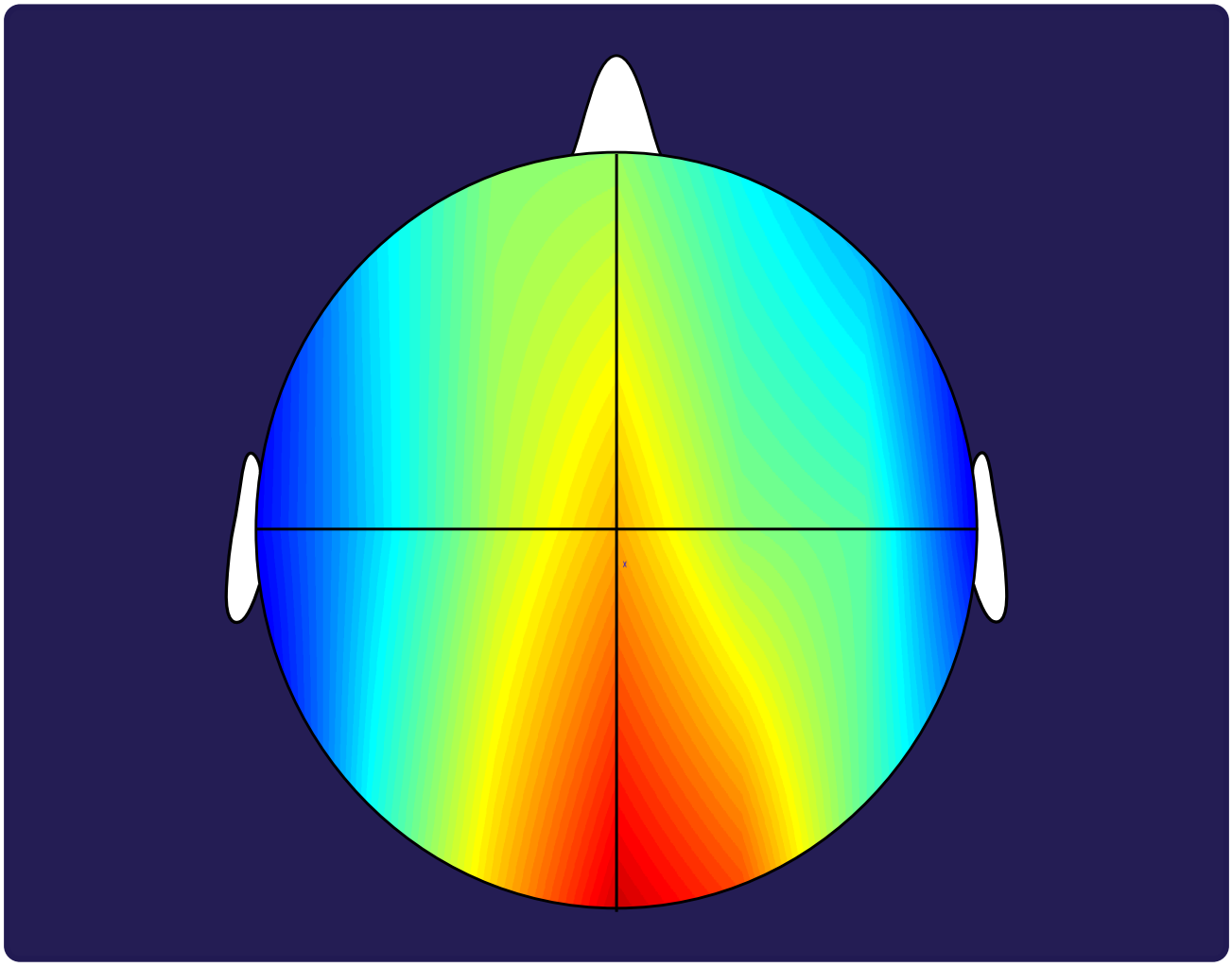
Neural effects of short term motor learning

- Christoffer Gøthgen & Mathias Brønd Sørensen



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Abstract:

Motor learning is important for human survival and is vital in rehabilitation of lost function. Increase in performance is not necessarily the best way of quantifying motor learning as it might be short lived and unable to transfer to similar skills. Furthermore it is impossible to know how the underlying neurophysiology changes. The aim of the present project was to investigate methods of quantifying short term motor learning within EEG features. The features investigated were the movement related cortical potential (MRCP), the event-related desynchronization/synchronization (ERD/ERS), corticomuscular coherence and brain waves from rest EEG. In order to assess the features an experiment was conducted including 19 subjects performing various motor tasks with their non-dominant hand, together with rest EEG sessions. Data obtained from the experiment were analyzed and statistically compared from the pre-session to the post-session in order to see effect of the intervention. Mean bereitschaftspotential, mean negative slope, peak movement potential, ERD/ERS following Pfurtscheller's method, coherence measures and center of mass from the heat map of power spectral density in rest EEG, was used in the analysis of the data. Subjects improved performance during the experiment, which was reflected as producing less errors during the intervention. Even though this was the case a significant change within the features was only seen as a posterior shift of the center of mass of heat maps and only in the beta band during the closed eyes rest session. No significant change was seen within any of the other features. If motor learning had been induced within the subjects it was not possible to quantify with the used features and equipment. Large variability suggests that EEG might not be a sensitive measure to evaluate the underlying neurophysiological changes associated with motor learning. More studies are needed to provide an accurate assessment of the possible neural changes measureable following short term motor training using other features of the EEG.

Dansk resume

Motorisk indlæring er vigtigt for den menneskelige overlevelse og er essentiel i forbindelse med rehabilitering af mistet funktion som det ses hos blandt andet hjerneskade patienter. Normalt måles fremgang alene på udførsel og præstation af den færdighed, der udøves, men dette kan til tider være en mangelfuld vurdering. Præstationsfremgang kan være kortvarig og ikke overførbart til andre færdigheder, der minder om den, der er trænet. Forskellige forskere har fundet bedre fastholdelse af ny-indlærte motoriske evner, hvis træningen varierer inden for træningssessionen, også selvom der opnås en hurtigere præstationsfremgang inden for træningssessionen ved at holde træningen simpel. Med dette in mente er der derfor brug for metoder, hvormed effekten af træningen kan vurderes udover selve præstationsfremgangen. Det ville kunne give en ekstra dimension af træningsevaluering til brug i rehabilitering til at kunne vurdere hvornår patienter har trænet tilstrækkeligt, eller det ville kunne bruges til at vurdere hvornår en kirurg er klar til at udføre operationer på mennesker. Derfor var formålet med dette projekt at undersøge muligheder for at kvantificere motorisk indlæring ved hjælp af egenskaber fra elektriske signaler fra hjernen (EEG).

19 forsøgspersoner udførte en motorisk færdighed ved at klemme på et håndtag til at måle kraft, mens en cursor på en skærm reagerede. Før, undervejs og efter blev EEG opsamlet fra 64 elektroder fordelt over hovedet samt muskelsignaler (EMG) fra underarmen. For at se om den motoriske træning havde effekt blev data fra forsøget analyseret og statistisk sammenlignet fra start-sessionen til slut-sessionen. Der blev udvalgt en række neurale signalegenskaber fra forskellige begivenheder i det elektriske hjerne- og muskelsignal. Et par sekunder før en bevægelse udføres kan der optages et forberedelsessignal, der gradvist falder i amplitude indtil bevægelsen udføres (movement related cortical potential, MRCP). For at karakterisere dette, blev det underinddelt i den initiierende del (bereitschafts potential, BP), den følgende del, hvor gradienten bliver mere negative (negative slope, NS') og selve bevægelsespotentialet (movement potential, MP). Ydermere sker der en desynkronisering (event-related desynchronization, ERD) og efterfølgende synkronisering (event-related synchronization, ERS) i neuronaktiviteten ved bevægelsesforberedelse og selve bevægelsen. Derudover blev der undersøgt hvorvidt, der var kohærens i frekvensaktiviten mellem hjerne og muskel, og hvorledes det ændres, og hvorvidt hjernebølger i hvile med åbne og lukkede øjne blev påvirket af den motoriske træning.

Forsøgspersonerne viste en forbedring i de motoriske færdigheder, ved at lave mindre fejl i slutningen af forsøget end i starten. Der var generelt stor variation i data og kun en af de neurale signalegenskaber ændrede sig statistisk signifikant. Der blev således observeret at hjerneaktiviteten flyttede sig posteriort i beta hjernebølgen mens forsøgspersonerne havde lukkede øjne. Dette kan indikere at motorisk indlæring havde fundet sted, men eftersom ingen af de andre signalegenskaber ændrede sig signifikant, er der stor usikkerhed. Der er brug for mere forskning for at give en nøjagtig vurdering af de mulige neurale ændringer, der kan måles efter kortvarig motorisk træning.

Preface

This project is the master thesis of Christoffer Gøthgen and Mathias Brønd Sørensen made during the final semester of Biomedical Engineering & Informatics at Aalborg University.

The thesis will give an insight into motor learning within humans both the use of different strategies and terms together with the underlying physiology. Pros and cons of different technologies used to determine neural effects of motor learning will be investigated with the goal of finding the most suitable technology to quantify changes associated with motor learning. With the use of a chosen technology there will be data collecting and analysis to investigate the physiological development occurring with motor training.

In the beginning of every chapter (apart from the introduction) text in italic will provide the reader with what is to be expected of the chapter. A summary of the problem area is provided in chapter 6 before the aim of the project is laid out.

Reading instruction

The Harvard method was used for references within the present report. If the reference is placed before the dot it is referring to the sentence, on the other hand if it is placed after the dot it is referring to the section. If the source have multiple authors the surname of the first author will be written followed by *et al.* - an example: [Jochumsen et al., 2015]. Figures without any references in the caption are self made. Any abbreviations used in the report will be written to its full extend followed by the abbreviation, first time mentioned and in headlines - an example: movement related cortical potential (MRCP).

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Chapter 1

Introduction

Motor control and motor learning are two of the most important aspects in human survival. Motor control refers to the planning and execution of movements, whereas motor learning is the process of improving a skill from practice. Motor learning can also be defined as an increasing accuracy, both temporal and spatial, of movements in relation to practice. Motor learning is essential for human activity. Without motor learning a driver would enter a car and look at the wheel and dashboard like it was the first time seeing it, every time the driver is entering the car. [Willingham, 1998] Neural understanding of motor control has made a considerable progress throughout the years, but there are still aspects that are influencing motor learning which remain unclear [Shmuelof and Krakauer, 2011, Kal et al., 2016, Heremans et al., 2016, Xiao et al., 2016]. Strategic groundwork for the different stages of motor learning have been investigated within several studies, for example a study by Taylor and Ivry [2012] looked into different stages regarding skill acquisition, movement strategies and motor adaptation. They concluded that further research of strategy development, within motor learning, could give insight into understanding progress in human performance. [Taylor and Ivry, 2012]

Many brain structures are involved with motor learning and depending on the motor learning task different brain regions are used. A meta-analysis by Hardwick et al. [2013] determined common brain structures used across 70 motor learning experiments. They found activation in dorsal premotor cortex, supplementary motor cortex, primary motor cortex, primary somatosensory cortex, superior parietal lobule, thalamus, putamen and cerebellum to be consistent across the motor learning tasks. They also found that activation of the basal ganglia and cerebellum were significantly stronger in tasks requiring greater motor demands and integration of sensory input. In tasks focusing on learning sequential motor behavior (e.g. pressing a button after a visual stimulus) activation in the cortical structures and the thalamus were significantly stronger. This indicates that a network of brain structures contribute to motor learning. [Hardwick et al., 2013] If the brain is damaged this network is disrupted resulting in the loss of motor skills. It is then necessary to re-learn lost motor skills through rehabilitation. For example: A definitive rehabilitation technique for brain damage following stroke has not been found therefore a combination of several techniques in combination is usually seen [Langhorne et al., 2009]. The importance in finding the right rehabilitation technique is immense for restoring lost function in patients suffering brain damage and is why studies have investigated how different motor learning tasks influence the aspects in motor learning. [Krakauer, 2006, Winstein et al., 2003] A review by Krakauer [2006] looked into training schedules and motor learning within healthy subjects and patients suffering from hemiparesis. Rehabilitation methods were presented which were based on motor learning, but an important issue were also raised regarding true recovery as opposed to compensatory movements or none retained motor skills. [Krakauer, 2006]

How motor training is planned matters and influences the robustness of motor learning. Immediate improvement in performance does not equal great retention of learning [Kantak and Winstein, 2012], which makes it harder to test for adequate motor learning and makes it hard to get feedback regarding the quality of the motor training. This is especially a problem within conditions where an acquired motor skill is lost, such as stroke. Within stroke rehabilitation there is a lack of strong evidence regarding the different treatment paradigms that exists. The issue being individual differences in treatment response and it is hard to quantify if a specific treatment is working [Laney et al., 2015]. Motor learning is however not limited to disease, but is also relevant

for medical professionals needing to acquire a certain skill, such as surgeons, before practicing it on human patients. An issue here is that there does not exist many objective methods to assess the physiologic part of their training [Glarner et al., 2015], and performance-based metrics does not necessarily translate into learning.

Therefore there is a need for an objective way of quantifying the physiological parts of motor learning.

Chapter 2

Motor learning

Before looking into how a new motor skill is learned in humans, it is important to get an understanding of how motor learning is defined, and what is effecting the learning of a new motor skill. This chapter will cover the processes associated with motor learning and how different practice strategies effects the learning of a motor task.

During the early stages of motor learning, new movements are highly dependent of sensory feedback and requires a high level of control. Performance is variable and slow, but with practice performance speed and accuracy increases and the amount of conscious sensory processing declines and becomes less important. [Halsband and Lange, 2006] Due to the nature of this, the initial stages of motor learning, is where the highest increase in performance is found and this increase declines in the latter stages. Fitts and Posner [1967] proposed a three stage model of this containing the cognitive, associative and autonomous stage. The cognitive stage is the early stage with a high level of cognitive activity and large parts of the movement being controlled consciously with variable performance. The associative stage is the intermediate stage, where movements are gradually being automatized, the cognitive activity is declining and performance stabilizes. The autonomous stage is the final stage, where conscious effort is no longer required to perform a movement and performance is consistent and efficient. [Taylor and Ivry, 2012] A visualization of this can be seen in figure 2.1.

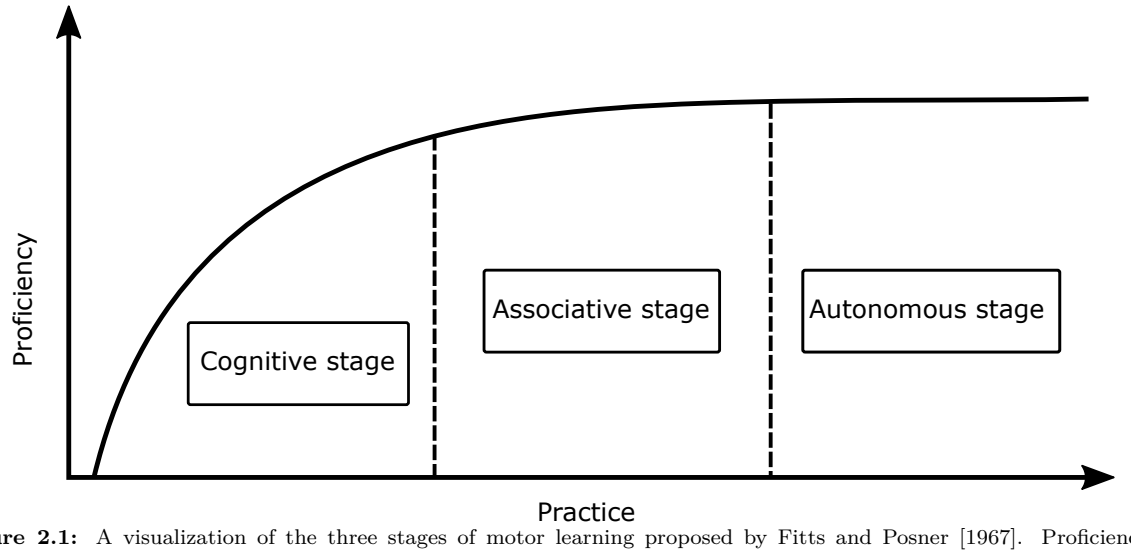


Figure 2.1: A visualization of the three stages of motor learning proposed by Fitts and Posner [1967]. Proficiency is increasing with the amount of practice and the highest increase is seen during the cognitive stage, it is attenuating in the associative stage and it is plateaued in the autonomous stage. With inspiration from Taylor and Ivry [2012].

2.1 Practice

The most important factor of the development of a motor skill is practice and that the practice leads to a performance improvement. [Krakauer, 2006] The most simple form of practice is performing the same movement repeatedly. This is often referred to as simple or massed practice [Krakauer, 2006], but might not be the most efficient way of learning. It has been found that introducing longer intervals of rest between repetitions and/or making the task vary from repe-

tition to repetition improves the performance in subsequent session of the skill as compared to simple practice. This is know as retention. [Krakauer, 2006, Kitago and Krakauer, 2013] Superior retention is seen with random-order practice compared to block-order/simple practice even though the performance is greater in the initial simple practice phase [Krakauer, 2006, Kantak and Winstein, 2012].

2.2 The learning-performance distinction

An important distinction is to be made about immediate improved motor performance during practice and whether the resilience of the skill is sustained over time. This is known as the learning-performance distinction. [Winstein et al., 2003, Kantak and Winstein, 2012] Practice done in a block-series manner may show a fast increase in performance but a degraded retention or transfer. Transfer is referred to as the use of the learned motor skill and how it is transferred to other or similar motor tasks. However practice done in a random-order may show slow increase in performance but will facilitate retention or transfer. This indicates that greater performance within practice does not necessarily equal to greater learning of the motor skill and *vice versa*. [Schmidt and Bjork, 1992]

Researchers use retention and/or transfer tests to assess if the improved immediate performance is translated into sustained improved flexible ability. [Winstein et al., 2003] Hence the retention test reflects the strength of the induced learning over time and the transfer test reflects the flexibility and generalization of the learning by using a variation of the skill trained as the test. [Kantak and Winstein, 2012] The timing of a test is also important; according to a review by Kantak and Winstein [2012], researchers utilize a retention test in the immediate time after practice (10 seconds to few hours) and/or a delayed test usually after 24 hours of the practice. The latter is thought to be more of a measure of relatively permanent learning and indirectly includes the result of processes occuring doing sleep related to learning. [Kantak and Winstein, 2012]

The difference between immediate improvement and retention may be a result of different processes happening in the brain during practice and post practice. [Kantak and Winstein, 2012] Galea et al. [2011] investigated this and found distinctive roles of the motor cortex and the cerebellum enhancing retention and immediate performance, respectively, by applying electrical stimulation to one area at a time. This indicates two different processes that are distinct, both in function and possibly anatomy.

2.3 Memory

Motor memory refers to the outcome of practice and learning and is the process regarding formation of motor skill into memory. Forming any memory can be divided into three processes: *Encoding*, *consolidation* and *retrieval*. [Robertson and Cohen, 2006] Although the processes are seen as distinct, there may be an overlap between them. During the acquisition phase, where the practice of a motor skill takes place, the encoding process is dominant. The stabilization and continued process of the acquired motor memory occurs under the consolidation process, where as the retrieval of the skill is under the so named process. The retrieval process is typical under a retention test where the subject needs to reproduce a motor skill. [Kantak and Winstein, 2012]

2.3.1 Encoding

The process termed encoding is associated with practice that have an end result in the formation of a motor memory and occurs under the acquisition phase. It is a cognitive processing of the information regarding the task performed and involve processes required for stimulus identification, response selection and execution. Once a motor action is executed with a certain force and timing the outcome is evaluated through feedback mechanisms and all these cognitive mechanism during the practice phase is considered to be the encoding. [Kantak and Winstein, 2012]

By manipulating practice the cognitive processes can be influenced during the encoding phase and enhance the retention. Two theories can be used for practice: Elaborative-distinctiveness hypothesis and the forgetting reconstruction hypothesis.

The elaborative-distinctiveness hypothesis suggests that by doing random-order practice it is possible for the subject to compare task-related information between them. For example learning tasks A, B and C in a random order, makes it possible for a learner/subject to make similarities between the tasks in the inter-trial interval (before starting a new trial). This is not possible with doing block training, for example performing task in order AAA will not make it possible for a learner/subject to make any similarities to task B or C. By doing the inter-trial comparison an enhancing and stronger memory representation is possible. [Kantak and Winstein, 2012]

The forgetting reconstruction hypothesis corresponds to the subject performing block-order task for a while and then performing random-order tasks. The performing of the block-order tasks will likely construct an action plan in the motor memory, but then by performing random-order tasks the subject needs to "forget" the previously acquired action plan and reconstruct a new one. This reconstruction can enhance the retention of the motor skill even though the performance in practice will decline. [Lee and Wishart, 2005, Kantak and Winstein, 2012]

2.3.2 Consolidation

Consolidation is seen as an "off-line" process that strengthens the motor memory and is occurring in the post-acquisition/post-practice phase. It may be seen as an improvement in performance between practice sessions or the resistance of the influence a secondary task might have on the motor memory of the primary task. [Robertson and Cohen, 2006] Consolidation is a crucial part of the retention of a motor skill, which was proven by Robertson et al. [2005]. They applied low-frequency rTMS to the primary motor cortex (M1) immediately after a practice session which resulted in the blocking of any "off-line" processing improvements [Robertson et al., 2005]. Furthermore an important part of consolidation and the retention of a motor skill is sleep. [Walker and Stickgold, 2004].

2.3.3 Retrieval

Retrieval of a motor memory is the essential part of motor learning. Once information is stored with practice it is the ability of bringing back the information acquired and use it again, that is defined as retrieval. It is the only measurement to investigate the extent of retention and if the motor skill is learned properly (the effectiveness of encoding and consolidation). Not a lot of studies have investigated the retrieval process, but studies have investigated the retention by fMRI with the BOLD sequence. Greater retention was found after random-order practice compared to block-order practice even though the performance of random-order was lower compared to block-order during practice. [Kantak and Winstein, 2012, Lin et al., 2011]

2.4 Motor control and performance

Voluntary movements are goal directed movements which improves with practice. The improvement is to withstand and correct, the learned movement, in the environment and perturbations of the body. The nervous system is able to do that through two control forms termed *feed-back control* and *feed-forward control*. When no experience exists with a specific movement the nervous system reacts directly on the sensory information given by a sensor (eg. muscle spindle). As mentioned before voluntary movements are goal directed meaning a certain state is desired and combining that with a disturbance to the system, an error signal is formed. The error signal then acts on an actuator (eg. muscle) to reach the desired state creating a *closed loop* for the whole system. This system is known as the feed-back control. [Kandel et al., 2011]

To give an example of the feed-back control, imagine holding an empty glass while someone is pouring water in it. The goal is to not spill any water on the floor meaning that the glass needs to be in the same place, a desired state. While the person is pouring, signals from different sensors are being compared to a *reference signal* which the desired state has created. If a mismatch between the signals occur, then an error signal is transferred to the muscles to upkeep the desired state. The end result is no water is spilled on the ground. The feed-back control is illustrated on figure 2.2.

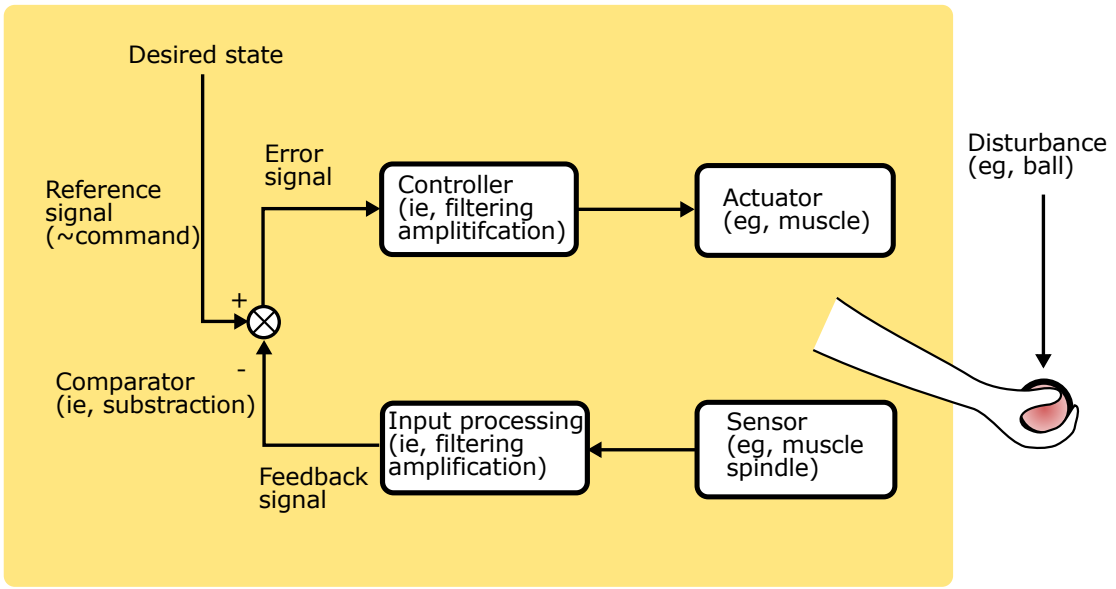


Figure 2.2: Feedback control. A disturbance by a ball creates a feedback signal from sensors (eg. muscle spindles). The feedback signal is compared with a reference signal from a desired state. The differences between these two signal results in an error signal that acts on a actuator (eg. muscle). With inspiration from Kandel et al. [2011]

By repetitively performing a movement several feedback-controls are done and experience is acquired. This is used for anticipating movements or actions and is used for the feed-forward control. The feed-forward control is often referred as an open-loop system but this term is rather misleading due to the control system reacting to some sort of sensory feedback (eg. visual feedback) and experience. So calling it the anticipatory control would be more explanatory. Feed-forward control is used in situations, where the motor system needs to control posture and movements. It is both used when anticipating a movement, but also in predicting an outcome of an action and is essential for rapid actions. A prime example is when to catch a ball, visual information from the eyes triggers the feed-forward control in producing an anticipatory command. This command is activating muscles in the arm in order to be able to catch the ball. By that a desired state is reached even though no direct contact is acquired. [Kandel et al., 2011, Wolpert et al., 2011] Feed-forward control is illustrated on figure 2.3.

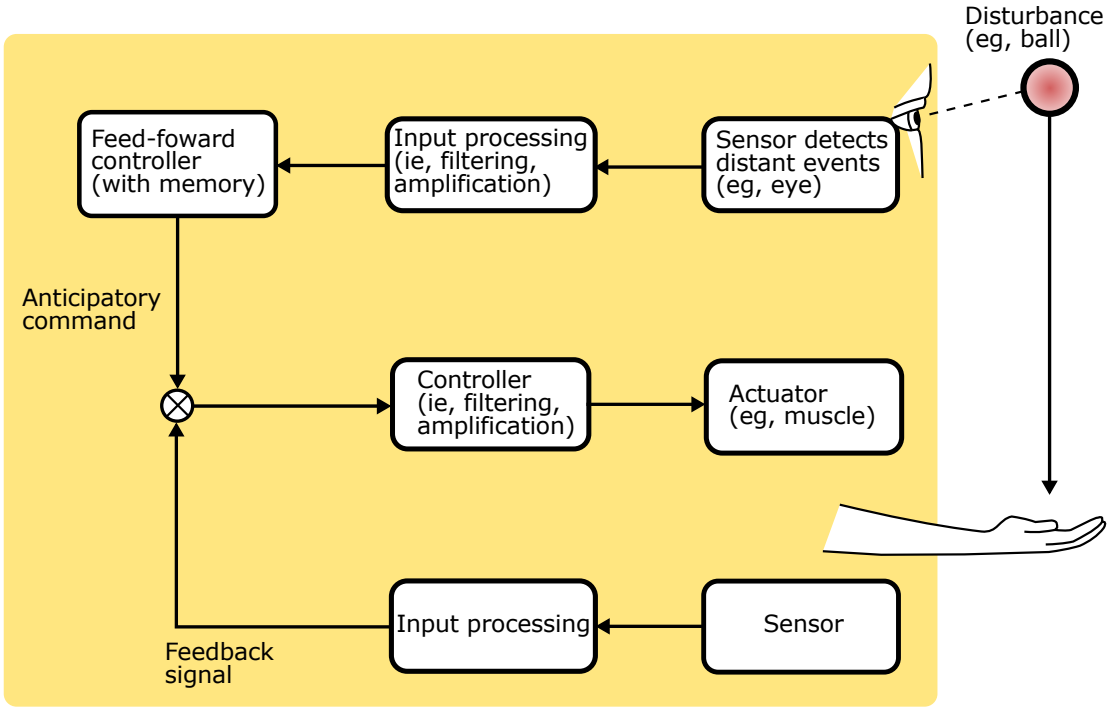


Figure 2.3: The feed-forward controller. A sensor detects a distant event (catching a ball) which triggers the feed-forward controller. The controller sends an anticipatory command to an actuator (eg. muscle) which reacts accordingly. If there is a mismatch between the effort required and the effort exerted a feedback signal is also incorporated in the response of the actuator. E.g. a familiar looking ball, but with twice the weight of what has been experienced earlier. With inspiration from Kandel et al. [2011]

Chapter 3

Physiology of motor learning

Previous chapter looked into the different aspects in the development of motor learning and different strategies in learning process and how it effects the outcome. In this chapter an insight will be provided of the underlying physiology in voluntary movements and the physiology of motor learning, known as plasticity. It is important to know the physiology in order to address all the aspects of motor learning and how it propagates in the human central nervous system.

3.1 Voluntary movements

Generation of voluntary movements is a vital component of motor learning as it involves both the preparation, planing and execution of a movement. Primary structures involved in the control of a voluntary movement are the primary motor cortex, premotor cortex and the supplementary motor areas. The premotor cortex and the supplementary motor areas are involved in motor planning and carrying out complex sequences of movements such as visually guided movements. The input comes from other cortical areas such as the pre-frontal cortex and the output is to the primary motor cortex, spinal cord, through the corticospinal tract, and spinal cord through the brainstem. For visually guided movements the information from the eye travels to the visual cortex and from there to the pre-frontal cortex. From the pre-fontal cortex the signal goes to the primary motor cortex which carries out the motor command via a connection through the spinal cord. [Kandel et al., 2011] The propagation of the signals is illustrated in figure 3.1.

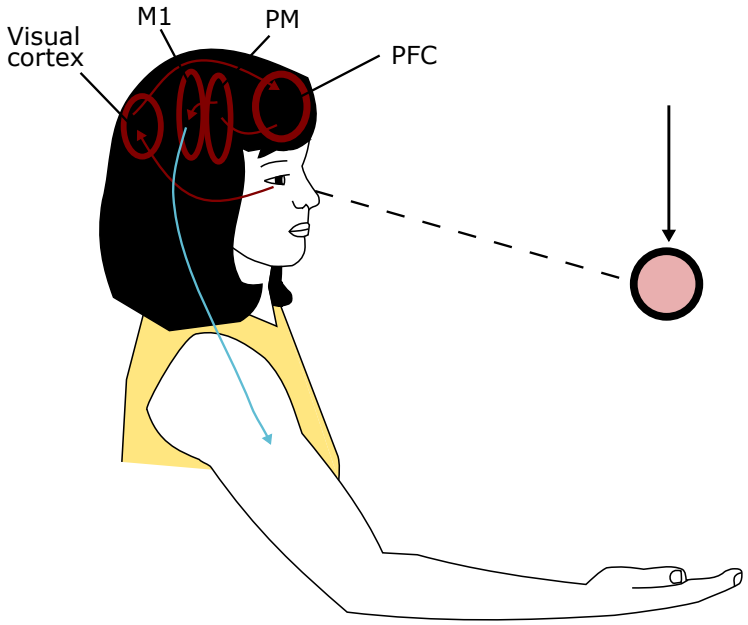


Figure 3.1: Propagation of the signals in a voluntary movement. Disturbance from ball creates visual input. From the eye the signal travels to the visual cortex whereafter it propagates to the prefrontal cortex (PFC). The signal then travels from PFC to the pre-motor cortex (PM) and to the primary motor cortex (M1) which initiates the motor command in the muscle(s). With inspiration from Kandel et al. [2011]

The primary motor cortex is the structure directly responsible for initiating motor commands and is controlling the selection and recruitment of motor units associated to the task. It has direct and indirect inputs, where the direct inputs are from somatosensory cortex, premotor cortex

and from the supplementary motor areas. The indirect inputs are from periphery, brainstem, thalamus, visual cortex, striatum, basal ganglia and the contra-lateral hemisphere. The primary motor cortex is in direct control of distal muscles which is important for precise movements. This means that it has axons directly to the spinal cord through the corticospinal tract. This region also has the lowest electrical stimulation threshold for eliciting a movement and by using this technique a mapping of the primary motor cortex was done and is known as the motor homunculus. Even though the motor homunculus show a somatotopic map of the primary motor cortex, muscles can still be activated from multiple sites in the brain creating an overlap meaning that different muscles can be recruited from different spots for different tasks. [Kandel et al., 2011, Flanders, 2008] The somatotopic motor map can be seen in figure 3.2.

