Fachbereich Erziehungswissenschaft und Psychologie
der Freien Universität Berlin

Neural correlates of covert and overt movements investigated by EEG/EMG with implications for brain-computer interfacing

Dissertation
zur Erlangung des akademischen Grades
Doktor der Philosophie (Dr. phil.) /
Doctor of Philosophy (Ph.D.)

Vorgelegt von Diplom-Psychologin
Friederike U. Hohlefeld[1,2,3]

Disputation an der Freien Universität Berlin: 17.12.2010

Erstgutachter:
Prof. Dr. Arthur M. Jacobs, Freie Universität, Berlin

Zweitgutachter:
Prof. Dr. Gabriel Curio, Charité – Universitätsmedizin Berlin

Direkter Supervisor:
Dr. Vadim V. Nikulin, Charité – Universitätsmedizin Berlin

Kontakt:

[1] Neurophysics Group, Department of Neurology
Charité – University Medicine Berlin
Hindenburgdamm 30, 12203 Berlin, Germany
[2] Neurocognitive Psychology Group, Department of Psychology
Free University Berlin, Germany
[3] Berlin School of Mind and Brain, Berlin, Germany

TABLE OF CONTENTS (short)

I. INTRODUCTION

II. STUDY 1 – Visual stimuli evoke rapid activation (120 ms) of sensorimotor cortex for overt but not for covert movements.

III. STUDY 2 – Detection of weak EMG motor responses in covert movements – comparing automatic procedures and visual inspection.

IV. STUDY 3 – Covert movements trigger repetition suppression in sensorimotor cortex as indicated by EEG dynamics.

V. GENERAL DISCUSSION

TABLE OF CONTENTS (detailed)

I. INTRODUCTION

II. STUDY 1 – Visual stimuli evoke rapid activation (120 ms) of sensorimotor cortex for overt but not for covert movements.

III. STUDY 2 – Detection of weak EMG motor responses in covert movements – comparing automatic procedures and visual inspection.

IV. STUDY 3 – Covert movements are associated with repetition suppression in sensorimotor cortex as indicated by EEG dynamics.

V. GENERAL DISCUSSION

i. Keywords

Alpha, abductor pollicis brevis (APB), beta, brain-computer interface (BCI), electroencephalography (EEG), electromyography (EMG), inhibition, intention, motor imagery, movement, quasi-movements.

ii. Abbreviations

ACC	accelerometer
APB	abductor pollicis brevis muscle
BCI	brain-computer interface
EEG	electroencephalography
EMG	electromyography
EPB	extensor pollicis brevis
fMRI	functional magnetic resonance imaging
FPB	flexor pollicis brevis
FPL	flexor pollicis longus
LRP	lateralized readiness potential
LRPrect	lateralized readiness potential from rectified signals
M1	primary motor cortex
MEG	magnetoencephalography
MVC	maximum voluntary contraction
RMS	root mean square
RP	readiness potential (“Bereitschaftspotential”)
RS	repetition suppression

iii. List of figures

iv. List of tables

v. Abstract

The present thesis investigates neural correlates of covert movements (i.e., motor imagery and quasi-movements) and overt movement execution in the human brain with electroencephalography (EEG), electromyography (EMG), and neurofeedback. Wittgenstein (1953) asked: “When I raise my arm, what is left over if I subtract the fact that my arm goes up?”

One answer could be, generally speaking, “motor cognition”: e.g., intending an action, preparing the movement, or merely imagining it – parts of our daily routine. Importantly, these processes are so-called “covert” movements when there is no externally observable muscle activity. However, even in covert motor processes there are distinct correlates of neural activity in sensorimotor networks in the brain. Investigating neural correlates of overt and covert movements is crucial, not only because movements enable daily communication and mobility but also in order to (partially) restore these abilities in “locked-in” patients, where the conscious mind is locked in a paralyzed body (e.g., due to amyotrophic lateral sclerosis or comatose states after traumatic head injury).

For this purpose neurofeedback-based methods can be utilized, such as brain-computer interface (BCI): The subject receives real-time feedback of the own neural brain activity which allows a statistical association of particular neural and cognitive states. This association is a prerequisite for learning to modulate the own brain activity which enables the control of external devices such as spelling programs or wheelchairs, without the need of muscular activity. For instance, the subject imagines left or right hand movements, computer algorithms classify the intention-related brain states and convert the neural signal into cursor movements on the screen.

In sum, the general framework for my thesis is the investigation of motor cognition from a neurophysiological perspective which has implications for optimizing BCI settings from the neuropsychological perspective (e.g., effective cognitive strategies for BCI). This is especially important for cases of BCI “illiteracy” where brain state discrimination is poor despite sophisticated technologies. One possible reason might be that there is no sufficiently strong neural signal to detect due to a suboptimal cognitive strategy of the given subject (e.g., poor imagination ability).

My thesis features neural correlates in the cortical sensorimotor system of overt movement execution and different types of covert movements, which per definition do not involve overt muscle contraction but only central processing in the brain. Two types of covert movements are investigated, motor imagery and the novel motor-cognitive skill of “quasi-movements” (introduced by Nikulin et al., 2008). The target movement in all present studies in the overt and covert conditions is the unilateral left and right thumb movement (abductor pollicis brevis muscle).

Quasi-movements are defined as volitional movements which are minimized in strength to such an extent that finally they become undetectable by external measures of muscle activity such as EMG. This state is achieved by training with EMG neurofeedback.

In contrast, *motor imagery* requires the mental simulation of “how a movement feels like” (i.e., proprioceptive simulation) without externally detectable muscle activity. Interestingly, while from the external viewpoint both skills are similar, they strongly differ on cognitive levels (quasi-movements: subjects report to intend “real” movements” – motor imagery: the subjects never intend to perform a movement but only its mental simulation) and on neural levels (stronger activation of sensorimotor networks in the brain by quasi-movement performance). Given the frequent findings of overlapping activation of sensorimotor neural substrates during the performance of overt or “covert” movements (i.e., not involving muscle contraction), this raises the question to what extent there are crucial differences between both motor modes. This aspect constitutes another main interest of my thesis, namely the short- and long-term neural dynamics of different action intentions, as well as the adaptability of neural networks to repeated cognitive-motor tasks (phenomenon of “repetition suppression”, see below), since communication via BCI involves many trial repetitions.

The present thesis comprises three studies, with the following key findings:

Study 1. Based on previous empirical findings it is assumed that overt and covert movements (e.g., motor imagery) engage similar or even the same neural substrates – in fact, neural activity in covert movement is often considered as a merely scaled-down copy of an overt movement. However, our study challenges this assumption: We investigate very early stages of stimulus processing in the sensorimotor cortices by utilizing high-temporal resolution EEG. Visual stimuli indicated left or right thumb movements (abductor pollicis brevis muscle; APB) in the overt and covert (motor imagery vs. quasi-movements) performance mode. We introduce the novel method of calculating stimulus-locked lateralized readiness potentials from *rectified* EEG signals (LRPrect), a method which overcomes problems associated with EEG signal variability due to polarity differences in the spatial distribution of neuronal sources. The LRPrect showed an activation already at 120 ms after stimulus onset (latN120) focally over sensorimotor cortices contralateral to the upcoming hand movement, yet only for overt but not covert movements. Thus the *prior* action intention might differentially route early stimulus-processing in the sensorimotor system, possibly contributing to significantly different later behavioral outcomes, i.e., movement generation or inhibition.

Study 2. Per definition a covert movement should not involve muscle contraction and also a brain-computer interface (BCI) should enable a non-muscular communication channel. Therefore, EMG monitoring is an important prerequisite in neurophysiological studies of covert movements and BCI. In fact it has been frequently demonstrated that covert movements in healthy subjects do involve occasional muscle responses, being only a small fraction of the normal movement's strength. This raises the question of how to adequately detect such trials in order to exclude them, if necessary, from the data set. Automatic/statistical procedures for EMG detection are frequently applied since they are less laborious than visual inspection. However, in contrast to previous studies we compare the suitability of these different approaches (automatic, statistical, visual inspection) for the detection of very weak and transient motor responses in the case of covert movements (left or right thumb, APB: motor imagery and quasi-movements). In fact we demonstrate that in contrast to automatic/statistical methods the visual inspection accurately detected these few, residual motor responses present in APB-EMG. Accordingly, we might hypothesize that despite the disadvantages of being a laborious and more subjective procedure, our findings suggest visual EMG inspection as a preferable strategy for the detection of weak motor responses occasionally present in covert movements in EMG.

Study 3. "Repetition suppression" (RS) refers to the decrease of neural activity to repeated external sensory stimuli and represents a fundamental characteristic of neural response organization. However, in our study we address the question whether RS can also be present without external sensory stimulation during the performance of repeated cognitive tasks, such as motor imagery. By the term "internally-driven RS" we refer to this scenario. The present study investigates for the first time the possibility of internally-driven RS during the repeated performance of covert movements, such as motor imagery and quasi-movements (left or right thumb movements, APB). Covert movements are associated with central brain activity but usually with none or negligible reafferent sensory feedback since the limb should remain at rest. Our results demonstrate that when subjects perform repetitive covert movements for trials of 1 min, there is significant recovery of EEG oscillations over sensorimotor cortices from initial suppression (often termed event-related desynchronization; ERD) back to resting baseline level.

After 58 sec only 20 % of the initial alpha ERD remains and 5 % of the initial beta ERD remains (overt movements: 34 % alpha, complete recovery in beta). There was no significant correlation between EMG and EEG dynamics. These results tentatively suggest that movement-related RS (here related to thumb movements) could be primarily internally-driven. One can speculate that this could also be the case also for other muscles and movement types.

Another important finding is a longer sustained neural activation for quasi-movements than for motor imagery (> 10 sec), suggesting quasi-movements as an effective strategy for long-term operation of a brain-computer interface (cf. also Nikulin et al., 2008), which requires the repeated performance of covert movements for many trials. Furthermore, the present results have implications for long-term neural correlates of action intentions and motor control.

In conclusion, the results of the present thesis showed that the study of neural correlates of action intention and the performance of overt and covert movements benefits from the investigation of neural and cognitive dynamics on different time scales (from milliseconds to minutes). This approach might contribute to a better understanding of the intricate relationship between the descriptive levels of neural and cognitive dynamics in the domain of movement control and motor cognition. Such knowledge might in the long-term also be helpful for the investigation of movement disorders and associated cognitive impairments (e.g., Parkinson), and for improving the discrimination of intention-related brain activity for patients in locked-in states, in order to restore communication and mobility via BCI technologies.

vi. Zusammenfassung (German abstract)

Die vorliegende Dissertation untersucht neuronale Korrelate von offener Bewegungsausführung und verdeckten Bewegungen (motorische Imagination, Quasi-Bewegungen) im menschlichen Gehirn mit Hilfe der Elektroenzephalographie (EEG), Elektromyographie (EMG) und Neurofeedback.

Wittgenstein (1953) stellte die Frage: „Was ist das, was übrig bleibt, wenn ich von der Tatsache, dass ich meinen Arm hebe, die abziehe, dass mein Arm sich hebt?“

Eine mögliche Antwort wäre, generell gesprochen, „motorische Kognition“: z. B. die Intention einer Handlung, motorische Vorbereitung einer Bewegung oder die mentale Vorstellung einer Bewegung – alles Teile unserer täglichen Routine.

Bei diesen genannten Beispielen sind tatsächliche Muskelkontraktionen zumeist nicht involviert. Daher wird auch von „verdeckten“ Bewegungen gesprochen, die nichtsdestotrotz begleitet werden von spezifischer neuronaler Aktivität in sensomotorischen Netzwerken. Die Untersuchung der neuronalen Realisierung von offenen und verdeckten Bewegungen ist insofern von fundamentaler Bedeutung, weil die tägliche Mobilität und Kommunikation erst durch Handlungsvorbereitung und motorische Bewegungen (z. B. des Sprechapparates) ermöglicht werden. Darüber hinaus können diese Fähigkeiten beeinträchtigt sein oder komplett fehlen, beispielsweise in so genannten „locked-in“ Patienten, bei denen der bewusste Geist eingeschlossen ist in einen vollständig gelähmten Körper (etwa durch Amyotrophische Lateralsklerose oder komatöse Zustände nach Schädel-Hirn-Trauma). In diesen Fällen kann die Erforschung neuronaler Korrelate motorischer Kognition (z. B. Handlungsintention), dazu beitragen, die Kommunikationsfähigkeit und Mobilität für solche Patienten (partiell) wiederherzustellen.

Eine Möglichkeit hierfür stellen Neurofeedback-basierte Verfahren dar, z. B. das Brain-Computer Interface (BCI): Der Proband erhält dabei ein Echtzeit-Feedback der eigenen neuronalen Aktivität im Gehirn. Dies ermöglicht es, verschiedene kognitive und neuronale Zustände statistisch miteinander zu verknüpfen und die neuronale Aktivität zielgerichtet zu modulieren, wodurch externe Anwendungen *ohne Muskelaktivität* kontrolliert werden können, z. B. Textverarbeitungsprogramme oder Rollstühle. Hierfür kann der Proband sich etwa linke oder rechte Handbewegungen vorstellen, wobei die mit dieser Handlungsintention korrelierte neuronale Aktivität von

Computeralgorithmen klassifiziert und beispielsweise in rechts-/linksgerichtete Cursorbewegungen auf dem Bildschirm konvertiert wird.
Zusammenfassend ist der allgemeine Rahmen der vorliegenden Dissertation die Untersuchung der motorischen Kognition aus einer neuropsychologischen Perspektive, vor allem in Hinblick auf die Optimierung von BCI: trotz sehr effektiver Algorithmen, basierend auf maschinellem Lernen, gibt es einen nicht unbeträchtlichen Anteil an Probanden, bei denen die Klassifizierung intentionskorrelierter neuronaler Aktivität nicht gut oder gar nicht funktioniert (auch „BCI illiteracy“ genannt, also das System kann die Intentionen des Nutzers nicht „lesen“). Dies kann beispielsweise der Fall sein, wenn kein ausreichend diskriminierbares neuronales Signal vorliegt, weil für einen Probanden eine bestimmte mentale Strategie nicht funktioniert (z. B. schlechtes Vorstellungsvermögen).

Die vorliegende Arbeit behandelt neuronale Korrelate der „offenen“ Bewegungsausführung (overt movements) und der so genannten „verdeckten“ Bewegungen (covert movements) ohne messbare Muskelaktivität, in unserem Fall die motorische Imagination und der neue motorisch-kognitive Prozess namens „Quasi-Bewegungen“ (eingeführt durch Nikulin et al., 2008). Die Zielbewegung in allen Studien ist die rechte und linke Daumenbewegung (musculus abductor pollicis brevis, APB).
Quasi-Bewegungen sind definiert als willkürliche Bewegungen, die in ihrer Stärke soweit minimiert werden, sodass sie letztendlich mit externen Messapparaturen der Muskelaktivität (z. B. EMG) nicht mehr registrierbar sind. Dieser Zustand wird durch ein Training mit EMG-Neurofeedback erreicht.
Im Gegensatz dazu impliziert die *motorische Imagination* eine mentale Simulation davon „wie sich eine Bewegung anfühlt“ (genau genommen: propriozeptive Simulation), ebenfalls ohne messbare Muskelaktivität. Obwohl bezüglich der Muskelaktivität beide „verdeckten Bewegungen“ als gleich erscheinen, unterscheiden sie sich auf kognitiver Ebene (Quasi-Bewegungen: Probanden berichten, dass sie eine „reale“ Bewegung intendieren vs. motorische Imagination: Probanden berichten, dass sie die Bewegung nur „im Kopf“ simulieren, ohne eine tatsächliche Bewegung ausführen zu wollen) und auf neuronaler Ebene (stärkere Aktivierung sensomotorischer neuronaler Netzwerke bei Quasi-Bewegungen).

In Übereinstimmung mit theoretischen Standpunkten, die verdeckte Bewegungen als sehr ähnlich zu offenen Bewegungen darstellen (abgesehen davon, dass die „finale“ Phase der Muskelkontraktion fehlt) haben viele Studien stark überlappende Aktivierungen in sensomotorischen Netzwerken gefunden. Diese robusten Ergebnisse werfen die Frage auf, inwiefern Unterschiede zwischen offenen und verdeckten Bewegungsformen bestehen. Diese Frage stellt ebenfalls ein zentrales Interesse der vorliegenden Dissertation dar: die kurz- und langfristigen neuronalen Dynamiken bei verschiedenen Handlungsintentionen sowie die Adaptation neuronaler Netzwerke (neuronale Plastizität) bei wiederholten kognitiv-motorischen Aufgaben (Stichwort „repetition suppression“, siehe unten), zumal die Kommunikation via BCI viele Wiederholungen von Trials erfordert.

Die Arbeit umfasst drei Studien mit den folgenden Hauptbefunden:
Studie 1. Es besteht generelle Übereinstimmung, dass offene und verdeckte Bewegungen assoziiert sind mit der Aktivierung sich stark ähnelnder oder gar gleicher neuronaler Substrate im Gehirn. In der Tat werden verdeckte Bewegungen, im Sinne der neuronalen Aktivierungsstärke, oftmals schlicht wie eine „verkleinerte“ Kopie einer offenen Bewegung behandelt. Unsere Studie hinterfragt diese Annahme: Wir untersuchen sehr frühe Stadien der Informationsverarbeitung (folgend einem Stimulus welcher rechte/linke Handbewegung indiziert) in den sensomotorischen Kortizes mit Hilfe der hohen zeitlichen Auflösung des EEGs. Visuelle Stimuli indizierten dabei linke oder rechte Daumenbewegungen (Abductor Pollicis Brevis Muskel; APB) für offene oder verdeckte Bewegungen (motorische Imagination, Quasi-Bewegungen).
Wir führen eine neue Methode für die Berechnung des stimulus-abhängigen Lateralisierten Bereitschaftspotentials (LRP – lateralized readiness potential) aus den *Absolutwerten* der EEG-Signale (LRPrect – LRP from rectified values) ein. Diese Methode hat den Vorteil, Problematiken der hohen Variabilität von EEG-Signalen, z. B. herrührend von Polaritätsunterschieden aufgrund der räumlichen Verteilung der neuronalen Quellen, zu überwinden. Das LRPrect zeigt bereits 120 ms nach dem Stimulus eine signifikante Aktivierung (latN120) fokal über den sensomotorischen Kortizes kontralateral zur aktiven Hand, allerdings nur für offene Bewegungen und nicht für die verdeckten. Dieses Ergebnis impliziert dass bereits die *vorausgehende* Handlungsintention (offen vs. verdeckt) in den frühen Stadien der

Informationsverarbeitung in neuronalen Netzwerken signifikante Unterschiede bewirkt. Dieses „priming“ könnte wesentlich dazu beitragen, dass eine spätere Bewegung zugelassen/ausgeführt oder gehemmt wird.

Studie 2. Eine Bewegung wird als „verdeckt“ (covert movement) definiert, wenn keine Muskelkontraktionen vorhanden bzw. messbar sind (z. B. motorische Imagination und Quasi-Bewegungen). Die Abwesenheit von Muskelaktivität ist ebenfalls theoretische Voraussetzung für ein BCI, welches nur aufgrund der Gehirnaktivität kontrolliert werden sollte. Daher ist die EMG-Überwachung eine wichtige Voraussetzung neurophysiologischer Studien von verdeckten Bewegungen und BCI. Mehrere Studien haben bereits gezeigt, dass entgegen der Definition verdeckte Bewegungen von gelegentlichen Muskelkontraktionen begleitet werden können, deren Stärke jedoch nur einen Bruchteil der normalen Bewegungsstärke beträgt. Diese Tatsache bedingt die Frage nach einer adäquaten Überwachung und Entdeckung solcher Minimalkontraktionen im Datensatz, um die betroffenen Datenabschnitte, falls gewünscht, vom Datensatz entfernen zu können. Für diese Zwecke werden zunehmend automatische/statistische Prozeduren verwendet wegen des geringeren Arbeits-/Zeitaufwandes als bei der visuellen (sprich manuellen) Inspektion der Datensätze. Im Unterschied zu früheren Studien vergleichen wir die Eignung verschiedener Verfahren, also automatischer, statistischer und visueller Verfahren, für die Entdeckung von sehr schwachen, flüchtigen Muskelkontraktionen vorkommend bei verdeckten Bewegungen (linker oder rechter Daumen, APB; Versuchsbedingungen motorische Imagination und Quasi-Bewegungen). Unsere Ergebnisse zeigen dass im Gegensatz zu automatischen und statistischen Methoden die visuelle Inspektion von APB-EMG Durchgängen mit diesen schwachen Muskelkontraktionen adäquat identifizieren konnte. Demzufolge können wir annehmen, dass visuell-manuelle Verfahren, trotz des höheren Arbeits-/Zeitaufwandes, besser geeignet sind für die Entdeckung von gelegentlichen, schwachen Muskelkontraktion bei verdeckten Bewegungen im EMG.

Studie 3. Das Phänomen “repetition suppression” (RS; wörtlich „Wiederholungsunterdrückung“) kennzeichnet die Abnahme neuronaler Aktivität bei wiederholter externer sensorischer Stimulation. Unsere Studie befasst sich mit der Frage, ob RS ebenfalls präsent ist, wenn keine externe Stimulation vorliegt während

der wiederholten Ausführung von kognitiven Aufgaben, z. B. mentaler Imagination von Bewegungen. Diese motorische Imagination, ebenso wie die sogenannten Quasi-Bewegungen, zählen zu den verdeckten Bewegungen, die von spezifischer neuronaler Aktivierung in Gehirn begleitet werden, jedoch mit keinem oder vernachlässigbarem externen sensorischen Feedback, weil der entsprechende Körperteil typischerweise ruht.

Die Probanden führten wiederholte offene oder verdeckte Daumenbewegungen aus (APB; motorische Imagination, Quasi-Bewegungen) für Durchgänge von 1 Minute Länge. Die zentrale Aktivierung sensomotorischer Netzwerke bei verdeckten Bewegungen ohne signifikante Muskelreaktionen ließ bei zunehmender Performanz-Dauer nach: nach initialer Blockade der alpha- und beta-Oszillationen (ereigniskorrelierte Desynchronisation; EKD) relaxierte die EKD zurück zum Baseline-Level. Nach 58 sec Performanz waren nur noch 20 % der initialen EKD im alpha-Band vorhanden und 5 % im beta-Band (zum Vergleich: für offene Bewegungen 34 % in alpha, vollständige Relaxation in beta). Die Korrelation zwischen EMG und EEG Dynamiken war nicht signifikant. Diese Ergebnisse könnten bedeuten, dass bewegungsassoziiertes RS allein durch *interne* wiederholte Stimulation hervorgerufen wird, ohne die Notwendigkeit von repetitiven externen sensorischen/propriozeptiven Inputs.

Ein weiteres wichtiges Ergebnis der vorliegenden Studie ist das Vorhandensein einer um mehr als 10 sec *längeren* Aktivierung sensomotorischer Netzwerke bei Quasi-Bewegungen im Vergleich zu motorischer Imagination. Dieses Ergebnis legt nahe, dass Quasi-Bewegungen eine vorteilhaftere Strategie für BCI sein könnten (siehe auch Nikulin et al., 2008), da beispielsweise für das Schreiben eines Briefes mit Hilfe eines BCI-kontrollierten Programms eine Vielzahl von wiederholten Durchgängen ausgeführt werden müssen. Darüber hinaus sind die Ergebnisse von Bedeutung für Studien der langzeitlichen neuronalen Realisation von Handlungsintentionen und exekutiver motorischer Kontrolle.

