta (13-30 Hz) frequency ranges. Figure 32 illustrates areas over the curve that were calculated.

Laterality index values range from -1 to 1. A value of -1 indicates complete right hemisphere predominance. A value of 1 indicates complete left hemisphere predominance. A value of 0 indicates equal amounts of ERD% at both electrode sites.

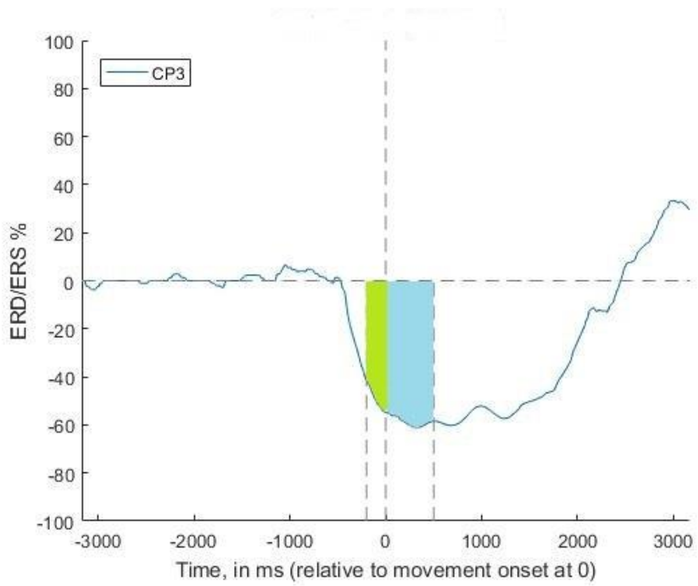


Figure 32 Illustration of areas over the curve for pre-movement onset (-200 to 0 ms), in green, and post-movement onset (0 to 500 ms), in blue.

To compare indices over each participant's three sessions, as laterality indices do not follow a linear relationship with the proportion of ERD between hemispheres, an additional indicator of laterality, L/R ratio, was calculated for comparison purposes by dividing ERD% values for the left hand side electrode (C3 or CP3) by ERD% values for the right hand side electrode (C4 or CP4). This was useful to quantify the degree of change of hemispheric laterality between sessions.

6.3 Results

6.3.1 Movement characteristics

Table 19 presents the number of movements retained for analysis, as well as mean reaction and movement times for all participants. Figure 33 shows box plots with further details about each participant's movement times.

Participant	Session	Number of movements	Mean reaction time	± SD	Mean movement time	± SD
H18	1	134	414	63	374	65
	2	142	406	78	327	45
	3	122	484	91	345	52
H19	1	125	588	114	413	85
	2	115	581	117	461	52
	3	117	621	103	444	49
H16	1	115	431	80	356	44
	2	108	476	108	397	48
	3	112	468	99	324	41
H15	1	128	350	55	207	25
	2	130	361	71	215	27
	3	119	366	78	192	25
H23	1	108	668	133	385	58
	2	115	600	137	387	47
	3	116	645	131	338	48
H26	1	137	337	53	255	38
	2	131	357	63	261	30
	3	133	363	63	276	26

Table 19 Number of movements retained for analysis, mean reaction times (in ms), and mean movement times for all participants (in ms).

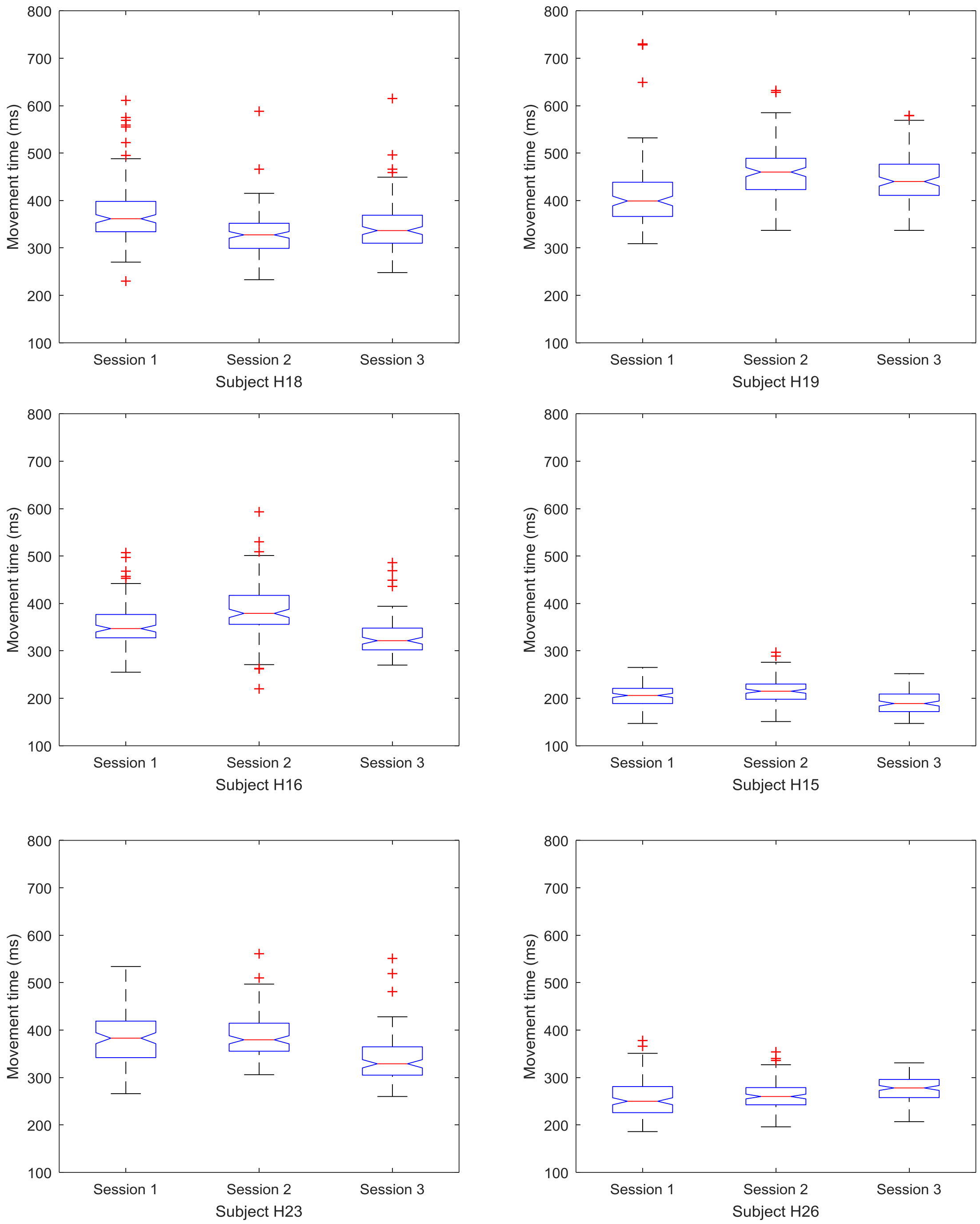


Figure 33 Box plots for each participant's movement times for three sessions (the red line in the centre of the box being the median, the edges of the box are the 25th and 75th percentiles, whiskers end at the most extreme values that are not considered outliers, and outliers are displayed with red crosses).

To compare each participant's mean movement times over three sessions, results from a one-way unbalanced analysis of variance (ANOVA) show that all participants had significantly different mean movement times (participant H18: [F = 26.16 (2, 395), p < 10^-6], participant H19: [F = 16.76 (2, 354), p < 10^-6], participant H16: [F = 44.58 (2, 332), p < 10^-6], participant H15: [F = 26.21 (2, 374), $p < 10^{-6}$], participant H23: [$F = 32.51$ (2, 336), $p < 10^{-6}$], participant H26: [$F = 16.5$ (2, 398), $p < 10^{-6}$]).

6.3.2 ERD/ERS

A preliminary examination of ERD/ERS time frequency maps and scalp maps revealed that participant H18 had low intensity alpha and beta ERD, with spatial and temporal patterns of movement-related ERD/ERS being difficult to recognise. For this reason, H18's data was not included for analysis. Literature findings from the brain-computer interface (BCI) research field report a small minority of individuals (healthy or otherwise) whose brain activity is difficult to detect with EEG. Hypotheses that would explain why this is include key active brain areas being located in the sulci of the brain, or deeper, or too close to other very active brain areas (Allison and Neuper 2010).

The variability of the following features of ERD/ERS was examined for each participant: intensity of alpha and beta ERD, lateralisation of alpha and beta ERD, beta ERD frequency range, beta ERS spatial distribution, beta ERS intensity, and beta ERS timing.

ERD/ERS time frequency maps and scalp maps for all participants are included on the accompanying USB drive for reference.

6.3.2.1 Intensity of alpha ERD

Peak alpha ERD% values

Figure 34 presents alpha ERD/ERS% over time plots for pairs of symmetrical electrodes (either C3/C4 or CP3/CP4) for all sessions. Non-significant ERD/ERS% is represented with a value of zero on the plots.

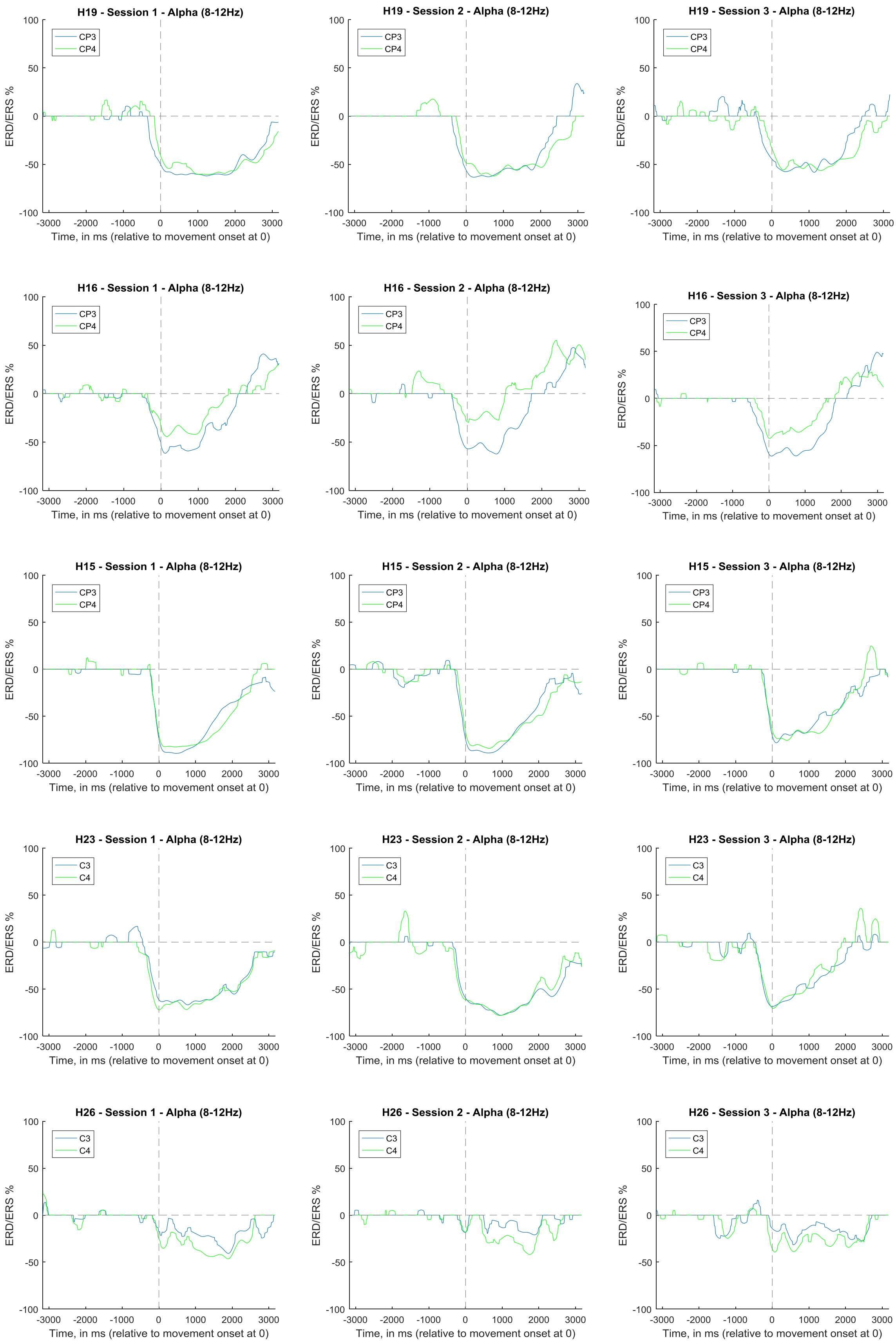


Figure 34 Plots of alpha ERD/ERS% over time for symmetrical electrodes C3/C4 or CP3/CP4. Each row presents plots for each participant’s three sessions.

These plots show that for participants H19, H16, H15, and H23, the intensity of alpha ERD% over time at either C3/C4 or CP3/CP4 was similar from session to session. Participant H26 however presented an atypical alpha ERD% curve with many fluctuations over time.

Table 20 presents peak alpha ERD% values for the electrode with the greatest alpha ERD% values from the plots above. When several peaks are present, they are approximately matched according to time and placed in the same row in order to compare values. For the purpose of visually highlighting peaks that differ the most from others, differences of more than 10 % between matched peaks' maximum and minimum ERD% values are highlighted in red.

	Session 1		Session 2		Session 3	
Participant (electrode)	Time	ERD%	Time	ERD%	Time	ERD%
H19 (CP3)	182	-58.0	198	-63.4	358	-57.7
	674	-61.0	594	-63.0		
	1231	-62.0			1135	-58.37
H16 (CP3)	118	-61.6	22	-57.0	70	-61.4
	722	-59.2	786	-62.3	738	-61.1
H15 (CP3)	214	-88.5	166	-86.8	118	-78.3
	482	-89.6	610	-89.1	406	-75.8
H23 (C4)	6	-72.0	86	-62.1	22	-70.5
	754	-71.7	926	-78.0		
H26 (C4)	118	-35.4	-6	-17.9	70	-39.3
					578	-38.7
	1895	-46.5	1755	-41.9		

Table 20 Alpha ERD% peak values for select electrodes for each participant's three sessions (times in ms). When several peaks are present, they are approximately matched according to time and placed in the same row in order to compare values. Values in red signify deviation greater than 10 % from other sessions' values at similar times.

A difference in peak alpha ERD% values (beyond the 10 % threshold, at 10.2 %) can be observed for session 3 for participant H15's first peak (-78.3 % compared to -88.5 % for session 1) as well as a larger difference of 13.8 % for the second peak (-75.8 % compared to -89.6 % for session 1). As for participant H26, as plots show atypical curves, it is not possible to make any meaningful conclusions.

Conclusion: Peak alpha ERD% values are generally similar (with values within 13.8 %) for four out of five participants. The number and timing of peaks varied greatly. Peak alpha ERD% values vary between participants.

6.3.2.2 Intensity of beta ERD

Peak beta ERD% values

Figure 35 presents beta ERD/ERS% over time plots for pairs of symmetrical electrodes (either C3/C4 or CP3/CP4) for all sessions.

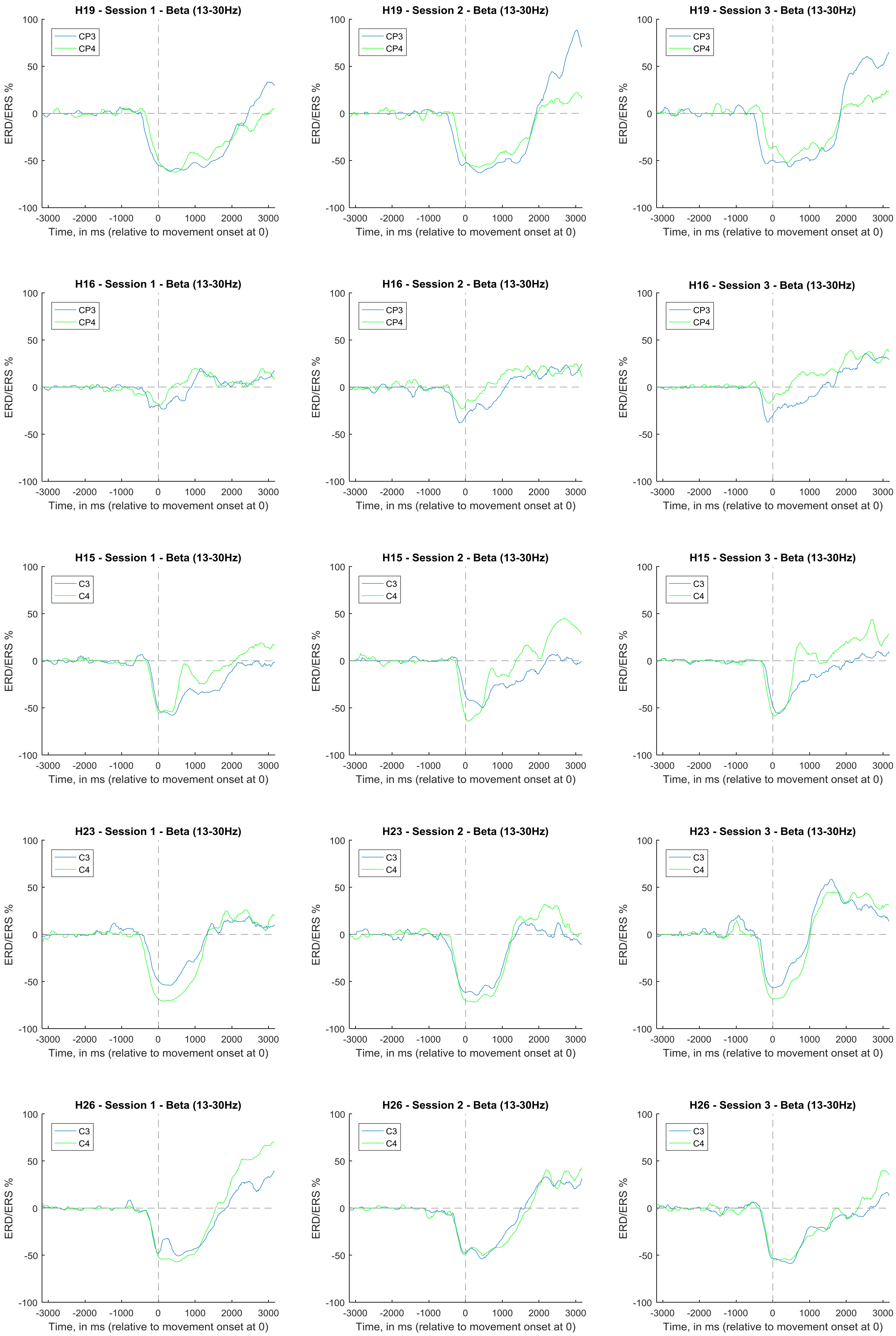


Figure 35 Plots of beta ERD/ERS% over time for symmetrical electrodes C3/C4 or CP3/CP4. Each row presents plots for each participant's three sessions.

These plots show that for participants H19, H15, H23, and H26, the intensity of beta ERD% over time at either C3/C4 or CP3/CP4 was similar from session to session. Participant H16 however had a lower beta ERD% peak for session 1.

Table 21 presents peak beta ERD% values for the electrode with the greatest beta ERD% values from the plots above. When several peaks are present, they are approximately matched according to time and placed in the same row in order to compare values. For the purpose of visually highlighting peaks that differ the most from others, differences of more than 10 % between matched peaks' maximum and minimum ERD% values are highlighted in red.

	Session 1		Session 2		Session 3	
Participant (electrode)	**Time**	**ERD%**	**Time**	**ERD%**	**Time**	**ERD%**
H19 (CP3)	-22	-54.4	-86	-55.4	-166	-53.5
	326	-61.1	390	-63.0	454	-56.7
	690	-60.2				
H16 (CP3)	-230	-22.1	-166	-38.2	-134	-37.2
	134	-23.4				
	658	-14.8	578	-23.7	406	-21.9
H15 (C4)	38	-55.5	70	-64.0	38	-58.8
	342	-54.2				
H23 (C4)	134	-70.6	246	-71.7	22	-68.4
			690	-65.7		
H26 (C4)	118	-54.1	-38	-49.5	70	-54.9
	482	-57.0	466	-50.2	454	-55.0

Table 21 Beta ERD% peak values for select electrodes for each participant's three sessions (times in ms). When several peaks are present, they are approximately matched according to time and placed in the same row in order to compare values. Values in red signify deviation greater than 10 % from other sessions' values at similar times.

A difference of 16.1 % in peak beta ERD% (beyond the 10 % threshold) can be observed for session 1 for participant H16 (-22.1 % compared to -38.2 % for session 2).

Conclusion: Peak beta ERD% values were generally similar (with values within 16.1 %). The number and timing of peaks varied greatly. Peak beta ERD% values varied between participants.

6.3.2.3 Hemispheric lateralisation of alpha ERD

Table 22 presents values for areas over the curve and laterality indices (LI), as calculated with alpha ERD% data for electrode pairs C3/C4 or CP3/CP4, for a period of 200 ms before movement onset and a period of 500 ms following movement onset. Laterality index values range from -1 to 1. A value of -1 indicates complete right hemisphere predominance. A value of 1 indicates complete left hemisphere predominance. A value of 0 indicates equal amounts of ERD% at both electrode sites. Participant H26 was not retained for this analysis, due to this participant's atypical alpha ERD% curve that includes many fluctuations over time.

Participant, electrodes, arm moved	Session	$A_{C3/CP3}$		$A_{C4/CP4}$		LI		L/R ratio	
		Pre 200	Post 500	Pre 200	Post 500	Pre 200	Post 500	Pre 200	Post 500
H19 CP3/CP4 Right	1	8224	28564	4208	24592	0.32	0.07	1.95	1.16
	2	8893	30499	6933	26659	0.12	0.07	1.28	1.14
	3	7460	26597	4140	24117	0.29	0.05	1.80	1.10
H16 CP3/CP4 Right	1	7380	27881	4360	19266	0.26	0.18	1.69	1.45
	2	9841	26557	3933	12273	0.43	0.37	2.50	2.16
	3	9127	28354	5908	18631	0.21	0.21	1.54	1.52
H15 C3/C4 Left	1	8671	42994	8139	40030	0.03	0.04	1.07	1.07
	2	9736	42199	7601	39246	0.12	0.04	1.28	1.08
	3	9124	35821	8283	36187	0.05	-0.01	1.10	0.99
H23 C3/C4 Left	1	9442	31029	12293	32719	-0.13	-0.03	0.77	0.95
	2	9620	32120	10665	31823	-0.05	0.00	0.90	1.01
	3	12321	31669	11753	30863	0.02	0.01	1.05	1.03

Table 22 Areas over the curve $A_{C3/CP3}$ and $A_{C4/CP4}$ (in ERD% * ms units) and laterality indices (LI) for alpha ERD% for either electrode pairs C3/C4 or CP3/CP4 for a 200 ms window before movement onset (Pre 200) and for a 500 ms window following movement onset (Post 500). L/R ratio = $A_{C3/CP3}$ / $A_{C4/CP4}$.

In order to interpret laterality indices and L/R ratio values, the researcher defined ranges for labelling laterality and variability. For the purpose of this study, laterality indices (LI) falling between -0.05 to 0.05 are deemed to indicate bilateral alpha ERD%, those between -0.15 to -0.05 and between 0.05 to 0.15 are deemed to indicate weak right and left hemispheric predominance, respectively, and any other values indicate either left or right hemispheric predominance. A difference of less than 20 % (0.20 when looking at differences between lowest and greatest L/R ratio values for each participant) indicates low variability between sessions. Any difference beyond 0.20 indicates variability between sessions. The term ‘contralateral’ refers to the hemisphere opposite to the side of the arm that was used to perform the movement, and ‘ipsilateral’ refers to the hemisphere on the same side of the arm used to perform the movement.

Table 23 presents the interpretation of the hemispheric lateralisation data using the described criteria.

Participant, arm moved	**Pre 200**	**Post 500**
H19 Right	sessions 1+3: contralateral dominant session 2: weak contralateral dominant (variable)	all sessions: weak contralateral dominant (low variability)
H16 Right	all sessions: contralateral dominant (variable)	all sessions: contralateral dominant (variable)
H15 Left	sessions 1 and 3: bilateral session 2: weak ipsilateral dominant (variable)	all sessions: bilateral (low variability)
H23 Left	session 1: weak contralateral dominant sessions 2 and 3: bilateral (variable)	all sessions: bilateral (low variability)

Table 23 Interpretation of hemispheric lateralisation data for alpha ERD% for a 200 ms window before movement onset (Pre 200) and for a 500 ms window following movement onset (Post 500).

For 'pre 200' results (200 ms preceding movement onset), for the two participants who performed right arm movements (H19 and H16), hemispheric lateralisation was contralateral dominant, with variable results between sessions (maximum difference in L/R ratio values were 0.67 and 0.96 for participants H19 and H16, respectively). For participants performing left arm movements (H15 and H23), bilaterality or weak contralateral and ipsilateral predominance was observed, with variable results between sessions (maximum difference in L/R ratio values were 0.21 and 0.28 for participants H15 and H23, respectively). For 'post 500' results (500 ms following movement onset), for those performing right arm movements, contralateral dominance was observed, with mixed variability (low variability for participant H19, and variability, with a maximum difference in L/R ratio values of 0.71 for participant H16). For those performing left arm movements, bilaterality was consistent, with low variability (maximum difference in L/R ratio values were 0.09 and 0.08 for participants H15 and H23, respectively).

Conclusion: Hemispheric lateralisation of alpha ERD% varied beyond a 0.20 difference (and up to 0.96 for participant H16) in L/R ratio values from session to session for a 200 ms period of time preceding movement onset. It was however more consistent (within 0.20 for L/R ratio values) for a 500 ms period of time after movement onset (for three out of four participants, as the other participant had a maximum difference of 0.71 in L/R ratio values) and was consistently of low variability for participants moving their left arm.

6.3.2.4 Hemispheric lateralisation of beta ERD

Table 24 presents values for areas over the curve and laterality indices (LI), as calculated with beta ERD% data for electrode pairs C3/C4 or CP3/CP4, for a period of 200 ms before movement onset and a period of 500 ms following movement onset. Laterality index values range from -1 to 1. A value of -1 indicates complete right hemisphere predominance. A value of 1 indicates complete left hemisphere predominance. A value of 0 indicates equal amounts of ERD% at both electrode sites.

Participant, electrodes, arm moved	Session	$A_{C3/CP3}$ Pre 200	$A_{C3/CP3}$ Post 500	$A_{C4/CP4}$ Pre 200	$A_{C4/CP4}$ Post 500	LI Pre 200	LI Post 500	L/R ratio Pre 200	L/R ratio Post 500
H19 CP3/CP4 Right	1	9442	28851	7383	29114	0.12	0.00	1.28	0.99
	2	10330	29032	7721	27266	0.14	0.03	1.34	1.06
	3	9929	25913	6528	22031	0.21	0.08	1.52	1.18
H16 CP3/CP4 Right	1	3879	8704	2865	3688	0.15	0.40	1.35	2.36
	2	6901	11054	4149	5625	0.25	0.33	1.66	1.96
	3	6604	10666	3078	2900	0.36	0.57	2.15	3.68
H15 C3/C4 Left	1	6461	27282	7818	25714	-0.10	0.03	0.83	1.06
	2	4061	21752	8201	28438	-0.34	-0.13	0.50	0.76
	3	5638	24911	8262	24676	-0.19	0.01	0.68	1.01
H23 C3/C4 Left	1	7976	25813	11936	34302	-0.20	-0.14	0.67	0.75
	2	11002	30122	12098	34261	-0.05	-0.06	0.91	0.88
	3	10080	23864	12178	31551	-0.09	-0.14	0.83	0.76
H26 C3/C4 Left	1	7160	19484	6872	26797	0.02	-0.16	1.04	0.73
	2	8117	23293	8621	22134	-0.03	0.03	0.94	1.05
	3	8578	27578	7822	26844	0.05	0.01	1.10	1.03

Table 24 Areas over the curve $A_{C3/CP3}$ and $A_{C4/CP4}$ (in ERD% * ms units) and laterality indices (LI) of beta ERD% for either electrode pairs C3/C4 or CP3/CP4 for a 200 ms window before movement onset (Pre 200) and for a 500 ms window following movement onset (Post 500). L/R ratio = $A_{C3/CP3}$ / $A_{C4/CP4}$.

Table 25 presents the interpretation of the hemispheric lateralisation data using the criteria described in the previous section.

Participant, arm moved	Pre 200	Post 500
H19 Right	all sessions: contralateral dominant (variable)	sessions 1 and 2: bilateral session 3: weak contralateral dominant (low variability)
H16 Right	all sessions: contralateral dominant (variable)	all sessions: contralateral dominant (variable)
H15 Left	all sessions: contralateral dominant (variable)	sessions 1 and 3: bilateral session 2: weak contralateral dominant (variable)
H23 Left	all sessions: contralateral dominant (variable)	all sessions: weak contralateral dominant (low variability)
H26 Left	all sessions: bilateral (low variability)	session 1: contralateral dominant sessions 2 and 3: bilateral (variable)

Table 25 Interpretation of hemispheric lateralisation data for beta ERD for a 200 ms window before movement onset (Pre 200) and for a 500 ms window following movement onset (Post 500).

For 'pre 200' results (200 ms preceding movement onset), for the two participants who performed right arm movements (H19 and H16), hemispheric lateralisation was contralateral dominant, with variable results between sessions (maximum difference in L/R ratio values were 0.24 and 0.96 for participants H19 and H16, respectively). For participants performing left arm movements (H15, H23, and H26), contralateral predominance was observed for two of these participants (H15 and H23), with variable results between sessions (maximum difference in L/R ratio values were 0.33 and 0.24 for participants H15 and H23, respectively), and bilaterality for the other participant (H26), with low variability. For 'post 500' results (500 ms following movement onset), for those performing right arm movements, a mix of bilaterality and contralateral dominance was observed, with mixed variability between sessions (maximum difference in L/R ratio values were 0.19 and 1.72 for participants H19 and H16, respectively). For those performing left arm movements, a mix of bilaterality and mostly weak contralateral dominance was observed, with variable results between sessions for two participants (maximum difference in L/R ratio values were 0.30 and 0.32 for participants H15 and H26, respectively), and low variability for one participant (H23).

Conclusion: Hemispheric lateralisation of beta ERD% was consistent (in that all sessions had the same laterality) for a 200 ms period of time preceding movement onset, but values did vary beyond a 0.20 difference (and up to 0.80) in L/R ratio values from session to session. Laterality was however less consistent for a 500 ms period of time after movement onset and values varied greatly from session to session (difference of up to 1.72 in L/R ratio values).

6.3.2.5 Beta ERD frequency range

The frequency range within the beta range (13-30 Hz) at which beta ERD occurred at symmetrical electrodes was determined by visually inspecting ERSP plots produced with EEGLAB's STUDY functions, by comparing plots for all three sessions side by side for each participant. Table 26 presents results for all sessions.

Participant	Electrode	Session 1	Session 2	Session 3
H19	CP3	17-30	17-30	17-30
	CP4	18-31	18-31	19-30
H16	CP3	14-21	15-22	15-23
	CP4	16-21	16-22	16-22
H15	C4	16-22	16-22	17-22
	C3	17-22	18-22	17-22
H23	C4	16-29	16-29	16-28
	C3	16-29	16-29	16-28
H26	C4	19-27	20-27	20-28
	C3	20-27	20-27	19-27

Table 26 Frequency ranges, in Hz, at which beta ERD occurs for all participants' sessions.

Conclusion: The frequency range at which beta ERD occurs from session to session was consistent from one session to another. Symmetrical electrodes presented with similar frequency ranges. Frequency ranges varied between participants.

6.3.2.6 Spatial distribution of beta ERS following movement

Scalp maps were visually inspected to examine the variability of the spatial distribution of beta ERS over each participant's three sessions, in terms of the location over which beta ERS was centred. For participants H19 and H15, little variability could be observed. Participant H19's beta ERS was centred at electrode site CP3, and at C4/CP4 for participant H15. For participant H16, some variability was observed in that for session 1, beta ERS was centred at Cz/CPz at its peak (then at C1/Cz). Then for session 2 it was centred at Cz, then spread to CP2/CP4/C1. For session 3, it was centred at Cz/C1, then also at CP1. Some variability could also be observed for participant H23, where beta ERS was centred at Cz/FCz (and remained centred at this location) for session 1, then at Cz for session 2, and at C3/CP3, FCz and CP4 for session 3. Participant H26 also presented with some variability. For session 1, beta ERS was centred around FCz/FC2/Cz/C2 initially, spreading to FCz/FC2/C2/C4; for session 2 it was centred at Cz initially, then spreading to Cz/CP1/CPz. For session 3, it was centred at Cz initially, to then spread to Cz/C2/C4.

Conclusion: The spatial distribution of beta ERS was similar, in terms of visual analysis, from one session to another for only two out of five participants. Most beta ERS occurred over the contralateral hemisphere (as anticipated), with some exceptions for some ipsilateral hemisphere electrodes involved in beta ERS for a small number of sessions.

6.3.2.7 Intensity of beta ERS following movement

Peak beta ERS% values following movement

Figure 36 presents beta ERS% over time plots for select electrodes for all sessions.

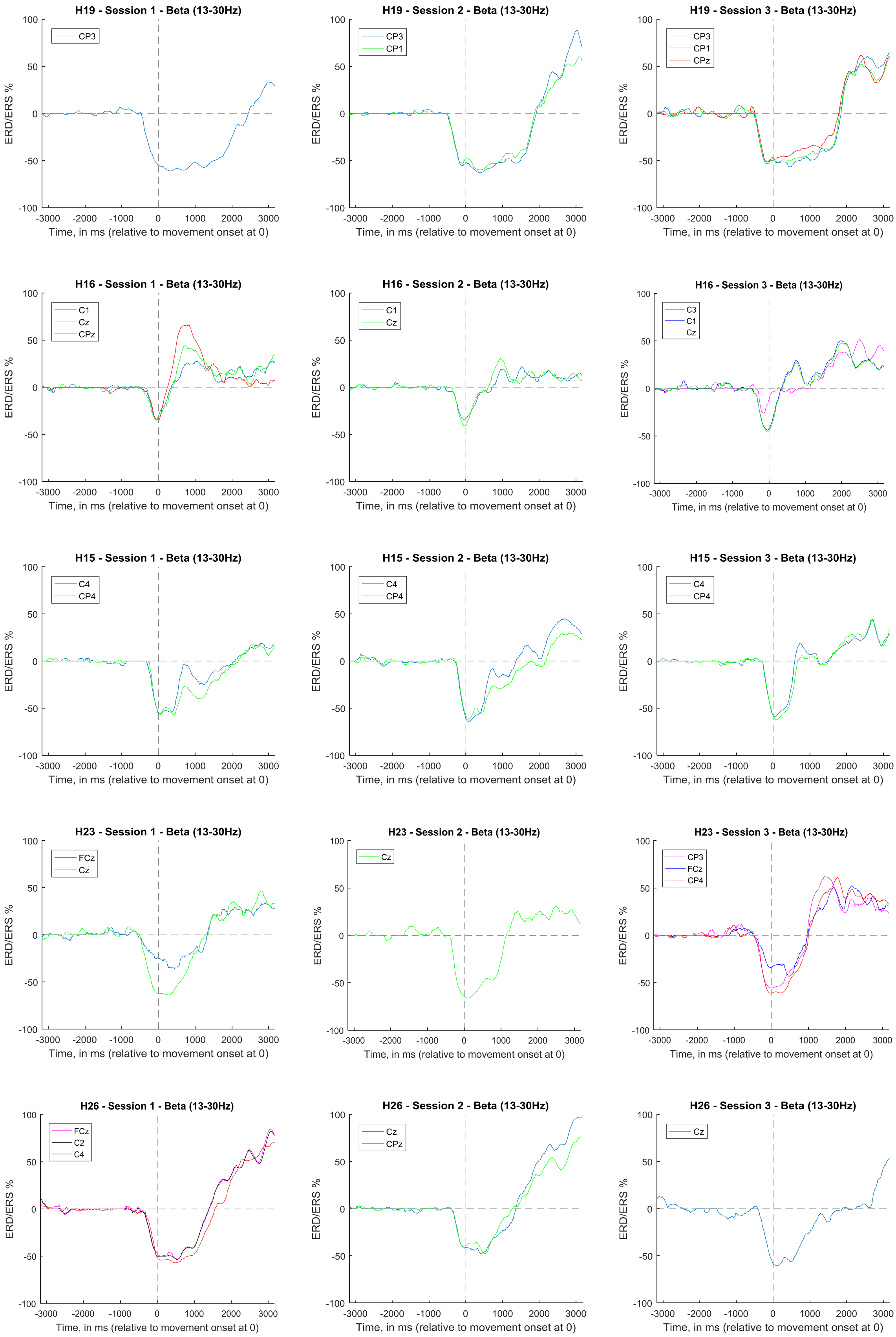


Figure 36 Plots of beta ERS% over time for select electrodes. Each row presents plots for each participant's three sessions.

Table 27 presents peak beta ERS% values for the electrode with the greatest beta ERS% values from the plots above. When several peaks are present, the most prominent are noted and are matched approximately according to time and placed in the same row in order to compare values. For the purpose of visually highlighting peaks that differ the most from others, differences of more than 10 % between matched peaks' maximum and minimum ERS% values are highlighted in red.

Participant, electrodes	Session 1		Session 2		Session 3	
	Time	ERS%	Time	ERS%	Time	ERS%
H19 **Session 1: CP3** **Session 2: CP3** **Session 3: CP3**	2991	33.3	3024	88.4	3168	64.7
H16 **Session 1: CPz** **Session 2: Cz** **Session 3: C1**	754	66.3	942	30.9	754	30.0
					1975	50.0
H15 **Session 1: C4** **Session 2: C4** **Session 3: C4**	706	-3.0	722	-7.9	738	18.9
	2799	18.8	2691	45.0	2707	44.2
H23 **Session 1: Cz** **Session 2: Cz** **Session 3: CP3**	1515	21.7	1435	25.4	1435	62.0
	2039	35.7	2071	25.5	2167	37.6
	2799	46.6	2499	30.5	2627	39.4
H26 **Session 1: FCz** **Session 2: Cz** **Session 3: Cz**	3040	84.3	3152	97.5	3168	53.6

Table 27 Beta ERS% peak values for select electrodes for each participant's three sessions (times in ms). When several peaks are present, they are approximately matched according to time and placed in the same row in order to compare values. Values in red signify a deviation greater than 10 % from other sessions' values at similar times.

Important differences in peak beta ERS% (beyond the 10 % threshold) were observed for all participants, with maximum differences ranging from 26.2 % (participant H15) to 55.1 % (participant H19).

Conclusion: Peak beta ERS% values varied from session to session for all participants. Peak beta ERS% values also varied between participants.

6.3.2.8 Timing of beta ERS% peaks following movement

Table 28 presents the range of timings for beta ERS% peaks, as calculated by the difference in time between the earliest and latest peaks for each participant over the three sessions.

Participant	Peak	Range (ms)
H19		177
H16		188
H15	first	32
	second	108
H23	first	80
	second	128
	third	300
H26		128

Table 28 Range of timings of beta ERS% peaks.

Apart from one slightly longer time range for one participants (participant H23's third peak, spanning over a 300 ms time range across sessions), ranges fell within 188 ms for all participants.

Conclusion: The timing of beta ERS% peaks were generally similar across sessions for all participants, within a 188 ms range for most peaks, and within a 300 ms range for one participant's third peak. There was variability between participants.

6.4 Discussion

This study's results answered the second research question: 'What is the variability over time of ERD/ERS measures during reaching for a small sample of healthy participants?'.

6.4.1 Movement characteristics

Considering the fact that it is not possible for participants to perform the reaching movement at the same speed at every movement and across sessions, some variability in mean movement times was expected. Even though all participants had statistically different mean movement times, the observed variability of mean movement times over sessions was deemed acceptable.

6.4.2 ERD/ERS

Movement-related ERD/ERS was elicited in most participants (apart from one participant, which had low intensity alpha and beta ERD) in the expected cortical areas and bandwidths.

To the researcher's knowledge, no published literature on movement-related ERD/ERS has included test-retest variability results, making comparisons with other experimental methods impossible. If such results were to be investigated and published, it would be useful to investigate these in order to identify factors, if any, that cause the most variability.

6.4.3 Limitations

Data from only a small sample of five participants was analysed. It is thus unknown whether a different or larger sample would provide similar results.

The age of participants does not reflect the general population (mean age 54.3 ± 16 years; range 25-71 years). This data would thus not be ideal to be used to characterise variation in ERD/ERS measures for younger individuals. As it is however expected that participants from the stroke participant group will be of similar age (as there are more older adults who have had a stroke than younger adults), this sample of participants is more appropriate.

Regarding the analysis of beta ERS, as it is present once movement and muscle contractions have ceased, the accuracy of results possibly depended on participants' ability to fully relax arm muscles following the end of the movement. Further analysis of EMG data would provide more insight into participants' abilities to consistently cease muscle contraction at the end of the movement over a number of sessions.

6.5 Conclusion

Variability of measures of ERD/ERS over time has been investigated in a small sample of healthy participants. These results were useful when investigating possible changes in ERD/ERS measures of individuals taking part in the stroke participant study (see Chapter 8), in that it was possible to determine whether any potential changes were due to natural variability or whether they were due to the effects of rehabilitation. Before results from the stroke participant study are presented, a study was carried out to determine average ERD/ERS measures in a larger group of healthy participants, for both left and right arm movements. Results of this study are presented in the next chapter.

Chapter 7: Healthy participant study

7.1 Introduction

In order to answer the third research question, ‘What are the characteristics of ERD/ERS measures during reaching for healthy participants?’, measures of ERD/ERS were characterised for a reaching movement in a healthy population by averaging data from a group of ten participants. This allowed for data from stroke participants, presented in the next chapter, to be compared to healthy participants’ measures of ERD/ERS.

7.2 Methods

7.2.1 Participants

Ten right-handed healthy participants (mean age 55.9 ± 13.3 years; range 35-67 years; four females and six males) were recruited and gave consent to participate in the study. Figure 37 provides details on recruitment. Table 29 presents characteristics of the ten individuals who participated.

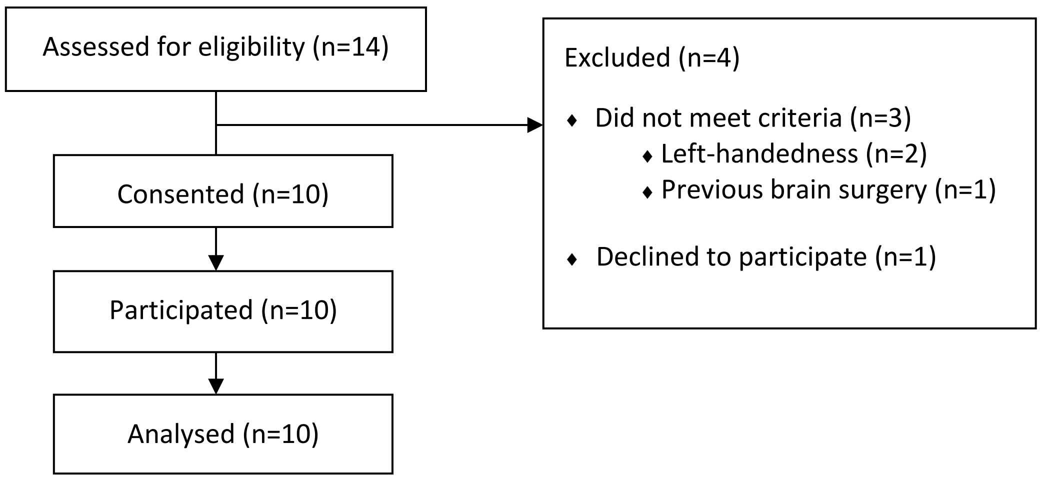


Figure 37 Recruitment of healthy participants.

Participant	Age (years)	Gender
H22	39	M
H24	59	F
H25	35	F
H27	63	F
H28	64	M
H29	62	M
H30	67	M
H31	66	M
H32	67	M
H33	37	F

Table 29 Healthy participants' characteristics.

7.2.2 Data recording

Each participant attended one recording session. A total of 20 EEG datasets were obtained (each of the ten participant had two datasets, one for left arm movements and another for right arm movements).

7.2.2.1 Motor task

All participants performed 160 cued reaching movements using the experimental setup described in Chapter 4. Participants first performed at least 80 movements with their left arm. The reaching device was then moved to the other side of the table, after which participants performed at least 80 movements with their right arm. Participants were given preparation instruction sheets prior to attending the recording session. Participants were asked to relax their arm muscles after reaching the end of the movement, and to avoid the production of signal artefacts caused by frowning, swallowing, and jaw or neck/shoulder tension.

7.2.2.2 EEG recording

The researcher carried out all recording sessions and collected data using the 35 channel EEG electrode configuration described in Chapter 4. All aspects of EEG recording were the same as for the test-retest variability study (see Chapter 6).

7.2.2.3 EMG and potentiometer data recording

All aspects of EMG and potentiometer data recording were the same as for the test-retest variability study (see Chapter 6).

7.2.3 Data processing and analysis

7.2.3.1 Data processing

All aspects of data processing were the same as for the test-retest variability study (see Chapter 6). As data was separated in different datasets for left and right arm movements, a total of 20 EEG datasets were processed.

7.2.3.2 Movement characteristics

Mean reaction and movement times (and standard deviations) were calculated using the same method as for all the previous studies.

Each participant's mean left and right mean movement times were compared. As samples for left and right movements have normal distributions but are of unequal size and variance, the Welch's t-test was carried out (by using MATLAB's 'ttest2' function) to determine whether left and right movement means were significantly different or not.

To compare all participants' mean movement times, a one-way unbalanced analysis of variance (ANOVA) was carried out (using MATLAB's 'anova1' function). This analysis was done for left and right arm movements separately.

7.2.3.3 ERD/ERS

Scalp maps, plots of ERD/ERS% over time, and peak ERD/ERS% values were calculated using the same methods as in the test-retest variability study (see Chapter 6).

When investigating movement-related EEG, brain areas of interest are those part of the motor cortex. The planning and execution of movement involves various areas: the dorsolateral prefrontal associative cortex, the premotor cortex, the supplementary motor area, the somatosensory cortex, the posterior parietal cortex, and the primary motor cortex (see Chapter 2 for an overview of the role of these areas and their activation sequence associated with planning and execution movement). When considering these areas as they relate to activity recorded from electrodes that are placed directly over them on the scalp, it should be taken into account that EEG has low spatial resolution, in that signals recorded at an electrode site will also include activity from surrounding areas due to their proximity to the electrode as well as to conductivity of the brain. As the electrode configuration used for this study included a relative large number of adjacent electrodes over rows F, FC, C, CP, and P, it was possible to produce scalp maps which were helpful to identify the relative contribution of different areas before, during, and following movement. For this study, electrodes that showed the greatest ERD in central rows FC/C/CP in close proximity to the areas over which electrodes C3 or C4 are located (as these areas, located centrally over the motor cortex, often present with the greatest ERD for movement of isolated joints (Pfurtscheller et al. 1999)), were considered as candidates for analysis of ERD. Scalp maps (see Figure 40 and Figure 41 for alpha ERD and Figure 45 for beta ERD), showed that the greatest ERD in the area near electrodes C3 or C4 occurs most often near electrode CP3 over the duration of the planning and execution of the movement, rather than near electrodes C3 or C4. For this reason the pair of electrodes CP3/CP4 was selected for analysis or ERD. A hypothesis that could explain this more posterior location is that movement of more than one joint at a time (as is the case for the reaching movement used in this study) possibly requires more information in the form of somatosensory, proprioceptive and visual inputs in order to determine the relative position of the upper limb and the movement's target end position. As this information is processed and transmitted (before and during movement) to the premotor and supplementary motor areas by the somatosensory and the posterior parietal cortices, which are located more posteriorly, it would follow that this area would play a greater part in the planning and execution of a reaching movement.

As for beta ERS following movement offset, as the greatest ERS was more localised to a small area, the electrodes with the greatest ERS were selected individually for each participant.

Hemispheric lateralisation of ERD

Lateralisation indices were calculated using the same methods as for the test-retest variability study (see Chapter 6).

7.3 Results

7.3.1 Movement characteristics

Table 30 presents the number of movements retained for analysis, as well as mean reaction and movement times for all participants. Figure 38 and Figure 39 show box plots with further details about each participant's movement times for left and right arm movements, respectively.

Participant	Number of movements (L=left, R=right)	Mean reaction time ± SD		Mean movement time ± SD	
		left	right	left	right
H22	L:79, R:80	470 ± 55	468 ± 72	295 ± 27	331 ± 53
H24	L:72, R:71	371 ± 73	401 ± 68	224 ± 27	217 ±20
H25	L:76, R:78	471 ± 78	507 ± 118	351 ± 55	337 ± 32
H27	L:75, R:78	433 ± 89	432 ± 80	256 ± 29	243 ± 29
H28	L:80, R:80	378 ± 58	403 ± 77	303 ± 35	372 ± 79
H29	L:70, R:73	483 ± 90	424 ± 73	264 ± 28	249 ± 25
H30	L:79, R:78	599 ± 106	530 ± 120	312 ± 28	276 ± 39
H31	L:81, R:80	487 ± 92	557 ± 123	503 ± 61	524 ± 85
H32	L:80, R:77	345 ± 60	406 ± 97	268 ± 26	295 ± 46
H33	L:78, R:78	474 ± 92	469 ± 81	385 ± 38	329 ± 39

Table 30 Number of movements retained for analysis, mean reaction times (in ms), and mean movement times (in ms).

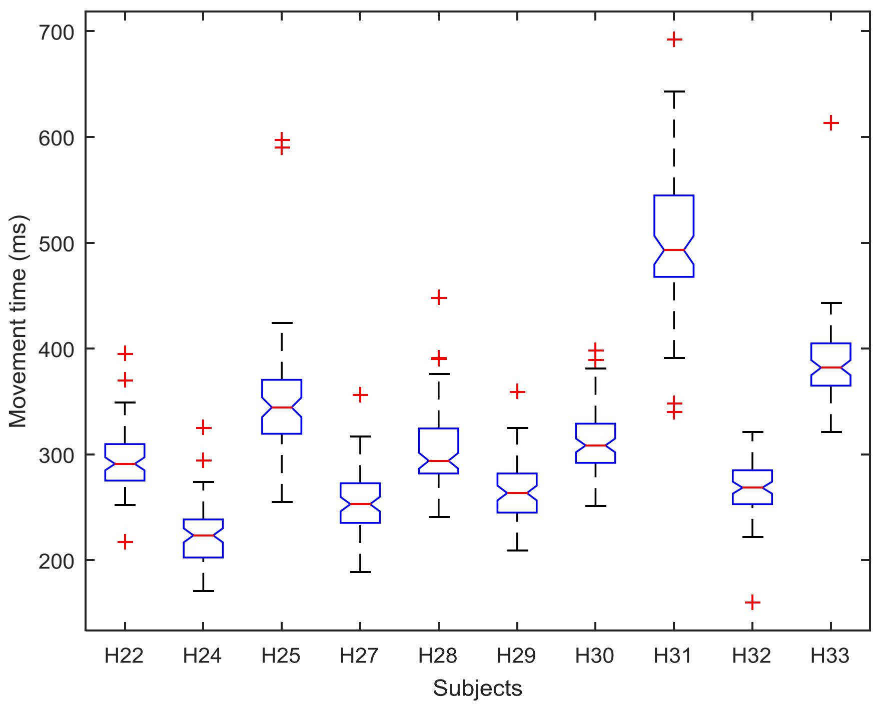


Figure 38 Box plots for each participant's movement times for left arm movements (the red line in the centre of the box being the median, the edges of the box are the 25th and 75th percentiles, whiskers end at the most extreme values that are not considered outliers, and outliers are displayed with red crosses).

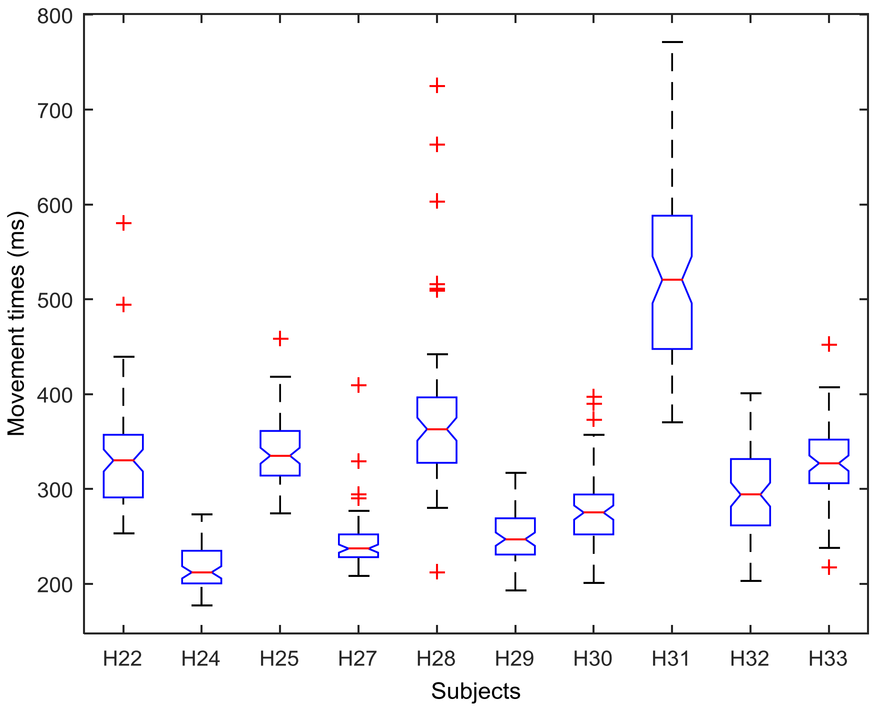


Figure 39 Box plots for each participant's movement times for right arm movements (the red line in the centre of the box being the median, the edges of the box are the 25th and 75th percentiles, whiskers end at the most extreme values that are not considered outliers, and outliers are displayed with red crosses).

Using Welch's t-test, results show that for only three out of the ten participants (H24, H25, and H31), left and right arm movement time means are not significantly different ($p < 0.05$).

When examining box plots for all participants, one participant's (H31) movement times were noticeably different from the majority, particularly for right arm movements (median of 520 ms compared to a range of medians varying between 212 and 363 ms for all other participants). A one-way unbalanced analysis of variance (ANOVA) showed that for left and right arm movements, all participants' mean movement times, when compared with each other, were significantly different ([$F = 361.09$ (9, 761), $p < 10^{-6}$] for left arm movements and [$F = 239.56$ (9, 763), $p < 10^{-6}$] for right arm movements).

7.3.2 ERD/ERS

ERD/ERS time frequency maps and scalp maps for all participants, as well as averaged scalp maps are included on the accompanying USB drive for reference.

7.3.2.1 Alpha ERD

Alpha ERD following the movement cue

Following the movement cue (at approximately -600 to -400 ms), scalp maps (see Figure 40) show that left and right arm movements have a contralateral hemisphere pre-movement alpha ERD over rows C, CP, and P, starting at approximately -600 to -400 ms, which becomes bilateral just before movement onset at around -200 to 0 ms. Maximum alpha ERD values before movement are found in the -200 to 0 ms time period.