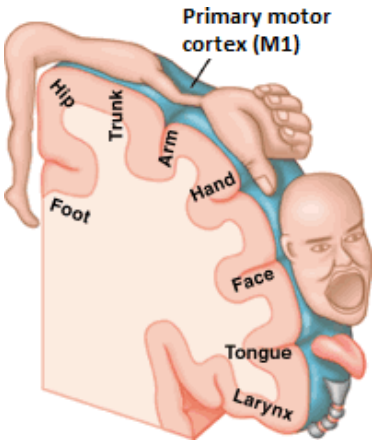
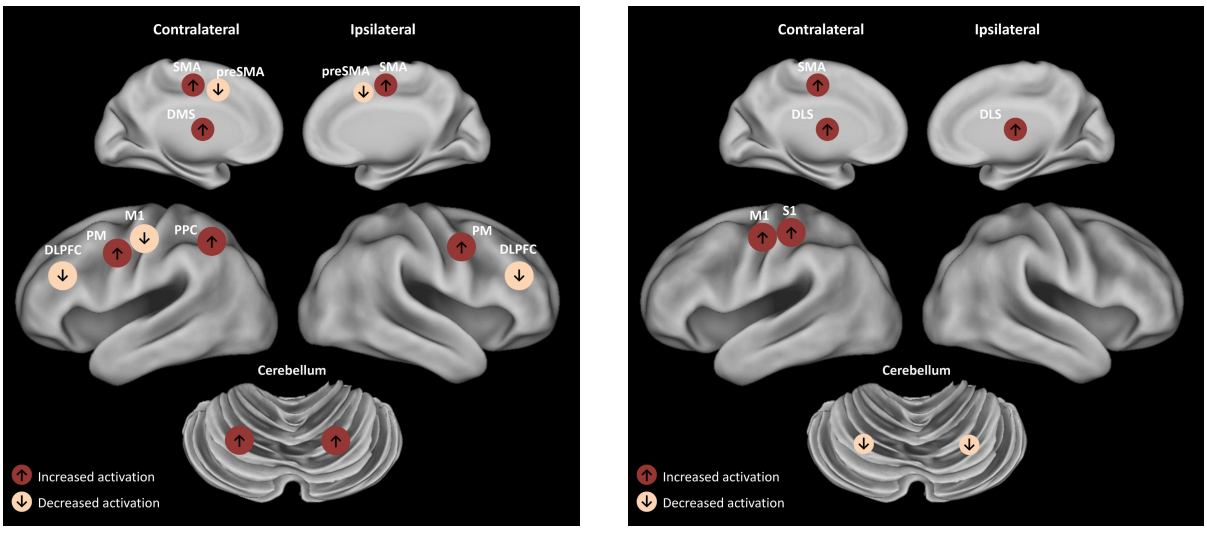


Figure 3.2: Illustration of the somatotopic map of the primary motor cortex. Modified from Schwerin [2013]

When voluntary movements are being repeated and becoming automated a basis of motor learning is laid out (see Chapter 2). Using BOLD fMRI a functional reorganization has been found in brain areas, which are associated with motor learning. In the initial stages of motor learning, regional activity is present in the dorsolateral prefrontal cortex, the primary motor cortex and the pre supplementary motor area. As learning progresses the regional activity of these areas decreases and an increase is seen in the premotor motor cortex, the supplementary area, regions within the parietal lobe, the striatum and the cerebellum. [Dayan and Cohen, 2011] This is illustrated on figure 3.3a.



(a) **(b)**

Figure 3.3: (a) Activation distribution within initial stages of motor learning. (b) Activation distribution within later stages of motor learning. DLPFC = dorsolateral prefrontal cortex. PM = premotor cortex. M1 = primary motor cortex. PPC = Posterior parietal cortex. SMA = supplementary motor area. DMS = Dorsomedial striatum. DLS = Dorsolateral striatum. S1 = primary somatosensory cortex. [Dayan and Cohen, 2011]

The later stages of motor learning are characterized by a progressive decrease in required attention, while being able to maintain performance. This is also reflected in brain activity as a shift from anterior to more posterior regions, thus indicating a decrease in executive function. The shift in activation patterns in the different brain regions are due to plastic properties of the brain. [Dayan and Cohen, 2011] This is illustrated on figure 3.3b.

3.2 Plasticity

The neurophysiologic aspect of skill learning is called *plasticity*. Neuro-plasticity refers to the constant change that the nervous system undergo from each sensory input, motor act and action potential. [Pascual-Leone et al., 2005]

Often plasticity is associated with positive changes such as learning a new instrument, storing memories or regaining lost functions in for example stroke patients. Plastic changes can however also be seen within various diseases such as phantom limb pain and dystonia. These are some of the consequences with the nervous system being this flexible in reorganization. [Pascual-Leone et al., 2005] Different types and forms of plasticity can occur within the nervous system. Axonal sprouting and unmasking of silent synapses can occur within post-stroke patients together with network re-learning [Wieloch and Nikolich, 2006]. Different neurotransmitters and receptors are also associated with both short-term and long-term plasticity [Lovinger, 2010]. Another plasticity form is cortical remapping which also is seen in stroke patient but can also be induced in healthy subjects. Cortical remapping refers to one brain area "taking over" responsibilities from a damaged or inhibited brain area. [Lee et al., 2003, Kandel et al., 2011] Two of the most important neuro-chemical mechanisms associated with learning and memory, are long term potentiation (LTP) and long term depression (LTD) [Purves et al., 2004].

3.2.1 Long term potentiation

LTP has been widely studied for many years within the hippocampus, but can occur within various places in the nervous system [Purves et al., 2004, Cooke and Bliss, 2006]. The LTP is the chemical, both cellular and molecular, and structural term for plasticity. It is a long lasting enhancement of the signal transmitter studied between the presynaptic terminal and post-synaptic neuron. [Purves et al., 2004] The post-synapse consists of two receptors; AMPA and NMDA. When a low frequency action potential travels through the presynaptic axon the neurotransmitter glutamate is released in the synaptic cleft and binds to both the AMPA and NMDA receptor. AMPA allows Na^+ to enter the cell which creates a small depolarization. NMDA receptors have a high permeability for Ca^{2+}, but due to a blockage by Mg^{2+} nothing can enter. This blockage can only be resolved at a high depolarization of the membrane allowing the NMDA to release the Mg^{2+}, but this is not possible at low frequencies. [Cooke and Bliss, 2006, Purves et al., 2004]

At higher frequencies more action potentials travels through presynaptic terminals allowing more glutamate to be released. This results in more AMPA receptors to be activated and stay active for a longer period. More Na^+ enters the cell by then generating a larger depolarization allowing NMDA to release its Mg^{2+} and the influx of Ca^{2+} begins. The influx contributes to LTP and can be divided into two phases: Early- and late-phase LTP. [Cooke and Bliss, 2006, Purves et al., 2004] The mechanism resulting in LTP is illustrated in figure 3.4.

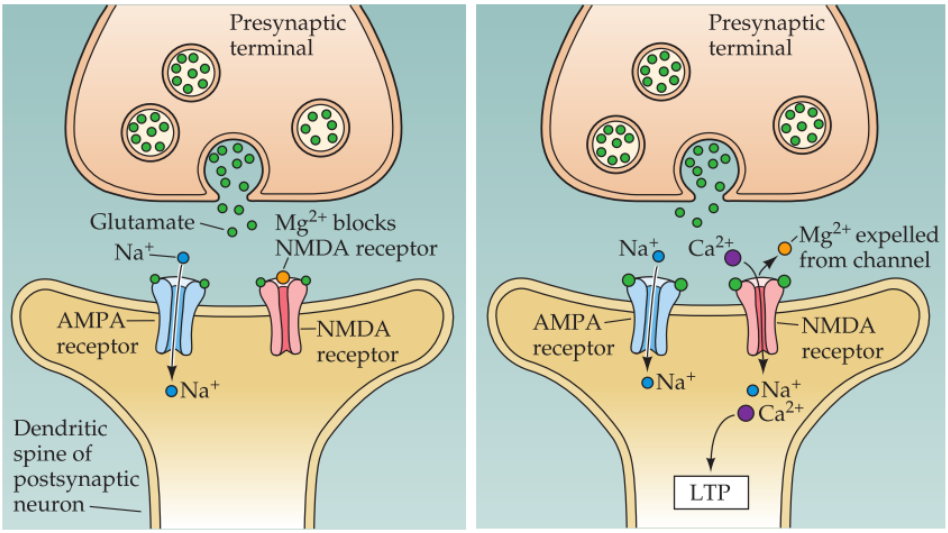


Figure 3.4: At resting potential at the post-synaptic membrane only Na^{+} can pass through the AMPA receptor due to a Mg^{2+} blockage at the NMDA receptor (left). At high frequencies a greater influx of Na^{+} occurs resulting in a depolarization of the membrane and the release of the Mg^{2+} from the NMDA receptor (right). Ca^{2+} enters the cell resulting in LTP. [Purves et al., 2004]

Early-phase LTP lasts a few hours and is characterized as the process of short influx of Ca^{2+}. The Ca^{2+} ions binds to their respected binding protein creating additional AMPA receptors on the post synaptic cell membrane resulting in the post-synaptic spine being more sensitive to glutamate. [Purves et al., 2004] The early phase of LTP is illustrated in figure 3.5.

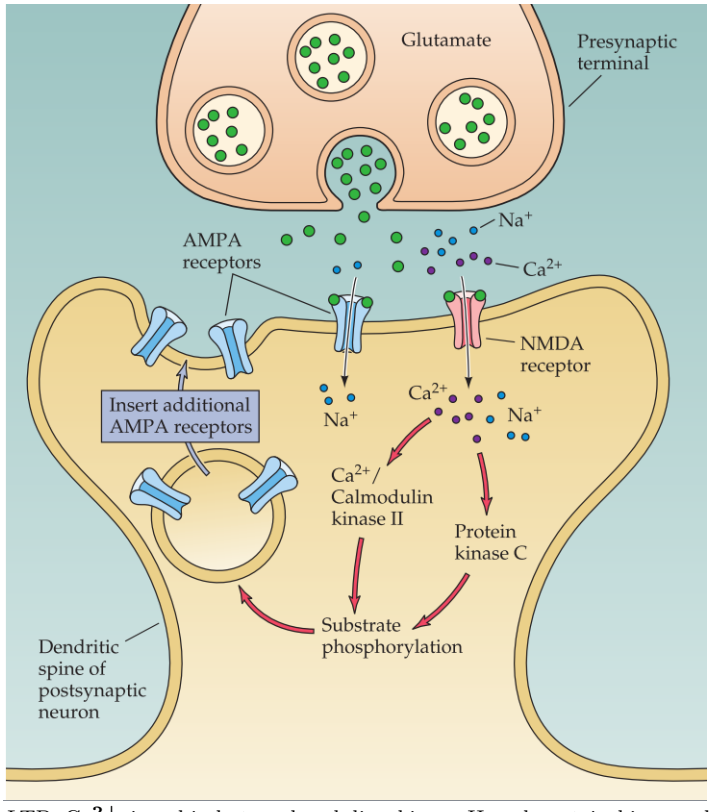


Figure 3.5: Early-phase LTP. Ca^{2+} ions binds to calmoduling kinase II and protein kinase which results in insertion of additional AMPA receptors making the membrane more sensitive to glutamate. [Purves et al., 2004]

Late-phase LTP can last from 24 hours to a life time and is characterized by the prolonged influx of Ca^{2+}. In addition to creating more AMPA receptors the increase of Ca^{2+} ions causes an increase of transcriptions factors with one of the outcomes being proteins that is referred to as growth factors. These growth factors plays a part in forming new synapses (structural plasticity) and is the basis for synaptic plasticity. [Purves et al., 2004] Late-phase LTP is illustrated in figure 3.6.

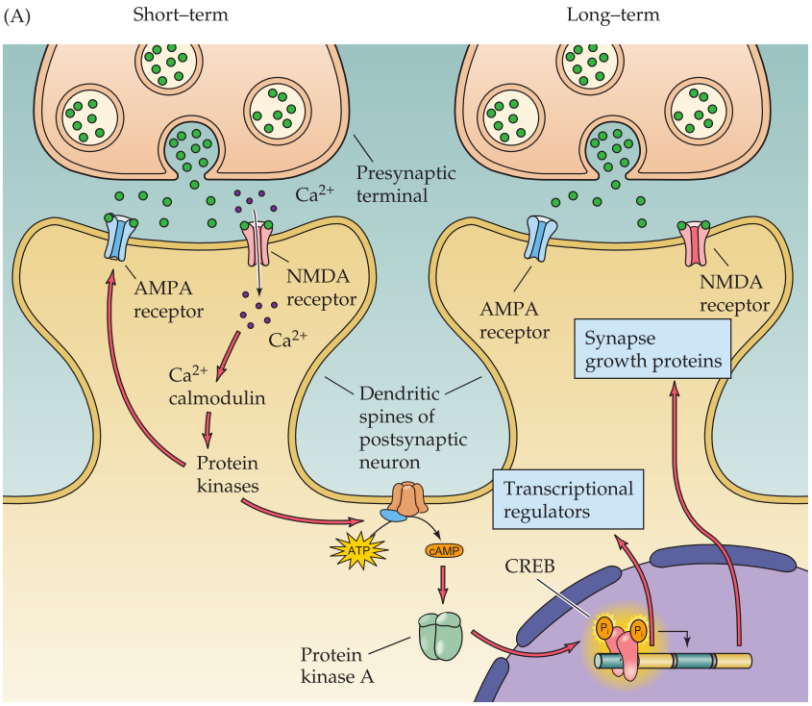


Figure 3.6: Late-phase of LTP. The long influx of Ca^{2+} forms transcriptional regulators and synapse growth proteins that is involved in the contruction of new synapses. [Purves et al., 2004]

3.2.2 Long term depression

An opposite, but just as crucial, mechanism in neuro-plasticity is the long term depression. If only LTP existed the synapses would reach some kind of maximum, where it would be impossible to encode new information. Therefore making strengthening of synapses useful, other mechanisms must selectively weaken specific sets of synapses. The mechanism that takes care of this is LTD. The process of LTD is somewhat similar as the LTP in the hippocampus, but where the LTP is related to a brief high frequency and a large influx of Ca^{2+}, the LTD is related to a long low frequency stimulation (around 1 Hz for 10-15 min). The low rise in Ca^{2+} activates protein phosphatases in the post-synaptic neuron which then causes internalization of the AMPA receptors, meaning the post-synaptic neuron loses AMPA receptors. This results in the post-synaptic neuron being less sensitive to glutamate. [Purves et al., 2004, Cooke and Bliss, 2006] LTD is also associated with the elimination of both the pre- and post-synaptic elements but the mechanisms are not fully understood [Collingridge et al., 2010]. The process of LTD is illustrated on figure 3.7.

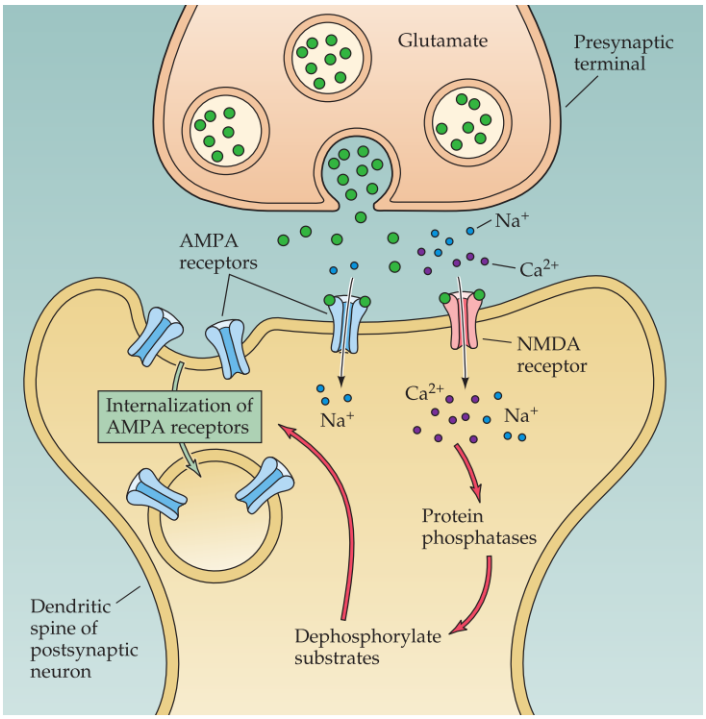


Figure 3.7: The long slow stimulation causes a a low rise of Ca^{2+} in the post-synaptic cell, which results in internalization of AMPA receptors. The sensitivity of the post-synapse decreases. [Purves et al., 2004]

3.2.3 Measuring LTP-/LTD-like plasticity

Measuring if LTP/LTD is induced have been investigating throughout several studies. The direct measurement and induction of LTP/LTD has been done *in vitro* but *in vivo* only LTP/LTD-like mechanisms can be observed. [Stefan et al., 2002, Monte-Silva et al., 2013] Criteria associated with LTP/LTD-like mechanisms are [Jochumsen et al., 2016]:

- Rapid onset
- Persistence on cessation of stimulation
- Associativity
- Specificity
- NMDA-receptor dependence

Rapid onset refers to the evolution of the plasticity and how rapidly it evolves (less than 30 min), whereas the persistence on cessation of stimulation refers to the plastic changes and how long they last (30-60 min) [Stefan et al., 2000]. Associativity and specificity within paired associative stimulation (PAS) refers to the time delay between the stimulation modalities and stimulation sites in order to resemble natural neural delays and physiology [Stefan et al., 2002]. The NMDA-receptor dependence can be investigated by inducing the drug dextromethorphan which blocks the receptor and compare the result with a placebo [Stefan et al., 2002, Monte-Silva et al., 2013]. All these criteria can induce cortical excitability changes which can be measured by different technologies.

Chapter 4

Quantifying motor learning

Being able to quantify the effects of motor training is pivotal to understand the underlying mechanisms, therefore in this chapter ways of quantifying motor training will briefly be outlined, both with respect to the skill being practiced and with respect to neural changes (plasticity) following training. Each of the sections will describe a specific technology, how it has been used to quantify plasticity and the limitation of use.

The effects of motor training can be measured directly on whatever performance measure is used in the practice session. This could include measuring the error the subject is producing over time, but could also include measures of the speed and the force used in the given task.

Multiple technologies have been utilized in assessing neural changes following some sort of intervention including functional magnetic resonance imaging (fMRI), positron emission tomography (PET), electroencephalography (EEG), magnetoencephalography (MEG) and transcranial magnetic stimulation [Chalovich and Eisenberg, 2005]. Other technologies such as near-infrared spectroscopy (NIRS) and transcranial direct current stimulation (tDCS) are also a possibility in assessing plasticity. The former is limited in measuring plasticity at the brain level due to thickness of the skull/scalp and skin [Minagawa-Kawai et al., 2008] and the latter having side effects such as pain, headaches, itching and fatigue [Brunoni et al., 2013].

4.1 Transcranial magnetic stimulation

TMS is a non-invasive magnetic stimulation and was introduced by Barker et al. [1985]. A magnetic field is generated, penetrating the scalp, creating an electrical field in the cortex. Since its publication it has been included in several areas of studies, where investigating plasticity is among them. It has also been used in combination with other techniques such as fMRI, EEG and EMG. [O'Shea and Walsh, 2007, Chalovich and Eisenberg, 2005] The coil used with TMS is usually a figure-of-eight shape because of the greatest intensity being in the center of the two circles forming the eight shape. The coil is placed directly on the scalp which results in a electric field in the underlying cortex. TMS can be done with different intensities, frequencies and be done as a single pulse or as repetitive tasks (rTMS). TMS can be used as an inhibitory or excitatory stimulation depending on the parameters set for the stimulation. Cortical inhibition can be produced by two single pulses separated with 5 milliseconds or less, while facilitation can be done by separating the pulses with 10 milliseconds or greater but no more than 30 milliseconds. By applying repetitive TMS at a frequency of 1 Hz depressing of cortical excitability can be done for at period of time, while at a frequency of 10 Hz or more can facilitate cortical excitability. [O'Shea and Walsh, 2007]

TMS has been used in several studies investigating plasticity, within the area of cortical motor mapping and excitability of the corticospinal pathways. This is done by stimulating a brain area related to motor control (e.g. motor cortex) and measuring the resulting motor evoked potential (MEP) in the muscle activated as a result of the stimulation. [Najib et al., 2011] Pascual-Leon et al. [1995] used TMS to investigate plasticity in the human motor cortex within subjects performing one-handed, five-finger exercise on the piano. After 5 days with 2 hours of daily practice they found the motor area representing long finger flexor and extensor muscles being enlarged, together with the threshold for activation being decreased. They found no changes in

the control group who underwent no piano practice but only TMS mapping of the cortex. This indicates that a plastic change occurred within the intervention group.

4.1.1 Limitations

By using TMS it is impossible to precisely assess a single neuron due to its electrical current affecting a cortical area. Furthermore it is also impossible to precisely determine how much of the cortical area is affected. [Bolognini and Ro, 2010] Even though different shapes of the coil can be used with TMS, it still has limitations in affecting deeper structures in the brain. TMS is mostly effective in structures close to the scalp, approximately 2-3 cm from the scalp. [Bolognini and Ro, 2010, Sliwinska et al., 2014] The spatial resolution of TMS is also relatively low, being approximately around 0.5-1 cm [Sliwinska et al., 2014]. In addition to these limitations when using high current TMS a loud click noise is induced which might cause head and neck muscles to contract [Bolognini and Ro, 2010]. Side effects is associated with TMS including; headache, local pain, toothache, neck pain, seizure induction with more, which indicate that several safety aspects must be considered [Rossi et al., 2009]. This is especially a concern for patients on specific medication, e.g. stroke patients [Rossi et al., 2009]. Another limitation is that with TMS it is not possible to obtain any knowledge of where the plastic changes occur, as it excites the entire pathway (from cortical level to target muscle) [Najib et al., 2011].

4.2 Magnetoencephalography

Magnetoencephalography (MEG) is the recording of the small magnetic fields generated by the electrical activity of the brain. Magnetic fields are not affected by biological tissue and hence the signals are not distorted by the scalp or skull. It does however decay with distance, why the MEG is most sensitive to superficial cortical activity. The magnetic fields are recorded with super-conducting quantum interference detectors (SQUID's), which are highly sensitive to small magnetic fields (recordings are in the range of 1-200 10^{-15} T). Being a super conductor requires extremely low temperatures (-270 °C) and measuring small magnetic fields requires a magnetically shielded room. MEG has both a high temporal and spatial resolution, but does not contain any structural information, why it is sometimes combined with MRI. [Singh, 2014]

MEG has been used to quantify plastic changes in multiple studies. Tecchio et al. [2006] used MEG to investigate plasticity in 18 stroke patients with monohemispheric infarction. They measured twice; once in the acute phase (5 days after infarction) and once in post-acute phase (around 6 months after infarction). The patients had partially of fully recovered functional capabilities. Using MEG in combination with electrical stimulation of the median nerves, the researchers were able to detect neural recruitment outside of the normally expected areas following functional improvement. They also found higher similarity between the affected hemisphere and the unaffected hemisphere in the post-acute phase recording, when comparing to the acute phase. Juenger et al. [2013] also used MEG to quantify neural changes following constrained induced movement training in children and adolescents with congenital hemiparesis. They found an increase in activation of the primary somatosensory cortex following functional improvement of the training.

4.2.1 Limitations

Despite the clear advantages and possibilities of usage, the MEG has some clear limitations. As mentioned before, it requires a specially designed room with magnetic shielding and it requires extreme cooling in order to function. [Singh, 2014] This makes the technology hard to relocate and expensive to establish [Wolpaw et al., 2002] and furhermore it is technically demanding to operate [Wolpaw et al., 2002].

4.3 Electroencephalography

EEG is a technique measuring the electrical currents produced by the billions of neurons in the human brain. Electrodes are placed directly on the scalp with some conductive media. These electrodes measures currents that flows during synaptic excitations of many pyramidal neurons that maximum have a current depolarization range of 20 mV. These currents are termed excitatory postsynaptic potentials (EPSPs) and their inhibitory counter parts are termed inhibitory postsynaptic potentials (IPSPs). EPSPs are the depolarization where as the IPSPs are the hyperpolarization of the postsynaptic membrane. [Teplan, 2002, Despopoulos and Silbernagl, 2003]

Due to the small current of a single EPSP (0.5 mV) several needs to be created to pass the threshold for an action potential to occur. The threshold can be surpassed by a summation of the EPSP's both temporal and spatial but also as a summation of EPSP's and IPSP's. Several EPSP's take place at the dendrites and are spatial summed at the axon hillock. With the spatial summation all the EPSPs occurs at the same time. Temporal summation is where a ESPS occurs at the dendrite and a secondary ESPS is time delayed but the summation of them both results in an action potential. The last summation form is the summation of IPSP's and EPSP's but still results in the threshold being passed. EEG is affected by all these processes but the signal is mostly affected by the ESPS's. [Teplan, 2002, Despopoulos and Silbernagl, 2003]

Different frequencies can appear in the EEG-signal and they represent different wakefulness of the individual [Teplan, 2002, Martini et al., 2012, Despopoulos and Silbernagl, 2003]:

- Delta (0.5-4 Hz): Associated with deep sleep
- Theta (4-8 Hz): May appear in sleep within normal adult for a short time. In some circumstances it is an indication of a brain disorder
- Alpha (8-13 Hz): Adults who are awake with their eyes closed
- Beta (13-30 Hz): Associated with concentration, stress or in a state of psychological tension
- Gamma (>30 Hz): Appears during learning activity

Several studies have investigated plasticity in delta waves using EEG as a technique [Assenza and Di Lazzaro, 2015]. A study by Huber et al. [2006] immobilized subject's arms during the day and at slow wave activity following sleep. They showed motor performance decline and motor evoked potentials decrease over contralateral sensorimotor cortex. This indicated local synaptic depression. [Huber et al., 2006]

4.3.1 Limitations

Even though EEG have a high temporal resolution (down to a few milliseconds) it still lacks a high spatial resolution due to volume conduction. EEG have a spatial resolution between 1 and several centimeters and by a comparison to for example fMRI, makes this resolution low. [Huettel et al., 2004, Assenza and Di Lazzaro, 2015] Furthermore the EEG-signal is of low amplitude and is sensitive to noise and the signal-to-noise-ratio (SNR) is relatively low, making it necessary to apply filters, amplifiers and record within a Faraday cage [Teplan, 2002].

4.4 Stretch reflex, H-reflex and F-waves

There exists different ways of investigating spinal excitability: The stretch reflex is the monosynaptic reflex which results in a muscle contraction as a response to the same muscle being stretched [Pierrot-Deseilligny Emmanuel, 2005]. The H-reflex is the electrical variant of the stretch reflex [Palmieri et al., 2004] and the F-wave a direct electrical stimulation of the motor neuron at a supramaximal intensity [Pierrot-Deseilligny Emmanuel, 2005].

The H-reflex is found by eliciting an electrical stimulus over a mixed nerve exiting both the efferent and afferent fibers resulting in an immediate muscle response from the excitement of the

efferent fibers and a delayed response from the afferent fibers synapsing onto the efferent fibers in the spinal cord. [Capaday, 1997] Hence it is a way to assess neural modulation at the spinal level, since a change in the H-reflex would indicate a change in the afferent transmission efficiency [Duclay et al., 2008]. Furthermore, change in the efferent response, also know as the M-wave, is a way of investigating peripheral adaptations, as the maximal M-wave represents the synchronous activation of all motor units for the targeted muscle [Pensini et al., 2002]. This is however not limited to neural modulation, but could include change in muscle size.

The F-wave is found by electrically stimulation the motor axon at a supramaximal stimulus, which produces first an M-wave, the product of the excitation along the axon path to the terminal, and then the F-wave, a "backfiring"/"reactivation" from the response propagating to the cell body in the spinal cord. The F-wave can be used as an expression of motor conduction to and from the spinal. [Pierrot-Deseilligny Emmanuel, 2005]

H-reflex experiments have primarily been used to investigate plastic changes in the spinal cord following resistance training. But even though changes were present (increase in strength and change in H-reflex) from a pre- to post-measurement, the changes were attributed to supraspinal mechanisms in the form of altered neural drive to agonist and antagonist muscles. [Pensini et al., 2002, Lagerquist et al., 2006, Duclay et al., 2008]

Klarner et al. [2016] investigated the effects of arm and leg cycling on stroke patients and used measures of the stretch reflex as an expression of neural plasticity. They found an increase in excitability of the stretch reflex of the soleus and the authors speculate that it could be due to altered pre synaptic inhibition in the spinal cord.

4.4.1 Limitations

In order to obtain the H-reflex the nerves innervating the targeted muscle need to be accessible by percutaneous electrical stimulation somewhere along the path before the spinal cord, thus not all muscles are able to be used [Misiaszek, 2003].

Another limitation to the H-reflex is that it is electrically induced and hence does not occur naturally. For instance, the muscle spindles are bypassed using this methodology and they play a part in the normal stretch reflex and are thought to adjust the output of the aforementioned reflex. A change in the H-reflex might therefore not translate into a change in the stretch reflex. [Palmieri et al., 2004]

Since the H-reflex is obtained by electrical stimulation a level of subject unpleasantness (with the degree dependent on the settings of the stimulator) is also to be accepted, [Capaday, 1997, Tucker et al., 2005] and a number of repetitions are required to obtain results, that are reliable [Brinkworth et al., 2007].