Die vorliegende Dissertationsarbeit macht deutlich, dass die Untersuchung neuronaler Korrelate von offenen und verdeckten Bewegungen von der Analyse der neuronalen und kognitiven Dynamiken auf verschiedenen zeitlichen Skalen profitiert (von Millisekunden bis hin zu Minuten). Dieser Ansatz könnte zu einem besseren Verständnis des Zusammenhangs zwischen beiden Beschreibungsebenen führen, der neuronalen und der kognitiven, sowohl im Bereich der Motorik als auch der motorischen Kognition. Dies könnte langfristig dazu beitragen, motorische Krankheiten und damit einhergehende kognitive Störungen (z. B. bei Parkinson) besser zu verstehen, und darüber hinaus die neuronalen Signaturen von Handlungsintentionen im Gehirn bei komplett gelähmten Patienten besser entschlüsseln zu können und somit die Kommunikation via eines Brain-Computer Interfaces zu optimieren.

Chapter 1

I. INTRODUCTION

1.1 General Introduction

"My goal is simple. It is a complete understanding of the universe,
why it is as it is and why it exists at all."
(Stephen W. Hawking, 1985)

"There are as many neurons in the brain as there are stars in the Milky Way galaxy."
(David Eagleman, 2007)

Approx. 100 billion nerve cells of the human brain are organized in a volume of approx. 1,500 cm^3 in amazing complexity, implying the fundamental impossibility of a *complete* understanding of brain functioning. While brain volume is constant since some 160,000 years (White et al., 2003), the complexity of human cognition and behavior rapidly increased until modern days, indicating that the brain's organization is the decisive factor rather than its volume. Already ancient anatomy allowed crucial insights into the brain's architecture; however, little was known about the functionality of the *living* brain. It took until the 1920s when Hans Berger measured the electrical activity of the human brain for the first time by electroencephalography (EEG; Berger, 1929). Since then different methods have been developed for non-invasively studying the living brain in action, allowing the spatial resolution up to a few millimeters by modern functional Magnetic Resonance Imaging (fMRI; Friston, 2009; Huettel et al., 2008), which strongly increased the knowledge about brain anatomy and neurophysiological functioning.

Furthermore, numerous studies have shown the intricate link between neural brain activity, cognition and behavior. Yet there are several cases when the link between brain/cognition and behavior is impaired/destroyed, for instance, in patients suffering from spinal cord lesions or brain stem stroke, or Amyotrophic Lateral Sclerosis (ALS) as in the case of the physicist Stephen Hawking. ALS is a progressive neurodegenerative disease, which affects the motor nervous system and leads to severe physical disabilities. In the final stage the patients have lost control over all muscles, resulting in complete paralysis: The conscious patients are locked in their body without being able to move or communicate any longer (Laureys et al., 2005). Critically, communication has been shown to be one of the most important factors for increasing the quality of life for ALS patients (Kübler et al., 2001; Lulé et al., 2009). Another important category of the so-called "locked-in states" are patients after severe head trauma, which seem to be in coma but actually are conscious and locked in their non-responsive body (disorders of consciousness: Kübler & Kotchoubey, 2007; Owen et al., 2006; Owen et al., 2009).

1.1.1 Investigating a mind-brain relationship by neurofeedback methods

In order to overcome the broken link between cognition and behavior in the case of neuromotor diseases, neuroscience has developed an effective method, the brain-computer interface (BCI), which can restore communication and mobility even in severe cases of completely locked-in patients. Via BCI the subject can control computer programs or external devices (e.g., wheelchairs) on the basis of brain activity alone, without muscular activity. The BCI detects neural correlates of the subject's action intention (e.g., "move left", "move right") and converts this neural signal into a technical control signal (e.g., cursor movement, moving the wheelchair, typing "yes" or "no") while the subject does not need to move any body limb. The essential feature of BCI is neurofeedback: The subject receives online feedback of its own intention-related neural brain activity and in turn learns to increase the control over the neural activity (Dornhege et al., 2007; Wolpaw et al., 2002). By the BCI method, i.e., "translate 'thought into action' by brain activity only" (Birbaumer, 2006, p. 529), completely locked-in patients can write letters or navigate in the internet (Birbaumer et al., 1999; Dornhege et al., 2007).

BCI technology is also beneficial for healthy subjects. Although here is no need for improving rehabilitation or communication, BCI could be utilized to monitor attention/alertness or cognitive workload in daily situations, for instance, car driving, aviation or security surveillance. If the system detects a mental overload, it might warn the user or automatically reduce the workload (Müller et al., 2008).

Furthermore, the scientific study of neurofeedback and BCI might be crucial for an understanding of a mind-brain relationship. Usually the relation between mental and neural states is not consciously accessible, as well expressed in Prinz' question: "Why don't we perceive our brain states?" (Prinz, 1992, p. 1). Yet neurofeedback enables subjects to perceive their own brain states (Kotchoubey et al., 2002), i.e., neural activity converted into a control signal, for instance cursor movement, and directly relating them to cognitive states, e.g., increased attention, intention to move left or right. It becomes clear that the relation between neurofeedback and cognition is two-way: Cognitive states modify neurofeedback and neurofeedback modifies cognitive states. Importantly, the “visualization” of a mind-brain relationship by neurofeedback also allows the understanding of cognitive states in a different way compared to mere introspection: For instance, when driving a car over a long distance, the subject can introspectively describe “My attention is low since I am tired”. Yet the subject is usually not aware of the fine-graded decrease of attention to a crucial level and will become conscious of it only *after* the attentional lapse (i.e., microsleep) has occurred. In contrast, a neurofeedback system monitoring attention-related brain signatures in real-time could predict attentional lapses in advance (O’Connell et al., 2009), which in turn could possibly also increase the introspective assessment of attentional (and other) cognitive states by the subject.

1.1.2 General outline of the thesis

Summarizing, modern neuroscience allows the non-invasive monitoring of brain activity and can make neural activity subject to conscious perception and voluntary control by neurofeedback/BCI methods. These methods can be utilized for a basic neurophysiological understanding of a mind-brain relationship, and furthermore can restore communication and mobility in patients suffering from neuromotor impairments. Given this framework, the main interest of the present thesis is the optimization of cognitive and neural states for effective neurofeedback-based BCI. A general outline of the main topics of my thesis is given in Figure 1.1.

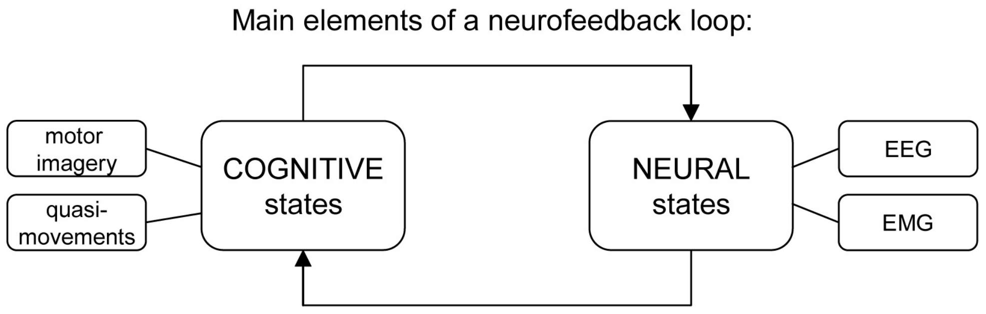


Figure 1.1. Outline of main Ph.D. framework.

Chapter 1 of my thesis gives an introduction to

a) neurofeedback and BCI in general (Chapter 1.1),
b) how “neural states” are measured in the present thesis (Chapter 1.2), i.e., with electroencephalography (EEG) and electromyography (EMG), and
c) “cognitive states”, i.e., related to the performance of motor imagery and quasi-movements (Chapter 1.3).

My thesis comprises three experimental studies (Chapters 2–4), whose aims are introduced in Chapter 1.4. The studies have been published in or have been submitted to international journals, so that Chapters 2–4 can be read as stand-alones; as a consequence some redundancy is unavoidable. The results of the studies are discussed in each chapter and are generally discussed in Chapter 5.

1.2 Introduction to neurofeedback and brain-computer interfacing

1.2.1 What is neurofeedback?

If you have never played tennis before and now you serve for the first time, probably the ball will not cross the net or will land outside of the opposite service box. However, when you try more often your performance will improve by learning. Learning depends on the interaction of the subject with the environment, i.e., receiving feedback of the own action (e.g., visual) and minimizing the error between the own intention/prediction (the ball should cross the net) and the actual outcome (the ball landed outside of the box). If you were sitting in front of a computer screen with EEG electrodes attached to your head and received real-time visual feedback of your own brain activity, you could learn how to voluntarily modulate the neural responses, much like learning how to serve in tennis. These examples make clear that feedback is essential for learning (cf. operant and classical conditioning) and that, given the appropriate setting, even the control of formerly “unconscious” processes such as brain activity can be learned to a certain extent.

“Biofeedback is a behavioral method of achieving or enhancing voluntary control of physiological processes“ (Shapiro, 1979, p. 24). More often the term neurofeedback is used when referring to the voluntary control of brain activity as measured by EEG. Research in human EEG neurofeedback dates back to pioneering work of the late 1960s (review in Budzynski, 1999; cf. also Kamiya, 1968; Rockstroh et al., 1984) and is very active until today, especially for medical purposes: frequent studies demonstrated the beneficial effects of EEG neurofeedback training, e.g., for epilepsy (Kotchoubey et al., 1996; Lubar, 1998) or attention deficit hyperactivity disorder (Gruzelier et al., 2006; Leins et al., 2007).

1.2.2 Brain-computer interfacing: Neurofeedback for communication and action

Vidal (1973) introduced the term “brain-computer interface” which basically establishes a “man-machine communication… [and] would indeed elevate the computer to a genuine prosthetic extension of the brain” (Vidal, 1973, p. 158). In his pioneering works Vidal discussed the feasibility of discriminating brain signatures in EEG and utilizing them for communication and control (Vidal, 1973, 1977; see also Dewan, 1967). This notion introduced a new perspective in neurofeedback research: The neurofeedback method is suitable for establishing a non-muscular channel for communication and action: If the derived neural signal (e.g., modulation of EEG alpha rhythms; cf. Chapter 1.3.1) is converted into a technical output signal by the help of a computer, the subject can control external devices by brain activity alone (Dornhege et al., 2007; Elbert et al., 1980; Farwell & Donchin, 1988; Wolpaw, 1991; Wolpaw et al., 2002).

In other words, a BCI translates the user’s intention directly into action, thus bypassing normal motor output channels (Birbaumer, 2006). This feature makes BCI a preferred tool for patients with neuromotor disorders, e.g., brain stem lesions, spinal cord injury or ALS, being able to control text spelling programs, prostheses or wheelchairs by means of a BCI (Kübler et al., 2001; Neuper, Müller-Putz et al., 2006). In healthy subjects BCI is developed for monitoring attention/workload, for instance, in car driving or piloting (Müller et al., 2008; cf. also Chapter 1.1).

Importantly, BCI research consists of two approaches: non-invasive approaches (e.g., EEG, fMRI, magnetencephalography, optical imaging; suitable for patients and healthy subjects) and invasive approaches (cortical or intracortical electrode implants for measuring even on the single neuron level; only in patients or animals; cf. Donoghue, 2002; Hochberg et al., 2006; Leuthardt et al., 2009; Nicolelis, 2001). The present thesis focuses on non-invasive EEG in healthy subjects, yet the studies’ implications are also transferable to invasive BCI settings.

BCI research benefits from powerful machine learning techniques which has reduced the training time for the subject from months to minutes (Dornhege et al., 2007;

Kübler et al., 2001; Blankertz et al., 2007; Vidaurre & Blankertz, 2010) as reflected in the motto “let the machines learn” of the Berlin Brain-Computer Interface (BBCI; Müller et al., 2008, p. 83). Recent studies demonstrated the remarkable speed of BCI-based communication, for instance, spelling 6–8 letters per minute (Müller et al., 2008) or achieving information transfer rates even up to ~ 37 bits per minute and very low error rates (Blankertz et al., 2007). State-of-the-art BCI utilizes sophisticated data recording techniques (e.g., high-density EEG, fMRI), established methods of artifact rejection, and advanced methods of neural signal detection and brain state classification. However, the main challenges of BCI research are of non-technical nature: for instance, the high intra-subject variability of neural signals or the choice of an appropriate mental strategy in order to achieve sufficient control over the brain activity, as discussed below.

Main components of a BCI: A BCI system consists of three main components:
a) USER
- generating and modulating the neurophysiological signal, e.g. measured by EEG (event-related potentials such as P300 or modulation of oscillatory alpha or beta rhythms: Chapter 1.2.3)
- usage of an effective cognitive strategy (e.g., motor imagery, quasi-movements: Chapter 1.3)

b) INTERFACE (cf. Blankertz et al., 2007; Wolpaw et al., 2002)
- signal preprocessing (spatial and temporal filtering, artifact rejection)
- feature extraction (e.g., independent component or common spatial pattern analysis)
- feature classification (e.g., linear discriminant analysis)
- establishing feature feedback (e.g., cursor movement) and online adjustment of feature classification (e.g., compensating for signal drifts according to increased subject’s tiredness)

c) APPLICATION (cf. review of Wolpaw et al., 2002)
- cursor movement, text spelling programs
- prosthesis, wheelchair, navigating in a virtual environment
- games (e.g., “Brain Pong”)

This main setup of a BCI system is also depicted in Figure 1.2. Notably, the results of the present thesis are of interest for all three components, as will be generally discussed in Chapter 5 and in the respective study sections.

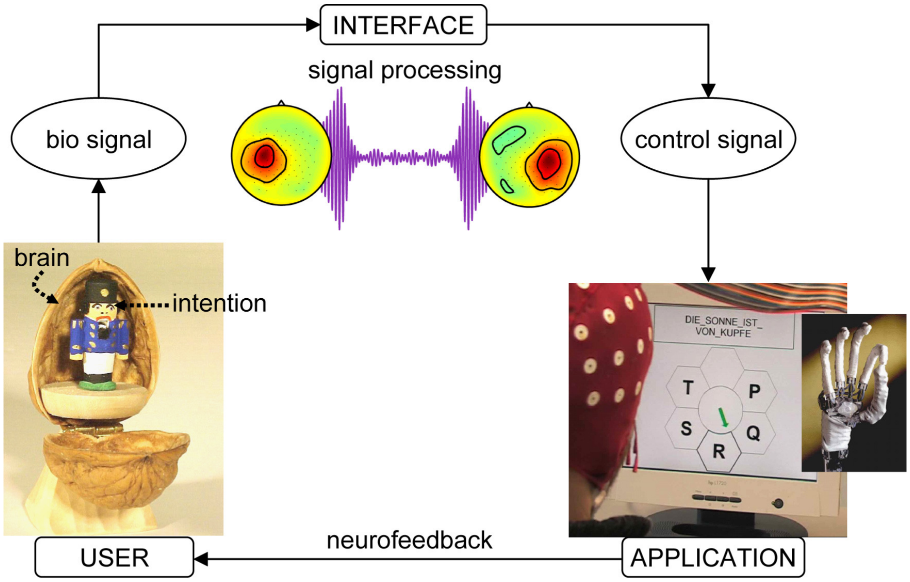


Figure 1.2. Main elements of a brain-computer interface (BCI).

1.2.3 Methods of BCI: Brief introduction to electroencephalography (EEG)

The EEG measures the electric neural activity of the brain, i.e., the voltage difference between two electrodes (or more pairs) on the scalp. The recorded voltage fluctuations usually are only tens of microvolts (µV) in amplitude and are assumed to be generated by the excitatory postsynaptic potentials of the apical dendrites of pyramidal neurons in the cerebral cortex (layers I–II). Importantly, a measurable EEG potential reflects the summated, synchronous activity of thousands of neurons (“dipoles”), which are in parallel orientation and radial to the scalp surface (Bear et al., 2007). Moreover, the macroscopic EEG reflects the superposition of many microscopic source populations across the cortex (volume conduction), also referred to as “neural cocktail party” phenomenon (Brown et al., 2001). The raw EEG recording contains a mixture of different frequencies, typically categorized as follows: delta rhythms (< 4 Hz), theta (4–7 Hz), alpha (8–13 Hz), beta (> 13 Hz), gamma (30–60 Hz), and higher frequencies. In general, the amplitude of oscillatory EEG is proportional to the number of synchronously active neurons, and the amplitude decreases with increasing frequency, i.e., smaller population of synchronized neurons (Pfurtscheller & Lopes da Silva, 1999). The dominance and amplitude of a frequency band, as determined for instance by Fourier Transform or Wavelet Analysis (Graimann & Pfurtscheller, 2006), is modulated by stages of consciousness (asleep---awake---alert), sensation/perception, movement, and cognition/emotion (general review: Niedermeyer & Lopes da Silva, 2004).

In general, EEG dynamics can be distinguished in phase-locked and non-phase-locked activation (Jung et al., 2001), which are emphasized by one of the following main analysis routes:

Event-related potentials (ERP): ERP reflect voltage fluctuations which are both time-locked and phase-locked to the occurrence of an event. These voltage fluctuations usually are very small compared to the large non-phase locked oscillatory activation (e.g., alpha rhythms), and in order to increase the signal-to-noise ratio, many stimulation trials are collected and subsequently averaged while the non-phase locked activity (considered here as “noise”) averages out (Kalcher & Pfurtscheller, 1995).

The ERPs can be locked to

a) an externally presented stimulus (i.e., forward averaging). ERP components with a latency of < 100 ms with respect to stimulus onset are termed exogenous. The endogenous components (> 100 ms) are of interest for neurocognitive studies of information processing (e.g., N200 for selective attention and error monitoring; P300 for stimulus evaluation, context-updating and memory; N400 for semantic processing; Duncan et al., 2009; Polich, 2007). If the first stimulus is a warning signal for a subsequent response, the contingent negative variation is elicited, reflecting expectation and response preparation (Rohrbaugh et al., 1976).

b) the motor response (i.e., backward averaging), e.g., the Readiness Potentials building up 1–2 sec before movement onset is assumed to reflect motor preparation (Kornhuber & Deecke, 1965).

An important treatment for stimulus- or response-locked data is the investigation of hemispheric differences, i.e., calculating lateralized event-related (readiness) potentials by subtracting EEG amplitudes of the ipsilateral hemisphere (with respect to the responding hand) from the contralateral hemisphere, such that a non-zero difference curve reflects differential engagement of sensorimotor networks. Study 1 of the present thesis (Chapter 2) deals with stimulus-locked lateralized readiness potentials and introduces a novel calculation method in order to overcome the variability of EEG signals due to polarity differences in the spatial distribution of neural sources.

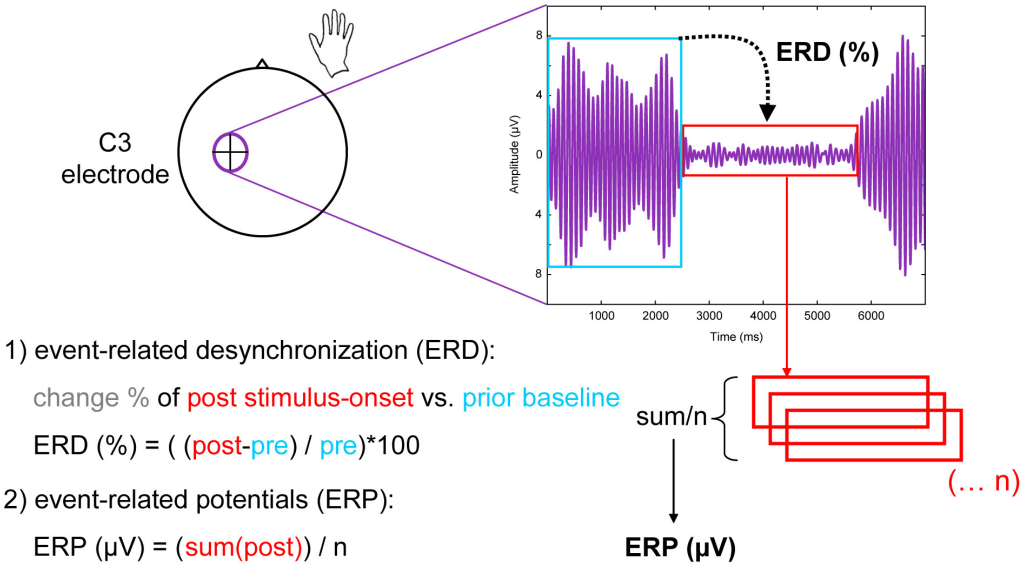
Oscillatory EEG – Event-related desynchronization (ERD): Oscillatory EEG dynamics reflect voltage fluctuations which are time-locked but not phase-locked to the occurrence of an event, e.g., alpha or beta oscillations. Several studies have demonstrated the amplitude decrease in oscillatory EEG (often referred to as induced "blocking" of rhythms) during sensory stimulation or movement preparation/execution or imagination (Adrian & Matthews, 1934; Berger, 1929; Gastaut et al., 1952; Jasper & Penfield, 1949; Nikouline, Linkenkaer-Hansen et al., 2000; Nikouline, Wikström et al., 2000; Pfurtscheller, 1981; Pfurtscheller & Lopes da Silva, 1999). The alpha/mu rhythms over sensorimotor cortices are also modulated by the mere imagination of a movement: during unilateral motor imagery the rhythms are blocked over the contralateral sensorimotor cortex (reviews: Lotze & Halsband, 2006; Neuper, Müller-Putz et al., 2006; Neuper, Wörtz et al., 2006).

This lateralization of intention-related brain signatures makes motor imagery an important strategy for BCI, since machine learning techniques can extract focal left- or right-hemispheric brain patterns and translate these signals into binary signals utilized for "left/right", "yes/no" or other in combination with text spelling programs into more complex outputs (Kübler et al., 2001; Müller et al., 2008; Wolpaw et al., 2002). Importantly, the main prerequisite of BCI is met with motor imagery, i.e., being based on brain activity alone and not on muscular output. Furthermore, motor imagery is applicable for healthy subjects and for patients (e.g., Neuper, Müller-Putz et al., 2006). Nevertheless BCI research is challenged by the fact that motor imagery strategies are not always effective in a considerable amount of subjects. The present thesis comprises a powerful alternative to the motor imagery paradigm dealing with the BCI "illiteracy" problem, as discussed below and in Chapter 1.3.

The modulation of oscillatory EEG is quantified as the percentage of amplitude/power increase or decrease with respect to a prior baseline: amplitude/power decrease (i.e., blocking of the rhythm) was termed "event-related desynchronization" (ERD), the amplitude/power increase (i.e., reappearance of rhythms) was termed "event-related synchronization" (ERS; Pfurtscheller & Aranibar, 1977; Pfurtscheller & Lopes da

Silva, 1999). Importantly, the terms ERD/ERS were criticized for implying a particular mechanism underlying the amplitude modulations, namely the desynchronization/synchronization of oscillatory neural activity. However, the disappearance/appearance of a macroscopic EEG rhythm might be due to different scenarios (e.g., activation/inactivation of neural population; cf. references in Erbil & Ungan, 2007). Therefore, alternative terms were suggested which do not assume a specific neural event underlying the changes in EEG rhythms, e.g., “movement-related modulation” and (Salmelin et al., 1995), “power change” (Gerloff et al., 1998), or “amplitude dynamics” (Erbil & Ungan, 2007). However, while being aware of the problem for simplicity the standard term ERD/ERS will be utilized throughout the text. The ERD measure is used in Study 3 of the present thesis (Chapter 4).

The calculation of both measures, ERP and ERD, are conceptualized in Figure 1.3. Importantly, there are ongoing debates about the appropriateness of each of these measures (review: Freeman & Holmes, 2005; Jacobs, 2006; Klimesch et al., 2007b; Makeig et al., 2004; Tallon-Baudry & Bertrand, 1999): Either oscillatory EEG might be considered as background noise and due to phase cancellation the oscillatory patterns average out, or ERP might be considered as noisy due to low signal-to-noise ratio (many trials are needed for the average). Furthermore, there are different models according to which ERP might be generated (e.g., Klimesch et al., 2007b; Nikulin et al., 2007; Sauseng et al., 2007; Sha et al., 2004). A detailed discussion of these issues is beyond the scope of the present introduction chapter. However, the rationale for using both measures in the present studies (ERP: Study 1; ERD: Study 3) is the large body of evidence that both measures ERP and ERD are highly sensitive to sensory, motor, and cognitive stimulation (cf. citations throughout the text above). Both measures have different advantages and can be actually applied on the same data set, emphasizing different aspects of the brain activity (cf. “local vs. global” discussion reviewed in Freeman & Holmes, 2005).