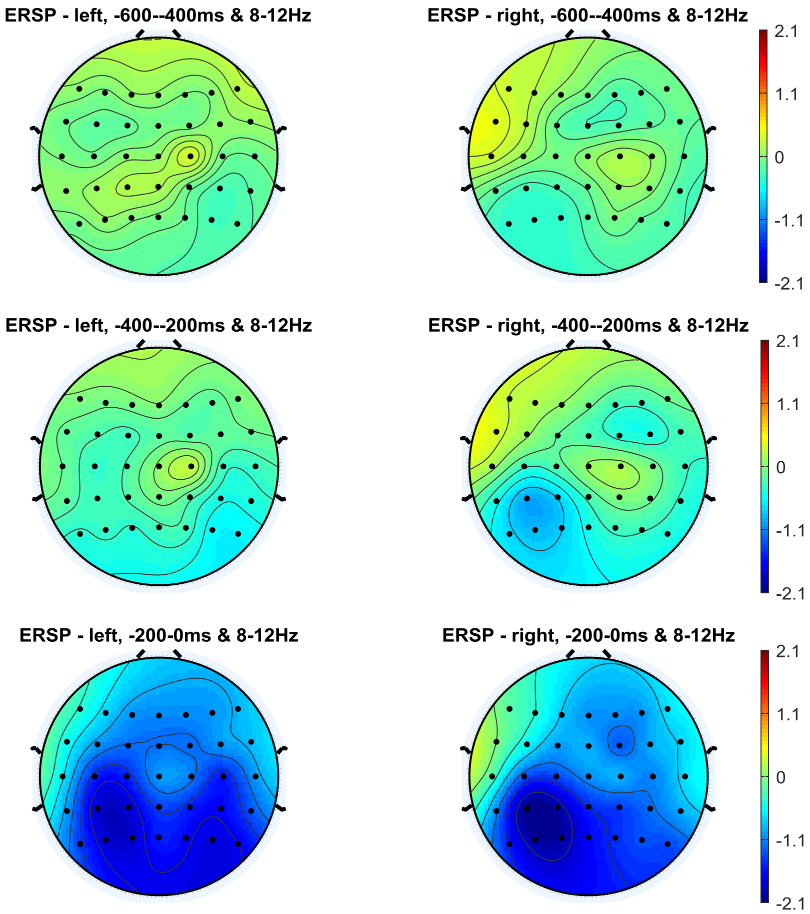


Figure 40 Series of scalp maps of grand averaged alpha ERD/ERS data (in dB) from all participants for left (left column) and right (right column) arm movements in 200 ms time intervals, from -600 to 0 ms before movement onset. Scalp maps are organised chronologically, starting from the top.

Alpha ERD during movement

Scalp maps (see Figure 41) show that during movement, left arm movement alpha ERD is bilateral with an ipsilateral hemisphere predominance. Right arm movement alpha ERD is present bilaterally with a contralateral hemisphere predominance. Maximum alpha ERD during and following movement occurs at 600 to 800 ms.

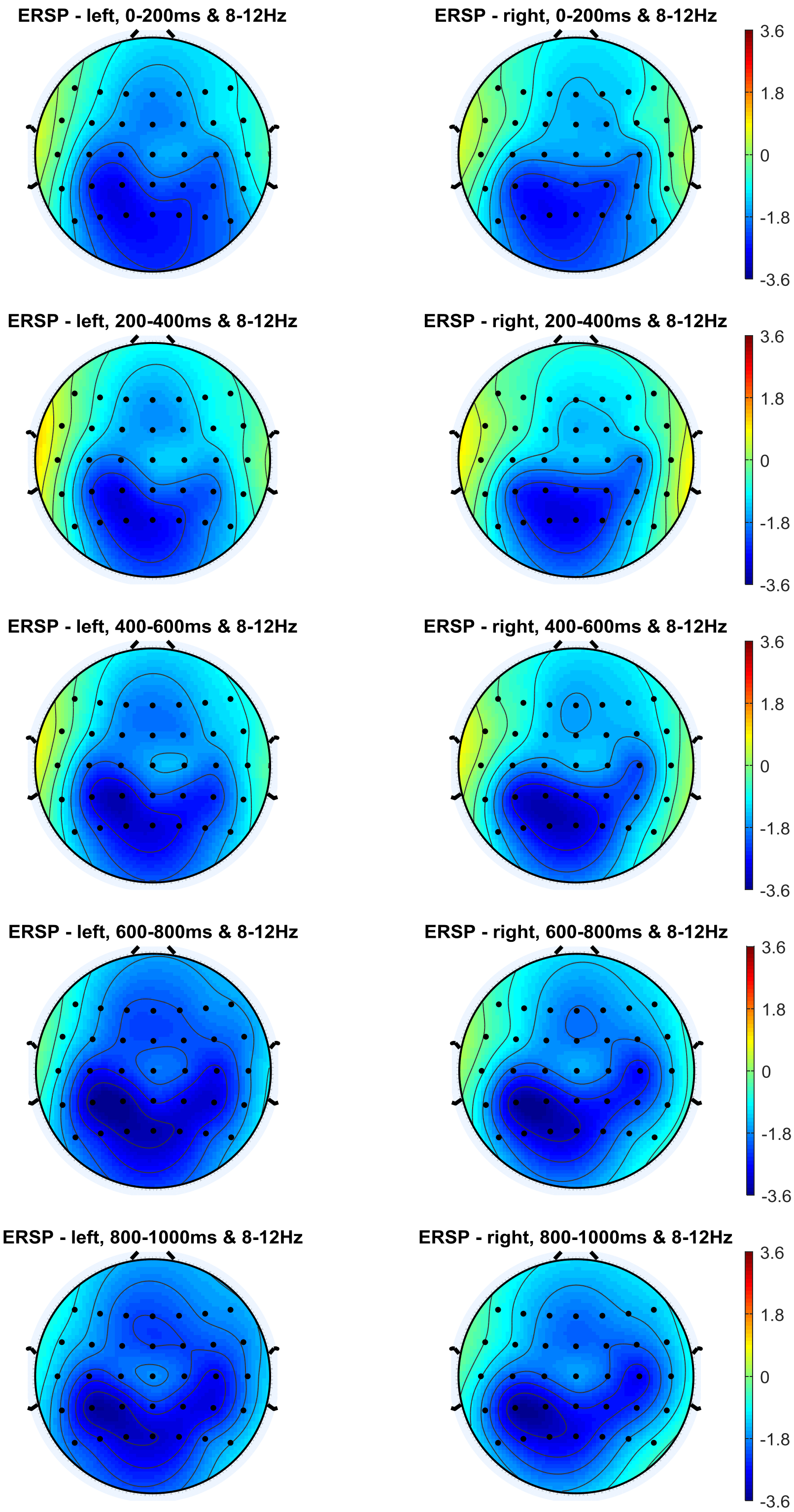


Figure 41 Series of scalp maps of grand averaged alpha ERD/ERS data (in dB) from all participants for left (left column) and right (right column) arm movements in 200 ms time intervals, from 0 to 1000 ms after movement onset. Scalp maps are organised chronologically, starting from the top.

Alpha ERD over time

Figure 42 presents time frequency ERD/ERS maps for electrode sites CP3 and CP4 for left and right arm movements.

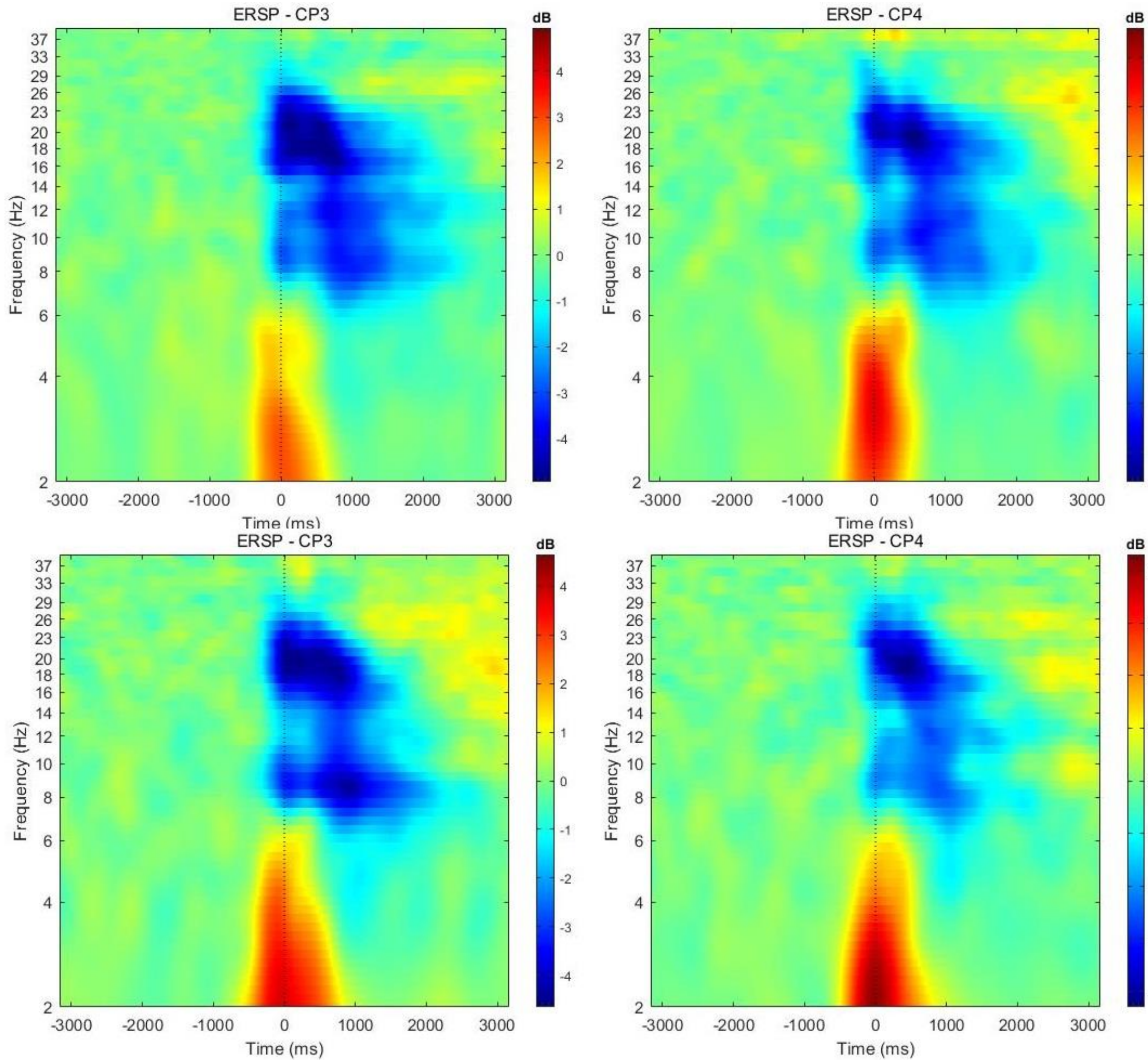


Figure 42 Grand average time frequency ERD/ERS maps for electrodes CP3/CP4 for left arm movements (top) and right arm movements (bottom).

Figure 43 shows alpha ERD% over time plots for electrode sites CP3 and CP4. For left arm movements, CP3 and CP4 have similar intensities before movement, followed by greater intensity for CP3 (ipsilateral hemisphere) just before and during movement. For right arm movements, CP3 has a greater intensity (contralateral hemisphere) than CP4 before and during movement.

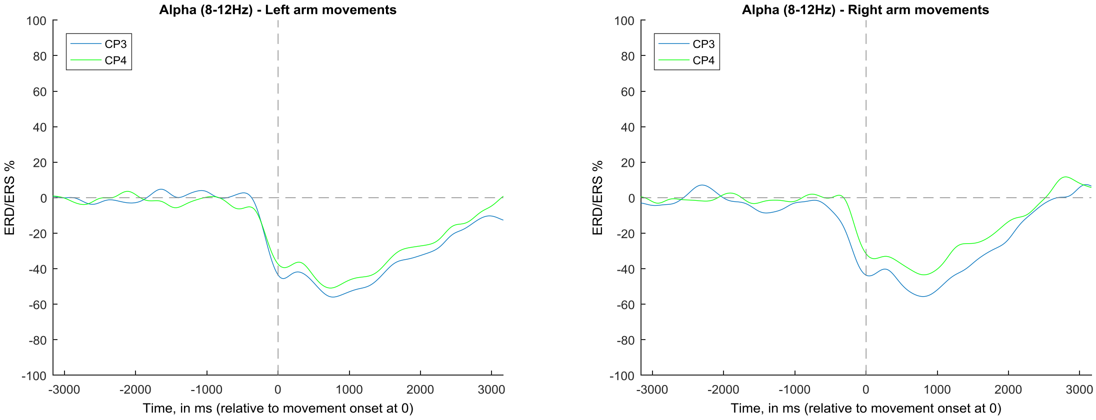


Figure 43 Grand average alpha ERD% over time plots for CP3 and CP4 electrode locations for left and right arm movements.

Peak alpha ERD%

Times and values of peak alpha ERD% for the electrode with the greatest alpha ERD% out of the two, electrode CP3, are shown in Table 31. There are two peak alpha ERD% values, one occurring shortly after movement onset, and another, after movement offset. The timings and values of peak alpha ERD% intensities are similar for left and right arm movements.

Left arm movements		Right arm movements	
Time (ms)	**ERD%**	**Time (ms)**	**ERD%**
68	-45.5	36	-44.0
768	-56.0	800	-55.7

Table 31 Grand average peak alpha ERD% times and values at electrode location CP3 for left and right arm movements.

Hemispheric lateralisation of alpha ERD%

Figure 44 presents scalp maps for averaged alpha ERD/ERS data for two periods of interest for the analysis of hemispheric lateralisation: a period of 200 ms before movement onset and a period of 500 ms following movement onset.

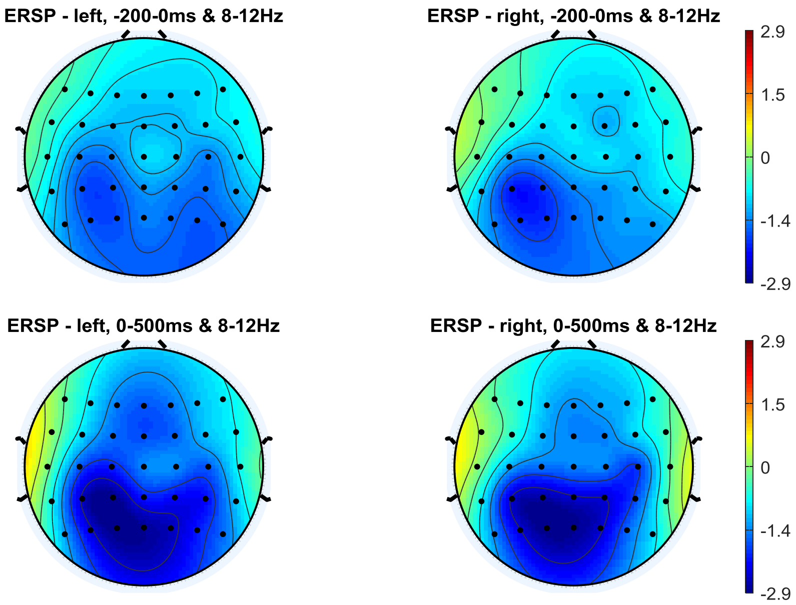


Figure 44 Scalp maps of grand averaged alpha ERD/ERS data (in dB) from all participants for left (left column) and right (right column) arm movements for a period of 200 ms before movement onset (top) and a period of 500 ms following movement onset (bottom).

Table 32 presents values for areas over the curve and laterality indices (LI), as calculated with alpha ERD% data for electrode sites CP3 and CP4, for left and right arm movements for a period of 200 ms before movement onset and a period of 500 ms following movement onset. Laterality index values range from -1 to 1. A value of -1 indicates complete right hemisphere predominance. A value of 1 indicates complete left hemisphere predominance. A value of 0 indicates equal amounts of ERD% at both electrode sites.

In order to interpret laterality indices and L/R ratio values, the researcher defined ranges for labelling laterality and variability. For the purpose of this study, laterality indices (LI) falling between -0.05 to 0.05 are deemed to indicate bilateral alpha ERD%, those between -0.15 to -0.05 and between 0.05 to 0.15 are deemed to indicate weak right and left hemispheric predominance, respectively, and any other values indicate either left or right hemispheric predominance. The term 'contralateral' refers to the hemisphere opposite to the side of the arm that was used to perform the movement, and 'ipsilateral' refers to the hemisphere on the same side of the arm used to perform the movement.

For left arm movements, alpha ERD% has a very weak predominance over the ipsilateral hemisphere before (LI = 0.06) and during (LI = 0.07) movement. For right arm movements, alpha ERD% is predominant over the contralateral hemisphere before movement (LI = 0.26). During movement, there is a weak contralateral hemisphere predominance (LI = 0.12). This lateralisation is more pronounced than for left arm movements.

Table 33 presents the interpretation of the hemispheric lateralisation data using the described criteria.

	A_{CP3}		A_{CP4}		Laterality Index (LI)	
	Pre 200	**Post 500**	**Pre 200**	**Post 500**	**Pre 200**	**Post 500**
Left arm movements	6270	21606	5515	18963	0.06	0.07
Right arm movements	7200	21134	4263	16767	0.26	0.12

Table 32 Grand average areas over the curve A_{CP3} and A_{CP4} (in ERD% * ms units) and laterality indices (LI) of alpha ERD% for left and right arm movements for electrode pairs CP3/CP4 for a 200 ms window before movement onset (Pre 200) and for a 500 ms window following movement onset (Post 500).

	Pre 200	Post 500
Left arm movements	weak ipsilateral dominant	weak ipsilateral dominant
Right arm movements	contralateral dominant	weak contralateral dominant

Table 33 Interpretation of hemispheric lateralisation data for alpha ERD% for a 200 ms window preceding movement onset (Pre 200) and for a 500 ms window following movement onset (Post 500).

7.3.2.2 Beta ERD/ERS

Beta ERD following the movement cue and during movement

Scalp maps (see Figure 45) of averaged beta ERD/ERS data show that before, during, and after the execution of the movement, beta ERD occurs more anteriorly (over rows C and CP) than alpha ERD. Pre-movement onset beta ERD starts at approximately -400 to -200 ms and maximum beta ERD before movement occurs during the -200 to 0 ms time period, over rows C and CP. For right arm movements, pre-movement onset beta ERD is more predominant over the contralateral hemisphere, and becomes bilateral starting from -200 to 0 ms. For left arm movements, beta ERD is bilateral before and during movement.

Beta ERD becomes bilaterally more localised bilaterally from about 200-400 ms for right arm movements and from about 400 to 600 ms for left arm movements. Maximum beta ERD during movement occurs during the 0 to 200 ms time period.

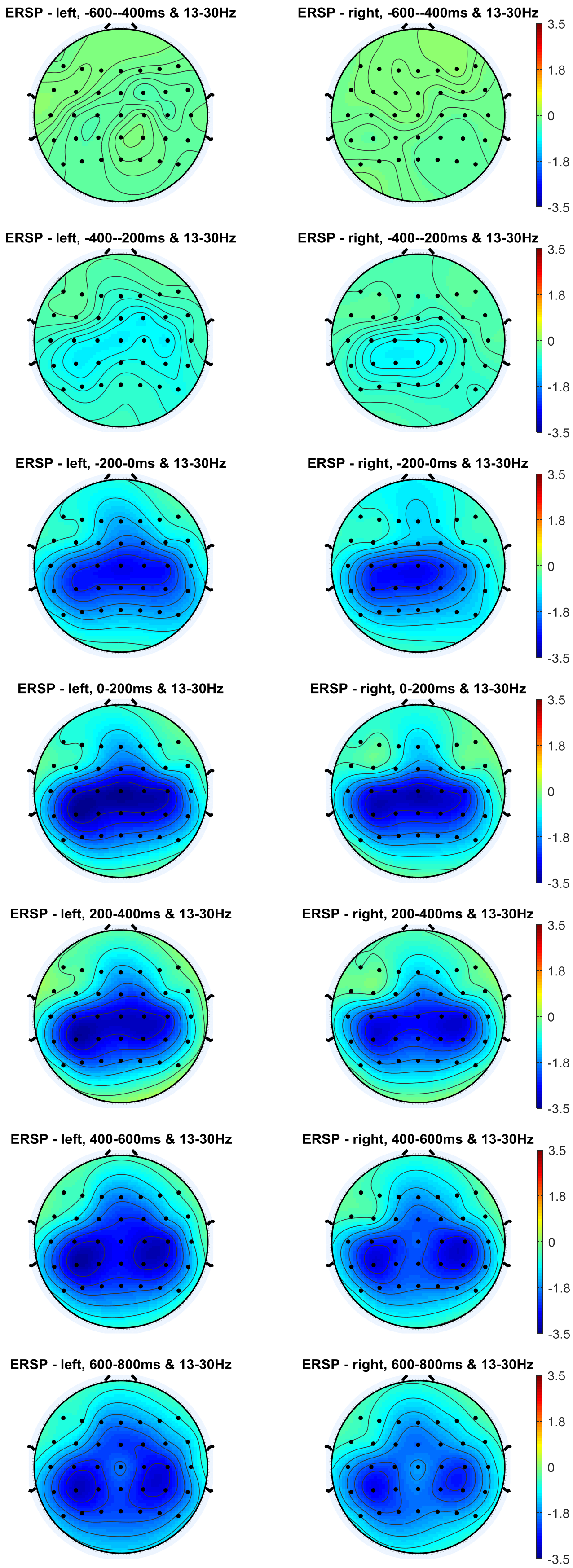


Figure 45 Series of scalp maps of grand averaged beta ERD/ERS data (in dB) from all participants for left (left column) and right (right column) arm movements in 200 ms time intervals, from -600 to 800 ms relative to movement onset. Scalp maps are organised chronologically, starting from the top.

Beta ERD over time

For time frequency ERD/ERS maps for electrode sites CP3 and CP4 for left and right arm movements, please refer to Figure 42 in the previous section.

Figure 46 shows beta ERD% over time plots for electrode sites CP3 and CP4. For left arm movements, CP3 and CP4 electrodes have similar beta ERD% intensities before movement, followed by greater beta ERD% for CP3 (ipsilateral hemisphere) during movement. For right arm movements, CP3 and CP4 electrodes have different beta ERD% intensities: greater for CP3 (contralateral hemisphere) than for CP4 before and during movement.

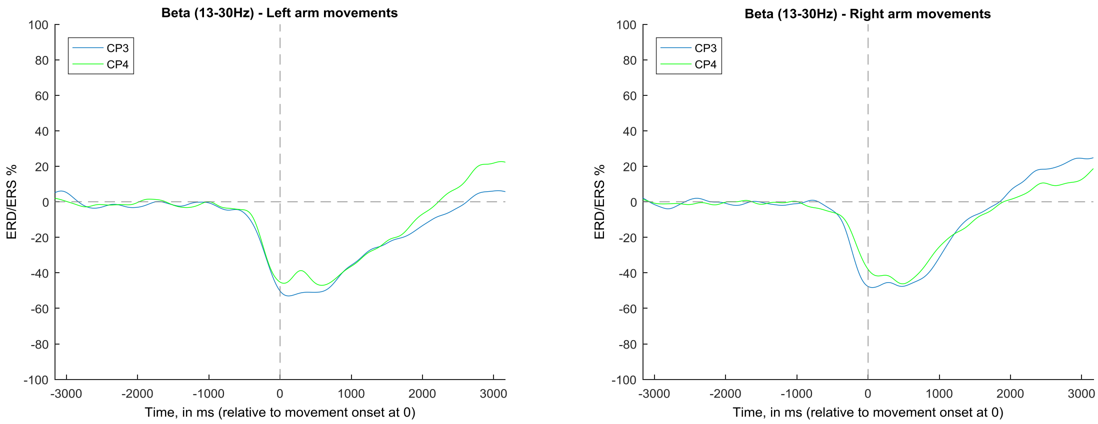


Figure 46 Grand average beta ERD/ERS% over time plots for CP3 and CP4 electrode for left and right arm movements.

Peak beta ERD%

Times and values of peak beta ERD% for the electrode with the greatest beta ERD% out of the two, electrode CP3, are shown in Table 34. There are two peak beta ERD% values, one occurring shortly after movement onset, and another, after movement offset (see Figure 46). The timings and values of peak beta ERD% intensities are similar for left and right arm movements.

Left arm movements		Right arm movements	
Time (ms)	ERD%	Time (ms)	ERD%
116	-53.0	68	-48.3
464	-51.0	480	-47.7

Table 34 Grand average peak beta ERD% times and values at electrode location CP3 for left and right arm movements.

Hemispheric lateralisation of beta ERD%

Figure 47 presents scalp maps for averaged alpha ERD/ERS data for two periods of interest for the analysis of hemispheric lateralisation: a period of 200 ms before movement onset and a period of 500 ms following movement onset.

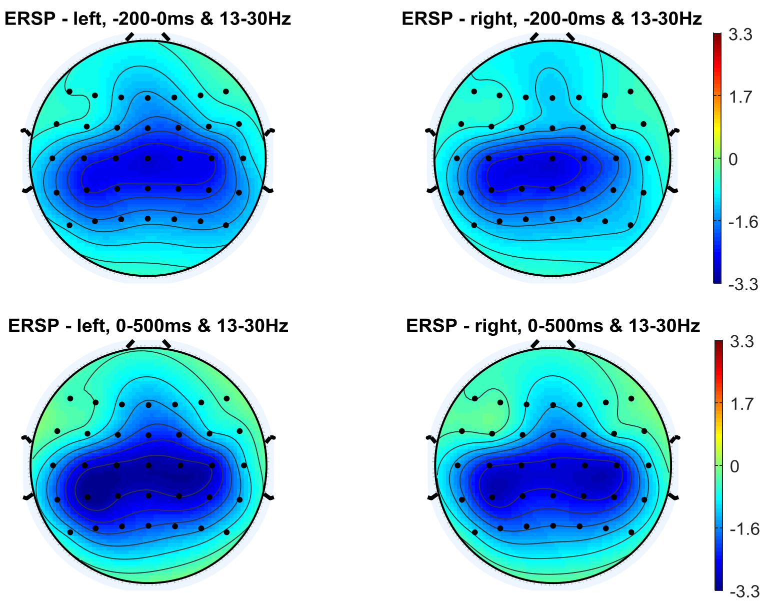


Figure 47 Scalp maps of grand averaged beta ERD/ERS data (in dB) from all participants for left (left column) and right (right column) arm movements for a period of 200 ms before movement onset (top) and a period of 500 ms following movement onset (bottom).

Table 35 presents values for areas over the curve and laterality indices (LI) for left and right arm movements for a period of 200 ms before movement onset and a period of 500 ms following movement onset. Laterality index values range from -1 to 1. A value of -1 indicates complete right hemisphere predominance. A value of 1 indicates complete left hemisphere predominance. A value of 0 indicates equal amounts of ERD% at both electrode sites.

In order to interpret laterality indices and L/R ratio values, the researcher defined ranges for labelling laterality and variability. For the purpose of this study, laterality indices (LI) falling between -0.05 to 0.05 are deemed to indicate bilateral alpha ERD%, those between -0.15 to -0.05 and between 0.05 to 0.15 are deemed to indicate weak right and left hemispheric predominance, respectively, and any other values indicate either left or right hemispheric predominance. For left arm movements, beta ERD% is bilateral before movement (LI = 0.03), and has a weak predominance over the ipsilateral hemisphere during movement (LI = 0.10). For right arm movements, beta ERD% is predominant over the contralateral hemisphere before movement (LI = 0.16). During movement, the laterality index value is at the limit of bilateral and weak contralateral hemisphere predominance (LI = 0.05). Table 36 presents the interpretation of the hemispheric lateralisation data using the described criteria.

	A_{CP3}		A_{CP4}		Laterality Index (LI)	
	Pre 200	**Post 500**	**Pre 200**	**Post 500**	**Pre 200**	**Post 500**
Left arm movements	7979	25449	7539	20921	0.03	0.10
Right arm movements	7939	23098	5732	20898	0.16	0.05

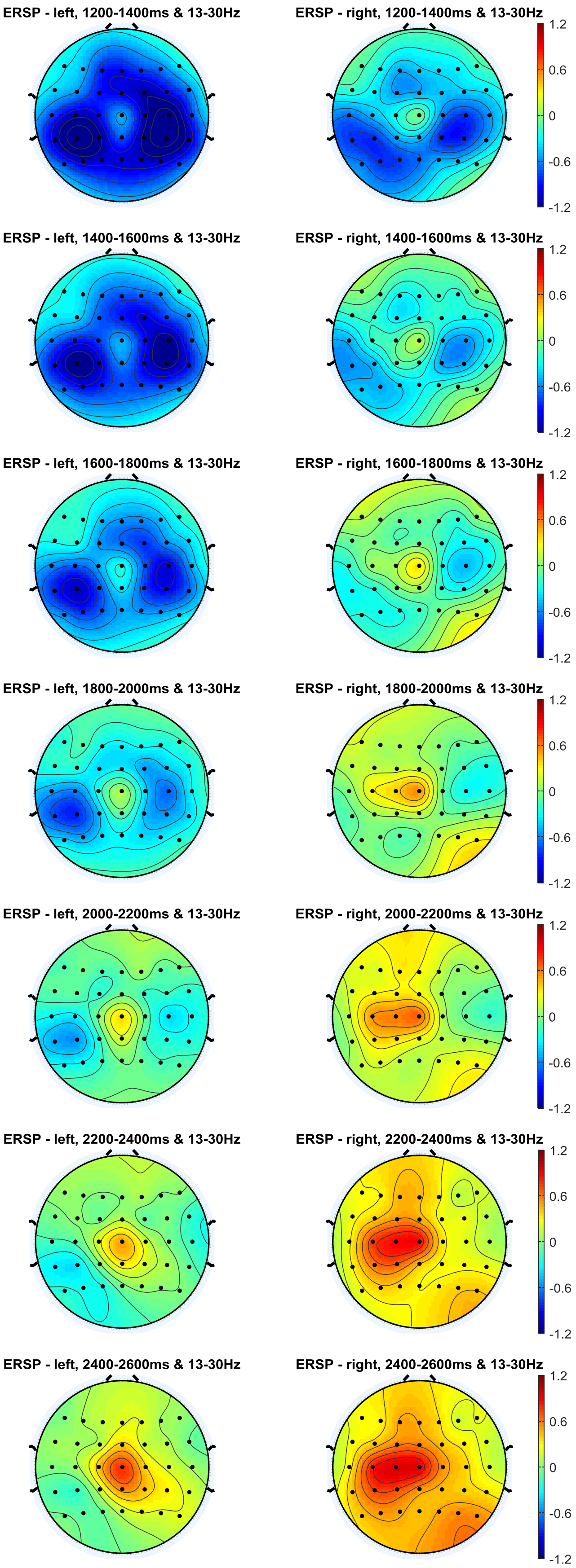
Table 35 Grand average areas over the curve A_{CP3} and A_{CP4} (in ERD% * ms units) and laterality indices (LI) for beta ERD% for left and right arm movements for electrode pairs CP3/CP4 for a 200 ms window before movement onset (Pre 200) and for a 500 ms window following movement onset (Post 500).

	Pre 200	**Post 500**
Left arm movements	bilateral	weak ipsilateral dominant
Right arm movements	contralateral dominant	bilateral/weak contralateral dominant

Table 36 Interpretation of hemispheric lateralisation data for beta ERD% for a 200 ms window preceding movement onset (Pre 200) and for a 500 ms window following movement onset (Post 500).

Beta ERS following movement

Scalp maps of averaged beta ERD/ERS data show that beta ERD becomes weaker for both left and right arm movements, locally around electrode site Cz from about 600 to 800 ms (see Figure 45). Above zero beta ERS values for right arm movement start earlier than for left arm movements at approximately 1200 to 1400 ms (see Figure 48). Above zero beta ERS values start later for left arm movements, at approximately 1800 to 2000 ms. Right arm movement beta ERS starts to be lateralised towards the contralateral hemisphere from approximately 1600 to 1800 ms, with peaks at electrode sites C3, C1, and Cz, occurring during the 2800 to 3000 ms time period. Left arm movement beta ERS starts to be lateralised towards the contralateral hemisphere from approximately 2200 to 2400 ms, with peaks at electrode sites Cz, CP2, and CP4, occurring during the 2600 to 2800 ms time period. Figure 49 shows beta ERD/ERS% over time plots for these electrodes.


ERSP - left, 1200-1400ms & 13-30Hz
ERSP - right, 1200-1400ms & 13-30Hz
ERSP - left, 1400-1600ms & 13-30Hz
ERSP - right, 1400-1600ms & 13-30Hz
ERSP - left, 1600-1800ms & 13-30Hz
ERSP - right, 1600-1800ms & 13-30Hz
ERSP - left, 1800-2000ms & 13-30Hz
ERSP - right, 1800-2000ms & 13-30Hz
ERSP - left, 2000-2200ms & 13-30Hz
ERSP - right, 2000-2200ms & 13-30Hz
ERSP - left, 2200-2400ms & 13-30Hz
ERSP - right, 2200-2400ms & 13-30Hz
ERSP - left, 2400-2600ms & 13-30Hz
ERSP - right, 2400-2600ms & 13-30Hz
1.2
0.6
0
-0.6
-1.2

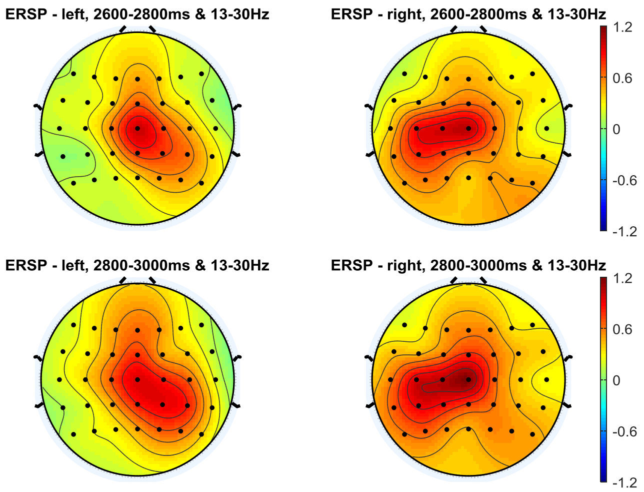


Figure 48 Series of scalp maps of grand averaged beta ERD/ERS data (in dB) from all participants for left (left column) and right (right column) arm movements in 200 ms time intervals, from 1200 to 3000 ms relative to movement onset. Scalp maps are organised chronologically, starting from the top.

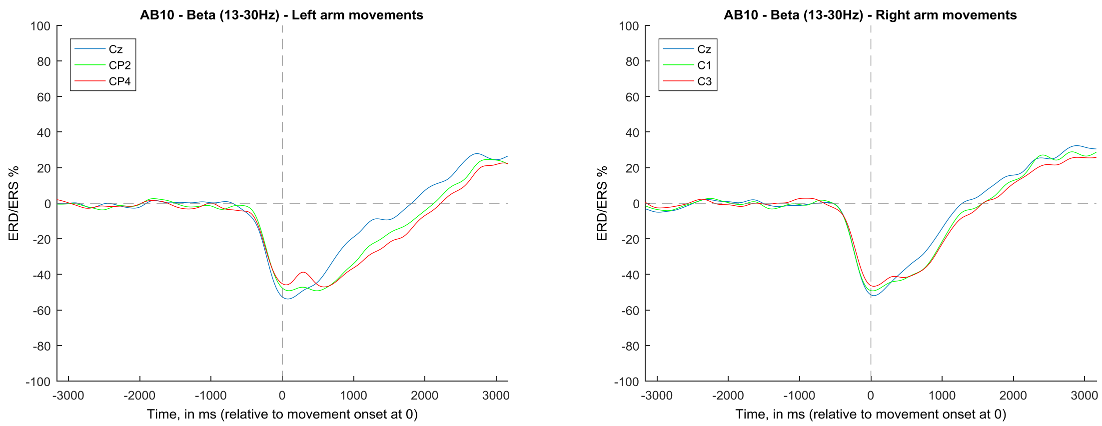


Figure 49 Grand average beta ERD/ERS% over time plots showing beta ERS% following movement for select electrode locations for left and right arm movements.

Peak beta ERS%

Times and values of peak beta ERS% for the electrode with the greatest beta ERS%, electrode Cz, are shown in Table 37. The timings and values of peak beta ERS% intensities are similar for left and right arm movements.

Left arm movements		Right arm movements	
Time (ms)	ERS%	Time (ms)	ERS%
2732	27.9	2892	32.4

Table 37 Grand average peak beta ERS% times and values at electrode location Cz for left and right arm movements.

7.4 Discussion

This study's results answered the third research question: 'What are the characteristics of ERD/ERS measures during reaching for healthy participants?'. Characteristics of alpha and beta ERD were defined for this experimental setup, including spatial distribution and timing, as well as hemispheric lateralisation and peak values for electrode sites CP3/CP4. For beta ERS, timing, spatial distribution and peak values for electrodes of interest were described.

7.4.1 Movement characteristics

As it is not always possible for participants to perform the reaching movement at the same speed, some variability was expected. One participant (H31) had noticeably longer movement times than the rest of the participant. As it is anticipated that some individuals taking part in the stroke participant study will also have longer movement times, longer movement times for this participant was not considered an issue.

7.4.2 Alpha ERD

The spatial distribution of alpha ERD is in accordance with literature findings, which show that when several joints are moved simultaneously, such as in whole arm movements, alpha ERD occurs over large areas and is not as spatially focused as for movement of individual joints (Pfurtscheller et al. 1999).

Characteristics of alpha ERD following the movement cue are in accordance with literature findings, in that right arm movements have a contralateral hemisphere pre-movement alpha ERD which becomes bilateral just before movement onset (Pfurtscheller and Lopes da Silva 1999).

Of note is the fact that before and during movement, for left arm movements, results show a weak ipsilateral predominance of alpha ERD, as demonstrated with hemispheric lateralisation calculations comparing alpha ERD% at electrode locations CP3 and CP4. Literature findings describe a bilateral spatial distribution of ERD, which can be observed for this study, but as right arm movements show a weak contralateral predominance, the same for left arm movements could have been anticipated.

7.4.3 Beta ERD

The spatial distribution of beta ERD shows peaks more anteriorly (over rows C and CP) than alpha ERD, in accordance with literature findings (Pfurtscheller and Lopes da Silva 1999). Also in accordance with literature findings is that results show that for left arm movements, beta ERD starts bilaterally and remains bilateral before movement onset (Bai et al. 2005). As it is the case with alpha ERD, a weak ipsilateral predominance can be observed during left arm movements, when a bilateral/contralateral hemispheric lateralisation could have been anticipated.

7.4.4 Beta ERS following movement

The spatial distribution of beta ERS is in accordance with literature findings, in that it is localised to the motor cortex (Pfurtscheller et al. 1999) and is dominant over the contralateral hemisphere (Pfurtscheller and Lopes da Silva 1999). In terms of timing, results are in not in accordance with literature findings that describe beta ERS starting at around 500 ms after the termination of movement, with peak values at 1000 ms after movement offset (Pfurtscheller and Lopes da Silva 1999). This is not observed in this study, where beta ERS begins at approximately 1800 ms after movement onset for left arm movements and 1200 ms for right arm movements. As the movement time is approximately 300 ms for both left and right arm movements, beta ERS starts at approximately 1500 ms after movement onset for left arm movements, and at 900 ms for right arm movements. The delay may be due to the nature of the movement in that participants may have held their arm after reaching the end of the reaching movement, instead of ceasing muscle contractions as soon as possible.

7.4.5 Limitations

The age of participants does not reflect the general population (mean age 55.9 ± 13.3 years; range 35-67 years). Literature findings shows that older adults exhibit a longer, greater, and more spatially diffused ERD over frontal and parietal areas, as opposed to more defined central regions for younger individuals (Derambure et al. 1993). This data would thus not be ideal to be used to compare ERD/ERS measures from younger individuals. As it is however expected that participants from the stroke participant group will be of similar age (as there are more older adults who have had a stroke than younger adults), these results could be more appropriate for comparison purposes.

7.5 Conclusion

Characteristics of ERD/ERS measures were defined for this experimental setup for a group of ten healthy participants, with many (but not all) being congruent with previous literature findings, though no other study used the same experimental setup and protocol. These results were used in the next study to compare ERD/ERS measures from a small sample of stroke participants.

Chapter 8: Stroke participant study

8.1 Introduction

In order to answer the fourth, fifth, and sixth research questions:

- Do characteristics of ERD/ERS measures during reaching in a small sample of stroke participants differ from those observed in healthy participants?
- What changes, if any, does a period of robotic rehabilitation cause in ERD/ERS measures during reaching in these stroke participants?
- For these stroke participants, is there an association between potential changes in ERD/ERS measures and changes in measures of upper limb impairment and function?

Measures of ERD/ERS were characterised for a reaching movement in a small sample of stroke participants before and after a period of robotic upper limb rehabilitation. They were then compared to healthy participants' averaged measures, and potential changes following rehabilitation were investigated.

8.2 Methods

8.2.1 Participants

Six right-handed stroke participants (mean age 50.8 ± 17.4 years; range 22-69 years; three females and three males) were recruited and gave consent to participate in the study. Figure 50 provides details on recruitment. Table 38 presents characteristics of the six individuals who participated. The location of stroke was sought from participants, but detailed information about whether it was sub-cortical, cortical, or mixed, was not always available.

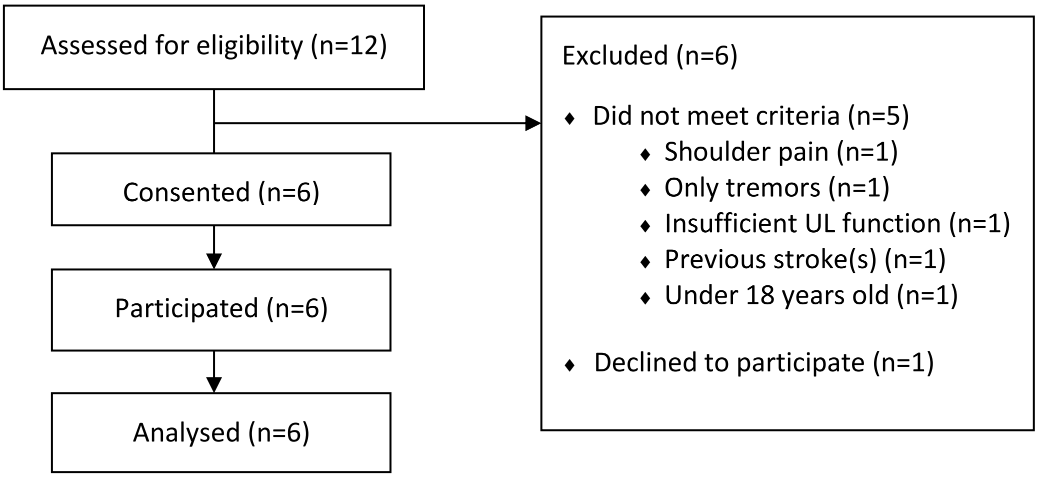


Figure 50 Recruitment of stroke participants.

Participants	Age (years)	Gender	Time since stroke (months)	Side affected	Stroke type and location	Baseline Fugl-Meyer score /66	Baseline ARAT score /57
P4	69	M	27	Right	Left haemorrhagic Partial Anterior Circulation Stroke (PACS)	55	54
P11	46	F	31	Right	Left basal ganglia ischemic stroke	64	57
P13	50	F	17	Right	Left frontal lobe haemorrhagic stroke	31	5
P9	22	F	134	Left	Right MCA territory ischemic stroke	51	23
P20	49	M	2	Left	Right basal ganglia ischemic stroke	52	51
P21	69	M	2	Left	Right ischemic stroke, unknown location	35	12

Table 38 Stroke participants' characteristics.

8.2.2 Data recording

Each participant attended four recording sessions, as per the measurement schedule described in Chapter 4. A total of 24 EEG datasets were obtained.

8.2.2.1 Motor task

All participants performed 150 cued reaching movements at each session, reaching forward as quickly as possible using the experimental setup described in Chapter 4. Participants used their affected arm to perform the reaching movement. Participants were given preparation instruction sheets prior to attending the recording session. Participants were asked to relax their arm muscles after reaching the end of the movement, and to avoid the production of signal artefacts caused by frowning, swallowing, and jaw or neck/shoulder tension.

8.2.2.2 EEG recording

The researcher carried out all recording sessions and collected data using the 35 channel EEG electrode configuration described in Chapter 4. All aspects of EEG recording were the same as for the test-retest variability study and the healthy participant study (see Chapters 6 and 7).

8.2.2.3 EMG and potentiometer data recording

All aspects of EMG and potentiometer data recording were the same as for the test-retest variability study and the healthy participant study (see Chapters 6 and 7).

8.2.2.4 Clinical assessments of impairment and function

The researcher filmed stroke participants as the Fugl-Meyer and ARAT assessments were administered for the affected upper limb at the beginning of all EEG recording sessions. They were also administered for the unaffected upper limb at the first session. A blinded assessor (Carolina Goncalves, physiotherapist experienced in using the assessments) viewed the films in random order and independently scored these assessments to ensure results were unbiased. Scores were recorded on scoring sheets (see Appendices O and P).

8.2.2.5 ArmeoSpring assessments

Three assessments from the ArmeoSpring system (‘A Goal’, ‘Vertical Catch’, and ‘Reaction Time’) were administered at the first rehabilitation session, at midpoint (at the fifth out of ten rehabilitation sessions), and at the last rehabilitation session. The ‘A Goal’ assessment consists of a timed activity where the participant is required to move an orange cross from a house icon to a grey target icon, then to return to the house icon, then to another target icon positioned at a different location than the first one, and so forth, until all targets have been reached (see Figure 51). The 'Vertical catch' assessment consists of a timed activity where the participant is required to move a target from ladybird to ladybird (each one being positioned at different locations on the screen), until all ladybirds have been reached (see Figure 52). The 'Reaction Time' assessment consists of a timed activity where the participant is required to move a fly swatter from a bench to a fly, then to return to the bench, then to another fly, and so forth, until all flies have been reached (see Figure 53). These assessments were all administered at the same level of difficulty for all participants: the 'A Goal' and 'Vertical catch' assessments were administered at level 2, and 'Reaction time' was administered at level 'Easy'. Scores were noted, including the percentage of the activity completed for each assessment, the hand path ratio (for 'A Goal' and 'Vertical Catch' activities), and time taken to complete all tasks within each assessment. The hand path ratio measures how well the user follows a straight line between targets. A perfect straight line trajectory has a hand path ratio of 1 and a hand path ratio of 2 would indicate a trajectory twice the length of a straight line between targets.

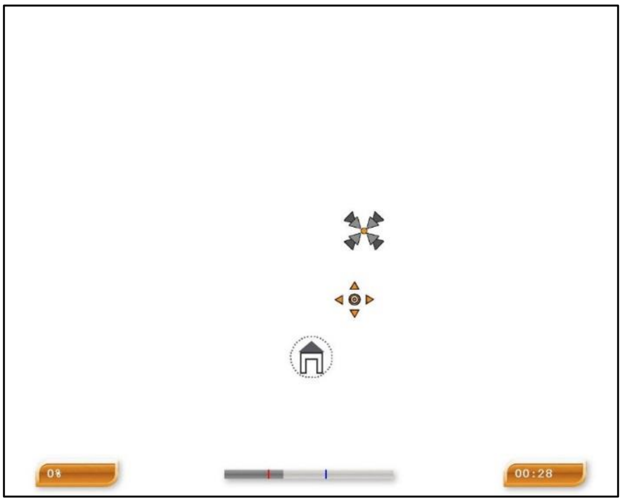


Figure 51 'A Goal' assessment
(Copyright of Hocoma AG (2011) reproduced with permission).

Figure 52 ‘Vertical catch’ assessment
(Copyright of Hocoma AG (2011) reproduced with permission).

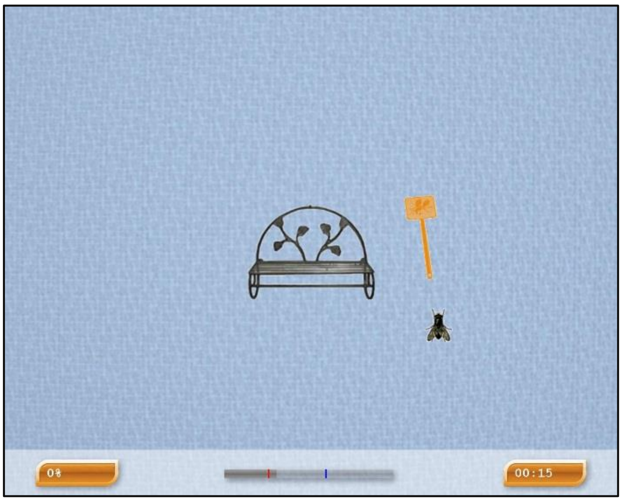


Figure 53 ‘Reaction time’ assessment
(Copyright of Hocoma AG (2011) reproduced with permission).

8.2.3 Data processing and analysis

8.2.3.1 Data processing

All aspects of data processing were the same as for the test-retest variability study and the healthy participant study (see Chapters 6 and 7).

8.2.3.2 Movement characteristics

Mean reaction and movement times (and standard deviations) were calculated using the same method as for all the previous studies. To compare each participant’s mean movement times over four sessions, a one-way unbalanced analysis of variance (ANOVA) was carried out (using MATLAB's 'anova1' function), followed by post-hoc multiple comparison tests with Tukey's honest significant difference criterion (using MATLAB's 'multcompare' function).

8.2.3.3 ERD/ERS

Scalp maps, plots of ERD/ERS% over time, and peak ERD/ERS% values were calculated using the same methods as for the test-retest variability study and the healthy participant study (see Chapters 6 and 7). For this study, ERD% plots and peak values were produced for pairs of symmetrical electrodes CP3/CP4, for direct comparison with those from the healthy participant group (see Chapter 7 for an explanation regarding the selection of electrodes for analysis).

Hemispheric lateralisation of ERD

Lateralisation indices were calculated using the same methods as for the test-retest variability study and the healthy participant study (see Chapters 6 and 7).

8.2.3.4 Clinical assessment scores

Total scores were calculated for the Fugl-Meyer (motor score of the upper extremity section only) and ARAT outcome measures, by adding up individual scores from every subtest.

8.2.3.5 ArmeoSpring assessments scores

Raw scores for the ArmeoSpring assessments (percentage of the activity completed for each assessment, hand path ratio, and time taken to complete the assessment) are reported in an unprocessed form.

8.3 Results

Results of this study are presented in a series of six case studies, with summaries presented at the end of each case study. The first three are for participants who moved their right arm during EEG recordings and the following three are for those who moved their left arm (reminders of which arm was moved are provided in the caption of all ERD/ERS figures and tables). When reference is made to the 'healthy group', this refers to averaged results from the healthy participant study described in Chapter 7. The term 'contralateral' refers to the hemisphere opposite to the side of the arm that was used to perform the movement, and 'ipsilateral' refers to the hemisphere on the same side of the arm used to perform the movement. ERD/ERS time frequency maps and scalp maps for all participants are included on the accompanying USB drive for reference.

8.3.1 Participant P4

At the time of the screening assessment, this participant presented with right-sided mild weakness (MRC grade 4) and mild range of motion restrictions in the upper limb, with some loss of dexterity and speed of movement. No spasticity was observed in his upper limb (Modified Ashworth Scale grade 0). At the time of his participation in the study, he reported difficulties with activities such as writing, throwing, shaving, for which he has been using his unaffected upper limb.

8.3.1.1 Clinical and ArmeoSpring assessment scores

Maximum scores for clinical assessments were achieved with the unaffected upper limb (57 for the ARAT and 66 for the Fugl-Meyer Assessment). Figure 54 presents clinical assessment scores achieved with the affected upper limb for participant P4's four sessions. Sessions 1 and 2 are pre-rehabilitation and sessions 3 and 4 are post-rehabilitation. Figure 55 and Figure 56 present time and hand path ratio scores for the ArmeoSpring assessments that were administered at the first rehabilitation session, at the fifth session, and at the last session. This participant reached 100 % of the target icons for each assessment.

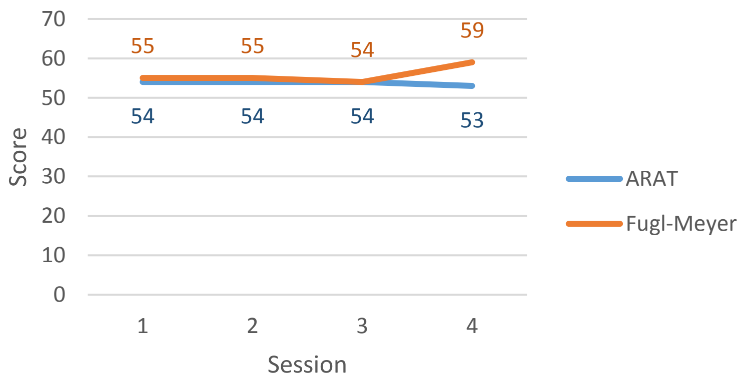


Figure 54 Participant P4's ARAT and Fugl-Meyer scores.

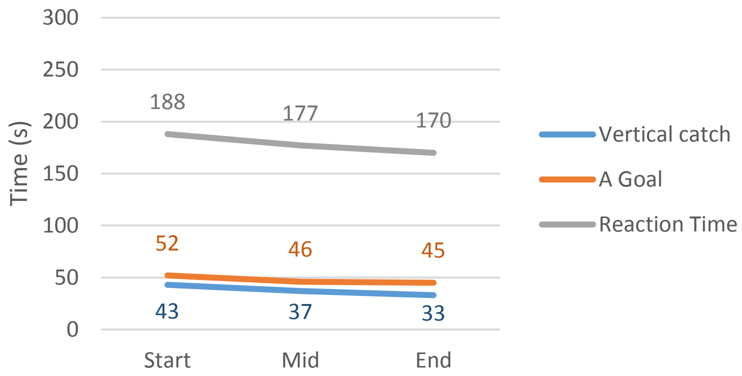


Figure 55 Participant P4’s ArmeoSpring assessment time scores (‘Start’: first rehabilitation session; ‘Mid’: fifth rehabilitation session; ‘End’: last rehabilitation session).

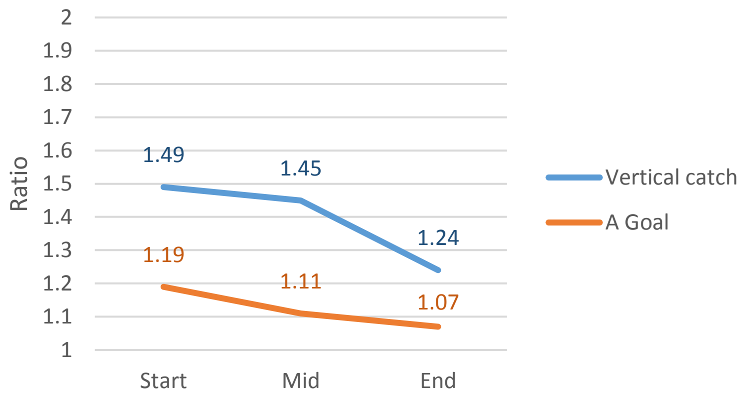


Figure 56 Participant P4’s ArmeoSpring assessment hand path ratio scores (‘Start’: first rehabilitation session; ‘Mid’: fifth rehabilitation session; ‘End’: last rehabilitation session).

Results show that for clinical assessments, scores for the ARAT were similar. For the Fugl-Meyer assessment, scores were similar for sessions 1 to 3, but an improvement of four points above pre-rehabilitation scores was observed at session 4. For the ArmeoSpring assessments, all time scores improved (from 188 to 170 for ‘Reaction Time’, from 52 to 45 for ‘A Goal’, and from 43 to 33 for ‘Vertical Catch’). Gains were also made with hand path ratio scores (from 1.49 to 1.24 for ‘Vertical Catch’ and from 1.19 to 1.07 for ‘A Goal’).

8.3.1.2 Movement characteristics

This participant moved their right arm during EEG recordings. Table 39 presents the number of movements retained for analysis, as well as mean reaction and movement times for participant P4. Figure 57 shows box plots with further details about each session’s movement times.

Corrupted computer files prevented access to data from the first 50 movements for session 1, resulting in only 100 movements available to pre-process.