As for the F-wave an obvious limitation is that motor neurons are never activated in the same manner in motor control as it is not a consequence of a synaptic event, why it is not a viable tool for assessing motor control. [Pierrot-Deseilligny Emmanuel, 2005]

4.5 Magnetic resonance imaging

MRI is a widely used and an essential imaging tool for diagnosing diseases in the central nervous system as well as in organs. The strength of MRI is the greater contrast it provides for soft tissues compared to plain radiography or computed tomography (CT). The technique of MRI is the measurement of the positively charged spinning nucleus of hydrogen, which is contained in water, tissues, proteins, lipids and other macromolecules, and how they react when applied in a magnetic field. [Edelman and Warach, 1993] The technique of MRI can produce different contrast, which determine what is shown in the image, by adding a gradient or radio-frequency. [Edelman and Warach, 1993, Huettel et al., 2004, Schild, 1990]

When locating activity or functioning of the human brain, fMRI is usually used. fMRI originates from MRI and is a sequence that can be applied to the MRI scanner. It can be made sensitive to changes in regional blood perfusion, blood volume or blood oxygenation that accompany neu-

ronal activity. By making it blood oxygenation level dependent (BOLD) a spatial resolution of a few millimeters and a temporal resolution of a few seconds can be achieved. [Huettel et al., 2004]

fMRI has been used in collaboration with several other techniques including TMS and has been used to investigate plastic changes both within motor learning [Pascual-Leone et al., 2005] but also within various diseases and injuries such as brain injuries, tumoral lesions, epilepsy etc. [Thomas et al., 2007]. A study by Pascual-Leone et al. [2005] asked subjects to perform the same rhythmic hand movement while lying in a fMRI scanner. They applied sham rTMS (no specification by the author), 1 Hz rTMS and 10 Hz rTMS to the contralateral motor cortex of the subjects and recorded fMRI scans again. Sham rTMS showed no changes, while the suppression of the motor cortex with 1 Hz rTMS showed an increased activation of the rostral supplementary motor cortex and of motor cortex ipsilateral to the moving hand. 10 Hz rTMS showed a excitability in the contralateral motor cortex and a decrease in activation of rostral supplementary motor cortex. This indicates that plastic changes can occur rapidly and be initiated by rTMS. [Pascual-Leone et al., 2005] The changes before and after the three session of rTMS with fMRI scans are illustrated on figure 4.1

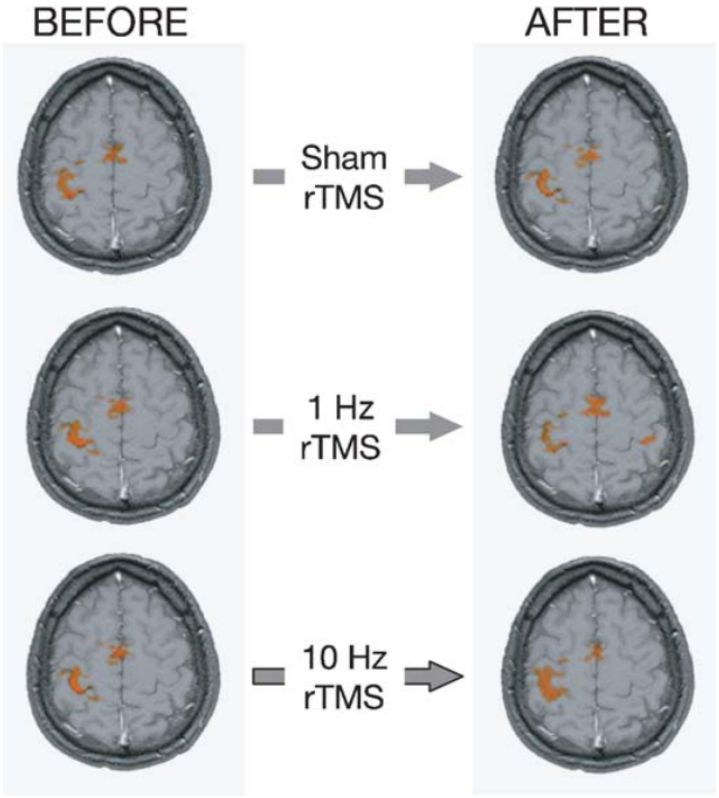


Figure 4.1: fMRI scans of before and after applying sham rTMS, 1 Hz rTMS and 10 Hz rTMS. Sham rTMS showed no real changes where as 1 Hz rTMS showed an increased activation of the rostral supplementary motor cortex and of motor cortex ipsilateral and 10 Hz rTMS showed an excitability in the contralateral motor cortex and a decrease in activation of rostral supplementary motor cortex. [Pascual-Leone et al., 2005]

A study by Karni et al. [1995] used BOLD fMRI signals in the primary cortex to investigate subjects performing finger movements. For the control group and the intervention group the activation of the primary cortex was comparable before practice but after a 4 week training period the pixels representing activation in the primary cortex for the intervention group was larger than the control group. The changes persisted for several months indicating that reorganization of the primary cortex is an indicator for retention of a motor skill. [Karni et al., 1995]

4.5.1 Limitations

By using fMRI a high spatial resolution can be obtained, but has its cost in temporal resolution. As mentioned before by using the BOLD fMRI a temporal resolution of a few seconds can be obtained but comparing that to EEG or MEG where a temporal resolution of 10-100 ms easily can

be obtained, then the temporal resolution of BOLD fMRI is low [Huettel et al., 2004]. Another limitation is the price of a MRI scanner which is high [Rentz, 2017].

4.6 Positron emission tomography

Positron emission tomography (PET) is a functional image technique that uses radioactive emitters to observe metabolic processes in the human body. Subjects are injected or asked to inhale a radiopharmaceutical, where the scan is performed seconds to minutes after allowing the transportation or uptake of the emitter. The decay of the radio-isotope results in a positively charged positron which hits a negatively charged electron resulting in an annihilation of both. This produces two high energy photons that are propagating in directly opposite directions and is captured as gamma rays by crystals and photo-multiplier tubes. PET can give highly detailed images of metabolic processes and help diagnosing several diseases including cancer. The spatial resolution of PET scans can vary but resolution of the center of view can be around 3.3-3.6 mm and 5 mm 20 cm from the center. [Ollinger and Fessler, 1997, Bailey et al., 2002] PET has also been used in investigating plasticity. The combination of rTMS and PET was done in a study by Lee et al. [2003]. They recorded PET scans of subjects performing a freely chosen finger movement after 30 minutes of 1 Hz rTMS to the primary motor cortex. They found that the primary motor cortex became less responsive to inputs from premotor and mesial motor areas and activity increased in the premotor cortex of the nonstimulated hemisphere.

4.6.1 Limitations

One of the big limitations with PET is the costs. The PET scanner itself is expensive but it also require cyclotron either on-site or close by to create isotopes. This is due to the relatively short half-time these isotopes have and if cyclotron is placed too far away, the isotope decays before usage is possible. [Ollinger and Fessler, 1997] Another limitation is that subjects must be exposed to radiation from the radiopharmaceutical in order to obtain images.

4.7 Combinations

Combination of technologies can give a greater insight to a problem than when only one technology is used. It can give the advantages of seeing changes within more than one area, for example by combining MRI and PET a change in anatomic structures together with a change in metabolic processes can be seen. As stated throughout this chapter multiple of the technologies mentioned have been used in combinations. TMS is obviously used in combination with EMG [Petersen et al., 2001], when assessing excitability, but has also been used en combination with MRI [Pascual-Leone et al., 2005], PET [Lee et al., 2003] and EEG [Lepage et al., 2008]. Furthermore EEG has been used in combinations with different technologies such as MRI [Toma et al., 2002] and EMG [Kristeva-Feige et al., 2002]. The combination of EEG/MEG and EMG is usually seen as coherence between the signals and is of interest due to the combination being able to solve the *binding* problem. The binding problem refers to the mechanisms in the link between two distinct locations that is processing the same information. In this case it is the linkage between brain and muscle and how they process information in order to reach the same goal. [Siemionow et al., 2010] EEG have a lackluster spatial resolution but in the combination with fMRI the spatial resolution can be increased while still keeping a high temporal resolution [Liu et al., 2006]. The combination of TMS and EEG can be used in investigating TMS induced motor evoked potentials (MEP) and EEG oscillations in relation. Combination of TMS-EEG can give insight into when and how activity in one area affect activity in other areas [Taylor et al., 2009].

Chapter 5

Literature review

Based on the information in the former chapters a research question will be presented to guide a systematic review of literature in this area. The research question will be followed by a research strategy including selection criteria, databases and search words. The chapter will end with the outcome(s) of the review.

Each of the measurements mentioned in the previous chapter can be used to quantify effects of motor learning. Measurements like TMS and H-reflex measure the effects in a direct manner with a stimulation being part of the modality, while measures such as MEG, EEG and fMRI are more of an indirect measurement. All of the measurements have pros and cons relating to the resolution; spatial and temporal, and to the availability. This is summed up in table 5.1, where the measurements are compared to each other.

Table 5.1: A relative comparison of the different measurements in terms of spatial resolution, temporal resolution and availability, from low to high based on the information provided in the previous chapter.

Technology	Spatial resolution	Temporal resolution	Availability
EEG	Low	High	High
MEG	High	High	Low
HMV	-	-	High
fMRI	High	Low	Low
TMS	Low	-	Medium
PET	Medium	-	Low

The H-reflex has primarily been used to investigate plastic changes associated with different types of resistance training or a change in maximal strength (see section 4.4). For motor skills requiring less effort it might not be suitable. Furthermore the electrical stimulation required to elicit the reflex might be painful for the subject. fMRI, MEG and PET seems unfeasible due to the cost of establishment and to the high requirements of use (and radiation for PET). The use of TMS has been reported to cause numerous side effects and it is a measurement which might introduce a plastic effect, just by being used (see section 4.1). This leaves EEG as the most viable option for further research. It is accessible and cheap compared to the other technologies and it has great temporal resolution. By including EMG, another accessible technology, it becomes possible to investigate the linkage between brain and muscle as a way to access plastic changes in the entire corticospinal pathway. Based on this decision the research question to guide a review of literature was formulated:

What has been shown using EEG and EEG-EMG coherence to quantify plastic changes in relation to motor learning?

5.1 Research strategy

An initial search was conducted with the keywords EEG and plasticity, to get an understanding of the field and to find relevant key words. This search resulted in hits in the range of 10,000 with a lot of results relating to EEG in relation to sleep and EEG connectivity. First off the sheer amount of work to systematically read and assess that number of articles is unfeasible in a project with a limited timeline and other objectives. The part sleep plays in the role of motor learning is beyond the scope of this project, why it was excluded. EEG connectivity was another frequent finding in the initial search and it is an area that is already well documented, why it was not pursued further. Another finding from the initial search was the use of features related to movement preparation in in the EEG, namely the movement related cortical potential and the event related desynchronization/synchronization. They have been used in different motor studies investigating the properties of the features for different limbs and different movements. It has also been utilized in different brain-computer interfaces using them as control signals or in relation to stroke rehabilitation. Because of this, these specific features were added as key words for the literature review.

5.1.1 Selection criteria

The studies must somehow be related to motor learning or training and investigate changes caused by this. The effects of motor learning might be different for animals and for humans, why the studies included in this review need to be done with human subjects. Studies investigating any pain in relation to motor learning was also excluded as it is established that pain can alter the effect of motor learning [Lamothe et al., 2014] and hence any change seen in relation to altered motor performance may be related to a change in pain for the subject. As mentioned above sleep and connectivity studies were also excluded.

5.1.2 Databases and keywords

The databases Pubmed, Embase, IEEE, ScienceDirect and the Cochrane library were used with the following keywords: EEG, motor learning, plasticity, EEG-EMG coherence, corticomuscular coherence, rest/resting EEG, Motor-related cortical potential, Event-related desynchronization/synchronization. A comprehensive list of searches including the specific keywords and the resulting hits can be found in appendix A.

5.1.3 Process of inclusion

Articles were screened at different levels for relevance. If the title seemed interesting with respect to the research question, the abstract was read and if it still fit the purpose, then the full text was assessed. The initial searches across databases yielded in 28810 hits. Using filters of the databases and adding keywords, the search results were narrowed to 2137 hits. The title of these were assessed and as a result 159 were selected for reviewing of abstracts. 70 articles were deemed relevant based on their abstract and the full text of these were read. 29 of those were found relevant and after removing redundant articles found on different databases a total of 21 articles were included in the review. The process is illustrated in figure 5.1.

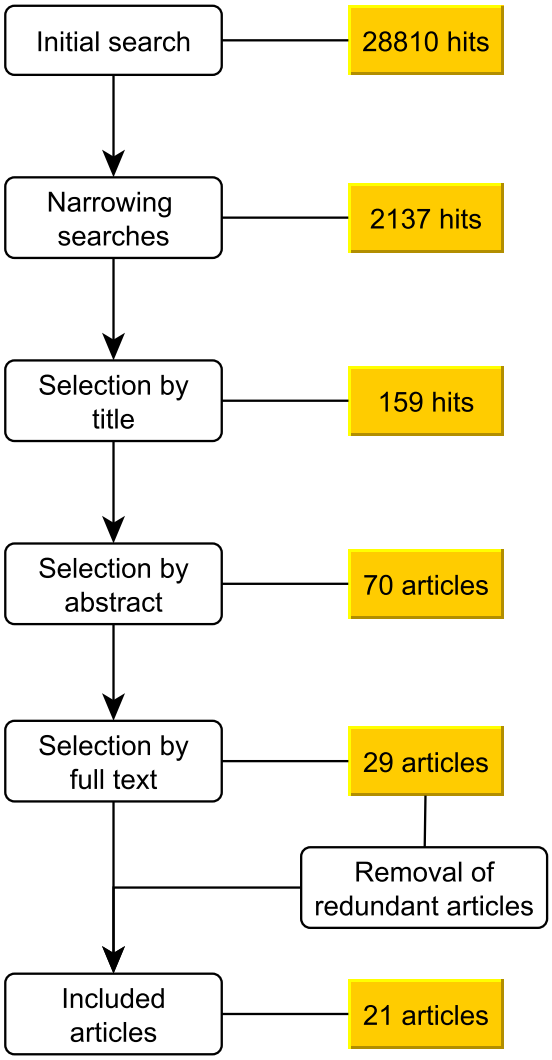


Figure 5.1: Overview of the process of the literature review.

The search was conducted from the 4th to the 16th of April 2017.

5.2 Outcome

The results of the literature review are presented in table 5.2 and 5.3. The results presented in the tables are only the results relevant to the research question presented above. Reports of tendencies or trends were also not included, meaning all results in the tables are of statistical significance.

Table 5.2: Included articles. ↓ = significant decrease, ↑ = significant increase, **MRCP microstate** = small segments of event related potentials, **CTLR** = contralesional/lesional activation ratio, **ERN** = error-related negativity, **SP** = spectral power, **MR(C)P** = movement related (cortical) potential, **RT** = reaction time, **RAP** = re-afferent potential, **ERD/ERS** = event related desynchronization/synchronization.

Study	Subjects (n)	Feature(s)	Outcome
Halder et al. [2005]	Healthy (10)	MRCP microstate	Two parts of motor training: Microstate 1: amplitude ↓ from part 1 to part 2 both runs. Microstate 2: amplitude ↓ from part 1 run 2 to part 2 run 2. Microstate 3: amplitude ↓ from part 1 to part 2 both runs.
Fang et al. [2015]	Stroke (10) Healthy (5)	Current Density, CTLR	Before movement onset: Control: no activation in right hemisphere. Patients: Substantial contralesional hemisphere activation. The nonlesional side source strength was significantly higher for stroke than control subjects. CTLR: Stroke higher in planning phase in Broadmann area 1,2,3,4
Bönstrup et al. [2015]	Young (15) Old (15)	Source SP analysis	Both groups: alpha power ↓ over bilateral motor cortices under finger movement session. 1 hour after learning alpha power ↓ in elderly group over bilateral motor cortices.
Smith and Staines [2006]	Healthy (10)	MRP	Early component of MRP max over central electrode sites onset latency 1300-1600 ms prior to movement onset. Early to late component occurred 100-150 ms and peaked within 100 ms post movement. Scalp distribution of late MRP left hemisphere and max over FC1. Larger RT decrease = larger early MRP amplitude. Last 40 repetitions: Early MRP ↑ in CZ, FCZ, RAP ↓ in CZ
Zhuang et al. [1997]	Healthy (13)	ERD	10 Hz max ERD when obtained full explicit knowledge and declining thereafter. Significant change in 10 Hz ERD power at C3 for 13 subjects between rest, random, implicit, full explicit, after-learning and random sequence block.
Yilmaz et al. [2013]	Stroke (5)	MRCP	CZ Peak-Amp was significantly larger before intervention at midline and ipsilateral central locations. Contralateral and midline frontal locations MRCP onsets earlier than during movements and after intervention (Pre and Post). Earlier MRCP onset at central electrodes during paretic compared to during healthy hand movements before intervention
Etnier et al. [1996]	Healthy (61)	Alpha power	Following the the first 10 acquisition trials, the experimental subjects had more alpha activity than the control subjects

Table 5.3: Included articles. ↓ = significant decrease, ↑ = significant increase, **MR(C)P** = movement related (cortical) potential, **PD** = Parkinson's disease, **ERD/ERS** = event related desynchronization/synchronization, **ROI** = region of interest, **SP** = spectral power, **MF** = mean frequency, **CMC** = corticomuscular coherence, **CDF** = cumulant density function, **SRTT** = serial reaction time task.

Study	Subjects (n)	Feature(s)	Outcome
Dirnberger et al. [2004]	Healthy (33)	MRCP	MRCP amplitude ↓ over the right hemisphere with repetitions. MRCP amplitude ↓ over entire scalp until a minimum was reached.
Moisello et al. [2015]	PD (15) Healthy (16)	ERD/ERS and Rest EEG	Left ROI: Beta ERS ↑ with practice in controls. Right ROI: Beta ERS ↑ with practice in controls. Frontal ROI: ERD ↓ with practice in both groups. Rest: ↑ in beta power over frontal and left area in controls.
Kranczioch et al. [2008]	Healthy (13)	ERS	9 Hz ERS larger in early compared to late runs in frontal and occipital ROI. Same for 13 Hz ERS
Lardon and Polich [1996]	Exercise (18) Control (18)	SP, MF in Rest EEG	SP: Exercise had less delta, more other bands compared to the control subjects. MF: exercise subjects had higher frequencies for delta, theta, beta-l, and beta-2 bands.
Assenza et al. [2015]	Healthy (20)	SP	Delta wave SP in resting EEG ↑
Perez et al. [2006]	Healthy (11)	CMC, CDF	CMC ↑ in 15-35 hz range, shift in peak frequency, largest peak in CDF ↑.
Hori et al. [2013]	Healthy (9)	CMC	CMC ↑ in alpha- and theta-range following virtual navigation training.
Klotz et al. [2013]	Healthy (15)	CMC	Change in gamma modulation, CMC ↑ following decrease in reaction time in a SRTT.
Mendez-Balbuena et al. [2011]	Healthy (14)	CMC, SP	CMC could be learned by subjects who did not show significance at beginning. CMC and SP ↑ with learning in both dynamic and static force tasks. Performance of all subjects ↑
Mendez-Balbuena et al. [2012]	Healthy (14)	CMC, SP	CMC could be learned by subjects who did not show significance at beginning. CMC and SP ↑ with learning in both dynamic and static force tasks.
Kristeva et al. [2007]	Healthy (8)	CMC, SP	Good performance in a visuomotor task was associated with significantly higher beta-range CMC and SP than bad performance.

Furthermore three reviews were included during the process. Hatfield et al. [2004] investigated the effects of practice over time including articles using spectral power, cognitive interference, interelectrode coherence, training, and event related potentials. In general they found cortical changes that happen over time with practice. It is argued that the changes associated with motor planning and execution are: less attentional demand and less cognitive interference. However, they also note that alterations of cortical signals can happen in a relatively short time frame.

Rueda-Delgado et al. [2014] looked at studies utilizing EEG and MEG to investigate the processes involved in motor learning, planning and execution, especially for task switching and dual tasks, using features such as movement related cortical potential, event related desynchronization and coherence. They found a correlation between performance improvement and a decrease of some of the components of the movement related cortical potential (the negative slope and

the motor potential), where as the early component, the bereitschafts potential, did not show changes. In line with Hatfield et al. [2004] they speculate that less neural resources are required when a subject becomes more proficient with the given motor skill.

Wright et al. [2011] reviewed articles investigating the movement related cortical potential in relation to motor training. They found differences in onset and amplitude for novice and expert performers: Experts produce a potential closer to the onset of the motor skill and of lower amplitude than novices. Similar changes are seen for novices practicing and the authors note that the movement related cortical potential may provide an adequate measure of assessing learning, rather than using improvement of performance as a lone indication.

Chapter 6

Aim

In this chapter a brief summary of the previous chapters with special emphasis on the findings from the literature review will be presented. This will be used to setup the aim of this project and to guide experimental procedures to investigate neural changes in relation to motor learning.

Motor learning is important for human survival. It is important to be able to quantify proper motor learning in areas of rehabilitation, as both time, motivation and effectiveness is of the essence. Motor learning as a term covers a wide range of processes such as practice, the learning-performance distinction and memory, which all contributes to an understanding of motor learning and the improvement of such. Several brain structures contributes to motor learning and the underlying physiological aspect is known as neural plasticity. By setting up certain criteria plasticity can be measured by different technologies. The technologies include TMS, MEG, EEG, stretch reflex, MRI (fMRI) and PET, but can also be used in combinations. All the technologies have their pros and cons regarding resolution and accessibility. Given those EEG was chosen as the focus of the present study.

Using key-words such as "EEG", "motor learning", "plasticity", "EEG-EMG coherence", etc. a literature review was conducted with the purpose of answering the following research question:

What has been shown using EEG and EEG-EMG coherence to quantify plastic changes in relation to motor learning?

21 studies were included in the review covering topics such as event related potentials, brain waves in resting EEG, event related desynchronization/synchronization and EEG-EMG coherence.

The studies that investigated the change of movement related cortical potential (MRCP) in the process of learning generally point in the direction, that the MRCP is changed both temporally and with respect to amplitude. As learning progresses the potential shifts closer to the movement onset, and the amplitude decreases, but with respect to which extend and what part of the signal, the findings are somewhat conflicting.

Only two of the included studies looked at the effects of motor learning on the resting EEG. One of them found an increase in spectral power of the delta wave, but the other one found the opposite: a decrease in delta waves, but an increase in other waves.

Three of the studies included in the review investigated event related desynchronization/synchronization (ERD/ERS). The general findings within these studies were that a decrease ERD following practice/motor learning occurs but the results regarding ERS are conflicting. One study found that ERS increased with practice whereas a different study found ERS being largest within the early runs compared to late of a training session.

Findings within coherence studies were, that coherence increases (or appears, if not present before) after motor learning. The studies however do not agree on which frequencies are affected. Within the six studies, that investigate coherence, three out of six utilize both a measure of coherence and spectral power within specific frequency ranges. Using both spectral power and corticomuscular coherence contains redundant information, as Kristeva et al. [2007] found that

the two are not independent of each other.

In general there is a lack of evidence/conflicting evidence within this field. Therefore the aim of this project is to investigate the neural changes associated with short-term motor learning using measures of EEG and corticomuscular coherence. The following measurements will be investigated:

- Movement related potential
- Event related desynchronization/synchronization
- Corticomuscular coherence
- Resting EEG brain waves

In order to accommodate the measures of interest an experiment will be conducted. The experiment will focus on short term motor learning in the non-dominant lower arm to induce movement related potential and event related desynchronization/synchronization for investigation. Corticomuscular coherence and resting brain waves will be recorded prior and after the motor learning has taken place to assess if any changes occurs following intervention.

Chapter 7

EEG measures

Prior to describing experimental procedures an explanation of in depth features of the EEG and corticomuscular coherence related to motor learning and motor execution will be provided to give an overview of the signal characteristics. With the information from this chapter the experiment can be designed to properly accommodate the collection of these features that will later be analyzed.

The interesting EEG frequency bands associated with motor learning that have been used in several studies are the alpha (8-13 Hz) and beta bands (13-31 Hz) [Lardon and Polich, 1996, Erbil and Ungan, 2007, Nakano et al., 2013]. Changes in different bands such as delta and theta bands have been investigated before [Lardon and Polich, 1996] but are less common. As presented in Chapter 5 several features of the EEG are related to motor learning and can change because of it. Features that will be presented in this chapter are the: Movement-related cortical potential (MRCP) and Event-related desynchronization/synchronization (ERD/ERS) within EEG frequency bands.

7.1 Movement-related cortical potential

EEG potentials recorded over the motor-cortex related to real or imaginary movement-stimuli is refered to as the MRCP. These changes are seen as a slow negative deflection in the EEG-signal and can be divided into parts of *planning/preparation*, *execution*, and *control of performance*. [Boye et al., 2008, Shakeel et al., 2015] Bereitschaftspotential (BP) or readiness potential (RP) corresponds to the planning/preparation and can have an onset of up to 2.0 seconds before the actual movement [Shibasaki and Hallett, 2006]. The execution of the voluntary movement is termed the motor potential (MP) and has the greatest negative amplitude of the MRCP [Shakeel et al., 2015]. Lastly the control of performance is called the movement-monitoring potential (MMP) which can be seen as an increase in amplitude of the EEG signal related to the MRCP [Boye et al., 2008]. The characteristics of the MRCP and its parts together with an EMG signal when performing a voluntary hand-movement is illustrated on figure 7.1. The two signals share the same time-axis to give a clear understanding of when the different parts appear in the MRCP in regard to the EMG-signal and what changes can be seen in the amplitude of the EEG.

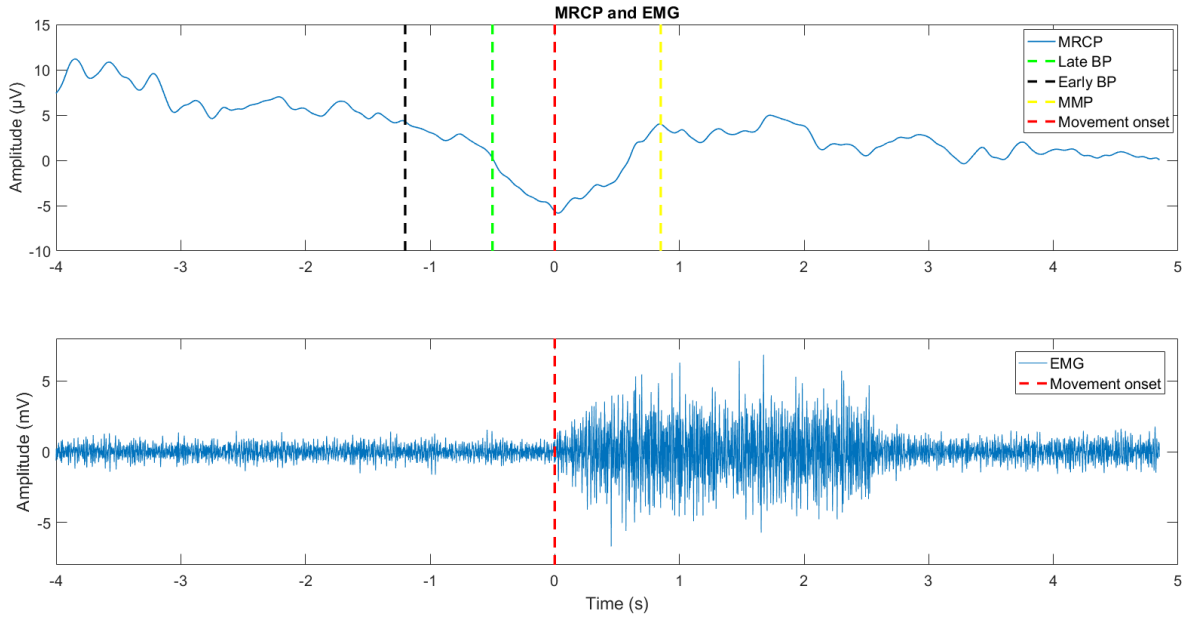


Figure 7.1: Illustration of a MRCP with a associated EMG signal. The MRCP is divided into the early BP (between black and green), late BP (between green and red), movement onset and MMP (between red and yellow).

7.1.1 Bereitschafts Potential

The BP or RP is a slow negative decrease in the EEG amplitude and can have an onset of up to 2 seconds before movement. Though the onset of the BP can vary in regard to the movement performed. For example in repetitive self paced movements performed every 5 seconds or longer an onset of the BP is seen much earlier compared to more natural movement execution, where the onset can be around 1-1.5 seconds before actual movement. This is due to the time available for the subject to plan the movement in an experiment compared to the limited time available in natural conditions. [Shibasaki and Hallett, 2006, Shakeel et al., 2015] BP can be divided into two parts: *Early BP* and *late BP*. The origin of the Early BP is in the pre-supplementary motor area (pre-SMA), the SMA and in the premotor cortex and has a small decrease in the EEG amplitude. The late BP has its onset 400 ms before the movement execution and has a steep negative gradient and is therefore also known as the *Negative Slope* (NS'). For hand movements the maximum amplitude of the late BP is seen over the contralateral central area or C1 and C2 for an international 10-20 EEG system. [Shibasaki and Hallett, 2006]

Several factors such as motor tasks and brain lesions can have an affect on the BP. Some of the factor can effect the BP in different ways. For example force exerted in isometric muscle contraction has been found having an affect on the last 100 ms of BP with a larger amplitude in regards to greater perceived effort versus the force itself. Other parts of the BP was not affected. [Slobounov et al., 2004, Shibasaki and Hallett, 2006] Speed and site of movement can also influence the amplitude of the BP. With speed it has been observed that onset of BP is closer to the movement onset the faster the movement is executed. A more negative late BP is related to movements in the proximal part of the upper extremity compared to the distal part. [Jankelowitz and Colebatch, 2002, Shibasaki and Hallett, 2006]

Contingent Negative Variation

Depending on the experimental setup the pre-movement components of the MRCP can have different terminology. The BP/RP reflects the planning/preparation for self-paced movement where as in cued movements the planning/preparation is described as being the contingent negative variation (CNV). [Brunia, 2003] The CNV have its onset 1-1.5 seconds before movement and consist of a O-wave and a terminal wave or E-wave which in general share the same characteristics as early and late BP [Shakeel et al., 2015, Rohrbaugh and Gaillard, 1983]. It has been discussed if there is any difference between BP and CNV but generally speaking the CNV has a larger am-

plitude, distributed differently and decreases more sudden compared to BP. Even though some have argued against CNV being different from BP, researchers can still agree that both reflect anticipatory behavior. [Brunia, 2003]

7.1.2 Motor Potential

MP or N-10 occurs right before the movement onset and the name N-10 is due to the peak being 10 ms from the corresponding EMG peak. MP is localized in the contralateral central scalp and is corresponding to the somatotopic movement site. [Shibasaki and Hallett, 2006]

7.1.3 Movement-monitoring potential

After the movement onset a rebound is seen in the EEG signal which is know as the movement-monitoring potential (MMP) or re-afferent potential [Jochumsen et al., 2013]. Several terminology can be used about MMP and can be divided into components that are all distributed differently over the scalp [Shibasaki and Hallett, 2006].

7.1.4 Computation of MRCP

For recording of the MRCP and all its components channel C1-C4 and Cz are vital, but the signal can be masked due to noise artifacts or signals lying in higher frequency bands. MRCP have an amplitude between 5 and 30 μV and occurs in the frequency band 0-5 Hz. Because of this it is necessary to make several recording of the same trial and thereafter average the background noise out. Ridding the signal of artifacts in higher order frequencies different filtering options should be considered. [Shakeel et al., 2015] Features that can be used to investigate the MRCP are mean BP, mean NS' and peak amplitude of MP. Furthermore the onset times of the MRCP parts can also be of interest. [Hatta et al., 2009]

7.2 Event-related desynchronization/synchronization

Changes such as desynchronization to the EEG alpha activity can occur following certain events. These changes are time-locked to the event but not phase-locked resulting in time-averaging techniques such as the MRCP are not able to detect them. Frequency analysis is able to detect these changes as power decreases or increases in a specific frequency band. This is due to either decreases or increases in the underlying neural activity. A power decrease in the frequency band is called Event-related desynchronization (ERD) and an increase is called Event-related synchronization (ERS). Event related potentials relates to the responses of cortical neurons in regard to changes in afferent activity, whereas ERD/ERS reflects changes between main neurons and interneurons that controls the frequency components of the EEG. [Pfurtscheller and Lopes, 1999]

Voluntary finger movements show a decrease in power within the alpha band (8-14 Hz, alpha ERD) over the sensorimotor areas and occurs around 1-2 seconds before movement onset. Furthermore an amplitude decrease is seen in the beta band (from 15-Hz to 25 Hz, beta ERD) and occurs even earlier than alpha ERD. A rebound of the amplitude (ERS) over the baseline occurs in the beta band, approximately 500 ms post-movement. [Pfurtscheller and Lopes, 1999, Erbil and Ungan, 2007] The interpretation of ERD/ERS lies in the meaning of synchronization and desynchronization of the underlying neural networks. Within desynchronization of the neural network small patches of neurons work in an independent desynchronized manner, giving the system maximal readiness and information capacity. This is seen with motor behavior where ERD is maximum before and around movement onset. In contrast synchronized neural network correlates to a deactivation of the cortical network giving a reduced information processing and little to no motor movement. That is why an increased power, ERS, is seen post-movement in actually both the alpha and lower beta band. [Pfurtscheller, 2001] Giving this Pfurtscheller [2001] hypothesized that the cortical network processing can take three different states: (i) resting state

where no information is processed (ii) activated state, known as ERD (iii) deactivated state, known as ERS.

Within explicit learning of for example voluntary finger movements an enhanced ERD in the frequency band 8-12 Hz is seen over the contralateral central regions, but once the movement is "learned" or becoming more automated a reduced ERD occurs [Pfurtscheller and Lopes, 1999]. This is also seen in the study by Zhuang et al. [1997].

7.2.1 Computation of ERD/ERS

Different techniques can be used to quantify ERD/ERS in the EEG signal, but this section only focuses on the power within a certain frequency band over a time course. First of all a certain band needs to be determined, usually alpha and lower beta band are chosen for voluntary movement as mentioned before. Furthermore it is important to have recordings of a few seconds before the event occurs to be used for baseline/reference in the calculations. [Pfurtscheller and Lopes, 1999] Four simple steps has been presented by Pfurtscheller and Lopes [1999] for calculating ERD/ERS:

1. Bandpass filtering for the chosen frequency band for all event-related trials
2. Squaring of the amplitude samples to obtain power samples
3. Averaging of power samples across all trials
4. Averaging over time samples to smooth the data and reduce the variability

These steps are illustrated in figure 7.2, where a raw EEG signal is taken through the steps mentioned above.