1) event-related desynchronization (ERD):

change % of post stimulus-onset vs. prior baseline

ERD (%) = ((post-pre) / pre)*100

2) event-related potentials (ERP):

ERP (µV) = (sum(post)) / n

Figure 1.3. Main approaches of EEG analysis.

Challenges of BCI research – machine learning and illiteracy: EEG-based BCI research is challenged by a number of technical obstacles (cf. review by Wolpaw et al, 2002; or McFarland et al., 2005): e.g., data quality (noisy signals, large intra- and inter-subject variability even within sessions), choice of the signal processing techniques (linear vs. non-linear), generalizability of results (from offline calibration of classifiers to online EEG feedback; healthy vs. impaired users; non-invasive vs. invasive methods), and reducing error rates (i.e., wrong classification of user's brain states). Furthermore, in the case of healthy, non-disabled subjects it is important to check for possible muscle activation contributing to the brain state discrimination, since a BCI requires non-muscular application control (only based on brain activity; cf. Type1-Type2 differentiation of neural activity in Study 2, Chapter 3.1).

However, one of the biggest challenges in BCI research is the "illiteracy" problem (Blankertz et al., 2010; Vidaurre & Blankertz, 2010): In approx. 15–30 % of the subjects the BCI is "illiterate", i.e., it cannot "read" the subject's brain signatures adequately and thus the application control is only mediocre or even impossible. One possible reason is the absence of detectable signals (e.g., no measurable mu rhythm or, if present, only little task-related modulation). This quite common "illiteracy" finding (in healthy subjects) is surprising with respect to the state-of-the-art data acquisition methods and sophisticated machine learning techniques. What else if not technical considerations could contribute to BCI illiteracy? Obviously, if the user cannot modulate his/her brain activity to a necessary extent, then even the best machine learning algorithm has no signal to detect. Accordingly, there might be clear psychological factors influencing BCI illiteracy: e.g., choosing an effective cognitive strategy (e.g., motor imagery might be a poor choice when the subject reports poor imagery abilities), task instructions, arousal and stress, effort and fatigue, motivation, prior (disappointing) BCI experiences. The present thesis features a novel motor-cognitive strategy, i.e., quasi-movements, which might overcome problems of BCI illiteracy (also cf. Nikulin et al., 2008) and represents a comprehensive paradigm for neurocognitive studies of action intention.

1.3 Cognitive states in “covert movements”: Motor imagery, quasi-movements

1.3.1 Continuity between overt and covert stages of action and perception

William James (1890, chapter 18) noted “that the cortical processes which underlie imagination and sensation are not quite as discrete as one at first is tempted to suppose”. He further considered “if a sensation of sound were only a strong imagination, and an imagination a weak sensation, there ought to be a border-line of experience where we never could tell whether we were hearing a weak sound or imagining a strong one”. This implies a continuum between “real” experience and introspective “imaginary” states in terms of neural brain activity and subjective experience. Although James himself did not fully agree with this notion, the continuity assumption has become widely accepted in modern neuroscience (Currie & Ravenscroft, 1997; Guillot & Collet, 2005; Jeannerod, 1994, 1995, 2001; Lotze & Halsband, 2006), as depicted in Figure 1.4.

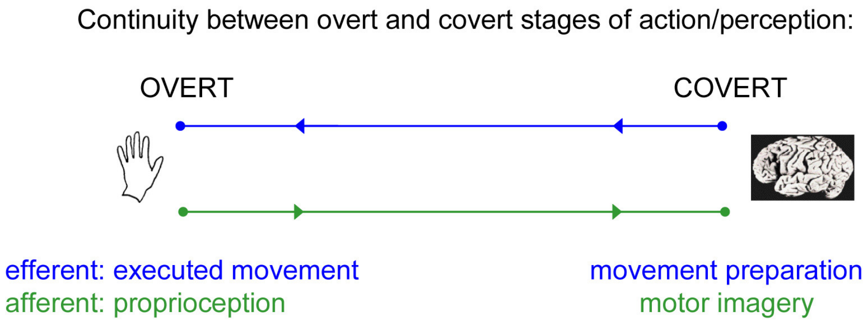

Continuity between overt and covert stages of action/perception:

Figure 1.4. The continuity assumption for brain activation and subjective experience.

More precisely, the continuity assumption holds for both efferent (top-down) and afferent (bottom-up) motor processes, i.e., action and perception. All overtly executed movements are assumed to be preceded by preparatory “covert” stages of action, for instance, movement intention or programming of the motor command. The “covert” counterpart of proprioception would be motor imagery, i.e., the conscious manipulation of sensory representations in memory (Richardson, 1969; Thomas, 1999; Tye, 1991). In neurophysiological terms, “covert” stages of action/perception refer to processes in the central nervous system excluding the effectors (i.e., muscles, alpha motor neurons) and receptors (i.e., muscle spindles, Golgi tendon organs).

1.3.2 Definition and characteristics of motor imagery

Brief history of mental imagery research: The philosophical consideration of mental imagery dates back to Aristotle and Descartes, proposing that mental images are basically picture-like copies of the external world. The “copy” theory was extended by the Empiricism tradition (e.g., Hobbes, Berkeley) by assuming that mental images, i.e., quasi-perceptual experiences, are recreated from perceptual data stored in memory which fade away over time, therefore mental images are always less detailed and “weaker” than actual perception (detailed reviews: Thomas, 1999; Thomas, 2010; Tye, 1991). The scientific research of mental imagery started in the 19th century, by assessing quantitative aspects of imagery abilities. Galton (1880) assumed that imagery abilities follow the Gaussian distribution, i.e., only few subjects form mental images being as clear and vivid as the “real” counterpart or reporting not being able to form mental images at all, while most subjects have images of moderate vividness. The influential “Questionnaire Upon Mental Imagery” (Betts, 1909) is used with modifications and shortenings until modern times (Isaac, Marks & Russell, 1986). The possible neural substrates of mental imagery in the brain and the similarities between perception and imagery in the different modalities (e.g., visual, kinesthetic) were extensively discussed by pioneers in experimental psychology (e.g., Wundt, James, Titchener; cf. review by Thomas, 2010), and subjected to behavioral experiments:

The classic Perky experiment (Perky, 1910) was one of the first experimental demonstration of a possible continuity between overt and covert stages of perception (cf. Figure 1.4 above). The subjects were asked to visually imagine different objects while looking at a screen in front of them. At different occasions objects were projected on the screen just above visibility threshold. Although the subjects reported later of not being aware of the “real” perception, the visual projection influenced details of their imagination. Therefore, the distinction between weak perception and vivid imagination appears to be blurred, as already noted by James (cf. citation above). The Perky effect has been reproduced (e.g., Segal & Fusella, 1970) and is an important method for investigating interference between visual images and actual perception (Craver-Lemley & Reeves, 1992; Farah, 1988).

With the cognitive revolution in the 1960s mental imagery became subject to extensive experimental investigation. Notably, early imagery research was mainly restricted to *visual* imagery: Shepard & Metzler (1971) published on the mental rotation of images, Kosslyn (1973) investigated the mental “scanning” of visual images. These and many subsequent studies suggested a *functional equivalence* between mental and actual images (Finke, 1980), e.g., the time to make a judgement about a visually rotated object is proportional to the amount of rotation necessary to align the object to a reference point, and the time it takes to mentally scan between different locations of a visual image is proportional to the actual physical distance.

Already in early EEG research there was an interest in possible neural correlates of mental imagery (e.g., Adrian & Matthews, 1934; Penfield; 1958). Recent neuroimaging studies demonstrated the remarkable similarity of neural substrates being activated during visual imagery and perception, for instance, primary visual cortex, parietal cortex, and fusiform face area (reviews: Kosslyn et al., 2001; Kosslyn et al., 1995; Bartolomeo, 2008). Importantly, in a recent fMRI study Ganis and colleagues (2004) showed that the voxels selectively activated during visual imagery were, without exception, a subset of those activated during perception.

Summarizing, behavioral and neuroimaging studies of mental/visual imagery demonstrated a strong similarity between imagery and perception in terms of cognitive and neural characteristics, supporting the assumptions of *continuity* and *functional/anatomic equivalence*. This is also assumed in the case of motor imagery, as reviewed below.

Definition of motor imagery: Motor imagery is often defined as mental simulation of a movement without activation of the effectors (Grush, 2004; Jeannerod, 2001;

Neuper et al., 2005). Specifically, motor imagery is assumed to involve “kinesthetic images; that is, … somatosensory feelings that a participant experiences when performing a movement him- or herself” (Munzert et al., 2009, p. 307). When additionally considering the general definition: “*Mental imagery refers to (1) all those quasi-sensory or quasi-perceptual experiences of which (2) we are self-consciously aware, and which (3) exist for us in the absence of those stimulus conditions that are known to produce their genuine sensory or perceptual counterparts”* (Richardson, 1969, pp. 2–3; italics in original), it becomes clear that by definition motor imagery is basically about evoking “motor images” by the simulation of proprioceptive input, and not about intending to simulate the motor command itself (Jeannerod, 1994; Kosslyn, Ganis et al., 2001; Moulton & Kosslyn, 2009).

Importantly, this so-called “kinesthetic motor imagery”, i.e., imagining proprioception/how it feels like to perform a certain action, is distinguished from “visual motor imagery”, i.e., visualizing body limb movements of oneself or another person (Guillot & Collet, 2005; Hall & Martin, 1997; Isaac et al., 1986; Jeannerod, 1994; Neuper, Müller-Putz et al., 2006; Stinear, Byblow et al., 2006). However, it is difficult to suppress accompanying visualimages, which might be reflected in the intricate coupling between the motor and the visual systems in the brain (Goodale et al., 2005; Lebedev & Wise, 2002). Therefore, it is not possible to control whether subjects perform genuine kinesthetic motor imagery. However, an important step is to assess imagery abilities via questionnaires and by precise task instructions (Sharma et al., 2006). The present thesis is concerned with kinesthetic motor imagery (simply referred to as “motor imagery”) while being aware of the fact that potential slight contamination by visual imagery is unavoidable.

Neural correlates of motor imagery: Numerous studies demonstrated the engagement of cortical and subcortical structures during motor imagery (reviews: Decety, 1996; Guillot & Collet, 2005; Jeannerod, 2001; Lotze & Halsband, 2006; Munzert et al., 2009; Sharma et al., 2006), as well as occasional muscular activation of the target limb (Jacobson, 1932; Gandevia et al., 1997; Guillot & Collet, 2005; Guillot et al., 2007; Hashimoto & Rothwell, 1999; Lebon et al., 2008; Shaw, 1938) and increased cortico-spinal excitability as evidenced by Transcranial Magnetic Stimulation (TMS; Stinear & Byblow, 2003; Stinear, Byblow et al., 2006). It is generally assumed that motor imagery and overt movements recruit (partially) overlapping neural networks in the motor systems, while the activation strength during motor imagery is considerably reduced compared to executed movements (Lotze & Halsband, 2006). This holds both for the central and the autonomous nervous system, and there is converging evidence from mental chronometry that the duration of imagined movements is similar to executed movements, and furthermore that motor imagery also seems to follow Fitts' law (Fitts, 1954; review in Guillot & Collet, 2005; Lotze & Halsband, 2006) stating that movement time increases with increasing task difficulty, e.g., imagining to place a stylus into squares of different sizes (Sirigu et al., 1996).

"Motor imagery corresponds to a subliminal activation of the motor system" (Jeannerod & Frak, 1999, p. 735), which in general holds for other types of covert movements. For present purposes only sensorimotor and parietal cortical regions will be reviewed here:

<u>a) Primary motor cortex (M1):</u> There are ambiguous reports on the activation of M1 (Brodman area BA 4) during motor imagery, depending on the method (high vs. low spatial resolution), task (imagination of simple vs. complex movements), motor imagery perspective (kinesthetic vs. visual), and EMG control. However, there is emerging evidence of M1 activation during motor imagery (review: Jeannerod, 2001) which seems to be somatotopically organized (Ehrsson et al., 2003; Sharma et al., 2008; Stippich et al., 2002). The apparent involvement of M1 during motor imagery indicates that the role of M1 for motor control is not purely executive, but is also related to motor attention or storage/access of motor programs. However, M1 activation seems to be not essential for motor imagery, since M1 lesions do not result in motor imagery impairments (Sirigu et al., 1995). Taken together, it might be the case that M1 activation during motor imagery is threshold-dependent (Lotze & Halsband, 2006), possibly from the input from secondary motor areas.

<u>b) Secondary motor areas:</u> Activations in the secondary motor areas (BA 6) during motor imagery have been reported consistently in dorsal and ventral premotor cortex (PMC) and posterior supplementary motor area (SMA). Secondary motor areas are assumed to be relevant for motor preparation and storage of motor plans, functions which might be employed during motor imagery (Jeannerod, 1994, 2001; Lotze & Halsband, 2006, Sharma et al., 2006).

<u>c) Primary somatosensory cortex:</u> The primary somatosensory cortex (S1; BA 3, 1, 2) is activated during motor imagery but reduced as compared to overt movements,

which might be due to the reduced afferent somatosensory feedback during imagery with absent or minor muscle discharge (Lotze et al., 1999; Solodkin et al., 2004).
d) Parietal cortex: Parietal activation (e.g., BA 7) has been demonstrated during motor imagery, and interestingly, rather for visual than kinesthetic motor imagery (Lotze & Halsband, 2006), e.g., mental rotation (Zacks, 2008). These results are in line with studies suggesting the importance of parietal cortices for the representation of space and body scheme, visuo-spatial aspects of movements, and visuo-motor mapping (Corradi-Dell'Acqua et al., 2009; Fleming et al., 2010; Shmuelof & Zohary, 2007); furthermore, patients with parietal lesions show impairments for estimating and integrating temporal and spatial aspects of motor imagery (like movement trajectory), or no ability to perform motor imagery at all (Jeannerod, 2001; Lotze & Halsband, 2006).
In sum, motor imagery is accompanied by the activation of various cortical and subcortical motor networks similar to those during executed movements. This gives rise to the assumption of shared neural networks, i.e., a common neural substrate being activated in both, overt and covert modes of action. This notion is strongly supported by the discovery of the so-called "mirror neurons" in monkeys (Gallese et al., 1996) and the "mirror system" in humans (Rizzolatti et al., 2001). In humans this network seems to consist of the inferior parietal lobule, the caudal sector (pars opercularis) of the inferior frontal gyrus, and the premotor cortex. The mirror system is activated by observation of actions performed by others (as well as by motor imagery), and this action "simulation" appears to contribute to the understanding of other's actions (Gallese et al., 2004).

Movement inhibition during motor imagery: Motor imagery might be accompanied by occasional muscular activation (review: Guillot & Collet, 2005), while in the majority of trials there are no detectable motor responses (e.g., Lotze et al., 1999), which is in agreement with the definition of motor imagery as movement/proprioceptive simulation without activation of the effectors (Jeannerod, 2001). Yet the presence of occasional muscle contraction during motor imagery suggests the investigation of motor inhibition: How does a covert movement become "covert"? Two complementary explanations have been proposed for explaining the absence of muscular activation during motor imagery (Jeannerod, 2001): The activation of the efferent motor system (especially primary motor cortex) is *subliminal*, therefore, no motor command is generated (i.e., passive inhibition of movements). It might also be the case that the subliminal or supra-threshold activation of efferent motor system is *paralleled by an inhibitory command*, resulting in a net zero outcome at the level of alpha motor neurons (i.e., active movement inhibition). In other words, movement residuals during motor imagery results from supra-threshold activation of efferent motor pathways and/or the possible “failure” of a parallel inhibitory command.

Besides the fact that it is difficult to experimentally distinguish between these scenarios, it is important to note that the occasional muscular activation should be rather an involuntary, automatic “byproduct” of the imagination: For motor imagery subjects are instructed to imagine proprioceptive/kinesthetic feedback (how it “feels like” to perform a movement). It is assumed that proprioception is simulated by using the efference copy of an issued motor command (forward-modeling; Grush, 2004; Wolpert & Gahramani, 2000; Wolpert et al., 2001). Therefore it might be conceivable that motor imagery involves the *automatic* production of a motor command, which is actively and/or passively inhibited (cf. also discussion of motor models in Chapter 5). These inhibitory mechanisms might be automatic as well – although subjects are instructed to avoid muscle activity, they are not instructed to imagine inhibitory commands per se. Congruent with this assumption might the observation that usually subjects can perform motor/visual imagery right away, without or with only little training (e.g., Pfurtscheller et al., 2008). The discussion of automatic/controlled inhibition is also crucial for an understanding of the novel phenomenon of quasi-movements, where in contrast to motor imagery the controlled, intentional inhibition of motor commands is essential for the task instructions and for the learning phase. Regarding possible neural correlates of motor inhibition is also topic of Study 1 (Chapter 2).

Key characteristics of motor imagery: Summarizing, the following notions regarding motor imagery are generally accepted and supported by neurophysiological evidence: shared networks, simulation, continuity, and equivalence. With respect to motor imagery: “motor imagery and motor execution overlap in their computational features and in their neural substrates” (Michelon et al., 2005, p. 811). Neurophysiological and introspective data support the notion of a continuity between both overt and covert motor states (Jeannerod, 2001).

Accordingly, motor imagery is considered as mental simulation of a movement, i.e., an imagined movement is anatomically and functionally equivalent to an overt movement (Finke, 1979; Finke, 1980; Grush, 2004; Jeannerod, 1994, 2001). However, although the simulation/equivalence notion is generally accepted in the research community, it is important to keep in mind the original definition of mental imagery as quasi-perceptual experience in the absence of stimuli (see above). For motor imagery this means evoking the sensation of *how it feels like* to perform a movement without its execution (e.g., S. Li et al., 2004). Therefore, the term *movement simulation* should be specified as *proprioceptive simulation* which in turn might automatically induce activation of central motor programs and efferent motor pathways due to a strong sensorimotor linkage in the case of forward modeling (cf. discussion in Chapter 5 and Wolpert & Gahramani, 2000). However, for simplicity this text utilizes the standard term “movement simulation”.

1.3.3 Quasi-movements: A novel motor-cognitive skill

The neurophysiological/-psychological characteristics of quasi-movements are comprised by Study 1–3 (Chapters 2–4). The study results are discussed in each chapter and generally discussed in Chapter 5.

Definition of quasi-movements: We introduced the novel skill “quasi-movements” in 2008 (Nikulin et al., 2008; cf. also Study 2, Chapter 3). Quasi-movements are defined “as volitional movements which are minimized by the subject to such an extent that finally they become undetectable by objective measures” (Nikulin et al., 2008, p. 727). The subject learns to reduce movement strength until EMG activity is indistinguishable from the baseline level of the muscle at rest. Performing a quasi-movement seems to be paradoxical task: performing a movement without performing it? Yet the simultaneous performance of these two logically contradicting tasks can be learned within half an hour of EMG neurofeedback, as described below. To the current date all but one of our subjects (n = 42), including myself, successfully learned how to perform quasi-movements. The key point of the training is to learn how to uncouple intentional and executional motor mechanisms: the intention and preparation of a movement, as reflected by different neural processes in the brain and spinal cord) does not necessarily need to culminate in the contraction of the target muscle. The subjects learn to sustain the movement intention/preparation but disrupt it from the final phase of the executive motor chain.

In this sense one can compare quasi-movements in healthy subjects to the so-called attempted movements in paralyzed patients or after amputation. For instance, when the patient tries to move his/her paralyzed hand, this attempted movement does not end up in the desired muscle contraction. In healthy subjects the equivalent to the patients' attempted movements was so far temporal transient ischemia, e.g., by a blood pressure cuff or curare, methods which are painful, uncomfortable and an unnatural condition for the subject, and cannot be used for extended experimental schedules (Gandevia & McCloskey, 1977; Gandevia et al., 1990).

These considerations make quasi-movements a unique paradigm for studying neural correlates of motor control and the functioning of the motor system in healthy subjects without contamination by peripheral proprioceptive activation. The latter notion is crucial, since basically all neurophysiological studies concerning overt movements are challenged by the fact that data recordings reflect a mixture of efferent motor processing and the reafferent sensory feedback from the moving limb. Quasi-movements represent an elegant solution to this problem, and furthermore the data is theoretically comparable to attempted movements in patients. Importantly, this is not the case when employing motor imagery in healthy subjects, since they intend to "mentally simulate a movement" but they never intend to actually execute this movement. In contrast, during quasi-movements all subjects reported to intend to perform genuine movements, they also reported to have a strong sense of movement, although objectively there were no detectable EMG responses, as reviewed below.

The utilization of quasi-movements is not restricted to healthy subjects but might also be beneficial to patients with neuromotor disorders, as discussed in Chapter 5.

Quasi-movements also represent an effective strategy for brain-computer interfacing, compared to standard motor imagery, as will be described below. Quasi-movements can be understood as a motor-cognitive skill, since it is learned by training similar to fine-graded motor control, e.g., learning to play piano. Before elaborating on the application of quasi-movements for BCI, we describe our developed training procedure how subjects learn to perform movements with undetectable motor responses in highly sensitive EMG.

Learning how to perform quasi-movements – EMG neurofeedback:

“Perform an abduction of your thumb (or any other movement) and let this movement be relatively small. Now try to minimize this movement even further, making it as small as possible”.

It is conceivable that potentially each body movement could be trained to become a quasi-movement. However, it is easier to start with a very simple movement with few or only one target muscle involved, as in the case of thumb abductions (abductor pollicis brevis muscle, APB). Once the principle is learned it could be generalized to other muscles or the activation of many muscles in combination. The key feature of quasi-movement training is neurofeedback. The target muscle is monitored by EMG and displayed to the subject. The subject reduces the EMG peaks by minimizing movement strength further and further, until motor responses become practically undetectable by EMG, i.e., EMG activation is at baseline level. By “baseline level” it is referred to the muscle being at rest. The length of the training is subject-dependent and usually takes up to 30 min.

It is very important for the quasi-movement training to choose a muscle which is very easy to measure by EMG, i.e., which has a high signal-to-noise ratio, as it is the case with APB. In practical terms: The subjects are asked to minimize the peak amplitude (which relate to muscle contraction) such that the peaks are barely above the baseline at a sensitivity of 50 µV per division (i.e., peak size of ~ 5 % if max. voluntary contraction is 1 mV). Then the sensitivity is increased to 20 µV/div (~ 2 % if max. voluntary contraction is 1 mV). During this phase the subjects familiarize themselves with performing very weak movements, since during normal daily practice even fine-graded motor control involves comparatively “strong” movements. When the subjects are able to perform these already miniscule movements (after ~ 15 min) the monitor is turned away and the researcher further trains the subjects by verbal feedback (~ 15 min).

This verbal feedback phase is the crucial part of the training since the subjects are asked to minimize the movement strength even further until the EMG activation is at baseline level, as seen by the researcher. After the initial familiarization the verbal feedback is the actual effective training phase. Importantly, when asking the subjects at this point they are convinced that they are still performing very weak movements. Once the performance is stable (or usually after the experiment) the subjects are debriefed that actually there were no measurable EMG responses any longer. This procedure (debriefing *after* the experiment) might be advantageous for naïve subjects from a non-scientific background in order to avoid confusion during the training and recordings, since an initial instruction such as “perform a movement without measurable EMG responses” might appear paradoxical and thus distract from learning the task. Once the novel skill of quasi-movements is learned and when subjects are debriefed, our experiences showed that the subsequent quasi-performance is not impaired. The subjects were surprised of the “zero” EMG, even when observing the traces in real time, and reported that they are still convinced of executing genuine movements (cf. task ratings in Nikulin et al., 2008 and Study 3 in Chapter 4). Summarizing, training quasi-movements is a multi-step procedure, where the subject learns to decrease movement strength and increase motor inhibition.