Session	Number of movements	Mean reaction time	SD	Mean movement time	SD
1	72	493	92	325	45
2	127	514	116	348	49
3	108	494	108	334	62
4	90	523	113	278	38

Table 39 Number of movements retained for analysis, mean reaction times (in ms), and mean movement times (in ms) for participant P4.

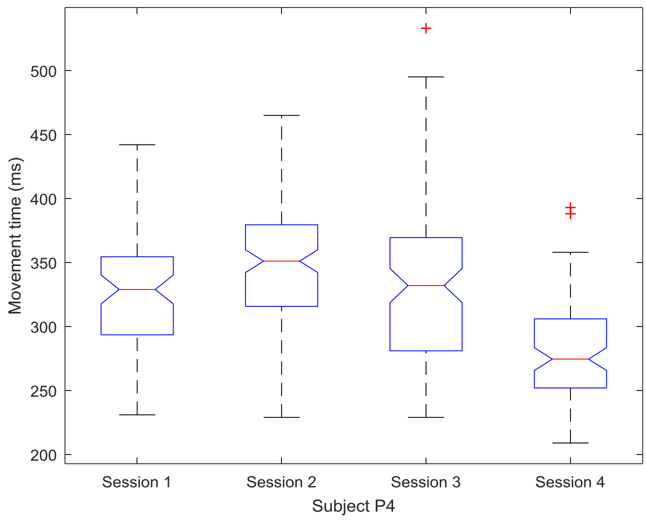


Figure 57 Box plots for participant P4's movement times for four sessions (the red line in the centre of the box being the median, the edges of the box are the 25th and 75th percentiles, whiskers end at the most extreme values that are not considered outliers, and outliers are displayed with red crosses).

To compare this participant's mean movement times over four sessions, results from a one-way unbalanced analysis of variance (ANOVA) show that all sessions, had significantly different mean movement times [F = 36.16 (3, 393), p < 10^-6]. Post-hoc multiple comparison tests with Tukey's honest significant difference criterion showed that some pairs of movement time means were not significantly different (for sessions 1 and 3, as well as for sessions 2 and 3). Session 4's mean movement time was lower than for the first three sessions.

8.3.1.3 Alpha ERD

Alpha ERD over time

Figure 58 presents time frequency ERD/ERS maps for electrode sites CP3/CP4 for participant P4, and shows that ipsilateral alpha ERD is less over electrode CP4 (on the ipsilateral hemisphere) than over electrode CP3. Averaged time frequency ERD/ERS maps for the healthy group are also displayed for comparison purposes. In this figure's caption, and in all other subsequent figures, when a reference is made to the maps' scale, this refers to the vertical colour-coded scale shown on the right hand side of the maps that indicates the degree of ERD/ERS.

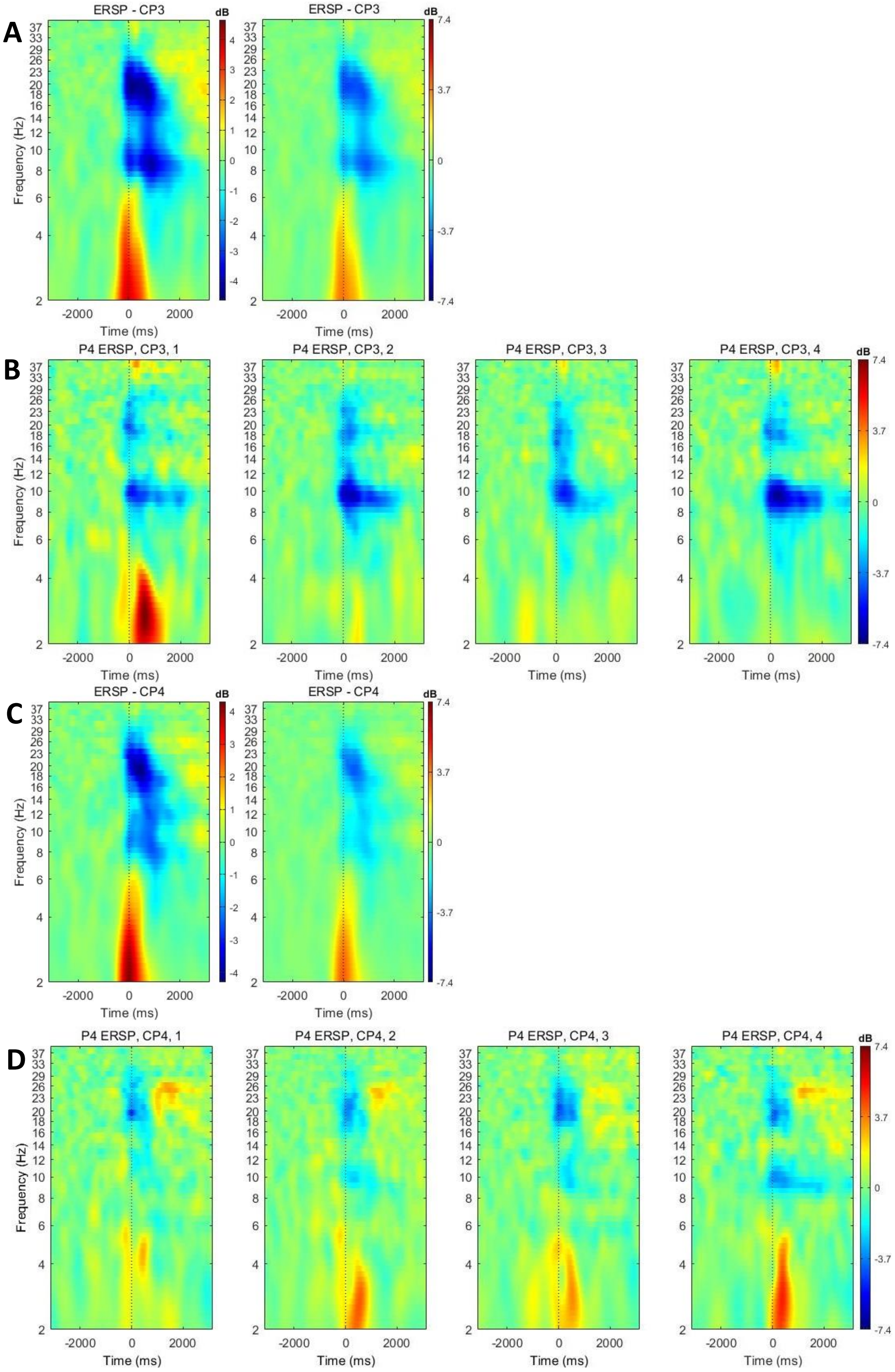


Figure 58 Time frequency ERD/ERS maps for CP3 for (A) the healthy group (two maps: original scale and adjusted to this participant's scale), (B) participant P4 sessions 1-4, and CP4 for (C) the healthy group (two maps as above), and (D) participant P4 sessions 1-4 (right arm movements).

Figure 59 presents alpha ERD/ERS% over time plots for pairs of symmetrical electrodes CP3/CP4 for all sessions. It can be observed that the relative difference of the intensity of alpha ERD% between electrode CP4 (on the ipsilateral hemisphere) and electrode CP3, is larger than for the healthy group. It can also be observed (on Figure 58 as well), that at session 4, alpha ERD at electrode location CP4 is greater in terms of intensity and time (it is longer) than at previous sessions.

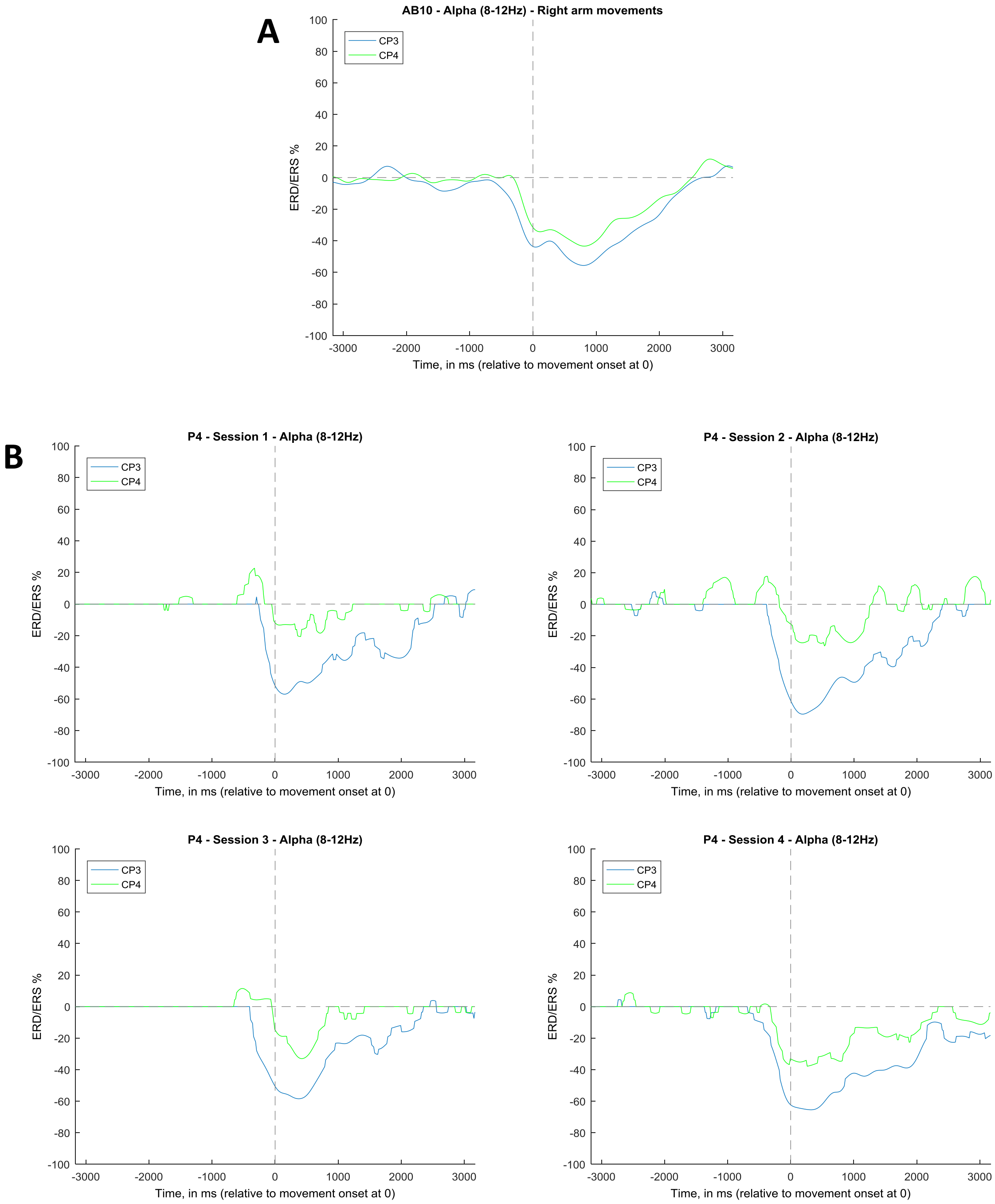


Figure 59 Plots of alpha ERD/ERS% over time for symmetrical electrodes CP3/CP4 for (A) the healthy group (averaged), (B) participant P4 (right arm movements).

Table 40 presents peak alpha ERD% values for electrode CP3 (the one with the greatest alpha ERD% values from the plots above). Peaks were approximately matched according to time and placed in the same row in order to compare values. Some variability can be observed in alpha ERD% peak values, but the pattern of variation is not indicative of changes due to rehabilitation. Values for the first peak for all sessions are greater than for the healthy group's average (-44.0 %).

Session 1		**Session 2**		**Session 3**		**Session 4**	
Time	ERD%	Time	ERD%	Time	ERD%	Time	ERD%
150	-57.0	182	-69.6	374	-58.5	326	-65.5
1723	-34.6	1611	-39.6	1627	-30.3	1831	-39.0

Table 40 Participant P4's alpha ERD% peak values for electrode CP3 for all sessions (times in ms) (right arm movements).

Hemispheric lateralisation

Figure 60 presents scalp maps of alpha ERD/ERS for a 200 ms window preceding movement onset and for a 500 ms window following movement onset for participant P4. Contralateral dominance can be observed for all sessions, before and after movement onset.

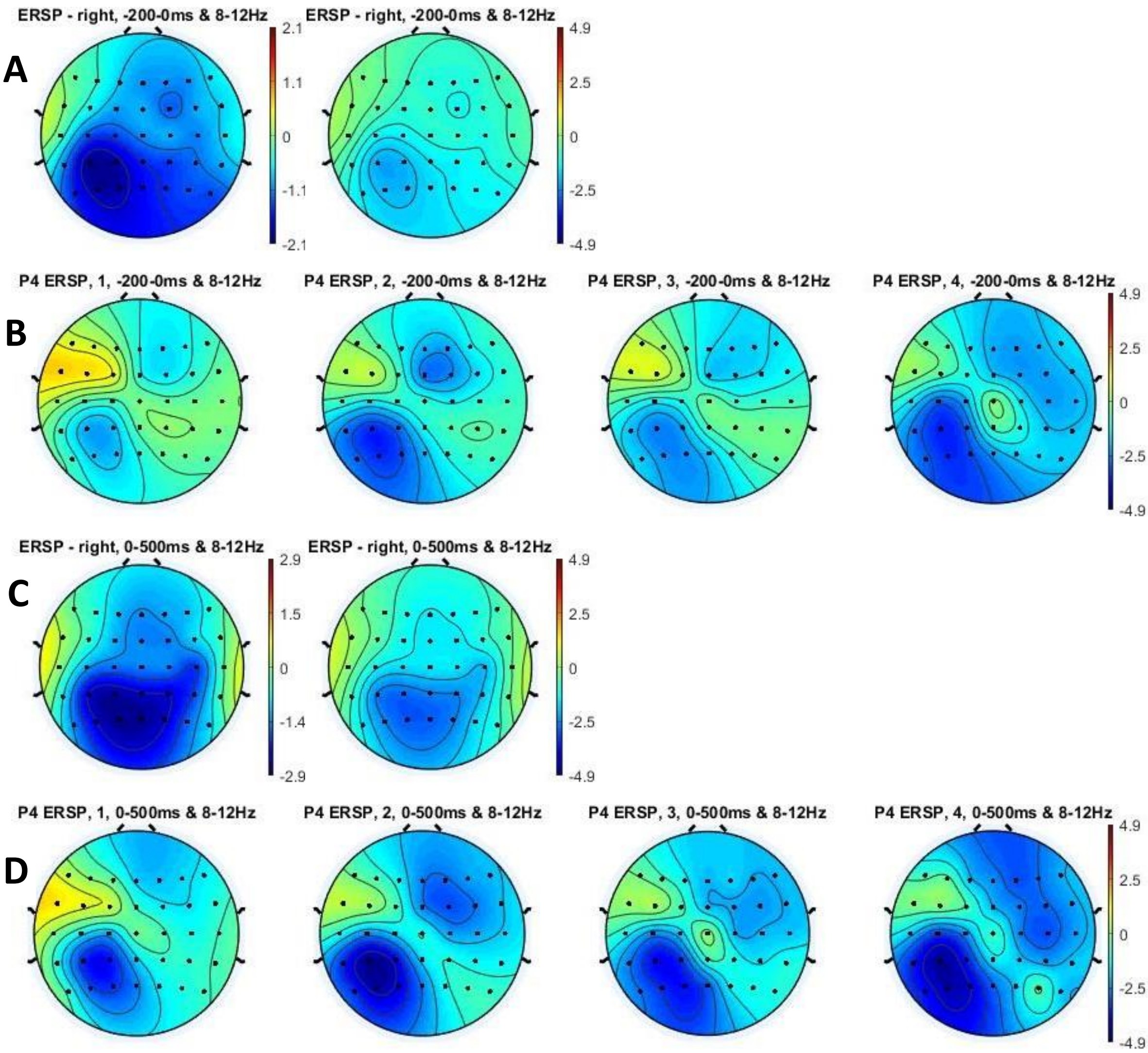


Figure 60 Scalp maps of alpha ERD/ERS for a 200 ms window preceding movement onset for (A) the healthy group (averaged; two maps: original scale and adjusted to this participant's scale), (B) participant P4 for sessions 1 to 4, and for a 500 ms window following movement onset for (C) the healthy group (two maps as above), and (D) participant P4 for sessions 1 to 4 (right arm movements).

Table 41 presents values for areas over the curve and laterality indices (LI), as calculated with alpha ERD% data for electrode pair CP3/CP4, for a period of 200 ms preceding movement onset and a period of 500 ms following movement onset. Laterality index values range from -1 to 1. A value of -1 indicates complete right hemisphere predominance. A value of 1 indicates complete left hemisphere predominance. A value of 0 indicates equal amounts of ERD% at both electrode sites.

Session	A_{CP3}		A_{CP4}		Laterality Index		L/R ratio	
	Pre 200	Post 500	Pre 200	Post 500	Pre 200	Post 500	Pre 200	Post 500
1	6772	26143	144	7184	0.96	0.57	47.02	3.64
2	9743	32824	1305	10737	0.76	0.51	7.46	3.06
3	8210	27695	342	12487	0.92	0.38	23.99	2.22
4	10285	31726	6100	17248	0.26	0.30	1.69	1.84

Table 41 Participant P4's areas over the curve A_{CP3} and A_{CP4} (in ERD% * ms units) and laterality indices for alpha ERD% for electrode pair CP3/CP4 for a 200 ms window preceding movement onset (Pre 200) and for a 500 ms window following movement onset (Post 500) (right arm movements). L/R values = A_{CP3} / A_{CP4}.

In order to interpret laterality indices and L/R ratio values, the researcher defined ranges for labelling laterality. For the purpose of this study, laterality indices (LI) falling between -0.05 to 0.05 are deemed to indicate bilateral alpha ERD%, those between -0.15 to -0.05 and between 0.05 to 0.15 are deemed to indicate weak right and left hemispheric predominance, respectively, and any other values indicate either left or right hemispheric predominance.

Table 42 presents the interpretation of the hemispheric lateralisation data using the described criteria.

Session	Pre 200	Post 500
1	contralateral dominant	contralateral dominant
2	contralateral dominant	contralateral dominant
3	contralateral dominant	contralateral dominant
4	contralateral dominant	contralateral dominant

Table 42 Interpretation of participant P4's hemispheric lateralisation data for alpha ERD% for a 200 ms window preceding movement onset (Pre 200) and for a 500 ms window following movement onset (Post 500) (right arm movements).

When compared to the healthy group, contralateral dominance is much greater for this participant. When looking at variations between sessions (see Table 41), results for hemispheric lateralisation show that the laterality index for a 200 ms period of time preceding movement onset is decreased for session 4 (from 0.96, 0.76, 0.92, for sessions 1 to 3, respectively, to 0.26 for session 4), well beyond any variability observed in the test-retest variability study described in Chapter 6 (the difference in L/R ratio values for this participant is 5.77 between the next lowest value at session 2, well beyond the maximum difference of 0.96 for the test-retest variability study group). This laterality index value (0.26) is equal to the laterality index observed for the healthy group.

For a 500 ms period of time after movement onset, laterality index values are consistently smaller for sessions 3 and 4 (following rehabilitation) than they are for sessions 1 and 2 (from 0.57, 0.51, for sessions 1 and 2, respectively, to 0.38 and 0.30 for sessions 3 and 4, respectively). The difference in L/R ratio values between session 2 and session 3 is 0.84, which is greater than the maximum difference of 0.71 found in the test-retest variability study.

8.3.1.4 Beta ERD

Frequency range

The frequency range within the beta range (13-30 Hz) at which beta ERD occurs at symmetrical electrodes CP3 and CP4 was examined by visually inspecting ERSP plots produced with EEGLAB's STUDY functions. Table 43 presents results for all sessions. Results are similar over sessions and for symmetrical electrodes.

Electrode	Session 1	Session 2	Session 3	Session 4
CP3	17-27	16-27	15-26	16-26
CP4	18-28	17-28	17-27	17-27

Table 43 Frequency ranges, in Hz, at which beta ERD occurs for participant P4's sessions.

Beta ERD over time

For time frequency ERD/ERS maps for electrode sites CP3 and CP4, please refer to Figure 58 in the previous section. Figure 61 presents beta ERD/ERS% over time plots for pairs of symmetrical electrodes CP3/CP4 for all sessions.

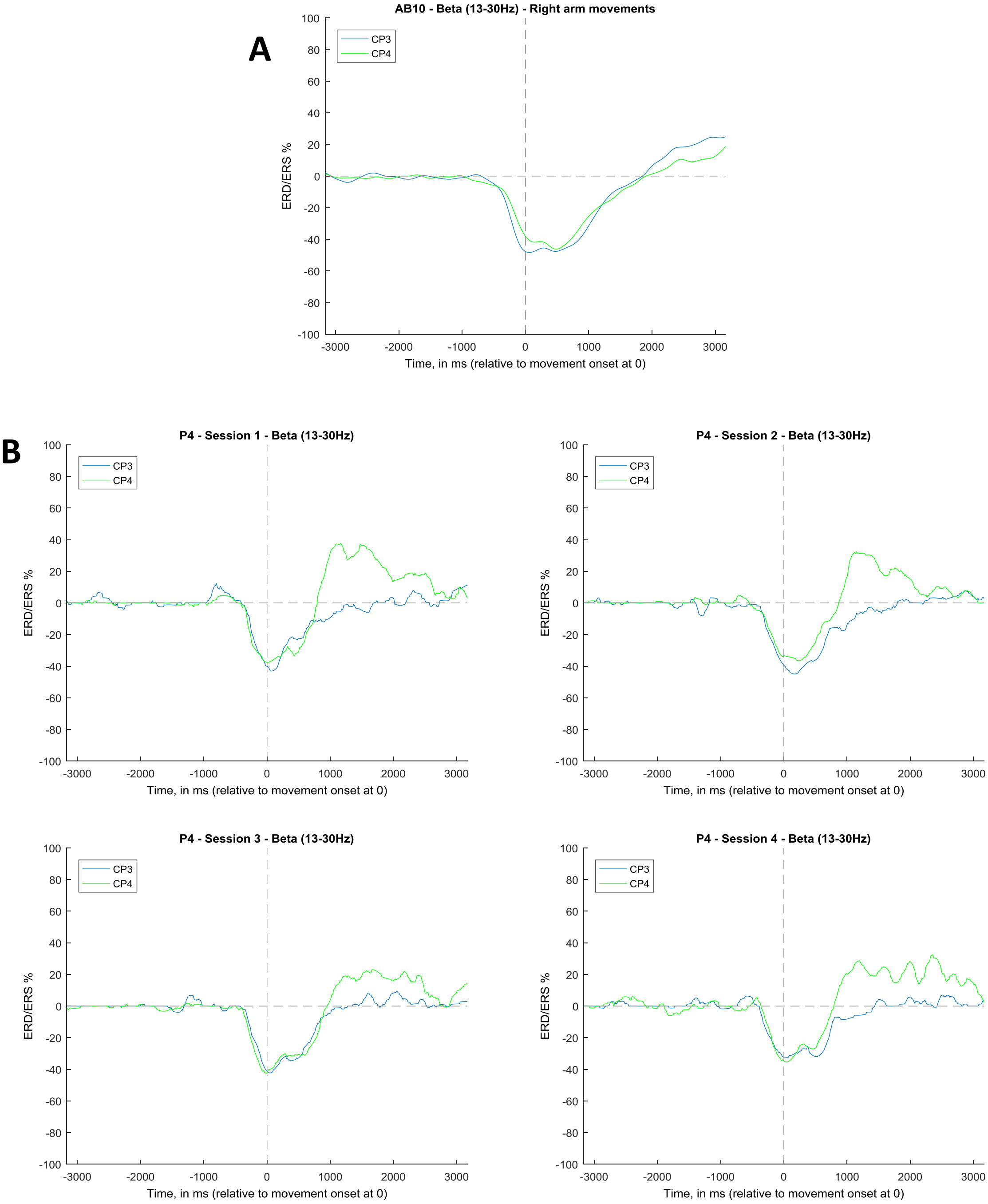


Figure 61 Plots of beta ERD/ERS% over time for symmetrical electrodes CP3/CP4 for (A) the healthy group (averaged), (B) participant P4 (right arm movements).

Table 44 presents peak beta ERD% values for electrode CP3 (the one with the greatest alpha ERD% values from the plots above). Peaks were approximately matched according to time and placed in the same row in order to compare values. Some variability can be observed in beta ERD% peak values, but the degree of variation is not indicative of changes due to rehabilitation, although the value for session 4's first peak is lower than for the first three sessions. Values for the first peak for all sessions are less than for the healthy group's average (-48.3 %).

Session 1		Session 2		Session 3		Session 4	
Time	ERD%	Time	ERD%	Time	ERD%	Time	ERD%
70	-43.1	166	-45.0	54	-42.2	54	-32.4
482	-23.32	454	-37.0	422	-31.6	514	-31.9

Table 44 Participant P4's beta ERD% peak values for electrode CP3 for all sessions (times in ms) (right arm movements).

Hemispheric lateralisation

Figure 62 presents scalp maps of beta ERD/ERS for a 200 ms window preceding movement onset and for a 500 ms window following movement onset for participant P4.

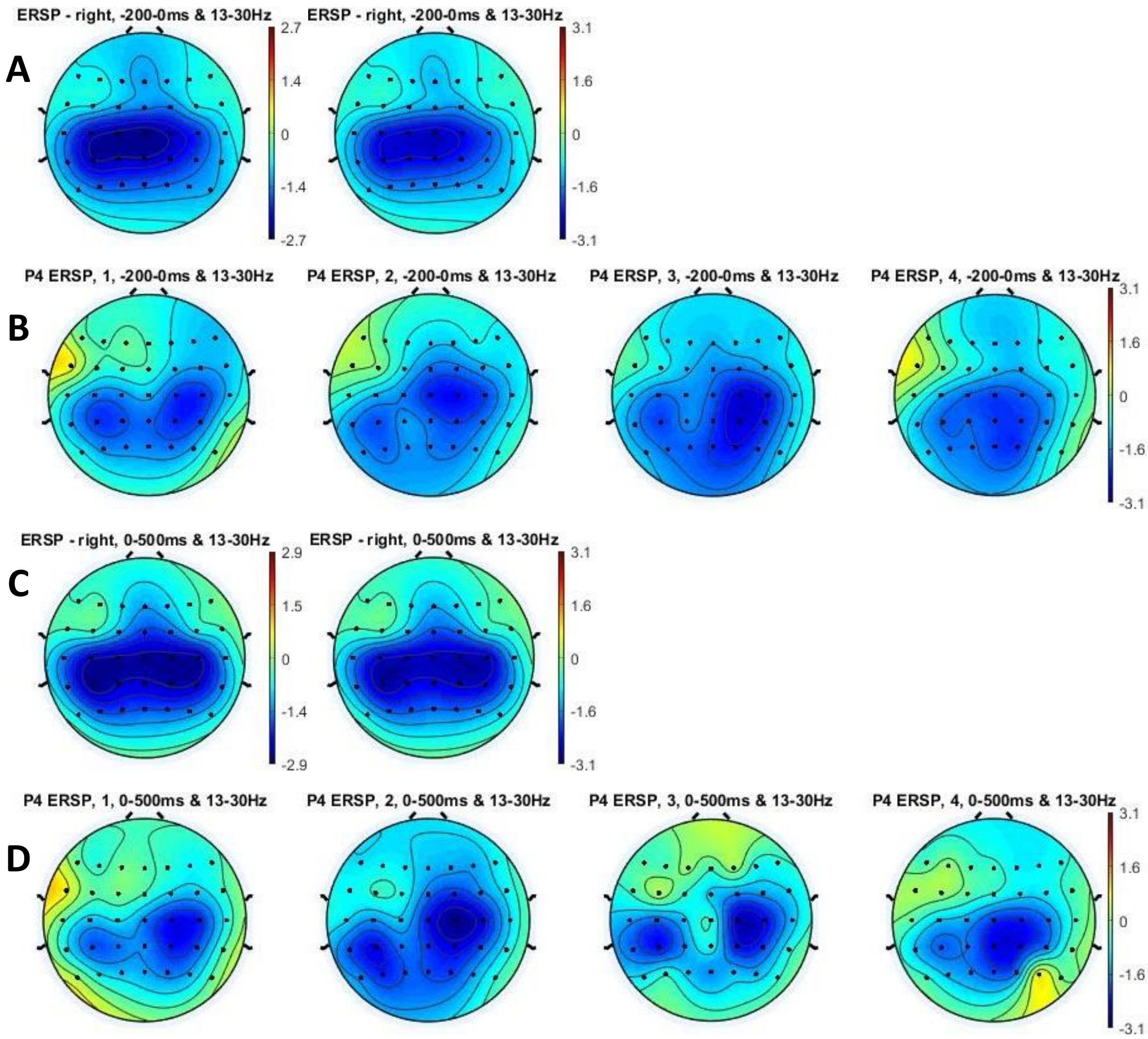


Figure 62 Scalp maps of beta ERD/ERS for a 200 ms window preceding movement onset for (A) the healthy group (averaged; two maps: original scale and adjusted to this participant's scale), (B) participant P4 for sessions 1 to 4, and for a 500 ms window following movement onset for (C) the healthy group (two maps as above), and (D) participant P4 for sessions 1 to 4 (right arm movements).

Table 45 presents values for areas over the curve and laterality indices (LI), as calculated with beta ERD% data for electrode pair CP3/CP4, for a period of 200 ms preceding movement onset and a period of 500 ms following movement onset.

Session	A_{CP3}		A_{CP4}		Laterality Index		L/R ratio	
	Pre 200	Post 500	Pre 200	Post 500	Pre 200	Post 500	Pre 200	Post 500
1	6368	15664	6443	16232	-0.01	-0.02	0.99	0.96
2	6149	20147	5431	16379	0.06	0.10	1.13	1.23
3	6107	17766	7181	16605	-0.08	0.03	0.85	1.07
4	5296	14635	5681	14231	-0.04	0.01	0.93	1.03

Table 45 Participant P4's areas over the curve A_{CP3} and A_{CP4} (in ERD% * ms units) and laterality indices for beta ERD% for electrode pair CP3/CP4 for a 200 ms window preceding movement onset (Pre 200) and for a 500 ms window following movement onset (Post 500) (right arm movements). L/R values = A_{CP3} / A_{CP4}.

Table 46 presents the interpretation of the hemispheric lateralisation data using the criteria described for alpha ERD in the previous section.

Session	Pre 200	Post 500
1	bilateral	bilateral
2	weak contralateral dominant	weak contralateral dominant
3	weak ipsilateral dominant	bilateral
4	bilateral	bilateral

Table 46 Interpretation of participant P4's hemispheric lateralisation data for beta ERD% for a 200 ms window preceding movement onset (Pre 200) and for a 500 ms window following movement onset (Post 500) (right arm movements).

When compared to the healthy group, hemispheric lateralisation of beta ERD% for a 200 ms period of time preceding movement onset for this participant is less contralateral dominant and more bilateral. For a 500 ms period of time after movement onset, it is congruent with results from the healthy group. The pattern of variation over sessions is not indicative of changes due to rehabilitation.

8.3.1.5 Beta ERS following movement

Spatial distribution

The spatial distribution was similar for all sessions, centred at Cz initially, then spreading to the ipsilateral hemisphere to C2/C4 (see Figure 63). This is unlike results from the healthy group, where beta ERS peaks occur at C3, C1, and Cz, over the contralateral hemisphere.

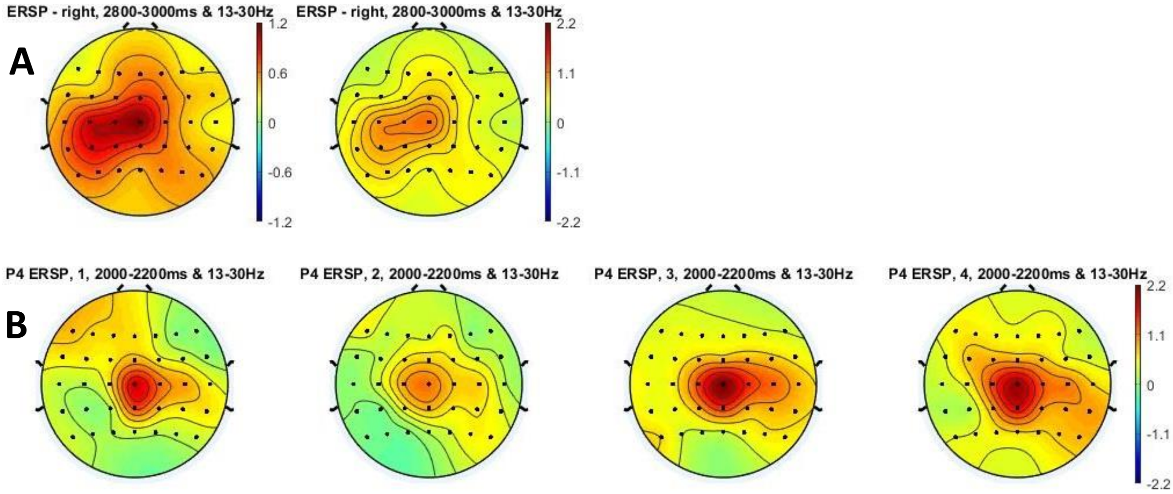


Figure 63 Scalp maps of beta ERS for (A) the healthy group (averaged; two maps: original scale and adjusted to this participant's scale), (B) participant P4 for sessions 1 to 4 (right arm movements).

Beta ERS over time

Figure 64 presents beta ERS% over time plots for electrodes Cz, C2, and C4 for all sessions.

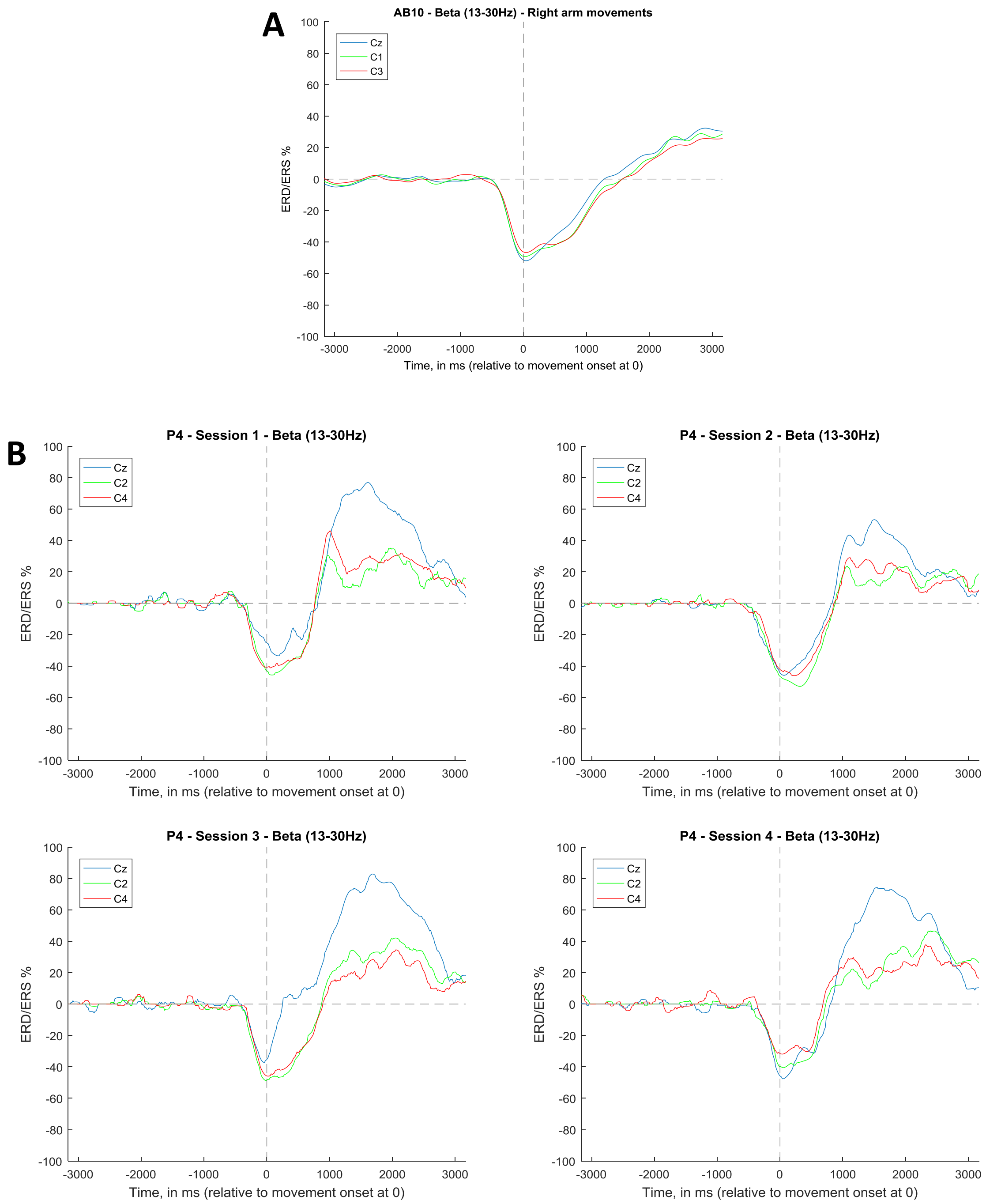


Figure 64 Plots of beta ERS% over time for (A) electrodes Cz, C1, and C3 for the healthy group (averaged), (B) electrodes Cz, C2, and C4 for participant P4 for all sessions (right arm movements).

Table 47 presents peak beta ERS% values for electrode Cz (the one with the greatest beta ERS% values from the plots above). The range of timings for beta ERS% peaks, as calculated by the difference in time between the earliest and latest peaks over the four sessions, is 192 ms. Some variability can be observed in the timing and peak values of beta ERS%, but the pattern of variation is not indicative of changes due to rehabilitation. Values for all sessions are greater than for the healthy group’s average (32.4 %).

Session 1		Session 2		Session 3		Session 4	
Time	ERS%	Time	ERS%	Time	ERS%	Time	ERS%
1611	77.0	1499	53.3	1691	82.9	1547	74.5

Table 47 Participant P4's beta ERS% peak values for electrode Cz for all sessions (times in ms) (right arm movements).

8.3.1.6 Summary and discussion of results

Participant P4's results for clinical assessments showed an improvement of four points following rehabilitation for the Fugl-Meyer assessment. This however occurred at session 4, whilst session 3, the first session after rehabilitation, showed no improvement from pre-rehabilitation measures. Gains were also made with hand path ratio and time scores for the ArmeoSpring assessments, suggesting that this participant improved their ability to move their arm with more control and precision.

Session 4's mean movement time was lower than for all other three sessions. As movement times depend on a variety of factors, such as the participant's alertness and motivation levels, it is not possible to say whether this increased speed of movement is solely due to improved arm function.

Some ERD/ERS measures deviated from the averaged results from the healthy group:

- The intensity of alpha ERD was less over the ipsilateral hemisphere than for the healthy group's average.
- Alpha ERD% peak values over the contralateral hemisphere were greater than for the healthy group's average.
- Hemispheric lateralisation of alpha ERD% was excessively more contralateral dominant before and after movement onset than for the healthy group.
- Hemispheric lateralisation of beta ERD% for a 200 ms period of time preceding movement onset was less contralateral dominant and more bilateral than for the healthy group.
- Beta ERS following movement was present over the ipsilateral hemisphere, rather than the contralateral hemisphere as seen in the healthy group.
- The intensity of beta ERS following movement was greater than for the healthy group's average.

Decreased ipsilateral hemisphere alpha ERD suggests that for this participant, interhemispheric inhibitory mechanisms may have been altered by stroke, by exerting an overactive interhemispheric inhibition resulting in a decreased ipsilateral alpha ERD.

Some changes in ERD/ERS measures could be attributed to the effects of rehabilitation:

- Alpha ERD was greater in terms of intensity and time (it was longer) over the ipsilateral hemisphere at session 4 than it was at previous sessions.
- The laterality index for alpha ERD% for session 4 for a 200 ms period of time preceding movement onset decreased and was equal to the one for the healthy group. This could however not be observed for session 3, the first session after rehabilitation.
- The laterality index for alpha ERD% for sessions 3 and 4 for a 500 ms period of time after movement onset decreased (at its lowest value at session 4), towards the value found for the healthy group.

Considering that the improvement for the Fugl-Meyer assessment score and the greatest changes in the laterality indices for alpha ERD% both occurred at session 4, this suggests that for this participant, improvements in arm function are associated with changes in laterality indices in the alpha range. These changes were mostly observed at session 4, which suggests that for this participant, the effects of rehabilitation required time to translate into improved arm function and changes in ERD/ERS measures.

8.3.2 Participant P11

At the time of the screening assessment, this participant presented with right-sided mild weakness in the upper limb (MRC grade 4), with some loss of dexterity and speed of movement in her hand. No spasticity was observed in her upper limb (Modified Ashworth Scale grade 0). At the time of her participation in the study, this participant reported only being able to lift light objects and sometimes using her unaffected side to carry out everyday activities.

8.3.2.1 Clinical and ArmeoSpring assessment scores

Maximum scores for clinical assessments were achieved with the unaffected upper limb (57 for the ARAT and 66 for the Fugl-Meyer Assessment). Figure 65 presents clinical assessment scores achieved with the affected upper limb for participant P11's four sessions. Sessions 1 and 2 are pre-rehabilitation and sessions 3 and 4 are post-rehabilitation. Figure 66 and Figure 67 present time and hand path ratio scores for the ArmeoSpring assessments that were administered at the first rehabilitation session, at the fifth session, and at the last session. This participant reached 100 % of the target icons for each assessment.

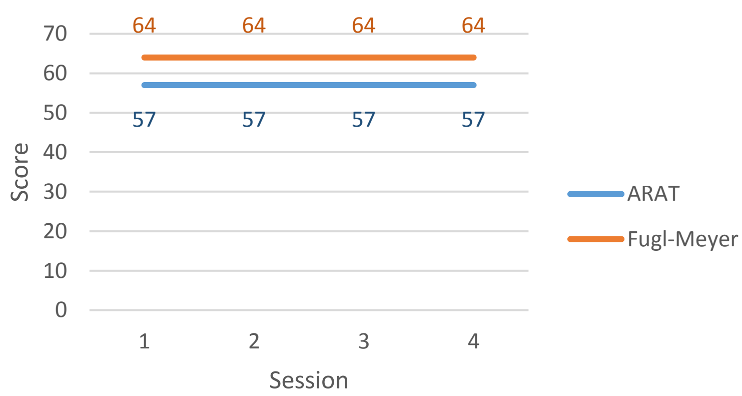


Figure 65 Participant P11's ARAT and Fugl-Meyer scores.

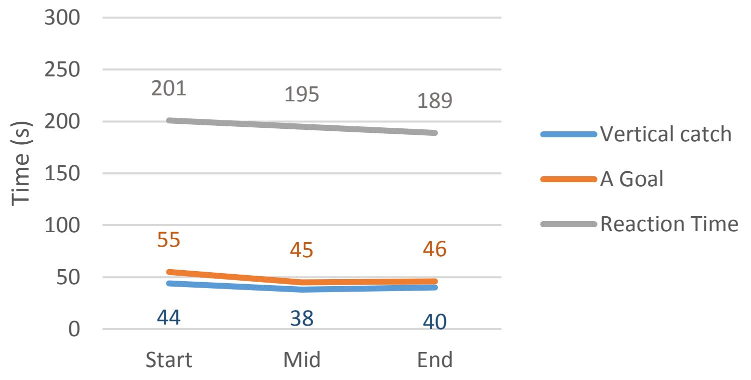


Figure 66 Participant P11's ArmeoSpring assessment time scores.

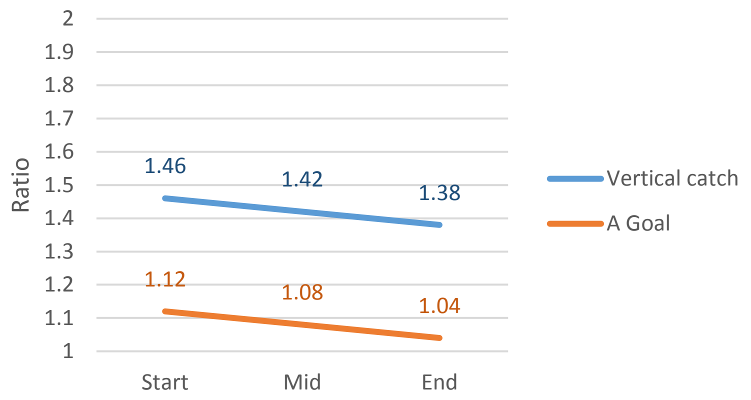


Figure 67 Participant P11's ArmeoSpring assessment hand path ratio scores.

Results show that for clinical assessments, all scores are equal across sessions, with this participant obtaining maximum scores for the ARAT, and almost maximum scores for the Fugl-Meyer assessment (64 out of 66). For the ArmeoSpring assessments, there were improvements in time scores (from 201 to 189 for 'Reaction Time', from 55 to 46 for 'A Goal', and from 44 to 40 for 'Vertical Catch'), and improvements were made for hand path ratio scores (from 1.46 to 1.38 for 'Vertical Catch' and from 1.12 to 1.04 for 'A Goal').

8.3.2.2 Movement characteristics

This participant moved their right arm during EEG recordings. Table 48 presents the number of movements retained for analysis, as well as mean reaction and movement times for participant P11. Figure 68 shows box plots with further details about each session's movement times. Mean reaction and movement times are not available for session 3 as there was a fault with the

EMG/potentiometer data acquisition board, which required replacement. As epochs were created using the movement cue instead of the movement onset for this session, ERD/ERS measures related to the timing of ERD/ERS are not available for this session.

Session	Number of movements	Mean reaction time	SD	Mean movement time	SD
1	110	352	80	276	24
2	125	366	92	298	27
3	88	unknown	unknown	unknown	unknown
4	134	373	81	282	23

Table 48 Number of movements retained for analysis, mean reaction times (in ms), and mean movement times (in ms) for participant P11.

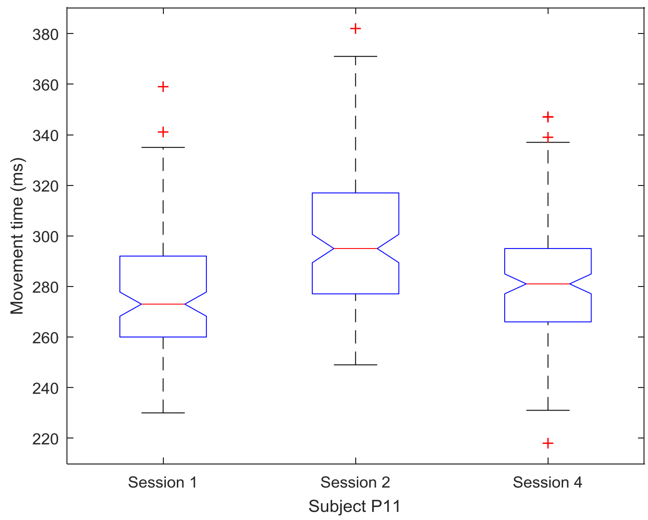


Figure 68 Box plots for participant P11's movement times for three sessions (the red line in the centre of the box being the median, the edges of the box are the 25th and 75th percentiles, whiskers end at the most extreme values that are not considered outliers, and outliers are displayed with red crosses).

To compare this participant's mean movement times over three sessions, results from a one-way unbalanced analysis of variance (ANOVA) show that all sessions had significantly different mean movement times [$F = 25.4$ (2, 366), $p < 10^{-6}$]. Post-hoc multiple comparison tests with Tukey's honest significant difference criterion showed that one pair of movement time means, for sessions 1 and 3, were not significantly different.

8.3.2.3 Alpha ERD

Alpha ERD over time

Figure 69 presents time frequency ERD/ERS maps for electrode sites CP3/CP4 for participant P11, where alpha ERS can be observed, particularly at electrode CP4, over the ipsilateral hemisphere. Averaged time frequency ERD/ERS maps for the healthy group are also displayed for comparison purposes.

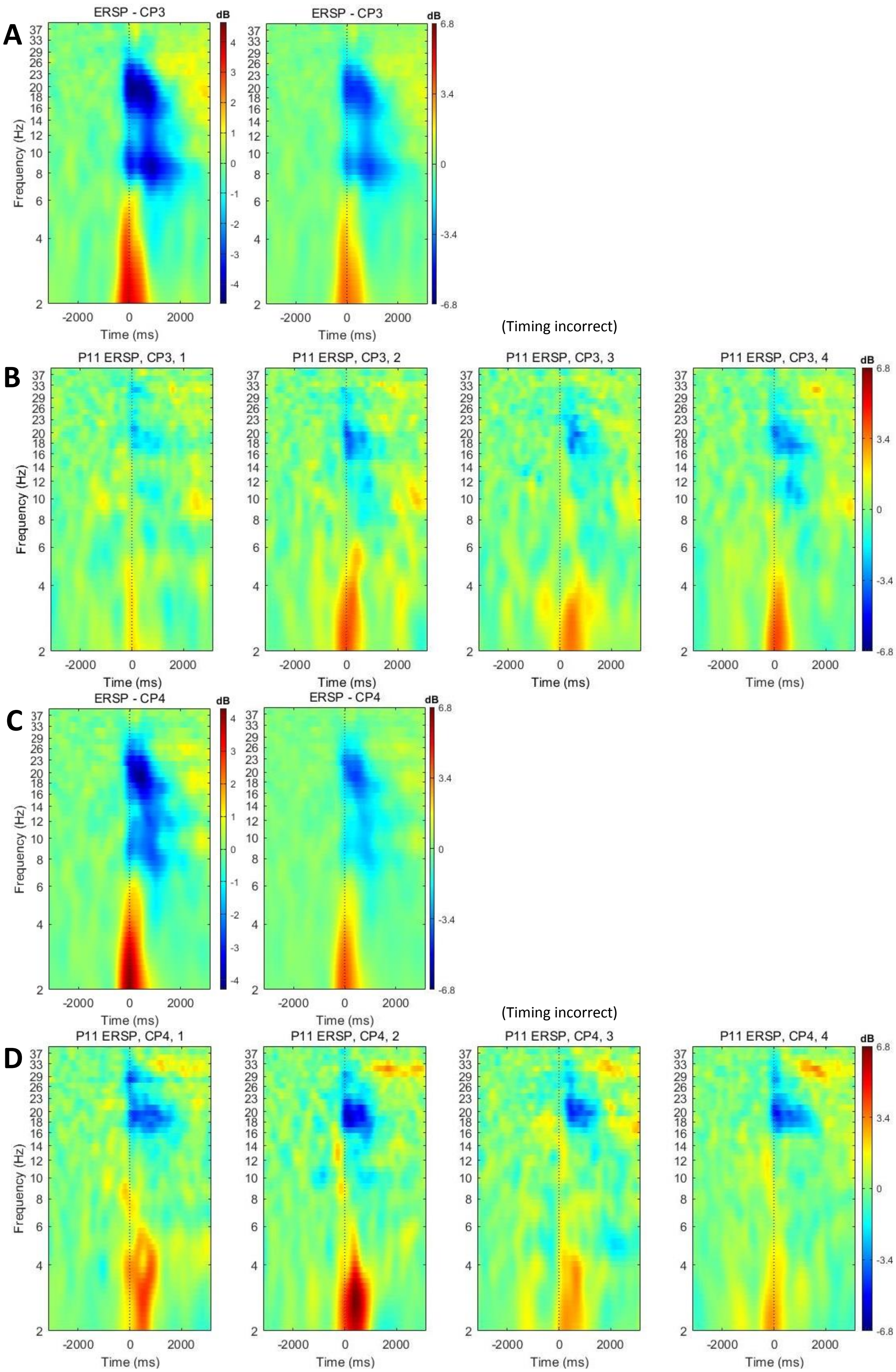


Figure 69 Time frequency ERD/ERS maps for CP3 for (A) the healthy group (two maps: original scale and adjusted to this participant's scale), (B) participant P11 sessions 1-4, and CP4 for (C) the healthy group (two maps as above), and (D) participant P11 sessions 1-4 (right arm movements).

Figure 70 presents alpha ERD/ERS% over time plots for pairs of symmetrical electrodes CP3/CP4 for all sessions. An atypical alpha ERD% can be observed, with alpha ERS% occurring before and during movement mostly at electrode CP4, on the ipsilateral hemisphere.

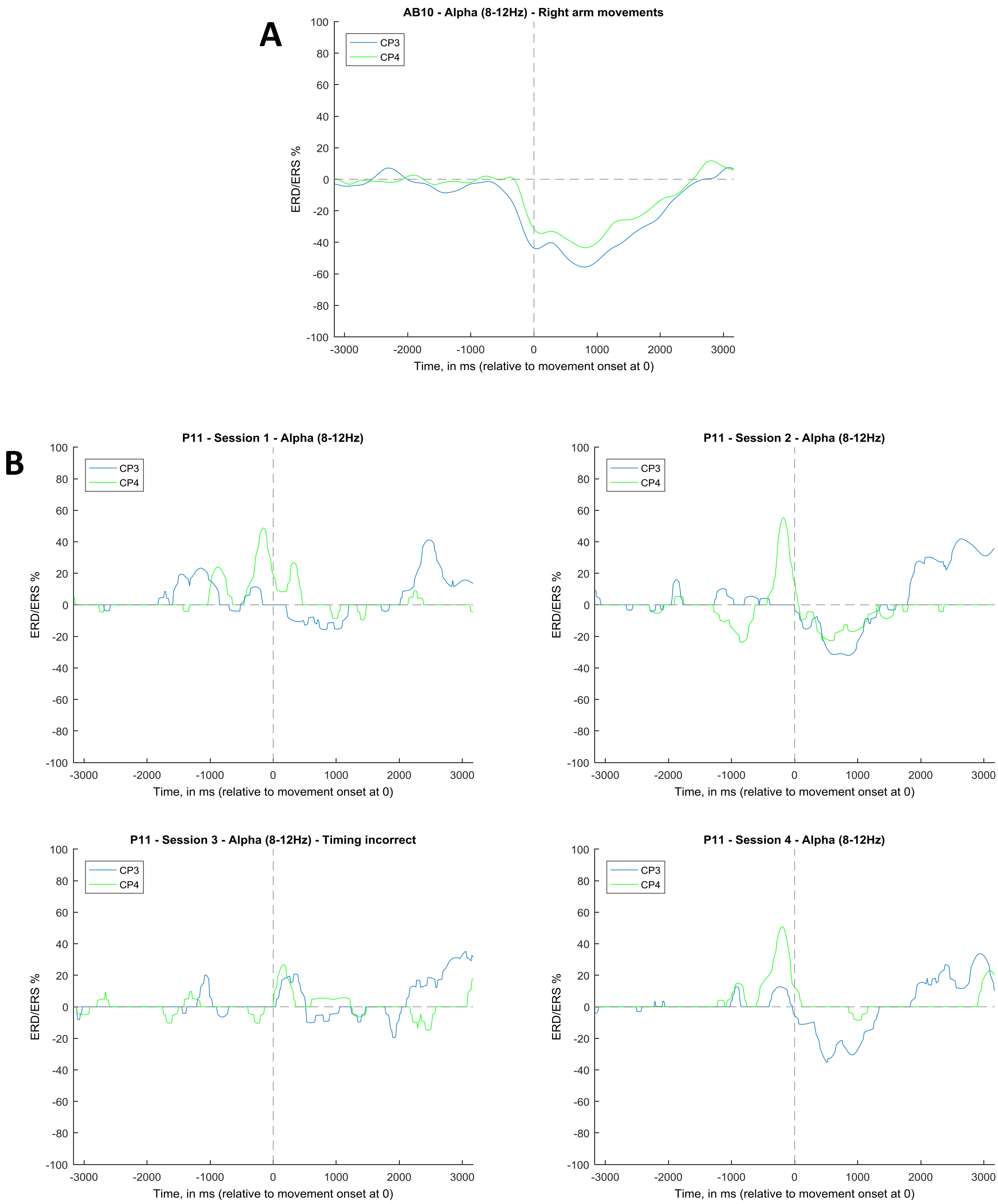


Figure 70 Plots of alpha ERD/ERS% over time for symmetrical electrodes CP3/CP4 for (A) the healthy group (averaged), (B) participant P11 (right arm movements). Timings for session 3 are incorrect.