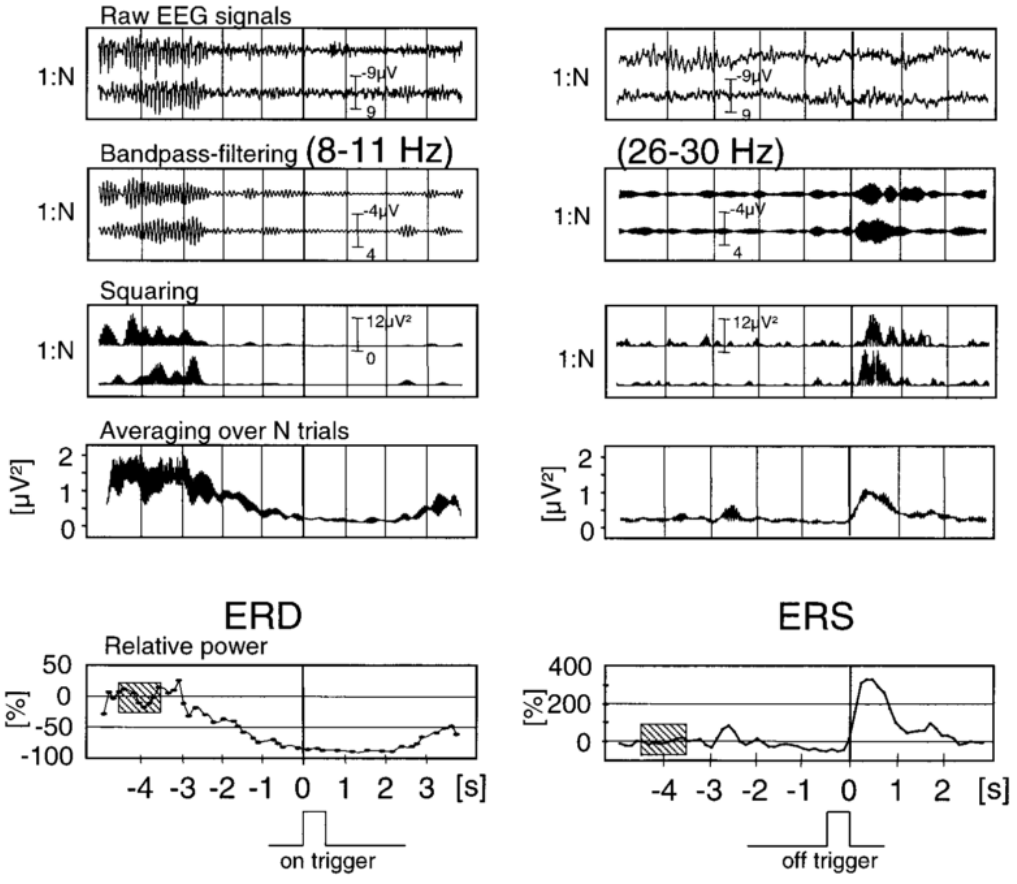


Figure 7.2: Computation process of ERD/ERS. In first row a raw EEG signal. Second row the EEG has been bandpass filtered. Third row a squaring has been done. Fourth row averaging over N trials has been done. Fifth and last row the relative power is presented. Both procceses for ERD and ERS are the same just within different frequency bands. [Pfurtscheller and Lopes, 1999]

The relative power for both ERD/ERS is presented as a percentage (see last row in figure 7.2), which is calculated as presented in equation 7.1.

$$\boldsymbol{ERD\% = \frac{(A - R)}{R} \cdot 100} \tag{7.1}$$

A is power in the frequency band of interest within the activity period, whereas **R** is the baseline or reference period. ERD is defined as a power decrease and ERS is defined as a power increase. [Pfurtscheller and Lopes, 1999, Pfurtscheller, 2001]

7.3 Corticomuscular coherence

The coupling between the cortical level and muscle can be measured via coherence and is referred to as corticmuscular coherence. Coherence is a measure of the coupling of two signals between specific frequency components [Perez et al., 2006]. It is an extension of the Pearson correlation and is hence a linear method of analyzing a linear interaction in the frequency domain. It can be seen as the correlation of two oscillatory activities indicating that there exists common frequencies of the motor command processing. [Mima and Hallett, 1999]

Adaptation of corticospinal input to the spinal motorneurons have been shown to occur during motor tasks with a high level of attention and precision, but such adaption has, according to Perez et al. [2006] not been investigated in motor learning prior to their study. The corticomuscular coherence activity is greatest during periods of steady contraction and disapears during isotonic contractions of the muscle [Perez et al., 2006, Kristeva et al., 2007].

Perez et al. [2006], Riquelme et al. [2014] suggest coherence in the beta (13-35 Hz) range may be descending corticospinal commands to recruit motor neurons. Riquelme et al. [2014] further suggest that coherence in the alpha bands (8-12 Hz) is an expression of pulsatile communication between brain and muscle. They add that coherence in the gamma band (30-45 Hz) might be related to fast integration of sensory inputs during self-paced phasic muscle contractions.

A possible explanation for the importance and implications of corticomuscular coherence was made by Aumann and Prut [2015]. They suggest that the oscillations in the beta range is present in a (almost) closed neural loop from the primary motor cortex to the muscle and back to the primary motor cortex (through the primary somatosensory cortex). This loop is thought to be essential in maintaining muscle and muscle synergy representation in the primary motor cortex. This is supported by the fact that oscillations can be measured at multiple sites through out the body with a phase delay approximately equivalent to the conduction speed of the neurons in the pathway. This is illustrated in figure 7.3.

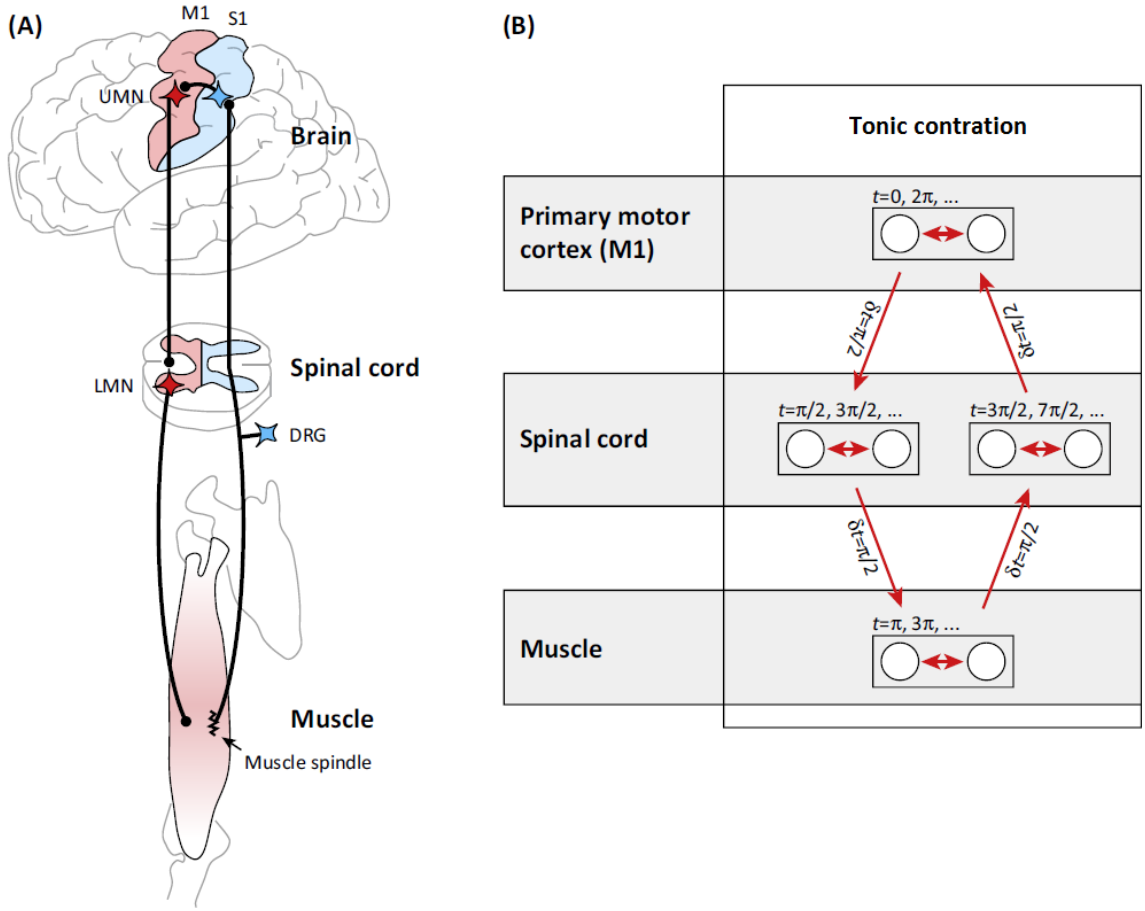


Figure 7.3: (A) The oscillatory activity is generated in the primary motor cortex (M1) propagating from upper motor neurons (UMN) through the spinal cord via lower motor neurons (LMN) and to the muscle. The contraction of the muscle activates the muscle spindle and a signal is propagating back through the spinal cord via dorsal root ganglia (DRG) to the primary somatosensory cortex (S1). (B) Illustrates the phase shift between the cortical level, the spinal cord level and the muscle. As indicated by the equations, the frequency remain the same, but the phase is delayed. Modified from Aumann and Prut [2015].

7.3.1 Computation of coherence

Corticomuscular coherence is computed by finding the cross power spectral density between a cortical signal (EEG, x) and a muscle signal (EMG, y). Furthermore the power spectral density of x and y, is calculated and by using the equation shown below the coherence between the signals is calculated:

$$C_{xy}(f) = \frac{|P_{xy}(f)|^2}{P_{xx}(f)P_{yy}(f)} \tag{7.2}$$

C_{xy} is the coherence between x and y, f is the frequency and P_{xy} is the power spectral density between x and y.

Coherence is constrained between 0 and 1 (as is correlation), where 0 indicates independence and 1 a total linear relationship. [Mima and Hallett, 1999]

For determining if the coherence measures are of statistical significance the significance limit needs to be calculated [Mima and Hallett, 1999]. This is done by calculating the confidence limit from the α (usually 95 %, 99 % or 99.9 %) and the number of segments, L, as of the following equation [Rosenberg et al., 1989, Hashimoto et al., 2010]:

$$CL(\alpha) = 1 - (1 - \frac{\alpha}{100})^{1/(L-1)} \tag{7.3}$$

Chapter 8

Experimental procedures

This chapter will contain a description of the experimental setup and procedures used for collecting data for further analysis. The procedures will be described in detail insuring reproducibility. A full experimental protocol can be found in Appendix B.

8.1 Study design

The present study was designed as as a pre-post study. Pre-post study design is an interventional study design, where measurements of an outcome before and after an intervention are performed. There are however some disadvantages by using pre-post study design: there is no control group and additional elements during the intervention is not controlled. [Thiese, 2014] The experiment was divided into pre-session, motor training and post-session. The pre- and post-session consisted of subjects performing three repetitions of maximal voluntary contraction (MVC) using a hand force transducer, three minutes of rest EEG both with eyes closed and open and coherence performance. The coherence performance consisted of subjects following triangles and squares with 5 % and 10 % of their MVC. The motor training consisted of in total 80 repetitions of low intensity palmar grasps using the force transducer. A break was provided after every 20th. 80 repetitions were chosen to minimize any effect of attention fatigue. The breaks in between repetitions were in order to prevent fatigue or concentration loss for the subject. The study design is illustrated on 8.1.

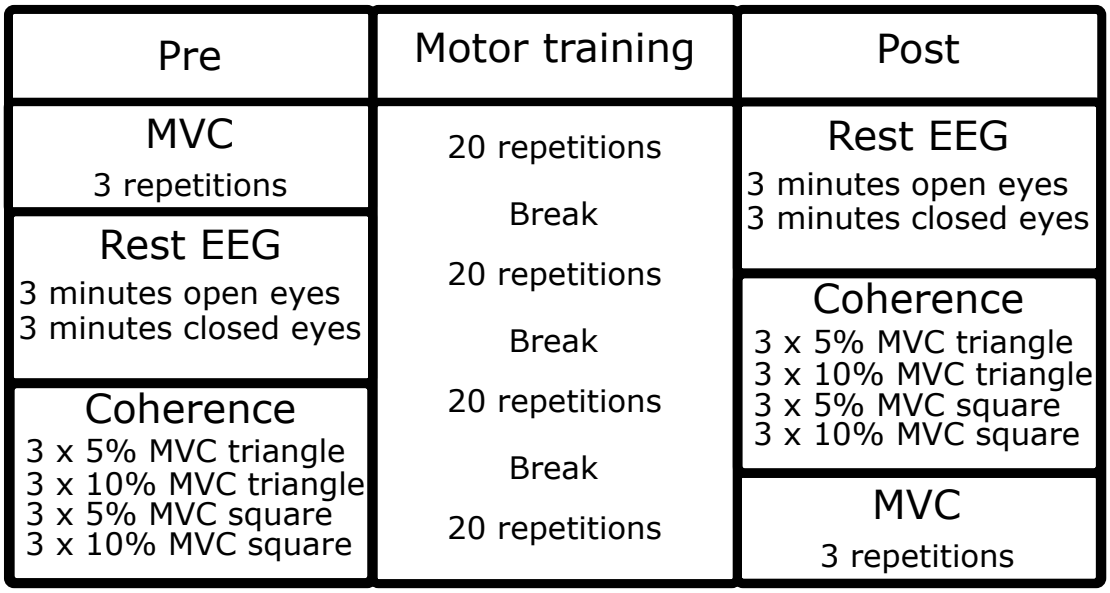


Figure 8.1: An overview of the experiment.

8.2 Subjects

Voluntary subjects were primarily recruited from the student and staff population at Aalborg University, where the study took place, with additional subjects being recruited by word of mouth. The criteria of inclusion were no neurologic condition and no nerve damage in upper limbs. Furthermore the subjects were asked to sleep at least 4-6 hours the night before (and to

feel rested) and not to drink coffee up to 4 hours before the experiment as both coffee [Dimpfel et al., 1993] and lack of sleep [Banks and Dinges, 2007] have been shown to alter brain activity. Prior to the experiment the subjects reported the amount of sleep, they had had the night before and the length of the experiment was also noted. 19 subjects were recruited (10 males and 9 females) with a mean age of 24.2 $\pm$ 1.87 years and 7 hours and 44 minutes $\pm$ 35 minutes of sleep. The experiment took on average 2 hours and 35 minutes $\pm$ 12 minutes. Out of the 19 subject one was left-handed. All subjects gave their written informed consent prior to participation. All procedures were approved by the local ethical committee (N-20130081).

8.3 Experimental setup

Subjects were placed in a comfortable chair approximately one meter from a monitor. The lighting of the room was adjusted to make the subjects most comfortable. Their non-dominant hand with the force transducer was placed with palm facing down on their thigh. A schematic of the physical experimental setup is illustrated in figure 8.2.

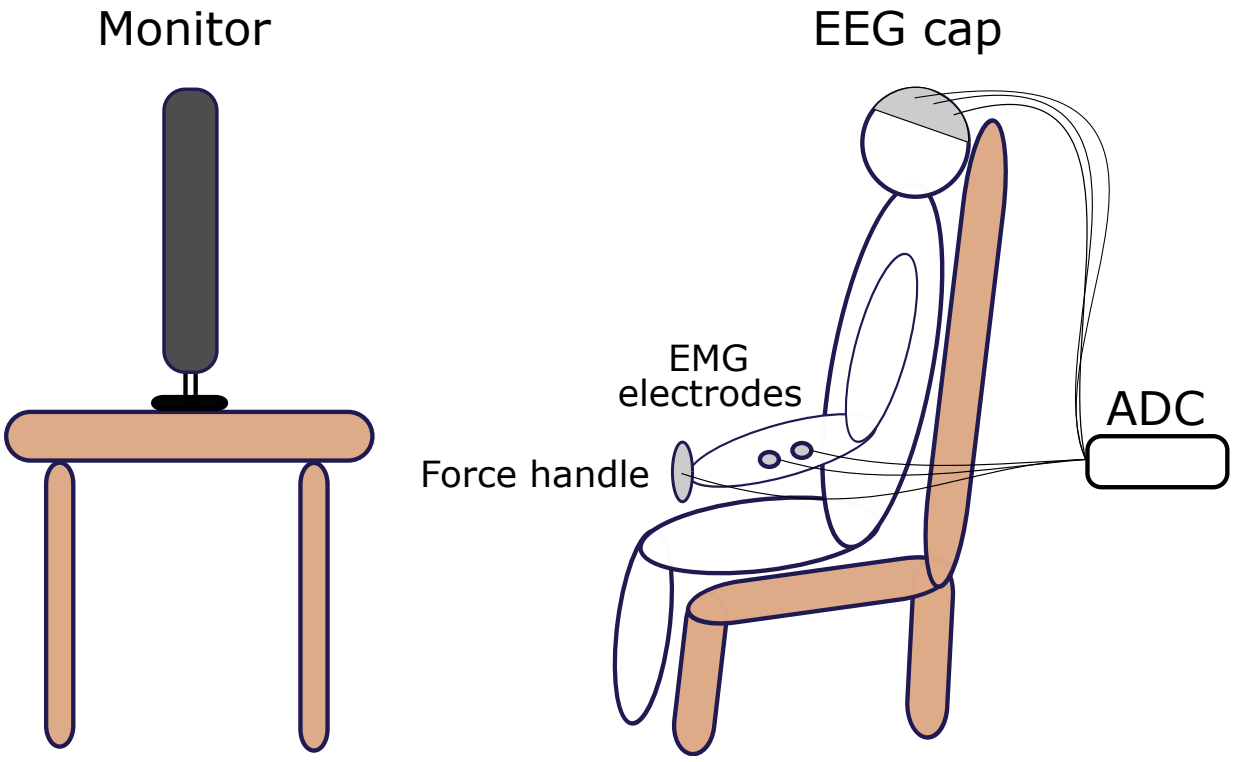


Figure 8.2: Schematic of the physical setup. Subjects were seated with the force transducer in their non-dominant hand.

EEG recordings

Using the g.tec g.HIamp 80-channel amplifier with active electrodes, 64 channels of EEG were recorded in accordance with the international 10-20 system using an EEG-cap (g.gammacap$^{\mathbf{2}}$). Subjects were asked to locate the top of their head with each hand, both with open and closed eyes. This was used as a guiding point for the Cz channel and the cap was then adjusted by finding the intersection between the coronar line from ear to ear and the sagittal line from inion to nazion. Each of the channels were prepared using electrode gel and a blunt syringe. The blunt syringe was used to stir the gel to make a connection to the scalp of the subject. Preperation of the channels was done until an impedance of $\leq$ 100 k$\mathbf{\Omega}$ was achieved. In figure 8.3 the electrodes can be seen. The sampling frequency was set at 4800 Hz.

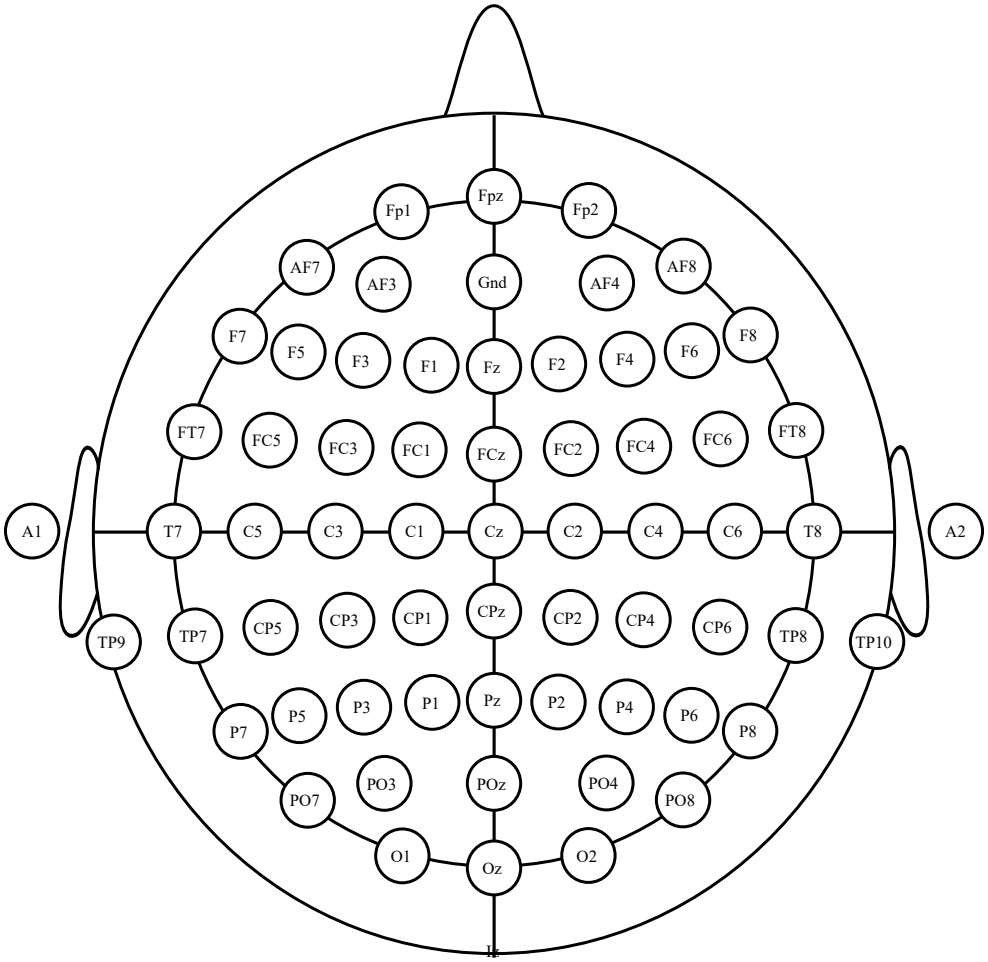


Figure 8.3: An overview of the EEG channels recorded.

EMG recordings

The recording of EMG was done with the g.tec g.HIamp 80-channel amplifier, a g.tec 16-channel electrode connector box and with surface electrodes (Ambu neuroline 720). The placement of the surface electrodes on the extensor bundle (primarily the extensor digitorum) and the flexor bundle of the forearm, was found using palpation during wrist flexion/extension and contraction of the non-dominant hand and with the atlas for electrode placement suggested by Cram [2011] as a starting point. Approximate sites for the electrodes can be seen in figure 8.4. The sampling frequency was set at 4800 Hz.

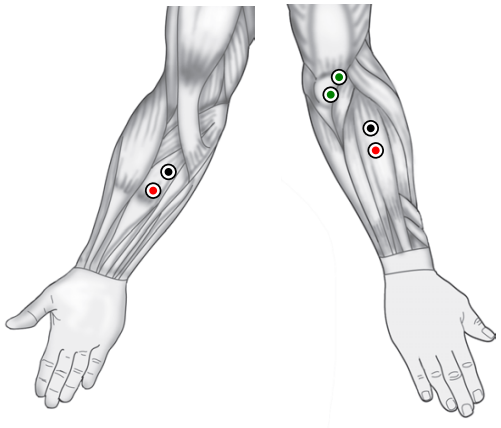


Figure 8.4: EMG recording electrodes used in the experiment. Modified from Cram [2011].

Force recordings

Force recordings were acquired using the Noraxon Scientific Handgrip Dynamometer. FollowMe (Knud Larsen, AAU) was used to collect the data and to provide visual feedback. The sampling frequency was set at 100 Hz.

8.3.1 Recording of maximum voluntary contraction

The subjects were asked to produce a MVC using the force transducer as fast as possible within a 5 second window after recieving a cue, followed by 2 minutes of break. This was repeated three times and the highest value was chosen as the MVC.

8.4 Motor training

In the motor training part of the experiment the subjects were presented with a random force track that they then were to follow to the best of their ability. When subjects applied pressure to the force transducer the cursor on the screen moved upwards, and when they stopped applying force the cursor moved downwards. The cursor moved from left to right as time progressed. The track was always 16 seconds long and the first 3 seconds were always a flat line indicating that no force should be produced. The maximum force required to follow the track was in all cases 5% of the MVC of the subject. This setup was chosen as the motor skills required to accurately control the force output was sufficiently challenging initially, but improved fast. The subject were asked to use their non-dominant hand to further make improvements possible.

During the initial 3 seconds, the subjects were asked not to blink and to keep their jaw still and focus on initiating the movement exactly at the 3 second mark as the period before the movement is where MRCP's can be recorded. An example of the track and trace can be seen in figure 8.5.

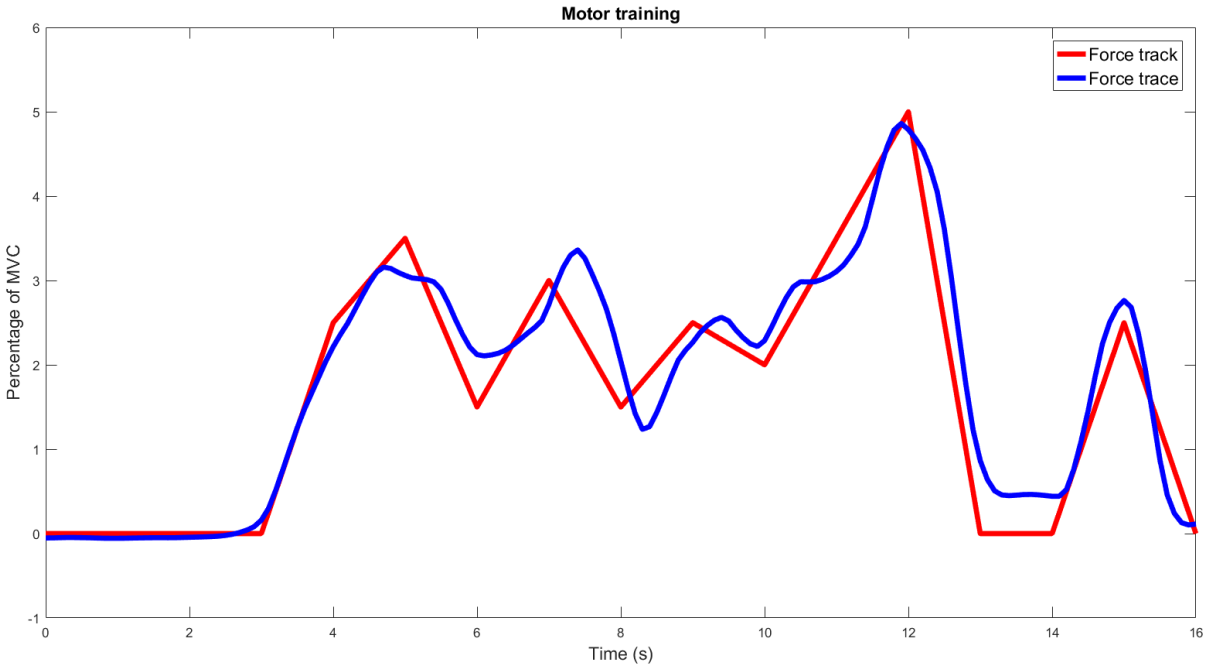


Figure 8.5: A typical example of a force track (red) and the corresponding subject force trace (blue) of one of the trials of the motor training.

Prior to the track beginning the subject was presented with a visual warning consisting of "1.. 2.. 3.. Go!". At the "Go!" a trigger was sent from the FollowMe to the ADC collecting the EEG and EMG data to use it as a trigger for initiation of a trial.

8.5 EEG-EMG coherence

Different contraction levels activate different motor units and the coticomuscular coherence is dependent on the muscle contraction and strength [Duchateau and Enoka, 2011, Conway et al., 2004]. Furthermore it has been hypothesized that the motor cortical neurons are most sensitive to forces in the low force range [Kristeva et al., 2007]. Because of this and preventing fatigue, it was chosen that subjects were to perform contractions at 5% and 10% of their MVC. Coherence is most prominent in isometric contractions [Pohja et al., 2005], why the force grip handle used in the experiment did not change in size with contraction levels making the contraction isometric.

The subjects were asked to follow two different shapes at two different intensities in a random order with each shape being repeated three times. The shapes can be seen in figure 8.6 and 8.7 and consisted of either a triangle or a square at 5% and 10% of the MVC of the subject. The triangle consisted of a three second delay, three seconds of rise to the target percentage of MVC, three seconds of decline and 3 seconds of tail time. The repetitions were spaced with an interval of 5 seconds and the subjects were asked to, by the best of their abilities, not to blink or do any head movement during the rise and decline of the shape. These two shapes were utilized to get recordings with increasing, declining and steady force output during isometric contractions.

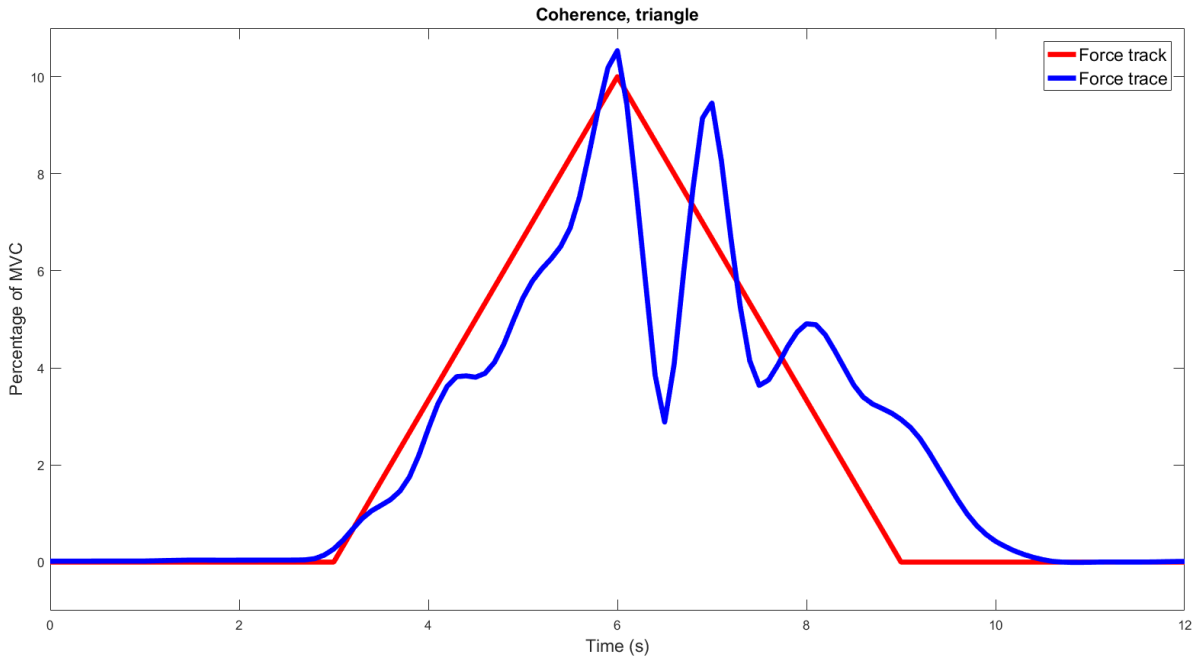


Figure 8.6: A typical example of the triangular shape. Following three seconds of delay, the subjects were asked to follow the incline and decline of the shape. The red line is the track the subjects were asked to follow and the blue line is a typical trace of a subject.

As for the square it consisted of a delay of 20 seconds, a rapid incline to the target percentage of MVC, a steady-state force output of 30 seconds, a rapid decline and 20 seconds of tail time. The repetitions were spaced with additional 50 seconds to minimize any effect of fatigue.