Quasi-movements – An effective strategy for brain-computer interfacing: As we have discussed above, quasi-movements represent a valuable strategy for studying movement organization by electrophysiological and neuroimaging methods, since there is no confounding reafferent sensory feedback. The latter makes quasi-movements suitable for BCI research, similar to motor imagery.

Motor imagery in healthy subjects for BCI has two important drawbacks: a) the strategy is conceptually inadequate when generalizing results to patients who try to operate the BCI via attempted movements (i.e., no intention of movement simulation but the actual execution is intended), and b) the modulation of neuronal activity often remains unsatisfactory in healthy subjects, resulting in poor BCI performance (i.e., BCI “illiteracy”, Chapter 1.2.3).

As we have already discussed, the quasi-movements paradigm overcomes drawback a). And concerning b), the quasi-movements paradigm was originally developed for the BCI illiteracy problem. We expected that, in contrast to standard motor imagery, the performance of quasi-movements would be associated with a stronger neural signal over sensorimotor cortices and with the increased classification accuracy of brain states. This hypothesis was confirmed by the data (Nikulin et al., 2008), since we demonstrated that in healthy subjects quasi-movements were associated with a significantly smaller classification error (~ 47% of relative decrease) for brain state discrimination in comparison to the errors obtained with standard motor imagery.

EMG control during quasi-movements: Continuous EMG monitoring is crucial for the training phase of quasi-movements and in order to assess successful task performance (i.e., no detectable motor responses). The researcher monitors the EMG traces throughout the experimental recordings and, if necessary and implemented in the specific experimental schedule, gives feedback to the subject or includes an additional short training phase. As already discussed above, the choice of the appropriate target muscle(s) for the movement (e.g., APB for thumb abduction) is very important, as well as the careful EMG preparation.

For EMG data analysis the visual inspection of single trials is crucial for the detection of motor responses, as well as the within- and across-subject testing for amplitude differences in the pre- and post-stimulus interval. Furthermore, machine learning techniques can be additionally applied. For the detailed single trial EMG analysis cf. Study 2 (Chapter 3).

Notably, we defined quasi-movements as movement performance with zero motor output, i.e., the muscle is at rest. Practically, it might be that this (infinitively) small motor output is not detectable by surface EMG, i.e., reflecting the activity of many motor units (although it has been shown that surface EMG might also reflect even single motor units activation: Roeleveld & Stegeman, 2002). However, even when utilizing invasive methods for single motor unit recordings it might be the case that other units are missed due to the low spatial resolution.

We are aware of the fact there is no final proof for a zero-finding. Nevertheless, in practical terms our main point is that the *EMG activity during quasi-movements is undetectable or at least as low as during motor imagery*. All the considerations above also apply to motor imagery studies, and we introduce a paradigm which is complementary to motor imagery and additionally has theoretical and practical advantages. Furthermore, it is important to demonstrate that occasional residual EMG responses during quasi-movements have no significant effect on EEG modulation (as we have demonstrated by extensive analysis, cf. Nikulin et al., 2008). It is an interesting question per se how much cortical EEG is modulated by extremely weak movements, i.e., ~ 1 % of max. voluntary contraction (EMG peak of ~ 10µV above resting baseline). Figure 1.5 shows an example of these occasional EMG residuals during quasi-movement performance (right hand), compared to concurrent EEG recordings from the contralateral sensorimotor cortex (channel C3, nose-referenced).

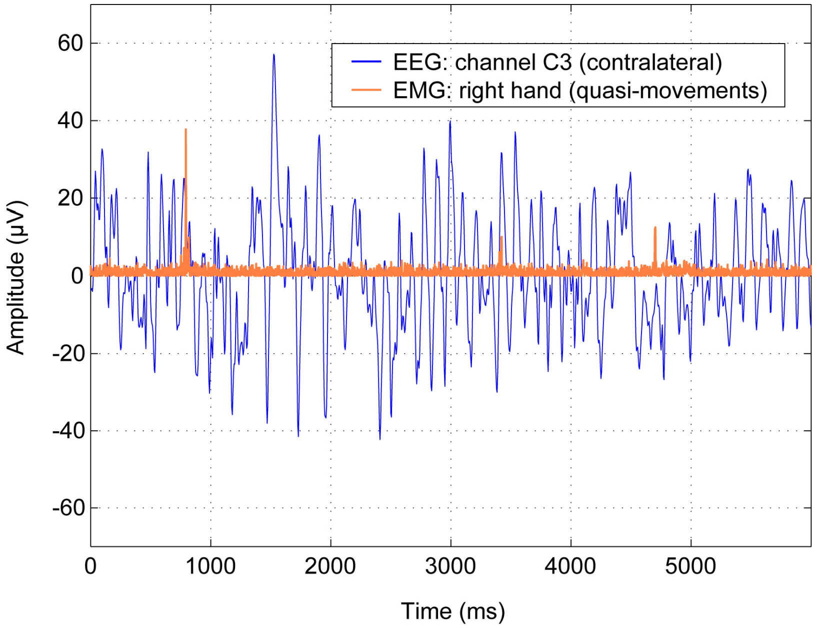


Figure 1.5. Occasional EMG responses during quasi-movements.
Concurrent EEG and EMG activation (representative subject from Study 3, single trial, right hand quasi-movements). EEG: band-pass filtered 0.5–40 Hz, nose-reference; EMG: high-pass 10 Hz, rectified.

If present, EMG residuals usually are of 10–40 µV above baseline, which is in the range of EEG voltage fluctuations. Another decisive factor is the training time for quasi-movements. The present studies involved naïve subjects performing quasi-movements for the first time (~ 30 min of training). It might be beneficial to employ a procedure where the subjects are involved for two or three sessions of neurofeedback trainings on different days for future studies, similar to schedules where subjects train motor imagery at home or in the lab for several times (e.g., Pascual-Leone et al., 1995).

Quasi-movements and the continuity assumption: As reviewed above, it is generally assumed that there is a continuum between overt and covert stages of action and perception in terms of neural activation and subjective experience (cf. Chapter 1.3.1 and Figure 1.4). Learning how to perform quasi-movements (i.e., the successive reduction of movement strength to a complete muscular quiescence) might represent a continuous transition process between overt and covert motor stages, as circumscribed as “border-line of experience” by William James (1890). The subjects start with an externally measurable behavior and in a self-paced manner end up in an internal cognitive state, in which they are still intending to perform a movement and feel strong proprioception, yet on the periphery there is no measurable muscle response any longer. Results from our previous study (Nikulin et al., 2008) could be interpreted as suggesting that there might be a continuum not only on the behavioral side but also in terms of brain activation (motor imagery < quasi-movements < overt movements). However, this assumption has to be investigated at different time scales, as shown by Study 1 (some hundred milliseconds) and Study 3 (up to 60 sec). For more details please also refer to Section 1.4 in the present chapter and Section 5.2.1 in the General Discussion.

Key characteristics of quasi-movements: Summarizing, quasi-movements represent a novel motor-cognitive skill, which can be employed in healthy (and potentially disabled) subjects. The neurophysiological and psychological investigation of quasi-movements contributes to a basic understanding of the organization and functioning of the motor system in the brain, and has important implications for studies of action intention, movement inhibition, brain-computer interfacing, and rehabilitation. We demonstrate that quasi-movements are accompanied by central motor activation but without/insignificant confounds from peripheral sensory feedback. Utilized in healthy subjects, the paradigm is better comparable with the attempted movements of patients with neuromotor disorders than motor imagery. Furthermore, the task of quasi-movements is precisely defined and easy to implement by means of EMG neurofeedback. In contrast to completely introspective motor imagery, which depends on the individual imagery abilities and reportability on behalf of the subject, quasi-movements represent a specific *motor skill*, which is explicitly trained and does not depend on subjective imagery abilities. Therefore, we can expect a higher degree of experimental control over subject compliance and reduce experimental variability due to precise task instructions.

The differences between quasi-movements and motor imagery are discussed in more detail (and incorporating the study results) in Chapter 5 and will be summarized here: Although both strategies seem very similar, i.e., absence of measurable muscle responses in EMG since movements should be performed only “in the head” and not by the muscles and recruitment of sensorimotor networks in the brain, there are fundamental differences between both tasks (cf. present results and Nikulin et al., 2008). Motor imagery and quasi-movements differ on the level of action intention (*proprioceptive/action simulation* vs. *motor execution with effectively zero muscular output*), on the level of subjective experience (higher “sense of movement” in quasi-movements), and on the level of brain dynamics in sensorimotor networks (stronger engagement by quasi-movements).

1.4 Short- and long-term dynamics of action intention

The general focus of my thesis is on the neural and cognitive correlates of action intentions on different time scales, i.e., short- and long-term dynamics. Action intentions can be distinguished into overt and covert types, i.e., overtly executed movements involving muscular contractions, and “covert movements” per definition without activation of the effectors.

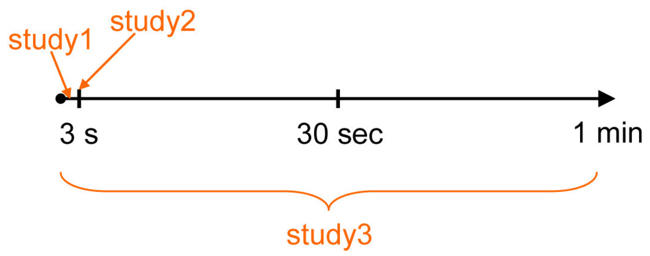
Covert movements are, for instance, attempted movements in patients with neuromotor impairments, movement preparation while waiting for a “go” signal, quasi-movements (i.e., movement performance with minimized muscle activation down to muscular quiescence), and motor imagery (i.e., mental simulation of a movement; more precisely, proprioceptive simulation since imagery is defined as quasi-perceptual experience without external input). My thesis concerns neural (EEG, EMG), behavioral, and introspective correlates of motor imagery and quasi-movement performance, compared to overt movements.

1.4.1 Summary of study aims

Neural correlates of action intention: An open question is how overt and covert action intentions manifest themselves in terms of neural activity in the brain. The majority of studies demonstrated the remarkable similarity of brain activation between both intentional modes. Nevertheless from an introspective viewpoint an imagined movement is fundamentally different from a “real” movement. Therefore, present and future neuroscientific research should also focus on the neural differences between overt and covert modes of action – is there a final “veto”, where and when does it unfold? Or are neural motor networks differentially primed by the action intention such that a veto is not necessary?

The *where* differences might be investigated by fMRI or MEG in future studies. However, the present thesis work focuses mainly on the *when* differences, given the high temporal resolution of EEG (milliseconds) but its comparatively low spatial resolution (centimeters): The present studies investigate neural correlates of action intentions on multiple time scales, i.e., from milliseconds up to minutes. Figure 1.6 depicts the general framework of the studies:

Short- and long-term dynamics of action intention:
quasi-movements vs. motor imagery vs. overt movements



Study 1 (~ 120 ms) – EEG Lateralized Readiness Potentials
Hohlefeld FU, Nikulin VV, Curio G (in press). Visual stimuli evoke rapid activation (120 ms) of sensorimotor cortex for overt but not for covert movements. Brain Research.

Study 2 (~ 3 sec) – EMG dynamics and brain-computer interfacing
Nikulin VV, Hohlefeld FU, Jacobs AM, Curio G (2008). Quasi-movements: A novel motor-cognitive phenomenon. Neuropsychologia 46, 727–742.

Study 3 (0–60 sec) – Repetition suppression in EEG alpha and beta dynamics
Hohlefeld FU, Nikulin VV, Curio G (submitted). Covert movements trigger repetition suppression of EEG in sensorimotor cortex.

Figure 1.6. Study aims: Neurocognitive characteristics of covert movements compared to overt movements on multiple time scales.

In the following the hypotheses driving my thesis' studies will briefly introduced. For a more detailed presentation please refer to the abstracts and introduction sections of the respective study.

Hypotheses – Study 1 (Hohlefeld et al., in press): We utilize the high temporal resolution of electroencephalography (EEG) in order to test two alternative hypotheses: 1) *similarity* or 2) *dissimilarity* of early stimulus-locked neuronal processes related to covert (motor imagery, quasi-movements) and overt hand movements (left/right thumb abduction: APB muscles), i.e., within the first 150 ms after stimulus onset in the Lateralized Readiness Potential (LRP) which is a well-established measure for studying inter-hemispheric differences in motor processing.

Importantly, we introduce a modification of this measure by deriving the LRP from rectified EEG signals (LRPrect) in order to overcome the problem of EEG/LRP signal variability related to polarity differences in the spatial distribution of neuronal sources. Please note that Study 2 has been carried out *before* Study 1, but the order has been switched for presentation purposes of my thesis (cf. Figure 1.6 above). The data pool of Study 1 consists of new data recordings and partly a re-analysis of the data from Nikulin et al. (2008).

Hypotheses – Study 2 (Nikulin, Hohlefeld et al., 2008): We hypothesize that the performance of covert thumb movements (i.e., quasi-movements and motor imagery) is not associated with detectable motor responses in the majority of trials (3 sec length) in highly sensitive EMG recordings of different muscles contributing to thumb movement as well as in accelerometer recordings. The results of these control experiments with additional subjects will be presented in my thesis. For the results and discussion of the main experiment with other subjects, regarding EEG data, brain state classification for BCI, EMG data analysis from APB muscle, and task ratings, please refer to Nikulin et al. (2008) and my diploma thesis (Hohlefeld, 2006). The main interest of the present analysis was the comparison of the sensitivity of the different statistical, automatic, and visual inspection methods for the detection of weak motor responses in EMG and accelerometer recordings which are occasionally present in covert thumb movements, since importantly, BCI should not rely on movement-related brain activity (or any other externally-driven activation).

Hypotheses – Study 3 (Hohlefeld et al., submitted): We addressed the hypothesis whether the phenomenon “repetition suppression” (RS), i.e., the decrease of neural activity to repeated external sensory stimulation, can also be present in the absence of sensory stimulation during the performance of a repetitive cognitive task, such as covert movements which per definition does not imply muscle contraction. For this purpose we recorded neuronal activity with multi-channel electroencephalography (EEG) when the subjects performed continuously either covert (i.e., motor imagery, quasi-movements) or overt repeated thumb movements over trials of 60 sec length. Importantly, frequent studies have shown that covert movements are associated with the activation of central sensorimotor networks in the brain (similarly to overt movements) while yet there are no detectable muscle responses in the majority of trials. We hypothesize that the neural dynamics of alpha and beta oscillations in both overt and covert movements show RS, i.e., the gradual recovery of sensorimotor rhythms with increasing movement repetitions across 60 sec. The presence of RS in covert movements with insignificant EMG contribution might tentatively indicate that movement-related RS could be primarily internally-driven.

Basic neurophysiological understanding of quasi-movements: The novel motor-cognitive skill “quasi-movements” has been recently introduced (Nikulin et al., 2008) and we showed that the performance of quasi-movements modulates sensorimotor networks similar to overt movements (and stronger than motor imagery) despite the EMG activity being at resting baseline level. However, further research was needed in order to reveal how this novel skill is implemented in the brain. Quasi-movements, especially in the training phase, depend on motor inhibition (i.e., progressive reduction of movement strength) which poses the question of possible neural correlates to such intentional, controlled inhibition. Furthermore, quasi-movements represent an interesting paradigm for studying motor cognition, i.e., action intention and sense of movement. In this respect the present dissertation represents an effort to further investigate the *differences* in neural correlates especially between quasi-movements, motor imagery, given that on the peripheral level both tasks do not imply muscle responses. For instance, given our previous assumption (discussed above and also suggested by Nikulin et al., 2008) of a continuity between overt and covert stages of action/perception in terms of neural processing (motor imagery < quasi-movements < overt movements), we were interested in whether the continuity assumption holds on different temporal scales (from milliseconds, Study 1, to minutes, Study 3). In sum, specific functional and anatomic knowledge is vital for the effective application of quasi-movements for studies of action intention, rehabilitation, and BCI.

Optimizing brain-computer interfacing: One of the main interests of my thesis is the optimization of BCI, i.e., integrating neurophysiological and psychological knowledge and applying it when designing experimental paradigms or brain state classifiers. BCI research has profited enormously by the development of machine learning techniques. However, interest in the systematic research of psychological factors has evolved only in the last few years (e.g., Adams et al., 2008; Burde &

Blankertz, 2006; Neumann et al., 2003; Nijboer et al., 2007). Yet the development of efficient mental strategies for BCI operation stagnates: motor imagery (of different body parts, visual vs. kinesthetic perspective), attention-based systems in oddball-paradigms (P300), and subjectively developed, individual strategies when learning to control slow-cortical potentials via operant conditioning (e.g., imagining a mental void vs. changing traffic lights; Neumann et al., 2003). However, we introduced the novel strategy of quasi-movements, a strategy which is easy to communicate to the subject and can be trained in a standardized way, i.e., the performance of quasi-movements does not depend on subjective imagery abilities.

Notably, a BCI creates a completely new, artificial situation for the brain: The brain receives real-time feedback of its own activity and controls the environment more directly than before, since the neural activity does not need to be translated into muscular output but is instantly read: the cursor becomes a novel limb. Indeed, subjects report that under ideal circumstances they do not “think” anymore about how to control the cursor, instead they simply “act” with it as if it were a naturally controlled movement (Neumann et al., 2003; Schwägerl, 2004). In this respect more research needs to be done in order to find out how this sense of agency emerges (Lynn et al., 2010) and how the brain adapts to the BCI environment per se in a long-term perspective. We demonstrate that the adaptation mechanism of repetition suppression has important implications for the design of BCI classifiers and experimental schedules.

Chapter 2

II. STUDY 1

Visual stimuli evoke rapid activation (120 ms) of sensorimotor cortex for overt but not for covert movements

To appear in: Brain Research (in press).

Friederike U. Hohlefeld[1,2,3], Vadim V. Nikulin[2,4], Gabriel Curio[2,4]

1) Berlin School of Mind and Brain, Berlin, Germany
2) Neurophysics Group, Department of Neurology,
   Charité – University Medicine Berlin, Germany
3) Department of Psychology, Free University Berlin, Germany
4) Bernstein Center for Computational Neuroscience, Berlin, Germany

Abstract

Overt and covert movements (e.g., motor imagery) have been frequently demonstrated to engage common neuronal substrates in the motor system. However, it is an open question whether this similarity is also present during early stages of stimulus-processing. We utilized the high temporal resolution of multi-channel electroencephalography (EEG) in order to test whether the prior action intention (overt vs. covert movements) differentially modulates early stimulus-processing stages in the cortical sensorimotor system. The subjects performed overt or covert movements contingent upon an instructive visual stimulus (indicating left or right hand performance). We introduced a novel measure, LRPrect, calculated as Lateralized Readiness Potentials from rectified EEG signals. This measure overcomes a problem related to the EEG signal variability due to polarity differences in the spatial distribution of neuronal sources. The LRPrect showed an activation already at 120 ms after stimulus onset (latN120) focally over sensorimotor cortices contralateral to the upcoming hand movement, yet only for overt but not covert movements. Thus the prior action intention differentially routes early stimulus-processing into the sensorimotor system, which might contribute to significantly different behavioral outcomes, i.e., movement generation or inhibition. The present results have implications for studies of motor inhibition and action intention.

Keywords: Electroencephalography, EEG, intention, lateralized readiness potential, LRP, motor imagery, movement, quasi-movements.

2.1 Introduction

An overt movement, i.e., the voluntary contraction of a muscle, is preceded by “covert” preparatory processes in the brain and spinal cord. On the other hand, the frequently studied phenomenon of kinesthetic motor imagery involves only covert motor processes: An imagined (covert) movement is assumed to have everything of a “real” movement except the overt muscle contraction (Currie & Ravenscroft, 1996; Jeannerod, 1994, 2001; Jeannerod & Frak, 1999; S. Li et al., 2004; Morton, 1994). Previous neuroimaging and electroencephalographic studies frequently demonstrated that motor imagery and overt movements share neuronal substrates, especially in primary and secondary motor areas (Bakker et al., 2007; Chatrian et al., 1959; Jacobson, 1932; Jankelowitz & Colebatch, 2002; Kranczioch et al., 2009; Lotze & Halsband, 2006; Stinear et al., 2006; Munzert et al., 2009; Wolpaw et al., 2002). Accordingly, motor imagery is defined as a mental/neuronal simulation of an overt movement without muscle contraction. Neuronal processing during motor imagery is often understood as a “scaled-down” version of the very same processes occurring during overtly executed movements (Finke, 1979, 1980; Grush, 2004; Jeannerod, 1994, 2001).

These quantitative differences in neuronal processing in the motor systems are obviously related to the absence of efferent motor commands (and reafferent sensory feedback) in the case of motor imagery. However, it is not clear whether differences between overt movements and motor imagery are already present in very early stages of neuronal processing, e.g., those associated with stimulus-processing and stimulus-response mappings (e.g., hand selection). By “early processes” we refer to the stimulus-locked neuronal activity preceding movement onset in electromyography (EMG), by “late processes” to neuronal activity at or after movement onset.

Two contrasting hypotheses capture these notions:

(1) The stimulus triggers neuronal events which are indistinguishable (i.e., very similar or identical) in early stimulus-processing stages of overt and covert movements. Only in later stages neuronal processes differ when the movement is executed or inhibited.

(2) Alternatively, on the basis of the prior intention the neuronal activity is routed differently immediately after the onset of the stimulus. Thus, the very early stimulus-response mappings in the motor system substantially differ, possibly contributing to movement generation or inhibition occurring at later stages in the neuronal activation chain. Both hypotheses can be straightforwardly tested: Observing early and, critically, stimulus-locked differences in neuronal activity between overt movements and covert movements would favor hypothesis (1). On the other hand, the absence of early activation differences would favor hypothesis (2).

In the present study we utilized the high temporal resolution of multi-channel electroencephalography (EEG) for testing differences of early (<150 ms) neuronal activity locked to a fully instructive stimulus requiring overt or covert hand movements. The analysis was focused on the first 150 ms after stimulus onset, since previous studies have shown that the motor/cognitive modulation of sensory responses might occur in this early time range (Alho, 1992; Bigman & Pratt, 2004; Carrillo-de-la-Peña et al., 2008; García-Larrea et al., 1995; Hatem et al., 2007; Loveless, 1977). We utilize the Lateralized Readiness Potential (LRP) as a well-established measure for studying inter-hemispheric differences in motor processing (Coles, 1989; de Jong et al., 1988; Eimer, 1998; Gratton et al., 1988; Hackley & Valle-Inclan, 1998; Osman & Moore, 1993) and motor imagery (Carrillo-de-la-Peña et al., 2008; Carrillo-de-la-Peña et al., 2006; Galdo-Álvarez & Carrillo-de-la-Peña, 2004; Kranczioch et al., 2009). We introduce a modification of this measure by deriving the LRP from rectified EEG signals (LRPrect). This procedure allows avoiding ambiguities in interpreting the traditional LRP, due to individual differences in the orientation and location of neuronal sources (cf. Methods section and Appendix below, Chapter 2.5).

The present study examines three different experimental conditions: overt movements and two types of covert movements, namely kinesthetic motor imagery and quasi-movements. Quasi-movements are defined as voluntary movements, which are minimized by the subject to such an extent that finally they become undetectable by measures of muscular activity (for instance EMG; cf. Nikulin et al., 2008, and Methods section). Thus, per definition both imagined and the “minimized” quasi-movements do not involve muscular contraction. Yet quasi-movements critically differ from motor imagery in cognitive and neurophysiological aspects (cf. Nikulin et al., 2008, for details). Firstly, during quasi-movement performance all subjects reported that they intended to perform a “real” movement instead of simulating it. Secondly, similar to motor imagery quasi-movements were also associated with the activation of contralateral sensorimotor cortices without concurrent muscle activation. However, this cortical activation was significantly stronger and more lateralized than during motor imagery (around ~ 1 sec after stimulus onset). Given these results we hypothesized quasi-movements to represent an intermediate stage in a continuum between imagined and overt movements (cf. Jeannerod, 1994, 2001) in terms of neuronal processing (Nikulin et al., 2008), which gives rise to the question of whether very early stimulus-processing (<150 ms) would be scaled in a similar way. Summarizing, the main interest of our study is whether the prior action intention (overt vs. covert movements) differentially modulates very early stimulus-processing stages in the cortical sensorimotor system.