Table 49 presents peak alpha ERD% values for electrode CP3 (the one with the greatest alpha ERD% values from the plots above). Peaks were approximately matched according to time and placed in the same row in order to compare values. Peak values for all sessions are less than for the healthy group's average (-44.0%).

Session 1		Session 2		Session 3		Session 4	
Time	ERD%	Time	ERD%	Time	ERD%	Time	ERD%
-	-	626	-31.5	-	-	514	-35.4
802	-15.8	850	-32.1	-	-	910	-30.5
-	-	-	-	unknown	-19.6	-	-

Table 49 Participant P11's alpha ERD% peak values for electrode CP3 for all sessions (times in ms) (right arm movements). When several peaks are present, they are approximately matched according to time and placed in the same row in order to compare values.

Hemispheric lateralisation

Figure 71 presents scalp maps of alpha ERD/ERS for a 200 ms window preceding movement onset and for a 500 ms window following movement onset for participant P11.

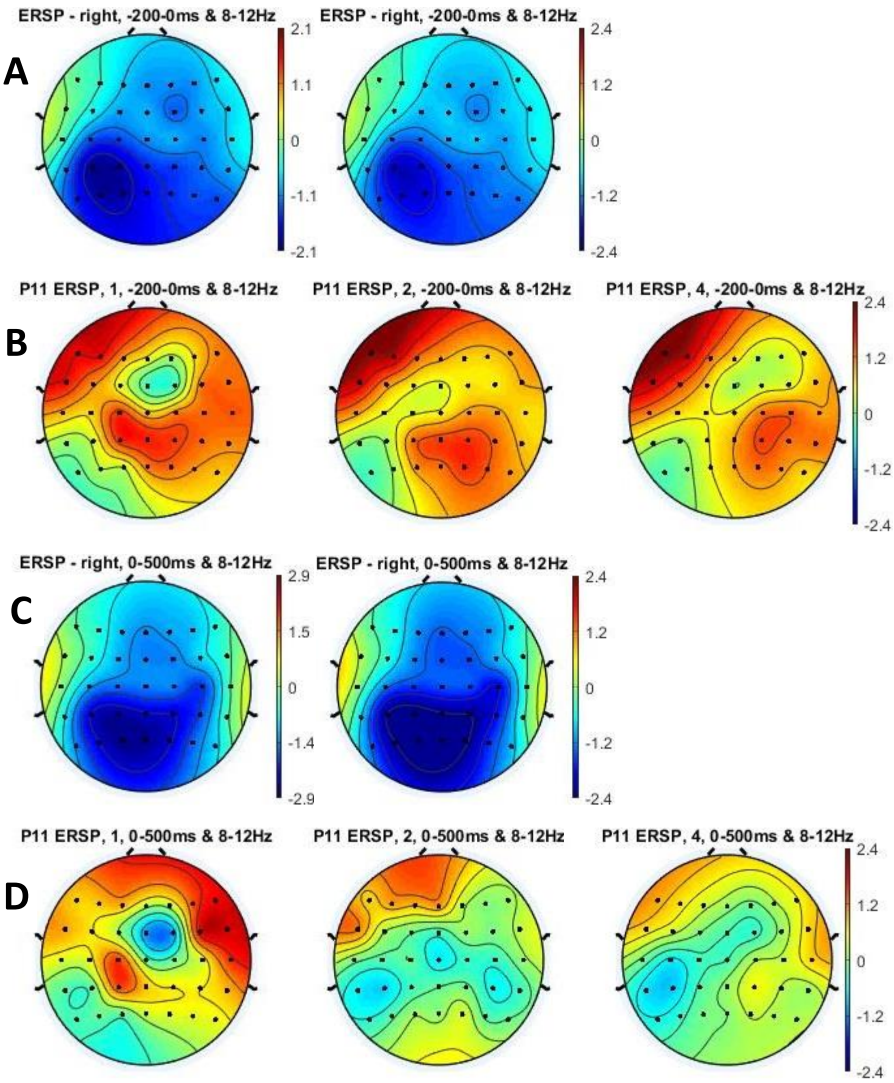


Figure 71 Scalp maps of alpha ERD/ERS for a 200 ms window preceding movement onset for (A) the healthy group (averaged; two maps: original scale and adjusted to this participant's scale), (B) participant P11 for sessions 1, 2, and 4, and for a 500 ms window following movement onset for (C) the healthy group (averaged; two maps as above), and (D) participant P11 for sessions 1, 2, and 4 (right arm movements). Scalp maps are not available for session 3.

Table 50 presents values for areas over the curve and laterality indices (LI), as calculated with alpha ERD% data for electrode pair CP3/CP4, for a period of 200 ms preceding movement onset and a period of 500 ms following movement onset. Laterality index values range from -1 to 1. A value of -1 indicates complete right hemisphere predominance. A value of 1 indicates complete left hemisphere predominance. A value of 0 indicates equal amounts of ERD% at both electrode sites.

Session	A_{CP3}		A_{CP4}		Laterality Index		L/R ratio	
	Pre 200	Post 500	Pre 200	Post 500	Pre 200	Post 500	Pre 200	Post 500
1	0	2796	0	0	-	1.00	-	-
2	0	6099	0	4471	-	0.15	-	1.36
4	1187	7631	0	0	1.00	1.00	-	-

Table 50 Participant P11's areas over the curve A_{CP3} and A_{CP4} (in ERD% * ms units) and alpha ERD% laterality indices for electrode pair CP3/CP4 for a 200 ms window preceding movement onset (Pre 200) and for a 500 ms window following movement onset (Post 500) (right arm movements). L/R values = A_{CP3} / A_{CP4}. Results are not available for session 3.

In order to interpret laterality indices and L/R ratio values, the researcher defined ranges for labelling laterality. For the purpose of this study, laterality indices (LI) falling between -0.05 to 0.05 are deemed to indicate bilateral alpha ERD%, those between -0.15 to -0.05 and between 0.05 to 0.15 are deemed to indicate weak right and left hemispheric predominance, respectively, and any other values indicate either left or right hemispheric predominance.

Table 51 presents the interpretation of the hemispheric lateralisation data using the described criteria. As alpha ERD% for this participant is atypical, hemispheric lateralisation data is different from the healthy group, and no pattern of change can be observed that would suggest improvement following rehabilitation.

Session	Pre 200	Post 500
1	-	contralateral dominant
2	-	weak contralateral dominant
4	contralateral dominant	contralateral dominant

Table 51 Interpretation of participant P11's hemispheric lateralisation data for alpha ERD% for a 200 ms window preceding movement onset (Pre 200) and for a 500 ms window following movement onset (Post 500) (right arm movements). Results are not available for session 3.

8.3.2.4 Beta ERD

Frequency range

The frequency range within the beta range (13-30 Hz) at which beta ERD occurs at symmetrical electrodes CP3 and CP4 was examined by visually inspecting ERSP plots produced with EEGLAB's

STUDY functions. Table 52 presents results for all sessions. Results are similar over sessions and for symmetrical electrodes.

Electrode	Session 1	Session 2	Session 3	Session 4
CP3	16-22	15-22	16-25	16-23
CP4	16-23	15-22	16-23	16-23

Table 52 Frequency ranges, in Hz, at which beta ERD occurs for participant P11's sessions.

Beta ERD over time

For time frequency ERD/ERS maps for electrode sites CP3 and CP4, please refer to Figure 69 in the previous section. Figure 72 presents beta ERD/ERS% over time plots for pairs of symmetrical electrodes CP3/CP4 for all sessions. It can be observed that beta ERD is greater at electrode CP4 (over the ipsilateral hemisphere) than at electrode CP3.

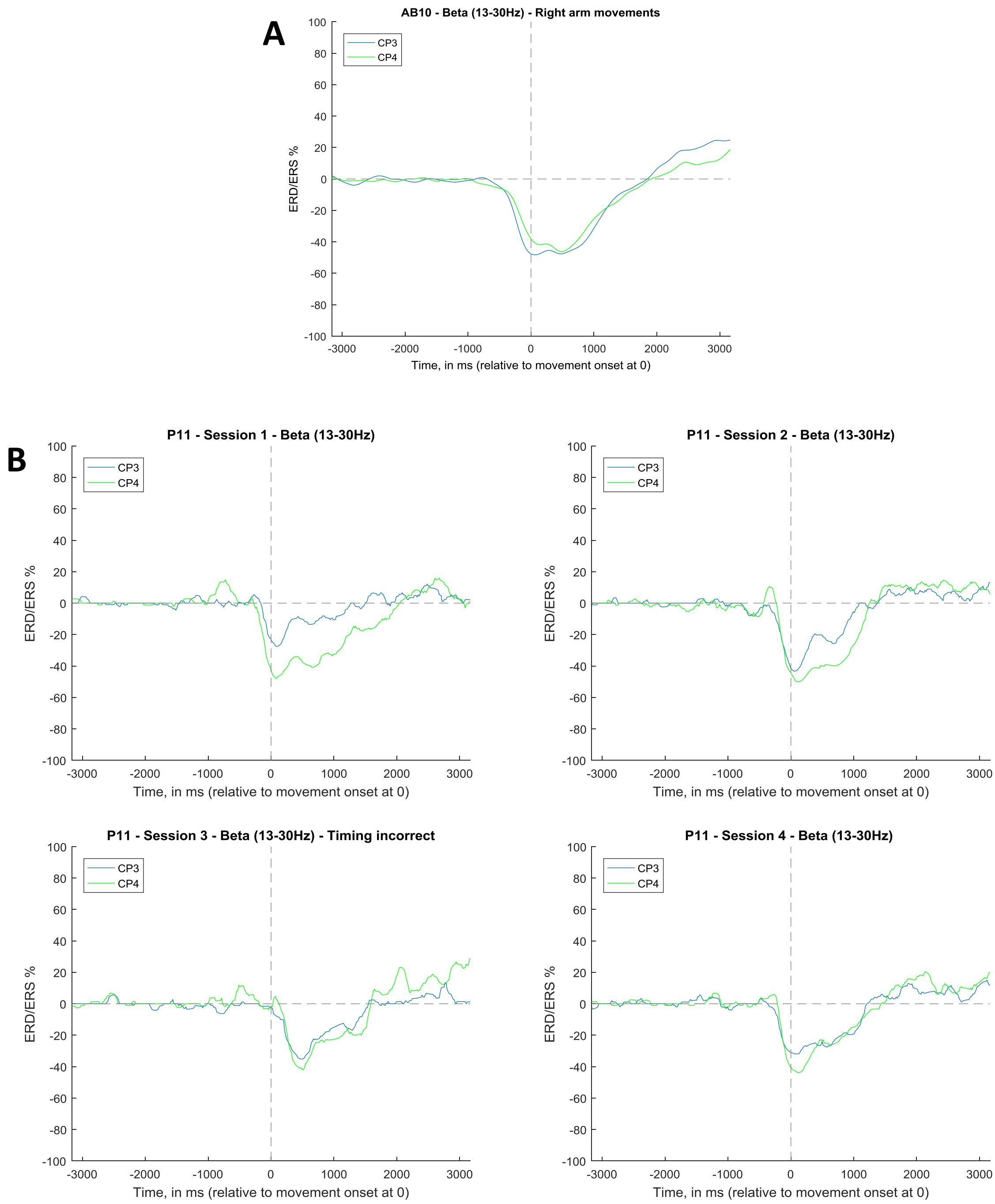


Figure 72 Plots of beta ERD/ERS% over time for symmetrical electrodes CP3/CP4 for (A) the healthy group (averaged), (B) participant P11 (right arm movements). Timings for session 3 are incorrect.

Table 53 presents peak beta ERD% values for electrode CP4 (the one with the greatest beta ERD% values from the plots above). Peaks were approximately matched according to time and placed in the same row in order to compare values. Some variability can be observed in beta ERD% peak values, but the pattern and degree of variation is not indicative of changes due to rehabilitation. Values for the first peak are generally similar to the one found for the healthy group's average (-48.3 %).

Session 1		Session 2		Session 3		Session 4	
Time	ERD%	Time	ERD%	Time	ERD%	Time	ERD%
86	-48.0	118	-50.1	unknown	-42.0	102	-44.0
642	-40.8	690	-39.9	-	-	610	-26.2

Table 53 Participant P11's beta ERD% peak values for electrode CP4 for all sessions (times in ms) (right arm movements). When several peaks are present, they are approximately matched according to time and placed in the same row in order to compare values.

Hemispheric lateralisation

Figure 73 presents scalp maps of beta ERD/ERS for a 200 ms window preceding movement onset and for a 500 ms window following movement onset for participant P11.

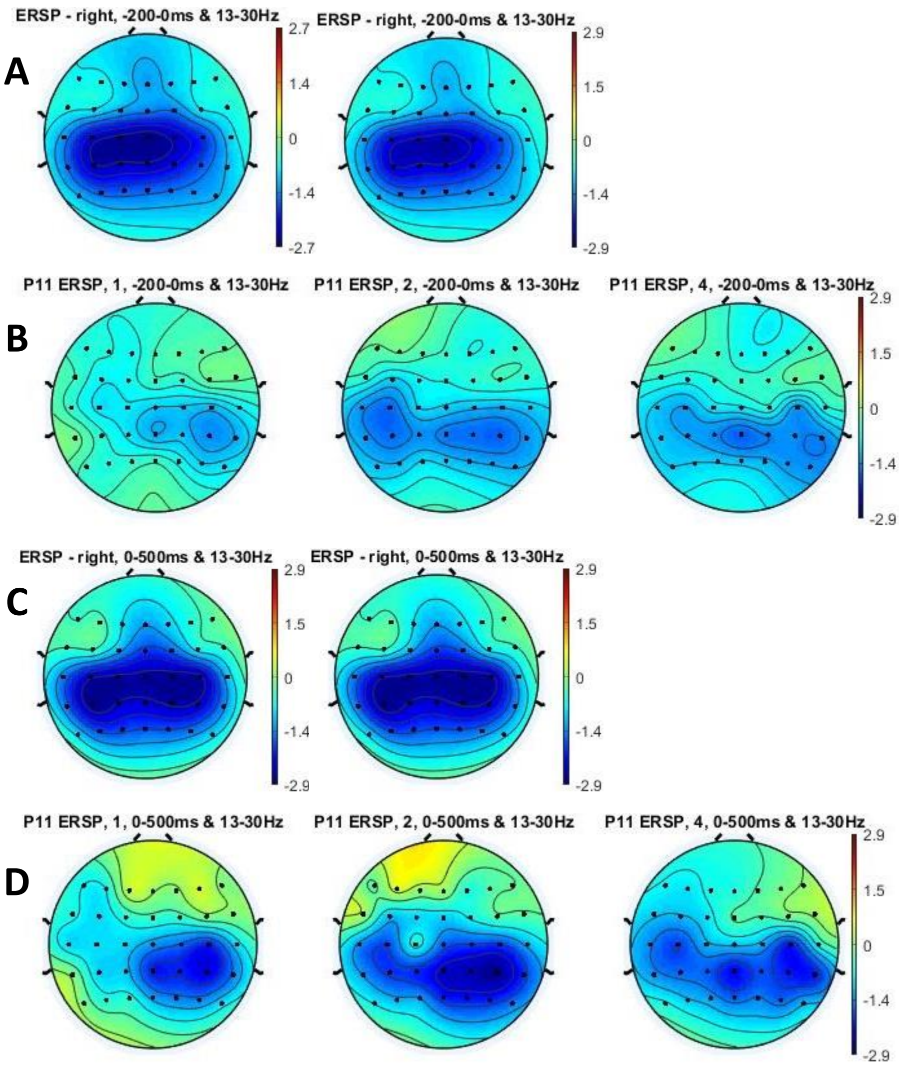


Figure 73 Scalp maps of beta ERD/ERS for a 200 ms window preceding movement onset for (A) the healthy group (averaged; two maps: original scale and adjusted to this participant's scale), (B) participant P11 for sessions 1, 2, and 4, and for a 500 ms window following movement onset for (C) the healthy group (averaged; two maps as above), and (D) participant P11 for sessions 1, 2, and 4 (right arm movements). Scalp maps are not available for session 3.

Table 54 presents values for areas over the curve and laterality indices (LI), as calculated with beta ERD% data for electrode pair CP3/CP4, for a period of 200 ms preceding movement onset and a period of 500 ms following movement onset.

Session	A_{CP3}		A_{CP4}		Laterality Index		L/R ratio	
	Pre 200	Post 500	Pre 200	Post 500	Pre 200	Post 500	Pre 200	Post 500
1	2003	8658	5067	19954	-0.43	-0.39	0.40	0.43
2	5521	15219	5865	22177	-0.03	-0.19	0.94	0.69
4	4710	13760	5051	17541	-0.03	-0.12	0.93	0.78

Table 54 Participant P11's areas over the curve A_{CP3} and A_{CP4} (in ERD% * ms units) and laterality indices for beta ERD% for electrode pair CP3/CP4 for a 200 ms window preceding movement onset (Pre 200) and for a 500 ms window following movement onset (Post 500) (right arm movements). L/R values = A_{CP3} / A_{CP4}. Results are not available for session 3.

Table 55 presents the interpretation of the hemispheric lateralisation data using the criteria described for alpha ERD in the previous section.

Session	Pre 200	Post 500
1	ipsilateral dominant	ipsilateral dominant
2	bilateral	ipsilateral dominant
4	bilateral	weak ipsilateral dominant

Table 55 Interpretation of participant P11's hemispheric lateralisation data for beta ERD% for a 200 ms window preceding movement onset (Pre 200) and for a 500 ms window following movement onset (Post 500) (right arm movements). Results are not available for session 3.

When compared to the healthy group, hemispheric lateralisation of beta ERD% for a 200 ms period of time preceding movement onset for this participant is not contralateral dominant as it is for the healthy group, but ipsilateral dominant for session 1 and bilateral for sessions 2 and 4). For a 500 ms period of time after movement onset, it is not congruent with results from the healthy group (weak contralateral dominance), in that all sessions present with ipsilateral beta ERD% dominance. The degree of variation over sessions is not indicative of changes due to rehabilitation.

8.3.2.5 Beta ERS following movement

Spatial distribution

The spatial distribution was similar for all sessions, centred at FCz/Cz initially, then spreading slightly to the ipsilateral hemisphere to FCz/FC2 (see Figure 74). This is different from results from the healthy group, where beta ERS peaks occur at C3, C1, and Cz, over the contralateral hemisphere.

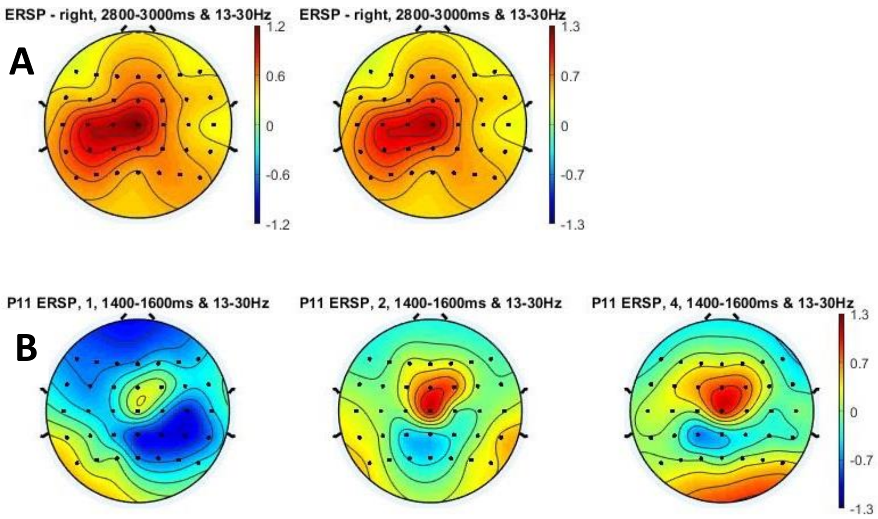


Figure 74 Scalp maps of beta ERS for (A) the healthy group (averaged; two maps: original scale and adjusted to this participant's scale), (B) participant P11 for sessions 1 to 4 (right arm movements). Scalp maps are not available for session 3.

Beta ERS over time

Figure 75 presents beta ERS% over time plots for electrodes FCz, FC2, and Cz for all sessions.

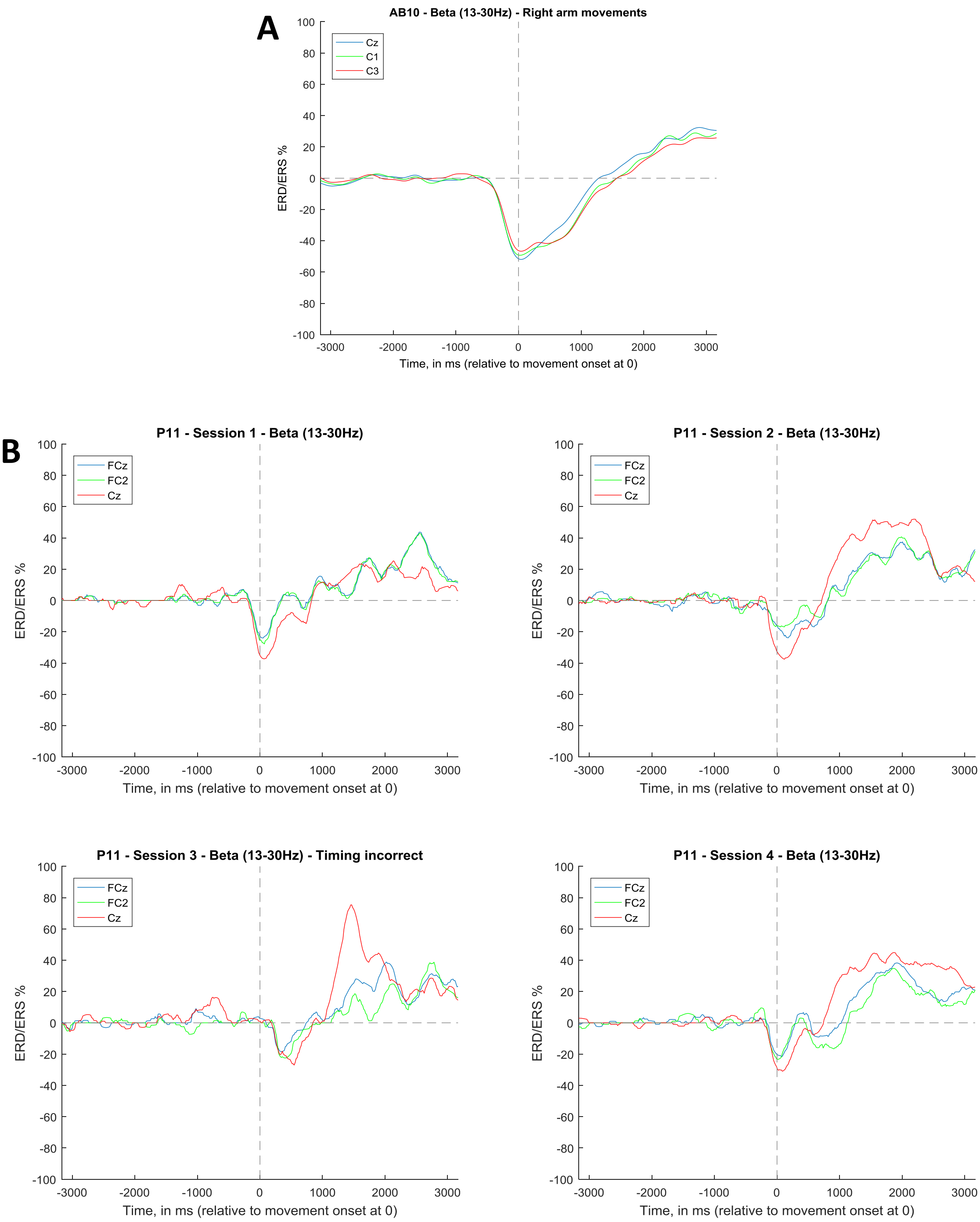


Figure 75 Plots of beta ERS% over time for (A) electrodes Cz, C1, and C3 for the healthy group (averaged), (B) electrodes FCz, FC2, and Cz for participant P11 for all sessions (right arm movements). Timings for session 3 are incorrect.

Table 56 presents peak beta ERS% values for electrodes Cz (the one with the overall greatest beta ERS% values from the plots above) and FCz, for session 1. Peaks were approximately matched according to time and placed in the same row in order to compare values. Due to the varying shape of the ERS% plots between sessions and the lack of clear single peak at some sessions, the matching of peaks is approximate. The range of timings for beta ERS% peaks, as calculated by the difference in time between the earliest and latest peaks over the three sessions, is 32 ms for the first peak, 16 ms for the second peak, and 108 ms for the third peak. Some variability can be observed in the timing and peak values of beta ERS%, but the pattern of variation is not indicative of changes due to rehabilitation. Most values for all sessions are greater than for the healthy group's average (32.4 %).

Session 1 (FCz)		**Session 2 (Cz)**		**Session 3 (Cz)**		**Session 4 (Cz)**	
Time	ERS%	Time	ERS%	Time	ERS%	Time	ERS%
-	-	1199	42.5	unknown	75.4	1167	35.7
-	-	1563	51.5	unknown	44.6	1547	44.5
1755	27.2	-	-	-	-	1863	44.9
-	-	2199	52.0	-	-	-	-
2563	43.7	-	-	-	-	-	-

Table 56 Participant P11's beta ERS% peak values for electrode FCz for session 1 and Cz for sessions 2, 3, and 4 (times in ms) (right arm movements). When several peaks are present, they are approximately matched according to time and placed in the same row in order to compare values.

8.3.2.6 Summary and discussion of results

Participant P11's results for clinical assessments showed no improvement following rehabilitation for the Fugl-Meyer assessment (improvements were not possible for the ARAT as this participant attained maximum scores at every session). Modest gains were however made with hand path ratio and time scores for the ArmeoSpring assessments, suggesting that this participant's ability to move their arm with more control and precision slightly improved.

Some ERD/ERS measures deviated from the averaged results from the healthy group:

- The spatial distribution and intensity of alpha ERD were atypical and weaker than for the healthy group, with alpha ERS occurring before movement over the ipsilateral hemisphere.
- Alpha ERD% peak values over the contralateral hemisphere were less than for the healthy group's average.
- Hemispheric lateralisation of beta ERD% was ipsilateral dominant or bilateral for a 200 ms period of time preceding movement onset, compared to contralateral dominant for the healthy group.

- Hemispheric lateralisation of beta ERD% for a 500 ms period of time following movement onset was ipsilateral dominant, rather than weak contralateral dominance for the healthy group.
- Beta ERS following movement was present over the ipsilateral hemisphere, rather than the contralateral hemisphere as seen in the healthy group.
- The intensity of beta ERS following movement was greater than for the healthy group's average.

Beta ERD ipsilateral dominance during movement suggests that for this participant, the ipsilateral hemisphere is compensating for impaired contralateral hemisphere function.

No changes in ERD/ERS measures could be attributed to the effects of rehabilitation.

This participant was able to obtain high scores on clinical assessments, despite her impairments. The ArmeoSpring assessments were however able to register subtle improvements in terms of speed and precision of movement. Even though her arm and hand level of function was high, a number of ERD/ERS measures were shown to deviate from those found in the healthy group.

8.3.3 Participant P13

At the time of the screening assessment, this participant presented with right-sided mild weakness in the upper limb (MRC grade 4) as well as moderate to severe range of motion restrictions. Hand function was severely limited. Spasticity was observed in her upper limb (Modified Ashworth Scale grade 2). At the time of her participation in the study, this participant reported being able to grasp objects with the help of the unaffected hand, but had difficulties releasing them.

8.3.3.1 Clinical and ArmeoSpring assessment scores

A maximum score of 57 for the ARAT was achieved with the unaffected upper limb, but a sub-maximal score of 65 (maximum score is 66) was given for this participant for the Fugl-Meyer Assessment. This is due to an incomplete forearm supination during the flexor synergy movement test item. Figure 76 presents clinical assessment scores achieved with the affected upper limb for participant P13's four sessions. Sessions 1 and 2 are pre-rehabilitation and sessions 3 and 4 are post-rehabilitation. Figure 77 and Figure 78 present time and hand path ratio scores for the ArmeoSpring assessments that were administered at the first rehabilitation session, at the fifth session, and at the last session. This participant reached 100 % of the target icons for each assessment.

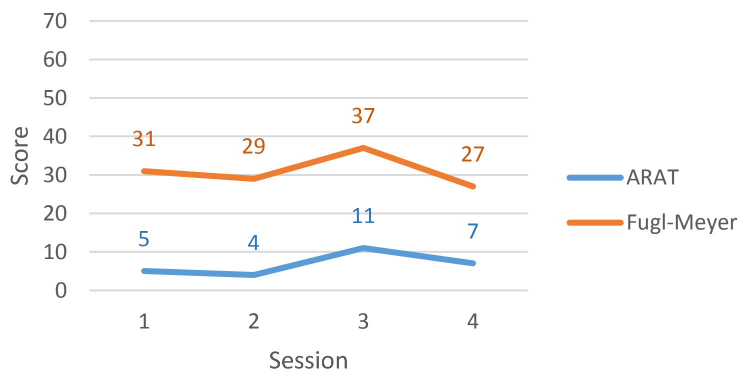


Figure 76 Participant P13's ARAT and Fugl-Meyer scores.

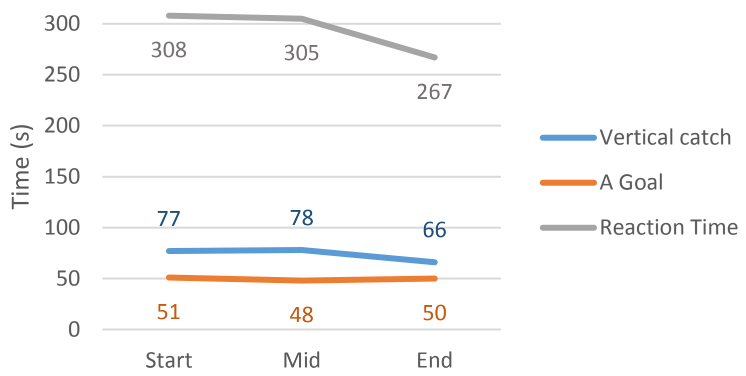


Figure 77 Participant P13's ArmeoSpring assessment time scores.

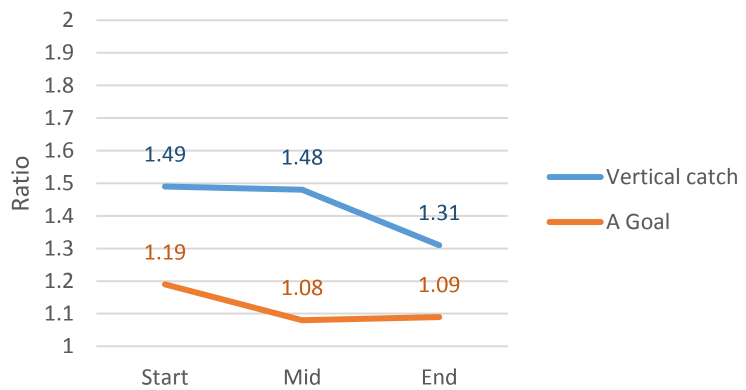


Figure 78 Participant P13's ArmeoSpring assessment hand path ratio scores.

Results show that for clinical assessments, ARAT scores improved at session 3 (up six points from the highest score before rehabilitation), followed by a decline at session 4, but with a higher score than at sessions 1 and 2 (score of seven for session 4 versus scores of five and four for sessions 1 and 2, respectively). For the Fugl-Meyer assessment, improvements also occurred at session 3 (up six points from the highest score before rehabilitation), followed by a score lower than ones attained before rehabilitation (score of 27 for session 4 versus scores of 31 and 29 for sessions 1 and 2, respectively). For the ArmeoSpring assessments, improvements were made for time scores (from 308 to 267 for 'Reaction Time', from 51 to 50 for 'A Goal', and from 77 to 66 for 'Vertical Catch'), as well as for hand path ratio scores (from 1.49 to 1.31 for 'Vertical Catch' and from 1.19 to 1.09 for 'A Goal').

8.3.3.2 Movement characteristics

This participant moved their right arm during EEG recordings. Table 57 presents the number of movements retained for analysis, as well as mean reaction and movement times for participant P13. Figure 79 shows box plots with further details about each session's movement times.

Session	Number of movements	Mean reaction time	SD	Mean movement time	SD
1	108	502	83	626	80
2	102	503	90	559	63
3	116	413	70	466	60
4	112	417	52	482	38

Table 57 Number of movements retained for analysis, mean reaction times (in ms), and mean movement times (in ms) for participant P13.

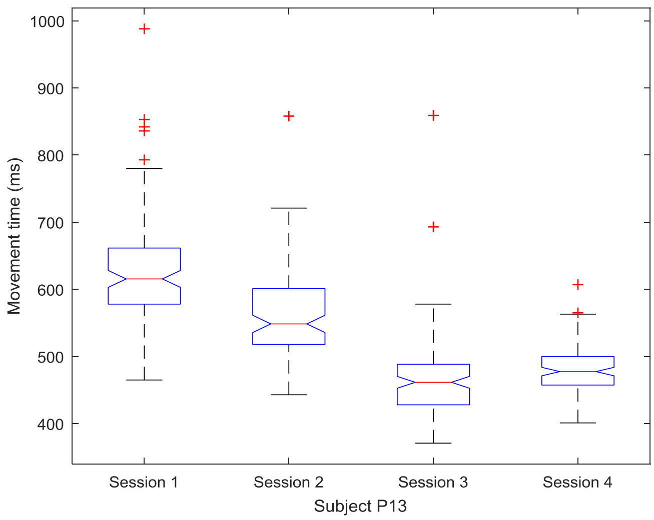


Figure 79 Box plots for participant P13's movement times for four sessions (the red line in the centre of the box being the median, the edges of the box are the 25th and 75th percentiles, whiskers end at the most extreme values that are not considered outliers, and outliers are displayed with red crosses).

To compare this participant's mean movement times over four sessions, results from a one-way unbalanced analysis of variance (ANOVA) show that all sessions had significantly different mean movement times [F = 157.76 (3, 434), p < 10^-6]. Post-hoc multiple comparison tests with Tukey's honest significant difference criterion showed that one pair of movement time means, for sessions 3 and 4, were not significantly different. Sessions 3 and 4's mean movement times were lower than for the first two sessions.

8.3.3.3 Alpha ERD

Alpha ERD over time

Figure 80 presents time frequency ERD/ERS maps for electrode sites CP3/CP4 for participant P13, where it can be observed that alpha ERD is greater at electrode CP4 (over the ipsilateral hemisphere) than it is at electrode CP3, particularly before movement onset. Averaged time frequency ERD/ERS maps for the healthy group are also displayed for comparison purposes.

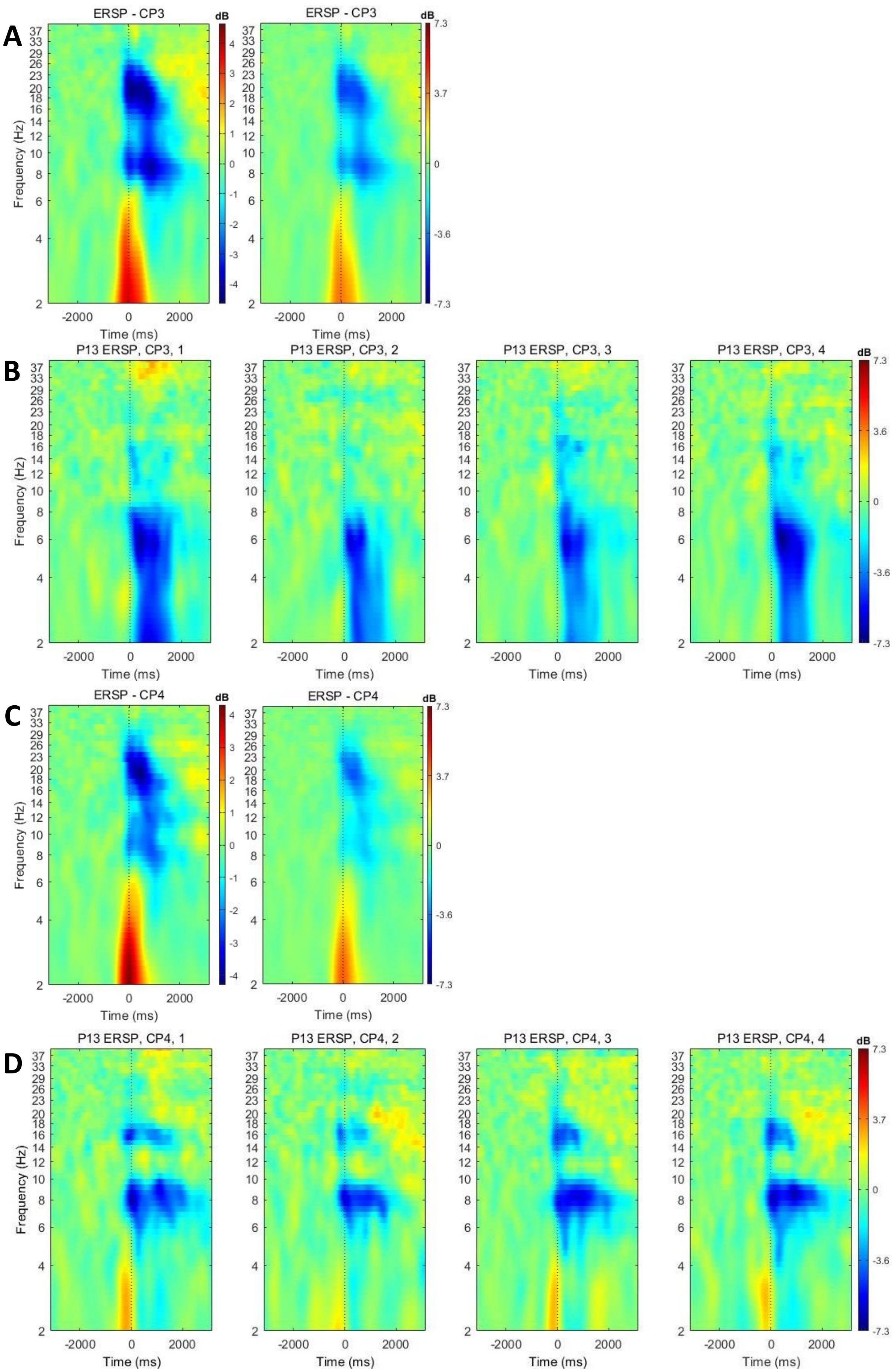


Figure 80 Time frequency ERD/ERS maps for CP3 for (A) the healthy group (two maps: original scale and adjusted to this participant's scale), (B) participant P13 sessions 1-4, and CP4 for (C) the healthy group (two maps as above), and (D) participant P13 sessions 1-4 (right arm movements).

Figure 81 presents alpha ERD/ERS% over time plots for pairs of symmetrical electrodes CP3/CP4 for all sessions. It can be observed that the intensity of alpha ERD% at electrode CP4, on the ipsilateral hemisphere, is generally greater than over the contralateral hemisphere.

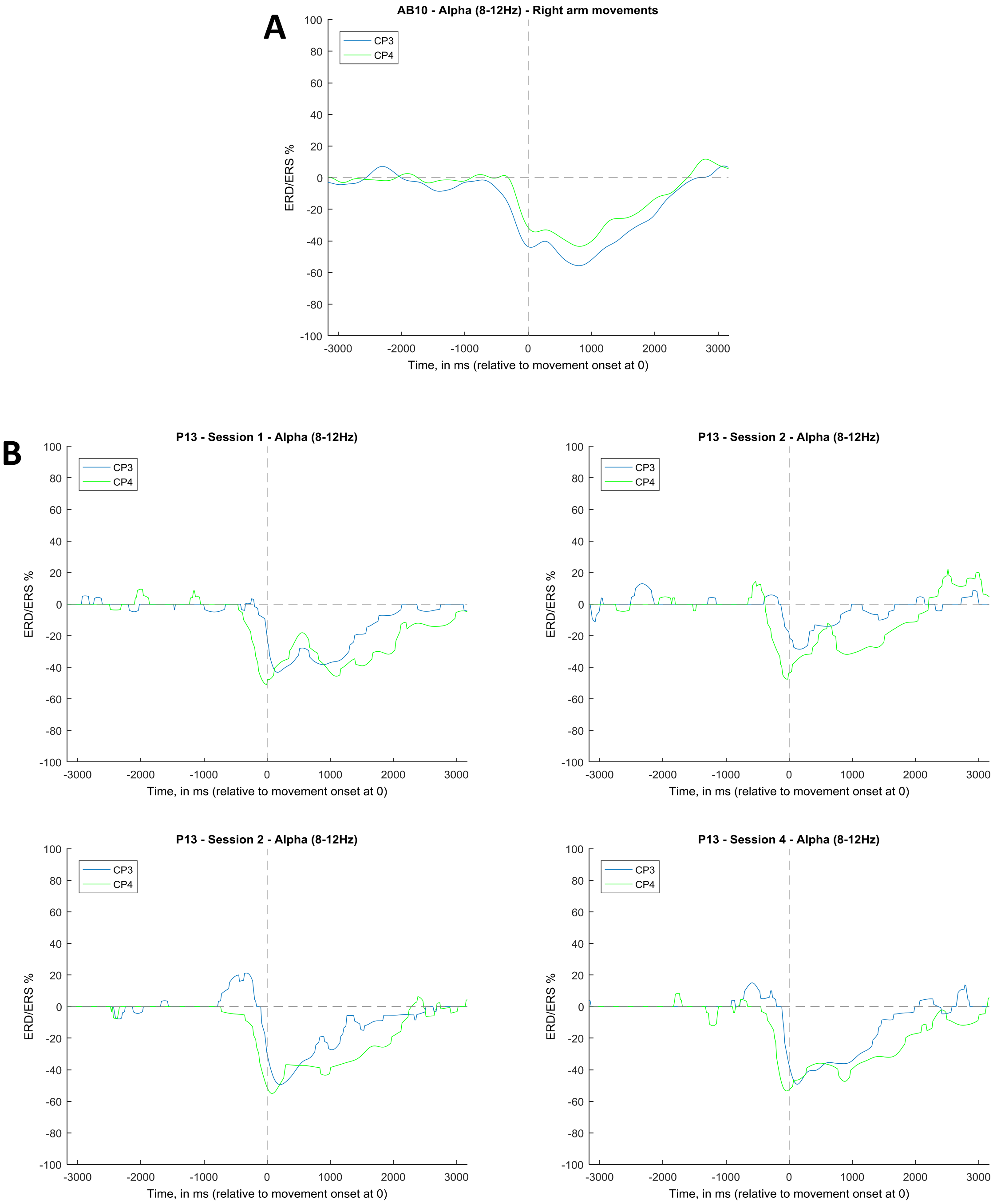


Figure 81 Plots of alpha ERD/ERS% over time for symmetrical electrodes CP3/CP4 for (A) the healthy group (averaged), (B) participant P13 (right arm movements).

Table 58 presents peak alpha ERD% values for electrode CP4 (the one with the greatest alpha ERD% values from the plots above). Peaks were approximately matched according to time and placed in the same row in order to compare values. Some variability can be observed in alpha ERD% peak values, and values are greater after rehabilitation, but the degree of variation is not clearly indicative of changes due to rehabilitation. Values for the first peak for all sessions are greater than for the healthy group's average (-44.0 %).

Session 1		**Session 2**		**Session 3**		**Session 4**	
Time	ERD%	Time	ERD%	Time	ERD%	Time	ERD%
-6	-50.9	-38	-47.6	70	-55.0	-38	-53.5
1103	-45.6	910	-31.8	910	-43.5	882	-47.4

Table 58 Participant P13's alpha ERD% peak values for electrode CP4 for all sessions (times in ms) (right arm movements).

Hemispheric lateralisation

Figure 82 presents scalp maps of alpha ERD/ERS for a 200 ms window preceding movement onset and for a 500 ms window following movement onset for participant P13. Ipsilateral dominance can be observed before movement onset.

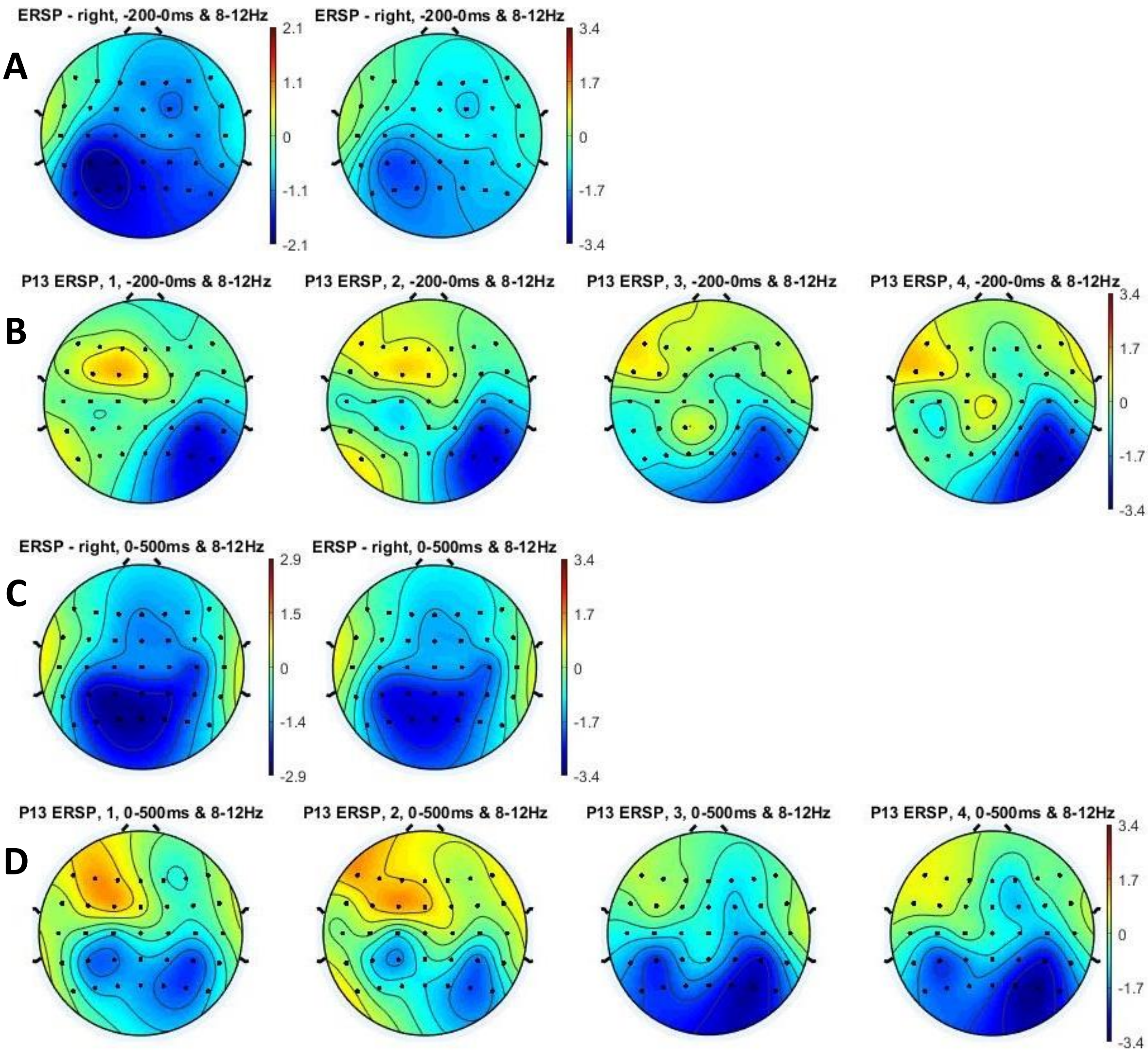


Figure 82 Scalp maps of alpha ERD/ERS for a 200 ms window preceding movement onset for (A) the healthy group (averaged; two maps: original scale and adjusted to this participant's scale), (B) participant P13 for sessions 1 to 4, and for a 500 ms window following movement onset for (C) the healthy group (averaged; two maps as above), and (D) participant P13 for sessions 1 to 4 (right arm movements).

Table 59 presents values for areas over the curve and laterality indices (LI), as calculated with alpha ERD% data for electrode pair CP3/CP4, for a period of 200 ms preceding movement onset and a period of 500 ms following movement onset. Laterality index values range from -1 to 1. A value of -1 indicates complete right hemisphere predominance. A value of 1 indicates complete left hemisphere predominance. A value of 0 indicates equal amounts of ERD% at both electrode sites.

Session	A_{CP3}		A_{CP4}		Laterality Index		L/R ratio	
	Pre 200	**Post 500**	**Pre 200**	**Post 500**	**Pre 200**	**Post 500**	**Pre 200**	**Post 500**
1	1379	18776	8389	17390	-0.72	0.04	0.16	1.08
2	1372	10944	7823	15611	-0.70	-0.18	0.18	0.70
3	1399	21808	6976	22122	-0.67	-0.01	0.20	0.99
4	2429	21319	9161	20756	-0.58	0.01	0.27	1.03

Table 59 Participant P13's areas over the curve A_{CP3} and A_{CP4} (in ERD% * ms units) and alpha ERD% laterality indices for electrode pair CP3/CP4 for a 200 ms window preceding movement onset (Pre 200) and for a 500 ms window following movement onset (Post 500) (right arm movements). L/R values = A_{CP3} / A_{CP4}.

In order to interpret laterality indices and L/R ratio values, the researcher defined ranges for labelling laterality. For the purpose of this study, laterality indices (LI) falling between -0.05 to 0.05 are deemed to indicate bilateral alpha ERD%, those between -0.15 to -0.05 and between 0.05 to 0.15 are deemed to indicate weak right and left hemispheric predominance, respectively, and any other values indicate either left or right hemispheric predominance.

Table 60 presents the interpretation of the hemispheric lateralisation data using the described criteria.

Session	Pre 200	Post 500
1	ipsilateral dominant	bilateral
2	ipsilateral dominant	ipsilateral dominant
3	ipsilateral dominant	bilateral
4	ipsilateral dominant	bilateral

Table 60 Interpretation of participant P13's hemispheric lateralisation data for alpha ERD% for a 200 ms window preceding movement onset (Pre 200) and for a 500 ms window following movement onset (Post 500) (right arm movements).

When compared to the healthy group, hemispheric lateralisation of alpha ERD% is different for both time periods. For a 200 ms period of time preceding movement onset, ipsilateral dominance can be observed for this participant, in comparison with contralateral dominance for the healthy group. For a 500 ms period of time after movement onset, bilateral (for sessions 1, 3, and 4) and ipsilateral dominance (for session 2) can be observed for this participant, in comparison with weak contralateral dominance for the healthy group.

When looking at variations between sessions, results for hemispheric lateralisation show that the laterality indices for a 200 ms period of time preceding movement onset are greater for sessions 3 and 4 (from -0.72 and -0.70 for sessions 1 and 2, respectively, to -0.67 and -0.58 for sessions 3 and 4, respectively), but this was well within the natural variability observed in the test-retest variability study described in Chapter 6 (the difference in L/R ratio values is only 0.11 between the maximum post-rehabilitation value at session 4 and the minimum pre-rehabilitation value at session 1, which falls below all maximum differences observed in the test-retest variability study), thus this trend cannot be attributed to the effects of rehabilitation.

For a 500 ms period of time after movement onset, some variability can be observed, but the pattern of variation is not indicative of changes due to rehabilitation.

8.3.3.4 Beta ERD

Frequency range

The frequency range within the beta range (13-30 Hz) at which beta ERD occurs at symmetrical electrodes CP3 and CP4 was examined by visually inspecting ERSP plots produced with EEGLAB's STUDY functions. Table 61 presents results for all sessions. Some incongruities were observed, in that for electrode CP3, session 2 presents with a narrow frequency range in which beta ERD occurs (15-16 Hz for session 2 versus 11-16 Hz, 11-18 Hz, and 11-17 Hz, for sessions 1, 3, and 4, respectively). In addition to this, electrode CP3 presents with ranges for sessions 1, 3, and 4, that are lower than for electrode CP4 (bottom of range at 11 Hz for electrode CP3 versus 13 or 14 Hz for electrode CP4).

Electrode	Session 1	Session 2	Session 3	Session 4
CP3	11-16	15-16	11-18	11-17
CP4	14-18	14-18	13-19	14-19

Table 61 Frequency ranges, in Hz, at which beta ERD occurs for participant P13's sessions.

Beta ERD over time

For time frequency ERD/ERS maps for electrode sites CP3 and CP4, please refer to Figure 80 in the previous section, where it can be observed that beta ERD is greater at electrode CP4 (over the ipsilateral hemisphere) than at electrode CP3. Figure 83 presents beta ERD/ERS% over time plots for pairs of symmetrical electrodes CP3/CP4 for all sessions.

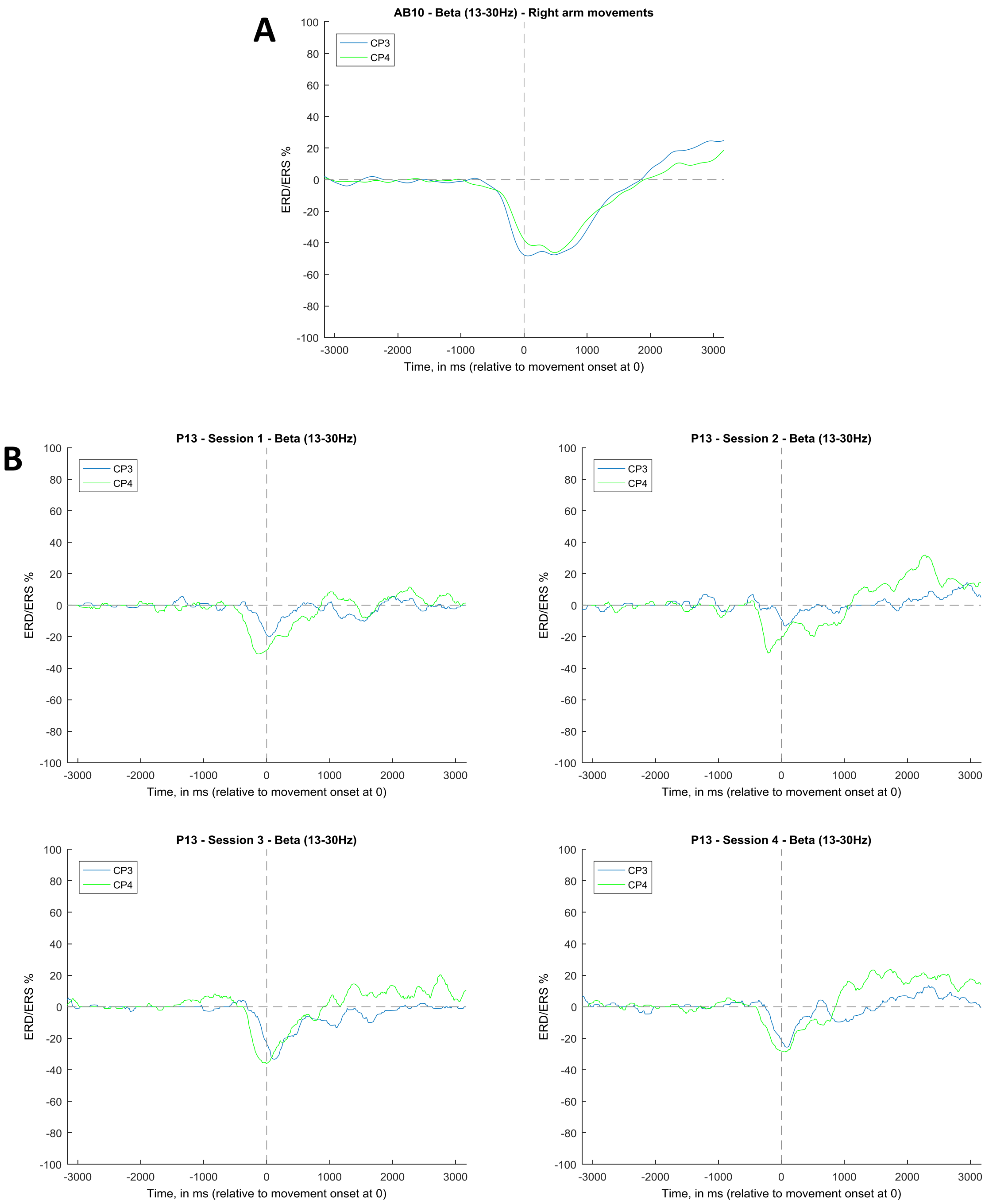


Figure 83 Plots of beta ERD/ERS% over time for symmetrical electrodes CP3/CP4 for (A) the healthy group (averaged), (B) participant P13 (right arm movements).