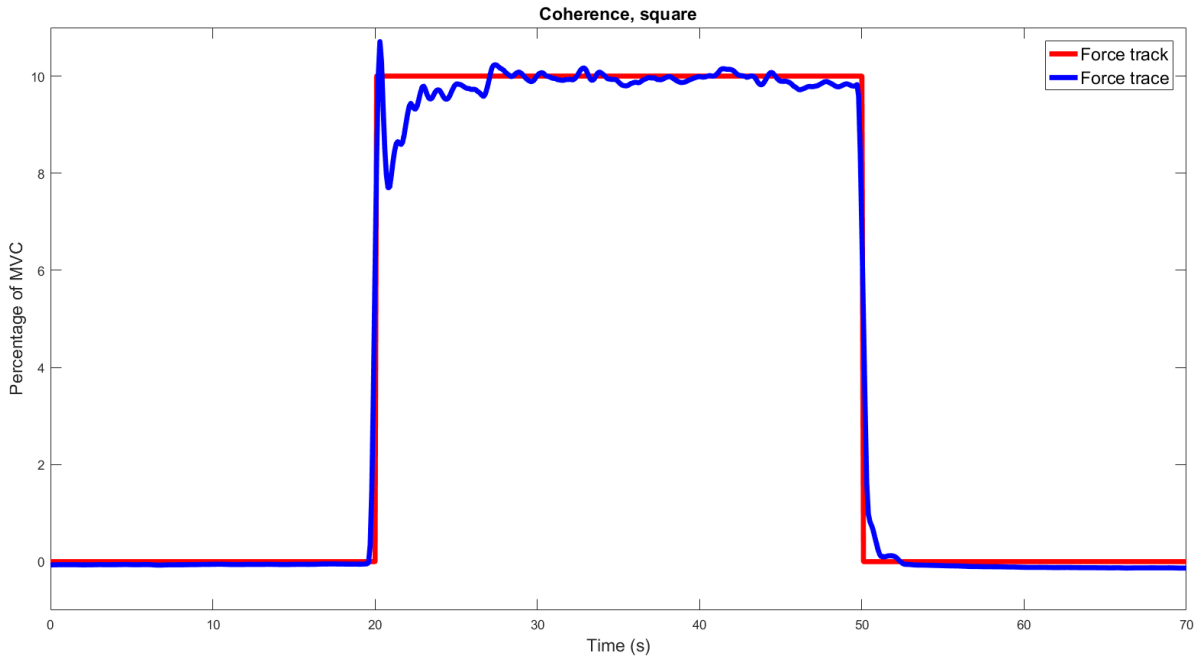


Figure 8.7: A typical example of the square shape. Following 20 seconds of delay, the subjects were asked to do a rapid increase in force to reach either 5 or 10 % of MVC and keep the contraction for 30 seconds. The red line is the track the subjects were asked to follow and the blue line is a typical trace of a subject.

8.6 Rest EEG

Resting EEG were recorded both with open eyes and closed eyes (each 3 minutes of length) in a predetermined randomized order. The length was chosen to ensure the data predominantly consisted of artifact free EEG signal. The subjects were asked to sit still and relax while the recordings were ongoing. For the open eyes recording, the subjects were asked to keep their gaze at a fixed location to minimize any potential from eye movement and changing visual impressions. Eyes open and closed for resting EEG was chosen due to different power in theta, alpha and beta band in relation to the state [Li, 2010].

Chapter 9

Data analysis

In this chapter analysis of the motor training, rest EEG and corticomuscular coherence executed in the experimental procedure, will be described. Each of the sections will begin with a flowchart presenting the reader with an overview of the process, which will then be described in detail.

9.1 Motor training

The analysis of the motor training trials will be focused on the MRCP and ERD/ERS in the time span before and around movement onset (-4:1 seconds). Data analysis of the motor training was divided into three segments: preprocessing, trial rejection and feature calculation. The flow of the data analysis is illustrated in figure 9.1.

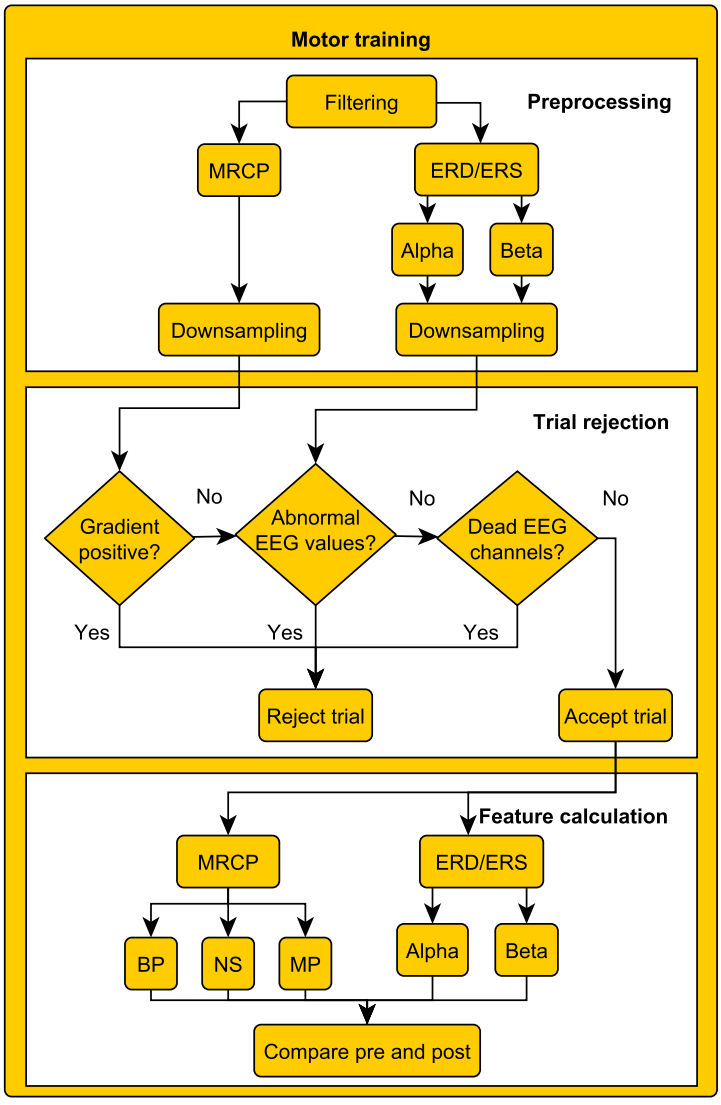


Figure 9.1: Flow diagram of motor training data analysis.

An overview of the time span is illustrated in figure 9.2. Data will be analyzed from four seconds before movement onset to one second after.

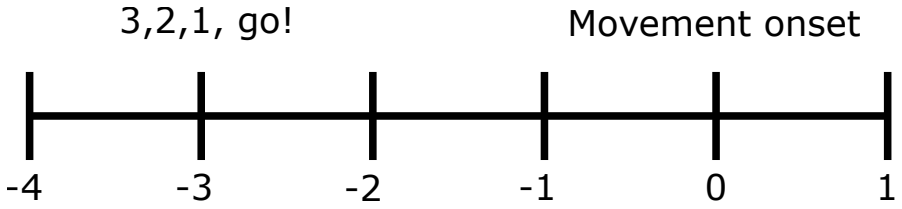


Figure 9.2: Overview of the time span in focus for data analysis of the motor training.

9.1.1 Preprocessing

It is desired to get a signal as detailed as possible. A contributor to that is the way the obtained EEG will be referenced. There are several ways for the signal to be referenced but within the present setup two channels (A1 and A2) was placed at the right and left earlobe with the intention of using them as reference. It was then later investigated which reference gave the most profound MRCP within a single channel over 20 trials. Three different types of reference was analyzed; right earlobe, left earlobe and linked earlobes. Of the three references the right earlobe resulted in the best and most detailed MRCP representation. The three different reference types is illustrated in figure 9.3.

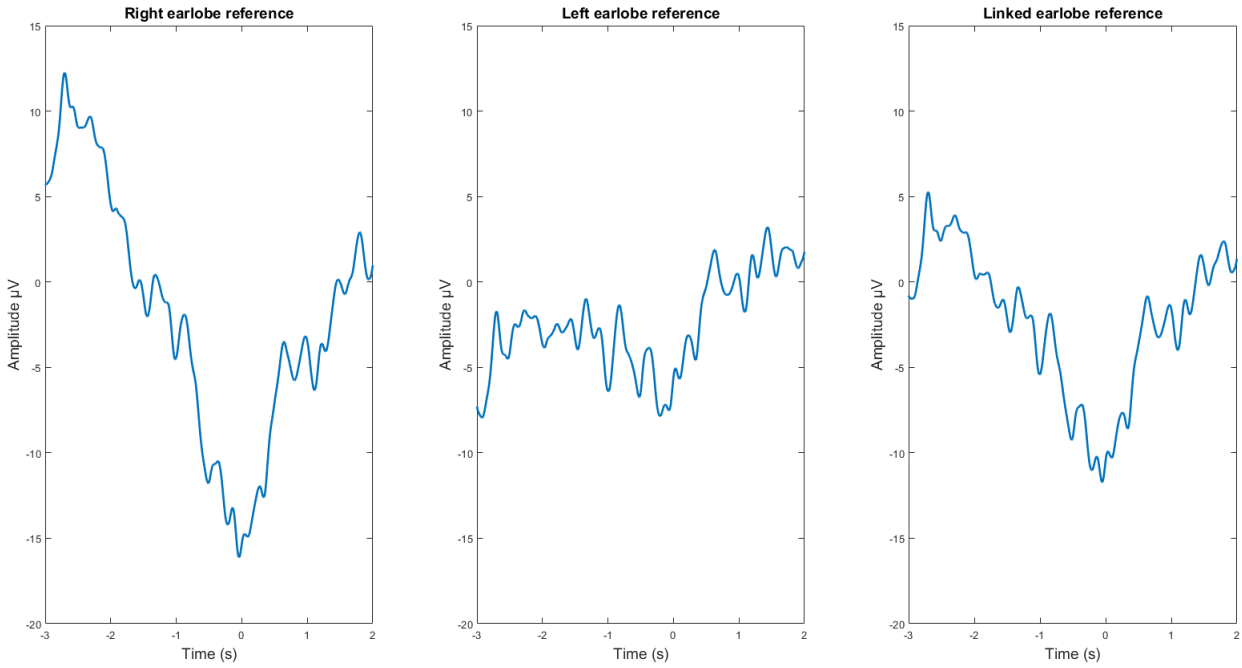


Figure 9.3: Representation of three different references; right earlobe, left earlobe and linked earlobe. Data were from subject 1, channel C2 and average over 20 trials.

The preprocessing step also consisted of filtering the data for the MRCP band (0.05-5 Hz) and for the alpha- and beta-ERD/ERS (alpha: 8-14 Hz, beta: 15-30 Hz) in all cases a second order zero-phase shift Butterworth filter was used. This was followed by a downsampling with a factor of 30 for the MRCP and 15 for the ERD/ERS. This was done to minimize the amount of data and to speed up the analysis, while still keeping a sampling frequency ten times higher than the highest expected frequency.

9.1.2 Trial rejection

Trials with data contaminated by noise artifacts can have a huge influence on the results, why trial rejection is crucial. Rejection of trials can be done as an automatic procedure or a visual inspection, where both have pros and cons. Visual inspection requires a certain amount of

experience within the field, but still includes the risk of being biased, opposed by an automated procedure which is bias free. However by using the automated approach the individuality is lost meaning that certain criteria used for some subjects might not be suitable for others. [Cohen, 2014] Despite the risks of using automatic procedures for rejecting trials, this approach was still chosen due to it being free of bias, the lack of experience from the authors in visual inspection and the amount of trials used in this study. Rejection criteria for motor training was focused in three areas: (i) Unnatural characteristics of the MRCP (ii) high values which exceeds the normal EEG signal range and (iii) dead channels corresponding to channels having no response.

Unnatural characteristics of the MRCP

As stated in section 7.1 the MRCP is reflected as a slow negative change in the EEG signal. Given that information a positive change within the interesting time range is not considered valid for MRCP feature calculation. In order to reject trials which behave in this manner different criteria was set up. Firstly channels of interest were included (this was consistent for all the areas of trial rejection in motor training). The gradient was calculated within a time span to see if it had a slow negative change or not. The time span was from 1.5 seconds before movement onset to movement onset (-1.5:0 s, see section 7.1), since this is the time span, where the MRCP declines the most resulting in the largest gradient. If the gradient had a positive value the removal of linear trends was performed. If the trial still had a positive gradient the trial was rejected. An example of a trial which had linear trends removed and was later accepted is illustrated in figure 9.4. Furthermore each channel had 80 trials of motor training and if more than 25 trials were rejected in the first half (first 40 motor training trials) or the same in the last half (last 40 motor trails), the channel was rejected. This is in line with Niemann et al. [1991] whom used 15 trials to record a successful MRCP.

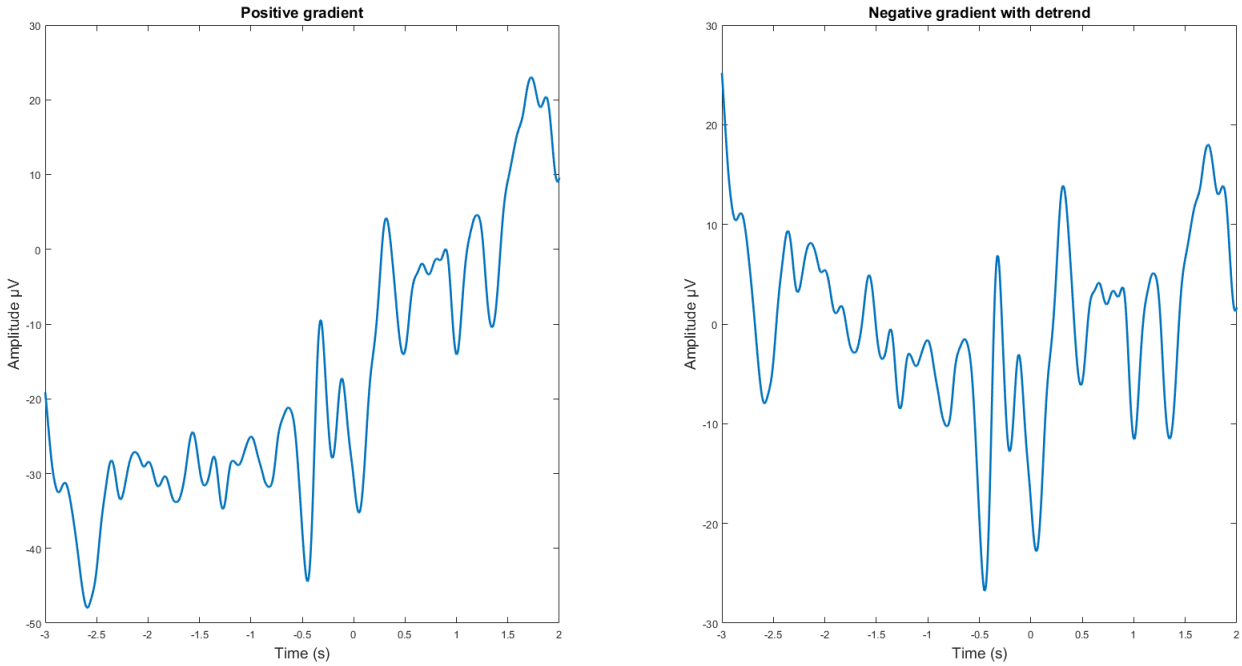


Figure 9.4: Data from subject number 6, channel C3, trial 11. Left figure is the original with a positive gradient. Right figure has had linear trends removed and now has a negative gradient.

Values outside of EEG range

The MRCP has a rather low amplitude ranging from 5 to 30 μV [Wright et al., 2011] but as a conservative measure in order not to exclude signal of physiological bearing the following rejection criteria was setup up: if the difference between the maximum and the minimum value was above 200 μV, the trial was rejected. The time span in which this difference was investigated, was from trial start to movement onset (-3:0 seconds). Channel rejection followed the same procedure as stated above with the gradient rejecting with respect to the 25 trials in either first half or the last half. An example of trial being rejected due to too high values is illustrated in figure 9.5.

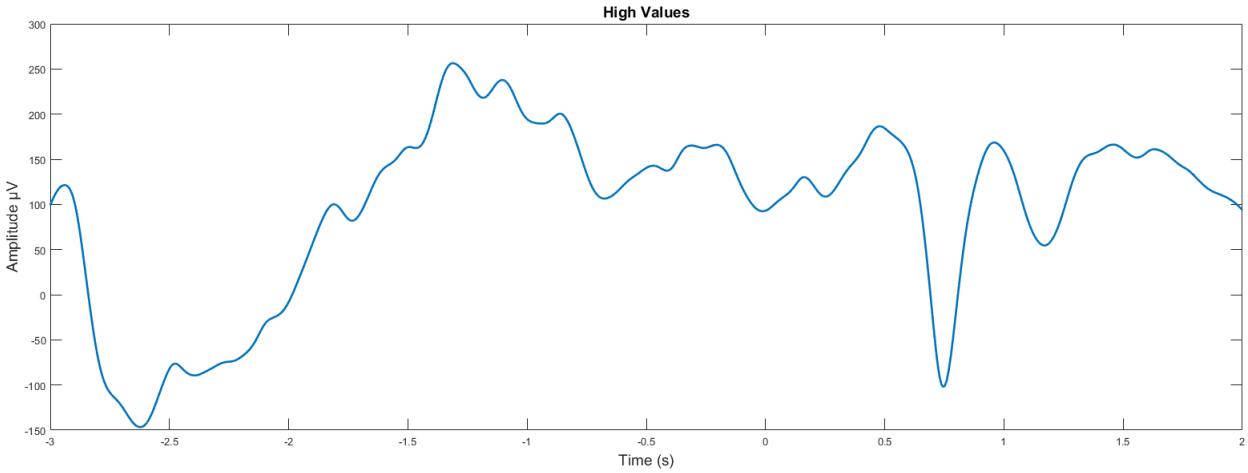


Figure 9.5: Data from subject number 7, channel F4, trial 72. The data included too high values which resulted in the trial being rejected.

Dead EEG channels

Rejection of trials which had no response, also known as "dead trials", followed the same procedure as rejection of high values. Instead of using a threshold of 200 μV, the rejection was done if the trials had an amplitude lower than 7 μV from maximum to minimum in the same time span as mentioned above (-3:0 seconds).

9.1.3 Feature estimation

The features were calculated for the channels FCz, FC2, FC4, Cz, C2, C4 as these channels cover the cortical area expected to be most active during preperation and execution of hand movements, which is in line with Shibasaki and Hallett [2006].

MRCP features

As stated in section 7.1 the MRCP can be divided into segments representing different aspects. The segments investigated were the BP, NS' and MP. With Hatta et al. [2009] and Niemann et al. [1991] used as inspiration the MRCP analysis was done on a mean trial of the first 15 non rejected trials in the first half (trial 1-40) and the last non rejected 15 trials in the second half (trial 41-80). The first and second half was then later compared to see if any changes occurred due to the intervention. The BP feature was then a mean calculation from 1.5 seconds to 450 ms before movement onset. The NS' was calculated in the same manner as the BP but in the interval 450 ms to 100 ms before movement onset. Lastly the peak value of MP was found as the maximum negative value in the time span 100 ms before movement to 100 ms after movement onset. The features are illustrated on figure 9.6

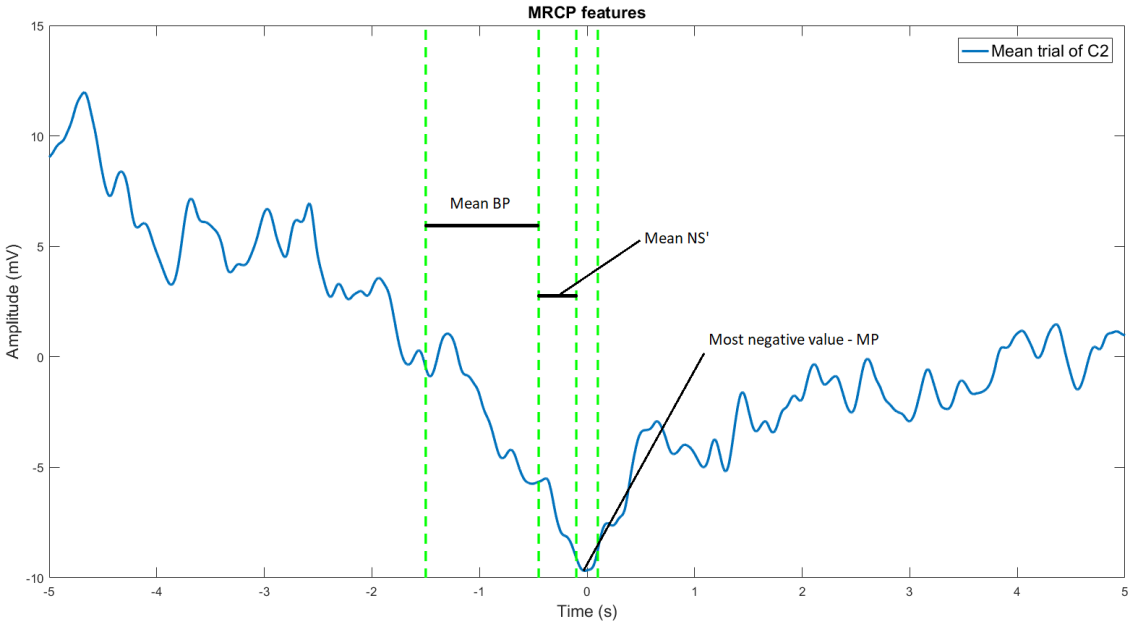


Figure 9.6: Illustration of the three features extracted from the mean trial of the MRCP for the first and last half, respectively. Data from subject 1 during the motor training trials.

ERD/ERS features

Following the method presented by Pfurtscheller and Lopes [1999] the data were first filtered in the bands; alpha (8-14 Hz) and beta (15-30 Hz). Later the data were squared and the mean across the trials was calculated for the first 15 non rejected trials and the last 15 non rejected trials, respectively. The relative ERD/ERS percentage was then found by dividing the period before movement onset and right after movement onset with a reference period (see equation 7.1 in section 7.2). The reference period was chosen to be four to two seconds before movement onset. The ERD was computed in the time span; two seconds before movement onset until the movement onset, where as the ERS was from movement onset to 1 second after. The ERD and ERS of the first and the last half were then compared. In figure 9.7 an illustration of the time spans used for the features can be seen.

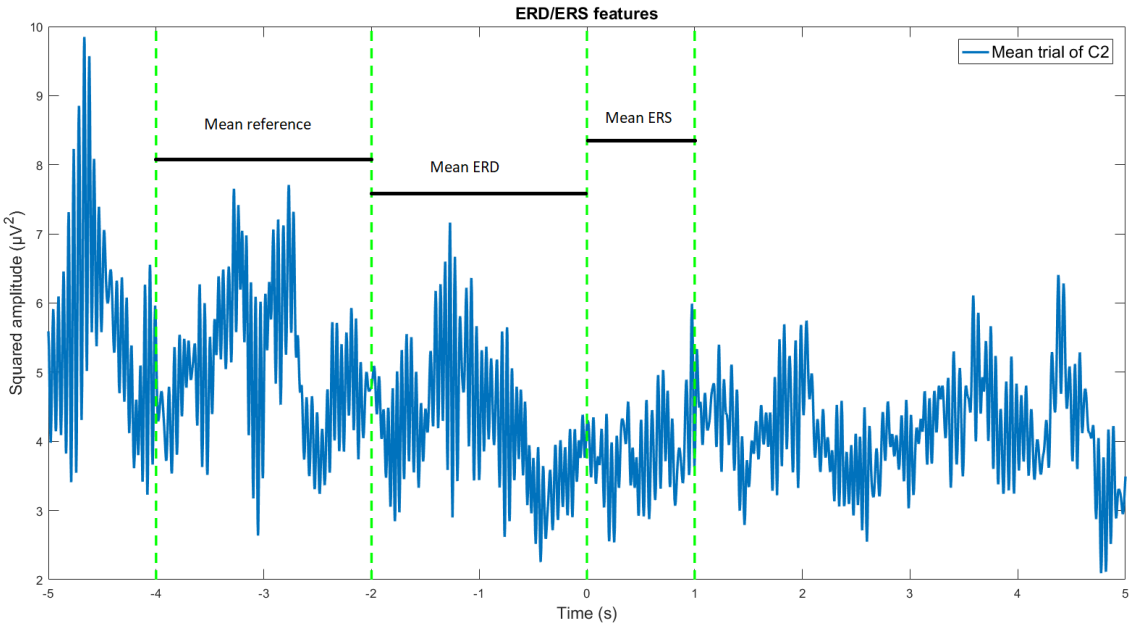


Figure 9.7: Illustration of the time spans of the ERD and ERS features. The ERD and ERS were divided by the reference following extraction, thus obtaining the ERD/ERS percentages. Data from subject 6 during the motor training trials.

9.2 Corticomuscular coherence

The analysis will be focused on the EEG-EMG coherence during the two types of shapes the subjects were asked to follow; triangle and square. Data analysis of the coherence estimation was divided into three segments; preprocessing, trial rejection and feature calculation. The flow of the data analysis is illustrated in figure 9.8.

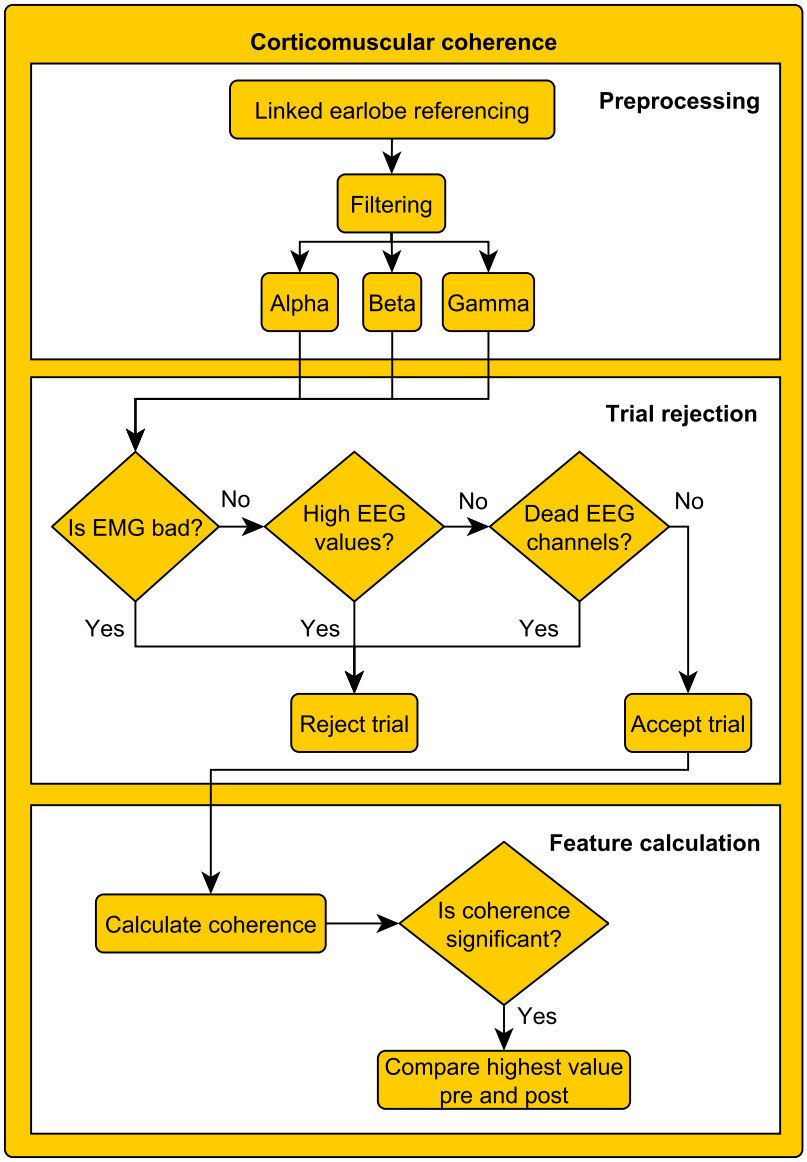


Figure 9.8: Flow diagram of coherence data analysis.

9.2.1 Pre processing

The EEG signal was referenced to both earlobes (linked earlobes) as done previously in coherence studies by Petersen et al. [2012] and Hori et al. [2013]. Both EEG and EMG signals were filtered to the alpha band (8-14 Hz), the beta band (15-30 Hz) and the gamma band (31-49 Hz) using a second order no-phaseshift Butterworth filter.

9.2.2 Trial rejection

For the corticomuscular coherence both the EMG and the EEG could potentially be contaminated by artifacts, why both had to be assessed.

EMG

Review of the EMG data revealed instances of EMG not rising during the periods of active contraction. An example of this can be seen in figure 9.9. The signal that was expected can be seen in 9.10.

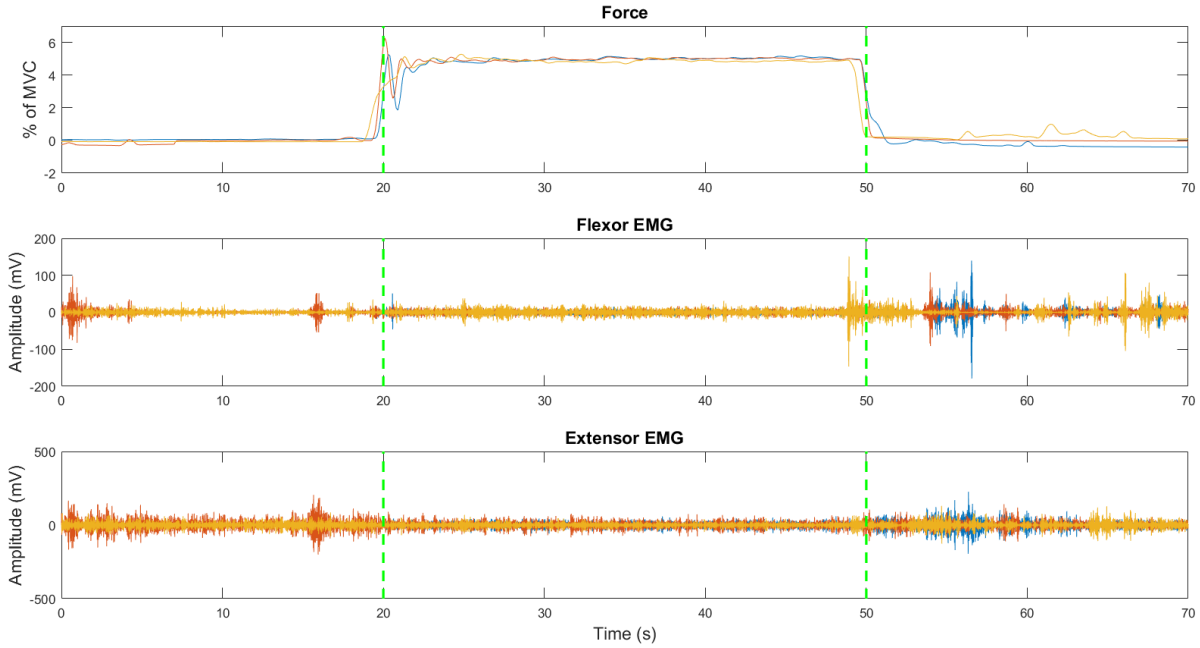


Figure 9.9: Force and EMG from subject 3 in the pre-session attempting to hold a contraction of 5 % MVC.

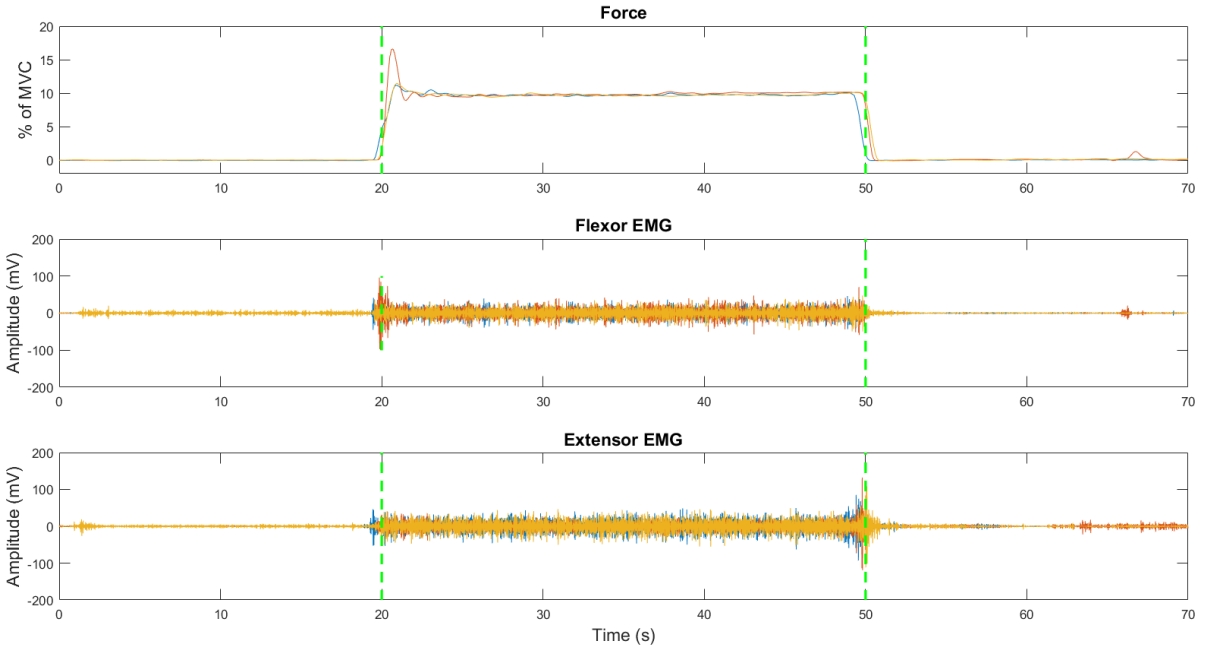


Figure 9.10: Force and EMG from subject 2 in the post-session attempting to hold a contraction of 10 % MVC.