2.2 Methods

2.2.1 Participants

Eighteen healthy subjects (mean age 28 years, range 19–48 years, 11 males, 7 females), without any history of neurological or psychiatric disorders, participated in the present study and gave informed consent. All subjects were right-handed (Edinburgh Handedness Inventory; Oldfield, 1971), having normal or corrected-to-normal vision. From our previous study (Nikulin et al., 2008) the data from the right-handed subjects were selected (N=13) for the present analysis, and five additional subjects were additionally recorded with the same experimental protocol (except for the “overt movements” condition).

2.2.2 Procedure

In a block design the subjects performed three experimental conditions, referred to as “overt movements”, “motor imagery” and “quasi-movements”. The visual stimuli, the letters “L” or “R” in the center of the computer screen (visual angle 4.8° x 3.4° on a grey background), indicated the left or right hand performance, respectively (random presentation, duration 3 sec, random variation of the inter-stimulus-interval 3±0.2 sec). One session lasted ~12 min, including two 30-sec breaks. Each experimental condition was recorded twice, resulting in six sessions. The sessions were presented in random order. Each session comprised 54 “L” and 54 “R” stimuli, resulting in 108 stimuli for each class.

Overt movements: The subjects performed overt thumb abductions (abductor pollicis brevis muscle). The movements were brisk, of medium force, and were executed with a frequency of ~2 Hz reacting to the “L” or “R” stimuli presented on the computer screen.

Motor imagery: The subjects imagined the thumb abduction with the same strength and frequency. The subjects were instructed to perform motor imagery from the first person perspective (egocentric) and to concentrate only on kinesthetic aspects of the imagined movement, while avoiding its visualization.

***Quasi-movements*: ** For quasi-movement performance the following instruction was given to the subjects: “Perform an abduction of your thumb and let this movement be relatively small. Now try to minimize this movement even further, making it as small as possible”. The main idea of quasi-movements is to train the subjects to initially perform overt movements (cf. “overt movements” task), but then to successively minimize the movement strength to such an extent that it becomes practically undetectable by EMG (Nikulin et al., 2008). For more details on the training procedure please refer to Chapter 1.3.3. The experimental procedures were approved by the Ethics Committee of Charité – University Medicine Berlin (Berlin, Germany).

2.2.3 Psychological measures

After finishing the EEG recordings the subjects were asked to fill out the Vividness of Motor Imagery Questionnaire (VMIQ; Isaac et al., 1986) in order to assess general imagery abilities. The VMIQ comprises two subscales referring to external (third-person perspective) and internal (first-person perspective) motor imagery. For the interest of the present study only the results of the “internal” subscale is reported. For additional subjective measures please refer to Nikulin et al. (2008).

2.2.4 EEG and EMG acquisition

EEG data were recorded by 120 Ag/AgCl electrodes positioned according to the 10–5 system (Oostenveld & Praamstra, 2001) with nasion reference. Surface EMG was recorded from the left and right abductor pollicis brevis muscle with Ag/AgCl electrodes. One electrode was positioned over the muscle belly and the other over the proximal base of the phalanx. EEG and EMG data were recorded by using BrainAmp amplifiers and BrainVision Recorder software (version 1.3; Brain Products GmbH, Munich, Germany). During the data acquisition EEG and EMG signals were band-pass filtered at 0.1–250 Hz and sampled at 1000 Hz. Offline analysis was carried out with Matlab (version 7; The MathWorks Inc., Natick, USA).

2.2.5 EMG data preprocessing and onset detection of motor responses

EMG data were high-pass filtered at 10 Hz (Butterworth filter, second order) and rectified. The data were segmented into epochs of 2500 ms length, starting 500 ms before stimulus onset. In order to improve the movement onset detection we applied the Teager-Kaiser energy operation (X. Li et al., 2007). In each epoch the onset of the overt thumb movement was manually determined.

2.2.6 EEG data preprocessing and artifact rejection

EEG data were decimated to 200 Hz. For analysis the most peripherally located electrodes (temporal and posterior) were excluded because of the possible contamination by muscular artifacts. For the final analyses 99 channels remained. EEG data were band-pass filtered at 0.5–40 Hz (Butterworth filter, second order). The data were segmented into epochs of 3200 ms length, starting 100 ms before the stimulus onset. Before averaging the data all epochs were carefully analyzed for the presence of physiological and technical outliers. The artifact rejection procedure was based on visual inspection of single trials and channels, and utilized Fast Independent Component Analysis with kurtosis as contrast function (Hyvärinen & Oja, 2000).

2.2.7 Calculation of the lateralized EEG components from rectified signals (LRPrect)

The present study focused on the hemispheric lateralization of early sensorimotor processes before movement onset, as reflected in the stimulus-locked LRP (de Jong et al., 1988; Gratton et al., 1988).

In contrast to previous studies we calculated the stimulus-locked LRP not from the raw amplitudes, but from *rectified* signal values (referred to as LRPrect; i.e., the LRP calculated from |µV|):

$$LRPrect = [\ (LH(|contra|-|ipsi|) + RH(|contra|-|ipsi|))/2\ ] * (-1)$$

where "LH" refers to left hand trials, "RH" to right hand trials, "contra" to an EEG electrode over the contralateral hemisphere and "ipsi" to the symmetric electrode over the ipsilateral hemisphere. After the derivation the LRPrect is baselined (prestimulus 100 ms). The inversion of the values (multiplication by -1) achieves that the LRPrect curve is deflected downwards (ie, negative) if the magnitude of the signal in the contralateral hemisphere is larger than in the ipsilateral hemisphere (and vice versa). Usually, unimanual motor response tendencies (e.g., motor preparation) are associated with a larger activation of the contralateral motor cortex, as reflected in the negativation of the lateralized EEG activity (Eimer, 1998; Kutas & Donchin, 1974, 1980; Rohrbaugh et al., 1976).

This novel LRPrect measure was introduced in order to overcome the variability in EEG signals produced by heterogeneous effects of signal polarity, e.g., related to the spatial distribution of neuronal sources (cf. extensive discussion in the Appendix below; and Gratton et al., 1988; Oostenveld et al., 2003;). The traditional LRP reflects shifts in polarity but does not allow definite conclusions about the signal's polarity or magnitude (i.e., absolute activation strength) in the *individual* hemispheres (Eimer & Schlaghecken, 2003). The LRPrect measure is complementary to the traditional LRP, since LRPrect indicates the magnitude difference of the individual hemispheres regardless of the signals' polarity (cf. Appendix below for more details and dipole simulations). This notion is common to the calculation of the global field strength, which is derived by rectification (or squaring) of the signals from all EEG electrodes (Lehmann & Skrandies, 1980; Murray et al., 2008). Accordingly, the LRPrect measure is especially suitable for lateralized stimulus-locked EEG processes, which are very early in time, transient in duration, and where the effect's polarity is unknown or might vary in polarity across/within subjects. The latter might be due to anatomical variations in the orientation of neuronal sources, or due to slight differences in electrode positioning (cf. Appendix below). In order to systematically study the spatial distribution of neuronal responses, the LRPrect was derived from 36 symmetric electrode pairs.

2.2.8 Statistical analyses

The present study is focused on the analysis of early changes in the neuronal activations related to overt and covert movements. Therefore we constrained the analysis to the first 150 ms following the presentation of visual stimuli (Alho, 1992; Bigman & Pratt, 2004; Carrillo-de-la-Peña et al., 2008; García-Larrea et al., 1995; Hatem et al., 2007; Loveless, 1977). The grand-average LRPrect derivation from the C3 and C4 channels (approx. located over primary motor cortices), a traditional location for deriving motor-related lateralized EEG potentials (e.g., Coles, 1989; Eimer, 1998; Kranczioch et al., 2009; Smulders et al., 1995), was tested by the one sample running t-test against zero in all three conditions in order to identify a time region of interest (Carrillo-de-la-Peña et al., 2006; Kranczioch et al., 2009). If a significant component could be identified the mean was taken in a 20 ms interval centered on the peak for the LRPrect derivation from C3 and C4 electrodes, as well as for the remaining 35 LRPrect channels. In order to objectively define a spatial ROI the following procedure was utilized. (1) The activity of all LRPrect channels (mean across time region of interest) were tested against zero with the t-test. (2) Importantly, the significant channels do not necessarily form a spatial cluster. However, if this is the case it might serve as an evidence for the spatial specificity of the studied phenomenon.

Subsequently the amplitude was averaged across the ROI channels and subjected to one-way ANOVA. Bonferroni correction was used for post hoc testing. If a ROI could be identified only in one experimental condition, this ROI was utilized also for the other conditions. The significance of the differences between the reaction times for the left and right hand (EMG onset) was estimated with the Wilcoxon-Mann-Whitney test. The significance level was set to $p = 0.05$.

2.3 Results

Already at ~ 120 ms after the onset of a visual cue the LRPrect derivation revealed significant differences between overt and covert movements: Firstly, the LRPrect curve showed a strong downward (i.e., negative) deflection for overt movements over sensorimotor cortices (referred to as latN120) but not for covert movements ("motor imagery" and "quasi-movements). This effect was not evident in frontal or occipito-parietal regions. Secondly, the LRPrect amplitude for covert movements did not significantly deviate from zero. Thirdly, the latN120 effect occurred much earlier than the onset of muscle contraction in the EMG (average ~ 460 ms).

2.3.1 Psychological measures

On average the subjects (N = 18) had "clear and reasonably vivid" motor imagery, as indicated by the kinesthetic motor imagery subscale (mean 2.3, SD = 0.7) of the Vividness of Movement Imagery Questionnaire (Isaac et al., 1986). For more results please refer to Nikulin et al. (2008).

2.3.2 EMG – onset of muscle contraction for overt movements

The single trial EMG onsets were determined in the "overt movements" condition (12 subjects) for the left and right hand performance, respectively. Since most of the data were not normally distributed (Lilliefors test), the median was calculated for all single trial onsets, separately for each hand and subject. There were no significant differences between left hand reaction times (median 470 ms) and right hand reaction times (median 451 ms) across subjects (p = 0.82, Wilcoxon-Mann-Whitney test), see Figure 2.1. Notably, the movement onsets varied considerably in the range from 300–640 ms.

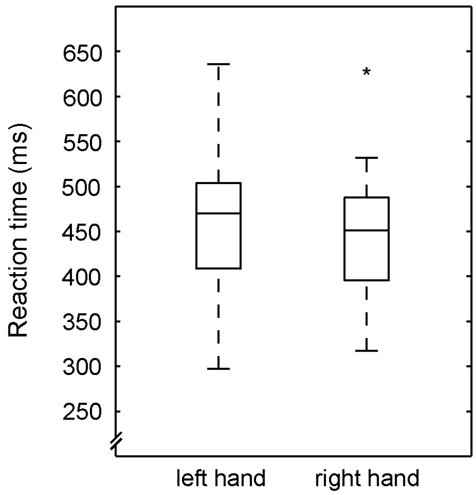


Figure 2.1. Average movement onset in EMG. *The figure shows the median EMG onset across trials in the "overt movements" condition, for all subjects (N=12) and separately for the left and right hand. The lines inside the boxes represent the median, the upper and lower error bars of the boxes show the 25th and 75th percentile, respectively. The maximum length of the whiskers is the median +/-1.5 * the interquartile range, outlier is represented by the star. There were no significant differences between the movement onsets of the left and right hand (p=0.82, Wilcoxon-Mann-Whitney test). However, the movement onsets varied considerably in the range of a few hundreds of milliseconds.*

2.3.3 EEG – hemispheric asymmetry (Lateralized Readiness Potential)

For the "motor imagery" condition 17 subjects were analyzed, 15 subjects for "quasi-movements" (one subject showed strong tonic EMG activation and another subject was excluded because of an insufficient amount of recorded data), and 12 subjects for "overt movements". One subject was completely excluded from the analysis because of not complying with the task instructions and having excessive amount of artifacts in the data. The analysis was focused on the first 150 ms after stimulus onset with respect to differences between overt and covert movements, as reflected by the stimulus-locked lateralized EEG activity. Figure 2.2 shows the grand-average LRPrect derived from the electrodes C3 and C4 (approx. located over the "hand area" of the primary motor cortices). For the "overt movements" condition the LRPrect shows a strong downward (i.e., negative) deflection with a peak latency of 120 ms (latN120), indicating a stronger activation of the hemisphere contralateral to the active hand. The lateralized EEG activity for both imagined and quasi-movements stayed approximately at zero baseline level. The one sample running t-test against zero revealed significant differences in the time range 120–125 ms (p = 0.03 and p = 0.02, respectively) only for the "overt movements" conditions. The average amplitude for each channel was calculated in the time interval of 110–130 ms (i.e., in a symmetric time window around the latN120 peak).

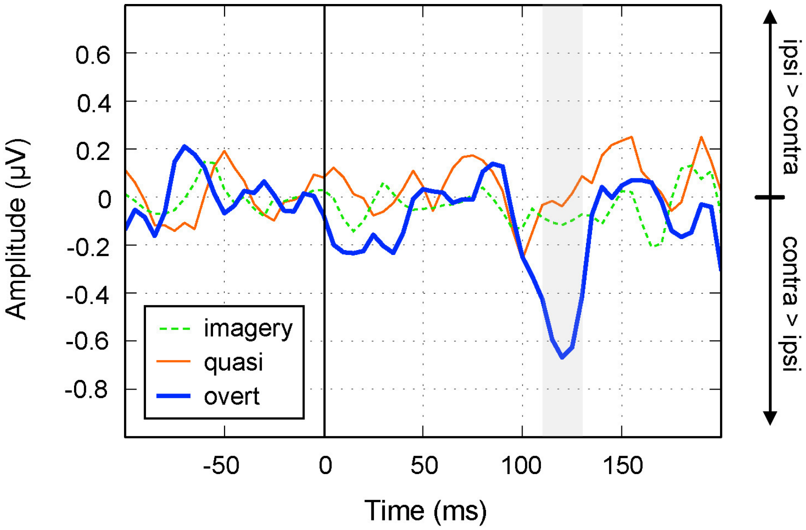


Figure 2.2. Grand-average of stimulus-locked LRPrect.
Overt – overt movements, quasi – quasi-movements, imagery – kinesthetic motor imagery, contra – contralateral hemisphere; ipsi – ipsilateral hemisphere. Zero indicates stimulus onset. Pre-stimulus baseline: 100 ms. Time interval of interest (grey shading): 110–130 ms. The grand-average across subjects is shown for the stimulus-locked LRPrect (from channels C3 and C4). Only for overt movements the LRPrect shows a negative deflection with a peak latency of 120 ms, indicating a stronger activation of the contralateral hemisphere.

A significant region of interest (ROI) could only be identified for the “overt movements” condition, consisting of four neighboring electrodes with a symmetric location over sensorimotor cortices (FFC5h/6h, C5/6, C3/4, CCP5h/6h) without significant frontal or occipito-parietal contribution. The activity in these channels significantly deviated from zero ($p < 0.01$) and the channels also formed a clear spatial cluster in the “overt movements” condition, whereas the “motor imagery” and “quasi-movements” conditions were not associated with significant activations in this early time interval (Figure 2.3).

Subsequently, the ROI amplitude was defined as the local average across the channels FFC5h/6h, C5/6, C3/4, and CCP5h/6h in the 110–130 ms time interval. The same ROI was also taken for both covert movement-conditions, “motor imagery” and “quasi-movements”, respectively. Figure 2.4 shows the grand-average across subjects for the ROI amplitudes from all three conditions. The ANOVA showed a significant main effect of “condition” ($F_{(2,41)} = 5.93$, $p = 0.005$). Post hoc testing showed that the LRPrect amplitude at ~120 ms for “overt movements” (mean ~ -0.55 µV) was significantly larger than the amplitude for “motor imagery” (mean ~ -0.05 µV, $p = 0.03$) and “quasi-movements” (mean ~ 0.06 µV, $p = 0.007$), respectively.

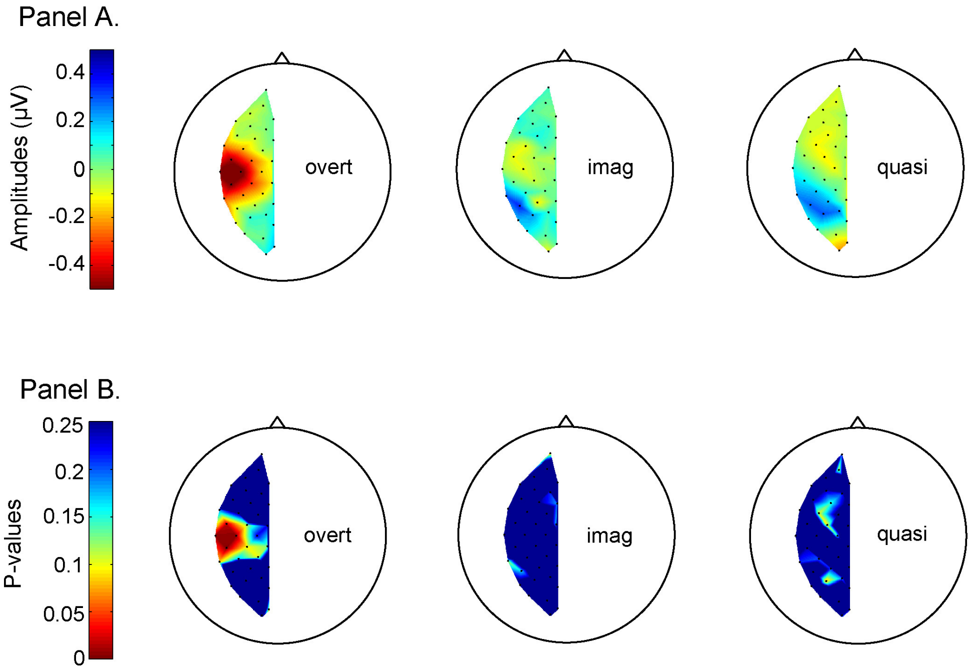


Figure 2.3. Region of interest in LRPrect.

Overt – overt movements, quasi – quasi-movements, imagery – kinesthetic motor imagery.
Panel A. The scalp maps for the grand-average LRPrect are shown (mean across 110–130 ms).
For convenience the scalp maps depict only electrodes on the left hemisphere, which are indicative for the LRPrect derived from the symmetric electrode pairs. The spatial topography demonstrates a spatial cluster only for the "overt movements" condition over sensorimotor cortices (FFC5h/6h, C5/6, C3/4, CCP5h/6h).
No such cluster is apparent for the covert movement-conditions (motor imagery, quasi-movements).
Panel B. When testing the activity of all LRPrect channels against zero (t-test), only for the "overt movements" condition significant deviations from zero were found for FFC5h/6h, C5/6, C3/4, and CCP5h/6h (p<0.01 for all channels). These channels also form a spatial cluster.

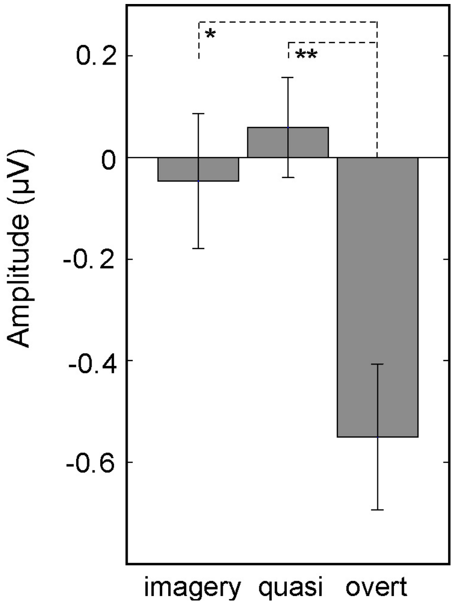


Figure. 2.4. Grand-average of LRPrect region of interest.
Overt – overt movements, quasi – quasi-movements, imagery – kinesthetic motor imagery.
*Bars represent the standard error of the mean. * p<0.05, ** p<0.01 (post hoc Bonferroni).*
The LRPrect is shown for the region of interest (averaged across channels FFC5h/6h, C5/6, C3/4, and CCP5h/6h) in the mean time range 110–130 ms for all experimental conditions.
The "overt movements" condition is significantly different from both covert movement conditions by showing a larger negativity over sensorimotor cortices, which indicates a stronger activation of the contralateral hemisphere than of the ipsilateral hemisphere.

2.4 Discussion

The present results provide evidence for early differences of neural processes between overt and covert movements. Already at 120 ms after the presentation of the instructive visual stimulus, the hemispheric lateralization of stimulus-locked EEG components is different over the sensorimotor cortices. This suggests a modulation of stimulus-processing activity in the sensorimotor cortices by the prior action intention. These results are in line with a growing body of evidence suggesting that imagined movements are not simply the “offline” equivalent of “real” movements (Dinstein et al., 2008; Gabbard et al., 2009; Rodriguez et al., 2008; Rodriguez et al., 2009). Previous results implied a strong similarity of overt and covert movements (Lotze & Halsband, 2006; Munzert et al., 2009) with respect to neural activations at late processing stages (which we defined with respect to movement onset or comparable interval in the case of motor imagery), which is in line with the simulation hypothesis (Finke, 1980; Grush, 2004; Jeannerod, 1994, 2001). However, a similarity in late processing (around or after movement onset) does not necessarily imply similar early neural activation, as the present data demonstrate.

2.4.1 Modulation of early stimulus-locked neural activity in sensorimotor cortices

Usually reaction times after visual cues in simple forced choice settings are on average ~ 400–500 ms (cf. Results and, e.g., Masaki et al., 2004). The present study investigated very early stimulus-locked EEG activity (~ 120 ms) – long before movement onset. For comparison, data from phase-locked as well as non-phase-locked EEG analyses, and monkey single cell recordings will be briefly reviewed with respect to early changes after stimulus onset for overt and covert movements.

Phase-locked EEG (LRP): The stimulus-locked LRP peaks at about 200–600 ms in the case of overt movements (Carrillo-de-la-Peña et al., 2006; de Jong et al., 1988; Eimer, 1998; Galdo-Alvarez & Carrillo-de-la-Peña, 2004; Gratton et al., 1988; Hackley & Valle-Inclán, 1998; Leuthold et al., 2004; Minelli et al., 2007; Wascher & Wauschkuhn, 1996) and for motor imagery at about 240–600 ms after stimulus onset (Carrillo-de-la-Peña et al., 2006; Galdo-Alvarez & Carrillo-de-la-Peña, 2004). Notably, one LRP study (Carrillo-de-la-Peña et al., 2008) demonstrated a two-step LRP activation with an earlier component: A precue informed about left/right hand selection while actual task performance (motor imagery or overt movements; block design) was withheld until a second imperative cue. At about 130 ms after the precue an LRP peak was observed which as expected did not differ in amplitude between both experimental conditions, since the hand was selected in both conditions alike but no task was executed yet. After the imperative cue, which fully specified the finger movement sequence and served as a “Go” signal for starting the performance, a second “late” LRP peak was observed (~ 200–300 ms after imperative cue onset) which was stronger for overt than for imagined movements. The authors interpreted the first “early” LRP as indication of neural processes reflecting hand selection in the sensorimotor cortices. This result is relevant for the present study, since we utilized a fully instructive cue specifying the hand selection. However, in contrast to the previous study, in the present design there was no precue (i.e., no preparatory period without task performance). Instead, the instructive cue required hand selection and immediate task performance, which allows testing differences in early stimulus-driven neural activity related to the performance of unilateral overt and covert movements.