Table 62 presents peak beta ERD% values for electrode CP4 (the one with the greatest beta ERD% values from the plots above). Peaks were approximately matched according to time and placed in the same row in order to compare values. Some variability can be observed in beta ERD% peak values, but the pattern and degree of variation is not indicative of changes due to rehabilitation. It was observed that sessions 1 and 2 peaks occur before movement onset (-134 and -214 ms for sessions 1 and 2, respectively), which was also observed in some healthy participant taking part in the test-retest variability study (see Chapter 6). It was however observed that at sessions 3 and 4, peaks occur later (at -6 and 70 ms for sessions 3 and 4, respectively). This change could not be attributed to the effects of rehabilitation, as timings varied greatly for healthy participants taking part in the test-retest variability study. Values for peaks for all sessions are less than for the healthy group's average (-48.3 %).

Session 1		**Session 2**		**Session 3**		**Session 4**	
Time	ERD%	Time	ERD%	Time	ERD%	Time	ERD%
-134	-31.0	-214	-30.5	-6	-36.1	70	-28.7

Table 62 Participant P13's beta ERD% peak values for electrode CP4 for all sessions (times in ms) (right arm movements).

Hemispheric lateralisation

Figure 84 presents scalp maps of beta ERD/ERS for a 200 ms window preceding movement onset and for a 500 ms window following movement onset for participant P13, where ipsilateral dominance can be observed.

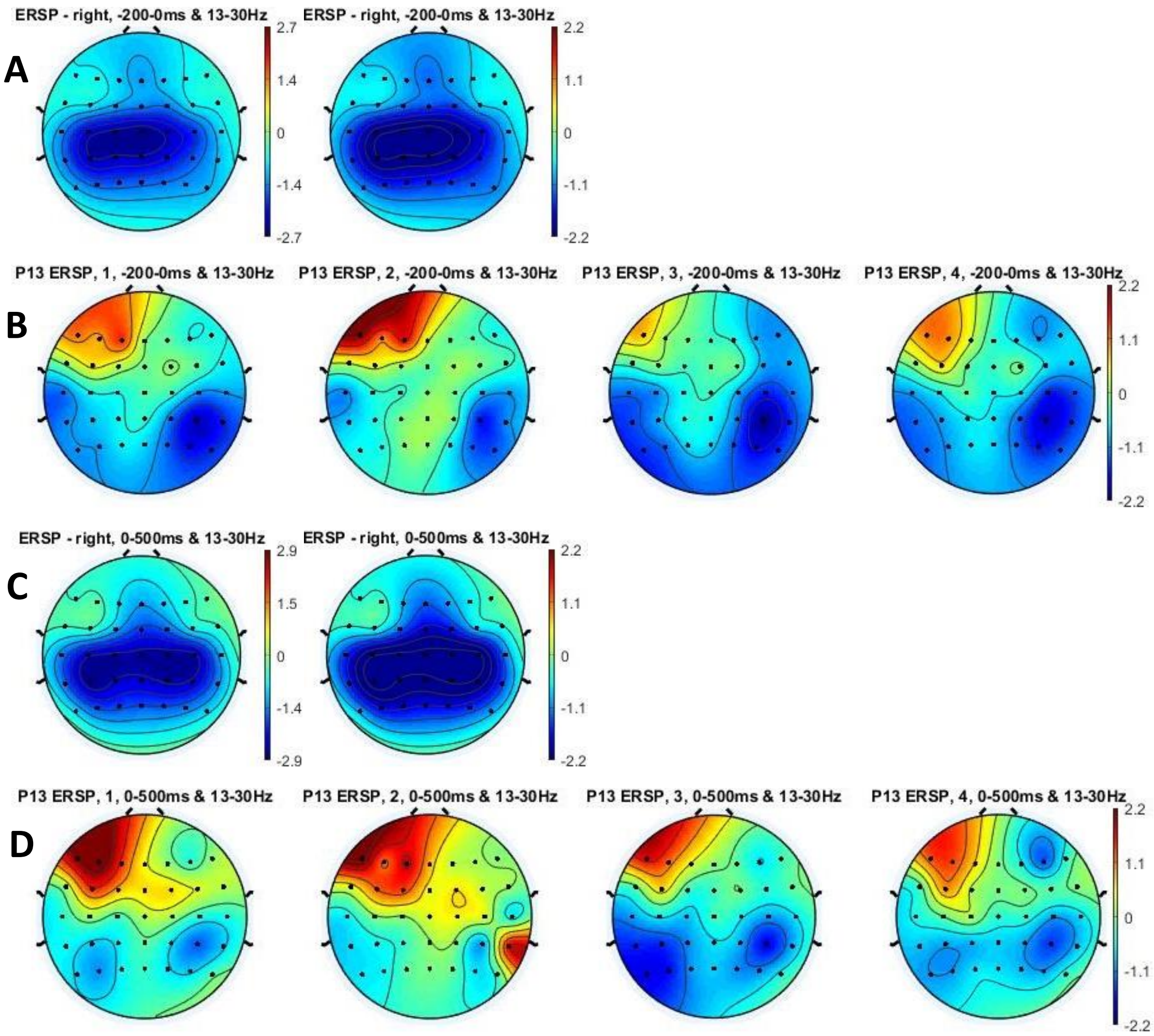


Figure 84 Scalp maps of beta ERD/ERS for a 200 ms window preceding movement onset for (A) the healthy group (averaged; two maps: original scale and adjusted to this participant's scale), (B) participant P13 for sessions 1 to 4, and for a 500 ms window following movement onset for (C) the healthy group (averaged; two maps as above), and (D) participant P13 for sessions 1 to 4 (right arm movements).

Table 63 presents values for areas over the curve and laterality indices (LI), as calculated with beta ERD% data for electrode pair CP3/CP4, for a period of 200 ms preceding movement onset and a period of 500 ms following movement onset.

Session	A_{CP3}		A_{CP4}		Laterality Index		L/R ratio	
	Pre 200	Post 500	Pre 200	Post 500	Pre 200	Post 500	Pre 200	Post 500
1	2028	5078	5770	9208	-0.48	-0.29	0.35	0.55
2	599	3301	4741	7146	-0.78	-0.37	0.13	0.46
3	2368	11969	6314	10932	-0.45	0.05	0.38	1.09
4	2693	6854	4681	9116	-0.27	-0.14	0.58	0.75

Table 63 Participant P13's areas over the curve A_{CP3} and A_{CP4} (in ERD% * ms units) and laterality indices for beta ERD% for electrode pair CP3/CP4 for a 200 ms window preceding movement onset (Pre 200) and for a 500 ms window following movement onset (Post 500) (right arm movements). L/R values = A_{CP3} / A_{CP4}.

Table 64 presents the interpretation of the hemispheric lateralisation data using the criteria described for alpha ERD in the previous section.

Session	Pre 200	Post 500
1	ipsilateral dominant	ipsilateral dominant
2	ipsilateral dominant	ipsilateral dominant
3	ipsilateral dominant	bilateral
4	ipsilateral dominant	weak ipsilateral dominant

Table 64 Interpretation of participant P13's hemispheric lateralisation data for beta ERD% for a 200 ms window preceding movement onset (Pre 200) and for a 500 ms window following movement onset (Post 500) (right arm movements).

When compared to the healthy group, hemispheric lateralisation of beta ERD% is different for both time periods. For a 200 ms period of time preceding movement onset, ipsilateral dominance can be observed for this participant, in comparison with contralateral dominance for the healthy group. For a 500 ms period of time after movement onset, ipsilateral dominance (for sessions 1, 2, and 4) and bilaterality (for session 3) can be observed for this participant, in comparison with bilateral/weak contralateral dominance for the healthy group.

When looking at variations between sessions, results for hemispheric lateralisation show that the laterality indices for a 200 ms period of time preceding movement onset are greater for sessions 3 and 4 (from -0.48 and -0.78 for sessions 1 and 2, respectively, to -0.45 and -0.27 for sessions 3 and 4, respectively), but this was well within the natural variability observed in the test-retest variability study described in Chapter 6 (the difference in L/R ratio values is 0.45 between the maximum post-rehabilitation value at session 4 and the minimum pre-rehabilitation value at session 2, which falls below the maximum difference observed in the test-retest variability study, which was 0.80), thus this trend cannot be confidently attributed to the effects of rehabilitation.

For a 500 ms period of time after movement onset, results for hemispheric lateralisation show that the laterality indices are greater for sessions 3 and 4 (from -0.29 and -0.37 for sessions 1 and 2, respectively, to 0.05 and -0.14 for sessions 3 and 4, respectively), but this was well within the natural variability observed in the test-retest variability study described in Chapter 6 (the difference in L/R ratio values is 0.63 between the maximum post-rehabilitation value at session 3 and the minimum pre-rehabilitation value at session 2, which falls below the maximum difference observed in the test-retest variability study, which was 1.72), thus this trend cannot be confidently attributed to the effects of rehabilitation. It is however noted that the greatest change occurred at session 3, which is when this participant scored the highest on clinical assessments.

8.3.3.5 Beta ERS following movement

Spatial distribution

A clear, recognisable pattern of beta ERS was found to only be present for two out of four sessions, and when present, in sessions 2 and 4, the spatial distribution was variable (see Figure 85). For session 2, it was centred at Cz and CPz, as well as over the ipsilateral hemisphere at C4, CP4, and CP6. For session 4, it was initially centred at Cz and C4, then spreading to CP4 and CP6 over the ipsilateral hemisphere This is different from results from the healthy group, where beta ERS peaks occur at C3, C1, and Cz, over the contralateral hemisphere.

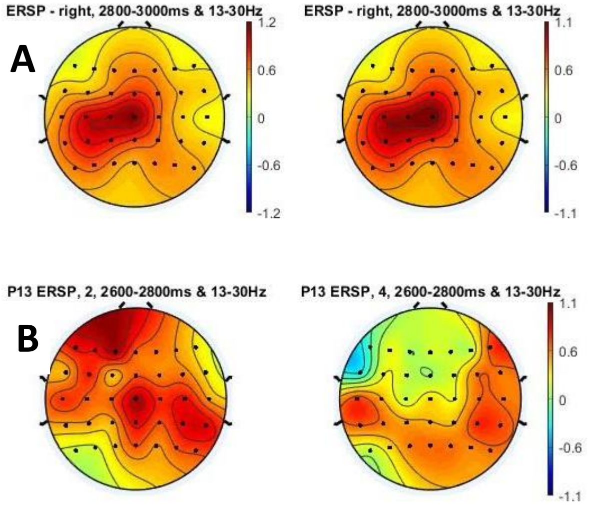


Figure 85 Scalp maps of beta ERS for (A) the healthy group (averaged; two maps: original scale and adjusted to this participant's scale), (B) participant P13 for sessions 2 and 4 (right arm movements).

Beta ERS over time

Figure 86 presents beta ERS% over time plots for select electrode locations for sessions 2 and 4.

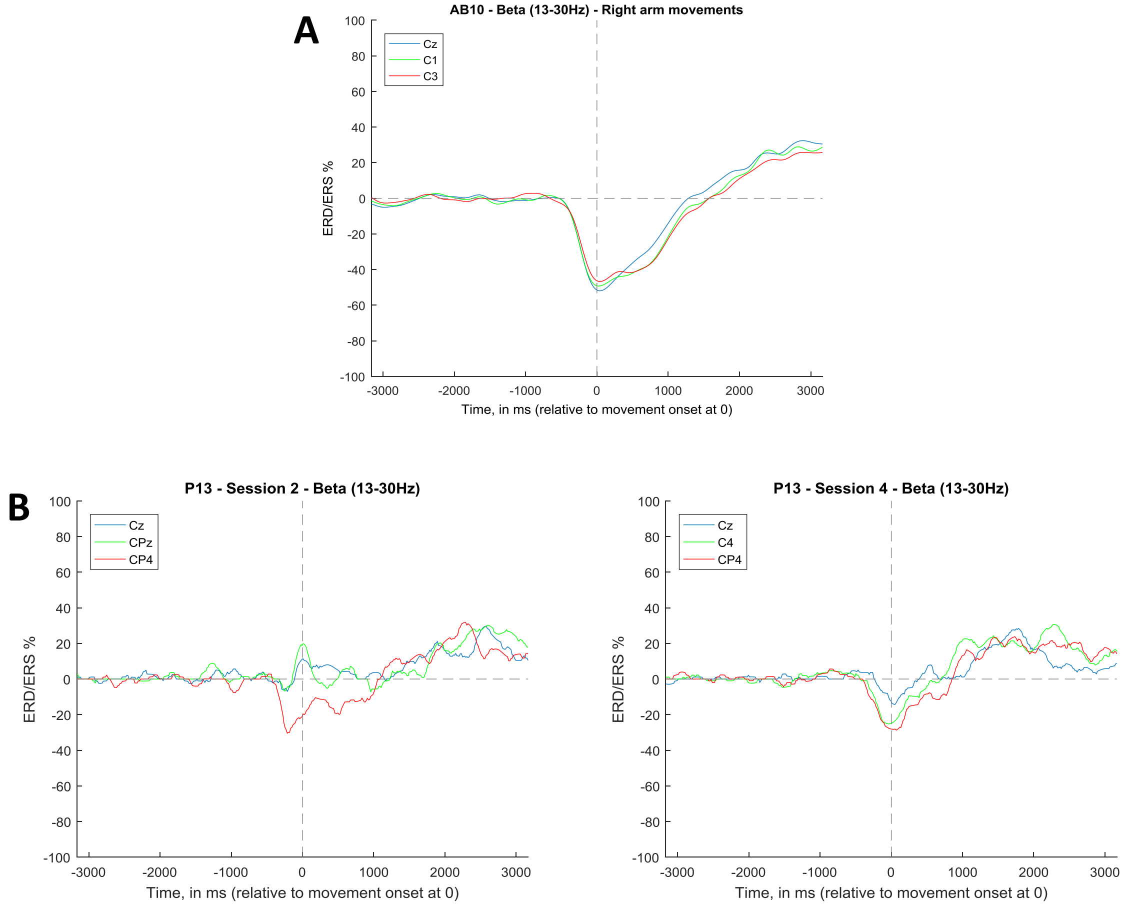


Figure 86 Plots of beta ERS% over time for (A) electrodes Cz, C1, and C3 for the healthy group (averaged), (B) select electrodes for participant P13 for sessions 2 and 4 (right arm movements).

Table 65 presents peak beta ERS% values for electrode CP4 for session 2 and C4 for session 4. The range of timings for beta ERS% peaks, as calculated by the difference in time between the earliest and latest peaks over the two sessions, is 16 ms. Values for both sessions are similar to the healthy group's average (32.4 %).

Session 2 (CP4)		**Session 4 (C4)**	
Time	ERS%	Time	ERS%
2275	31.8	2291	30.7

Table 65 Participant P13's beta ERS% peak values for select electrodes (times in ms) (right arm movements).

8.3.3.6 Summary and discussion of results

Participant P13’s results for clinical assessments showed an improvement of six points for the ARAT at session 3 following rehabilitation. This was however followed by a decline at session 4. For the Fugl-Meyer assessment, scores improved by six points at session 3, and also declined at session 4. Gains were also made with hand path ratio and time scores for the ArmeoSpring assessments, suggesting that this participant improved their ability to move their arm with more control and precision.

Session 3 and 4’s mean movement times were lower than for the first two sessions. As movement times depend on a variety of factors, such as the participant’s alertness and motivation levels, it is not possible to say whether this increased speed of movement is solely due to improved arm function.

Some ERD/ERS measures deviated from the averaged results from the healthy group:

- Alpha ERD occurred mostly over the ipsilateral hemisphere before movement, rather than occurring predominantly over the contralateral hemisphere for the healthy group.
- Alpha ERD% peak values over the ipsilateral hemisphere were greater than for the healthy group’s average.
- Hemispheric lateralisation of alpha ERD% for a 200 ms period of time preceding movement onset was ipsilateral dominant, rather than contralateral dominant as seen in the healthy group.
- Hemispheric lateralisation of alpha ERD% for a 500 ms period of time following movement onset was bilateral and ipsilateral dominant, rather than weak contralateral dominant as seen in the healthy group.
- Beta ERD% peak values over both hemispheres were less than for the healthy group’s average.
- Hemispheric lateralisation of beta ERD% for a 200 ms period of time preceding movement onset was ipsilateral dominant, rather than contralateral dominant for the healthy group.
- Hemispheric lateralisation of beta ERD% for a 500 ms period of time following movement onset was ipsilateral dominant, rather than bilateral/weak contralateral dominant for the healthy group
- Beta ERS following movement was only present for two out of four sessions.
- Beta ERS following movement was present over the ipsilateral hemisphere, rather than the contralateral hemisphere as seen in the healthy group.

Differences were found in the beta frequency range at which beta ERD occurred. For this participant, the range observed for the electrode on the contralateral hemisphere, CP3, was lower than for symmetrical electrode CP4.

For this participant, hemispheric lateralisation of alpha and beta ERD results suggest that the ipsilateral hemisphere is compensating for impaired contralateral hemisphere function.

No changes in ERD/ERS measures could be attributed to the effects of rehabilitation despite important improvements in upper limb function at session 3.

8.3.4 Participant P9

This participant and the following participants (presented in subsequent sections) performed left arm movements during EEG recordings. Reminders of which arm was moved are provided in the caption of all ERD/ERS figures and tables.

This participant sustained a stroke as a child and took part in this study many years later, as an adult. At the time of the screening assessment, this participant presented with left-sided mild weakness (MRC grade 4) as well as moderate range of motion restrictions in the upper limb. Hand function was severely limited. Spasticity was observed in her upper limb (Modified Ashworth Scale grade 1+).

8.3.4.1 Clinical and ArmeoSpring assessment scores

Maximum scores for clinical assessments were achieved with the unaffected upper limb (57 for the ARAT and 66 for the Fugl-Meyer Assessment). Figure 87 presents clinical assessment scores achieved with the affected upper limb for participant P9's four sessions. Sessions 1 and 2 are pre-rehabilitation and sessions 3 and 4 are post-rehabilitation. The blinded assessor declared that they assumed that session 1 was the first assessment that was carried out when they scored the Fugl-Meyer assessment as the participant stated "I've never done this before" at item 'Grasp B: extended index and thumb', with four items to go until the end of the assessment. As this occurred towards the end of the assessment, and it was the last to be scored out of the four, becoming unblinded at this point would have not affected scores significantly. The blinded assessor also declared that they assumed that one of the assessment they scored was the second assessment (they were not correct as it was the third) as the participant stated "I remember this test" just before the last item of the Fugl-Meyer assessment ('Finger-to-nose'). As the blinded assessor stated she didn't know whether this was before or after the intervention, it would have not affected scores significantly.

Figure 88 and Figure 89 present time and hand path ratio scores for the ArmeoSpring assessments that were administered at the first rehabilitation session, at the fifth session, and at the last session. This participant reached 100 % of the target icons for each assessment.

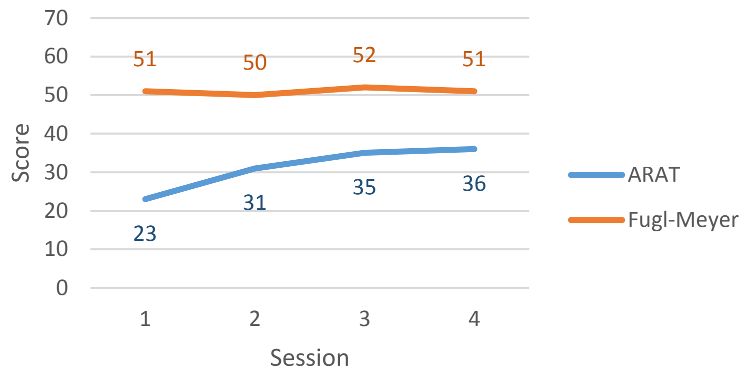


Figure 87 Participant P9's ARAT and Fugl-Meyer scores.

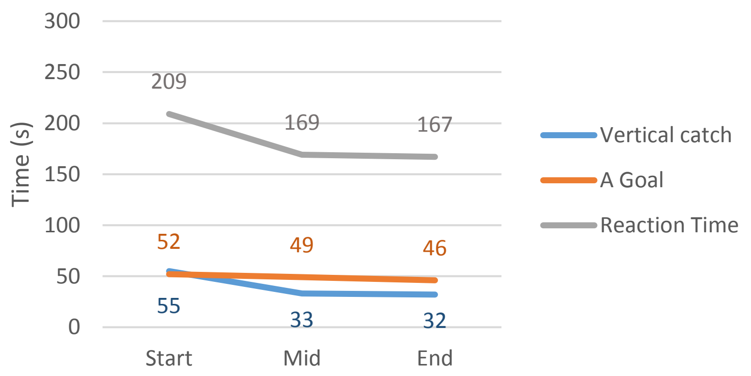


Figure 88 Participant P9's ArmeoSpring assessment time scores.

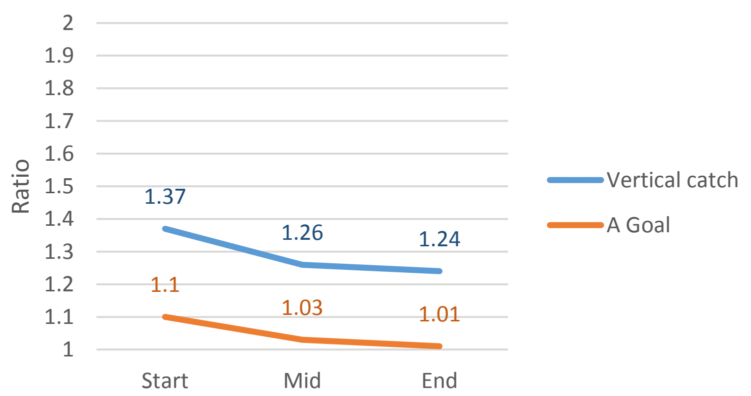


Figure 89 Participant P9's ArmeoSpring assessment hand path ratio scores.

Results show that for clinical assessments, ARAT scores improved at session 3 (up four points from the highest score before rehabilitation at session 2) which were maintained at session 4 (up five points from the highest score before rehabilitation at session 2). For the Fugl-Meyer assessment, no important changes occurred. For the ArmeoSpring assessments, improvements were made for time scores (from 209 to 167 for 'Reaction Time', from 52 to 46 for 'A Goal', and from 55 to 32 for 'Vertical Catch'), as well as for hand path ratio scores (from 1.37 to 1.24 for 'Vertical Catch' and from 1.1 to 1.01 for 'A Goal').

8.3.4.2 Movement characteristics

This participant moved their left arm during EEG recordings. Table 66 presents the number of movements retained for analysis, as well as mean reaction and movement times for participant P9. Figure 90 shows box plots with further details about each session's movement times. The number of movements for this participant is lower as the raw data contained a high number of artefacts.

Session	Number of movements	Mean reaction time	SD	Mean movement time	SD
1	75	503	66	269	38
2	67	489	83	307	40
3	84	513	89	324	29
4	92	507	87	354	34

Table 66 Number of movements retained for analysis, mean reaction times (in ms), and mean movement times (in ms) for participant P9.

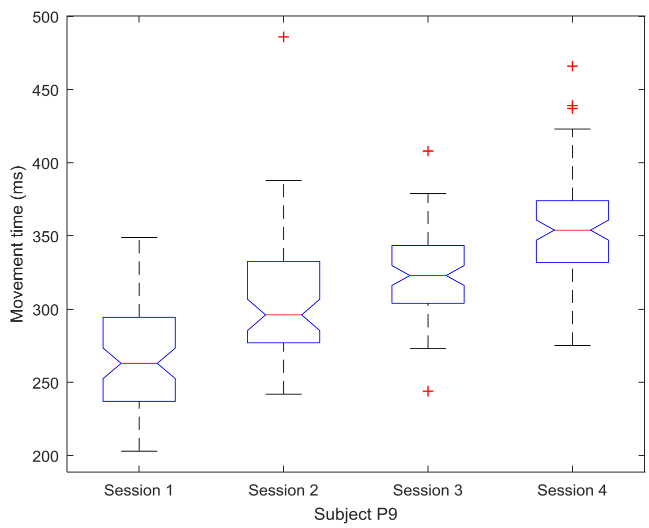


Figure 90 Box plots for participant P9's movement times for four sessions (the red line in the centre of the box being the median, the edges of the box are the 25th and 75th percentiles, whiskers end at the most extreme values that are not considered outliers, and outliers are displayed with red crosses).

To compare this participant's mean movement times over four sessions, results from a one-way unbalanced analysis of variance (ANOVA) show that all sessions had significantly different mean movement times [$F = 84.13$ (3, 314), $p < 10^{-6}$]. Post-hoc multiple comparison tests with Tukey's honest significant difference criterion showed that none of the pairs of movement time means were not significantly different. Session 3 and 4's mean movement times were greater than for the first two sessions.

8.3.4.3 Alpha ERD

Alpha ERD over time

Figure 91 presents time frequency ERD/ERS maps for electrode sites CP3/CP4 for participant P9, where it can be observed that alpha ERD is greater at electrode CP3 (over the ipsilateral hemisphere) than at electrode CP4. Averaged time frequency ERD/ERS maps for the healthy group are also displayed for comparison purposes.

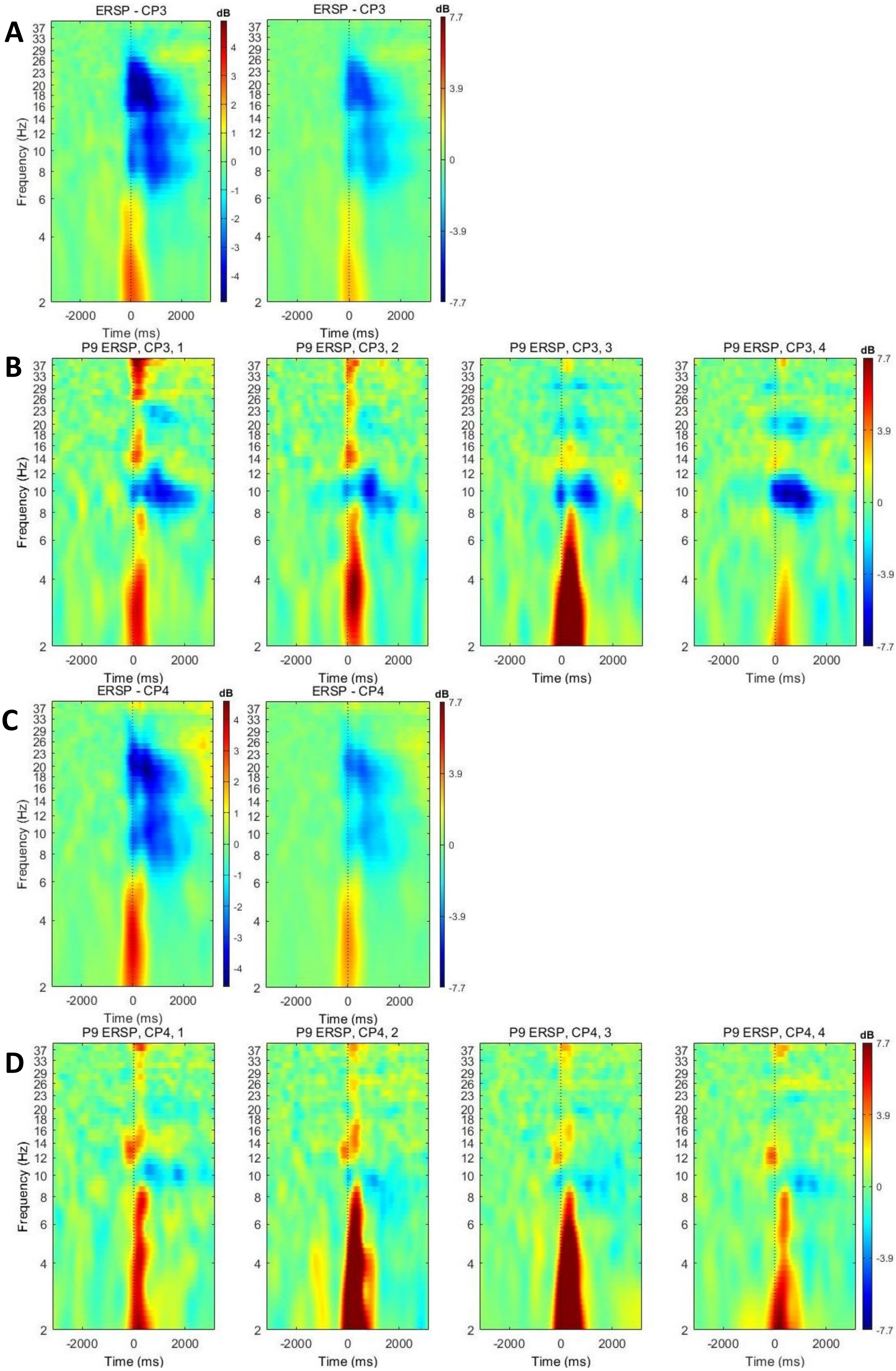


Figure 91 Time frequency ERD/ERS maps for CP3 for (A) the healthy group (two maps: original scale and adjusted to this participant's scale), (B) participant P9 sessions 1-4, and CP4 for (C) the healthy group (two maps as above), and (D) participant P9 sessions 1-4 (left arm movements).

Figure 92 presents alpha ERD/ERS% over time plots for pairs of symmetrical electrodes CP3/CP4 for all sessions. An atypical alpha ERD% can be observed, with alpha ERS% occurring before and during movement mostly at electrode CP4, on the contralateral hemisphere.

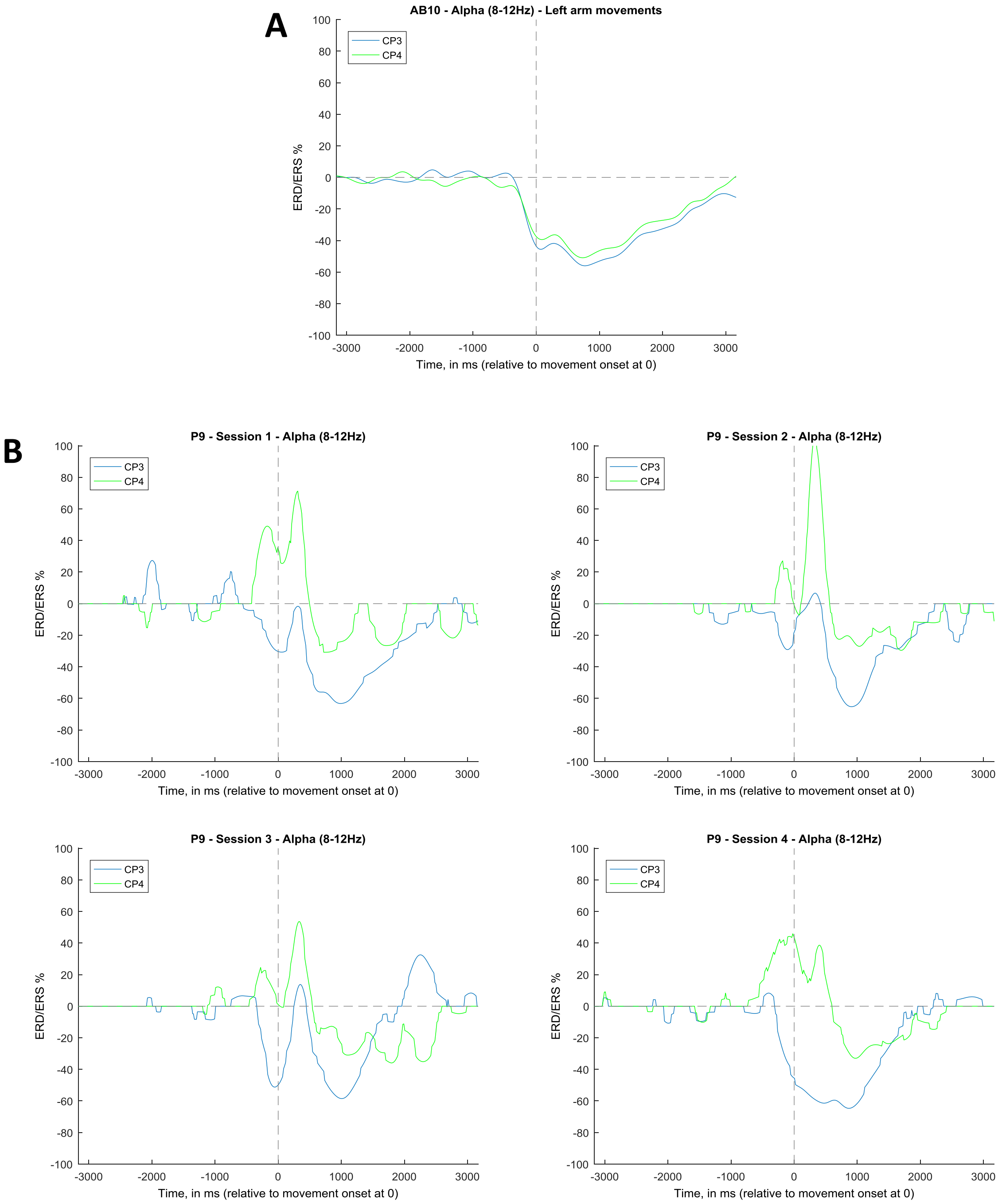


Figure 92 Plots of alpha ERD/ERS% over time for symmetrical electrodes CP3/CP4 for (A) the healthy group (averaged), (B) participant P9 (left arm movements).

Table 67 presents peak alpha ERD% values for electrode CP3 (the one with the greatest alpha ERD% values from the plots above). Peaks were approximately matched according to time and placed in the same row in order to compare values. Some variability can be observed in alpha ERD% peak values, but the pattern of variation is not indicative of changes due to rehabilitation.

The only observation that could relate to a possible improvement is that at session 4, electrode CP3 no longer shows alpha ERS% during movement. Values for the second peak (less affected by alpha ERS during movement) for all sessions are similar or greater than the healthy group's average (-56 %).

Session 1		**Session 2**		**Session 3**		**Session 4**	
Time	ERD%	Time	ERD%	Time	ERD%	Time	ERD%
54	-30.7	-102	-29.1	-54	-51.3	-	-
990	-63.2	910	-65.3	1007	-58.5	866	-64.7

Table 67 Participant P9's alpha ERD% peak values for electrode CP3 for all sessions (times in ms) (left arm movements).

Hemispheric lateralisation

Figure 93 presents scalp maps of alpha ERD/ERS for a 200 ms window preceding movement onset and for a 500 ms window following movement onset for participant P9, where ipsilateral dominance can be observed before movement onset.

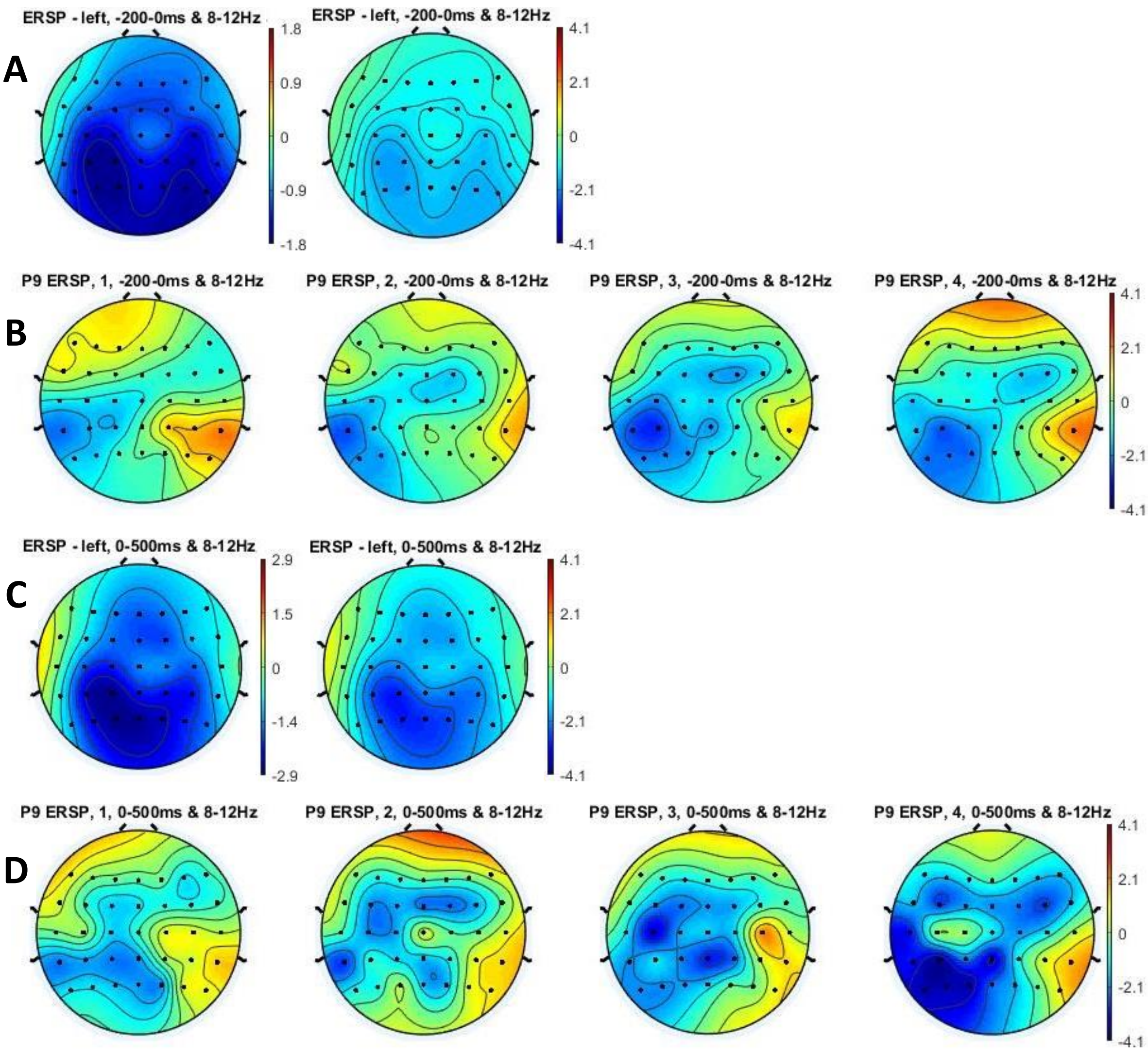


Figure 93 Scalp maps of alpha ERD/ERS for a 200 ms window preceding movement onset for (A) the healthy group (averaged; two maps: original scale and adjusted to this participant's scale), (B) participant P9 for sessions 1 to 4, and for a 500 ms window following movement onset for (C) the healthy group (averaged; two maps as above), and (D) participant P9 for sessions 1 to 4 (left arm movements).

Table 68 presents values for areas over the curve and laterality indices (LI), as calculated with alpha ERD% data for electrode pair CP3/CP4, for a period of 200 ms preceding movement onset and a period of 500 ms following movement onset. Laterality index values range from -1 to 1. A value of -1 indicates complete right hemisphere predominance. A value of 1 indicates complete left hemisphere predominance. A value of 0 indicates equal amounts of ERD% at both electrode sites.

Session	A_{CP3}		A_{CP4}		Laterality Index		L/R ratio	
	Pre 200	**Post 500**	**Pre 200**	**Post 500**	**Pre 200**	**Post 500**	**Pre 200**	**Post 500**
1	4986	9663	0	0	1.00	1.00	-	-
2	5242	1363	0	0	1.00	1.00	-	-
3	9053	6236	0	0	1.00	1.00	-	-
4	6961	27632	0	0	1.00	1.00	-	-

Table 68 Participant P9's areas over the curve A_{CP3} and A_{CP4} (in ERD% * ms units) and laterality indices for alpha ERD% for electrode pair CP3/CP4 for a 200 ms window preceding movement onset (Pre 200) and for a 500 ms window following movement onset (Post 500) (left arm movements). L/R values = A_{CP3} / A_{CP4}.

In order to interpret laterality indices and L/R ratio values, the researcher defined ranges for labelling laterality. For the purpose of this study, laterality indices (LI) falling between -0.05 to 0.05 are deemed to indicate bilateral alpha ERD%, those between -0.15 to -0.05 and between 0.05 to 0.15 are deemed to indicate weak right and left hemispheric predominance, respectively, and any other values indicate either left or right hemispheric predominance.

Table 69 presents the interpretation of the hemispheric lateralisation data using the described criteria.

Session	Pre 200	Post 500
1	ipsilateral dominant	ipsilateral dominant
2	ipsilateral dominant	ipsilateral dominant
3	ipsilateral dominant	ipsilateral dominant
4	ipsilateral dominant	ipsilateral dominant

Table 69 Interpretation of participant P9's hemispheric lateralisation data for alpha ERD% for a 200 ms window preceding movement onset (Pre 200) and for a 500 ms window following movement onset (Post 500) (left arm movements).

Due to the absence of alpha ERD for electrode CP4 during the periods of interest, hemispheric lateralisation is completely ipsilateral dominant for this participant, which is different from results for the healthy group, where a weak ipsilateral dominance is observed before and movement onset.

8.3.4.4 Beta ERD

Frequency range

The frequency range within the beta range (13-30 Hz) at which beta ERD occurs at symmetrical electrodes CP3 and CP4 was examined by visually inspecting ERSP plots produced with EEGLAB's STUDY functions. Table 70 presents results for all sessions. An incongruity was observed, in that for electrode CP4, beta ERD occurred within a narrower frequency range than for electrode CP3.

Electrode	Session 1	Session 2	Session 3	Session 4
CP3	17-25	18-24	19-25	19-24
CP4	20-22	18-20	20-21	20-21

Table 70 Frequency ranges, in Hz, at which beta ERD occurs for participant P9's sessions.

Beta ERD over time

For time frequency ERD/ERS maps for electrode sites CP3 and CP4, please refer to Figure 91 in the previous section. Figure 94 presents beta ERD/ERS% over time plots for pairs of symmetrical electrodes CP3/CP4 for all sessions. Beta ERS% can be observed to occur at both electrode sites before and during movement. An observation that could relate to a possible improvement is that at sessions 3 and 4, both electrodes CP3 and CP4 show a reduced beta ERS% during movement, with the greatest reduction occurring at CP3.

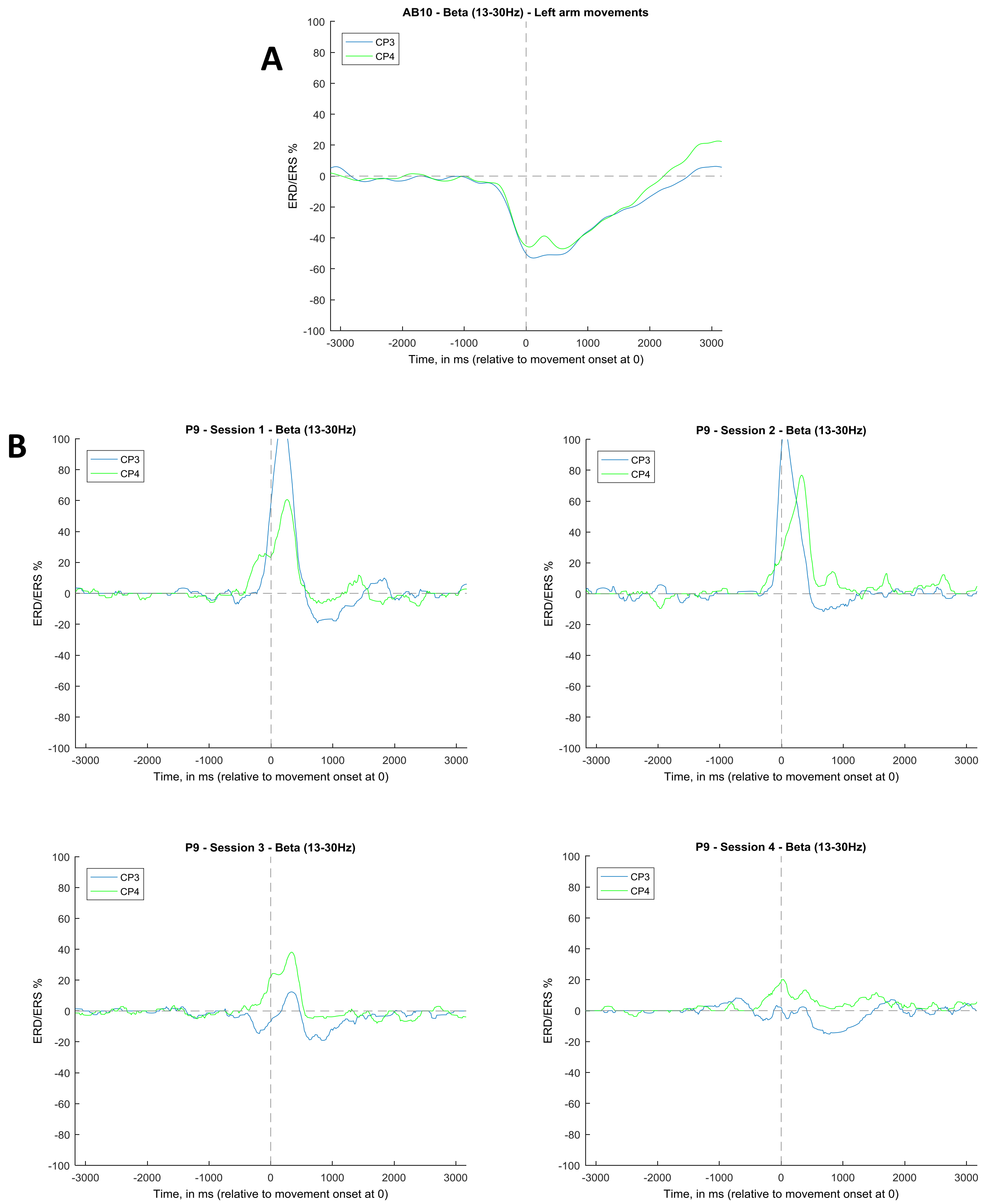


Figure 94 Plots of beta ERD/ERS% over time for symmetrical electrodes CP3/CP4 for (A) the healthy group (averaged), (B) participant P9 (left arm movements).

Table 71 presents peak beta ERD% values for electrode CP3 (the one with the overall greatest beta ERD% values from the plots above). Peaks were approximately matched according to time and placed in the same row in order to compare values.

Session 1		Session 2		Session 3		Session 4	
Time	ERD%	Time	ERD%	Time	ERD%	Time	ERD%
754	-19.1	674	-11.5	850	-19.1	786	-15.2

Table 71 Participant P9's beta ERD% peak values for electrode CP3 for all sessions (times in ms) (left arm movements).

Some variability can be observed in beta ERD% peak values, but the pattern of variation is not indicative of changes due to rehabilitation. Values are less than for the healthy group's average (-51 %).

Hemispheric lateralisation

Figure 95 presents scalp maps of beta ERD/ERS for a 200 ms window preceding movement onset and for a 500 ms window following movement onset for participant P9.

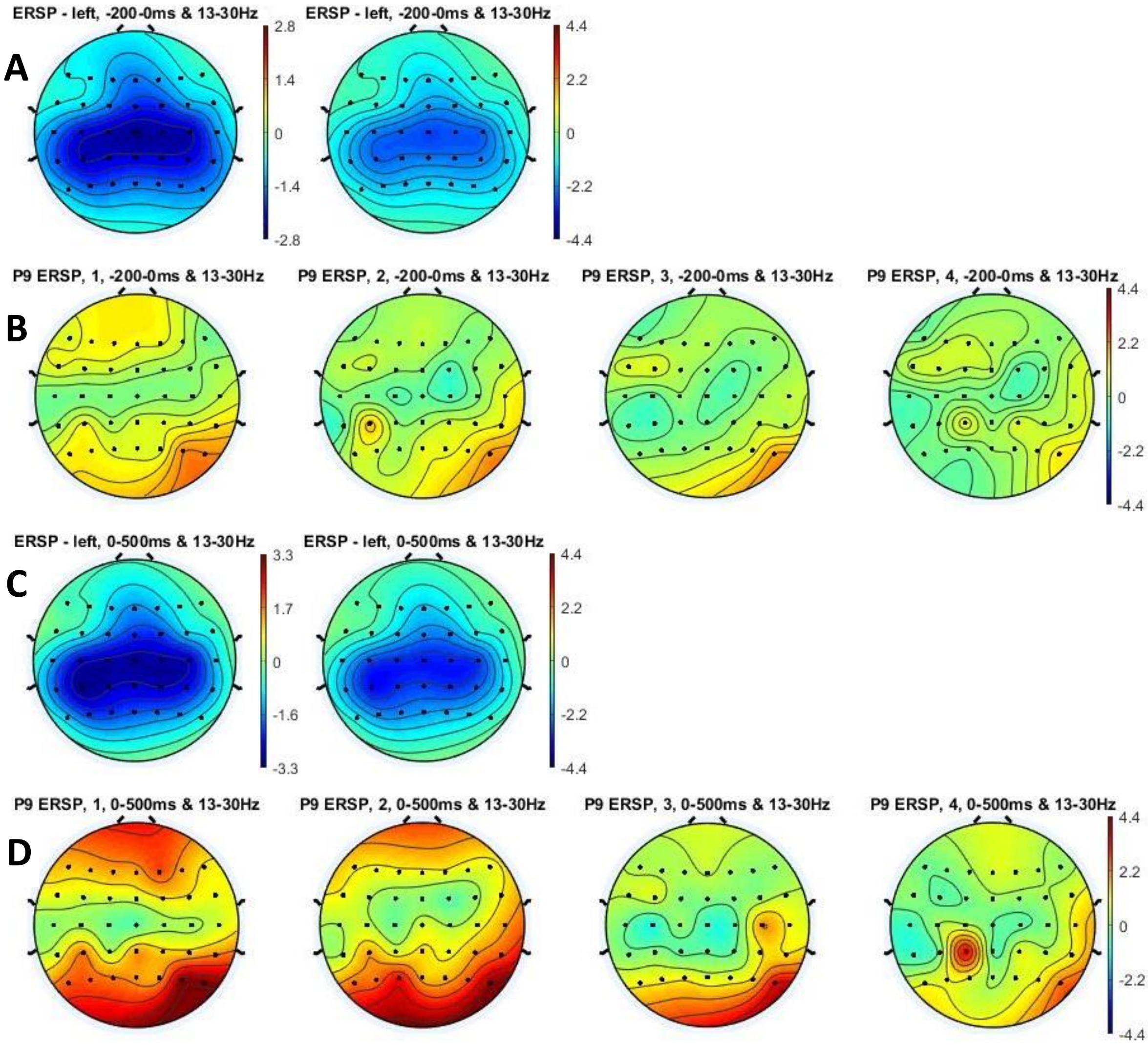


Figure 95 Scalp maps of beta ERD/ERS for a 200 ms window preceding movement onset for (A) the healthy group (averaged; two maps: original scale and adjusted to this participant's scale), (B) participant P9 for sessions 1 to 4, and for a 500 ms window following movement onset for (C) the healthy group (averaged; two maps as above), and (D) participant P9 for sessions 1 to 4 (left arm movements).

As no beta ERD% occurs at electrode CP4 within a 200 ms window preceding movement onset and a 500 ms window following movement onset, hemispheric lateralisation is completely ipsilateral dominant when beta ERD% is present at electrode CP3. This is different from results for the healthy group, where a weak ipsilateral dominance is observed before and movement onset. Table 72 presents hemispheric lateralisation of beta ERD% for participant P9.

Session	Pre 200	Post 500
1	-	-
2	-	-
3	ipsilateral dominant	ipsilateral dominant
4	ipsilateral dominant	ipsilateral dominant

Table 72 Participant P9's hemispheric lateralisation for beta ERD% for a 200 ms window preceding movement onset (Pre 200) and for a 500 ms window following movement onset (Post 500) (left arm movements).

8.3.4.5 Beta ERS following movement

Spatial distribution

The spatial distribution was variable over sessions (see Figure 96). It was initially centred at Cz for all sessions, then spreading to FCz/FC2/Cz for session 1, to C3/C1/Cz over the ipsilateral hemisphere for sessions 2 and 4. For session 3, it remained centred at Cz. This is different from results from the healthy group, where beta ERS peaks occur at Cz, CP2, and CP4, over the contralateral hemisphere.

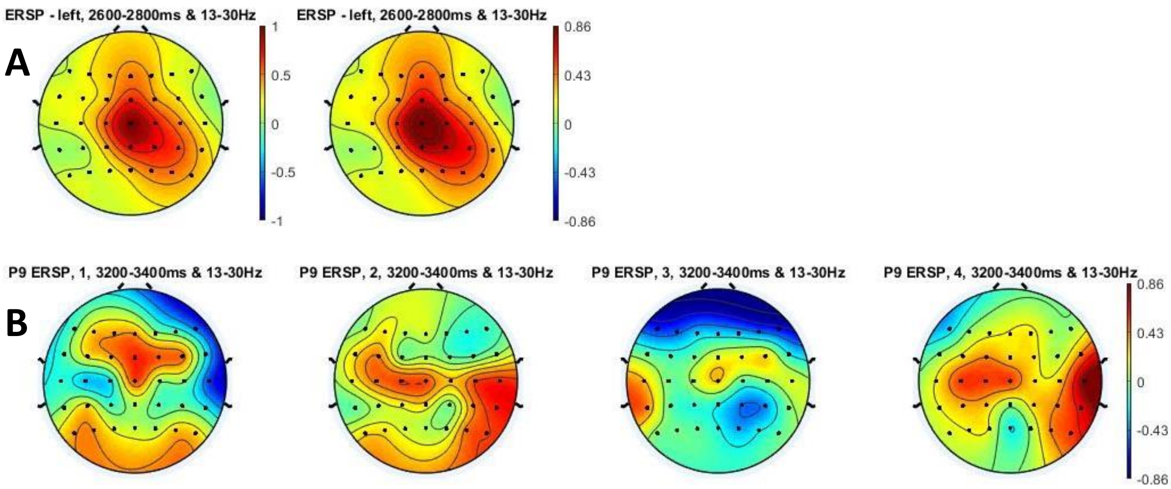


Figure 96 Scalp maps of beta ERS for (A) the healthy group (averaged; two maps: original scale and adjusted to this participant's scale), (B) participant P9 for sessions 1 to 4 (left arm movements).

Beta ERS over time

Figure 97 presents beta ERS% over time plots for select electrodes for all sessions.