This led to the inclusion of the following trial acceptance criteria: Root mean square of the EMG during the contraction must be two times larger than the root mean square of the baseline signal in a period without contraction.

Values outside of EEG range

Rejections of trials due to values being outside the normal EEG range follows some of the same principles as in the corresponding paragraph in section 9.1.2. Since there was not a lot of trials (three repetitions pre and post) and since a short spike of a high value might not effect the entire sequence that much, the rejection criteria was implemented slightly different. The data within the active period were rectified (by taking the absolute value) and if the mean value within this period was above 100 μV (corresponding to 200 μV peak-to-peak), the trial was rejected.

Dead EEG channels

Rejections of dead EEG channels follows the same principles as in the corresponding paragraph in section 9.1.2. Dead channels were detected within the 24-46 seconds for the square and 3-9 seconds for the triangle coherence. These ranges are illustrated on figure 9.12 and 9.13, presented further down.

9.2.3 Coherence calculation

Corticomuscular coherence was calculated using equation 7.2 in section 7.3 via the built-in MATLAB function *mscohere*. It is an estimation of the magnitude-squared coherence, using Welch's averaged, modified periodogram method of calculating the cross-power spectral density (CPSD) and the power spectral density (PSD). Welch's method is a way to improve the PSD estimation, by dividing a signal into n bins in order to minimize variance. The higher the n, the lower the variance, but this will also result in lower resolution. Since the signal is divided into segments, the signal is abruptly cut resulting in altered frequencies (referred to as spectral leakage), why different window functions can be used on the segments to minimize this. [Bronzino, 2000] For the coherence analysis 1 second bins were used with a Hamming window and no overlap.

According to Mima and Hallett [1999] the corticomuscular coherence roughly follows the somatotopic map (see figure 3.2 in section 3.1), why the same channels as in the previous section were included (FCz, FC2, FC4, Cz, C2 and C4) together with the EMG signals of the flexors and extensors of the lower arm, respectively. Following the calculation it was tested if the coherence was significant and if so, the highest coherence value within the respective bands were compared pre and post. This means that the coherences being compared were not necessarily at the same frequency, but within the same band. This is illustrated in figure 9.11.

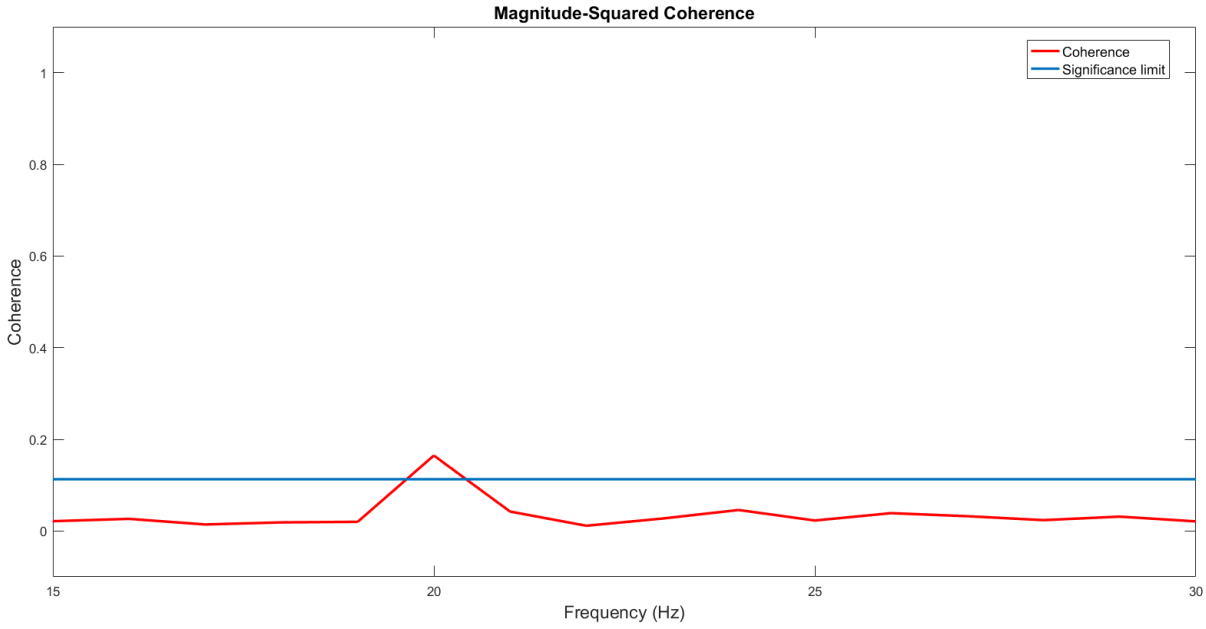


Figure 9.11: An example of the coherence feature for the beta band. The coherence value at the peak above the significance limit was used as a feature and compared to another value from the opposite session. Data from subject 3 in the pre-session attempting a square of 5 % MVC.

Square

For analysis of the square shape coherence, the initial and final 4 seconds of active data were discarded in an attempt to only use data of (relatively) steady-state force output. This is illustrated in figure 9.12.

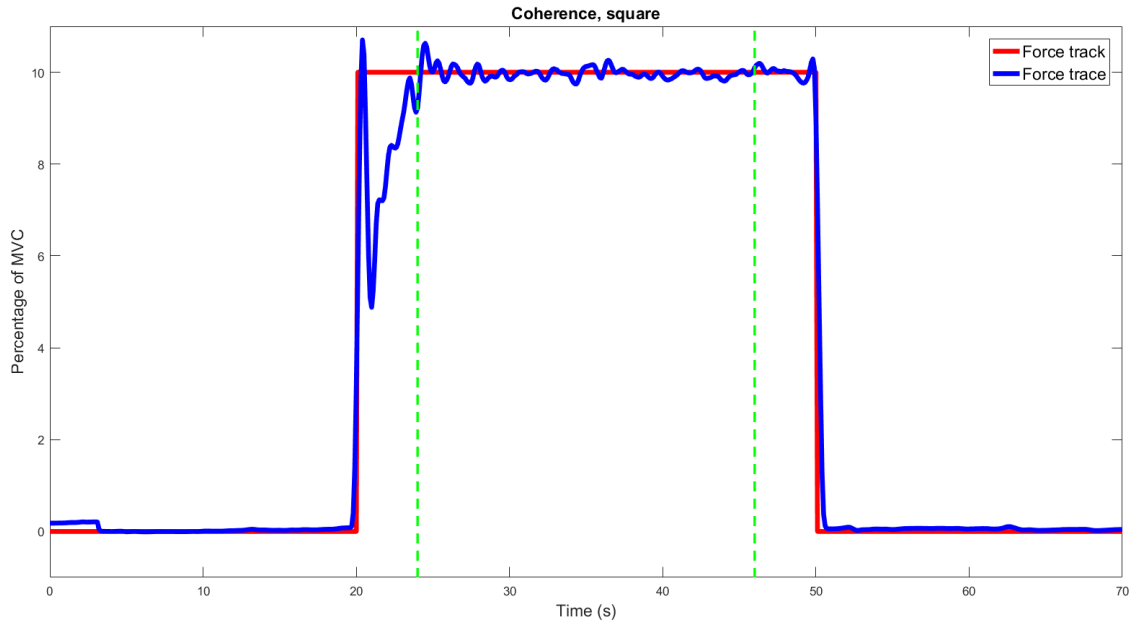


Figure 9.12: Force data from subject 6 in the pre-session attempting to hold a force out of 10 % MVC. The green vertical dotted lines at 24 and 46 seconds indicate the period of data used.

Triangle

For analysis of the triangle shape coherence none of the active data were discarded due to the short time span of the recording. Instead it was split into two: the ascending part from 3-6 and the descending part from 6-9 seconds. It is believed that the coherence is affected differently in these two situation of contraction, [Mima and Hallett, 1999] why they were treated separately. This is illustrated in figure 9.13.

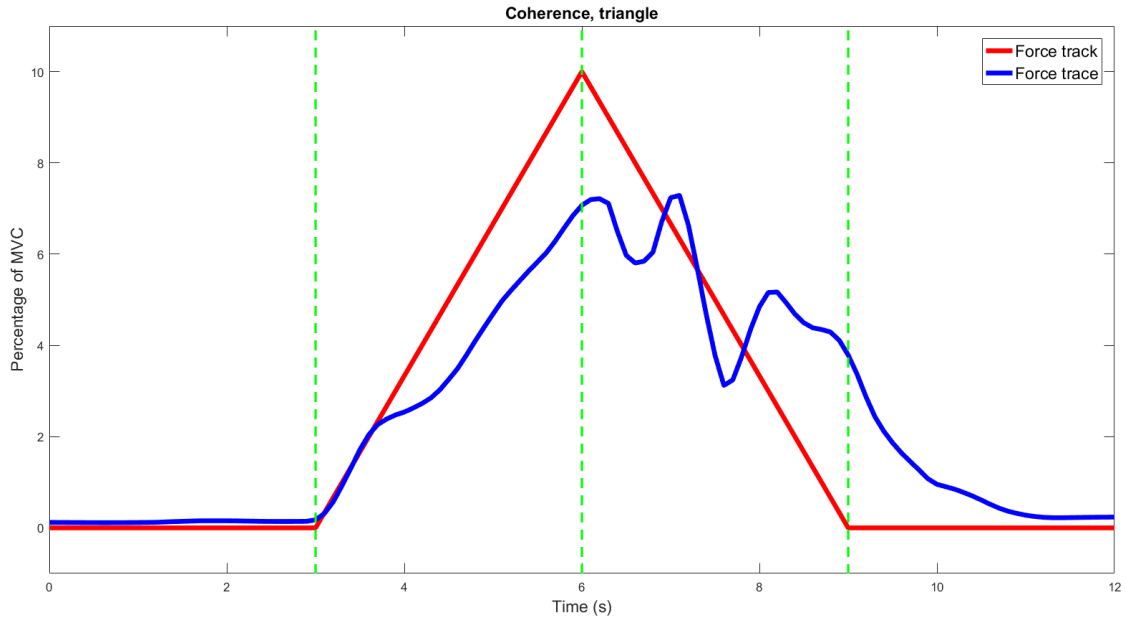


Figure 9.13: Force data from subject 6 in the pre-session attempting the force triangle of 10 % MVC. The green vertical dotted lines indicate the two seperated periods of data used from 3-6 and from 6-9 seconds. The first is the ascending part, where force increase and the second is the descending part, where force is declining.

9.3 Rest EEG

Analysis of the data obtained in the rest EEG segments was focused on channels: F1-F8, Fz, FCz, FC1-FC6, FT8, FT7, T7, T8, Cz, C1-C6, TP7, TP8, CPz, CP1-CP6, Pz and P1-P8. The analysis consisted of three segments; preprocessing, channel rejection and feature calculation, which is illustrated in the flow diagram in figure 9.14. Data were analyzed over the whole time span of the rest EEG part of the experiment, meaning that data were analyzed over a time span of 3 minutes both for when the subjects had their eyes open and closed.

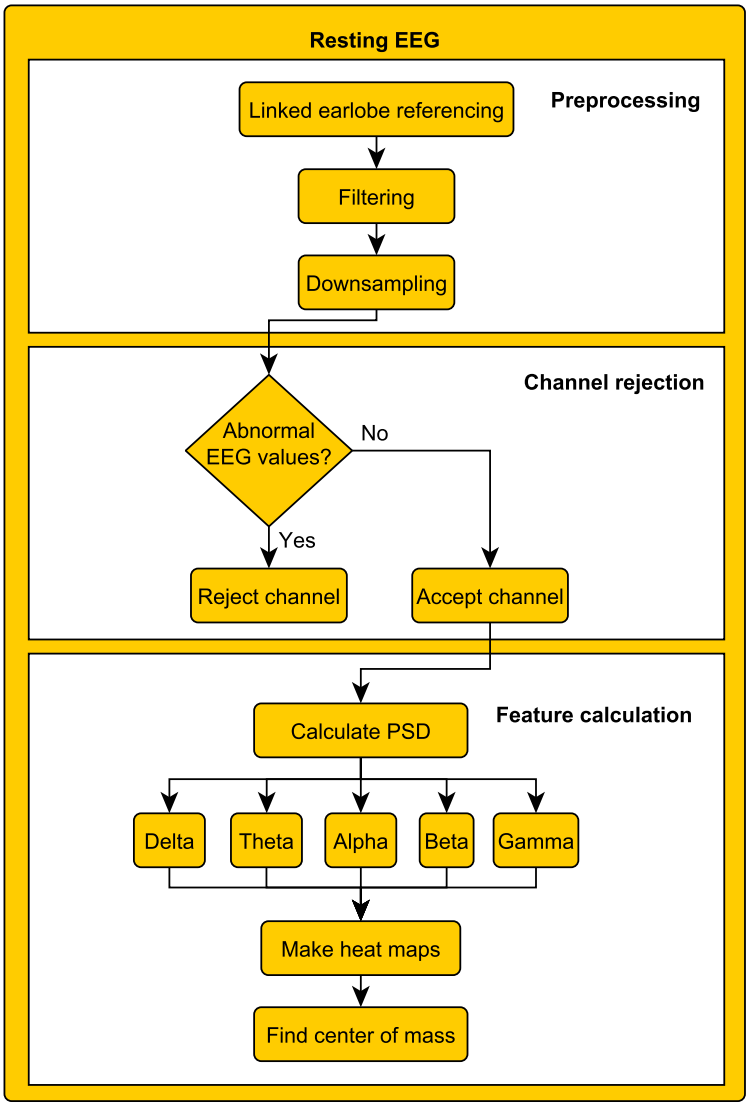


Figure 9.14: Overview of the data analysis of the rest EEG.

9.3.1 Preprocessing

The data were filtered from 0.5 to 49 Hz and were later divided into the frequency bands; delta (0.5-4 Hz), theta (5-7 Hz), alpha (8-14 Hz), beta (15-30 Hz) and gamma (30-49 Hz). Following filtering, the data were downsampled with a factor of 10. Since no movements was performed during this session it was decided to reference the data as a linked earlobe reference, meaning that half of each earlobe was used as reference.

9.3.2 Channel rejection

Since one rest session is considered one trial, no trial rejection was implemented to prevent loss of too much data. Instead channel rejection was implemented to insure the data integrity. The criteria for rejection of channels consisted of analyzing PSD within the frequency bands together with the EEG signal in the time domain and if the value exceeded normal values, the channel was rejected. For visual presentation heat maps were developed where each of the channels were used as their own pixel. The channels were aligned like the international 10-20 electrode-system. A colorbar was assigned to the heat map where high values had the color red to dark red and low values had the color blue to dark blue. In order to give greater detail to the image linear interpolation was done. An example of a channel with extreme high values is illustrated in figure 9.15. The channel T8 is causing the saturation of the heat map with values around $12 \cdot 10^5$ $\boldsymbol{\mu V^2/Hz}$.

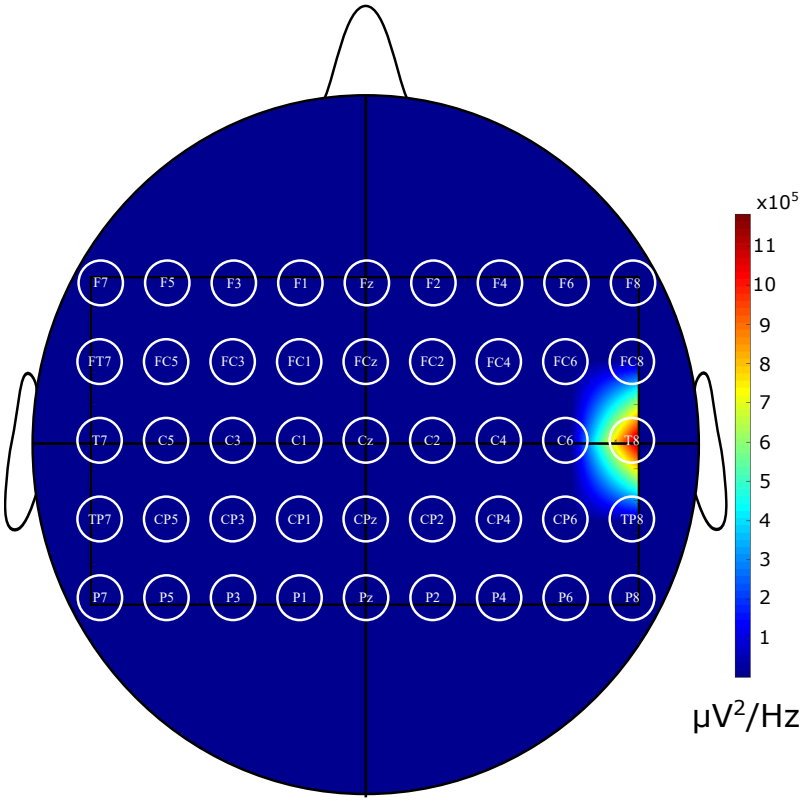


Figure 9.15: Heat map from subject 19 within the delta band, post-session with open eyes. Channel T8 had extremely high values resulting in the heat map being saturated around that channel and details being lost.

By looking at the EEG data it was apparent that throughout this session the amplitude was outside normal EEG limits and was possibly a result of issues with the equipment. The EEG data corresponding to the T8 channel in figure 9.15 is illustrated in figure 9.16.

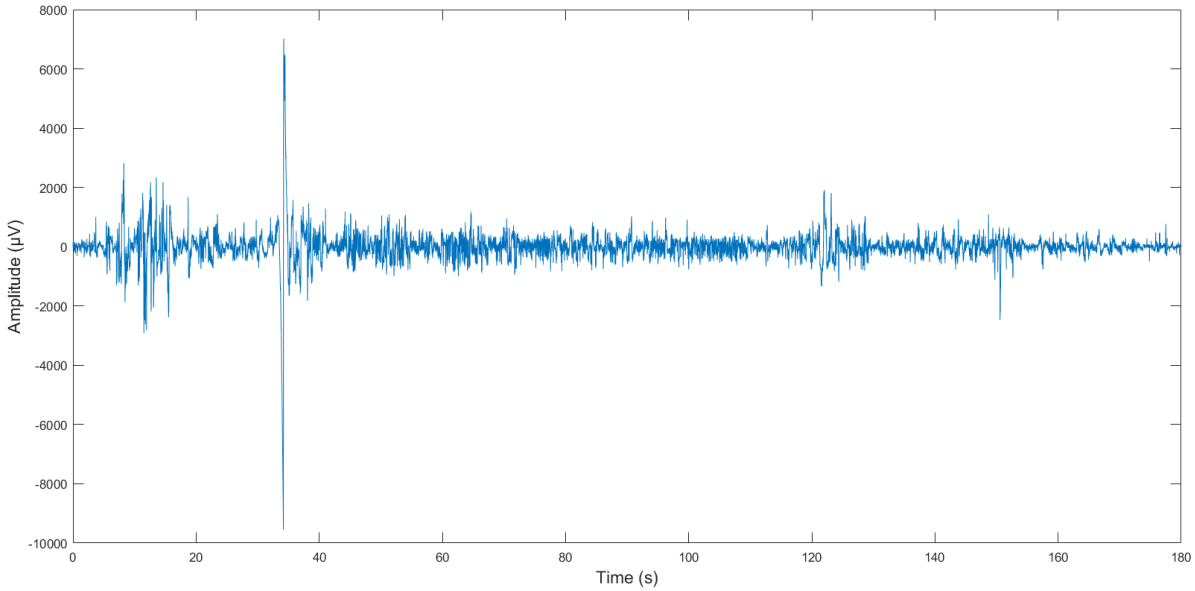


Figure 9.16: The EEG signal from subject 19 in channel T8 in the post-session with open eyes.

Channel T8 was rejected but to keep the symmetry of the heat maps channel F7, FT7, T7, TP7, P7, F8, FT8, TP8 and P8 was also rejected. This was done for all subjects due to it being a consisting problem and the additional channels not being of crucial interest. Furthermore channel F4 showed the same tendencies as T8, which is illustrated in figure 9.17.

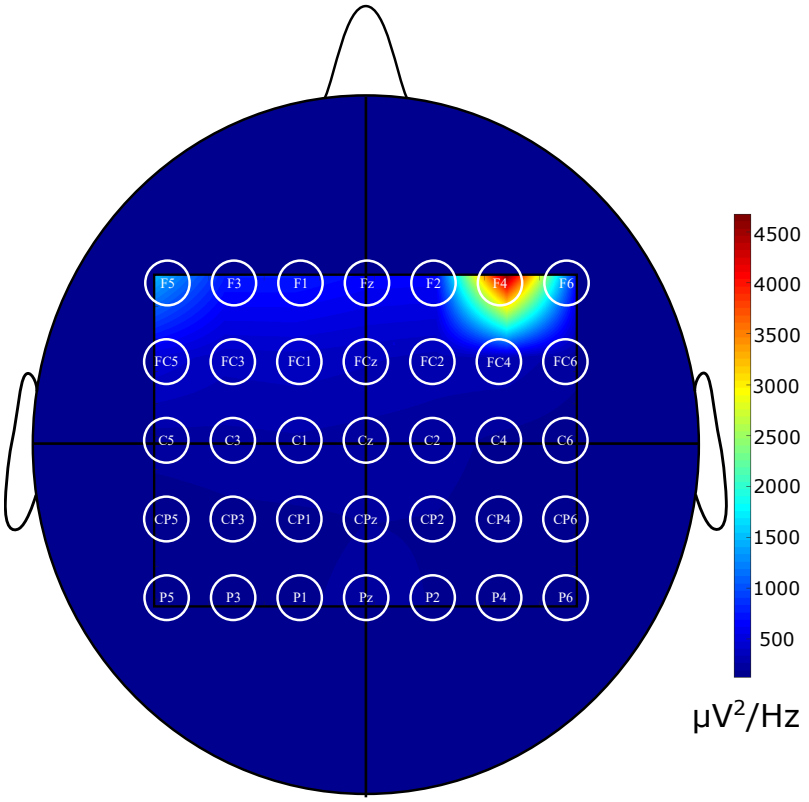


Figure 9.17: Subject 11 within delta band, post-session with open eyes. Channel F4 had values outside the normal EEG range.

Channel F4 was rejected along side channel F1-F6, Fz, P1-P6 and Pz. Furthermore a single subject (subject 7) was rejected due to high values in channel FCz, which was not seen in any other subjects. Channels which ended up being included in the analysis of rest EEG is illustrated in green in figure 9.18. Red channels indicates the channels which were rejected in the first iteration whereas the blue were the rejected channels in the second iteration.

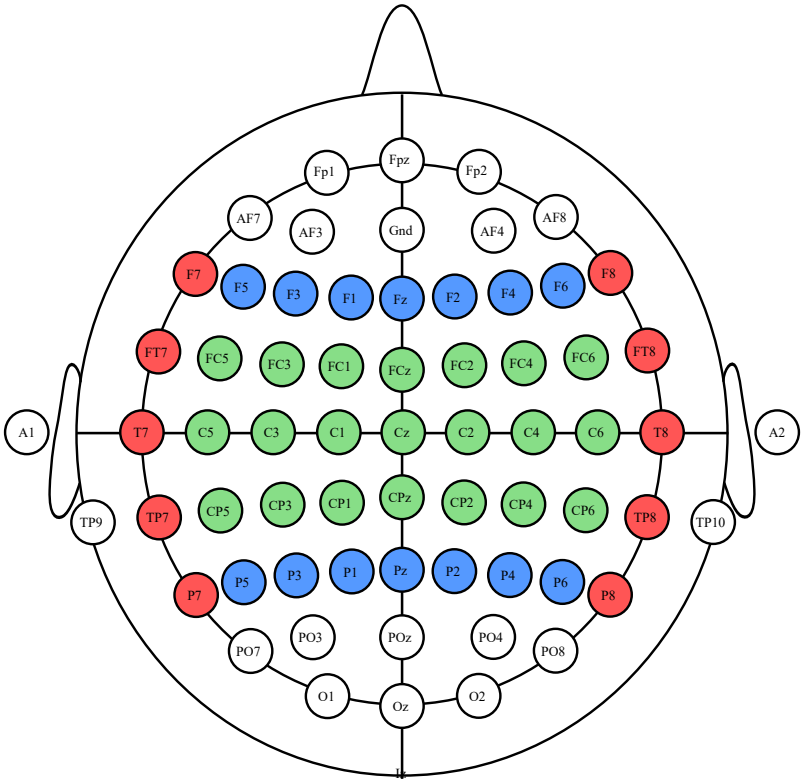


Figure 9.18: Channels included in the analysis of rest EEG. Red indicates the firstly rejected channels and blue indicates secondly rejected channels. Green indicates the included channels.

9.3.3 Feature calculation

Power spectral density was calculated with Welch's method (see section 9.2.3) within the frequency bands of delta, theta, alpha, beta and gamma. PSD within these frequencies was calculated for each channel both pre and post as well as data where the subjects had their eyes closed and open. The PSD was summed for each frequency band and in order to have a measure for comparing pre- and post-sessions center of mass was calculated.

Center of mass is the point $\overline{\boldsymbol{x}}$ where the moment of a system is equal to zero. The center of mass is given by [Adams and Essex, 2010]:

$$\overline{\boldsymbol{x}} = \frac{\boldsymbol{M_{x=0}}}{\boldsymbol{m}} \tag{9.1}$$

Where $\boldsymbol{m}$ is the total mass of the system and $\boldsymbol{M_{x=0}}$ is the total moment about x=0 [Adams and Essex, 2010]. Given an 2D example, the center of mass is calculated as a coordinate where $\boldsymbol{x}$ and $\boldsymbol{y}$ is obtained separately. The x-coordinate is calculated as follows:

$$\boldsymbol{COM_x} = \frac{\boldsymbol{m_1 \cdot x_1 + m_2 \cdot x_2 \ldots}}{\boldsymbol{m_1 + m_2 \ldots}} \tag{9.2}$$

And for the y-coordinate:

$$\boldsymbol{COM_x} = \frac{\boldsymbol{m_1 \cdot y_1 + m_2 \cdot y_2 \ldots}}{\boldsymbol{m_1 + m_2 \ldots}} \tag{9.3}$$

The intention of using center of mass is not to get the point with the highest activity but rather a measure which trend toward areas of peak activity. Given that the subjects are compared pre and post to the motor training a precise measurement for peak activity is not necessarily valuable, but the change in overall location might be. In theory it is possible if two high activities is equally distributed that center of mass is given as the exact midpoint, which is a factor to have in mind when reviewing the results.

9.4 Statistics

Firstly it was tested if the subjects improved in their performance. This was done using first the Shapiro-Wilk test for normality then followed by a paired t-test/Wilcoxon signed-rank test depending on the normality. In all cases statistical significance was assumed if the p-value <0.05.

9.4.1 Motor training

The features from the MRCP and the ERD/ERS were compared using a two-way repeated measures ANOVA with the factors time (pre and post) and channels (FCz, FC2, FC4, Cz, C2 and C4) as done by [Hatta et al., 2009]. The Greenhouse-Geisser correction was used if sphericity was violated for channels since it had more than two levels. One analysis was conducted for each feature.

9.4.2 Coherence

The highest coherence value from the coherence calculation of the different bands were first compared to the significance limit, to see if the coherence was significant. If more than half the subjects ($9\leq$) had significant coherence in both the pre-session and the post-session, they were compared using a paired t-test/Wilcoxon signed-rank test depending on the result of the Shapiro-Wilk test for normality.

9.4.3 Rest

The coordinates of the center of mass calculated from the heat maps for each of the sessions were compared with a paired t-test/Wilcoxon signed-rank test depending on the Shapiro-Wilk test for normality. This was repeated for the five brain waves being investigated and for both sessions; open and closed eyes.

Chapter 10

Results

In this chapter the results will be described. Firstly the motor performance of the subjects is presented following the features of motor training, coherence and rest EEG. The data of the left handed subject were flipped about the sagittal axis during the data analysis and included in the same manner as the right handed data.

10.1 Performance measure

A prerequisite for the remainder of the results is that the subjects improved their performances. This was defined as the subjects producing force close to the presented shape they were to follow, and the error they made was defined as the distance from the measured force to the shape. For each of the 80 trials, the amount of error made was summed and meaned across subjects. This is illustrated in figure 10.1.

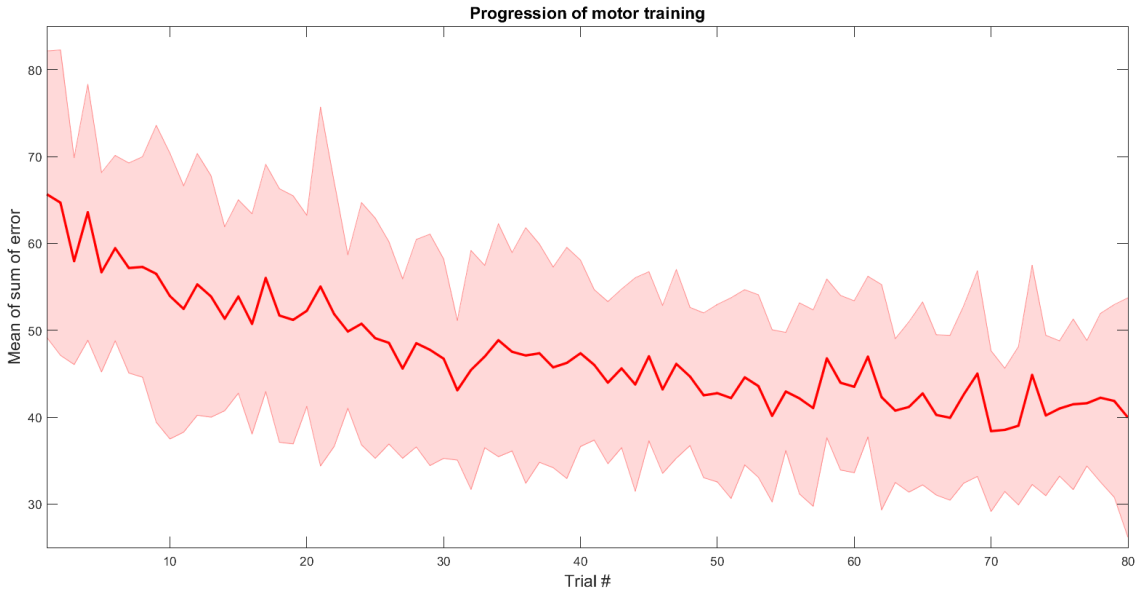


Figure 10.1: Mean of all subjects sum of error for each trial with standard deviation as the shaded error along the curve.

The plot shows a decreasing trend and to insure this was the case, the first and the last trial was compared statistically. The data were normally distributed (first trial: $p = 0.384$ and last trial: $p = 0.340$) and there was a significant decrease from first trial to last trial ($t(18) = 5.568$, $p < 0.001$).

10.2 Motor training

Results of the motor training consists of statistical analyses of the MRCP features and ERD/ERS. Trial rejection resulted in 2701/8640 trials in the MRCP being rejected where as in the ERD/ERS 105/8640 trials were rejected (18 subjects · 6 channels · 80 trials). An overview of the rejected trials can be found in table 10.1. Subject 7 was not included in the analysis due to too many rejected trials in the FCz channel. The analysis is for the remaining 18 subjects.

Table 10.1: Rejection of trials overview

	MRCP	ERD/ERS (alpha + beta)
High values (trials)	103	105
Gradient (trials)	2598	-
Dead trials	-	-

The features of the MRCP; BP, NS' and MP, did not differ significantly from the pre- to the post-session ($p = 0.709$, $p = 0.21$, $p = 0.938$). There was no significant difference between the channels within the BP feature ($p = 0.084$), but within both NS' and MP a significant difference was found ($p = 0.033$, $p = 0.003$). Post hoc analysis revealed difference between FCz and Cz for NS' and FC4 and Cz together with FC4 and C2 for MP. Looking at the interaction between the two factors time and channels, no significance was found for any of the features (BP: $p = 0.763$, NS': $p = 0.796$, MP: $p = 0.846$). An overview of the p-values together with their corresponding F-values can be found in table 10.2.