***Non-phase locked EEG*:** When preparing or executing unilateral overt finger movements, non-phase-locked EEG activity (event-related desynchronization, ERD) peaks at about 600 ms after visual stimulus onset (Müller-Gerking et al., 2000; Pfurtscheller & Neuper, 1994), at about 200–900 ms for unilateral motor imagery (Neuper, Müller-Putz et al., 2006; Neuper, Wörtz et al., 2006; Nikulin et al., 2008; Pfurtscheller et al., 1999; Pfurtscheller et al., 2008), and at ~ 700 ms for quasi-movements (Nikulin et al., 2008). Importantly, in all three conditions the stimulus-locked ERD occured focally over the sensorimotor cortex contralateral to the performing hand, and the ERD was strongest and most lateralized for overt movements compared to covert movements, and stronger for quasi-movements than for motor imagery (Nikulin et al., 2008). Importantly, the significant ERD lateralization in the case of covert movements indicates that among possible programming parameters of movement at least hand selection is involved.

Single cell recordings from motor cortex: The “hand-selection” interpretation above is in line with single neuron monkey data, which showed that the primary motor cortex starts discharging as early as 60–80 ms, with a maximum discharge at about 100–150 ms after the onset of a visual cue indicating unilateral hand movements (Georgopoulos et al., 1982; cf. also Requin & Riehle, 1995; Kwan et al., 1985). Comparable latencies of ~ 100 ms are present in motor cortex single cells during a precue period indicating the preparation of subsequent movements in different directions (Riehle & Requin, 1995). Taken together, these data strongly suggest that very early stimulus-locked neural activity in the primary motor cortices might reflect early visuomotor stimulus-response mappings, e.g., left or right hand selection, movement direction or programming of other motor parameters before the motor command is issued (Carrillo-de-la-Peña et al., 2008; Georgopoulos et al., 1982; Requin & Riehle, 1995; Riehle & Requin, 1995).

***Early motor programming (hand selection) and stimulus-response mappings*:**
In the present study we investigated stimulus- (phase-) locked LRP after the onset of a fully instructive visual cue (no precue presented) calling for immediate left or right hand performance of either covert movements (motor imagery, quasi-movements) or overt movements in a block design. Importantly, we demonstrate very early (120 ms) significant lateralized EEG activation only for overt movements but not for covert movements. Importantly, this early peak most likely is not related to movement execution per se, i.e., generation of the motor command. This is because the peak is quite narrow (~ 40 ms), thus indicating a high level of neural synchronization with respect to the stimulus onset. Such transient activation would not be visible if it were locked to the onset of the movement, since the movement latencies varied considerably in a range of hundreds of milliseconds (300–600 ms). Also the early latency of the peak (cf. references above) suggests that it might reflect stimulus-response mapping and/or response selection (left or right hand), in line with the results from Carrillo-de-la-Peña et al. (2008). First we will discuss apparent differences between early modulation of phase-locked and non-phase-locked EEG. Then we discuss the absence of significant early LRP modulation in the case of motor imagery and potential neural mechanisms.

Why no early lateralization (120 ms) for overt movements in the majority of LRP studies (> 200–600 ms)? Importantly, we utilized a different calculation method, i.e., we calculated LRP from *rectified* EEG signals (LRPrect). Importantly, LRPrect indicates only magnitude differences of the individual hemispheres and not polarity. This is especially relevant for EEG processes, where the effect's polarity is unknown or might vary across/within subjects. It might be the case that the very early activation of the contralateral sensorimotor cortex in the present study is very transient and of variable polarity, and therefore is more likely to be extracted by the LRPrect method. Moreover, we used a very simple alternative forced choice task with centralized visual stimuli (in contrast to, e.g., Wascher & Wauschkuhn, 1996), without (partially) informative precues (in contrast to, e.g., Galdo-Alvarez & Carrillo-de-la-Peña, 2004), and in our case only a simple, non-goal directed motor response of unilateral thumb abduction was required (in contrast to button presses, e.g., Hackley & Valle-Inclán, 1998). Possibly very early and transient stimulus-locked effects in the motor system might be well extractable by a simplified experimental design, which eliminates as many potential confounding factors as possible, in combination with a sensitive measure such as the LRPrect.

Why no early lateralization (120 ms) for overt movements in previous ERD studies (> 200–600 ms)? An absence of significant early activity (120 ms) in previous ERD studies (e.g., Müller-Gerking et al., 2000), might be due to the fact that such extremely early, stimulus-induced modulations of (sensori-) motor cortex activity, in our case most likely related to hand selection, are phase-locked, very transient and of small amplitude (compared to the relatively gross modulations of non-phase-locked spontaneous EEG). Such activity might be more likely to be detectable by calculating phase-locked activity such as the LRP. The same argumentation would also hold for absent early ERD changes for motor imagery. Importantly, it has been assumed that overt and covert movements share much of motor programming/planning (e.g., encoding of movement direction, force, body limb) except for the generation of an efferent motor command (Jeannerod, 1994, 2001; Stinear et al., 2006). However, it is an open question whether the *timing* of neural activation related to motor programming and stimulus-response mappings is similar to overt movements, as will be discussed below.

2.4.2 Dissimilarity of early neural processing during overt and covert movements

The present study presents converging evidence from two covert motor processes, where no significant early lateralized EEG peak (120 ms, referred to as latN120) was observable: kinesthetic motor imagery and the recently introduced quasi-movements (Nikulin et al., 2008). Neural correlates of motor representations, related to motor planning, movement initiation, and motor control, are distributed networks in the motor system (Blakemore et al., 2002; Brass & Haggard, 2008; Desmurget et al., 2009; Haggard, 2008; Kühn et al., 2008; Munzert et al., 2009).

Despite frequent findings of overlapping neural substrates for overt and covert movements (Lotze & Halsband, 2006; Munzert et al., 2009), there are open questions concerning the actual *differences* between both tasks in terms of neural processing in the brain on different time scales and the spatial distribution of interacting neural populations. While late stages in neural processing after stimulus onset (i.e., at the time where a movement would occur, after some 300–500 ms) are similar in terms of EEG activation (e.g., contralateral sensorimotor cortex activation in traditional LRP with weaker amplitude in the case of motor imagery; Galdo-Alvarez & Carrillo-de-la-Peña, 2004), very early stages of stimulus-processing might differ, as the present study demonstrated. In the following, different interpretations will be discussed regarding the absence of significant latN120 in covert movements, which might in general contribute to the absence of later muscle contraction.

Why there is no significant early (120 ms) lateralization of stimulus-locked EEG in the case of covert movements? As reviewed above, the very early activity (< 150 ms) in the primary motor (single cell data) and sensorimotor cortices (EEG data) strongly suggest that neural processing at this time most likely reflects stimulus identification and stimulus-response mappings, e.g., hand selection (Carrillo-de-la-Peña et al., 2008; Georgopoulos, 1982; Requin & Riehle, 1995). Interestingly, experimental evidence supported the assumption of “sensory” neurons in the monkey primary motor cortex being reactive not to visual stimuli per se, but only when the stimulus indicated a forthcoming motor response (Requin & Riehle, 1995; Riehle, 1991; Kwan et al., 1985), i.e., such neurons are stronger reactive in stimulus- than in response-locked data which might reflect processes of stimulus identification. Another population of “sensorimotor” neurons, equally reactive in both stimulus-locked and response-locked data, might reflect stimulus-response mappings (Requin & Riehle, 1995).

*1) Multiple response preparation: Effect of block design.* The assumption of the latN120 being related to hand selection is strongly supported by the present experimental design: In a block design (i.e., overt or covert movement conditions) the subjects performed with either the left or right hand. The only movement parameter unknown to the subject was the left/right selection of the hand, as indicated by the randomized visual cue calling for immediate task performance. All other parameters (muscle, force, speed, performance mode: “overt” or “covert”) were fully specified in advance in each block. In fact, (pre-)motor areas can represent multiple response alternatives in advance, i.e., specifying “how to do” before an external stimulus indicates “what to do” (or even both in parallel). The more information accumulates, different competing action alternatives are gradually eliminated until a final decision is made and the response is executed. Such mechanism would allow quick adaptation to continuously changing environmental demands (Bastian et al., 2003; Cisek, 2007; Cisek & Kalaska, 2005). In sum, the latN120 *difference* between overt and covert movements most likely is due to a specific combination of performance mode, i.e., prior action intention (“how to do”: overt movement, motor imagery, quasi-movement with unilateral thumb, speed ~ 2 Hz), and stimulus-induced hand selection (“what to do”: left or right). In the case of overt movements the latN120 might then reflect the early release of an already completely pre-planned action, i.e., the peak reflecting a signal for “left/right decision” and “forthcoming immediate action”, and after this stimulus-response mapping the signal is transmitted to the motor output networks. In the case of covert movements this processing stage might be simply omitted, inhibited, or delayed (see below). Alternatively, for covert movements there might be no motor preplanning in advance, so there is nothing which could be released. However, given experimental evidence of occasional, subliminal EMG responses during covert movements (Guillot et al., 2007; Lebon et al., 2008), it is more likely that covert movements involve motor pre-planning, an assumption also supported by preparatory LRP modulations for motor imagery in delayed response paradigms (Carrillo-de-la-Peña et al., 2008; Kranczioch et al., 2009).

*2) Effect of motor inhibition (reactive vs. preemptive).* (A) *Reactive inhibition*. It has been assumed that motor imagery is basically a fully prepared overt movement minus the motor command (Jeannerod, 1994, 2001; Stinear et al., 2006). The movement is reactively inhibited after stimulus onset. The absence of the LRPrect peak might be indicative of such a reactive inhibitory mechanism. Importantly, based on the peak timing and argumentation above, the target here would be not the blocking the cortico-spinal volley. Instead it might be a prevention of stimulus-response mappings from reaching the motor output networks.

(B) *Preemptive inhibition*. It might be the case that the absence of the LRPrect peak in covert movements reflects the cortical motor system being in an insusceptible mode (subthreshold-idling) in this early time frame, due to a general decrease of excitability. Since all three experimental conditions were presented in different blocks, the brain could fine-tune for the optimal performance of the specific motor task. Such tuning might lead to a *preemptive* movement inhibition (cf. also Jaffard et al., 2008) in the case of covert movements, reflected by the absence of the latN120. The stimulus-response mappings might occur in areas related to higher order motor cognition, for instance, in the parietal cortex (discussed below), while the responsiveness of the motor cortex is modulated by the prior action intention.

The common notion for both accounts (reactive vs. preemptive inhibition) is that the initial activation of the motor cortex, observed only in the “overt movements” condition, might reflect the “openness” of the motor cortex for subsequently activating motor effectors.

3) Effect of time scales. It is an open question whether the *timing* of early stimulus-locked neural activation related to motor planning (e.g., stimulus identification, stimulus-response mappings) is similar between overt and covert movements – an assumption not supported by the present results. This opens the interesting discussion of *when* differences in motor planning might occur (and not *whether* it occurs at all, pre- or post-stimulus time interval). It might be possible that, for instance, hand selection occurs in motor imagery considerably later compared to overt movements, which could be in line with significant ERD/LRP changes starting at 200 ms for motor imagery (e.g., Galdo-Alvarez & Carrillo-de-la-Peña, 2004; Pfurtscheller et al., 2008). It might also be possible that the hand selection occurs at about 120 ms, but elsewhere (e.g., parietal cortices). Furthermore, it might be the case that motor planning in covert movements does not occur in advance, as for overt movements, but instead begins *after* stimulus onset, which would also cause a delay and some variability in the neural responses.

In general, it is important to note that it is an implicit assumption of these interpretations, that motor planning (motor selection and specification) and executive stages are sequentially dissociable. However, it might also be the case that motor performance is based on parallel rather than sequential processing (Cisek, 2007), in addition to the possibility that neural stimulus-processing operates on different time scales for covert and overt movements. Yet there is an important serial aspect in the present data, since the LRPrect peak is tightly synchronized to the stimulus, and that certain aspects of motor planning (e.g., final response selection and “openness” of the motor cortex for subsequent execution) cannot occur *before* the external stimulus. Importantly, the present data strongly suggests that the prior action intention (overt vs. covert) modifies such early stages of stimulus-processing in the sensorimotor networks.

Another important notion concerns our initial hypothesis of quasi-movements representing an intermediate stage in a continuum between imagined and overt movements (cf. Jeannerod, 1994, 2001) in terms of neural processing, as suggested by previous results on alpha-ERD with latencies > 700 ms (Nikulin et al., 2008). However, the present study clearly demonstrated that very early stimulus-processing (120 ms) is not scaled in a similar way – significant LRPrect activation is present only in the “overt movements” condition. Therefore, one might assume that the time scale of neural processing is crucial for the interpretation of similarities/differences between neural correlates of overt and different types of covert movements.

2.4.3 Implications for studies of motor representation and action intention

Previous studies have implied that overt, covert, and observed actions engage common motor representations (Finke, 1979; Jeannerod, 1994, 2001). These representations are differentially engaged, depending on the action intention (Haggard, 2005). It seems intuitively appealing to identify the main difference between motor imagery and executed movements with inhibitory mechanisms suppressing the motor output. However, this notion is challenged by the case study of patient CW, who had bilateral parietal lesions after stroke. While performing motor imagery CW was not aware that he actually executed the movements (Schwoebel et al., 2002; Wilson, 2003). This study and others strongly suggest that the parietal cortices are crucial for higher motor cognition, for instance, forming movement intentions (overt vs. covert), sensorimotor integration, and motor inhibition (Andersen

& Buneo, 2002; Hesse et al., 2006; Lotze & Halsband, 2006; Rushworth et al., 2003; Thoenissen et al., 2002).

On the basis of our EEG results, we assume that already the prior intention (Brass & Haggard, 2008; Haggard, 2008; Majdandzić et al., 2007; Pacherie, 2008) can put the motor system into a “covert” or “overt” mode of brain functioning (Jaffard et al., 2008; Raichle et al., 2001; Raichle & Snyder, 2007). This default brain mode would then influence all neural stages in the information processing chain. The present results suggest that the operational modes (“overt-external” vs. “covert-internal”) involve different neural processing – not only at the relatively late stages of task performance (i.e., around muscle contraction), but already at the initial processing stages.

2.4.4 Outlook

The results of the present study demonstrate that “movements in the mind” differ from “real movements” already at the first 120 ms after an instructive visual stimulus. Importantly, this difference is not related to the execution of the movement per se, it rather indicates dissimilar stimulus processing at early stages of response selection and stimulus-response mapping in the motor system, probably modulated by the prior action intention. However, later neural activations can be anatomically and functionally equivalent, as shown in previous studies. Further research might focus on neural correlates of prior action intention in the primary and secondary motor cortices.

Acknowledgements

FH is supported by the Berlin School of Mind and Brain. VVN and GC are partially supported by the Berlin Bernstein Center for Computational Neuroscience.

2.5 Appendix

2.5.1 Lateralized Readiness Potentials from rectified EEG signals (LRPrect)

Theoretically eight cases are conceivable for constituting different amplitude aspects of a given LRP curve, as graphically demonstrated in Figure 2.5. Some of the cases might appear counterintuitive, but can be explained for instance by suboptimal electrode placement with respect to the source, or the source does not have a radial orientation with respect to the recording electrode (cf. Figure 2.6 for dipole simulations).

For the traditional LRP different calculation methods have been introduced that are mathematically equivalent (Eimer, 1998). Regardless of the calculation, the LRP emphasizes hemispheric polarity differences, whereas the LRPrect is complementary by considering only magnitude differences. The complementing features of both approaches become clear in Figure 2.5, where the LRP and LRPrect are identical in two out of eight cases. In the other cases the measures emphasize different aspects of the neuronal processing in the hemispheres.

The virtue of the LRPrect becomes clear in situations such as case 4 in Figure 2.5 (panel 4, upper row), as an example of the performance of unilateral overt or covert movements. The recording electrode, located over the contralateral motor cortex, shows strong positivity whereas the symmetric ipsilateral electrode shows weak negativity. The traditional LRP shows an upward deflection indicating “ipsi more negative than contra”, which would be interpreted as an incorrect motor response (e.g., left hand preparation for right stimulus).

However, the unexpected positivity in the contralateral hemisphere (e.g., electrode C3 for right hand performance) might simply arise from a neuronal source which does not have a radial orientation with respect to the electrode, as illustrated by the dipole simulations in Figure 2.6. In such a case, the projection of the electrical field is different from the unipolar orientation with respect to the surface. Therefore, a bipolar field is visible in the EEG derivations, and the C3 detects a positive field. However, since the LRPrect does not consider polarity but only source strength, it would reflect “contra > ipsi”, being interpreted as correct motor response. In general, EEG data show large intra- and inter-subject variability in signal polarity, for instance due to:

a) anatomical variations in source orientation in the cortex and its corresponding electric fields,

b) suboptimal electrode placement over the source due to EEG cap position and variations in head size, or

c) superposition of local and global source activity.

The LRPrect measure is complementary to the traditional LRP, allowing the unambiguous evaluation of the magnitude differences in the individual hemispheres.

Figure 2.5. Exhaustive case distinction for constituting the LRP and LRPrect. Contra, c – contralateral hemisphere, ipsi, i – ipsilateral hemisphere, a.u. – arbitary units. All logically possible cases are shown which can constitute the LRP.
The first column (per row in a panel) shows the amplitude in the contralateral hemisphere and the second column the ipsilateral hemisphere (blue lines). Rectified values (i.e., taking absolute values) are indicated by the green dotted lines. The third column shows the subtraction of the contralateral values from the ipsilateral values (blue line), and the same for the rectified values (green dotted line). The fourth column shows the traditional LRP (blue line) and the LRPrect (green dotted line). A downward deflection depicts more negative values for the contralateral hemispheres in the case of the traditional LRP, and a stronger magnitude of the values in the case of the LRPrect (and vice versa for an upward deflection). For simplicity, this is indicated by “c>i” and “i>c”, respectively. The inversion of the values for LRPrect (i.e., (|c|-|i|)*-1) is done for the convenience of having a downward deflection for both measures in the case of “contra stronger ipsi”.

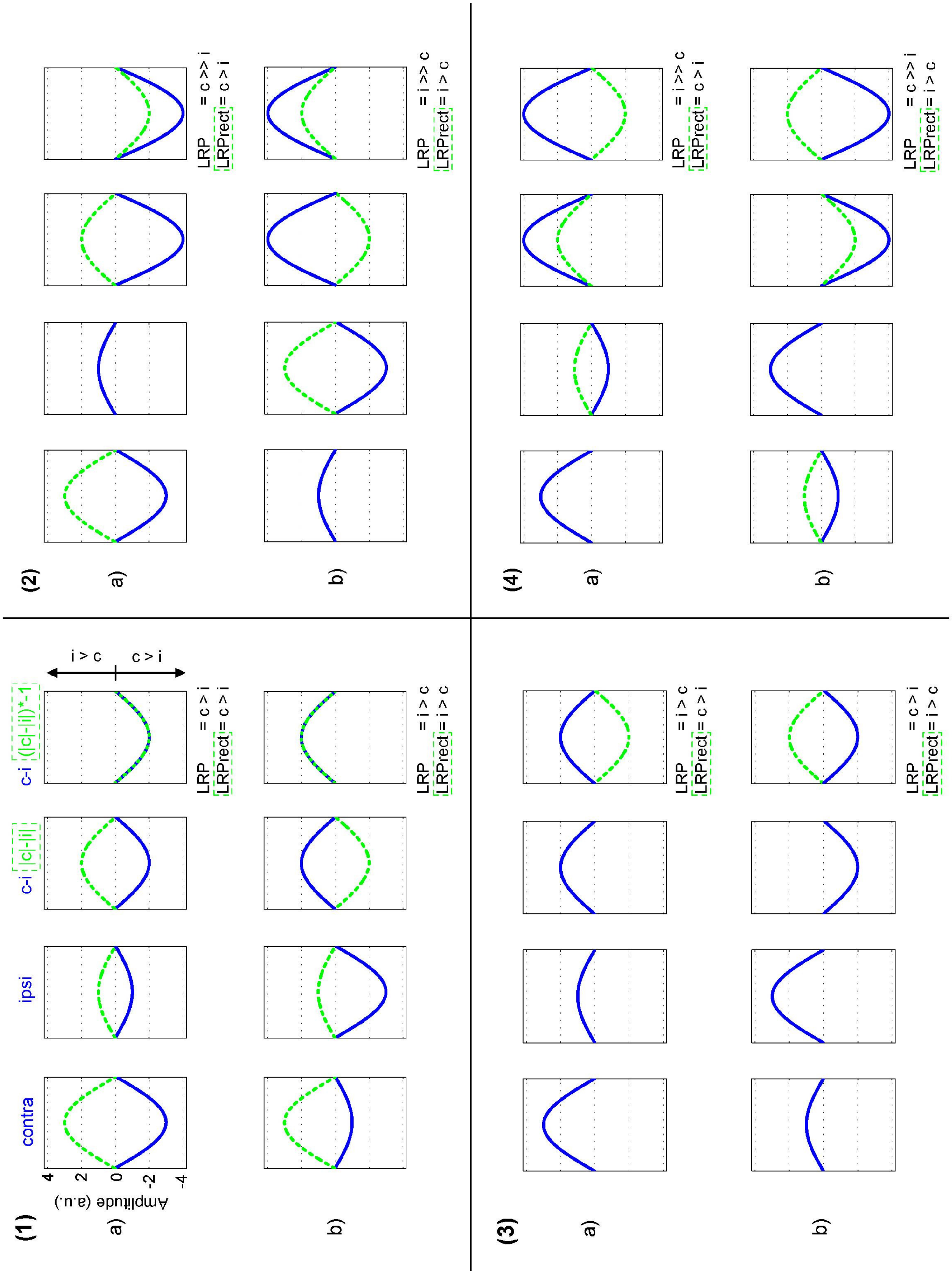
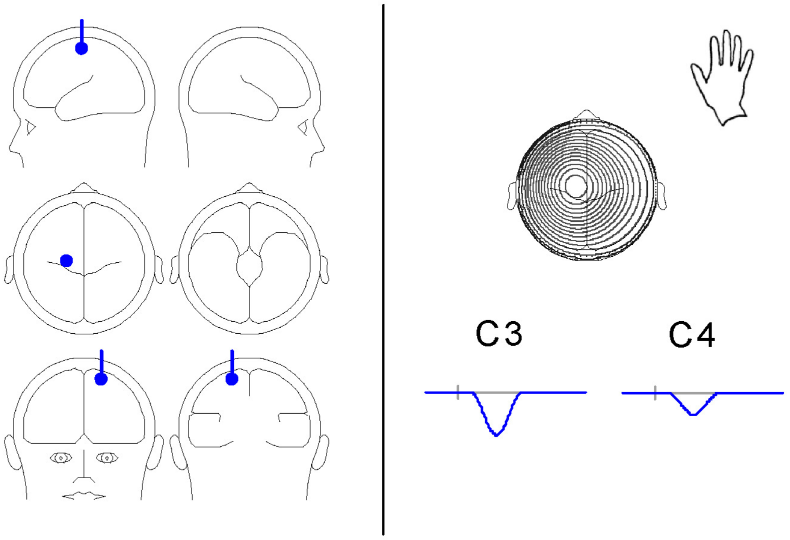


Figure 2.5. Exhaustive case distinction for constituting the LRP and LRPrect.