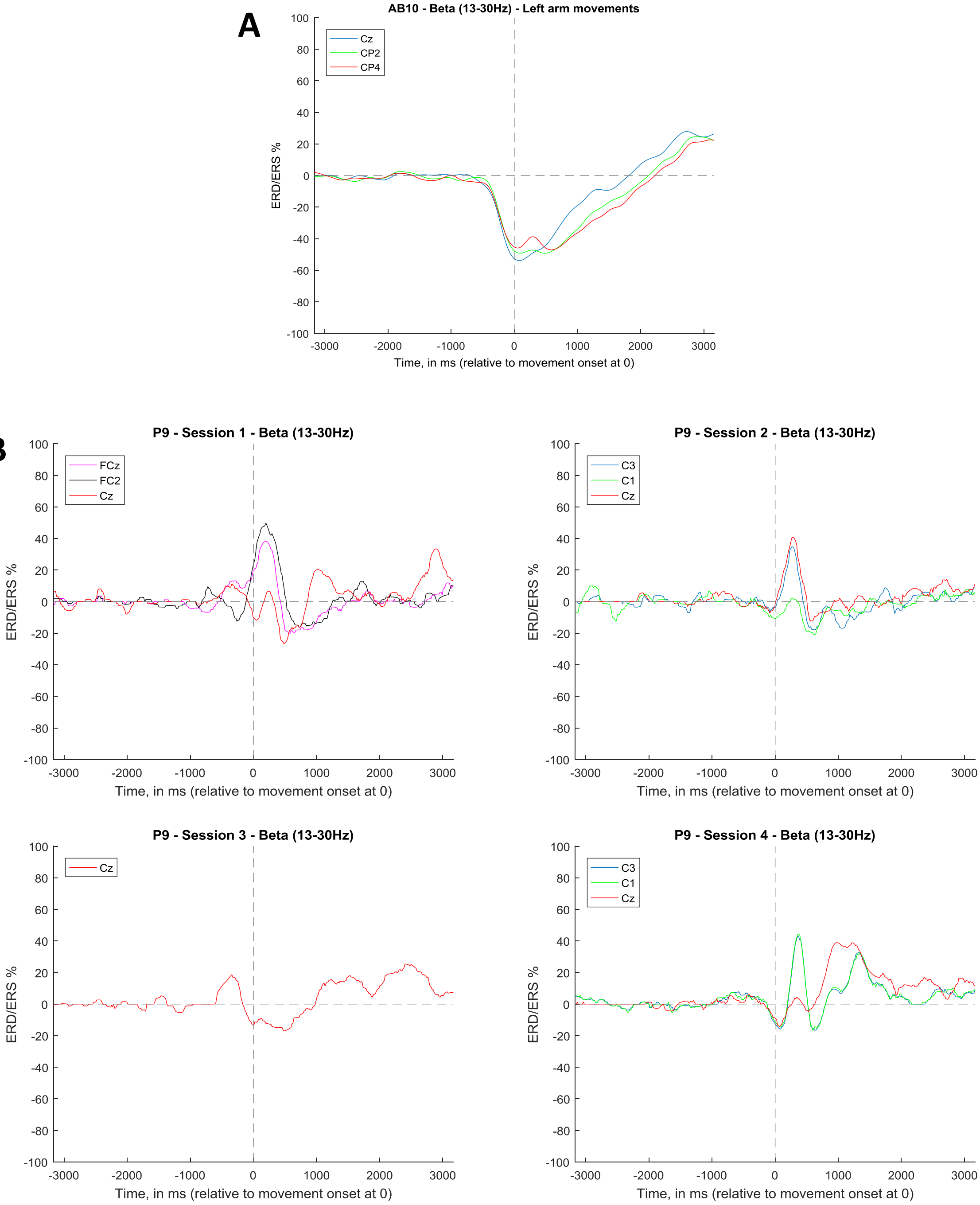


Figure 97 Plots of beta ERS% over time for (A) electrodes Cz, CP2, and CP4 for the healthy group (averaged), (B) select electrodes for participant P9 for all sessions (left arm movements).

Table 73 presents peak beta ERS% values for electrode Cz (the one with the greatest beta ERS% values after movement from the plots above). Due to the number of peaks and variety of times present over sessions, the difference in timing of peaks was not analysed. Values vary greatly when compared to the healthy group's average (27.9 %).

Session 1		Session 2		Session 3		Session 4	
Time	ERS%	Time	ERS%	Time	ERS%	Time	ERS%
1023	20.3	-	-	-	-	974	38.9
-	-	-	-	1531	18.2	-	-
-	-	-	-	2403	25.4	-	-
2895	33.5	2719	14.3	-	-	-	-

Table 73 Participant P9's beta ERS% peak values for electrode Cz for all sessions (times in ms) (left arm movements). When several peaks are present, they are approximately matched according to time and placed in the same row in order to compare values.

8.3.4.6 Summary and discussion of results

Participant P9's results for clinical assessments showed an improvement of five points following rehabilitation for the ARAT. Gains were also made with hand path ratio and time scores for the ArmeoSpring assessments, suggesting that this participant's ability to move their arm with more control and precision improved.

Some ERD/ERS measures deviated from the averaged results from the healthy group:

- The spatial distribution of alpha ERD was atypical, with alpha ERS occurring before and during movement over the contralateral hemisphere. Alpha ERD occurred mostly over the ipsilateral hemisphere.
- Beta ERS occurred during movement over both hemispheres.
- Beta ERD% peak values over the ipsilateral hemisphere were less than for the healthy group's average.
- Hemispheric lateralisation of both alpha and beta ERD was completely ipsilateral dominant for a 200 ms period of time preceding movement onset and a 500 ms period of time following movement onset.
- Beta ERS following movement was present over the ipsilateral hemisphere for two out of four sessions, rather than over the contralateral hemisphere as seen in the healthy group.

Differences were found in the beta frequency range at which beta ERD occurred. For this participant, the range observed for the electrode on the contralateral hemisphere, CP4, was narrower than for symmetrical electrode CP3, suggesting impaired contralateral hemisphere function.

For this participant, hemispheric lateralisation results suggest that the ipsilateral hemisphere is compensating for impaired contralateral hemisphere function.

Some changes in ERD/ERS measures could be attributed to the effects of rehabilitation:

- Electrode CP3, on the ipsilateral hemisphere, no longer showed alpha ERS during movement at session 4, resulting in a more typical pattern of movement-related alpha ERD found for the healthy group.
- At sessions 3 and 4, both electrodes CP3 and CP4 show a reduced beta ERS during movement, with the greatest reduction occurring at CP3, over the ipsilateral hemisphere.

For this participant, improvements in arm function are associated with a reduction of abnormal alpha and beta ERS during movement.

8.3.5 Participant P20

At the time of the screening assessment, this participant presented with left-sided mild weakness (MRC grade 4) and mild range of motion restrictions in the upper limb, with some loss of dexterity and speed of movement in his hand. No spasticity was observed in his upper limb (Modified Ashworth Scale grade 0).

8.3.5.1 Clinical and ArmeoSpring assessment scores

A maximum score of 66 for the Fugl-Meyer assessment was achieved with the unaffected upper limb, but a sub-maximal score of 56 (maximum score is 57) was given for this participant for the ARAT assessment. This is due to going over the five second time limit to complete one of the ball bearing test items in the 'Pinch' section. Figure 98 presents clinical assessment scores achieved with the affected upper limb for participant P20's four sessions. Sessions 1 and 2 are pre-rehabilitation and sessions 3 and 4 are post-rehabilitation. Figure 99 and Figure 100 present time and hand path ratio scores for the ArmeoSpring assessments that were administered at the first rehabilitation session, at the fifth session, and at the last session. This participant reached 100 % of the target icons for each assessment.

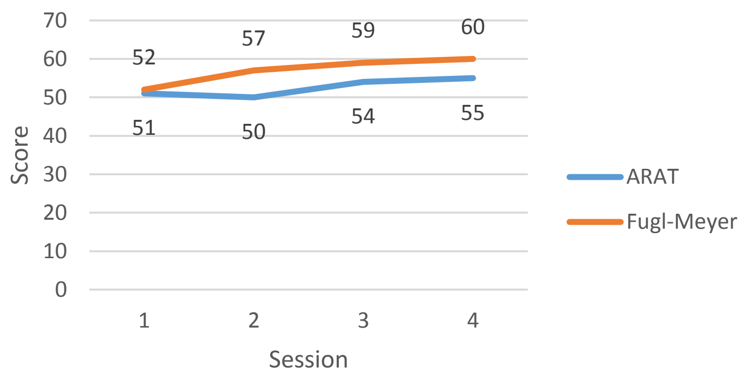


Figure 98   Participant P20's ARAT and Fugl-Meyer scores.

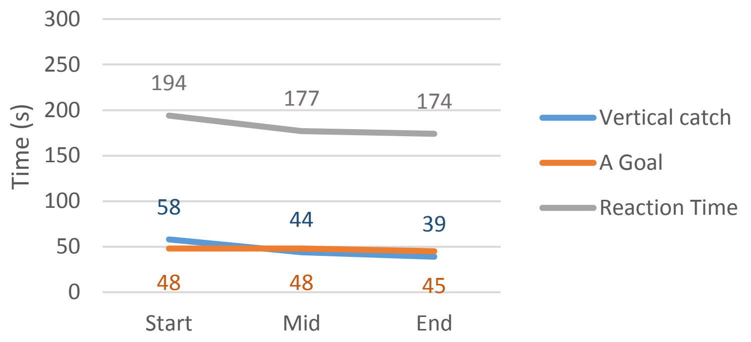


Figure 99 Participant P20's ArmeoSpring assessment time scores.

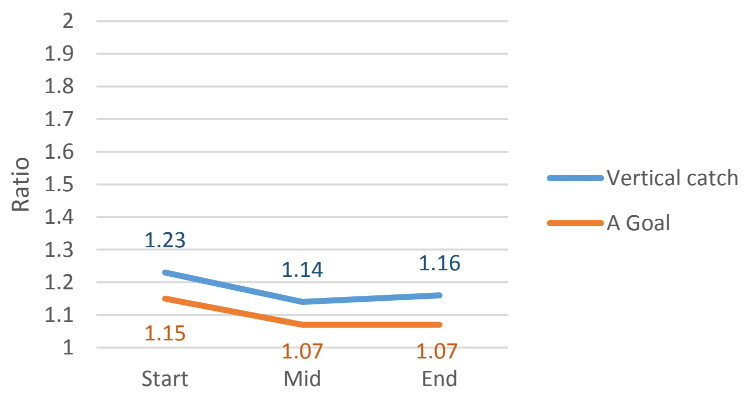


Figure 100 Participant P20's ArmeoSpring assessment hand path ratio scores.

Results show that for clinical assessments, ARAT scores improved at session 3 (up three points from the highest score before rehabilitation), followed by a further improvement at session 4 (up another point). For the Fugl-Meyer assessment, improvements also occurred at session 3 (up two points from the highest score before rehabilitation), followed by a further improvement at session 4 (up another point). For the ArmeoSpring assessments, improvements were made for time scores (from 194 to 174 for 'Reaction Time', from 48 to 45 for 'A Goal', and from 58 to 39 for 'Vertical Catch'), as well as for hand path ratio scores (from 1.23 to 1.14 for 'Vertical Catch' and from 1.15 to 1.07 for 'A Goal').

8.3.5.2 Movement characteristics

This participant moved their left arm during EEG recordings.

Table 74 presents the number of movements retained for analysis, as well as mean reaction and movement times for participant P20. Figure 101 shows box plots with further details about each session's movement times.

Session	Number of movements	Mean reaction time	SD	Mean movement time	SD
1	137	470	82	492	64
2	108	531	89	603	105
3	122	485	79	541	61
4	110	559	83	591	77

Table 74 Number of movements retained for analysis, mean reaction times (in ms), and mean movement times (in ms) for participant P20.

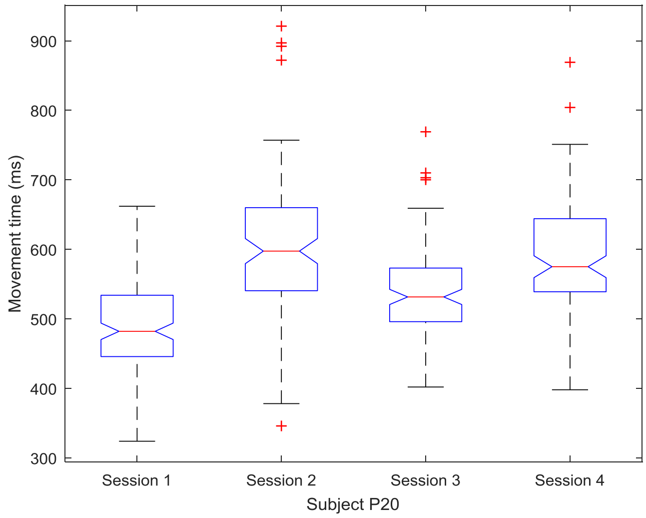


Figure 101 Box plots for participant P20's movement times for four sessions (the red line in the centre of the box being the median, the edges of the box are the 25th and 75th percentiles, whiskers end at the most extreme values that are not considered outliers, and outliers are displayed with red crosses).

To compare this participant's mean movement times over four sessions, results from a one-way unbalanced analysis of variance (ANOVA) show that all sessions had significantly different mean movement times [F = 53.03 (3, 473), p < 10^-6]. Post-hoc multiple comparison tests with Tukey's honest significant difference criterion showed that one pair of movement time means, for sessions 2 and 4, were not significantly different.

8.3.5.3 Alpha ERD

Alpha ERD over time

Figure 102 presents time frequency ERD/ERS maps for electrode sites CP3/CP4 for participant P20. Averaged time frequency ERD/ERS maps for the healthy group are also displayed for comparison purposes.

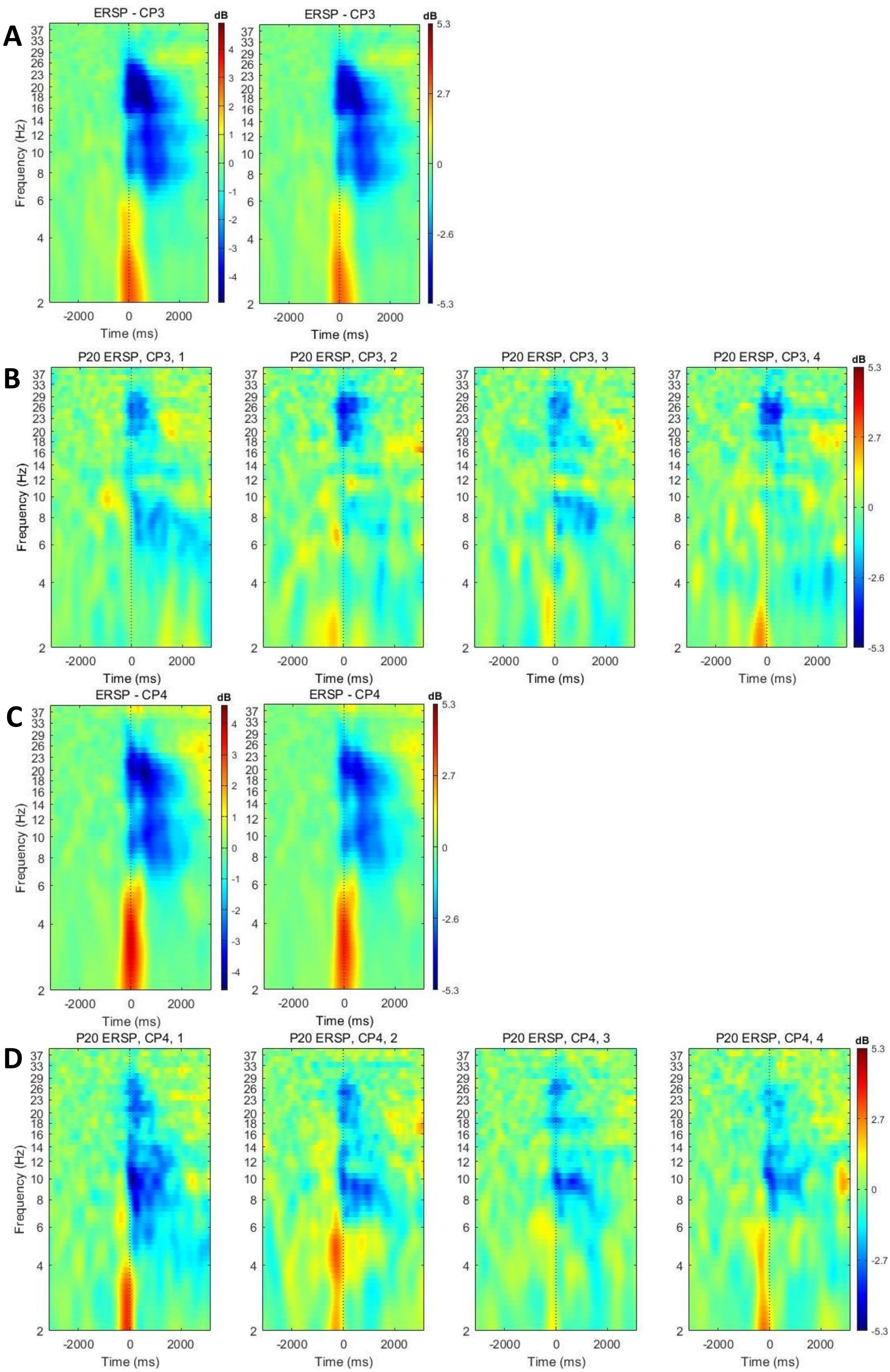


Figure 102 Time frequency ERD/ERS maps for CP3 for (A) the healthy group (two maps: original scale and adjusted to this participant's scale), (B) participant P20 sessions 1-4, and CP4 for (C) the healthy group (two maps as above), and (D) participant P20 sessions 1-4 (left arm movements).

Figure 103 presents alpha ERD/ERS% over time plots for pairs of symmetrical electrodes CP3/CP4 for all sessions. It can be observed that the relative difference of the intensity of alpha ERD% between electrode CP3 (on the ipsilateral hemisphere) and electrode CP4, is larger than for the healthy group.

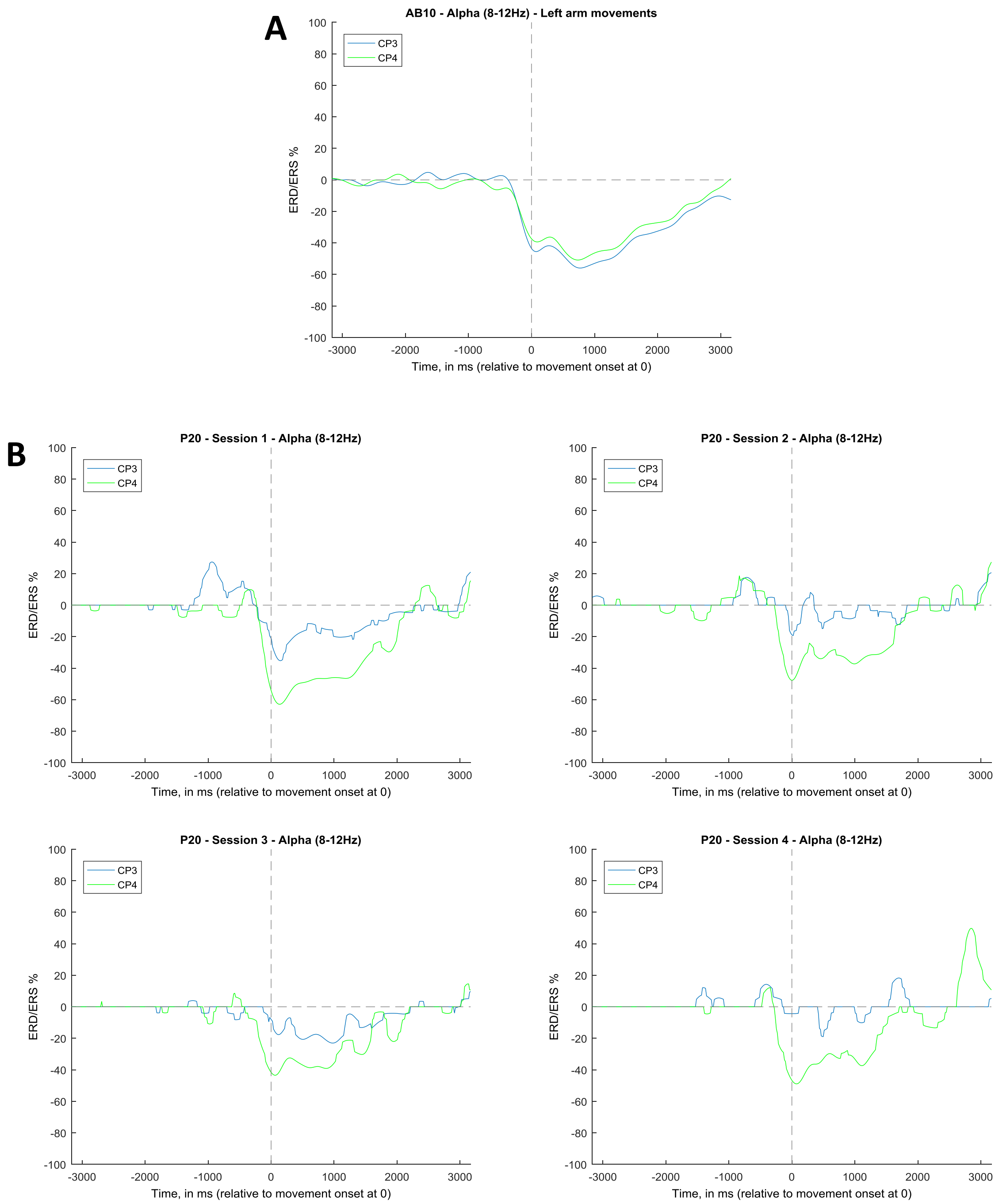


Figure 103 Plots of alpha ERD/ERS% over time for symmetrical electrodes CP3/CP4 for (A) the healthy group (averaged), (B) participant P20 (left arm movements).

Table 75 presents peak alpha ERD% values for electrode CP4 (the one with the greatest alpha ERD% values from the plots above). Peaks were approximately matched according to time and placed in the same row in order to compare values. Some variability can be observed in alpha

ERD% peak values, but the pattern of variation is not indicative of changes due to rehabilitation. Values for the first peak are generally similar to the one found for the healthy group's average (-45.5 %).

Session 1		**Session 2**		**Session 3**		**Session 4**	
Time	ERD%	Time	ERD%	Time	ERD%	Time	ERD%
134	-62.9	6	-47.7	70	-43.5	70	-48.9
1183	-46.5	990	-37.3	882	-39.1	1103	-37.4

Table 75 Participant P20's alpha ERD% peak values for electrode CP4 for all sessions (times in ms) (left arm movements).

Hemispheric lateralisation

Figure 104 presents scalp maps of alpha ERD/ERS for a 200 ms window preceding movement onset and for a 500 ms window following movement onset for participant P20, where it can be observed that alpha ERD is contralateral dominant before and after movement onset.

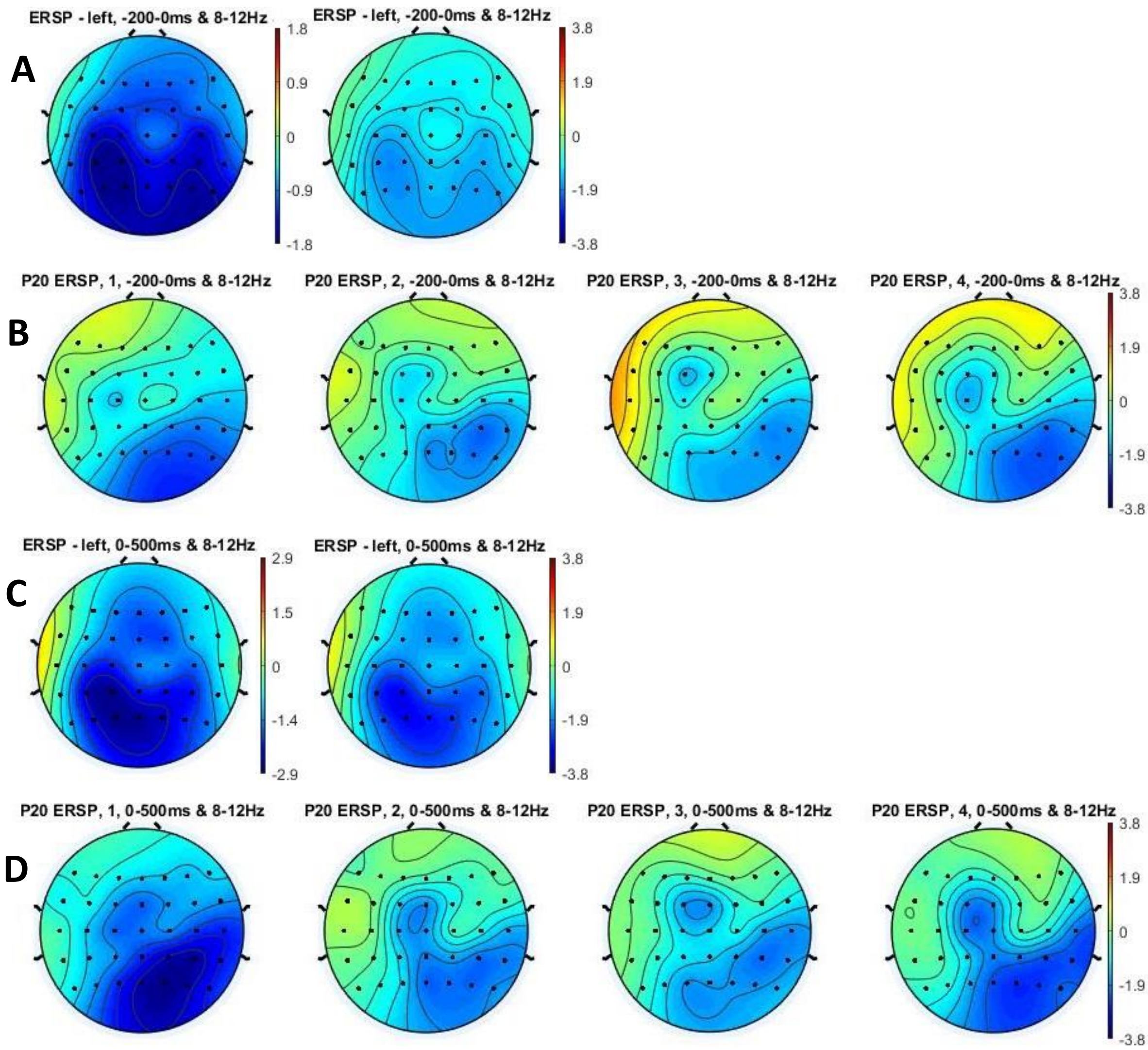


Figure 104 Scalp maps of alpha ERD/ERS for a 200 ms window preceding movement onset for (A) the healthy group (averaged; two maps: original scale and adjusted to this participant's scale), (B) participant P20 for sessions 1 to 4, and for a 500 ms window following movement onset for (C) the healthy group (averaged; two maps as above), and (D) participant P20 for sessions 1 to 4 (left arm movements).

Table 76 presents values for areas over the curve and laterality indices (LI), as calculated with alpha ERD% data for electrode pair CP3/CP4, for a period of 200 ms preceding movement onset and a period of 500 ms following movement onset. Laterality index values range from -1 to 1. A value of -1 indicates complete right hemisphere predominance. A value of 1 indicates complete left hemisphere predominance. A value of 0 indicates equal amounts of ERD% at both electrode sites.

Session	A_{CP3}		A_{CP4}		Laterality Index		L/R ratio	
	Pre 200	Post 500	Pre 200	Post 500	Pre 200	Post 500	Pre 200	Post 500
1	2417	12659	6254	27806	-0.44	-0.37	0.39	0.46
2	907	2578	7241	16972	-0.78	-0.74	0.13	0.15
3	659	7064	5961	18216	-0.80	-0.44	0.11	0.39
4	322	1647	6831	20208	-0.91	-0.85	0.05	0.08

Table 76 Participant P20's areas over the curve A_{CP3} and A_{CP4} (in ERD% * ms units) and alpha ERD% laterality indices for electrode pair CP3/CP4 for a 200 ms window preceding movement onset (Pre 200) and for a 500 ms window following movement onset (Post 500) (left arm movements). L/R values = A_{CP3} / A_{CP4}.

In order to interpret laterality indices and L/R ratio values, the researcher defined ranges for labelling laterality. For the purpose of this study, laterality indices (LI) falling between -0.05 to 0.05 are deemed to indicate bilateral alpha ERD%, those between -0.15 to -0.05 and between 0.05 to 0.15 are deemed to indicate weak right and left hemispheric predominance, respectively, and any other values indicate either left or right hemispheric predominance.

Table 77 presents the interpretation of the hemispheric lateralisation data using the described criteria.

Session	Pre 200	Post 500
1	contralateral dominant	contralateral dominant
2	contralateral dominant	contralateral dominant
3	contralateral dominant	contralateral dominant
4	contralateral dominant	contralateral dominant

Table 77 Interpretation of participant P20's hemispheric lateralisation data for alpha ERD% for a 200 ms window preceding movement onset (Pre 200) and for a 500 ms window following movement onset (Post 500) (left arm movements).

When compared to the healthy group, this participant's hemispheric lateralisation of alpha ERD% is different for both time periods. For this participant, contralateral dominance can be observed, in comparison with weak ipsilateral dominance for the healthy group. When looking at variations between sessions, results for hemispheric lateralisation show that laterality indices for a 200 ms period of time preceding movement onset show increased contralateral predominance after rehabilitation. For a 500 ms period of time after movement onset, the pattern of variation is not indicative of changes that could be associated with rehabilitation.

8.3.5.4 Beta ERD

Frequency range

The frequency range within the beta range (13-30 Hz) at which beta ERD occurs at symmetrical electrodes CP3 and CP4 was examined by visually inspecting ERSP plots produced with EEGLAB's STUDY functions. Table 78 presents results for all sessions. Results are similar over sessions and for symmetrical electrodes.

Electrode	Session 1	Session 2	Session 3	Session 4
CP3	18-30	17-30	17-30	17-30
CP4	17-29	17-29	17-28	17-27

Table 78 Frequency ranges, in Hz, at which beta ERD occurs for participant P20's sessions.

Beta ERD over time

For time frequency ERD/ERS maps for electrode sites CP3 and CP4, please refer to Figure 102 in the previous section, where it can be observed that beta ERD is greater at sessions 2 and 4 at electrode CP3 (over the ipsilateral hemisphere) than it is at electrode CP4. Figure 105 presents beta ERD/ERS% over time plots for pairs of symmetrical electrodes CP3/CP4 for all sessions.

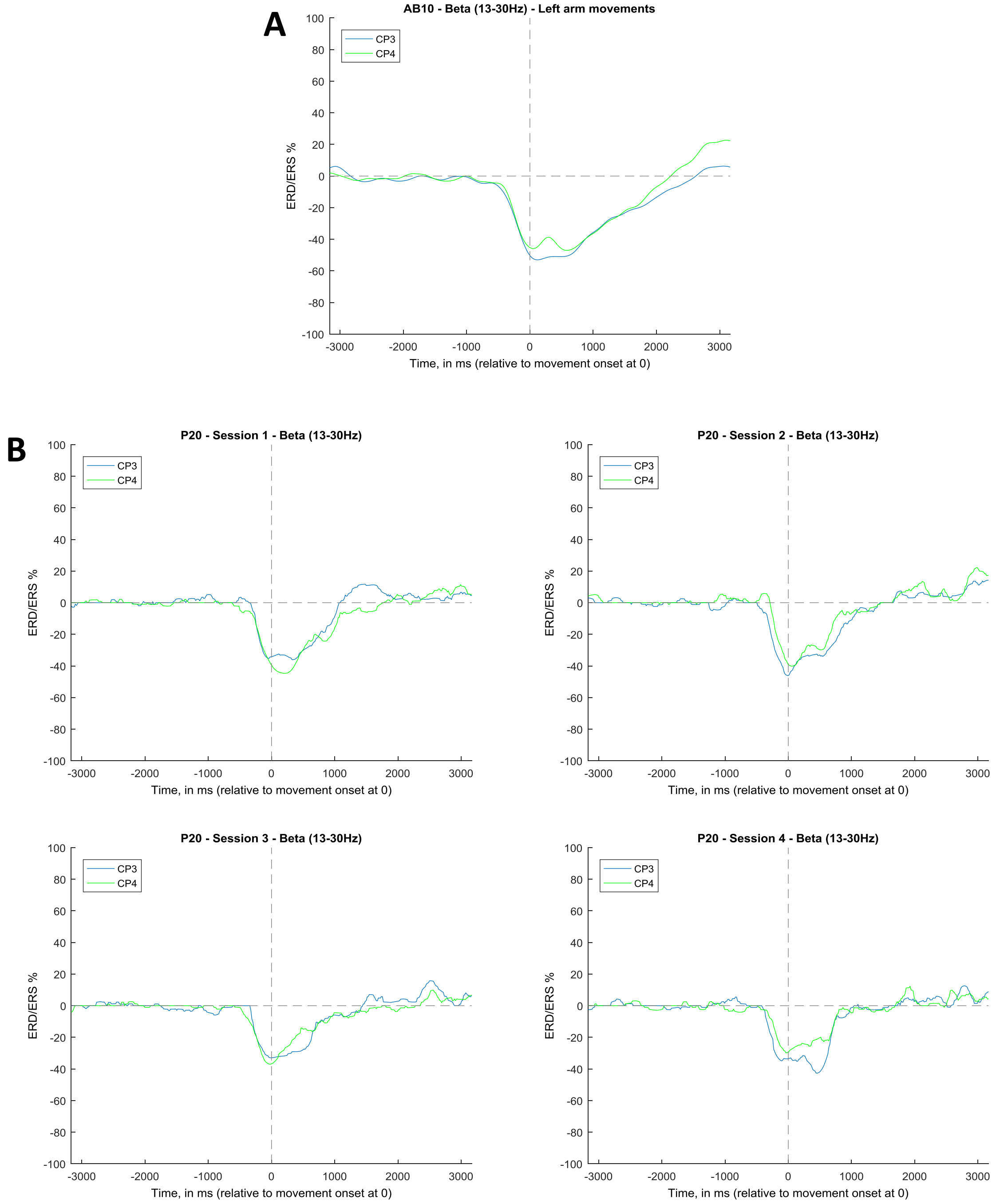


Figure 105 Plots of beta ERD/ERS% over time for symmetrical electrodes CP3/CP4 for (A) the healthy group (averaged), (B) participant P20 (left arm movements).

Table 79 and Table 80 present peak beta ERD% values for electrode CP3 and CP4, as neither has the greatest beta ERD% peak values over all four sessions. Peaks were approximately matched according to time and placed in the same row in order to compare values. Some variability can be observed in beta ERD% peak values, but the pattern and degree of variation is not indicative of changes due to rehabilitation. Maximum values between both electrodes for the first peak for each session were less than for the healthy group's average (-53 %).

Session 1		Session 2		Session 3		Session 4	
Time	ERD%	Time	ERD%	Time	ERD%	Time	ERD%
-38	-35.2	-6	-46.1	-6	-33.0	-102	-35.0
342	-36.1	546	-34.0	-	-	454	-42.7

Table 79 Participant P20's beta ERD% peak values for electrode CP3 for all sessions (times in ms) (left arm movements).

Session 1		Session 2		Session 3		Session 4	
Time	ERD%	Time	ERD%	Time	ERD%	Time	ERD%
214	-44.7	54	-40.1	-22	-37.0	-38	-29.8
834	-24.3	514	-29.9	642	-16.4	562	-22.8

Table 80 Participant P20's beta ERD% peak values for electrode CP4 for all sessions (times in ms) (left arm movements).

Hemispheric lateralisation

Figure 106 presents scalp maps of beta ERD/ERS for a 200 ms window preceding movement onset and for a 500 ms window following movement onset for participant P20.

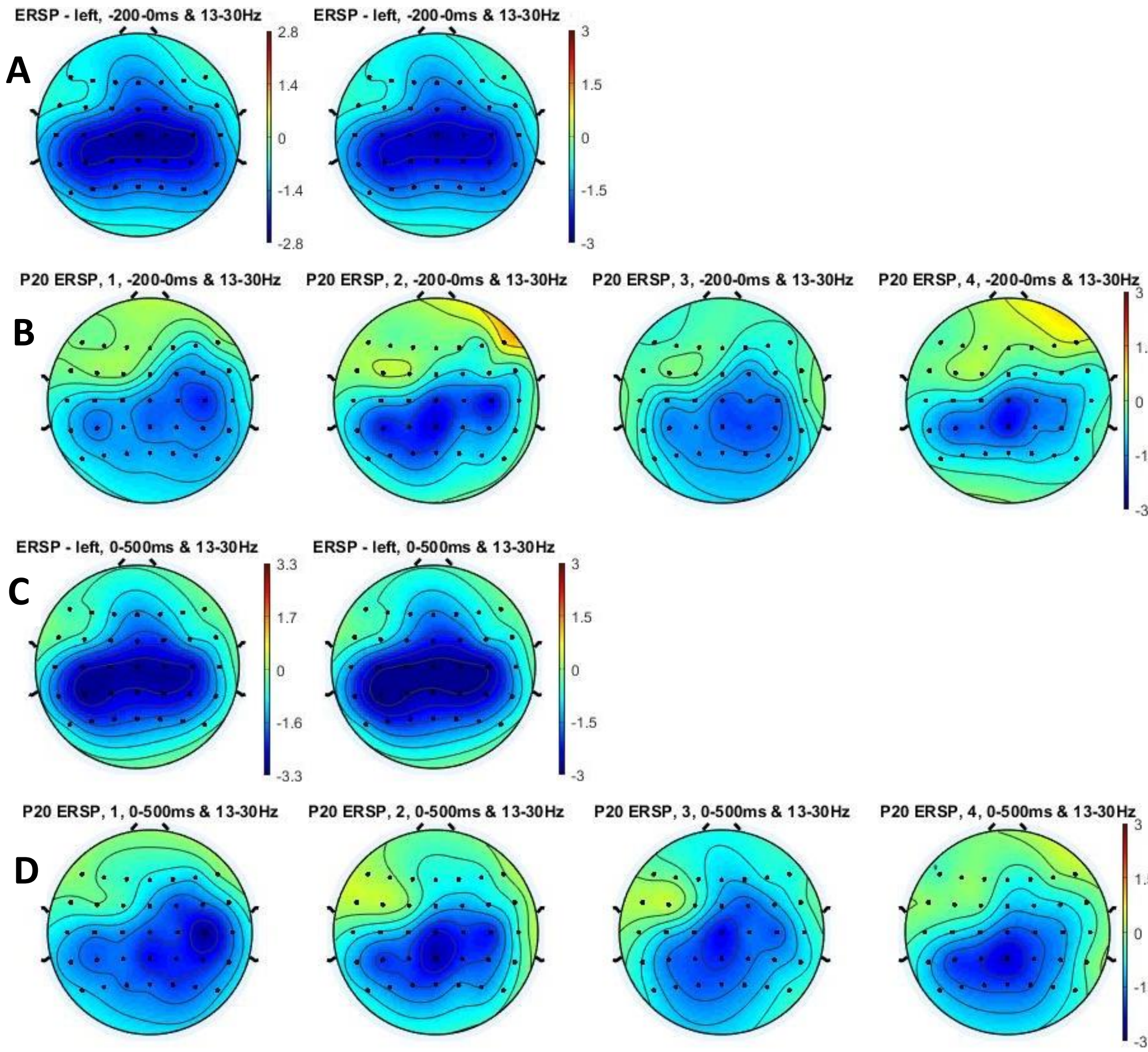


Figure 106 Scalp maps of beta ERD/ERS for a 200 ms window preceding movement onset for (A) the healthy group (averaged; two maps: original scale and adjusted to this participant's scale), (B) participant P20 for sessions 1 to 4, and for a 500 ms window following movement onset for (C) the healthy group (averaged; two maps as above), and (D) participant P20 for sessions 1 to 4 (left arm movements).

Table 81 presents values for areas over the curve and laterality indices (LI), as calculated with beta ERD% data for electrode pair CP3/CP4, for a period of 200 ms preceding movement onset and a period of 500 ms following movement onset.

Session	A_{CP3}		A_{CP4}		Laterality Index		L/R ratio	
	Pre 200	Post 500	Pre 200	Post 500	Pre 200	Post 500	Pre 200	Post 500
1	6065	16556	5956	20091	0.01	-0.10	1.02	0.82
2	7627	17735	5669	16016	0.15	0.05	1.35	1.11
3	5676	15094	6428	12581	0.06	0.09	0.88	1.20
4	6436	17730	4941	12040	0.13	0.19	1.3	1.47

Table 81 Participant P20's areas over the curve A_{CP3} and A_{CP4} (in ERD% * ms units) and laterality indices for beta ERD% for electrode pair CP3/CP4 for a 200 ms window preceding movement onset (Pre 200) and for a 500 ms window following movement onset (Post 500) (left arm movements). L/R values = A_{CP3} / A_{CP4}.

Table 82 presents the interpretation of the hemispheric lateralisation data using the criteria described for alpha ERD in the previous section.

Session	Pre 200	Post 500
1	bilateral	weak contralateral dominant
2	weak ipsilateral dominant	bilateral
3	weak ipsilateral dominant	weak ipsilateral dominant
4	weak ipsilateral dominant	ipsilateral dominant

Table 82 Interpretation of participant P20's hemispheric lateralisation data for beta ERD% for a 200 ms window preceding movement onset (Pre 200) and for a 500 ms window following movement onset (Post 500) (left arm movements).

When compared to the healthy group, hemispheric lateralisation of beta ERD% for a 200 ms period of time preceding movement onset for this participant was slightly different, in that it was mostly weak ipsilateral dominant, in comparison with bilaterality for the healthy group. For a 500 ms period of time following movement onset, there was much variation for this participant, in comparison with weak ipsilateral dominance for the healthy group, with variations over sessions showing changes towards an increased ipsilateral dominance.

8.3.5.5 Beta ERS following movement

Spatial distribution

The spatial distribution was similar for all sessions, centred at CPz initially (with a slight variation for session 3, where it was also centred at Cz in addition to CPz), then spreading to the contralateral hemisphere towards C4 (see Figure 107). This was slightly different from results from the healthy group, where beta ERS peaks occurred, at Cz, CP2 and CP4.

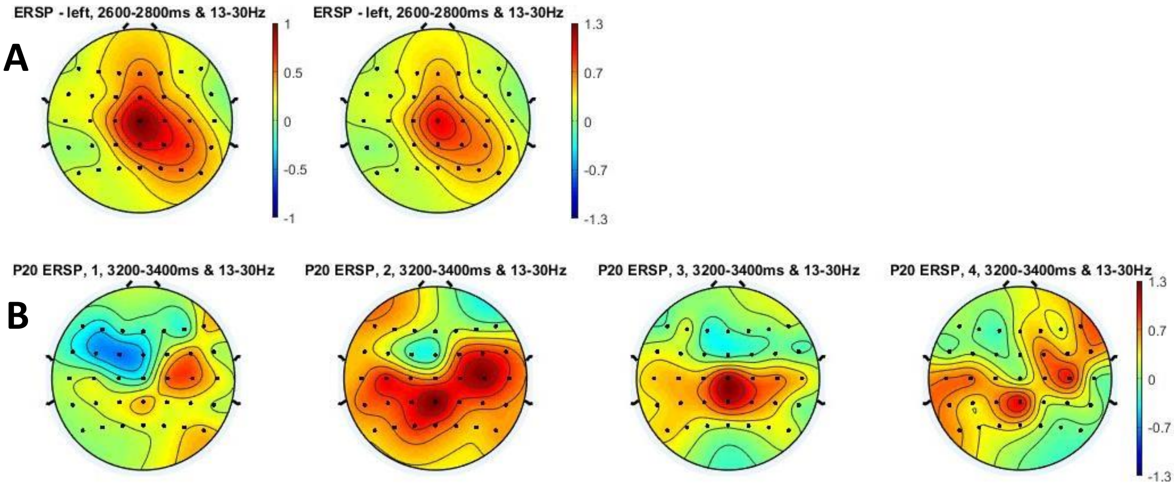


Figure 107 Scalp maps of beta ERS for (A) the healthy group (averaged; two maps: original scale and adjusted to this participant's scale), (B) participant P20 for sessions 1 to 4 (left arm movements).

Beta ERS over time

Figure 108 presents beta ERS% over time plots for select electrodes for all sessions.

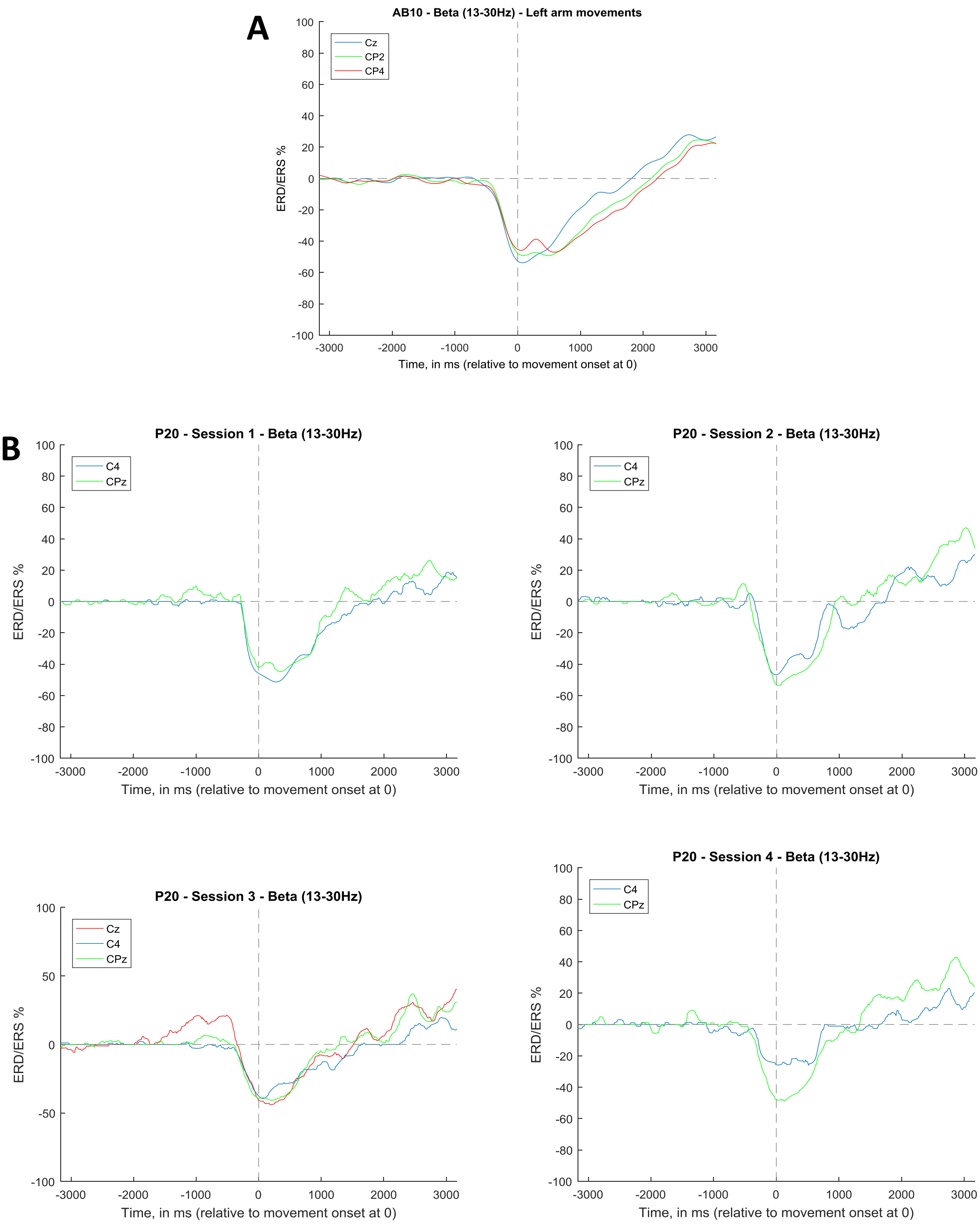


Figure 108 Plots of beta ERS% over time for (A) electrodes Cz, CP2, and CP4 for the healthy group (averaged), (B) select electrodes for participant P20 for all sessions (left arm movements).

Table 83 presents peak beta ERS% values for electrode CPz (the one with the greatest beta ERS% values from the plots above). The range of timings for beta ERS% peaks, as calculated by the difference in time between the earliest and latest peaks over the four sessions, is 557 ms. Some variability can be observed in the timing and peak values of beta ERS%, but the pattern of variation is not indicative of changes due to rehabilitation. Most values for all sessions are greater than for the healthy group’s average (27.9 %).

Session 1		Session 2		Session 3		Session 4	
Time	ERS%	Time	ERS%	Time	ERS%	Time	ERS%
2719	26.4	3024	47.0	2467	36.9	2847	42.6

Table 83 Participant P20’s beta ERS% peak values for electrode CPz for all sessions (times in ms) (left arm movements).

8.3.5.6 Summary and discussion of results

Participant P20’s results for clinical assessments showed an improvement of four points following rehabilitation for the ARAT assessment. For the Fugl-Meyer assessment, scores improved by three points. Gains were also made with hand path ratio and time scores for the ArmeoSpring assessments, suggesting that this participant’s ability to move their arm with more control and precision improved.

Some ERD/ERS measures deviated from the averaged results from the healthy group:

- The relative intensity of alpha ERD (in relation to the contralateral hemisphere) was less over the ipsilateral hemisphere than for the healthy group.
- Hemispheric lateralisation of alpha ERD% before and during movement was contralateral dominant, rather than weak ipsilateral dominant for the healthy group.
- Beta ERD% peak values over both hemispheres were less than for the healthy group’s average.
- Hemispheric lateralisation of beta ERD% was weak ipsilateral dominant for a 200 ms period of time preceding movement onset, compared to bilateral for the healthy group, and varied greatly for a 500 ms period of time following movement onset.
- Beta ERS% peak values following movement were greater than for the healthy group’s average.

Decreased ipsilateral hemisphere alpha ERD suggests that for this participant, interhemispheric inhibitory mechanisms may have been altered by stroke, resulting in an overactive inhibitory influence over the ipsilateral hemisphere.

No changes in ERD/ERS measures could be attributed to the effects of rehabilitation despite improvements in upper limb function at sessions 3 and 4.

8.3.6 Participant P21

At the time of the screening assessment, this participant presented with left-sided mild weakness (MRC grade 4) and moderate range of motion restrictions in the upper limb. Hand function was severely limited. Spasticity was observed in his upper limb (Modified Ashworth Scale grade 1+).

8.3.6.1 Clinical and ArmeoSpring assessment scores

A maximum score of 57 for the ARAT was achieved with the unaffected upper limb, but a sub-maximal score of 65 (maximum score is 66) was given for this participant for the Fugl-Meyer Assessment. This is due to an incomplete forearm supination during the flexor synergy movement test item. Figure 109 presents clinical assessment scores achieved with the affected upper limb for participant P21's four sessions. Sessions 1 and 2 are pre-rehabilitation and sessions 3 and 4 are post-rehabilitation. Figure 110 and Figure 111 present time and hand path ratio scores for the ArmeoSpring assessments that were administered at the first rehabilitation session, at the fifth session, and at the last session. This participant reached 100 % of the target icons for each assessment, except for the 'A Goal' assessment administered at the first rehabilitation session, where this participant reached 66 % of the target icons before reaching this assessment's time limit.

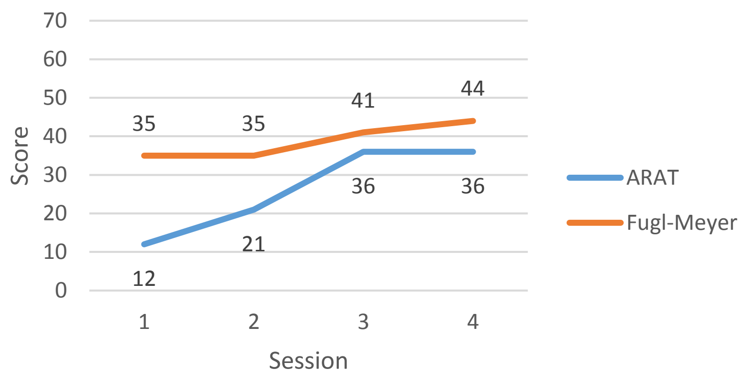


Figure 109 Participant P21's ARAT and Fugl-Meyer scores.

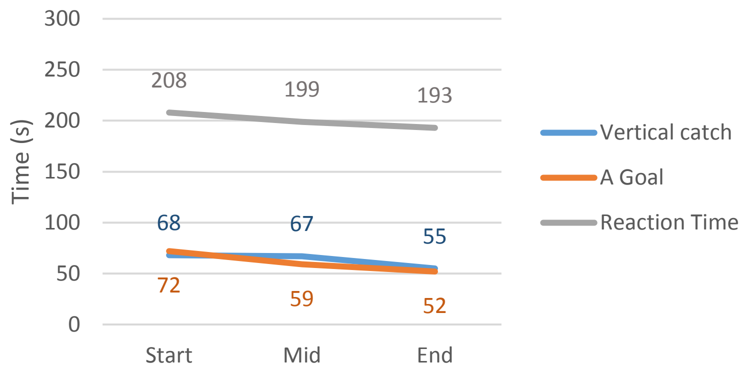


Figure 110 Participant P21's ArmeoSpring assessment time scores.

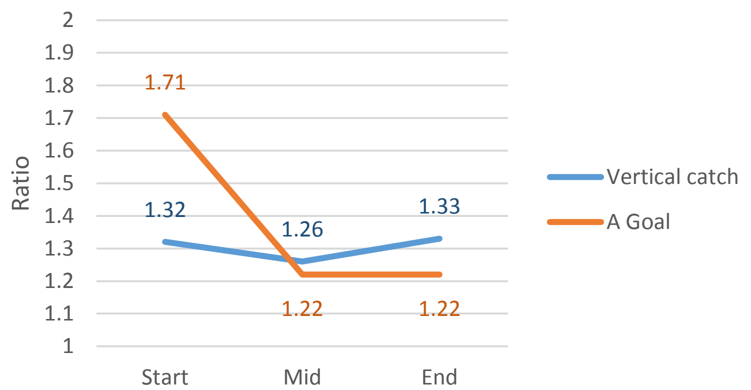


Figure 111 Participant P21's ArmeoSpring assessment hand path ratio scores.

Results show that for clinical assessments, Fugl-Meyer scores improved at session 3 (up six points from the highest score before rehabilitation), followed by a further improvement at session 4 (up another three points). For the ARAT, scores improved, up 15 points after rehabilitation. For the ArmeoSpring assessments, improvements were made for time scores (from 208 to 193 for 'Reaction Time', from 72 to 52 for 'A Goal', and from 68 to 55 for 'Vertical Catch'), as well as for hand path ratio scores (1.71 to 1.22 for 'A Goal').

8.3.6.2 Movement characteristics

This participant moved their left arm during EEG recordings. Table 84 presents the number of movements retained for analysis, as well as mean reaction and movement times for participant P21. Figure 112 shows box plots with further details about each session's movement times. The number of movements retained for analysis for session 4 is lower than the others due to a high number of movements with reaction times exceeding one second.

Session	Number of movements	Mean reaction time	SD	Mean movement time	SD
1	110	637	116	1104	214
2	115	609	138	970	211
3	115	661	121	793	169
4	86	607	132	825	160

Table 84 Number of movements retained for analysis, mean reaction times (in ms), and mean movement times (in ms) for participant P21.

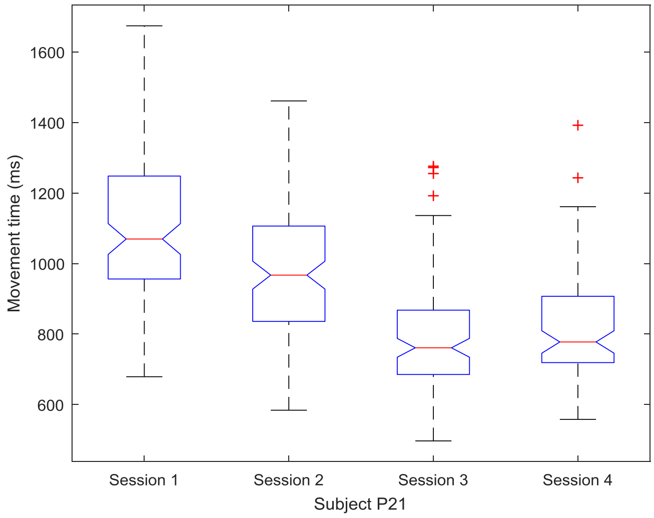


Figure 112 Box plots for participant P21's movement times for four sessions (the red line in the centre of the box being the median, the edges of the box are the 25th and 75th percentiles, whiskers end at the most extreme values that are not considered outliers, and outliers are displayed with red crosses).