Table 10.2: Overview of statistical results from MRCP features. The results are divided into the difference between the pre- and post-session, difference between the channels and the interaction between the main effects.

	BP	NS'	MP
Difference Pre/Post	$F(1,17) = 0.147$ $p = 0.709$	$F(1,17) = 1.676$ $p = 0.21$	$F(1,17) = 0.006$ $p = 0.938$
Between channel	$F(5,85) = 2.019$ $p = 0.084$	$F(3.11,52.92) = 3.095$ $\mathbf{p = 0.033}$	$F(3.01,51.2) = 5.369$ $\mathbf{p = 0.003}$
Interaction	$F(2.82,47.88) = 0.369$ $p = 0.763$	$F(2.55,43.33) = 0.296$ $p = 0.796$	$F(2.88,48.87) = 0.260$ $p = 0.846$

The mean values of the features with their corresponding standard deviations in the pre- and post-session is illustrated as bar plots in figure 10.2.

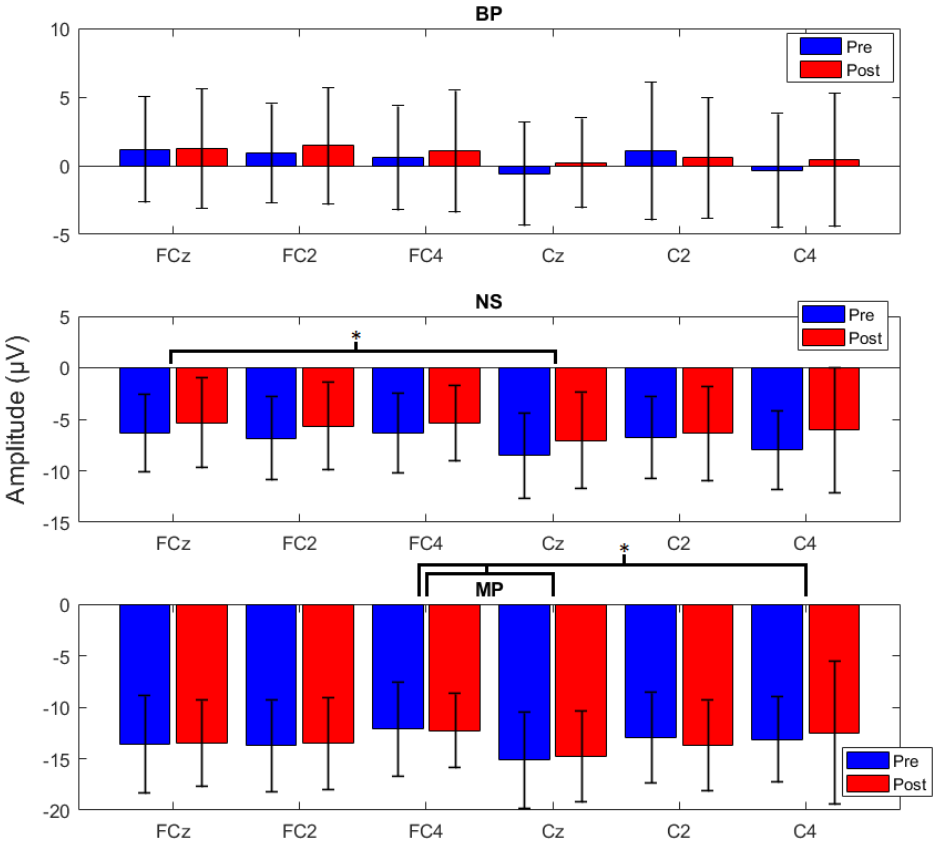


Figure 10.2: Bar plots of mean values from MRCP across subjects in both pre- and post-session with their standard deviations. * = $p<0.05$.

ERD-alpha and ERD-beta did not differ significantly from the pre-session to the post-session ($p = 0.053$, $p = 0.064$). For the difference between channels a statistical significance was only found within the ERD-alpha ($p = 0.042$) but not within ERD-beta ($p = 0.597$). Furthermore the interaction between the factors showed no significant difference ($p = 0.33$, $p = 0.474$). Post hoc analysis revealed no difference between the channels pairwise. For the ERS-alpha and ERS-beta no significance was found between the pre- and post-session. Significant difference between the channels were only found for ERS-alpha ($p = 0.014$) but not for ERS-beta ($p = 0.364$). Post hoc analysis revealed difference between C4 and FCz, FC2, and Cz in ERS-alpha. No interaction was found for both ERS-alpha and ERS-beta ($p = 0.576$, $p = 0.791$). Overview of statistical results can be found in table 10.3 for ERD and in table 10.4 for ERS.

Table 10.3: Overview of statistical results from ERD-alpha and ERD-beta with p-values and F-values.

	ERD	
	Alpha	Beta
Difference Pre/Post	$F(1,17) = 4.326$, $p = 0.053$	$F(1,17) = 3.928$, $p = 0.064$
Between channel	$F(2.69,45.67) = 3.063$, $\mathbf{p = 0.042}$	$F(2.45,41.72) = 0.581$, $p = 0.597$
Interaction	$F(2.71,46.01) = 1.167$, $p = 0.33$	$F(2.76,46.99) = 0.833$, $p = 0.474$

Table 10.4: Overview of statistical results from ERS-alpha and ERS-beta with p-values and F-values.

	ERS	
	Alpha	Beta
Difference Pre/Post	$F(1,17) = 0.198$, $p = 0.662$	$F(1,17) = 0.109$, $p = 0.745$
Between channel	$F(2.53,42.99) = 4.265$, $\mathbf{p = 0.014}$	$F(2.3,39.06) = 1.059$, $p = 0.364$
Interaction	$F(2.56,43.53) = 0.628$, $p = 0.576$	$F(2.63,44.67) = 0.312$, $p = 0.791$

The mean values of ERD-alpha, ERD-beta, ERS-alpha and ERS-beta with their corresponding standard deviations is illustrated as bar plots in figure 10.3

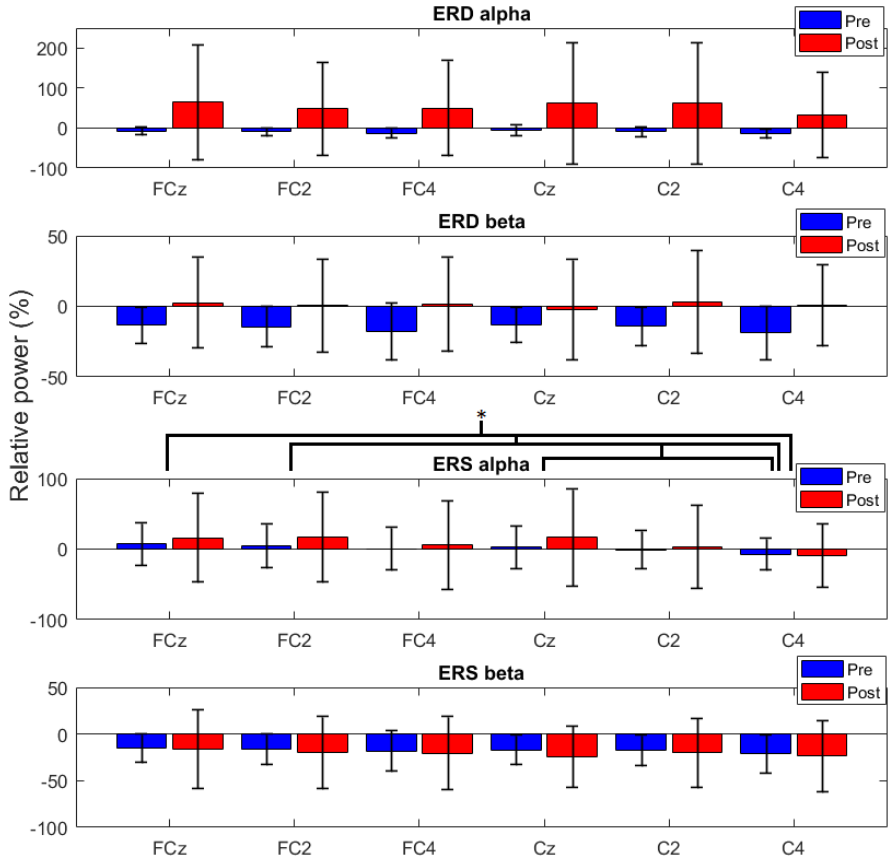


Figure 10.3: Bar plots of the mean values with their corresponding standard deviations from ERD and ERS across subjects within the alpha and beta frequency bands. * = $p<0.05$.

10.3 Corticomuscular coherence

Trial rejection in the coherence part consisted of rejection based on the EEG and the EMG. This meant that trials might be rejected if either or both were contaminated. The results of the trial rejection can be seen in table 10.5.

Table 10.5: Rejection of trials overview. 18 subjects · 3 repetitions · 2 sessions · 2 intensities · 3 frequency bands.

	Square		Triangle	
Bad EMG (trials)	Ext	Flex	Ext	Flex
	45/648	33/648	54/648	57/648
High EEG values (trials)	-		-	
Dead trials	6/648		39/648	

After trial rejection the remaining results were tested against the significance limit calculated via equation 7.3 in section 7.3. The significance limit for the square coherence was 0.1329 and for the triangle coherence it was 0.7764. The difference between the two, is due to the amount of data segments available for the square coherence as opposed to the short time frame of the triangles. The number for subjects having significance coherence in both the pre-session and post-session of the different repetitions across the selected channels can be seen in the following tables. As mentioned in section 9.4 if half or more of the subjects had significant coherence in both the pre-session and the post-session, they were statistically compared.

10.3.1 Triangle coherence

In table 10.6 the alpha wave coherence of the triangle repetitions can be seen.

Table 10.6: Triangle alpha wave coherence. The number of subjects with significant coherence in both pre- and post-session can be seen for the different repetitions across the selected channels. Ext = extensor EMG, flex = flexor EMG.

	Triangle ascending				**Triangle descending**			
	5% MVC		10% MVC		5% MVC		10% MVC	
Channels	Ext	Flex	Ext	Flex	Ext	Flex	Ext	Flex
FCz	0	1	0	0	0	1	0	1
FC2	0	0	0	0	1	0	0	0
FC4	0	0	0	0	0	0	0	0
Cz	0	1	0	0	0	1	1	0
C2	0	0	0	0	1	0	1	0
C4	0	0	0	0	0	0	0	0

In table 10.7 the beta wave coherence of the triangle repetitions can be seen.

Table 10.7: Triangle beta wave coherence. The number of subjects with significant coherence in both pre- and post-session can be seen for the different repetitions across the selected channels. Ext = extensor EMG, flex = flexor EMG.

	Triangle ascending				**Triangle descending**			
	5% MVC		10% MVC		5% MVC		10% MVC	
Channels	Ext	Flex	Ext	Flex	Ext	Flex	Ext	Flex
FCz	2	1	0	0	1	2	0	1
FC2	0	1	0	2	0	3	0	0
FC4	1	2	1	0	0	3	0	1
Cz	0	0	0	0	0	1	0	0
C2	1	1	0	0	0	2	0	0
C4	2	2	2	0	0	2	0	0

In table 10.8 the gamma wave coherence of the triangle repetitions can be seen.

Table 10.8: Triangle gamma wave coherence. The number of subjects with significant coherence in both pre- and post-session can be seen for the different repetitions across the selected channels. Ext = extensor EMG, flex = flexor EMG.

	Triangle ascending				**Triangle descending**			
	5% MVC		10% MVC		5% MVC		10% MVC	
Channels	Ext	Flex	Ext	Flex	Ext	Flex	Ext	Flex
FCz	0	1	1	1	0	2	0	0
FC2	0	1	0	1	0	1	0	0
FC4	0	1	1	2	0	1	1	0
Cz	2	1	1	2	0	1	0	0
C2	1	1	0	1	0	1	1	0
C4	1	1	0	1	0	3	0	0

None of the repetitions of triangle coherence reached the required number of subjects for further statistical analysis.

10.3.2 Square coherence

In table 10.9 the alpha, beta and gamma wave coherence of the square repetitions can be seen.

Table 10.9: Square coherence for each wave. The number of subjects with significant coherence in both pre- and post-session can be seen for the different repetitions across the selected channels. The repetitions used for further analysis are highlighted in bold. Ext = extensor EMG, flex = flexor EMG. Session where more than half the subjects had significant coherence are highlighted.

	Square alpha waves				**Square beta waves**				**Square gamma waves**			
	5% MVC		10% MVC		5% MVC		10% MVC		5% MVC		10% MVC	
Channels	Ext	Flex	Ext	Flex	Ext	Flex	Ext	Flex	Ext	Flex	Ext	Flex
FCz	0	2	3	3	5	**10**	3	4	4	**10**	**9**	7
FC2	2	2	4	1	3	7	3	2	1	**9**	5	**10**
FC4	1	2	3	5	4	8	4	3	1	**9**	7	6
Cz	1	0	3	4	6	5	6	4	6	6	**9**	6
C2	3	0	3	3	5	7	4	3	3	6	5	4
C4	5	1	4	4	6	7	6	3	4	5	**9**	6

The highlighted cells from the table above were then compared pre to post. No significance was found for any channels of any sessions. The statistical results can be seen in table 10.10.

Table 10.10: Statistics of the different EEG and EMG combinations, that had the required amount of data for statistical analysis. Ext = extensor EMG, flex = flexor EMG.

Square coherence			
Channels	**Normally distributed**		**Change**
	Pre	Post	
Beta 5 % MVC			
FCz-Flex	p <0.001	p <0.001	z = -0.255, p = 0.799
Gamma 5 % MVC			
FCz-Flex	p <0.001	p = 0.007	z = -0.968, p = 0.333
FC2-Flex	p = 0.001	p <0.001	z = -1.244, p = 0.214
FC4-Flex	p = 0.002	p <0.001	z = -1.244, p = 0.214
Gamma 10 % MVC			
FCz-Ext	p = 0.016	p <0.001	z = -0.652, p = 0.515
Cz-Ext	p = 0.005	p <0.001	z = -1.007, p = 0.314
C4-Ext	p = 0.024	p = 0.017	z = -0.059, p = 0.953
FC2-Flex	p <0.001	p <0.001	z = -1.682, p = 0.093

In figure 10.4 the mean and standard deviation of the coherence used for statistical analysis is illustrated.

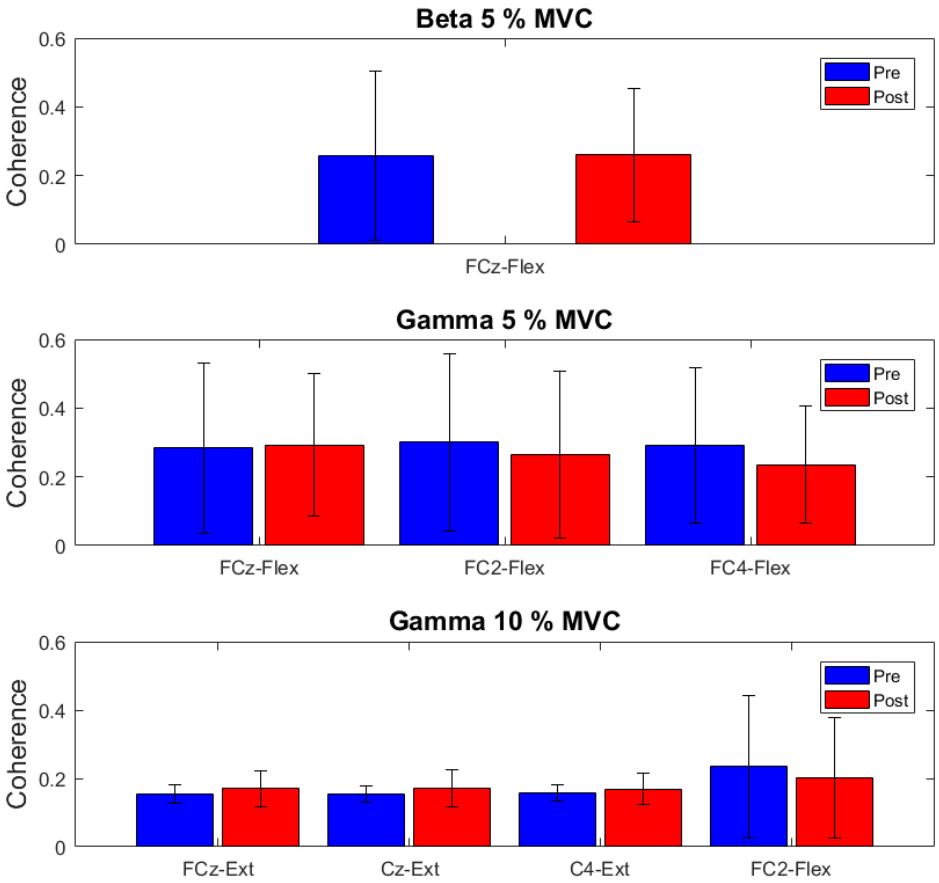


Figure 10.4: Bar plot of the coherence divided into the frequency bands beta and gamma with 5 % and 10 % MVC. Ext = extensor EMG, flex = flexor EMG.

10.4 Rest EEG

No trials were rejected following analysis of the rest EEG data, however subject 7 was excluded from the analysis due to abnormally high values in FCz.

10.4.1 Open eyes

The coordinates of the center of mass within the different frequency bands were tested if they were normally distributed. All coordinates were normally distributed except the y-coordinate pre- an post-session within the theta frequency band ($p = 0.024$, $p = 0.026$) and y-coordinate in the post-session within the gamma band ($p = 0.009$). It was tested if the center of mass had a significant shift in either the x- or y-direction but no significant shift was found within any of the frequency bands. An overview of the statistical results can be found in table 10.11 for the x-coordinate and in table 10.12 for the y-coordinate.

Table 10.11: Overview of statistical results for the x-coordinate in rest EEG open eyes divided into the frequency bands. P-values and their corresponding t- and z-values is presented.

X			
Waves	Normally distributed		Shift
	Pre	Post	
Delta	$p = 0.607$	$p = 0.854$	$t(17) = -0.616$ $p = 0.546$
Theta	$p = 0.134$	$p = 0.958$	$t(17) = -1.812$ $p = 0.634$
Alpha	$p = 0.396$	$p = 0.307$	$t(17) = -1.812$ $p = 0.088$
Beta	$p = 0.308$	$p = 0.375$	$t(17) = -1.732$ $p = 0.101$
Gamma	$p = 0.516$	$p = 0.794$	$t(17) = -1.748$ $p = 0.099$

Table 10.12: Overview of statistical results for the y-coordinate in rest EEG open eyes divided into the frequency bands. P-values and their corresponding t- and z-values is presented.

Y			
Waves	Normally distributed		Shift
	Pre	Post	
Delta	p = 0.300	p = 0.116	t(17) = -0.050, p = 0.961
Theta	p = 0.024	p = 0.026	z = -1.983, p = 0.053
Alpha	p = 0.468	p = 0.966	t(17) = -1.844, p = 0.083
Beta	p = 0.809	p = 0.638	t(17) = 1.179, p = 0.255
Gamma	p = 0.637	p = 0.009	z = -0.022, p = 0.983

A bar plot is shown in figure 10.5 with the mean values and standard deviations of x- and y-coordinate within the frequency bands and in pre- and post-session.

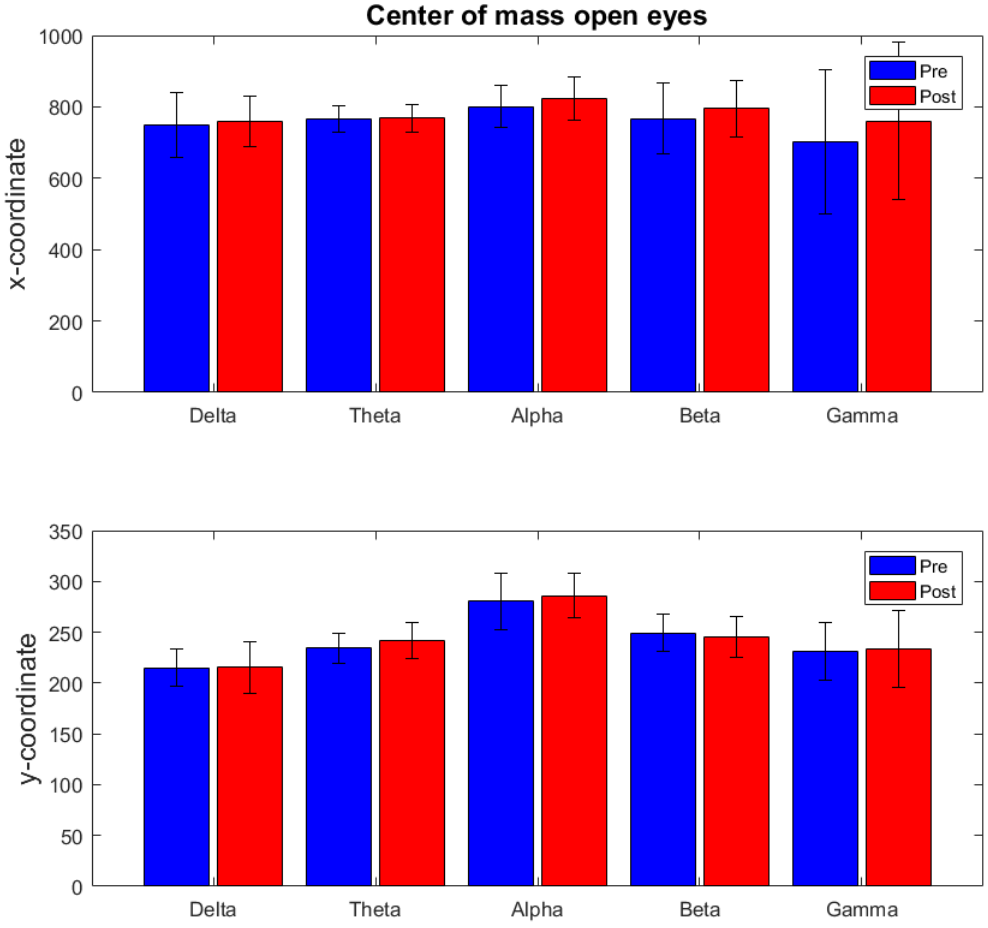
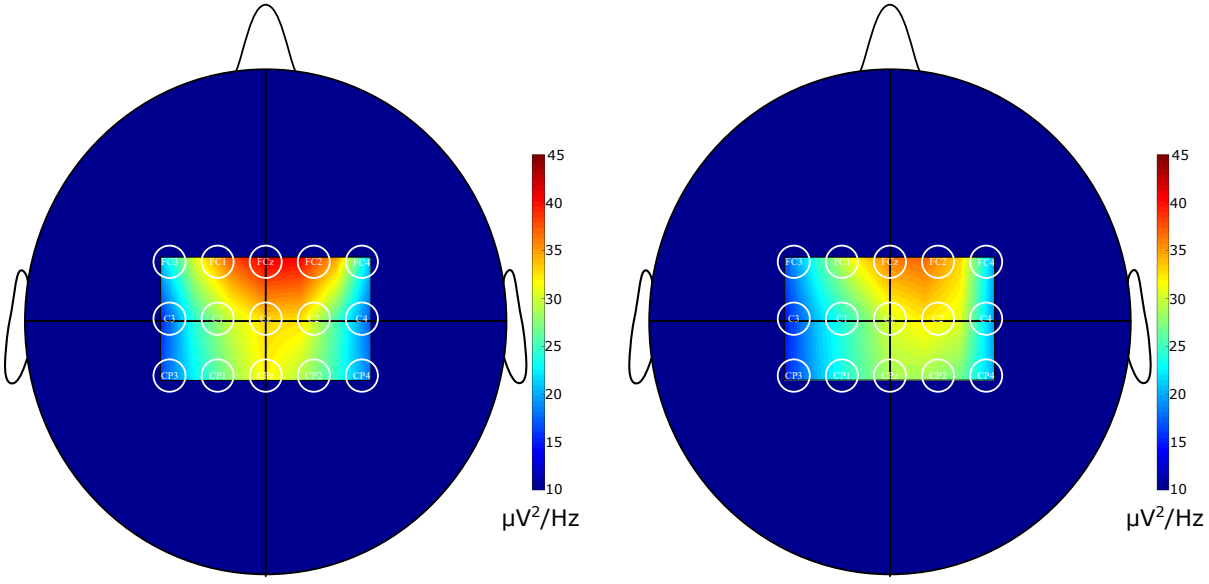


Figure 10.5: Barplot of rest EEG session with open eyes. The plots are divided in x- and y-coordinate, with pre and post together with the frequency bands.

An example of a heat map constructed from the PSD values of the channels and interpolated for greater detail, is shown in figure 10.6. The heat map is from subject 3 and values from the alpha frequency band. There seems to be greater activity in the pre-session in the channels FCz and FC2, but the center of mass did not differ significantly.



(a) (b)

Figure 10.6: (a) Heat map for subject three in the pre-session of rest EEG with open eyes within the alpha band. (b) Heat map for subject three in the post-session of rest EEG with open eyes within the alpha band.

10.4.2 Closed eyes

Testing if the coordinates were normally distributed resulted in x and y in the post-session within the delta band being not normally distributed ($p = 0.034$, $p < 0.001$). Furthermore the x-coordinate in pre-session alpha, x and y in post-session beta and post-session for both the coordinates in gamma were not normally distributed. There was a significant shift posteriorly for the beta band as the only one ($p = 0.008$). Overview of the results can be found in table 10.13 for the x-coordinate and table 10.14 for the y-coordinate.

Table 10.13: Statistical results of rest EEG closed eyes for x-coordinate, where p-values and their corresponding t- and z-values is presented.

X			
Waves	Normally distributed		Shift
	Pre	Post	
Delta	$p = 0.126$	$p = 0.034$	$z = -0.719$, $p = 0.472$
Theta	$p = 0.661$	$p = 0.640$	$t(17) = -0.392$, $p = 0.700$
Alpha	$p = 0.038$	$p = 0.321$	$z = -0.065$, $p = 0.948$
Beta	$p = 0.091$	$p = 0.004$	$z = -0.457$, $p = 0.647$
Gamma	$p = 0.803$	$p = 0.030$	$z = -0.283$, $p = 0.777$

Table 10.14: Statistical results of rest EEG closed eyes for y-coordinate, where p-values and their corresponding t- and z-values is presented.

Y			
Waves	Normally distributed		Shift
	Pre	Post	
Delta	$p = 0.514$	$p < 0.001$	$z = -1.285$, $p = 0.199$
Theta	$p = 0.401$	$p = 0.502$	$t(17) = -0.747$, $p = 0.465$
Alpha	$p = 0.924$	$p = 0.297$	$t(17) = 0.442$, $p = 0.664$
Beta	$p = 0.209$	$p = 0.213$	$\mathbf{t(17) = 3.030, p = 0.008}$
Gamma	$p = 0.306$	$p = 0.318$	$t(17) = 0.372$, $p = 0.715$

A bar plot of the mean values and standard deviation within the frequency bands and in the pre- and post-session can be seen in figure 10.7.

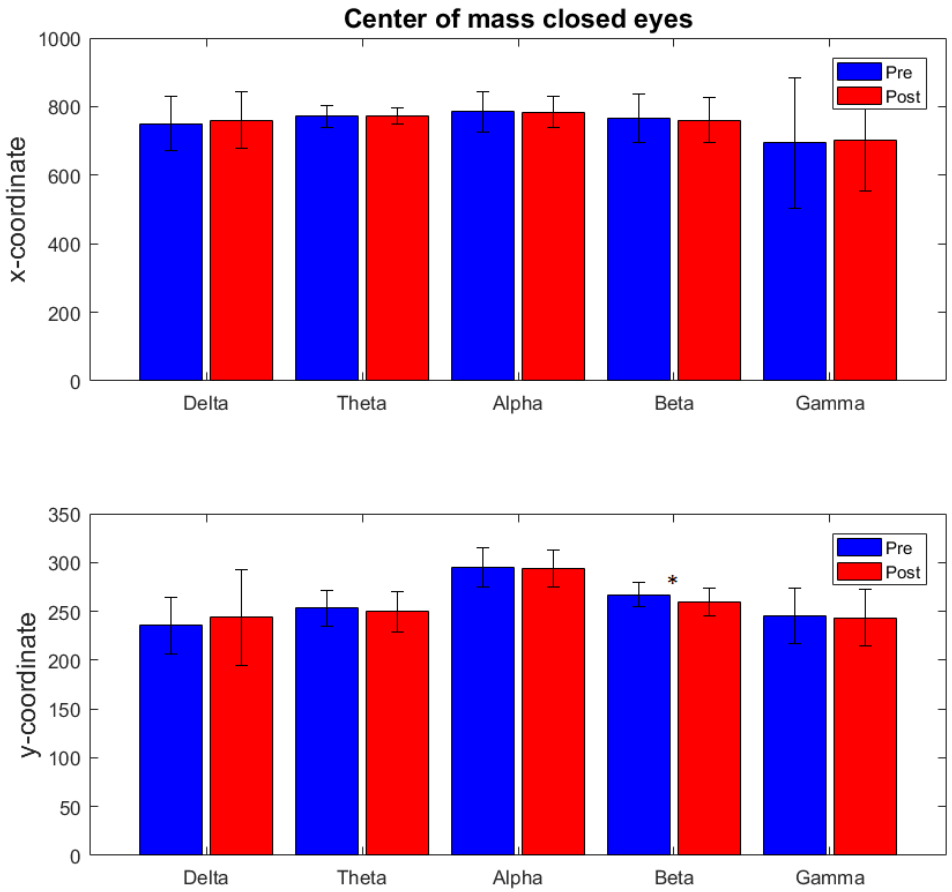


Figure 10.7: Barplot of rest EEG session with closed eyes. The plots are divided in x- and y-coordinate, with pre and post together with the frequency bands.

A heat map from subject 18 with PSD values within the alpha band is shown in figure 10.8. There seems to be more activity in the pre-session in channel CPz, but it is radiating a little towards Cz. In the post-session the radiation towards the Cz channel is becoming more profound together with a higher activity around CP1 and CP2. But no significant difference was found in the center of mass.

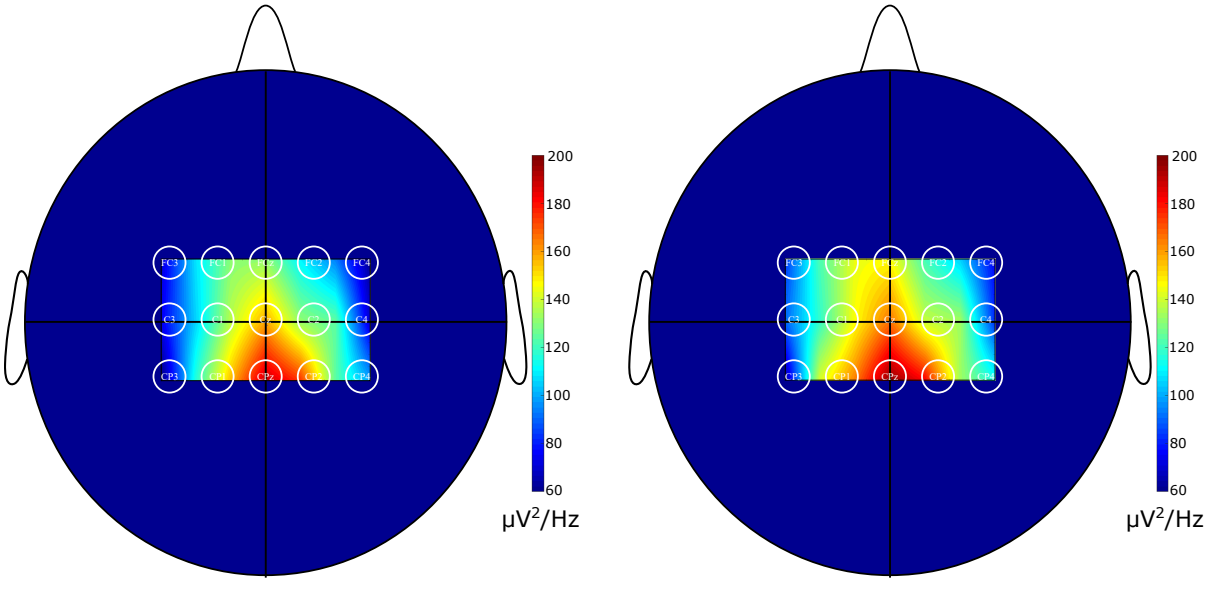


Figure 10.8: (a) Rest EEG close eyes heat map from subject 18 within the alpha band in the pre-session. (b) Rest EEG close eyes heat map from subject 18 within the alpha band in the post-session.