(A) Radial source orientation, contralateral motor cortex



(B) Tilted source orientation, contralateral motor cortex

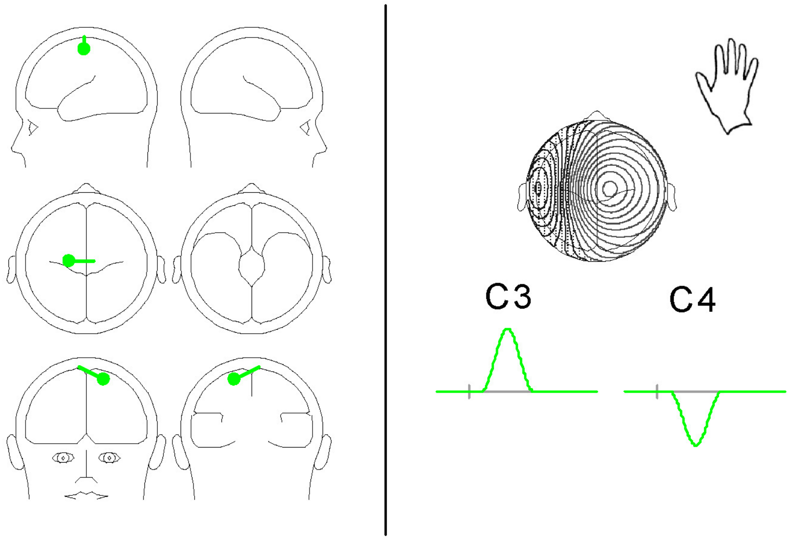


Figure 2.6. Dipole simulation.

Panel A. In the case of overt or covert unilateral hand movements (here the right hand), there is a negativation of the contralateral surface EEG electrode over the “hand” area of the primary motor cortex (C3).

Panel B. A tilt in the orientation of the neuronal source (away from the radial position) gives rise to a *positive* signal in the surface electrode C3.

Figures were created by DipoleSimulator software, (c) P. Berg (2009).

Chapter 3

III. STUDY 2

Detection of weak motor responses in covert movements – comparing automatic procedures and visual inspection

Parts of the text and results have been published in:
Quasi-movements: A novel motor-cognitive phenomenon.
Neuropsychologia (2008), 46, 727–742

Friederike U. Hohlefeld[1,2,3], Vadim V. Nikulin[2,4], Arthur M. Jacobs[3], Gabriel Curio[2,4]

1) Berlin School of Mind and Brain, Berlin, Germany
2) Neurophysics Group, Department of Neurology,
Charité – University Medicine Berlin, Germany
3) Department of Psychology, Free University Berlin, Germany
4) Bernstein Center for Computational Neuroscience, Berlin, Germany

Abstract

It is assumed that covert movements, for instance motor imagery (i.e., mental simulation of movement-related proprioceptions), involve central neural processing in the brain without activation of the target muscle. Frequent studies utilize covert movements for investigating movement organization in the brain, since studies involving overt movements are always challenged by the fact that the recorded signals represent a mixture between efferences (movement preparation, motor command) and afferences from the moving limb. Furthermore, covert movements are frequently utilized for brain-computer interfacing (BCI): for instance, the discrimination of brain states related to left or right hand motor imagery enables the control of external devices without the need of muscle activation. This paradigm is often studied in healthy subjects in order to develop algorithms and experimental paradigms for paralyzed patients. Importantly, the prerequisite for a covert movement is the absence of muscle contraction, e.g., in electromyography (EMG), therefore monitoring the muscle activity and identifying trials with motor responses is of critical importance for data analysis and interpretation.

In the present study we investigate different methods (statistical, automatic, and visual inspection) for detecting occasional motor responses in EMG and accelerometer recordings during two different types of covert movements, i.e., motor imagery and quasi-movements (introduced by Nikulin et al., 2008) in different muscles contributing to unilateral thumb movements (e.g., abductor pollicis brevis, APB).

Extensive single trial analysis of EMG and accelerometer data of the different muscles demonstrated the absence of detectable motor responses during the performance of quasi-movements and motor imagery in the majority of trials. Notably, we demonstrate the superior recording sensitivity in the case of APB muscle for EMG monitoring of thumb movements. Moreover, our results suggest visual EMG inspection as advantageous strategy compared to automatic procedures for the detection of weak and transient motor responses occasionally present in covert movements.

Keywords: Abductor pollicis brevis, APB, Brain-computer interface, EEG, EMG, intention, motor cortex, motor imagery

3.1 Introduction

Executed movements are the only known natural way by which individuals are able to communicate with the environment. This includes a broad repertoire of motor activities such as skilled limb and finger movements, locomotion, eye movements, vocalization etc. We define movement performance as a sequence of neuronal activations related to carrying out a motor intention, which culminates in the contraction of a muscle. The latter is also referred to as movement execution or motor response. However, there are examples when the activation of neuronal motor structures does not produce a motor response, i.e., in the case of so-called covert movements. For instance, patients with neuromuscular impairments intend and try to execute a movement but do not succeed because of damage in the central or peripheral nervous system. Another example is kinesthetic motor imagery, which is defined as mental simulation of a movement without activation of the effectors (Decety, 1996; Guillot & Collet, 2005; Haggard, 2005; Jeannerod, 1994, 1995, 2001; Lotze & Halsband, 2006; Michelon et al., 2006; Neuper et al., 2005). However, kinesthetic motor imagery differs in one important aspect from the mentioned pathological cases – there is no intention to execute a movement. Another covert movement type is the novel skill “quasi-movements” (introduced by Nikulin et al., 2008), which are neither movement execution nor motor imagery. Quasi-movements are defined as volitional movements which are minimized by the subject to such an extent that finally they become undetectable by objective measures of muscle activity, e.g., electromyography (EMG). The performance of quasi-movements requires training: Healthy participants learn to minimize movement strength until EMG activity is indistinguishable from the resting baseline.

Summarizing, covert movements has been frequently shown to involve central neural processing in the brain, especially in the sensorimotor cortical and subcortical networks, showing a substantial overlap with those areas active during the execution of overt movements (review: Lotze & Halsband, 2006; Munzert et al., 2009), yet per definition covert movements should not involve the activation of the target muscle. Importantly, covert movements are frequently used in studies investigating movement organization in the brain, since recordings of brain activity during overt movements are always challenged by the fact that the recorded signals represent a mixture between efferences (movement preparation, motor command) and afferences from the moving limb (see also the distinction between two types of neural activity discussed below).

Covert movements are also frequently utilized for brain-computer interfacing (BCI): for instance, the discrimination of EEG patterns associated with left or right hand motor imagery enables the control of external devices without the need of muscle activation. The motor imagery-based BCI is often studied in healthy subjects for developing algorithms and experimental paradigms for paralyzed patients.

Notably, in principle two types of neural activity in the brain could serve as signal for BCI:

a) *Type 1*: Modulations of neural brain activity which *cannot* be predicted on the basis of external events occurring outside of the brain, e.g., associated with attention or mental imagery.

b) *Type 2*: Modulations of neural brain activity which are predictable on the basis of external events, e.g., associated with visual stimulation and sensory input in general or proprioceptive feedback in the case of movements.

Ideally, a “genuine” BCI should only rely on Type 1 neural activity. However, practice is often challenged by Type 2: For instance, given the occasional EMG responses in the case of motor imagery, it is not clear whether BCI control is achieved by imagery-related brain activity (Type 1, top-down) or by modulations in brain activity due to peripheral feedback from the joints, skin, and muscle receptors (Type 2, bottom-up).

These notions emphasize the necessity for EMG-monitoring of the muscle activity in studies involving covert movements, especially BCI (Vaughan et al., 1998). The identification of trials containing motor responses is of critical importance for data analysis and interpretation. Therefore in the present study we investigated different methods (and visual inspection, statistical and machine learning methods) for detecting occasional motor responses in EMG and accelerometer recordings during two different types of covert movements, i.e., motor imagery and quasi-movements in different muscles contributing to unilateral thumb movements. The present study is also of relevance for the ongoing debate on whether automatic procedures are advantageous compared to visual inspection (Hodges & Bui, 1996; Reaz et al., 2006), and in contrast to previous studies testing different methods on overt movements with (moderately) strong motor responses (Castellini et al., 2009; X. Li et al., 2007), i.e., with a relatively high signal-to-noise ratio, we address this issue in the case of *weak and transient* motor responses occasionally present in covert movements.

We compare the sensitivity of the different methods and hypothesized that a) that EMG monitoring is more suitable than accelerometer (higher sensitivity for measures of electrical muscle activity than for measures of physical displacement), and b) that compared to other muscles contributing to thumb movements, the APB muscle is most suitable for the detection of possible motor responses in EMG, since APB is a flat, superficially located muscle. Therefore even its smallest activations are detectable in EMG since the contracting muscle fibers are close to the recording surface electrode, resulting in a better signal-to-noise-ratio (Roeleveld & Stegeman, 2002; Roeleveld et al., 1997).

3.2 Methods

In this investigation I will report on the control experiments with additional subjects for the study of Nikulin et al. (2008). For the results from the other subjects and the discussion of the main experiment (regarding EEG data, brain state classification for BCI, EMG data analysis from APB muscle, task ratings) please refer to Nikulin et al. (2008) and my diploma thesis (Hohlefeld et al., 2006).

3.2.1 Participants

Two subjects (age 24 and 34 years, 1 male) without any history of neurological or psychiatric disorders participated in the present study and gave informed consent. Both subjects were right-handed according to the Edinburgh Handedness Inventory (Oldfield, 1971) and had corrected-to-normal vision.

3.2.2 Tasks and stimuli

Please refer to Study 1, Chapter 2.2.2.

3.2.3 Experimental conditions

For details please refer to Study 1 (Chapter 2.2.2) and Chapter 1.3.3. Experimental procedures were approved by the Ethics Committee of Charité – University Medicine, Berlin, Germany.

3.2.4 Data acquisition

EMG data were recorded with Ag/AgCl electrodes, using BrainAmp amplifiers and BrainVision Recorder software (Brain Products GmbH, Munich, Germany), and were band-pass filtered between 0.1–250 Hz and digitized at a rate of 1000 Hz. EMG was recorded from the left and right APB with one electrode located over the muscle belly and the other over the proximal base of the phalanx. For the offline analysis EMG data was high-pass filtered at 10 Hz. In addition three other muscles were recorded contributing to the thumb movement (one extensor, two flexors): In one subject the right and left extensor pollicis brevis (EPB) and flexor pollicis longus (FPL) muscles were recorded in addition to APB. In another subject the right and left EPB and flexor pollicis brevis (FPB) muscles were recorded together with APB. In these two subjects we also recorded the movement of the left thumb with an accelerometer (model BP-BM-40, Brain Products GmbH, Munich, Germany) with the sensitivity 300 mV/g and the threshold 0.0002 g, where g is 9.8 m/s^2. The accelerometer was a one-dimensional sensor and was positioned on the proximal phalanx of the left thumb with the principal measurement axis being adjusted along the direction of abduction. Although the sensor was one-dimensional it could detect any tangential component of acceleration, which fitted the goal of our measurements – to detect possible movements but not to reconstruct the trajectory. Since both subjects were right handed, the left thumb was chosen since we would expect more motor responses in the non-dominant hand.

3.2.4 Data analysis – automatic classification

An automatic classification of EMG and ACC epochs was performed on the basis of root-mean square (RMS) values in the post-stimulus interval (epoch ranging from 70–3300 ms), in order to discriminate between the “left” and “right” stimulus class (i.e., left or right hand performance of imagined, quasi- or overt movements). The classification procedure is essentially the same as utilized for the EEG brain state classification (cf. Blankertz et al., 2007; Nikulin et al., 2008; Shenoy et al., 2006): The logarithm of variance (i.e., RMS) was calculated for each epoch for each hand, and then the epochs were classified by Linear Discriminant Analysis (LDA; Fisher, 1936; Friedman, 1989) whether belonging to the “left” or “right” stimulus class. LDA, a frequently used method for brain state and EMG classification (Blankertz et al., 2008), yields the optimal (minimized least squares error) linear separation between two (or more) classes by minimizing the within-class variance and maximizing the between-class variance. The LDA discriminant function is also referred to as “classifier”, which describes the optimal separation between classes.

The classification is verified by a cross-validation procedure: The main idea is to use one part of the data set for training the classifier, and to test the classifier on the other part, i.e., how well the classifier performs on “new” data not used for the training. The data set containing all epochs was divided into eight non-overlapping parts, then the linear classifier was trained on 7/8 of the set and tested on the remaining 1/8. This procedure was run eight times, and in each run the percentage of misclassified epochs (left class erroneously as right class and vice versa) was calculated for the test data set. After all runs the percentage values of misclassified epochs were averaged, referred to as “classification error”. A zero classification error corresponds to the perfect classification of motor responses belonging to the “left” and “right” class, whereas the classification error of 0.5 refers to random classification of the two classes. The 95% confidence intervals for the classification error of 0.5 were obtained by Monte Carlo simulations.

3.2.6 Data analysis – statistical comparison

In order to test for the presence of motor responses in EMG and ACC in the “motor imagery” and “quasi-movements” conditions, two statistical analyses were performed: First, the averaged power values of the pre- (-1000–0 ms) and post-stimulus (70–3300 ms) intervals were compared separately for each condition and hand. Secondly, the averaged power values of the post-stimulus interval were compared between conditions, separately for each hand. For both analyses the Wilcoxon-Mann-Whitney test was used. The reason for applying this non-parametric test was the fact that the RMS values were not normally distributed. The significance level was set to $p = 0.05$.

3.2.7 Data analysis – visual inspection

The power values of EMG and ACC data were segmented into epochs ranging from 70 to 3300 ms with respect to stimulus onset. Each single epoch was visually inspected by the researcher, separately for the left and right hand. Importantly, during the inspection the researcher did not know whether a given epoch belonged to the “left” or “right” stimulus class, therefore avoiding possible bias for the detection of motor responses. Some epochs contained excessive amounts of background muscle activity and were excluded from the analysis since they compromised the ability to detect weak motor responses. We quantified the amount of epochs containing motor responses with the “detection rate”: the percentage of the total number of epochs with correct motor responses to the total number of epochs. Epochs with correct motor responses were those with only left hand movements detected for the “left” class epochs, and only right hand movements for the “right” class epochs (i.e., only unilateral hand activation with respect to the target stimulus). For the “overt movements” condition the detection rate should be 100 %, while for the “motor imagery” and “quasi-movements” conditions the detection rate should be rather small.

Visual detection involves the identification of a motor response depending on the following characteristics: sharp onset of the peak, larger magnitude compared to the pre-stimulus baseline (e.g., 15 µV peak compared to 3 µV baseline in the case of

EMG) and duration (e.g., > 50 ms compared to ~ 10 ms of tonic muscle activation in EMG). Visual detection is a subjective procedure and the thresholds are naturally difficult to verbalize, nevertheless studies have demonstrated a high reliability of the ratings across several days and high accuracy compared to automatic methods (Hodges & Bui, 1996).

3.3 Results

Figure 3.1 depicts the average EMG and ACC activity in a single subject for left hand performance in all three experimental conditions, averaged across epochs (similar results for the other hand and for the other subject).

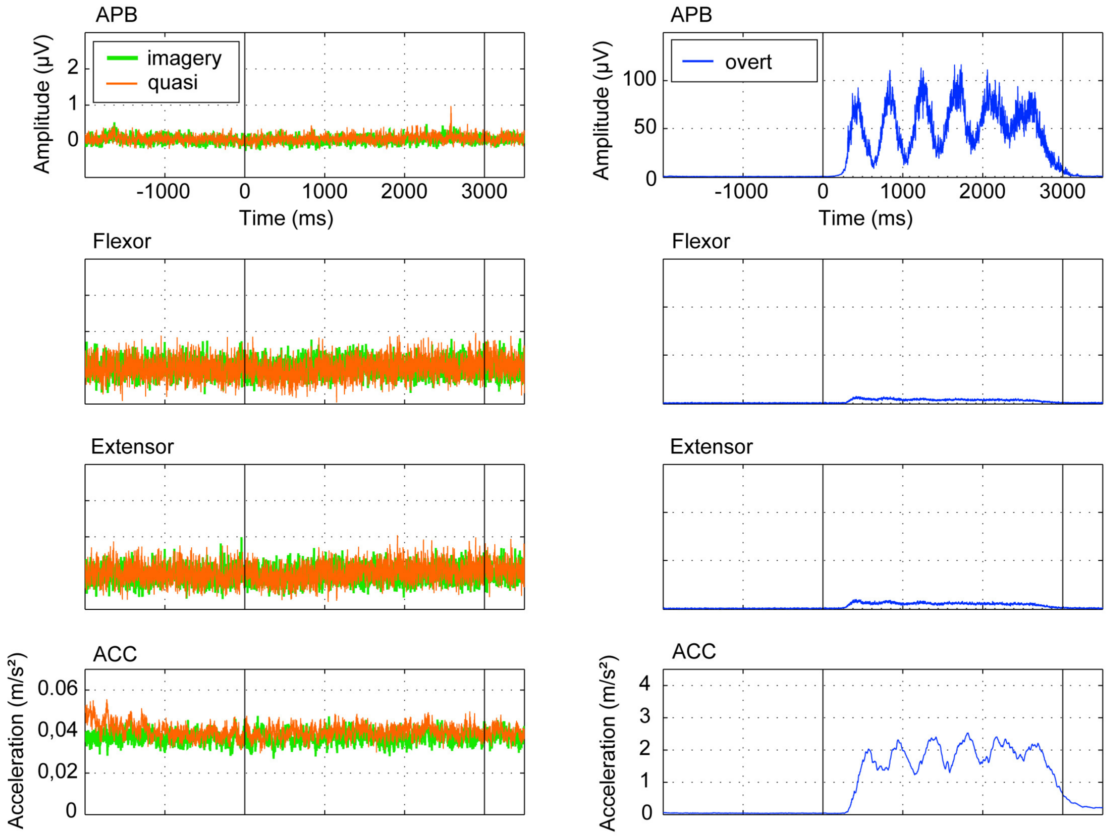


Figure 3.1. Single subject (S16) data, averaged across epochs, from EMG and accelerometer recordings during left hand performance (thumb movement). *APB – abductor pollicis brevis; ACC – accelerometer; imagery – motor imagery; overt – overt movements; quasi – quasi-movements.*

Figure 3.1 illustrates that for both the “motor imagery” and “quasi-movements” conditions the EMG and ACC activity is at baseline level during task performance in all three muscles (APB, flexor, and extensor). In the case of overt movements the

APB and ACC recordings from the thumb show clear motor responses, while the other two muscles did not show such strong motor activity. Notably, in the "overt movements" condition the amplitude of EMG responses in the additionally measured muscles (extensor and flexors) was at least two times smaller (range 2–14 times) than the amplitude of APB responses, which could indicate both stronger activation and superior recording conditions for the latter one (cf. also Figure 3.1 and Table 3.1). The results from the visual inspection were confirmed by objective machine learning methods and statistical comparisons.

3.3.1 Automatic classification

The LDA and cross-validation procedures revealed that the discrimination between "left" and "right" single trials both in the "motor imagery" and the "quasi-movements" condition was at chance level for all three muscles (APB, flexor, extensor) and for ACC recordings, cf. Table 3.1. In the "overt movements" condition the classification error was very low with an average error of ~ 0.2, (i.e., only 2 % of misclassified epochs). The non-zero error in the case of overt movements could be due to the subject missing one stimulus or performing with the wrong hand.

Condition/muscle	Subject	APB	EPB	FPL	FPB	A/E/F	ACC
Motor imagery	S16	0.51	0.46	0.44	--	0.48	0.44
	S11	0.57	0.56	--	0.53	0.55	0.55
Quasi-movements	S16	0.49	0.49	0.5	--	0.5	0.49
	S11	0.5	0.48	--	0.51	0.56	0.55
Overt movements	S16	0.01	0.01	0.04	--	0.01	0.02
	S11	0.02	0.02	--	0.02	0.02	0.02

Table 3.1. Mean classification error of EMG and movement acceleration in the post-stimulus interval. *APB – abductor pollicis brevis, EPB – extensor pollicis brevis, FPL – flexor pollicis longus, FPB – flexor pollicis brevis, A/E/F – classification based on the combination of all three muscles, ACC – accelerometer, (--) the muscle was not measured in this subject. For the "motor imagery" and "quasi-movements" conditions none of the classification errors significantly deviated from 0.5, i.e., the classification of "left" vs. "right" single trials was at chance level.*

In the case of "motor imagery" and "quasi-movements" conditions the classification error was also at chance level even when utilizing the combined the data from all three muscles for classification. Please note that some deviations from the 0.5 value were random (p > 0.05), as found on the basis of confidence levels obtained with multiple random permutations of the values belonging to the “left” and “right” class.

3.3.2 Statistical comparison

The following Table 3.2 depicts the pre- and post-stimulus RMS values from the different conditions and muscles/ACC.

Cond./ muscle	**Subj.**	**APB L**	**APB R**	**EPB L**	**EPB R**	**FPL/B L**	**FPL/B R**	**ACC L**
Motor imagery	S16							
	pre	1.45	1.53	3.29	1.63	3.33	1.05	43495.14
	post	1.47	1.51	3.34	1.61	3.37	1.05	43501.19
	S11							
	pre	1.90	1.65	2.43	2.80	3.28	2.27	308.43
	post	1.88	1.64	2.45	2.79	3.29	2.29	305.73
Quasi-movem.	S16							
	pre	1.51	1.66	3.64	1.90	3.97	1.17	45974.43
	post	1.54	1.68	3.70	1.92	3.98	1.18	45979.97
	S11							
	pre	1.59	1.67	2.54	3.15	3.19	2.18	1252.37
	post	1.61	1.66	2.56	3.13	3.19	2.19	1257.92
Overt movem.	S16							
	pre	1.53	1.75	3.22	2.33	3.12	1.71	4971.37
	post	103.70	65.71	9.46	13.45	7.29	7.49	49619.48
	S11							
	pre	1.85	1.59	2.50	3.07	3.15	2.27	581.34
	post	41.51	31.77	8.31	9.03	20.42	15.53	2198.99

Table 3.2. Mean RMS values (µV) of EMG and ACC recordings.
APB – abductor pollicis brevis, EPB – extensor pollicis brevis, FPL – flexor pollicis longus, FPB – flexor pollicis brevis, ACC – accelerometer, pre – pre-stimulus interval (-1000–0 ms), post – post-stimulus interval (70–3300 ms), RMS – root mean square values, L = left hand activation for the “left” stimulus class, R = right hand activation for the “right” stimulus class.

The most important analysis was pre- vs. post-stimulus comparison – whether there is an increase of activity during the performance of “motor imagery” or “quasi-movements” compared to the resting baseline before stimulus onset. The testing revealed that there were no significant differences between the pre- and post-stimulus EMG/ACC activity within each condition, muscle, hand, and subject (p > 0.05).

Another interest was the comparison of the muscle activity *between* both conditions, separately for the pre- and post-stimulus intervals and hands. Summarizing, out of 28 comparisons (4 data sources for the left hand, 3 data sources for the right hand, 2 intervals, 2 subjects) 13 comparisons were significant ($p < 0.05$), where 11/13 times the EMG or ACC activity was slightly stronger for the “quasi-movements” condition than for “motor imagery”. This slightly increased activity was present in both the pre- and the post-stimulus intervals, indicating that the performance of quasi-movements might be associated with a slight general increase of baseline muscle activity (cf. also Table 3.2 for RMS values). However, this tendency was not present in the analysis of the EMG data from 15 other subjects, cf. Nikulin et al. (2008).

3.3.3 Visual detection of motor responses

Table 3.3 shows the results of the visual inspection of EMG and ACC single trials (detection rate).

Condition/muscle	Subject	APB	EPB	FPL	FPB	ACC
Motor imagery	S16	6 %	1 %	2 %	--	1 %
	S11	4 %	3 %	--	3 %	1 %
Quasi-movements	S16	8 %	3 %	2 %	--	0 %
	S11	3 %	4 %	--	3 %	3 %

Table 3.3. Visual detection of motor responses (detection rate).
APB – abductor pollicis brevis, EPB – extensor pollicis brevis, FPL – flexor pollicis longus, FPB – flexor pollicis brevis, ACC – accelerometer, (--) the muscle was not measured in this subject. The detection rate (i.e., percentage of epochs with detected motor responses) is given for the left hand performance in ACC, and averaged across left and right hand for EMG recordings.