To compare this participant's mean movement times over four sessions, results from a one-way unbalanced analysis of variance (ANOVA) show that all sessions had significantly different mean movement times [F = 60.01 (3, 422), p < 10^-6]. Session 3 and 4's mean movement times were lower than for the first two sessions. Post-hoc multiple comparison tests with Tukey's honest significant difference criterion showed that one pair of movement time means, for sessions 3 and 4, were not significantly different. Mean movement times for this participant were higher than mean movement times for all other participants taking part in this study.

8.3.6.3 Alpha ERD

Alpha ERD over time

Figure 113 presents time frequency ERD/ERS maps for electrode sites CP3/CP4 for participant P21, where it can be observed that alpha ERD is much greater for participant P21 than it is for the healthy group.

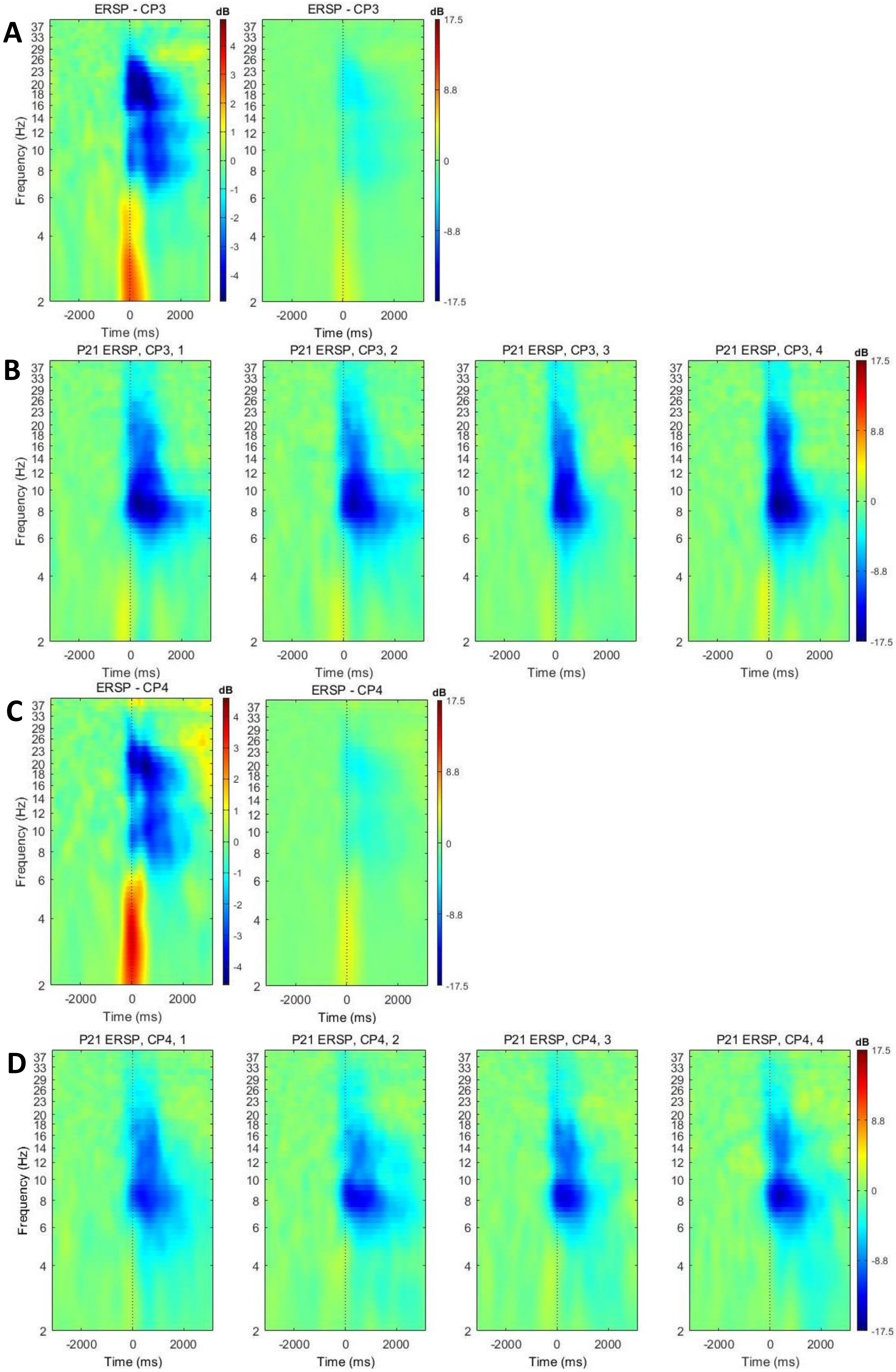


Figure 113 Time frequency ERD/ERS maps for CP3 for (A) the healthy group (two maps: original scale and adjusted to this participant's scale), (B) participant P21 sessions 1-4, and CP4 for (C) the healthy group (two maps as above), and (D) participant P21 sessions 1-4 (left arm movements).

Figure 114 presents alpha ERD/ERS% over time plots for pairs of symmetrical electrodes CP3/CP4 for all sessions.

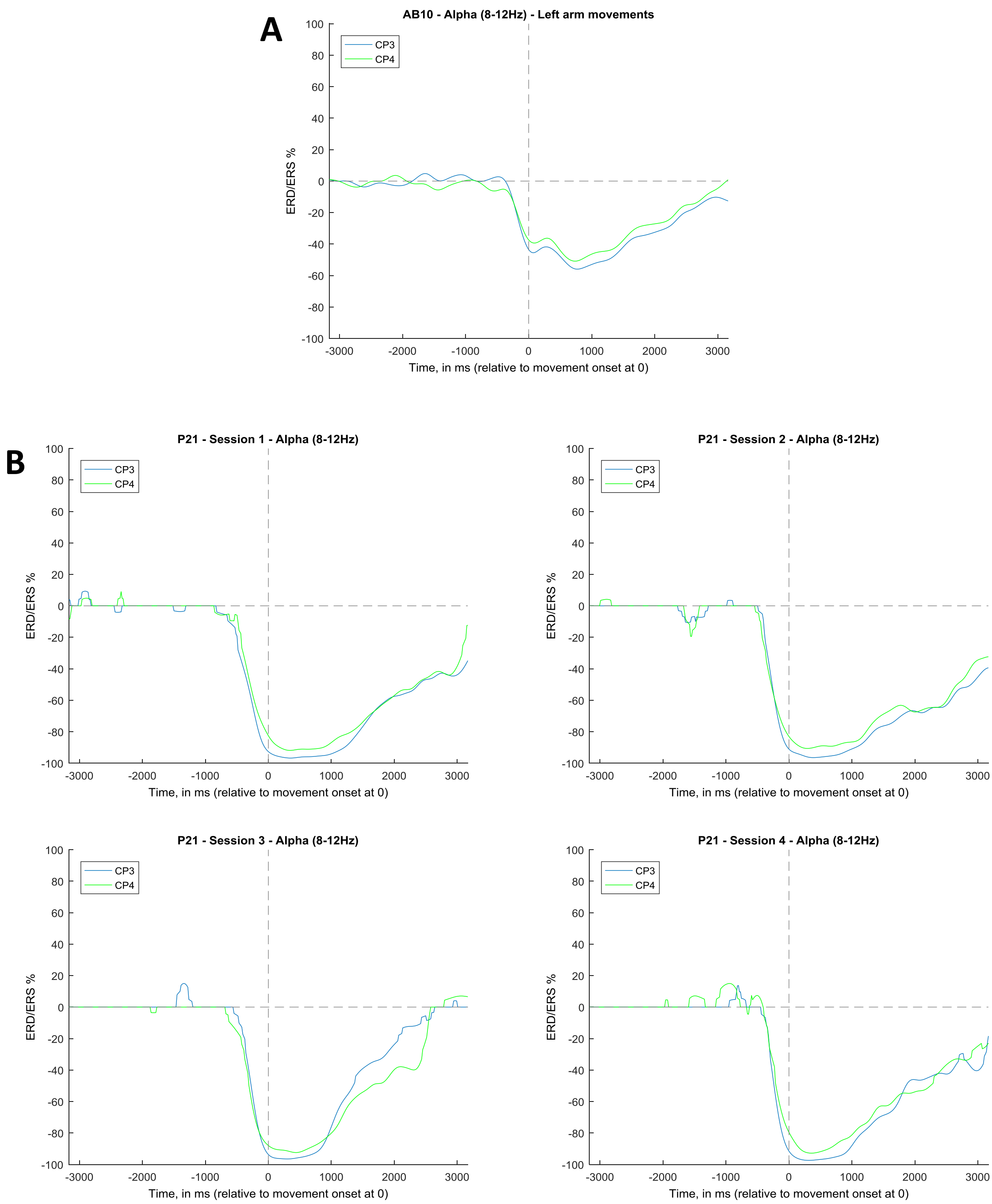


Figure 114 Plots of alpha ERD/ERS% over time for symmetrical electrodes CP3/CP4 for (A) the healthy group (averaged), (B) participant P21 (left arm movements).

Table 85 presents peak alpha ERD% values for electrode CP3 (the one with the greatest alpha ERD% values from the plots above). Peaks were approximately matched according to time and placed in the same row in order to compare values. Peak alpha ERD% values are high, with little variability between sessions. Peak values are greater than those for the healthy group's average (-56 %).

Session 1		Session 2		Session 3		Session 4	
Time	ERD%	Time	ERD%	Time	ERD%	Time	ERD%
358	-96.7	390	-96.4	310	-96.5	310	-97.4

Table 85 Participant P21's alpha ERD% peak values for electrode CP3 for all sessions (times in ms) (left arm movements).

Hemispheric lateralisation

Figure 115 presents scalp maps of alpha ERD/ERS for a 200 ms window preceding movement onset and for a 500 ms window following movement onset for participant P21. It can be observed that alpha ERD occurs over large areas over both hemispheres before and during movement.

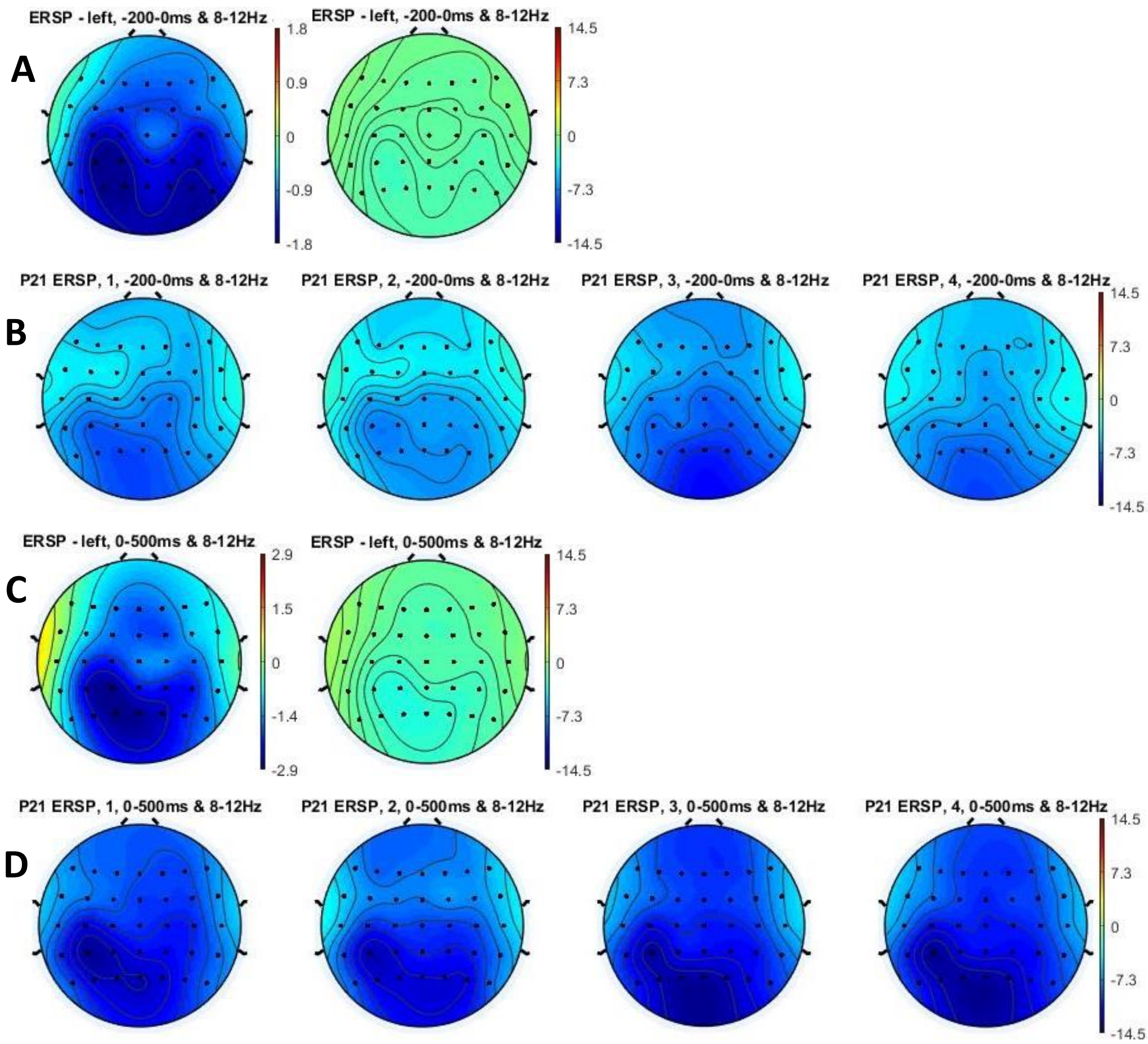


Figure 115 Scalp maps of alpha ERD/ERS for a 200 ms window preceding movement onset for (A) the healthy group (averaged; two maps: original scale and adjusted to this participant's scale), (B) participant P21 for sessions 1 to 4, and for a 500 ms window following movement onset for (C) the healthy group (averaged; two maps as above), and (D) participant P21 for sessions 1 to 4 (left arm movements).

Table 86 presents values for areas over the curve and laterality indices (LI), as calculated with alpha ERD% data for electrode pair CP3/CP4, for a period of 200 ms preceding movement onset and a period of 500 ms following movement onset. Laterality index values range from -1 to 1. A value of -1 indicates complete right hemisphere predominance. A value of 1 indicates complete left hemisphere predominance. A value of 0 indicates equal amounts of ERD% at both electrode sites.

Session	A_{CP3}		A_{CP4}		Laterality Index		L/R ratio	
	Pre 200	Post 500	Pre 200	Post 500	Pre 200	Post 500	Pre 200	Post 500
1	16319	47135	14218	44189	0.07	0.03	1.15	1.07
2	15675	46718	14322	43746	0.05	0.03	1.09	1.07
3	16170	47229	15772	44784	0.01	0.03	1.03	1.05
4	15237	47407	13008	44219	0.08	0.03	1.17	1.07

Table 86 Participant P21's areas over the curve A_{CP3} and A_{CP4} (in ERD% * ms units) and alpha ERD% laterality indices for electrode pair CP3/CP4 for a 200 ms window preceding movement onset (Pre 200) and for a 500 ms window following movement onset (Post 500) (left arm movements). L/R values = A_{CP3} / A_{CP4}.

In order to interpret laterality indices and L/R ratio values, the researcher defined ranges for labelling laterality. For the purpose of this study, laterality indices (LI) falling between -0.05 to 0.05 are deemed to indicate bilateral alpha ERD%, those between -0.15 to -0.05 and between 0.05 to 0.15 are deemed to indicate weak right and left hemispheric predominance, respectively, and any other values indicate either left or right hemispheric predominance.

Table 87 presents the interpretation of the hemispheric lateralisation data using the described criteria.

Session	Pre 200	Post 500
1	weak ipsilateral dominant	bilateral
2	bilateral	bilateral
3	bilateral	bilateral
4	weak ipsilateral dominant	bilateral

Table 87 Interpretation of participant P21's hemispheric lateralisation data for alpha ERD% for a 200 ms window preceding movement onset (Pre 200) and for a 500 ms window following movement onset (Post 500) (left arm movements).

When compared to the healthy group, this participant's hemispheric lateralisation of alpha ERD% was similar with slight differences. Variations over sessions are not indicative of changes due to rehabilitation.

8.3.6.4 Beta ERD

Frequency range

The frequency range within the beta range (13-30 Hz) at which beta ERD occurs at symmetrical electrodes CP3 and CP4 was examined by visually inspecting ERSP plots produced with EEGLAB's STUDY functions. Table 88 presents results for all sessions. Some incongruities were observed, in that the range within which beta ERD occurred was indistinguishable from the one within which alpha ERD occurred. In addition to this, the range was narrower for electrode CP4, on the contralateral hemisphere.

Electrode	Session 1	Session 2	Session 3	Session 4
CP3	6-25	6-25	6-25	6-25
CP4	6-20	6-20	6-20	6-20

Table 88 Frequency ranges, in Hz, at which beta ERD occurs for participant P21's sessions.

Beta ERD over time

For time frequency ERD/ERS maps for electrode sites CP3 and CP4, please refer to Figure 113 in the previous section. Figure 116 presents beta ERD/ERS% over time plots for pairs of symmetrical electrodes CP3/CP4 for all sessions.

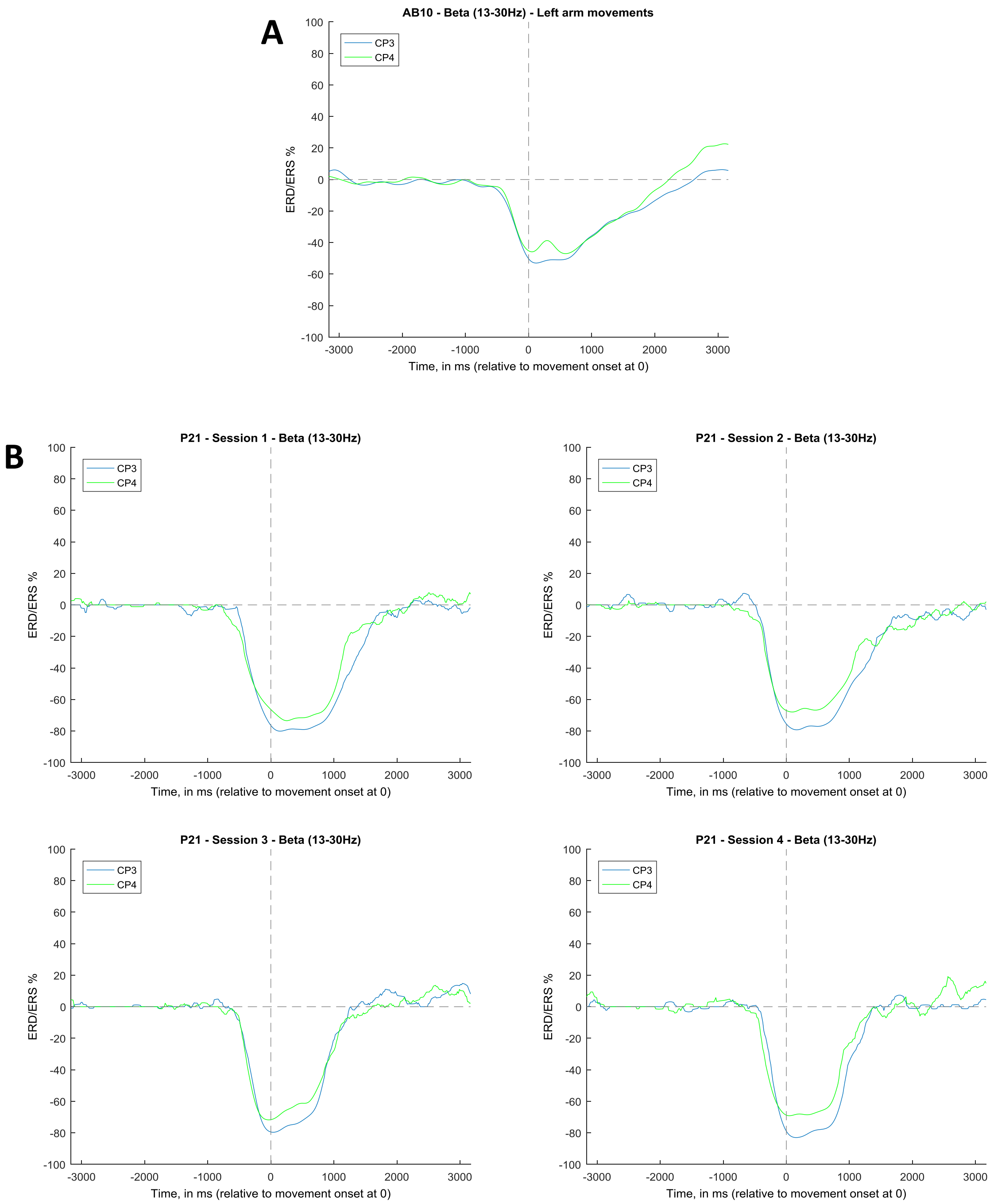


Figure 116 Plots of beta ERD/ERS% over time for symmetrical electrodes CP3/CP4 for (A) the healthy group (averaged), (B) participant P21 (left arm movements).

Table 89 presents peak beta ERD% values for electrode CP3 (the one with the greatest beta ERD% values from the plots above). Peaks were approximately matched according to time and placed in the same row in order to compare values. Peak beta ERD% values are high, with little variability between sessions. Values are greater than those for the healthy group's average (-53 %).

Session 1		Session 2		Session 3		Session 4	
Time	ERD%	Time	ERD%	Time	ERD%	Time	ERD%
150	-80.1	166	-79.3	38	-79.6	150	-83.0

Table 89 Participant P21's beta ERD% peak values for electrode CP3 for all sessions (times in ms) (left arm movements).

Hemispheric lateralisation

Figure 117 presents scalp maps of beta ERD/ERS for a 200 ms window preceding movement onset and for a 500 ms window following movement onset for participant P21.

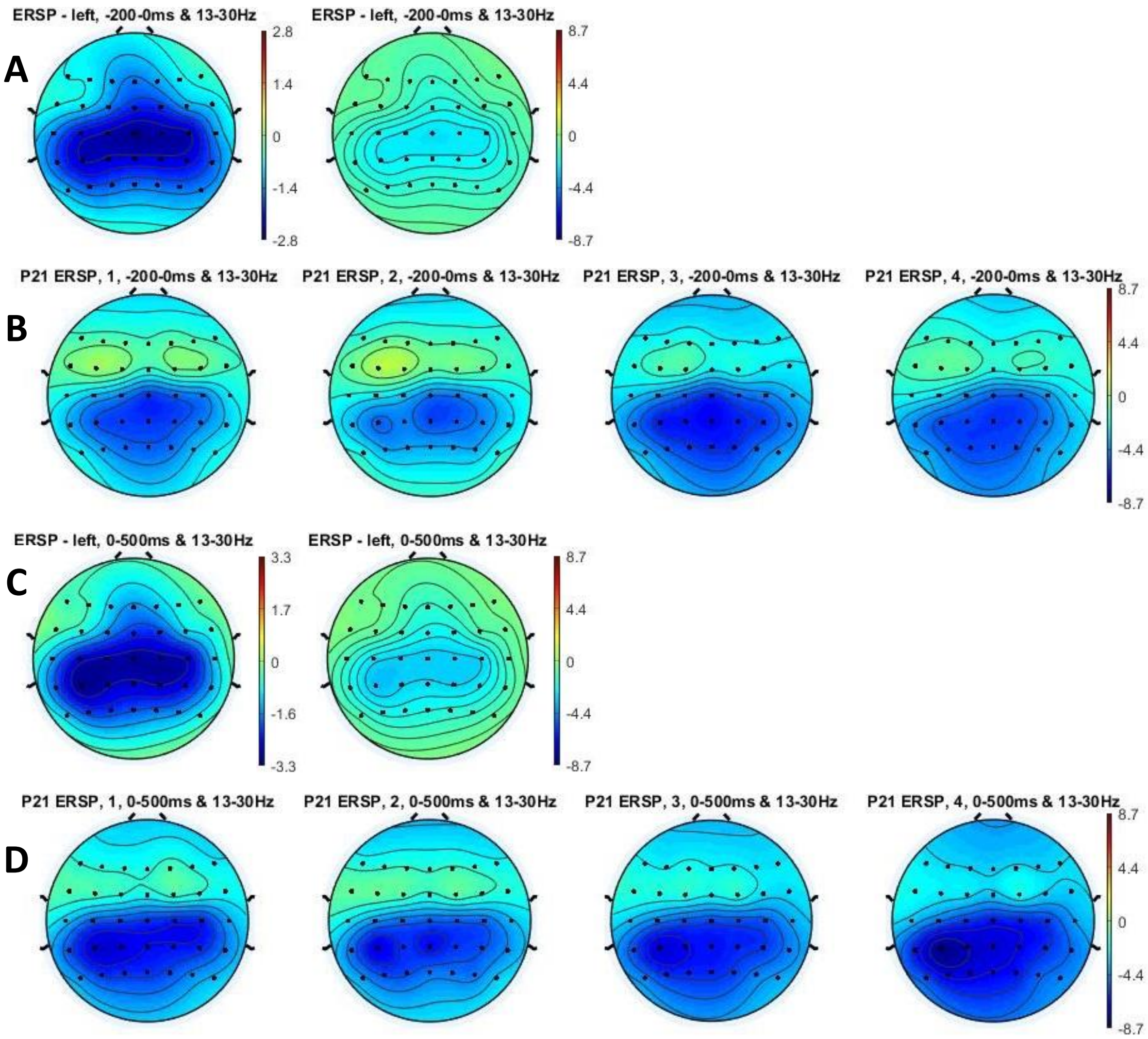


Figure 117 Scalp maps of beta ERD/ERS for a 200 ms window preceding movement onset for (A) the healthy group (averaged; two maps: original scale and adjusted to this participant's scale), (B) participant P21 for sessions 1 to 4, and for a 500 ms window following movement onset for (C) the healthy group (averaged; two maps as above), and (D) participant P21 for sessions 1 to 4 (left arm movements).

Table 90 presents values for areas over the curve and laterality indices (LI), as calculated with beta ERD% data for electrode pair CP3/CP4, for a period of 200 ms preceding movement onset and a period of 500 ms following movement onset.

Session	A_{CP3}		A_{CP4}		Laterality Index		L/R ratio	
	Pre 200	Post 500	Pre 200	Post 500	Pre 200	Post 500	Pre 200	Post 500
1	13220	38921	11850	35183	0.05	0.05	1.12	1.11
2	12851	38278	11957	32845	0.04	0.08	1.07	1.17
3	14368	37544	13524	32448	0.03	0.07	1.06	1.16
4	12873	39895	12328	33603	0.02	0.09	1.04	1.19

Table 90 Participant P21's areas over the curve A_{CP3} and A_{CP4} (in ERD% * ms units) and laterality indices for beta ERD% for electrode pair CP3/CP4 for a 200 ms window preceding movement onset (Pre 200) and for a 500 ms window following movement onset (Post 500) (left arm movements). L/R values = A_{CP3} / A_{CP4}.

Table 91 presents the interpretation of the hemispheric lateralisation data using the criteria described for alpha ERD in the previous section. When compared to the healthy group, this participant's hemispheric lateralisation of beta ERD% was similar.

Session	Pre 200	Post 500
1	bilateral	bilateral
2	bilateral	weak ipsilateral dominant
3	bilateral	weak ipsilateral dominant
4	bilateral	weak ipsilateral dominant

Table 91 Interpretation of participant P21's hemispheric lateralisation data for beta ERD% for a 200 ms window preceding movement onset (Pre 200) and for a 500 ms window following movement onset (Post 500) (left arm movements).

8.3.6.5 Beta ERS following movement

Spatial distribution

The spatial distribution varied for all sessions (see Figure 118). It was initially centred at Cz/CPz, except for session 1, where it was at Cz only. It then spread bilaterally (towards C3 and C4) for all sessions except session 2 (where it remained centred around Cz/CPz), with variations in intensity and spatial distribution, where for session 1 it was mostly to Cz/C2, for session 3 it was mostly to C3/Cz/CPz/C4, and mostly to Cz/CPz/C4 for session 4. This is different from results from the healthy group, where beta ERS peaks occur at Cz, CP2, and CP4, over the contralateral hemisphere.

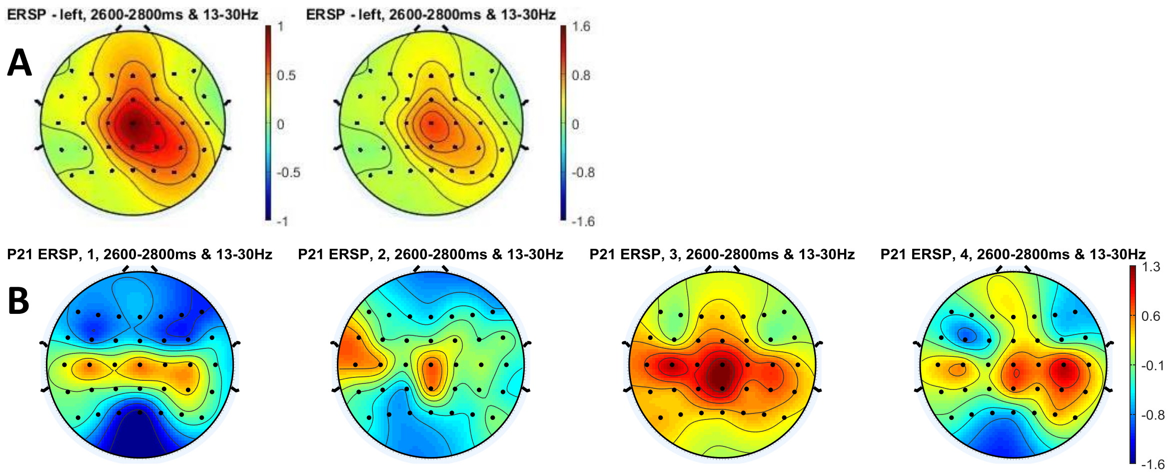


Figure 118 Scalp maps of beta ERS for (A) the healthy group (averaged; two maps: original scale and adjusted to this participant's scale), (B) participant P21 for sessions 1 to 4 (left arm movements).

Beta ERS over time

Figure 119 presents beta ERS% over time plots for select electrodes for all sessions.

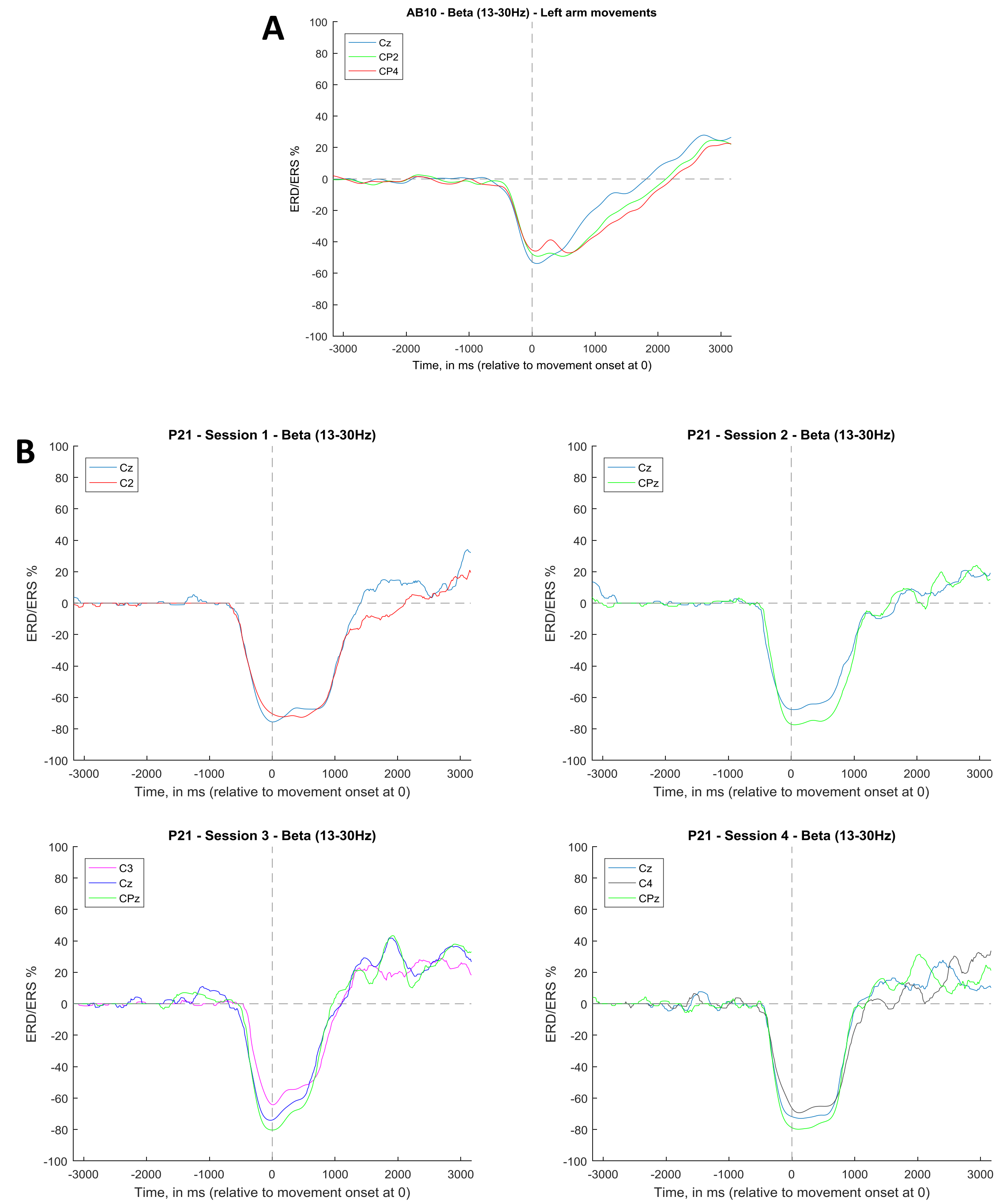


Figure 119 Plots of beta ERS% over time for (A) electrodes Cz, CP2, and CP4 for the healthy group (averaged), (B) select electrodes for participant P21 for all sessions (left arm movements).

Table 92 presents peak beta ERS% values for electrodes with the greatest ERS% values from the plots above: Cz for session 1 and CPz for all other sessions. The range of timings for beta ERS% peaks, as calculated by the difference in time between the earliest and latest peaks over the four sessions, is 252 ms for the first peak and 209 ms for the second peak. Values for all sessions vary greatly and are at times greater, and at times less than the healthy group's average (27.9 %).

Session 1 (Cz)		Session 2 (CPz)		Session 3 (CPz)		Session 4 (CPz)	
Time	ERS%	Time	ERS%	Time	ERS%	Time	ERS%
1787	15.0	1787	9.4	1911	43.4	2039	31.4
3120	34.0	2943	24.1	2911	38.0	3088	24.6

Table 92 Participant P21's beta ERS% peak values for select electrodes (times in ms) (left arm movements).

8.3.6.6 Summary and discussion of results

Participant P21's results for clinical assessments showed an improvement of nine points following rehabilitation for the Fugl-Meyer assessment, and of 15 points for the ARAT. Gains were also made with hand path ratio and time scores for the ArmeoSpring assessments, suggesting that this participant's ability to move their arm with more control and precision improved.

Mean movement times for sessions 3 and 4 were lower than for the first two sessions. As movement times depend on a variety of factors, such as the participant's alertness and motivation levels, it is not possible to say whether this increased speed of movement is solely due to improved arm function.

Some ERD/ERS measures deviated from the averaged results from the healthy group:

- Alpha ERD% peak values over both hemispheres were greater than for the healthy group's average.
- Beta ERD% peak values over both hemispheres were greater than for the healthy group's average.
- Beta ERS following movement was present over both hemispheres, rather than only over the contralateral hemisphere as seen in the healthy group.

Differences were found in the beta frequency range at which beta ERD occurred. For this participant, the range observed was indistinguishable from alpha ERD, and the range for the electrode on the contralateral hemisphere, CP4, was narrower than for symmetrical electrode CP3, suggesting impaired contralateral hemisphere function.

No changes in ERD/ERS measures could be attributed to the effects of rehabilitation despite important improvements in upper limb function at sessions 3 and 4. This suggests that there are mechanisms of cortical recovery that are not quantifiable using the ERD/ERS measures used in this study.

8.4 Discussion

This study's results answered the fourth, fifth, and sixth research questions:

- Do characteristics of ERD/ERS measures during reaching in a small sample of stroke participants differ from those observed in healthy participants?
- What changes, if any, does a period of robotic rehabilitation cause in ERD/ERS measures during reaching in these stroke participants?
- For these stroke participants, is there an association between potential changes in ERD/ERS measures and changes in measures of upper limb impairment and function?

Results show that for all the participants who took part in this study, a number of characteristics of ERD/ERS measures were different from averaged ERD/ERS measures described in the healthy participant study (see Chapter 7).

As stroke participants' measures of ERD/ERS were compared to averaged measures of ERD/ERS for healthy participants (a limitation of this study, discussed in the next section), and results from the test-retest variability study showed that measures of intensity of ERD/ERS can vary greatly between individuals, these comparisons do not necessarily indicate differences that can be attributed to stroke. The remainder of this discussion will therefore focus on findings relating to hemispheric lateralisation.

The first observations that can be made relate to ERD measures of hemispheric lateralisation for the planning phase of movement. Abnormal ipsilateral hemisphere predominance prior to movement onset was observed in two of the six participants, in both the alpha and beta range (P13 and P9). This is in accordance with previous literature findings that reported ipsilateral predominance in some stroke participants, with improvements (in the form of an increased contralateral activation) possible with time (Tangwiriyasakul et al. 2014), which was however not observed in this study.

The presence of a reduced alpha ERD for participants P4 and P20 over the ipsilateral hemisphere (relative to alpha ERD over the contralateral hemisphere) during movement indicates that ipsilateral hemisphere function has possibly been affected by stroke for these participants, and suggests that this may have occurred as a result of a compromised interhemispheric inhibitory mechanism, resulting in an excessive inhibitory influence over the ipsilateral hemisphere. This result differs from examples of imbalanced inhibition influences mentioned in the literature, where ipsilateral hemisphere activity is predominant and contralateral hemisphere activity is suppressed by a dysfunctional interhemispheric inhibition mechanism (Alia et al. 2017). A possible explanation for this difference is that ipsilateral hemisphere activity predominance is often observed in individuals with severe impairments. In this study, participants P4 and P20 had high levels of upper limb function, with scores above 50 for both ARAT and Fugl-Meyer clinical assessments. A tentative hypothesis to explain this result could be that as contralateral hemisphere function recovered, interhemispheric inhibition mechanisms remained or became imbalanced.

ERS was observed to occur in two participants before or during movement. Participant P11 presented with alpha ERS before movement over the ipsilateral hemisphere, and participant P9 showed alpha and beta ERS during movement, over the contralateral hemisphere for alpha ERS and bilaterally for beta ERS. For participant P11, a possible explanation relates to an excessive inhibitory influence over the ipsilateral hemisphere in the alpha frequency range (as for the beta frequency range, ipsilateral hemisphere activity was dominant). For participant P9, this can be explained by the fact that beta ERD occurred over the anterior portion of the area where it typically occurs. It is unknown why beta ERS occurred in the posterior portion of this area. To the researcher's knowledge, no published literature on movement-related ERD/ERS has reported ERS occurring before or during movement with stroke participants.

As per previously reported literature findings for some stroke participants (Alia et al. 2017), hemispheric lateralisation of ERD was found to be predominant over the ipsilateral hemisphere in three participants, in the beta frequency range during movement (participant P11) and in both the alpha and beta ranges before and during movement (participants P13 and P9). This suggests that for these participants, the ipsilateral hemisphere is compensating for impaired contralateral hemisphere function.

Beta ERS following movement was predominantly found to occur over the ipsilateral hemisphere for four out of six participants (consistently for participants P4, P11, P13, and inconsistently for participant P9, for two out of four session), in line with previous literature findings that showed that hemispheric lateralisation of post-movement ERS was predominant on the ipsilateral hemisphere for some stroke participants, with improvements possible with time (Eder et al. 2006), which was however not observed in this study. Results from the test-retest variability study (see Chapter 6) showed that some healthy participants presented with ipsilateral beta ERS following movement, but this was not frequent, and inconsistently across sessions for those who did. As post-movement beta ERS is present when the motor cortex deactivates (Pfurtscheller and Lopes da Silva 1999), this result would suggest that contralateral hemisphere activity may have difficulty returning to an idle state following the end of the movement for these participants.

Despite five out of six participants improving on upper limb function as measured by clinical assessments (all except participant P11), only two of these (participants P4 and P9) showed changes in ERD/ERS measures that could be attributed to the effects of rehabilitation, demonstrating, for these patients, an association with changes in measures of upper limb impairment and function. These changes related to hemispheric lateralisation of alpha ERD for participant P4, demonstrated by a decrease of excessive contralateral predominance (when compared to healthy participants), and to a hypothesised normalisation of interhemispheric inhibitory mechanisms demonstrated by a decrease in abnormal alpha and beta ERS during movement for participant P9. In some participants, some trends were observed that would suggest changes due rehabilitation, but these changes were within natural variability parameters described in the test-retest variability study (see Chapter 6). The absence of changes in ERD/ERS clearly attributable to rehabilitation in three participants (P13, P20, and P21) suggests that improved motor function is not necessarily reflected in changes of intensity or hemispheric lateralisation of ERD/ERS that are reported in the literature (Tangwiriyasakul et al. 2014). This is the most clearly illustrated by results for participant P21, who had the greatest increases in clinical assessment scores out of all participants. This participant presented with some of the most stable ERD/ERS measures across sessions. They were however the only one who presented with very high bilateral alpha and beta ERD, when compared to the other participants and the healthy group. This suggests a joint effort from both hemispheres, free of any strong interhemispheric inhibitory mechanism. The absence of changes in ERD/ERS measures in the presence of improved upper limb function in three participants (participants P13, P20, and P21) could however suggest alternative explanations. Measures of ERD/ERS used in this study may not be sufficiently responsive to the degree of improvements observed in upper limb function observed in individuals taking part in this study. It is not clear whether this might be the case as the participant who improved the most, participant P21, was not one of the participants who showed changes in ERD/ERS measures that could be attributed to the effects of rehabilitation. Another possible explanation could be that rehabilitation sessions need to occur over a longer time period to allow neural connections to reorganise in a way that would translate into changes in measures of ERD/ERS that would follow a clearer trend of recovery. This was observed for participant P4, whose changes were mostly observed at session 4 and not at session 3, immediately after the end of the rehabilitation programme. This explanation is however debateable as it would be expected that cortical activity changes are required for improved motor function, or that at least both would simultaneously influence and reciprocally induce changes in each other. Another potential explanation relates to the fact that a reaching movement, involving several joints, was used for this study. When several joints are moved simultaneously, ERD is not as spatially focused and occurs over large cortical areas, including precentral, central, and posterior areas (Pfurtscheller et al. 1999). This might result in changes being less apparent than they would have been had a finger, hand, or wrist movement been performed.

Limitations

This study's sample size was small and cortical changes attributed to rehabilitation were sparse. These results therefore did not provide an extensive answer as to how improvements in motor function facilitated by robotic upper limb rehabilitation affected cortical activity after stroke in these participants. Another limitation refers to the fact that only two participants were in the subacute phase of stroke, with the remaining four being in the chronic phase of stroke, who typically have a lower potential for recovery. It was also not possible to recruit participants with more severe impairments, as minimum movement requirements for the use of the ArmeoSpring rehabilitation device as well as for EEG data collection were in some cases too great for potential participants to take part in the study. Recruitment of participants was a challenge, and it is hypothesised that this was due to improved post-discharge rehabilitation services (in the public health service) in the local area that offer intensive rehabilitation over a number of weeks after discharge from hospital.

Stroke participants' measures of ERD/ERS were compared to averaged measures of ERD/ERS for healthy participants, and differences were reported as such. This comparison is however limiting in that it is possible that stroke participants' measures did not deviate from some individual results from the healthy participant group. Further work to examine data in more detail could be carried out to analyse individual ERD/ERS measures for every healthy participant, and to subsequently identify the range of results across all healthy participants, which would allow for a more detailed comparison and increased robustness of results.

Another limitation concerns scores obtained with the ArmeoSpring assessments. It is unknown whether greater scores where exclusively due to improved upper arm function. It is possible that increased familiarity with the system and practice (as the rehabilitation programme involved similar movements using the same device) accounted for superior scores. To determine whether this is the case, a study involving healthy participants being assessed in the same way would be helpful.

EMG data was recorded at the same time as EEGs but not used for analysis. It had been considered that corticomuscular coherence could also be investigated, but further research into this area revealed that corticomuscular coherence only occurs during maintained isometric contractions (Niedermeyer and Lopes da Silva 2005), which were not part of the required movement task for this study.

8.5 Conclusion

Measures of ERD/ERS were characterised for a reaching movement in a small sample of stroke participants before and after a period of robotic upper limb rehabilitation. They were compared to those observed in healthy participants, and changes following rehabilitation were investigated. The next chapter concludes the thesis with a summary of findings, and proposals for potential future research.

Chapter 9: Conclusion

This chapter concludes the thesis by presenting the findings of all the studies reported in the thesis, as well as proposals for future research.

9.1 Summary of findings

1. Are recruitment procedures, data collection and data analysis methods developed for this study effective to investigate ERD/ERS measures during reaching?

Results from the feasibility study showed that data collection and data analysis methods were effective, in that results were reasonable with regards to movement-related ERD/ERS being elicited in all participants in the expected cortical areas and bandwidths, in line with previous movement-related EEG literature findings (see Chapter 5). Issues relating to recruitment, recording of EEG data, and data processing were identified and solutions proposed for subsequent studies.

2. What is the variability over time of ERD/ERS measures during reaching for a small sample of healthy participants?

A test-retest variability study determined the degree of variability of ERD/ERS measures for a reaching movement among healthy participants (see Chapter 6). These results were used to investigate changes in ERD/ERS measures of individuals taking part in the stroke participant study, to determine whether changes were due to natural variability or whether they could be attributed to the effects of rehabilitation.

3. What are the characteristics of ERD/ERS measures during reaching for healthy participants?

Measures of ERD/ERS were characterised for a reaching movement in a healthy population by averaging data from a group of ten participants, with many being congruent with previous literature findings (see Chapter 7). Results were used to compare ERD/ERS measures from a small sample of individuals taking part in the stroke participant study.

4. Do characteristics of ERD/ERS measures during reaching in a small sample of stroke participants differ from those observed in healthy participants?

Measures of ERD/ERS were characterised for a reaching movement in a small sample of stroke participants before and after a period of robotic upper limb rehabilitation. They were then compared to healthy participants' averaged measures, and changes following rehabilitation were investigated (see Chapter 8).

- All participants had a number of characteristics of ERD/ERS measures that were different from averaged ERD/ERS measures observed in the healthy participant study.
- Two participants (P4 and P20) presented with reduced alpha ERD over the ipsilateral hemisphere, indicating that ipsilateral hemisphere function was affected by stroke for these participants, and suggests that this may have occurred as a result of a compromised interhemispheric inhibitory mechanism, resulting in an excessive inhibitory influence over the ipsilateral hemisphere.
- Hemispheric lateralisation of ERD was found to be predominant over the ipsilateral hemisphere in three participants (P11, P13, and P9), suggesting that the ipsilateral hemisphere is compensating for impaired contralateral hemisphere function.
- Beta ERS following movement was predominantly found to occur over the ipsilateral hemisphere for four participants (consistently for participants P4, P11, P13, and inconsistently for participant P9), suggesting that, as post-movement beta ERS is present when the motor cortex deactivates, contralateral hemisphere activity may have difficulty returning to an idle state for these participants.

5. What changes, if any, does a period of robotic rehabilitation cause in ERD/ERS measures during reaching in these stroke participants?

6. For these stroke participants, is there an association between potential changes in ERD/ERS measures and changes in measures of upper limb impairment and function?

Two participants showed changes in ERD/ERS measures that could be attributed to the effects of rehabilitation, with associations made with measures of upper limb impairment and function. These changes related to hemispheric lateralisation of alpha ERD, as demonstrated by a decrease of excessive contralateral predominance (when compared to healthy participants), and to a hypothesised normalisation of interhemispheric inhibitory mechanisms demonstrated by a decrease in abnormal alpha and beta ERS during movement.

9.2 Limitations and potential future research

9.2.1 Start of muscle contractions and movement onset

In this study movement onset markers were determined by using data from the potentiometer that was attached to the reaching device. Movement onset was set to the time at which the movable trough of the reaching device started moving. As stabilisation of the scapula and of the glenohumeral joint is required prior to the start of shoulder flexion (required for a reaching movement), muscle contraction of the serratus anterior, rhomboids, levator scapulae, trapezii, and of rotator cuff muscles are occurring prior to movement. The implication is that a delay occurs between the start of muscle contractions and the time of the movement onset as it was determined in this study, which potentially decreases the accuracy of the timings of the pre- and post- movement onset phases. To investigate this delay, EMG could be recorded (in both healthy and stroke participants) over further muscles involved in reaching to determine individual muscles' time lags in relation to the time at which displacement of the trough begins. Findings would help determine the extent of this delay and to ascertain whether using EMG instead of data from a potentiometer might be preferable as a means of setting movement onset marker times.

9.2.2 Movement repetitions and fatigue

In this study participants were required to perform 150 movement repetitions with each arm (except for those part of the healthy participant group, who performed 80 with each arm). Although reaching movements were performed with the forearm supported and over a time period of approximately 45 minutes with breaks between blocks of 25 movements, it is possible that muscle fatigue may have gradually affected EEG signals over time, particularly for stroke participants, whose affected arms often fatigue more quickly than healthy participants'. To investigate a potential pattern of change, ERD/ERS measures from movements performed at the beginning of a recording session could be compared to those performed towards the end of the session. If findings show that fatigue significantly affects ERD/ERS measures, a smaller number of movement repetitions could be used, ensuring that it is sufficient to produce reliable results whilst avoiding the effects of fatigue over time.

9.2.3 Test-retest variability study sample size

As mentioned in Chapter 6, data from a small sample of five healthy participants was analysed to examine test-retest variability of ERD/ERS measures. In order to obtain a better estimate of the range of measures found in the general population, further work could involve increasing the sample size by recruiting additional participants to this study.

9.2.4 Spatial distribution of ERD/ERS

In this study the individual spatial distribution of ERD/ERS was not examined objectively. A preliminary visual inspection of scalp maps did not result in any obvious findings however this could be further explored more systematically by using objective analysis methods. This could be achieved by applying a centre of gravity calculation to each scalp map's area of ERD to determine potential patterns of differences and displacements. This analysis would be helpful to further characterise test-retest variability in healthy participants, to determine whether there are differences between healthy and stroke participants, and to identify any potential patterns of change as a result of stroke participants undergoing a period of rehabilitation.

9.2.5 Further investigation of responsiveness

The lack of identifiable cortical activity changes attributed to rehabilitation and improved motor function in the stroke participant study indicates that further work is required to determine the responsiveness of the methods used, in terms of dosage of the rehabilitation programme over time, the movement performed during recordings, and the period of time over which measurements are made. Such an investigation could thus involve stroke participants attending rehabilitation sessions over a longer period of time, performing a single joint movement during EEG recordings (in addition to a reaching movement), with measurements taking place over a number of months to establish in what conditions cortical activity changes attributable to rehabilitation can be observed.

9.2.6 MRCP analysis

In this study movement-related ERD/ERS measures were analysed. It would also be possible to analyse the EEG data collected as part of this study in an additional way, by examining movement-related cortical potentials (MRCPs). As part of this analysis, MRCP amplitude, length, and spatial localisation would be examined in line with previous studies. It is unknown whether analysis of MRCPs would be more effective than ERD/ERS measures in identifying cortical activity changes attributable to rehabilitation.

9.2.7 Implications for stroke rehabilitation research

Even though the number of participants for the stroke participant study was small, the variety of results observable, in terms of ERD/ERS measures and presence or absence of changes associated with improved motor function after rehabilitation, indicates that stroke affects individuals' cortical activity in different ways and that patterns of recovery (even though only two participants showed changes that could be attributed to rehabilitation) also vary between individuals. This supports the concept of tailored individual rehabilitation programmes that would take into account the neural status of the individual, such as the integrity of the corticospinal tract as measured with TMS and EMG, as well as measures of cortical activity such as those used for this study, and known effects of rehabilitation modalities on motor cortex activity.

As some of the stroke participants' ERD/ERS measures of hemispheric laterality were affected in this study, interventions that can modulate interhemispheric inhibition mechanisms would be of particular interest. Non-invasive brain stimulation (NIBS) techniques, such as TMS, theta-burst stimulation (TBS), and transcranial direct current stimulation (tDCS) could be used to counter a maladaptive lateralisation of cortical activity by increasing or decreasing the excitability of ipsilesional and/or contralesional hemispheres (Alia et al. 2017). In addition to this, other rehabilitation modalities that have been shown to have an effect on hemispheric excitability such as mirror therapy, which can increase the excitability of neurons over the ipsilesional hemisphere (Garry et al. 2005), or bilateral therapy, which can increase cortical activity over the contralesional hemisphere (Luft et al. 2004a), could also be considered for future research in which analysis of ERD/ERS measures developed for this study could be used to monitor cortical activity responses.

9.3 Conclusion

Current research efforts in the field of restorative neuroscience aim to further understand brain function after stroke and the effects of various rehabilitation approaches on motor cortex activity. For this to occur, measurement tools with adequate psychometric properties are required to assess and monitor motor cortex activity over time. They can be used to investigate and identify patterns of cortical recovery, based on several factors such as baseline upper limb motor function and neural status, time since stroke, and effects of rehabilitation modalities. This knowledge will allow clinicians to make improved informed predictions of an individual's cortical and motor function recovery, as well as to further guide their choices of rehabilitation modalities.

The results of this study have contributed to this area of stroke research through initiating the creation and development of a method to examine movement-related cortical activity among people who have had a stroke, as measured by analysis of ERD/ERS during a standardised reaching movement. Test-retest variability of ERD/ERS measures were investigated in a small group of healthy participants, and averaged data from another group was analysed to characterise ERD/ERS measures in a healthy sample of participants. The same measures were then characterised for a small group of stroke participants, before and after a period of robotic upper limb rehabilitation. Results from the present study warrant further work to investigate the responsiveness of the methods used with a view to develop a model of cortical recovery after stroke based on ERD/ERS measures that could then be tested with a larger group of participants.

Appendices

Appendix A Ethical Approval

NHS

National Research Ethics Service
SOUTHAMPTON & SOUTH WEST HAMPSHIRE
RESEARCH ETHICS COMMITTEE (A)

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CM/sta

05 February 2010

Mr Sebastien Pollet
Occupational Therapist,
MPhil/PhD student (University of Southampton)
Southampton City NHS Primary Care Trust
Western Community Hospital
William McLeod Way, Millbrook
Southampton
SO16 4XE

Dear Mr Pollet

Study Title:	**Cortical activity changes among stroke patients following robotic upper limb rehabilitation as measured by EEG during reaching movements.**
REC reference number:	**09/H0502/126**
Protocol number:	**5**

Thank you for your letter of 01 February 2010, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Vice-Chair.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Ethical review of research sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

The Committee has not yet been notified of the outcome of any site-specific assessment (SSA) for the non-NHS research site(s) taking part in this study. The favourable opinion does not therefore apply to any non-NHS site at present. I will write to you again as soon as one Research Ethics Committee has notified the outcome of a SSA. In the meantime no study procedures should be initiated at non-NHS sites.