Chapter 11

Synthesis

This chapter will include a summary of the aim and the findings, followed by a discussion of the results and the methods. The chapter ends with a conclusion on the project.

11.1 Discussion

The aim of the present project was to investigate short term motor learning within EEG features. The features investigated were the MRCP, more specifically the BP, NS' and MP, the ERD/ERS, corticomuscular coherence and waves from rest EEG. In order to assess the features an experiment was conducted including 19 subjects performing various motor tasks with their non-dominant hand, together with rest EEG sessions. Data obtained from the experiment were analyzed and statistically compared from the pre-session to the post-session in order to see effect of the intervention. Subjects improved performance during the experiment, which was reflected as producing less errors during the intervention. Even though this was the case a significant change within the features was only seen as a posterior shift of the center of mass of heat maps and only in the beta band during the closed eyes rest session. No significant change was seen within any of the other features.

11.1.1 Results

As it was apparent throughout the result chapter, there were no neural changes following the motor training in the measures utilized in this project. In fact the only feature which changed significantly was during the closed eyes rest session, as the center of mass shifted posteriorly in the beta band. The lack of change in the features might be because of several reasons. One possibility could be that the performance improvement was simply not enough to equal a measureable change in the majority of the features utilized. Maybe the subjects were not far enough on the learning curve as the performances did not seem to plateau, meaning the motor tasks were not yet in a phase of being automatized (i.e. still in the cognitive phase of the model presented in figure 2.1 in chapter 2).

Performance outcome

In the present study the subject significantly improved performance during the intervention. Of the four articles studying MRCP only one investigated behavioral performance where a significant difference was found. Smith and Staines [2006] had an experiment which focused on reaction time from pre- to post-training, where they found significant decrease in reaction time along with change in features. As this was not found in the present study, explanations of the conflicts can be due to the differences in study design. Since Smith and Staines [2006] focused on reaction time and did not include any force measurements, this might indicate force measures as being less optimal, when the goal is to quantify neural change. Furthermore no force measures were done in the study done by Dirnberger et al. [2004], where subjects were to press a button in self-paced manner. They also found amplitude differences in the MRCP following the intervention. If force is to be included into the experiment it can be discussed if the amount of MVC should be higher than what was done in the present study. The MVC was at maximum 5 %, which is low compared to the study by Halder et al. [2005], where MVC between 10-40 % was used. They

also had sessions where subjects needed to produce 40 % MVC [Halder et al., 2005]. Therefore an effect on the MRCP features may have been seen if a higher MVC was used during the motor training. The motor training consisted of 80 repetitions which in comparison to other studies is rather low. Studies found in the literature review regarding MRCP (chapter 5) had at least 200 repetitions in total [Dirnberger et al., 2004, Halder et al., 2005, Smith and Staines, 2006] but within ERD/ERS less repetitions is seen, from 90-100 repetitions [Zhuang et al., 1997, Kranczioch et al., 2008, Moisello et al., 2015], still more than in the present study. Within coherence studies 35-150 repetitions [Kristeva et al., 2007, Mendez-Balbuena et al., 2012] is seen where as in rest no repetitions were performed [Lardon and Polich, 1996]. A difference in the MRCP features may have been discovered if subjects were to perform more repetitions during motor training. However this would extent the experimental time to the point where fatigue could have an influence. The other studies were able to fit around 200 repetitions in the same time span due to their motor training being simpler and less time consuming. The movement performed in the present study consisted of various force intensities (up to 5 % MVC) depending on the force track, which is much more complex in comparison to the studies Dirnberger et al. [2004], Halder et al. [2005], Smith and Staines [2006] where movements consisted of, finger tapping, ball squeezing and wrist flexion and extension. It can then be discussed if MRCP and ERD/ERS are valid EEG features for quantifying motor learning within more complex movements.

MRCP

The MRCP features did not differ significantly and had a high standard deviation compared to their respective mean values (especially for the BP and NS' feature). The high inter-subject variance might suggest that more subjects were needed in order to obtain a valid mean value of the respective features. The studies investigating MRCP had subjects ranging from 10-33 healthy subjects with motor training of 36-45 minutes and 5 stroke subjects with one month of motor training.

Previously, changes in the MRCP have been observed in relation to motor learning in multiple studies [Dirnberger et al., 2004, Halder et al., 2005, Smith and Staines, 2006, Yilmaz et al., 2013]. The general finding was a lower amplitude and a potential closer to movement onset following motor training, which was not found in this project as none of the features, quantifying the MRCP, changed. The time perspective of the three studies on healthy subjects are in line with the amount of time subjects in the present project used on the motor training part of the experiment. The number of subjects varied by Dirnberger et al. [2004] having more, while Halder et al. [2005], Smith and Staines [2006] had fewer, eliminating these factors as possible explanations.

Three out of four included articles Dirnberger et al. [2004], Smith and Staines [2006], Yilmaz et al. [2013] all used features extracted from the MRCP in the time domain in the immediate time period before and after. Dirnberger et al. [2004] used af mean of 20 trials to calculate 3 features, which were mean values of specific time intervals before movement onset: 1500-1000 ms, 1000-500 ms and 500-0 ms. Smith and Staines [2006] used 40 trials to quantify the early component, start of negativity (1300-1800 ms before movement onset), late component, sharper negativity with peak (100-150 ms to around movement onset) and reafferent potential following the late component. Yilmaz et al. [2013] did not specify the number of repetitions they had, but they looked at MRCP onset and the peak amplitude. The features used in the present project covered the same time period/latencies and quantified most of the same events, also eliminating features and latencies as possible explanations for the difference in results.

ERD/ERS

No significant changes were to be found in ERD/ERS results in both beta and alpha bands. There was however a much greater variation in the results during the post-session compared to the pre-session for both the frequency bands in the ERD/ERS. This indicates that the results in the post-session had much more uncertainty and that the subjects responded very differently to the intervention. Furthermore the standard deviation in both pre- and post-session were large

compared to the mean value. Changes within the ERD and the ERS have previously been found by other researchers. [Zhuang et al., 1997, Kranczioch et al., 2008, Moisello et al., 2015] The general finding was a decreased ERD-alpha and beta following motor training, while there was no consensus on changes inflicted to the ERS in the bands. The specific bands however differed across the studies where Zhuang et al. [1997] used an alpha band from 9-11 Hz, Kranczioch et al. [2008] used an alpha band from 8-12 Hz and beta from 13-21 Hz and Moisello et al. [2015] used a beta band from 15-30 Hz. The present study used an alpha band from 8-14 Hz and a beta band from 15-30 Hz, which was a little bit different from at least Zhuang et al. [1997] and Kranczioch et al. [2008]. Whether any difference would have occurred if the bands were different is to be doubted due to Moisello et al. [2015] finding a difference utilizing a similar band. The individual differences may suggest that subject-specific ERD/ERS should be used to quantfiy changes; however, this needs to be addressed in future studies.

The ERD/ERS studies all had fewer subjects and a similar experimental time, and they were all able to find differences following motor training.

Corticomuscular coherence

No significant changes were found within the corticomuscular coherence results, but one thing which was apparent was the variation in the extensor EMG (figure 10.4). The gamma frequency band with 10 % MVC had much lower variation in the coherence between the EEG channels and the extensor EMG channel compared to the flexor EMG channel. This might indicate that coherence is more relevant for the extensor muscles when performing palmar grasps as done in the present study. Multiple researchers have found changes in corticomuscular coherence in relation to motor learning. [Perez et al., 2006, Kristeva et al., 2007, Mendez-Balbuena et al., 2011, 2012, Hori et al., 2013, Klotz et al., 2013] They do however not agree in which frequency ranges the changes are present. No changes were found in corticomuscular coherence in the present project in any of the explored frequency ranges. However 9-10 subjects were found to have significant coherence several times with different MVC percentage within both the pre- and post-session. This was not found with the triangle coherence, indicating that the design of this force track was not able to elicit coherence between the EEG and EMG. This is however a known issue, as other researchers have highlighted the problem of reliably recording coherence in all subjects in a sample [Hashimoto et al., 2010, Mendez-Balbuena et al., 2012] The purpose of the triangle shaped force track for coherence measures was to assess different isometric contraction states, but if this shape is to be used, higher MVC percentage and more repetitions would be suggested. The design of the square coherence was expected to yield similar results as it was similar to the studies by Kristeva et al. [2007] and Mendez-Balbuena et al. [2012]. The difference however was the percentage in MVC which was 4 % in Kristeva et al. [2007] and 8 % in Mendez-Balbuena et al. [2012]. Furthermore Mendez-Balbuena et al. [2012] had a dynamic aspect in their study which was not included in the present study. Calculation differences from the present study to studies investigating coherence was minimal as the bin size in Kristeva et al. [2007] was 512 ms compared to 1000 ms in the present study. All of the coherence studies have a lower number of subjects and were still able to find changes. Multiple of the studies did not specify the time frame of the motor training involved, why this might be a source of different results. One thing that was not investigated in this project is whether the motor training made subjects have significant corticomuscular coherence (if it was not present in the pre-session), as it was found by Mendez-Balbuena et al. [2011, 2012]. This is a possibility, but it seems unlikely as none of the remaining coherence features showed any significant changes.

If the goal is to find features to quantify the neural effects of motor learning, coherence should perhaps not be considered for further studies, or at the very least the protocol should be optimized in such a manner that coherence is estimated for the most subjects possible. From the present project the coherence during steady-state force (the square shape) within the gamma band had the most useful data.

Resting EEG

The effect of motor learning on the resting EEG has not been investigated a lot, as only two studies were found previously having researched the area. [Lardon and Polich, 1996, Assenza et al., 2015] However both of them were able to find differences, but conflicting. The studies had a similar number of subjects compared to the present project, but their respective setups were very different, why it is hard to compare their results to each other and to the present project.

The posterior shift seen in the beta bands during resting EEG with closed eyes sessions is however in line with the findings presented in section 3.1. It is noted that the later stages of motor learning is characterized in a shift from anterior to more posterior regions, indicating a decrease in executive function, which would suggest motor learning had occurred.

In general it should also be noted that the rest features had the lowest relative variation compared to their mean values.

11.1.2 Study design

The present study included a pre-session, an intervention and a post-session. While the rest and coherence measures were from the pre- and post-session, the MRCP and the ERD/ERS of the motor training was found directly from the intervention data. Multiple of the studies found in the literature review does not employ a similar setup, instead a pre-session measurement followed by a motor training session (sometimes different from that being used for measuring features) and then a post-session recording. Some of the advantages of this include the possibility of varying the motor training slightly from the recording sessions, making the measurement have an element of a transfer test, which has been proposed as a better way of assessing learning (see chapter 2). The primary disadvantages of this compared to the design employed in the present study is that it would have added time to an already long experiment. Furthermore it would have introduced a possibility of having subjects improve from the pre- to the post-session merely by the unintended practice of performing movements for the recording of the MRCP and ERD/ERS. This could then be accounted for by including a control group not doing motor training as an intervention, which would mean recruiting substantially more subjects.

11.1.3 Data rejection

Trial rejection resulted in 31.3 % of the trials being rejected in the analysis of MRCP and 1.25 % in the ERD/ERS analysis. Furthermore high values in the crucial channel FCz resulted in exclusion of subject 7. The high percentage of rejection in the MRCP analysis may be due to equipment issues or insufficient preparation of subjects. Before any recordings were done all channels were prepared with conducting gel and it was made sure that the impedance were under 100 k Ω. Furthermore subjects were asked not produce any unwanted movements (eye blinking, clenching of the jaw etc.) in the desired time span. With this in mind it cannot be ruled out that the equipment used for the experiment was not able to adequately record a signal with such a low signal-to-noise ratio as the MRCP. Stricter control of unwanted movement could have been applied, but the majority of the rejected trials were from a positive gradient, which would not have been induced by eye activity or head movement. In addition whole channels were rejected during the data analysis of rest EEG, further indicating that there might have been issues regarding the equipment.

Of the four studies from the literature review investigating MRCP only one reported their rejection rate. The study by Smith and Staines [2006] had an average rejection rate of 9.6 % of the epochs which was approximately 3-4 per condition making the rejection rate in the present study being extremely high. Whether a rejection rate of 9-10 % is normal within such a procedure is not known due to other studies not reporting it. If it is the case other equipment should be taking into consideration when performing an experiment investigating MRCP features than what has been used in the present study and possibly tighter control of unwanted movements.

The EMG rejection in corticomuscular coherence was ranging from 5-9 % where especially the triangle shape had a large rejection rate. The rejection criteria for the EMG was if RMS of

the active period was below or equal to two times RMS of the baseline prior to movement. A possibility could be to do a RMS test of the EMG prior to recording, to minimize the amount of coherence trials being rejected due to improper EMG signals. Furthermore more repetitions could have been added, especially for the square coherence, as a lot of data were discarded if a trial was contaminated. A possibility would be to break the 30 seconds of steady-state force output into three repetitions of 10 seconds. That would have meant 9 repetitions in the same time as used with the present method compared to the existing 3, minimizing the amount of rejected data if only part of a trial had contaminated signals. It can also be discussed if the EMG electrodes were placed correctly or a more strict control of the placement should have been performed. Since the electrodes were placed primarily on the flexor and extensor bundle a more extensive investigation of the muscles involved in the grip motion performed could have been done. This may have helped in the cases, where little to no EMG signal was present, especially in the 5 % MVC where a more optimal electrode placement could have produced higher amplitude signal.

11.1.4 Limitations

The result of the performance measure showed a significant decrease in error comparing the first trial to the last. Given this a performance increase have taken place but as the other features indicate not necessarily motor learning. As described in section 2.2 a performance increase is not necessarily equal to motor learning, which raises the question if motor learning have been induced in the subjects. If motor learning has been induced within the subjects it has not been possible to quantify with the used features and equipment. Given that, other features of the EEG should be investigated.

Changes shown in relation to motor learning might also be specific to the type of task [Krakauer and Mazzoni, 2011]. The studies selected during the literature review included an array of different motor training tasks including reaction time tasks, visuomotor tasks, virtual navigation tasks, etc. Furthermore the studies had different types of subject as some included Parkinson's disease patients or stroke patients, which raises the question if any effect measured is task and/or subject type specific, possibly making it harder to compare.

11.1.5 Implications and future studies

If changes had been found, one or more of the features could have been used as a way to quantify and/or evaluate motor learning. This could be used in assessing rehabilitation or skill progress of surgeons (or similar professions with a skill component). Furthermore EEG features might have been a viable alternative to studies using TMS to quantify plastic changes in the corticospinal pathway, as TMS can be unpleasant/painful for subjects and as it contains no information of where in the pathway a change happens. The results from the present study does however suggest that the chosen features might not be optimal in any of these cases. Features had a relatively high standard deviation compared to their means and only one measure changes significantly as performance increased. Even though correlation between features and performance was not investigated, these results suggest that there would be none. As mentioned above features such based on the MRCP have previously been used to quantify motor learning in simple movements, but the clinical value in measuring improved ability/less attentional effort in tapping a finger is probably limited. Whether the goal is to quantify rehabilitation or skill progression, future studies should have motor training that resembles the training that is utilized normally in order to find appropriate neural features.

Future studies could also investigate additional brain areas. According to Dayan and Cohen [2011] the cerebellum is highly active in the initial stages of motor learning, why investigation of short term motor learning could benefit from including a measure that quantifies cerebellum activity. Furthermore to insure that learning is measured and not only a short lived performance enhancement, a retention test could be utilized preferably 24 hours after training.

11.2 Conclusion

Short term motor learning did not result in neural changes measured using EEG features during movement preparation, resting brain waves or corticomuscular coherence. This is partly in conflict with existing literature, as multiple of the selected features previously have been used to show changes following motor learning. More studies are needed to provide an accurate assessment of the possible neural changes measureable following short term motor training.

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Appendix A

Searches

Searches regarding changes in EEG and selected features of EEG can be found in table A.1. The searches regarding coherence can be found in table A.2. The searches regarding rest EEG can be found in A.3.

Table A.1: Searches regarding EEG.

Keywords (search string)	Database	Hits	Selected titles	Selected abstracts	Selected full texts
EEG motor learning	PubMed	2035	-	-	-
EEG Plasticity motor learning	PubMed	133	29	12	4
EEG motor learning	Embase	1962	-	-	-
EEG Plasticity motor learning	Embase	225	19	8	1
EEG motor learning	ScienceDirect	22914	-	-	-
EEG Plasticity motor learning NOT sleep (filter: Only articles in journals)	ScienceDirect	309	8	3	3
EEG motor learning	IEEE	229	9	4	2
EEG motor learning	Cochrane	36	1	1	1
EEG motor learning event related (desynchronization OR synchronization)	PubMed	59	5	2	2
EEG motor learning event related (desynchronization OR synchronization)	Embase	39	1	0	-
EEG motor learning event related (desynchronization OR synchronization)	ScienceDirect	125	3	2	2
EEG motor learning event related (desynchronization OR synchronization)	IEEE	7	0	-	-
EEG motor learning event related (desynchronization OR synchronization)	Cochrane	0	-	-	-
EEG motor learning movement related cortical potential	PubMed	53	7	3	2
EEG motor learning movement related cortical potential	Embase	44	5	4	2
EEG motor learning movement related cortical potential	ScienceDirect	42	3	2	1
EEG motor learning movement related cortical potential	IEEE	-	-	-	-
EEG motor learning movement related cortical potential	Cochrane	-	-	-	-

Table A.2: Searches regarding coherence.

Keywords (search string)	Database	Hits	Selected titles	Selected abstracts	Selected full texts
EEG EMG Coherence motor learning	PubMed	3	3	2	1
EEG EMG Coherence motor learning	Embase	7	5	4	3
EEG EMG Coherence motor learning	ScienceDirect	698	-	-	-
EEG EMG Coherence motor learning (filter: Only articles in journals)	ScienceDirect	269	24	6	0
EEG EMG Coherence motor learning	IEEE	1	0	0	0
EEG EMG Coherence motor learning	Cochrane	0	0	0	0
Corticomuscular coherence motor learning	PubMed	4	4	4	2
Corticomuscular coherence motor learning	Embase	7	5	5	4
Corticomuscular coherence motor learning (filter: Only articles in journals)	ScienceDirect	51	18	5	1
Corticomuscular coherence motor learning	IEEE	1	0	0	0
Corticomuscular coherence motor learning	Cochrane	0	-	-	-

Table A.3: Searches regarding resting EEG.

Keywords (search string)	Database	Hits	Selected titles	Selected abstracts	Selected full texts
(rest OR resting) EEG motor learning	PubMed	91	1	0	0
(rest OR resting) EEG motor learning	Embase	126	2	1	0
(rest OR resting) EEG motor learning NOT Sleep NOT Connectivity	ScienceDirect	269	6	2	1
(rest OR resting) EEG motor learning	IEEE	3	1	0	0
(rest OR resting) EEG motor learning	Cochrane	4	0	0	0

Appendix B

Experimental Protocol

B.1 Purpose

The purpose of this experiment is to collect EEG and EMG from a subject performing short term motor training with their non-dominant hand. Recordings will be done before, during and after the motor training.

B.2 Selection criteria

- Have no neurological conditions
- Have no nerve damage in arms of torso
- Have not done resistance training involving the lower arm 8-12 hours before
- Have slept a minimum of 4-6 hours

B.3 Method

Before starting the experiment the table regarding sex, age, etc. and questionnaire needs to be filled out together with the consent form. Measurements will be done on a seating subject. The subject will be well informed about the process of the experiment and of any risks that might be associated with participating. The experiment consists of three sessions: pre motor training, motor training and post motor training.

- Pre motor training:
  - 3 MVC recordings will be performed
  - 3 minute resting EEG recordings will be performed on the subject with closed eyes
  - 3 minute resting EEG recordings will be performed on the subject with open eyes
  - EEG-EMG coherence training
- Motor training:
  - The subject will execute 3 test trials to get the understanding of the task
  - The training consists of in total 80 trials with a 60-120 seconds break after every twentieth trial
  - Each trial lasts 26 seconds with 16 seconds of tracking, 4 seconds of preparing and 5-6 seconds between trials
- Post motor training:
  - 3 minute resting EEG recordings will be performed on the subject with closed eyes
  - 3 minute resting EEG recordings will be performed on the subject with open eyes
  - EEG-EMG coherence
  - 3 MVC recording will be performed

B.4 Material List

- EEG-EMG Amplifier - g.tec g.HIamp 80-channel amplifier
  - Power cable
  - USB cable
  - USB dongle
  - Connector-cable x 2
  - Connector power cable
- EMG connector pad - g.tec 16-channel electrode connector box
  - EMG to surface electrodes x 2
  - EMG to BNC cable
  - Custom made EMG electrode-to-amplifier cables x 2
- EEG connector pad - g.tec 64-channel active electrode driver box
  - EEG Cap - g.gammacap^{2}
- Hand force transducer - Noraxon Scientific Handgrip Dynamometer
- Force amplifier - 390 Sensor Supply Noraxon
  - BNC cable
- Surface electrodes - Ambu Neuroline 720
- Conduction gel - g.tec g.GAMMAgel
- Conductive and abrasive paste - spes medica everi
- Syringes
- Alcohol swabs

B.5 Physical setup

B.5.1 Before the subject arrives

1. Connect the EEG and EMG amplifier to the power and to the computer via the USB
2. Connect the USB dongle
3. Connect the EMG and EEG connector pads to the amplifier as shown in figure B.1

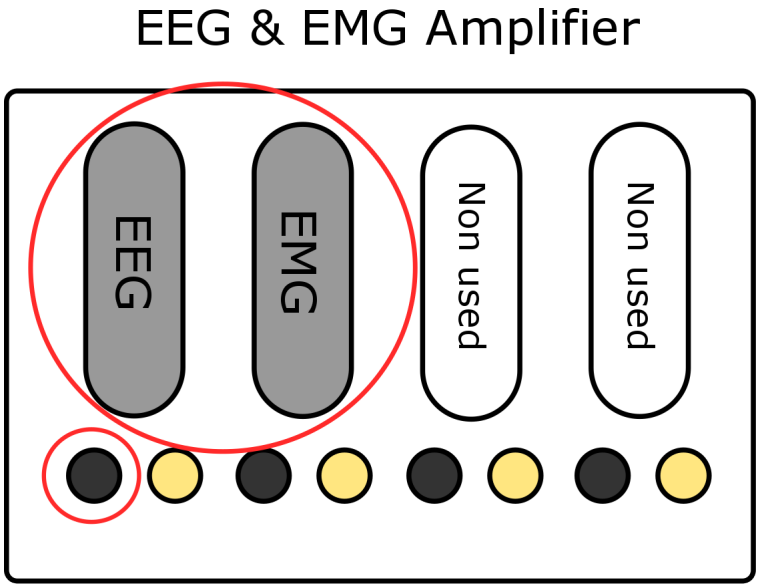

Figure B.1: Amplifier

4. Connect the two EMG surface electrode cables and the EMG-BNC cable as shown in figure B.2

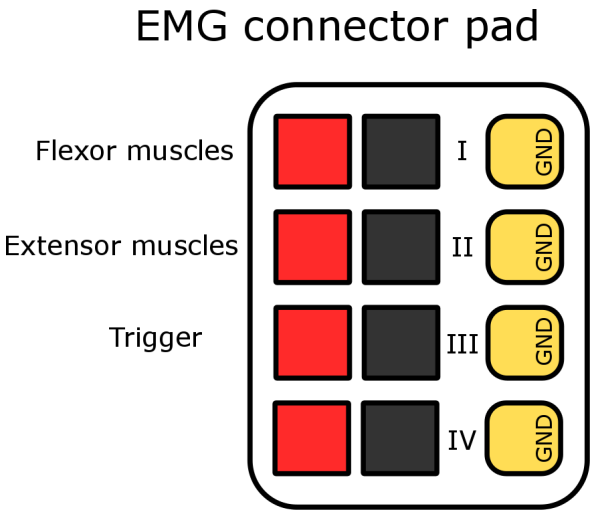

Figure B.2: EMG connector pad.

5. EMG-BNC cable should go to User 1 on the ADC.

6. The hand force transducer should be connected to the force amplifier as shown in figure B.3

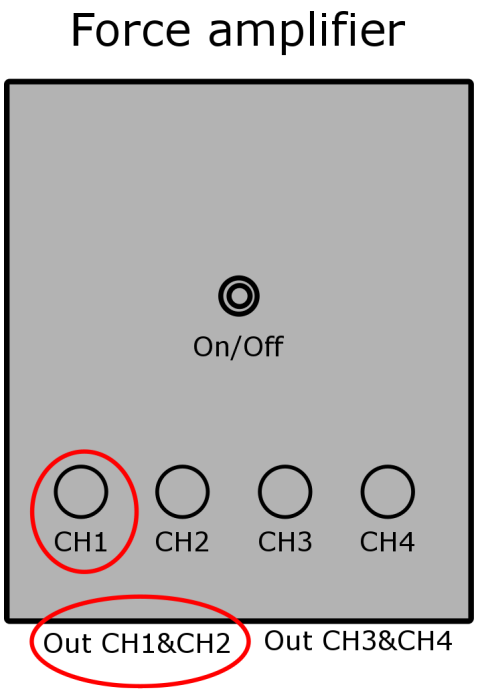

Figure B.3: Force-amplifier

7. The output of the force amplifier should go to the ADC0 on the ADC.
8. Turn on EEG-EMG amplifier and force amplifier.
9. On the computer run Follow Me and g.tec program.

B.5.2 After the subject arrives

1. Put on the EEG cap on the subject and apply gel in all channels.

How to put on the cap:

- Put on the cap
- Make the subject point to the top of his/her head with left and right hand
- Do this again with closed eyes
- Align channel Cz with this point
- Check if the point is roughly in the intersection between the line from ear to ear and the line from inion the nasion
- Otherwise measure

2. Prep the earlobes of the subjects with alcohol swabs, put conductive gel on earclip and put on the clip electrodes.
3. Prep the subjects non-dominant arm with abrasive gel and alcohol swabs and apply surface electrodes on the following sites illustrated on figure B.4.

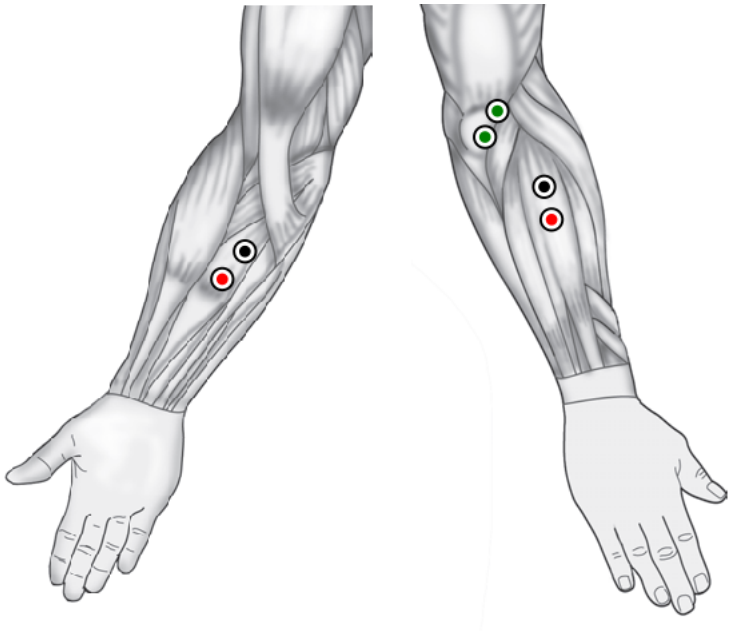

Figure B.4: Electrode placements

B.6 Procedure

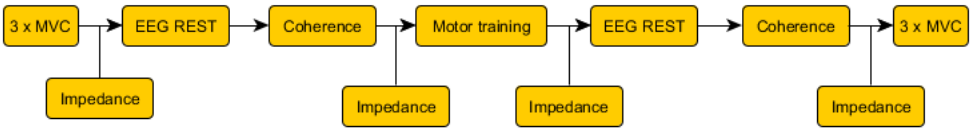

Figure B.5: Experiment flow.

1. Start PC
2. Connect equipment as shown in "Physical setup - Before subject arrives"
3. Open "Follow me" and "g.tec"
4. In "g.tec" load setup "ST10_setup.xml"
5. Welcome subject
6. Present them with the consent form
7. Fill out the sex, age, etc. table and questionnaire form
8. Explain what is going to happen
9. Connect equipment as shown in "Physical setup - After subject arrives"
10. Check impedances in "g.tec" (located under tools, press start)
11. Prep electrodes until they all have under 100 kΩ (green)
12. Press "Play" in "g.tec" to check connection of EMG electrodes (they are located from channel 66 to 70)
13. Have the subject flex and extend the wrist while looking at the EMG channels
14. Have the subject blink and clench their jaw while looking at the EEG channels

15. Start stopwatch
16. Perform 3 MVC recordings in "Follow Me", by choosing MVC from the drop down menu
17. 2 minute break between each MVC recordings
18. Note down MVC
19. Take a screenshot of impedances, save under the corresponding subject folder as: "subject-number_imp_pre_pre.png"
20. Take force pressure thing from subject
21. Test the EMG and EEG by looking at the signals
22. Perform the two sessions of resting EEG
    - For the eyes open, shut off screens, turn main screen and have the subject focus at the ”T”
    - When ready press record, set recording time to 3 minutes and select folder with the subject number and name it accordingly: "subject number (with 0, if below 10)"_pre/-post_rest_open/closed. E.g.: 05_pre_rest_open
23. EMG-EEG coherence with square and triangles (check order in lab notes) set the drop down to track and setup the following way:
    - If 5/10 % triangle:
      - Baseline: 0
      - Delay: 3
      - Risetime: 3
      - Target: 5/10
      - HoldTime: 0
      - FallTime: 3
      - TailTime: 3
      - Interval Range: 5-5
      - Cont.: X
      - SAVE: X
      - Scale
    - If 5/10 % square:
      - Baseline: 0
      - Delay: 20
      - RiseTime: 0
      - Target: 5/10
      - HoldTime: 30
      - FallTime: 0
      - TailTime: 20
      - Interval Range: 50-50
      - Cont.: X
      - SAVE: X
      - Scale
24. Instruct the subject not to blink or clench jaw during the active part of the trials

25. Save the files accordingly - Start EEG recording 5 sec before:
    - EEG-EMG: "Subject number"_pre/post_triangle/square_5/10
        - Remove time limitation from the EEG recording
    - Force: "Subject number"_pre/post_triangle/square_5/10_force
26. Take a screenshot of impedances, save under the corresponding subject folder as: "subject-number_imp_pre_post.png"
27. In "Follow Me" set the drop down to track, press special and apply the following settings:
    - Baseline: 0
    - Delay: 3
    - RiseTime: 1
    - Target: 5
    - Holdtime: 1.5
    - FallTime: 0
    - TailTime: 0
    - Interval Range: 5-6
    - Mark Cont.
    - SAVE: X
    - Scale
    - Special
28. Do 3 runs with the subject while explaining the goal and emphasizing no blinking or swallowing during the initial three seconds after the go
29. Discard the data file that was saved during the training runs
30. Instruct the subject that they will do 20 repetitions and then receive a break
31. Press record in "g.tec" and select the folder corresponding to the subject name. Name the file accordingly: "subject number"_EEG_MT_"trial number (1-4)"
32. Press start in "Follow Me" when ready
33. Press start in "Follow Me" after the twentieth run and stop the recording in "g.tec"
34. Find the saved file of "Follow Me", move it to the corresponding subject folder and rename it accordingly: "subject number"_force_MT_"trial number (1-4)" E.g.: 07_force_MT_1
35. Continue this procedure until 80 trials (4 segments of 20) are completed
36. Take a screenshot of impedances, save under the corresponding subject folder as: "subject-number_imp_post_pre.png"
37. Perform the resting EEG recordings again using the same procedure (and same order) as mentioned above
    - Remove transducer
    - For the eyes open, shut off screens, turn main screen and have the subject focus at the ”T”
    - When ready press record, set recording time to 3 minutes and select folder with the subject number and name it accordingly: "subject number (with 0, if below 10)"_pre/-post_rest_open/closed. E.g.: 05_pre_rest_open

38. Perform the EMG-EEG coherence using the same procedure as mentioned above
39. Take a screenshot of impedances, save under the corresponding subject folder as: "subject-number_imp_post_post.png"
40. Perform 3 MVC recordings in "Follow Me", by choosing MVC from the drop down menu
41. Thank the subject
42. Stop stopwatch - note down time