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

<u>Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.</u>

This Research Ethics Committee is an advisory committee to South Central Strategic Health Authority

The National Research Ethics Service (NRES) represents the NRES Directorate within the National Patient Safety Agency and Research Ethics Committees in England

For NHS research sites only, management permission for research ("R&D approval") should be obtained from the relevant care organisation(s) in accordance with NHS research governance arrangements. Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at http://www.rdforum.nhs.uk. *Where the only involvement of the NHS organisation is as a Participant Identification Centre, management permission for research is not required but the R&D office should be notified of the study. Guidance should be sought from the R&D office where necessary.*

Sponsors are not required to notify the Committee of approvals from host organisations.

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	*Version*	*Date*
Covering Letter		11 November 2009
REC application		06 October 2009
Protocol	5	28 October 2009
Investigator CV: Mr S Pollet		11 November 2009
Participant Consent Form: Collect Medical Information	1	09 September 2009
Participant Consent Form: Healthy	2	23 September 2009
GP/Consultant Information Sheets	1	09 September 2009
Evidence of insurance or indemnity		14 October 2009
Letter from Sponsor		29 October 2009
Referees or other scientific critique report: Cheryl Metcalf		10 September 2009
Questionnaire: Health	1	09 September 2009
Thank you Letter	1	09 September 2009
Feedback Form	1	09 September 2009
Referees or other scientific critique report: Geert Verheyden		10 September 2009
Investigator CV: Professor J Burridge		27 February 2009
Participant Information Sheet: Stroke	5	21 January 2010
Participant Information Sheet: Healthy	5	21 January 2010
Participant Consent Form: Stroke	3	21 January 2010
Advertisement	2	21 January 2010
Timetable of Sessions	2	21 January 2010
Response to Request for Further Information		01 February 2010

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Now that you have completed the application process please visit the National Research Ethics Service website > After Review

You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the website.

The attached document *"After ethical review – guidance for researchers"* gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Progress and safety reports
- Notifying the end of the study

The NRES website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

We would also like to inform you that we consult regularly with stakeholders to improve our service. If you would like to join our Reference Group please email referencegroup@nres.npsa.nhs.uk.

09/H0502/126	**Please quote this number on all correspondence**

Yours sincerely

Dr Chris Markham
Vice-Chair

Email: scsha.SWHRECA@nhs.net

Enclosures: "After ethical review – guidance for researchers" *SL- AR2*

Copy to: *Mrs Christine McGrath, Southampton University Hospital NHS Trust*

This Research Ethics Committee is an advisory committee to South Central Strategic Health Authority

The National Research Ethics Service (NRES) represents the NRES Directorate within the National Patient Safety Agency and Research Ethics Committees in England

Appendix B R&D Approvals

Southampton City NHS
Primary Care Trust

Shared Research Management & Governance Service
2nd Floor, Adelaide Health Centre
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Tel: 023 8060 8925

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Sebastien Pollett
69 Newlands Avenue
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SO15 5EQ

Wednesday, 14 April 2010

Dear Mr Pollett

Study: Cortical changes in stroke following rehabilitation
Research Ref: MWP/005/10

I am pleased to tell you that the above project has been approved by the Southampton City Primary Care Trust.

R&D approval is separate from ethics approval and is also essential for the conduct of research within NHS trusts. It is subject to the following requirements.

1) It is a condition of the approval that the project is carried out according to Good Clinical Practice and within the guidelines of the NHS Research Governance Framework. You have responsibility for ensuring that you and any co-workers adhere to the protocol agreed by the ethics committee.

2) If there are any alterations to the protocol after the study has commenced, you must inform the Research Ethics Committee and the Trust Research Management & Governance (RM&G) Office.

3) It is my duty to remind you that as Chief Investigator you may be required to provide us with project monitoring and outcome information.

In the event that you have applied to have this study adopted onto the UKCRN Clinical Research Portfolio, we take this opportunity to remind you of your responsibility for uploading accrual data for our organisation should adoption subsequently be confirmed and we become a participating site. (http://www.ukcrn.org.uk/index/clinical/portfolio_new/P_accrual.html)

Please do not hesitate to contact us should you require any additional information or support

Yours sincerely

Dr R Patel
R&D Lead

Trust Headquarters, Oakley Road, Southampton SO16 4GX
Telephone: 023 8029 6904 Fax: 023 8029 6960
Website: www.southamptonhealth.nhs.uk

Southampton University Hospitals NHS Trust NHS

Please reply to: Research and Development
Duthie Building (Trust) MP138
Southampton General Hospital
Tremona Road Southampton SO16 6YD

Telephone: 02380 794245
Fax: 02380 798678
E-mail: Victoria.McArdell@suht.swest.nhs.uk

Mr Sebastien Pollet
Uni of S/ton
School of Health Sciences
Postgraduate student office
Highfield Campus Building 45
Southampton
SO17 1BJ

29 March 2010

Dear Mr Pollet

ID: rhm neu0151 Cortical activity changes among stoke patients following robotic upper limb rehabilitation as measured by EEG during reaching movements

EudraCT:

Thank you for submitting all the required documentation for Trust R&D approval. I write to inform you that your study has full SUHT R&D approval. Please find attached the Conditions of Trust R&D approval which you are obliged to adhere to.

You are required to keep copies of all your essential documents relating to this study. Please download a copy of the relevant Investigator Site File template from the R&D website: http://tinyurl.com/p8vuek.

Your project is subject to R&D monitoring and you will be contacted by our office to arrange this.

Please note: A condition of approval is that any changes need to be timeously notified to the R&D office. This includes providing copies of:

. All NRES substantial amendments and favourable opinions;
. All Serious Adverse Events (SAEs);
. NRES Annual Progress Reports;
. Annual MHRA Safety Reports;
. NRES End of Study Declaration;
. Notifications of significant breaches of GCP or protocol

Please quote the above RHM No. on any correspondence with our office.

Should you, or any of your team, require training in any of the policies and procedures required to ensure compliance with the conditions of approval, please refer to the R&D Training website http://tinyurl.com/prkd65 for an up-to-date calendar of training events.

Yours singerely

Victoria McArdell
Research Governance Officer

Appendix C Sponsorship

Southampton University Hospitals NHS Trust NHS

Please reply to: Research and Development
Duthie Building (Trust) MP138
Southampton General Hospital
Tremona Road Southampton SO16 6YD

Telephone: 02380 794245
Fax: 02380 798678
E-mail: Victoria.McArdell@suht.swest.nhs.uk

Mr Sebastien Pollet
Uni of S/ton
School of Health Sciences
Postgraduate student office
Highfield Campus Building 45
Southampton
SO17 1BJ

29 October 2009

Dear Mr Pollet

ID: rhm neu0151 Cortical activity changes among stoke patients following robotic upper limb rehabilitation as measured by EEG during reaching movements

Re: NHS Research Governance and Identification of Nominated Research Sponsor

I am writing to confirm that Southampton University Hospitals NHS Trust is prepared to act, in principle, as sponsor for this study under the terms of the Department of Health Research Governance Framework for Health and Social Care.

SUHT's final acceptance of sponsorship responsibilities is dependent on full R&D approval, which will incorporate evidence of adequate funding to conduct your study.

SUHT fulfills the role of research sponsor in ensuring management, monitoring and reporting arrangements for research. I understand that you will be acting as the principal investigator responsible for the daily management for this study, and that you will be providing regular reports on the progress of the study to the Trust on this basis.

I would like to take this opportunity to remind you of your responsibilities under the terms of the Research Governance Framework for researchers, principal investigators and research sponsors, that it is a requirement of the terms and conditions of approval that you become fully conversant with the Research Governance Framework on Health and Social Care document which is available from : http://www.dh.gov.uk/en/Policyandguidance/Researchanddevelopment/index.htm

Please do not hesitate to contact us should you require any additional information or support.

May I also take this opportunity to wish you every success with your research.

Yours sincerely

Victoria McArdell

Research Governance Officer

Appendix D Insurance

UNIVERSITY OF Southampton

Mr Sebastien Pollet
School of Health Sciences
University of Southampton
University Road
Highfield
Southampton
SO17 1BJ

19 February 2010

Dear Mr Pollet

Professional Indemnity and Clinical Trials Insurance

RGO REF - 6762 NHS R&D RHM - NEU0151
REC No - 09/H0502/126

Project Title Cortical Activity Changes Among Stroke Patients Following Robotic Upper Limb Rehabilitation as Measured by EEG During Reaching Movements

Participant Type:	No Of Participants:	Participant Age Group:	Notes:
Patients	20	Adults	
Healthy volunteers	20	Adults	

We have now received notification of NRES approval; we can confirm that insurance is now activated and you may now begin your project.

Good luck with your project.

Yours sincerely

Mrs Ruth McFadyen
Insurance Services Manager

Tel: 023 8059 2417
email: hrm@soton.ac.uk

cc: File

Finance Department, University of Southampton, Highfield Campus, Southampton SO17 1BJ United Kingdom
Tel: +44 (0) 23 8059 5000 Fax: +44 (0) 23 8059 2195 www.southampton.ac.uk

Appendix E Participant Information Sheet

Participant Information Sheet

for healthy participants

Study Title:	Cortical activity changes among stroke patients following robotic upper limb rehabilitation as measured by EEG during reaching movements.
Researcher:	Sebastien Pollet This research study forms the basis for the award of an MPhil/PhD from the University of Southampton.
Ethics number:	09/H0502/126

Please read this information carefully before deciding to take part in this research. If you are happy to participate you will be asked to sign a consent form.

What is the research about?

The first part of the study will examine what happens in the brains of people who have had a stroke when they move their arm. People who have never had a stroke, like yourself, are also required for comparison purposes. In this study, brain activity is measured using electroencephalography (EEG), which involves placing a cap containing recording electrodes over your head to measure your brain's electrical activity (see Figure 1). A special gel is used underneath each electrode to make sure the electrical signals from the brain reach the recording electrodes (there are hair-washing facilities within the EEG lab to wash away the gel once recording is finished). The cap is connected to a computer to record the signals. Electrodes are placed over your arm to detect when you start moving it. Additional electrodes will be placed next to your eyes to record when you blink (as blinking distorts the data), and on your ears (as a reference electrode). To measure brain activity, you will be asked to reach forwards with one of your arms several times using a reaching device.

Figure 1. Electroencephalography (EEG) cap (Neuroscan 2008)

How will I know if I can take part?

If you are interested in participating in the study, you will need to contact the researcher (contact details are included at the end of this document). The researcher will then visit you to answer all the questions you may have. If you are still interested, the researcher will need to make sure that you meet all requirements before you officially participate in the study. To do this, the researcher will ask you to complete a health questionnaire. If all criteria are met, you will be formally invited to participate in the study. If you accept, you will be asked to sign a consent form.

Do I have to take part?

It is your choice whether you participate or not. There is nothing to do if you do not wish to participate.

What will happen to me if I take part?

The study requires that you visit the University of Southampton for a total of 3 times, over 2 weeks. Sessions will consist of recording EEG brain signals while you reach forward several times. Figure 2 shows the timeline of sessions.

Figure 2. Timeline of sessions

How will I get to the University of Southampton?

You will need to make your own way to the campus. The researcher will however offer to contribute up to £5 per visit to cover your transport costs. Free car parking is available.

Are there any benefits in my taking part?

Results from the study will add to what is known about brain activity in people who have had a stroke. This may benefit people who have strokes in the future, if these results lead to the development of better rehabilitation techniques. It is not expected that you will benefit directly as a result from your participation in the study.

Are there any risks involved?

There are no known physical or psychological risks associated with EEG data collection. There is also a small risk of skin allergy to gels used for EEG data collection.

Will my participation be confidential?

Only your GP will be informed of your participation in this study, with your permission. To ensure confidentiality, all information about you will be kept in locked filing cabinets, in a locked office at the University of Southampton. Anonymisation will be achieved by physically separating information about you into two separate folders. Anonymisation is about keeping your personal information (for example name, date of birth, medical information) apart from your EEG data. Personal information will be stored in a filing cabinet and the rest of the information in another. A number will be assigned to you, which will be used to link both sets of information. The researcher will ensure that all the information that is kept on digital media (such as computers and memory sticks) is password-protected. Guidelines from the University of Southampton Data Protection Policy will be followed.

What happens if I change my mind?

You have the right to withdraw at any time during the study without giving an explanation. If you do withdraw, your legal rights will not be affected.

What happens if something goes wrong?

If you have a concern or a complaint about this study you should contact Martina Prude, Head of the Governance Office, at the Research Governance Office (Address: University of Southampton, Building 37, Highfield, Southampton, SO17 1BJ ; Tel: +44 (0)23 8059 5058; Email: rgoinfo@soton.ac.uk . If you remain unhappy and wish to complain formally Martina Prude can provide you with details of the University of Southampton Complaints Procedure. This research study is covered by the University of Southampton Professional Indemnity and Clinical Trials Insurance.

I'm interested in the study. Where can I get more information?

Please contact the researcher, **Sebastien Pollet**, either:

- by phone : 0798 366 7610
- by mail: Sebastien Pollet
  Building 45 (Faculty of Health Sciences)
  Highfield Campus
  University of Southampton
  Southampton
  SO17 1BJ
- by email: sebastien.pollet@soton.ac.uk

You may also contact **Professor Jane Burridge**, who is supervising the study:

- by phone : 02380 598885
- by mail: Professor Jane Burridge
  Building 45 (Faculty of Health Sciences)
  Highfield Campus
  University of Southampton
  Southampton
  SO17 1BJ
- by email: J.H.Burridge@soton.ac.uk

For independent advice about participating in research, you may contact **Martina Prude**, Head of the Governance Office at the University of Southampton (please see 'What happens if something goes wrong?' section above for contact details).

Appendix F Participant Information Sheet

Participant Information Sheet

for healthy participants

Study Title:	Cortical activity changes among stroke patients following robotic upper limb rehabilitation as measured by EEG during reaching movements.
Researcher:	Sebastien Pollet This research study forms the basis for the award of an MPhil/PhD from the University of Southampton.
Ethics number:	09/H0502/126

Please read this information carefully before deciding to take part in this research. If you are happy to participate you will be asked to sign a consent form.

What is the research about?

The first part of the study will examine what happens in the brains of people who have had a stroke when they move their arm. People who have never had a stroke, like yourself, are also required for comparison purposes. In this study, brain activity is measured using electroencephalography (EEG), which involves placing a cap containing recording electrodes over your head to measure your brain's electrical activity (see Figure 1). A special gel is used underneath each electrode to make sure the electrical signals from the brain reach the recording electrodes (there are hair-washing facilities within the EEG lab to wash away the gel once recording is finished). The cap is connected to a computer to record the signals. Electrodes are placed over your arms to detect when you start moving them. Additional electrodes will be placed next to your eyes to record when you blink (as blinking distorts the data), and on your ears (as a reference electrode). To measure brain activity, you will be asked to reach forwards with both of your arms several times using a reaching device.

Figure 1. Electroencephalography (EEG) cap (Neuroscan 2008)

How will I know if I can take part?

If you are interested in participating in the study, you will need to contact the researcher (contact details are included at the end of this document). The researcher will then visit you to answer all the questions you may have. If you are still interested, the researcher will need to make sure that you meet all requirements before you officially participate in the study. To do this, the researcher will ask you to complete a health questionnaire. If all criteria are met, you will be formally invited to participate in the study. If you accept, you will be asked to sign a consent form.

Do I have to take part?

It is your choice whether you participate or not. There is nothing to do if you do not wish to participate.

What will happen to me if I take part?

The study requires that you visit the University of Southampton once. The session will consist of recording EEG brain signals while you reach forward several times.

How will I get to the University of Southampton?

You will need to make your own way to the campus. The researcher will however offer to contribute up to £5 per visit to cover your transport costs. Free car parking is available.

Are there any benefits in my taking part?

Results from the study will add to what is known about brain activity in people who have had a stroke. This may benefit people who have strokes in the future, if these results lead to the development of better rehabilitation techniques. It is not expected that you will benefit directly as a result from your participation in the study.

Are there any risks involved?

There are no known physical or psychological risks associated with EEG data collection. There is also a small risk of skin allergy to gels used for EEG data collection.

Will my participation be confidential?

Only your GP will be informed of your participation in this study, with your permission. To ensure confidentiality, all information about you will be kept in locked filing cabinets, in a locked office at the University of Southampton. Anonymisation will be achieved by physically separating information about you into two separate folders.

Anonymisation is about keeping your personal information (for example name, date of birth, medical information) apart from your EEG data. Personal information will be stored in a filing cabinet and the rest of the information in another. A number will be assigned to you, which will be used to link both sets of information. The researcher will ensure that all the information that is kept on digital media (such as computers and memory sticks) is password-protected. Guidelines from the University of Southampton Data Protection Policy will be followed.

What happens if I change my mind?

You have the right to withdraw at any time during the study without giving an explanation. If you do withdraw, your legal rights will not be affected.

What happens if something goes wrong?

If you have a concern or a complaint about this study you should contact Martina Prude, Head of the Governance Office, at the Research Governance Office (Address: University of Southampton, Building 37, Highfield, Southampton, SO17 1BJ ; Tel: +44 (0)23 8059 5058; Email: rgoinfo@soton.ac.uk . If you remain unhappy and wish to complain formally Martina Prude can provide you with details of the University of Southampton Complaints Procedure. This research study is covered by the University of Southampton Professional Indemnity and Clinical Trials Insurance.

I'm interested in the study. Where can I get more information?

Please contact the researcher, **Sebastien Pollet**, either:

- by phone : 0798 366 7610
- by mail: Sebastien Pollet
  Building 45 (Faculty of Health Sciences)
  Highfield Campus
  University of Southampton
  Southampton
  SO17 1BJ
- by email: sebastien.pollet@soton.ac.uk

You may also contact **Professor Jane Burridge**, who is supervising the study:

- by phone : 02380 598885
- by mail: Professor Jane Burridge
  Building 45 (Faculty of Health Sciences)
  Highfield Campus
  University of Southampton
  Southampton
  SO17 1BJ
- by email: J.H.Burridge@soton.ac.uk

For independent advice about participating in research, you may contact **Martina Prude**, Head of the Governance Office at the University of Southampton (please see 'What happens if something goes wrong?' section above for contact details).

Appendix G Health Questionnaire

Health Questionnaire

(Healthy Participants)

Study Title:	Cortical activity changes among stroke patients following robotic upper limb rehabilitation as measured by EEG during reaching movements.
Researcher:	Sebastien Pollet
Ethics number:	09/H0502/126

Information will only be used for the purposes of the study.

Guidelines from the University of Southampton Data Protection Policy will be followed.

Name of participant: ………………………………………………………………………...

Date of birth: ……………………………………………………………………………………….

Please complete all sections.

If you answer 'yes' to any question, please give details in the spaces provided.

Medical History

Have you ever had or do you have now, any of the following?

	Yes	**No**	**Not Sure**
Neurological disorder affecting central or peripheral nervous system, such as: • Epilepsy • Seizures/fits • Stroke (CVA) • Multiple sclerosis (MS), • Alzheimer's disease • Dementia • Parkinson's disease (PD) • Autism • Traumatic brain injury • Cerebral palsy • or other If yes: ______________________	☐	☐	☐
Musculoskeletal condition or pain affecting joints, muscles, bones in the arm (shoulder, elbow, arm, wrist, hand, fingers) If yes: ______________________	☐	☐	☐
Visual impairment/eye conditions If yes: ______________________	☐	☐	☐
Abnormal skin sensations, such as numbness, tingling, tickling, itching or burning If yes: ______________________	☐	☐	☐

Have you ever had or do you have now, any of the following?

	Yes	No	Not Sure
Contraindicated sitting position If yes: ____________________	☐	☐	☐
Cognitive deficits (memory, attention, problem-solving) If yes: ____________________	☐	☐	☐
Any other medical condition, physical or mental, not mentioned above If yes: ____________________	☐	☐	☐

Medication

Are you taking:

	Yes	No	Not Sure
Medication affecting the nervous system, such as: • Antidepressants • Anti-anxiety tablets • Sleeping tablets • Neuroleptics • Antiepileptics • Benzodiazepines • Dopamine • D-amphetamine • or other If yes: ____________________	☐	☐	☐

Participation in other studies

	Yes	No	Not Sure
Are you involved or planning to be involved in any other research study? If yes: ____________________	☐	☐	☐

Hand Dominance

Please mark the box that best describes which hand you use for the activity in question

	Always Left	Usually Left	No Preference	Usually Right	Always Right
Writing	☐	☐	☐	☐	☐
Throwing	☐	☐	☐	☐	☐
Scissors	☐	☐	☐	☐	☐
Toothbrush	☐	☐	☐	☐	☐
Knife (without fork)	☐	☐	☐	☐	☐
Spoon	☐	☐	☐	☐	☐
Match (when striking)	☐	☐	☐	☐	☐
Computer mouse	☐	☐	☐	☐	☐

I declare that the information on this form is true to the best of my knowledge.

Name of participant (print name)……………………………………………………………

Signature of participant…………………………………………………………………

Date…………………………………………………………………………………………

Appendix H Consent Form

UNIVERSITY OF Southampton

Consent Form

(Healthy Participants)

Study Title:	Cortical activity changes among stroke patients following robotic upper limb rehabilitation as measured by EEG during reaching movements.
Researcher:	Sebastien Pollet
Ethics number:	09/H0502/126

Please initial the boxes if you agree with the statements:

I have read and understood the information sheet (version 6, dated 15/8/12) and have had the opportunity to ask questions about the study ☐

I agree to take part in this research project and agree for my data to be used for the purpose of this study ☐

I give permission to the researcher to inform my GP of my participation in this study ☐

I understand my participation is voluntary and I may withdraw at any time without my legal rights being affected ☐

(Optional) I would like to receive a brief summary describing the study's results when it is completed. ☐

Name of participant (print name)…………………………………………………………

Signature of participant………………………………………………………………….

Name of Researcher (print name) ……………………………………………………….

Signature of Researcher…………………………………………………………………..

Date……………………………………………………………………………………….

Appendix I Participant Information Sheet

Participant Information Sheet

for people who have had a stroke

Study Title:	Cortical activity changes among stroke patients following robotic upper limb rehabilitation as measured by EEG during reaching movements.
Researcher:	Sebastien Pollet This research study forms the basis for the award of an MPhil/PhD from the University of Southampton.
Ethics number:	09/H0502/126

Please read this information carefully before deciding to take part in this research. If you are happy to participate you will be asked to sign a consent form.

What is the research about?

The first part of the study will examine what happens in the brains of people who have had a stroke when they move their arm. In this study, brain activity is measured using electroencephalography (EEG), which involves placing a cap containing recording electrodes over your head to measure your brain's electrical activity (see Figure 1). A special gel is used underneath each electrode to make sure the electrical signals from the brain reach the recording electrodes (there are hair-washing facilities within the EEG lab to wash away the gel once recording is finished). The cap is connected to a computer to record the signals. Additional recording electrodes are placed over your arm to detect when you start moving it. Additional electrodes will be placed next to your eyes to record when you blink (as blinking distorts the data), and on your ears (as reference electrodes). To measure brain activity, you will be asked to reach forwards with your affected arm several times using a reaching device. Brain signals will also be recorded from people who haven't had a stroke for comparison purposes.

Figure 1. Electroencephalography (EEG) cap (Neuroscan 2008)

The second part of the study will be about finding out if brain signals in people who have had a stroke improve after a period of rehabilitation. You will receive 10 sessions of training, using the Armeo rehabilitation robot. The Armeo is an interactive activity system which encourages repetition of arm and hand movements (see Figure 2).

Figure 2. Armeo rehabilitation robot, arm orthosis and screen, and virtual activity (Hocoma AG 2009)

The Armeo will not move the arm for you, but will provide physical support to counterbalance the effects of gravity which will help you move it farther. If you have access to the Internet, information about the Armeo can be found on Hocoma's website (the company who manufactures the Armeo) on www.hocoma.com/products/armeo/armeospring. A video demonstrating the Armeo is also available on that website, and can also be watched on www.youtube.com/watch?v=5Lv7YLG2i1Y. Brain signals recorded before and after rehabilitation will be compared to see if rehabilitation makes a difference, and to see if they return to the kind of brain signals people who haven't had a stroke have.

The third part of the study will be about finding out if improvements in brain signals match the improvements seen with tests that look at how well your arm and hand can be used. For example, can you pick up an object and place it on a shelf? These tests will be done before and after rehabilitation. The idea behind this is to see if electroencephalography (EEG) could be used to measure recovery after stroke in the same way that movement tests are used.

Why am I being considered for this study?

You are being approached because you have suffered a stroke. If you are interested in participating in the study, you will need to contact the researcher (contact details are included at the end of this document). The researcher will then visit you (or speak to you over the phone) to answer all the questions you may have. If you are still interested, the researcher will need to make sure that you meet all requirements before you officially participate in the study. To do this, the researcher will ask you some questions. If you meet all preliminary requirements, the researcher will arrange an assessment session with you at the University of Southampton. If all criteria are met, you will be formally invited to participate in the study. If you accept, you will be asked to sign a consent form.

Do I have to take part?

It is up to you whether you participate or not. There is nothing to do if you do not wish to participate. If you decide not to take part, the standard of care you receive will not be affected in any way.

What will happen to me if I take part?

The study requires that you visit the University of Southampton for a total of 15 times. This includes the assessment session, 10 visits for rehabilitation sessions and 4 visits to record brain signals and to test how well you can move your arm and hand. All rehabilitation and measurement sessions will last for approximately 2 hours. Figure 3 shows the timeline of measurement and rehabilitation sessions.

Figure 3. Timeline of measurement and rehabilitation sessions

The assessment session will consist of tests to make sure:

- one of your arms is affected by the stroke
- you are truly right-handed
- you are able to reach forwards enough times for EEG recording
- there is not too much spasticity in your affected arm
- you can see and perceive things around you correctly
- your thinking skills (such as memory and attention) are within normal limits

Measurement sessions will consist of:

- recording EEG brain signals while you reach forward several times
- testing how well you can move your arm and hand (these tests will be filmed and scored by another researcher)

Rehabilitation sessions will consist of training with the Armeo rehabilitation robot:

- adjustment of Armeo: 10 minutes
- 4 X 20 minute work periods = 80 minutes
- 3 X 10 minute rest periods = 30 minutes

How will I get to the University of Southampton?

You will need to make your own way to the campus. The researcher will however offer to contribute up to £5 per visit to cover your transport costs. Free car parking is available.

Are there any benefits in my taking part?

Results from the study will add to what is known about brain activity in people who have had a stroke. This may benefit people who have strokes in the future, if these results lead to the development of better rehabilitation techniques. It is unknown whether this study will directly benefit you, as studies looking at whether the Armeo helps people move their arm better usually have patients use it for a longer period of time.

Are there any risks involved?

There are no known significant physical or psychological risks associated with the use of the Armeo rehabilitation robot or with EEG data collection. The Armeo is a CE-marked commercially available system and is used clinically worldwide. As fatigue may result from prolonged use, the researcher will monitor this at intervals during rehabilitation sessions. There is also a small risk of skin allergy to gels used for EEG data collection.

Will my participation be confidential?

Only your GP will be informed of your participation in this study, with your permission. To ensure confidentiality, all information about you will be kept in locked filing cabinets, in a locked office at the University of Southampton. Anonymisation will be achieved by physically separating information about you into two separate folders. Anonymisation is about keeping your personal information (for example name, date of birth, medical information) apart from your EEG data and test scores. Personal information will be stored in a filing cabinet and the rest of the information in another. A number will be assigned to you, which will be used to link both sets of information. The researcher will ensure that all the information that is kept on digital media (such as computers and memory sticks) is password-protected. Guidelines from the University of Southampton Data Protection Policy will be followed.

What happens if I change my mind?

You have the right to withdraw at any time during the study without giving an explanation. If you do withdraw, your legal rights will not be affected.

What happens if something goes wrong?

If you have a concern or a complaint about this study you should contact Martina Prude, Head of the Governance Office, at the Research Governance Office (Address: University of Southampton, Building 37, Highfield, Southampton, SO17 1BJ ; Tel: +44 (0)23 8059 5058; Email: rgoinfo@soton.ac.uk) . If you remain unhappy and wish to complain formally Martina Prude can provide you with details of the University of Southampton Complaints Procedure. This research study is covered by the University of Southampton Professional Indemnity and Clinical Trials Insurance.

I'm interested in the study. Where can I get more information?

Please contact the researcher, **Sebastien Pollet**, either:

- by phone : 0798 366 7610
- by mail: Sebastien Pollet
  Postgraduate Office
  Building 45 (Faculty of Health Sciences)
  Highfield Campus, University of Southampton
  Southampton
  SO17 1BJ
- by email: sebastien.pollet@soton.ac.uk

You may also contact **Professor Jane Burridge**, who is supervising the study:

- by phone : 02380 598885
- by mail: Professor Jane Burridge
  Building 45 (Faculty of Health Sciences)
  Highfield Campus, University of Southampton
  Southampton
  SO17 1BJ
- by email: J.H.Burridge@soton.ac.uk

For independent advice about participating in research, you may contact **Martina Prude**, Head of the Governance Office at the University of Southampton (please see 'What happens if something goes wrong?' section above for contact details).

Appendix J Consent Form

Southampton NHS
University Hospitals NHS Trust

Consent form to collect medical information

Study Title:	Cortical activity changes among stroke patients following robotic upper limb rehabilitation as measured by EEG during reaching movements.
Researcher:	Sebastien Pollet
Ethics number:	09/H0502/126

Information will only be used for the purposes of the study.
Guidelines from the University of Southampton Data Protection Policy will be followed.

Please <u>initial</u> the boxes if you agree with the statements.

I give permission to the researcher to collect information from my medical notes. ☐

I give permission to the researcher to speak to health professionals involved in my care. ☐

I understand I may withdraw my consent at any time without my legal rights being affected. ☐

Name of participant (print name)……………………………………………………………
Signature of participant……………………………………………………………………
Name of Researcher (print name) …………………………………………………………
Signature of Researcher……………………………………………………………………
Date……………………………………………………………………………………………

Appendix K Assessment session scoring sheet

Assessment session scoring sheet

Name:________________________________
d.o.b.:________________________________

Date of assessment: ________________________________

MRC Muscle Grading

	0	No muscular activity
	1	Minimal contraction of muscle but insufficient to move a joint
	2	Contraction of muscle sufficient to move a joint with gravity eliminated*
	3	Muscle contraction sufficient to move a joint against gravity but not against resistance
	4	Muscle contraction sufficient to move a joint against gravity and mild/moderate resistance
	5	Normal power, muscle contraction sufficient to resist firm resistance

*For a grade of **2**, participants are required to be able to extend their elbow sufficiently to complete the reaching movement required for EEG data collection.

Modified Ashworth Scale

	0	No increase in muscle tone
	1	Slight increase in muscle tone, manifested by a catch and release or by minimal resistance at the end of the ROM when the affected part is moved **from full flexion to extension within one second (count: "one thousand and one")**
	1+	Slight increase in muscle tone, manifested by a catch, followed by minimal resistance throughout the remainder (less than half) of the ROM
	2	More marked increase in muscle tone through most of the ROM, but affected parts easily moved
	3	Considerable increase in muscle tone, passive movement difficult
	4	Affected part rigid in flexion or extension

EEG data collection test

Patient is able to perform _______ reaching movements with cues, with pauses of two minutes between each block of 25 movements.

Star Cancellation Test

Total number of small stars crossed out with a pencil: ________ (pass criteria **≥44**)

Hand Dominance

Please mark the box that best describes which hand you use for the activity in question

	Always Left	**Usually Left**	**No Preference**	**Usually Right**	**Always Right**
Writing	☐	☐	☐	☐	☐
Throwing	☐	☐	☐	☐	☐
Scissors	☐	☐	☐	☐	☐
Toothbrush	☐	☐	☐	☐	☐
Knife (without fork)	☐	☐	☐	☐	☐
Spoon	☐	☐	☐	☐	☐
Match (when striking)	☐	☐	☐	☐	☐
Computer mouse	☐	☐	☐	☐	☐

Appendix L Consent Form

Southampton UNIVERSITY OF

Consent Form
for people who have had a stroke

Study Title:	Cortical activity changes among stroke patients following robotic upper limb rehabilitation as measured by EEG during reaching movements.
Researcher:	Sebastien Pollet
Ethics number:	09/H0502/126

Please initial the boxes if you agree with the statements:

I have read and understood the information sheet (version 5, dated 21/1/10) and have had the opportunity to ask questions about the study.

I agree to take part in this research project and agree for my data to be used for the purpose of this study.

I give permission to the researcher to inform my GP of my participation in this study

I agree to being filmed while performing movement tests and for video footage to be viewed by an external assessor for analysis.

(Optional) I agree to the use of video footage for teaching and research presentations.

(Optional) I would like to receive a brief summary describing the study's results when it is completed.

I understand my participation is voluntary and I may withdraw at any time without my legal rights being affected.

Name of participant (print name)……………………………………………………

Signature of participant…………………………………………………………

Name of Researcher (print name) …………………………………………………

Signature of Researcher………………………………………………………

Date………………………………………………………………………………

Appendix M Letter to GP

18 November 2015

Dr X
X Surgery
Southampton
XXXX XXX

Dear Dr X,

This letter is to hereby inform you that one of your patients, X Xxxxx (d.o.b. xx/xx/xx), will be participating in a research study at the University of Southampton.

This study will be investigating cortical activity changes following stroke, and includes both a stroke patient group and healthy volunteers. The study involves four sessions of electroencephalographic (EEG) brain wave recording and ten 2-hour sessions of arm training using an interactive upper limb rehabilitation system.

Should you have any questions or concerns, please do not hesitate to contact me for further information.

Best regards,

Sebastien Pollet
Researcher
Building 45 (Faculty of Health Sciences)
University of Southampton
Highfield Campus
Southampton
SO17 1BJ

phone: 0798 366 7610
email: sebastien.pollet@soton.ac.uk

Appendix N Letter to thank participants

21 July 2016

Dear X,

I would like to thank you again for participating in the study. I would particularly like to acknowledge your efforts to attend all sessions, as this study was very demanding for participants in terms of the number of times they needed to visit the university. I would also like to thank you for your patience.

Once the study is over, you will be receiving a brief summary describing the study's results, if you have agreed to this on the consent form you signed at the beginning of the study.

It was a pleasure to meet you.

Again, thank you for participating.

With best wishes,

Sebastien Pollet
Researcher
Faculty of Health Sciences
University of Southampton

Appendix O Fugl-Meyer scoring sheet

Subject I.D.: ______________ Assessor: ___________________
Assessment No.: ___________ Signature: ___________________
Date:

FUGL-MEYER ARM SCORE

Primarily assessed side: left ☐ or right ☐

A. SHOULDER-ELBOW-FOREARM

I REFLEX-ACTIVITY
(patient sitting, verbalise the findings)

Biceps *Triceps* *Finger flexors*

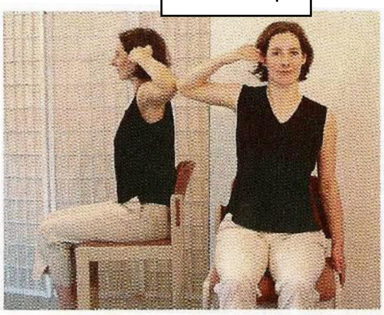
Biceps/finger flexors
- no reflex-activity ☐ 0
- reflex-activity ☐ 2

Triceps
- no reflex-activity ☐ 0
- reflex-activity ☐ 2

/4

II ACTIVE MOVEMENTS IN SYNERGIES
(patient sitting with the back against the backrest)

thumb up



a) Flexor synergy: "hand to your (ipsilateral) ear" with shoulder retraction

	none	partial	perfect
forearm supination:	☐ 0	☐ 1	☐ 2
elbow flexion:	☐ 0	☐ 1	☐ 2
shoulder outw rotation:	☐ 0	☐ 1	☐ 2
shoulder abduction (90°)	☐ 0	☐ 1	☐ 2
shoulder elevation:	☐ 0	☐ 1	☐ 2
shoulder retraction:	☐ 0	☐ 1	☐ 2

can assist

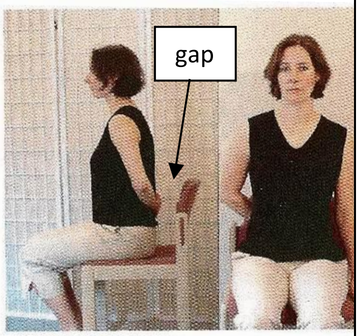
knees apart

b) Extensor synergy: "palm of hand on (contralateral) knee" from flexor synergy (eventually passive)

	none	partial	perfect
forearm pronation:	☐ 0	☐ 1	☐ 2
elbow extension:	☐ 0	☐ 1	☐ 2
shlder addctn + int rot	☐ 0	☐ 1	☐ 2

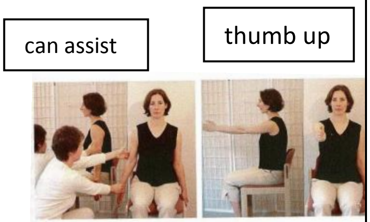
/18

III DYN. FLEXOR+EXTENSOR SYNERGY (patient sitting)



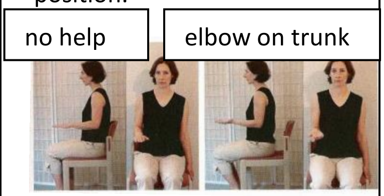
a) Hand to lumbar spine
"bring the back of your hand on your back"

- the specific detail cannot be performed at all, or used compensatory movements ☐ 0
- hand behind ant sup iliac spine but does not reach the spine ☐ 1
- the detail is performed faultlessly ☐ 2



b) Shoulder flexion 0° to 90°
elbow extended, forearm in midposition
"bring your extended arm up, thumb upwards".
The assessor may assist the patient to get into the starting position.

- arm immediately in abduction or elbow in flexion ☐ 0
- cannot cover full range or shoulder abduction and/or elbow in flexion occurs ☐ 1
- the detail is performed faultlessly ☐ 2



c) Pro-Supination of the forearm
(elbow flexed 90°, shoulder 0°)

- starting position impossible and/or no pro-supination ☐ 0
- starting position possible and kept during the movement, limited pro-supination ☐ 1
- the detail is performed faultlessly ☐ 2

CHECK PASSIVE ROM TO CHECK THAT PATIENT COVERS IT COMPLETELY

/6

IV ACTIVE MOVEMENT, WITH LITTLE OR NO SYNERGY
(patient sitting)

a) Shoulder abduction 0° - 90°
(elbow fully extended and forearm pronated)

- immediately supinated and/or elbow flexed ☐ 0
- partly performed or elbow is flexed or fore-arm cannot be kept in pronated position ☐ 1
- the detail is performed faultlessly ☐ 2

can assist / thumb up  *b) Shoulder flexion 90° - 180°* (arm in 0° abduction, elbow extended and forearm in midposition) "bring extended arm up, thumb up". The assessor may assist the patient to get into the starting position. no help  *c) Pro-Supination of forearm* (shoulder 30° - 90° flexion, elbow in extension) Score against the passive RoM, don't mistake the rotation of the glenohumeral joint.	- arm immediately in abd. or elbow flexed ☐ 0 - arm not immediately in abduction and/or elbow in flexion or cannot cover full ROM ☐ 1 - the detail is performed faultlessly ☐ 2 - starting position impossible and/or no pro-sup ☐ 0 - starting position possible and kept during the movement, limited pro-sup ☐ 1 - the detail is performed faultlessly ☐ 2 CHECK PASSIVE ROM TO CHECK THAT PATIENT COVERS IT COMPLETELY	**/6**
V NORMAL REFLEX-ACTIVITIES Only assessed if in the previous section total score = 6	a) not assessed (because score of A. IV < 6) ☐ 0 b) assessed: - ≥ 2 of 3 reflex-activities are markedly hyperactive ☐ 0 - 1 reflex markedly hyperactive or ≥ 2 lively ☐ 1 - no hyperactive reflexes and no more than 1 lively ☐ 2	**/2**

B. WRIST		
can assist elbow maintain 90°  with slight resistance *a) Wrist in 15° dorsal flexion* (shoulder 0°, elbow 90°, forearm fully pronated) Assessor may bring and keep the elbow in the required position.	palm down - 15° dorsiflexion not achieved ☐ 0 - 15° dorsiflexion performed, no resistance ☐ 1 - 15° can be maintained against slight resistance ☐ 2	

can assist elbow maintain 90°

max flex./ext.

__b) Max. wrist flexion - extension__

(shoulder in 0°, elbow 90°, forearm pronated) Assessor may support the elbow in the required position.

palm down

- no active repeated movements ☐ 0
- active movements less than passive range ☐ 1
  (but need to have both flexion and extension)
- detail is fully and adequately performed ☐ 2

CHECK PASSIVE ROM TO CHECK THAT PATIENT COVERS IT COMPLETELY

can assist elbow maintain 0°

palm down

with slight resistance

__c) Wrist stability in 15° dorsiflexion__

(shoulder slightly flexed and/or abducted, elbow extended, forearm pronated) Assessor may support the elbow in this position.

- 15°dorsiflexion to required position not possible ☐ 0
- 15° wrist position possible, no resistance ☐ 1
- 15° can be maintained against slight resistance ☐ 2

can assist elbow maintain 0°

palm down

__d) Max. wrist flexion - extension__

(shoulder slightly flexed and/or abducted, elbow extended, forearm pronated) Assessor may support the elbow if needed.

- no active repeated movements ☐ 0
- active movements less than passive range ☐ 1
  (but need to have both flexion and extension)
- detail is fully and adequately performed ☐ 2

CHECK PASSIVE ROM TO CHECK THAT PATIENT COVERS IT COMPLETELY

can assist elbow maintain 90°  palm down  *e) Circumduction of the wrist* (shoulder 0°, elbow 90°). Assessor may provide support for the forearm but not restrain it.	- circumduction cannot be performed ☐ 0 - jerky or incomplete movements ☐ 1 - detail is fully and adequately performed ☐ 2	**/10**

C. HAND (assessor may support the elbow in 90° position; not the wrist)		
can assist elbow maintain 90° and to start from full extension  forearm in neutral *a) Flexion of the fingers*	- no flexion ☐ 0 - some, but not full active flexion ☐ 1 - full active flexion compared with the unaffected hand ☐ 2	
can assist elbow maintain 90° and to start from full flexion  forearm in neutral *b) Extension of the fingers* from the position of full flexion (passive)	- no extension ☐ 0 - some, but not full ext. or release of an active mass flexion grasp ☐ 1 - full active extension, compared with the unaffected hand ☐ 2	

apply resistance to finger flexion

- required position not possible ☐ 0
- grasp is weak ☐ 1
- grasp maintained against relatively great resistance ☐ 2

c) Grasp A: extension MCP, flexion PIP and DIP

grasp is tested against resistance

can assist elbow maintain 90°

thumb CMC and thumb IP must be at 0°

warn patient of sudden horizontal tug

palm down

paper between thumb and index

- the function cannot be performed ☐ 0
- scrap of paper kept in place, not against a slight tug ☐ 1
- scrap of paper is held well against a tug ☐ 2

d) Grasp B: extended index and thumb

patient should perform a pure thumb adduction (holding a scrap of paper against a horizontal tug away from the patient)

can assist elbow maintain 90°

pencil between thumb and index pulpae

warn patient of sudden upwards tug

forearm in neutral

- the function cannot be performed ☐ 0
- pencil kept in place, not against a slight tug ☐ 1
- pencil is held well against a tug ☐ 2

e) Grasp C: pulpa thumb against the pulpa of the index (holding a pencil against a vertical tug)

can assist elbow maintain 90°

tip-ex bottle between thumb and index (anywhere)

warn patient of sudden upwards tug

forearm in neutral

- the function cannot be performed ☐ 0
- cylinder kept in place, not against a slight tug ☐ 1
- cylinder is held well against a tug ☐ 2

f) Grasp D: volar surface of the thumb and index against each other

(holding a cylinder-shaped object against a vertical, upwards tug)

palm down

g) Grasp E: spherical grasp
(grasping a tennis ball with forearm pronated and holding it against a downwards tug)

can assist elbow maintain 90°

hold tennis ball underneath patient's hand

warn patient of sudden downwards tug

- the function cannot be performed ☐ 0
- ball grasped, not held against a slight tug ☐ 1
- ball grasped, well held against a tug ☐ 2

/14

D. COORDINATION/ SPEED
(no compensation of trunk - head allowed)

starting position

blindfold

AS FAST AS POSSIBLE

if cannot reach start position, score 0

no compensating movements of trunk/head allowed

Finger-to-nose test:
eyes closed, starting position is abduction, 5 times

time right:
________seconds

time left:
_______seconds

a) *Tremor (oscillations during the trajectory)*	marked ☐ 0	slight ☐ 1	no ☐ 2
b) Dysmetria (error in endpoint destination)	pronounced or unsystematic ☐ 0	slight and systematic ☐ 1	no ☐ 2
c) Time compare time affected to unaffected side	> 6 sec slower ☐ 0	2-5 sec slower ☐ 1	< 2 sec slower ☐ 2

/6

TOTAL MOTOR FUNCTION, UPPER LIMB	**/66**

Appendix P ARAT scoring sheet

Action Research Arm Test

Subject I.D.: ______________
Assessor: ________________
Assessment No.: __________
Signature: _______________
Date: ___________________

-Table 75cm, armless chair 46cm (table: mid-abdomen, Δ30cm chair/table
-Trunk 15cm from table
-Trunk remains in contact with backrest – no leaning (remind regularly)
-Feet remain in contact with the floor
-Start position: 2 palms on table (except Gross Movement subtest)
-Hand lies lateral to testing object
-Unaffected side first for each subtest, then affected side
-Practice allowed. Score based on best performance. Not penalised if object is dropped and relifted.

Scoring:

3 = Performs test normally, in < 5 s, with appropriate body posture, normal hand/arm movement components.

2 = Completes test, but takes abnormally long time (5-60 seconds), or has great difficulty (abnormal hand (e.g. use of wrong grasp) or arm (e.g. elbow does not flex as required) movement components, or abnormal body posture (e.g. used as a substitute for impaired movements).

1 = Performs test partially (within 60s). For grasp/grip/pinch subtests, cannot get score of 1 for arm movements only. Must initiate some form of hand movement that achieves holding and lifting the object. Pushing an object is not sufficient.

0 = Can perform no part of test – given when unable to complete any part of the hand or arm movement components within 60 seconds.

a. Subtest Grasp

		Left	Right
1.	**Block 10 cm** (If score = 3, total = 18 and -> GRIP)		
2.	**Block 2.5 cm** (If score = 0, total = 0 and -> GRIP)		
3.	**Block 5 cm**		
4.	**Block 7.5 cm**		
5.	**Ball 7.5 cm** – examiner can stabilise tin lid		
6.	**Stone** – examiner can reposition on long side if falls to its side		
	SUBTOTAL *GRASP*	**/18**	**/18**

b. Subtest Grip

7.	**Pour water from glass to glass (pronation)**(If score = 3, total = 12 and ->PINCH)			
8.	**Tube 2.25 cm** (If score=0, total =0 and ->PINCH)	move from closer position to further away position (30cm)		
9.	**Tube 1 cm**			
10.	**Washer over Bolt -** examiner can stabilise tin lid			
	SUBTOTAL *GRIP*		**/12**	**/12**

c. Subtest Pinch examiner can stabilise tin lid

11.	**Ball bearing, 6mm, ring finger + thumb** (If score = 3, total = 18 and -> GROSSMT)		
12.	**Marble index finger and thumb** (If score = 0, total = 0 and -> GROSSMT)		
13.	**Ball bearing, middle finger and thumb**		
14.	**Ball bearing, index finger and thumb**		
15.	**Marble ring finger and thumb**		
16.	**Marble middle finger and thumb**		
	SUBTOTAL *GRASP*	**/18**	**/18**

d. Subtest Gross Movement

	Start with both hands pronated on lap, head still and in neutral position.		
17	**Place palm of hand behind head** (not behind neck) (If score = 3, total = 9, If score = 0, total =0)		
18	**Place palm of hand on top of head** (not on forehead)		
19	**Palm of hand to Mouth** (not the chin)		
	SUBTOTAL *Gross Movement*	**/9**	**/9**

	TOTAL *ACTION RESEARCH ARM TEST*	**/57**	**/57**

Appendix P

Task Number	Task Materials and Details	Hand Movement Components	Arm Movement Components
1-4	Blocks: displace vertically to shelf	Hand voluntarily opens to the size of the block. Any type of grasp involving the thumb and fingers in opposition is acceptable.	a. Forearm is between midposition and pronation. b. Elbow flexed when first grasping object and then extends to reach top of shelf. c. Shoulder flexion to reach top of the shelf, and shoulder stabilization to maintain position as object is released onto shelf. d. Thumb and finger extension to release the object.
5	Cricket ball: displace vertically to shelf	Spherical grasp; fingers and thumb slightly flexed and abducted to the size of the ball.	
6	Sharpening stone: displace vertically to shelf	Lateral grip; sharpening stone is between the pad of thumb and the radial side of the index finger at or near interphalangeal joints.	
7	2 cups: pour water from one cup to another	Cylindrical grasp around cup	a. Forearm pronation to pour, then forearm supination to return cup to table. b. Thumb and finger extension to release the cup.
8-9	Alloy tubes: displace from starting plank to target plank	Any type of grasp, such as 3 jaw-chuck pinch, involving the pads of the thumb opposed with pads of any number of fingers in order to grasp the alloy tube	a. Forearm is between midposition and pronation. b. Elbow is sufficiently extended to reach the distal target plank. c. Shoulder movement and stabilization to maintain position
10	Washer: displace distally from tin to target plank	Pincer or 3 jaw-chuck grasp, with pads of the thumb and fingers in opposition, in order to grasp the washer	as object is released. d. Thumb and finger extension to release tube/washer.
11, 13, 14	Ball bearing, from tin on table, vertically displaced to tin on shelf	Opposition of pads of ring finger and thumb, middle finger and thumb, and index finger and thumb, respectively	a. Forearm is between midposition and pronation. b. Elbow flexed when first grasping object, then extends to reach top of shelf. c. Shoulder flexion to reach top of shelf and shoulder stabilization to maintain position as object is released.
12, 15,16	Marble, from tin on table, displace vertically to tin on shelf	Opposition of pads of index finger and thumb, ring finger and thumb and middle finger and thumb, respectively	
17-19	Hand from lap to various pericranial positions	Palmer side of hand (hand does not need to be open) reaches to back side of head, to top of head, and to mouth, respectively	a. Forearm pronation and supination. b. Full elbow flexion c. Shoulder abduction, flexion, and external rotation.

(Yozbatiran et al., 2008)

Appendix Q Preparation instruction sheet

Preparation instructions for EEG recordings

Thank you for agreeing to take part in this research project. Your contribution is extremely important. Preparing for your visit will ensure that the information we collect will be really useful. Please read this sheet carefully and try to practice the things we suggest for a few days before your visit.

On the day of your visit:

1) Please wash your hair before coming to the lab (on the day or the night before), but **avoid using hair conditioner (includes 2-in-1 products)** or **any styling product** (shampoo is fine).

2) Wear a top **that allows access to the front and sides of your shoulder** (loose short sleeves are best), where some electrodes will be placed. Please ensure that your top's sleeves can be pushed up in a way that the side of your shoulder can be uncovered.

As you will have gel in your hair after we finish recording, you will be able to wash your hair in the lab – we have a sink with an electric shower over it. We have shampoo, conditioner, a hairdryer, a mirror, and fresh towels. You may wish to bring a comb or brush to style your hair. Some people prefer to wear a hat and wash their hair at home (although the hat will have some gel on it when removed). The gel is water-soluble: it can be completely washed away by water (it does not stain or leave marks). If the appearance of your hair is very important to you, you may want to avoid planning activities after the session as it might not be possible for you to recreate your hairstyle as you would at home.

How to prepare:

Electroencephalography (EEG) is very sensitive and picks up very small electrical signals from the brain. In this study, EEG is recorded whilst you reach forward 150 times (over about an hour) with one of your arms. Your arm will be placed in a "reaching device" (see picture), which ensures that the reaching movement is the same every time you do it.

EEG is so sensitive that it also picks up electrical signals when muscles close to the head are used, for example:

-when you move your head or eyes to look at something
-when you move or tense up your jaw, or purse your lips
-when you swallow, yawn, sneeze, or cough
-when you frown, or grimace with effort

This means that when EEGs are recorded:

-Your whole body (from your head all the way down to your toes) needs to be as still as possible (think of the wax figures at the Madame Tussauds museum in London!), except of course for your arm that will be doing the reaching movement.

-You need to fix your gaze (where you look) on a coloured square on a screen in front of you. The square is red then turns green when you need to reach forward (this will be explained at your first visit).

-You need to relax your jaw, as the jaw muscles go all the way up to your temples and so quite near to your brain.

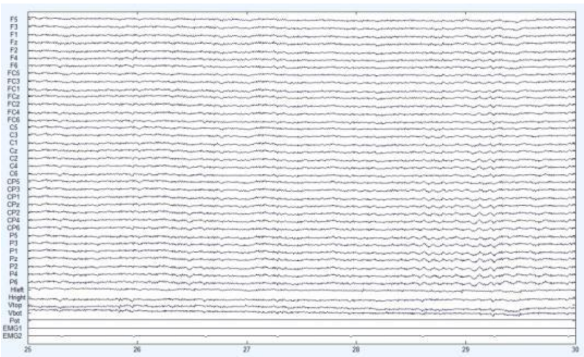
Keeping still like this can be difficult for some people so it would help if you practiced doing the following on the few days before your visit:

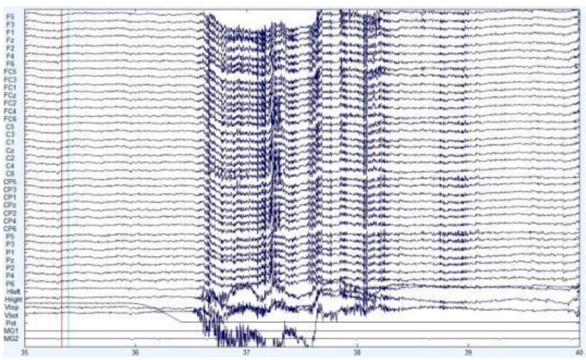
-sit comfortably in an armchair or sofa
-place your feet flat on the ground
-place one hand on your lap
-place the arm that you will move (the researcher will let you know which one) to your side
-fix where you look on an object in front of you (could be something on your wall)
-do this for 10-15 seconds, staying completely still and not moving your eyes to look anywhere else. Continue breathing normally and continue blinking your eyes when needed – this is okay!

Now pay attention to your jaw. Let it go, and relax it. It should drop a little. It might feel a bit strange, as most of us hold it in place. Your jaw should be completely relaxed – your upper and lower teeth should not be touching each other.

Now place your hands on your temples and feel the muscle contractions when you move your jaw, even slightly. You should feel the muscles move when you do this. This is what we are trying to avoid when recording EEGs. Frowning or raising eyebrows during recordings should also be avoided.

You can see the difference in the recordings (each line is for one electrode on the head):





Person is still, fixes their gaze, and

Person has jaw tension, or looks

The image on the left shows smooth, straight lines (which is good). You can see on the image on the right that jaw tension, looking away, or moving the head makes the lines go wiggly. This means that the data about that reaching movement cannot be used. If lots of data is lost in this way, results will not be accurate.

It is very important that you do your best to follow these instructions.

<u>Practicing the following will help you to do this:</u>
-Still sitting in an armchair or sofa as before, fix your gaze on that object again but this time let your jaw relax and keep it relaxed for about 15 seconds
-now do a few reaching movements with your arm (one about every 10 seconds), reaching quickly for an imaginary object in front of you, and bring your arm back to your side. Try only moving your arm from the shoulder down, avoiding clenching your jaw, or tensing up your neck, your face or your forehead when you reach forward. Make sure that your upper body continues to be very still when you reach forward, as much as possible, and that your jaw stays relaxed. To achieve this, you will need to pay attention to your jaw, forehead, and upper body regularly.

Thank you for practicing this. It will make a big difference to the quality of the data. If you have any questions please don't hesitate to contact me.

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