As expected during the performance of covert movements only few epochs (mean = 3 %, range 1–8 % out of 108 epochs) contained detectable motor responses. Importantly, when comparing the different muscles with ACC recordings it becomes clear that the EMG recording of the APB muscle has a slightly higher detection rate than the other data sources, indicating this recording as being the most sensitive. Furthermore, in most of the cases the detection rate in ACC recording is lower (8 out of 12 cases) or equal (4 out of 12 cases) to the detection rate in EMG of any muscle contributing to the thumb movement.

Summarizing, the present analyses demonstrated that in the case of automatic classification and statistical comparison of pre- and post-stimulus muscle activity in covert movements, there were no significant motor responses in EMG and ACC recordings. In contrast, visual inspection by an expert revealed that on average there were detectable motor responses in 3 % of the epochs, and the detection rate was higher in EMG recordings than in ACC. The highest detection rate, i.e., highest sensitivity, was in the EMG recordings of the APB muscle.

3.4 Discussion

In the present analysis we tested different muscles (APB, extensor pollicis brevis, flexor pollicis longus/brevis) for their contribution to the performed task, i.e., left or right thumb abduction contingent upon an instructive visual stimulus. By this we addressed the possible scenario that even if there are no detectable motor responses in the APB muscle during the performance of imagined and quasi-movements, there might be residual EMG activation in *other* muscles contributing to thumb movements. We also addressed the concern whether the accelerometer recording is more suitable for the detection of APB activations than the surface EMG. We discuss our results with respect to the ongoing debate on whether automatic detection methods are preferable over visual inspection.

The present results have implications for studies involving covert movements in general, since per definition covert movements should not involve muscle contraction, therefore the monitoring of muscle activity is a necessity. The absence of motor responses is also crucial for the operation of a BCI, since the self-paced modulation of brain activity should not rely on peripheral muscle activity.

In our study the APB muscle showed the highest signal-to-noise ratio and is optimal for determining motor responses in the case of thumb movements, compared to other, more distant muscles also contributing to thumb movements.

3.4.1 Automatic classification of motor responses

Summarizing, the results of the automatic single trial classification showed that the discriminability of the “left” and “right” class trials on basis of EMG was at chance level (i.e., classification error of ~ 0.5) both for the “quasi-movements” and “motor imagery” conditions. This classification at chance level was present in all three muscles (separately and combined classification), as well as in the accelerometer recordings. Taken together, the random classification in all data sources suggests that the recordings of different muscles (or accelerometer) in addition to the target APB muscle did not improve the detection of possible motor responses in the "quasi-movements" and "motor imagery" conditions. Therefore, in order to minimize experimental effort we suggest that it might be sufficient to perform recordings from the most sensitive muscle (in the present case APB).

Automatic EMG classification is frequently utilized in BCI research and for prosthesis control (Chen et al., 2010; Castellini et al., 2009; Vaughan et al., 1998). Such machine learning techniques or threshold-based approaches (cf. Abbink et al., 1998) overcome the disadvantage of laborious singe trial visual inspection. However, the automatic procedures strongly depend on the signal-to-noise level of the motor responses. This is not a crucial issue for prosthesis control, since EMG is measured from remaining muscles where the EMG signal is strong, e.g., shoulder muscles in the case of arm amputation.

Importantly, utilizing automatic EMG classification in BCI context for the purpose of detecting possible muscle responses during covert movements, e.g., motor imagery, is problematic: The challenge for automatic procedures is the high variability of EMG responses, especially regarding the very weak (~ 20–50 µV, i.e., if the maximum voluntary contraction were 1 mV, cf. Study 3 in Chapter 4 or Liguori et al., 1992, this would be 2–5 %) and transient (< 100 ms) motor responses occasionally present in motor imagery or quasi-movements.

While the visual inspection by an expert can discriminate such residual weak motor response even from tonic background EMG of the same amplitude, while a variance- or threshold-based approach would fail in this scenario. Moreover, other challenges are physiological artifacts such as heartbeats or mechanical artifacts due to wire movement or slightly loosened electrode contacts, where even sophisticated correction methods (e.g., independent component analysis, template matching) are not always efficient (cf. discussion in Hodges & Bui, 1996; Reaz et al., 2006). In such cases the automatic rejection of artifact epochs might result in unnecessary data loss – the alternative would be visual pre-screening of single trials by the expert, while the actual inspection of epochs for presence of motor responses does not take much more time.

3.4.2 Advantages of visual inspection

Summarizing, we demonstrate the superior recording sensitivity of the APB muscle for EMG monitoring of thumb movements: Firstly, the magnitude of motor responses in the “overt movements” condition was much higher in APB compared to the flexor/extensor muscles. Secondly, the visual detection rate in both “motor imagery” and “quasi-movements” conditions was highest for EMG of APB muscle (on average 5 %). Importantly, the detection rate was higher for EMG (i.e., all three muscles) than for ACC recordings (on average 4 % vs. 1 %, respectively), suggesting the higher sensitivity of monitoring electrical muscle activity compared to only the mechanical displacement of the limb.

Automatic methods have been shown to be quite accurate in the detection of moderately strong EMG responses of “normal” movements (i.e., approx. ≥ 1 mV; cf. Abbink et al., 1998; Li et al., 2007). However, in the case of very weak and transient EMG responses (< 50 µV), e.g., present during the performance of motor imagery or quasi-movements, visual inspection is preferable over automatic procedures, despite the disadvantage of being more time-consuming. Moreover, visual inspection depends on the subjective thresholds/experience of the researcher, which is often discussed as a disadvantage.

However, in the case of low signal-to-noise ratio and variable characteristics of transient, weak EMG responses this expert experience turns into an advantage, since the automatic EMG classification was at chance level for the ACC and all EMG recordings of four muscles contributing to the thumb movement, as well as the statistical comparison of the muscle activity in the pre- vs. post-stimulus interval. Yet the visual inspection revealed that weak motor responses were present in a small amount of the epochs (~ 4 % averaged across both conditions). In one of both subjects the detection rate for quasi-movements was slightly larger (2 %) than for motor imagery (cf. Table 3.3) and there was a slight increase (RMS 0.1 µV) of the average EMG activity for quasi-movements (Table 3.2). Importantly, this slightly increased EMG activation was present in both the pre- and post-stimulus intervals (which might speak for general tonic muscle activity) and in both hands. Therefore and resulting from our previous analysis, the tonic or occasional weak transient EMG responses could not explain the pronounced and time-specific changes observed in the EEG dynamics, as we have also demonstrated by extensive data analysis in our study for both “motor imagery” and “quasi-movement” conditions (cf. data and discussion in Nikulin et al., 2008).

3.4.3 Outlook

In agreement with previous studies (review: Guillot & Collet, 2005) we found that the majority of trials during the performance of covert movements (i.e., motor imagery, quasi-movements) were not associated with detectable motor responses in different data sources (EMG of three muscles, ACC). However, such residual motor responses in covert movements were of weak and transient nature, sometimes embedded in tonic muscle activity. This low signal-to-noise ratio in the case of covert movement conditions makes the detection of motor responses difficult for automatic and/or statistical procedures. In fact we demonstrate that in contrast to automatic methods the visual inspection accurately detected these few, residual motor responses. Accordingly, despite the disadvantages of being a laborious and more subjective procedure, our findings suggest visual EMG inspection as preferable strategy for the muscle monitoring in covert movements. Future studies might compare the accuracy of visual and automatic procedures in invasive EMG recordings of weak motor responses (10–50 µV strength) as they are naturally occurring in covert movements in a minority of trials. In order to increase the number of trials, another strategy might be to train subjects via EMG neurofeedback to intentionally produce such weak motor responses in every trial. Furthermore, future studies might concentrate on neural correlates of very weak movements in the brain, since such fine-graded motor control is part of motor routines in daily life.

Acknowledgements

FH is supported by the Berlin School of Mind and Brain. VVN and GC are partially supported by the Berlin Bernstein Center for Computational Neuroscience.

Chapter 4

IV. STUDY 3

Covert movements are associated with repetition suppression in sensorimotor cortex as indicated by EEG dynamics

Shortened version of this manuscript submitted under the title:
Covert movements trigger repetition suppression of EEG in sensorimotor cortex.

Friederike U. Hohlefeld[1,2,3], Vadim V. Nikulin[2,4], Gabriel Curio[2,4]

1) Berlin School of Mind and Brain, Berlin, Germany
2) Neurophysics Group, Department of Neurology,
Charité – University Medicine Berlin, Germany
3) Department of Psychology, Free University Berlin, Germany
4) Bernstein Center for Computational Neuroscience, Berlin, Germany

Abstract

The well-known phenomenon of repetition suppression indicates the decrease of neural responses to repeated externally presented sensory stimuli (e.g., visual), and it is often interpreted as habituation and/or response optimization. However, in our study we address the question whether RS can be also present in the absence of external sensory stimulation during the performance of repeated cognitive tasks (referred to as “internally-driven” RS), such as motor imagery.

The present study investigates for the first time the possibility of internally-driven RS, during the repeated performance covert movements, such as motor imagery and quasi-movements. Importantly, covert movements have been frequently shown to engage central motor processing in the brain, while the limbs remain at rest. We recorded multi-channel electroencephalography (EEG) when the subjects performed continuously either covert (i.e., motor imagery, quasi-movements) or overt repeated thumb movements (abductor pollicis brevis muscle) over trials of 60 sec length.

We observed a significant recovery of alpha and beta EEG oscillations after initial power decrease (also termed event-related desynchronization, ERD) in sensorimotor cortices towards baseline level during covert movements: After 58 sec ~ 20 % in the initial ERD remained in the alpha band and ~ 5 % in beta (for comparison in overt movements: ~ 34 % of remaining ERD in alpha, complete recovery in beta), Importantly, there were no significant differences of EMG activity during covert movements between pre- and task intervals, also not between imagined and quasi-movements (average EMG activity ~ 2 µV), and no significant correlation between EMG and EEG activity.

These results might tentatively suggest that RS could be associated with internally-driven rhythmic stimulation alone in the case of covert thumb movement performance, in absence of external sensory stimulation and without the significant contribution of proprioceptive input. Hypothisizing further, it is not entirely unlikely that *any* repeated cerebral activation, internally or externally-driven, might be associated with RS, which could reflect the adaptation to stereotyped activation in neural networks. The present results have important implications for motor control, studies of neural correlates of action intentions, and brain-computer interfacing.

***Keywords*:** Abductor pollicis brevis, alpha, beta, BCI, EEG, EMG, ERD, intention, motor imagery, quasi-movements, repetition suppression.

4.1 Introduction

The repeated presentation of external sensory stimuli (e.g., visual, auditory) is associated with decreased neural activity, referred to as “repetition suppression” (RS). This fundamental phenomenon is assumed to reflect the plasticity of neural networks, adaptation, learning, and response optimization to repeated input in the brain (Desimone, 1996; Friston, 2005; Grill-Spector et al., 2006; Henson, 2003).

An open question is whether RS would occur also in case of internally-triggered repetitive neural activations, i.e., without external sensory stimuli during the performance of repeated cognitive tasks not involving overt muscle contraction, e.g., covert movements such as motor imagery.

The investigation of RS in covert movements, compared to other potential cognitive tasks, is of interest to the present study since the results might allow an interpretation with respect to motor imagery-based brain-computer interfacing (BCI), and it has also implications for the central-peripheral discussion in the case of RS during overt movement execution.

4.1.1 Movement-related repetition suppression (RS): The central-peripheral discussion

How does the brain control repeated movements? Movement repetition belongs to our daily motor repertoire (e.g., walking, typing). During the online control the brain has to deal with continuous information flows: preparing and issuing motor commands (efferent flow) and processing sensory feedback from the moving limb (reafferent flow). A single study (Erbil & Ungan, 2007) reported that during movement execution RS occurs in sensorimotor cortices in electroencephalography (EEG), specifically in alpha oscillations (8–12 Hz) but not in beta dynamics (15–28 Hz). The interpretation of this result is not straightforward: Is movement-related RS due to central-efferent or peripheral-reafferent neural activation (pro central: Doyle et al., 2008; Rodrigues et al., 2009; Schillings et al., 2006; Schnitzler et al., 1997 – pro peripheral: Alegre et al., 2002; Alegre et al., 2003; Erbil & Ungan, 2007)?

This issue is not easy to address methodologically, since recordings of electroencephalographic and neuroimaging data reflect a mixture of central activity and sensory feedback, since an executed movement is necessarily accompanied by reafferent feedback. In order to overcome this difficulty one could study movement-related RS in healthy subjects with temporary blockade of the target muscles (e.g., by inducing transient ischemia) or in patients with neuromotor lesions (e.g., spinal cord injury, amputation) or deafferented patients. However, the mentioned possibilities allow only restricted conclusions regarding healthy/normal motor control. However, the experimental design of the present study allows to approach the central-peripheral discussion from another angle: If RS also occurs during covert movements, e.g., motor imagery or quasi-movements without overt muscle contraction (see below), then central, internally-driven processes might dominate RS since the sensory feedback is absent or minimal, when the limbs remain at rest.

4.1.2 Motor imagery and quasi-movements

Motor imagery is defined as the mental simulation of a movement (i.e., simulation of proprioceptive aspects of a movement) without activation of the target muscles (Finke, 1979, 1980; Grush, 2004; Jeannerod, 1994, 2001). Importantly, frequent studies have demonstrated that covert movements (e.g., motor imagery, also movement preparation) share neural substrates, especially in primary and secondary motor areas, with overt movement execution (Bakker et al., 2007; Chatrian et al., 1959; Jacobson, 1932; Jankelowitz & Colebatch, 2002; Kranczioch et al., 2009; Lotze & Halsband, 2006; Munzert et al., 2009; Nikulin et al., 2008; Stinear et al., 2006; Wolpaw et al., 2002). These data gave rise to the assumption of a continuum of neural activation in the brain between overt and covert stages of action and perception (Jeannerod, 2001).

In contrast, during quasi-movements, a novel motor-cognitive skill introduced by Nikulin et al. (2008), the subjects learn to execute a genuine movement with lowest possible motor output, i.e., effectively the muscles are at rest. Importantly, our previous study (Nikulin et al., 2008) has demonstrated that motor imagery and quasi-movements crucially differ in cognitive and neurophysiological aspects, although from an external viewpoint they are similar since usually no detectable muscle contractions are generated in both conditions. Yet imagined and quasi-movements differed with respect to the motor intention (simulated vs. minimized movement) and regarding the neural activation in contralateral sensorimotor cortices (stronger and more lateralized activation for quasi-movements). Comparing both covert conditions with overt movements in the present study allows dissecting the contributions of central/peripheral effects and action intentions on movement-related RS.

4.1.3 Electroencephalographic amplitude dynamics for quantifying RS

In order to quantify RS in EEG we utilize the stimulus-locked amplitude dynamics of alpha (8–12 Hz) and beta (15–25 Hz) oscillations. During the preparation, execution or even imagination of movements the amplitude of oscillatory EEG decreases over sensorimotor areas (Adrian & Matthews, 1934; Berger, 1929; Gastaut et al., 1952; Jasper & Penfield, 1949; Lotze & Halsband, 2006; Munzert et al., 2009; Wolpaw et al., 2002). This effect was termed “event-related desynchronization” (ERD; Pfurtscheller & Aranibar, 1977; Pfurtscheller & Lopes da Silva, 1999), i.e., the percentage of amplitude/power decrease with respect to a prior baseline or “event-related synchronization” (ERS) for amplitude/power increase (see Methods section). The terms ERD/ERS were criticized for implying a particular mechanism underlying the amplitude modulations, namely the desynchronization/synchronization of oscillatory neural activity. While being aware of this issue we will use the standard terms ERD/ERS in the present text.

Importantly, RS is defined as amplitude decrease over time to repeated stimulation (see above). However, in the case of oscillatory EEG rhythms RS refers to a "recovery" of the dynamics towards a prior baseline, i.e., smaller ERD values or even ERS. Importantly, this recovery indicates the reappearance of sensorimotor rhythms after initial stimulus-induced "blocking" (Chatrian et al., 1959), thus RS in EEG oscillations actually denotes an *increase* of amplitude.

4.1.4 Review of EEG dynamics in repetitive overt movements

Neural correlates of different movement parameters are frequently studied, e.g., speed, force or complexity (Kranczioch et al., 2010; Romero et al., 2000; Yuan et al., 2010), but little is known about the long-term dynamics of movement-related neural activation. Usually the movements are studied in isolation, i.e., few movements in a short trial of few seconds, single movements with long inter-movement-interval (IMI), longitudinal data are not reported (Cassim et al., 2000; Hashimoto & Rothwell, 1999; Schlaug et al., 1996; Stancák & Pfurtscheller, 1995; Stancák & Pfurtscheller, 1996), or data are collapsed across the long trial as in the case of functional magnetic resonance imaging (fMRI; Ehrsson et al., 2003; Formaggio et al., 2008; Wu et al., 2008; Wu et al., 2004).

Some EEG evidence comes from movement-related cortical potentials (e.g., the Readinesspotential). With increasing repetition the potential amplitude decreases (i.e., towards baseline) for non-fatiguing movements requiring little attentional monitoring (i.e., 50 % of maximum voluntary contraction; Freude & Ullsperger, 1987). Conversely, when the movements required high muscular effort and/or high attentional monitoring the negative potential amplitude was increased, interpreted by the authors as a centrally-guided compensatory mechanism, also indirectly evidenced by the presence of potential decreases *before* movement onset (Dirnberger et al., 2004a, Dirnberger et al., 2004b; Freude & Ullsperger, 1987; Johnston et al., 2001; Schillings et al., 2006).

At this point it is important to remind that the Readinesspotential (only few seconds before and after movement onset) is computed as the average from many movement-locked trials so that the temporal information are lost. Another approach would be to collect long trials of continuous movements and lock the data to the *beginning* of the trial (i.e., to the stimulus or first movement onset) and not to the single movements, and subsequently average the trials to enhance the signal-to-noise ratio.

So far a single study provided such data (Erbil & Ungan, 2007). In this study the subjects performed self-paced repetitive finger movements with an inter-movement-interval of 2 sec. The movements were performed for a 30 sec period, followed by 30 sec rest before the next performance. The ERD in the alpha range gradually (but not fully) recovered towards baseline during movement performance, whereas beta-ERD did not recover but remained sustained until the end of the 30 sec period. The authors discussed the question whether the observed RS effect in the alpha range might be due to central (top-down) or peripheral (bottom-up) processing, concluding that the “gradual recovery observed in the present study [in alpha] is probably related to a habituation in the somatosensory cortex to repeated afferent inflow” (p. 54). In contrast, the beta dynamics seem “to be an index of the cortical mechanism that governs the sequences of active movement” (p. 53) and therefore “an EEG amplitude change that would be related to motor activity should also be a steady one” (p. 54). In this respect it is important to note that it has been frequently argued that, very broadly speaking, both alpha (mu) and beta-ERD are associated with motor processes. Yet experimental data have supported the view of (in no way clear-cut) differences in the susceptibility of neural activity in the different bands: Beta-ERD might be rather associated with executive initiation and termination of a movement, whereas alpha-ERD rather reflects motor attention/intention and somatosensory processing (e.g., Erbil & Ungan, 2007; Pfurtscheller et al., 1998; Ritter et al., 2009). Concluding, the central-peripheral discussion remains rather speculative and an alternative experimental paradigm is needed, as provided by the present study.

4.1.5 Study aims: Repetition suppression in covert movements?

Can RS in the neural brain activity be present in the absence of repeated external stimuli and with absent/minimized proprioceptive input, for instance during the performance of repetitive covert movements or possibly other repetitive cognitive tasks? The present study utilizes multi-channel EEG to studying repetitive brisk covert (motor imagery, quasi-movements) and overt movements (unilateral left/right thumb), performed with a speed of 1 Hz contingent upon an instructive auditory stimulus for periods of 1 min. The overt movements were performed with intermediate strength, i.e., ~ 50% of max. voluntary contraction in order to avoid muscular fatigue or too high attentional load (cf. Freude & Ullsperger, 1987).

The stimulus-locked amplitude dynamics (i.e., ERD/ERS) are analyzed in the frequency ranges of alpha (8–12 Hz) and beta (15–25 Hz). Compared to the 30 sec period of the previous study (Erbil & Ungan, 2007) we deliberately increased the trial length to 1 min in order to investigate RS in oscillatory EEG dynamics over a longer time period. Since the previous study did not observe RS effects in the beta range within 30 sec perhaps the beta dynamics need more time to recover. The present study investigates the following hypotheses:

A) If we observe RS (i.e., recovery of alpha dynamics towards baseline) in overt but not in covert movements, then the sensory feedback from the moving limb is required for the occurrence of RS in neural dynamics.

B) If we observe RS in covert movements then rather central processing (top-down) in the brain, without involving the effectors, is sufficient to trigger RS. This hypothesis would be also strengthened by observing RS in overt movements in the beta frequency range, since beta dynamics were shown to be primarily associated with executive (top-down) motor control (cf. Erbil & Ungan, 2007; Pfurtscheller et al., 1998).

The mechanisms of RS are far from being understood. The results of the present study are of importance for a basic neurophysiological understanding of neural adaptation mechanisms and for studying neural correlates of (long-term) action intentions (Haggard, 2008). Furthermore, the results are of critical relevance for brain-computer interfacing, which relies on the detection of neural signatures of repeated action intentions (Wolpaw et al., 2002).

4.2 Methods

4.2.1 Participants

Fifteen healthy subjects (mean age 27 years, range 23–31 years, 6 males), without any history of neurological or psychiatric disorders, participated in the present study and gave written informed consent. All subjects were right-handed (Edinburgh Handedness Inventory; Oldfield, 1971) and had normal or corrected-to-normal vision.

4.2.2 Procedure

The subjects performed three experimental tasks, referred to as “motor imagery”, “quasi-movements”, and “overt movements”, respectively (see below). The subject sat in a comfortable armchair, the forearms placed on the armrests with palms up while fixating a cross on the wall in the front (distance 1.6 m). For the experimental conditions the acoustic stimuli were presented via loudspeakers located in the front of the subject (distance 1.6 m).

The stimuli were the words “left”, “right”, and “stop”, spoken by a female voice in a neutral tone. The beginning of a trial (duration 60 sec) started either with the “left” or “right” stimulus, referring to the performance with the left or right hand (i.e., left or right class), respectively. The trial was terminated by the “stop” stimulus. In the “stop” period (duration 45 sec, ± 5 sec random variation), the subject rested with relaxed hands. Eight trials (four “left” and four “right” trials) comprised one block (duration ~ 15 min). Each experimental condition was recorded in two blocks, resulting in eight trials per hand and condition (“motor imagery”, “quasi-movements”). For the “overt movements” condition only one block was recorded (resulting in four trials per hand). The order of “left” and “right” trials was counterbalanced across blocks. The order of the experimental blocks was alternating (e.g., two blocks of “motor imagery” were never recorded in direct succession), and the order of blocks was counterbalanced across subjects. The “overt movements” block was either recorded as the first or as the last block (the order was counterbalanced across subjects). Before the “overt movements” block the maximum voluntary muscle contraction was recorded (1 min tonic contraction). The subject was deliberately not asked to control the occurrence of eye blinks during the recordings, in order to avoid confounding the subject’s performance with additional cognitive load. The experimental procedures were approved by the Ethics Committee of Charité – University Medicine Berlin (Berlin, Germany).

Rest: The subjects were asked to fixate the cross mark in the front. In a continuous recording the subjects first relaxed with eyes open (4 min) and then with eyes closed (1 min). These data were recorded before all other experimental sessions.

Overt movements: The subjects performed continuous overt thumb abductions (target muscle abductor pollicis brevis muscle). The movements were brisk and of medium force (i.e., ~ 50 % of max. voluntary contraction), and were executed with a frequency of ~ 1 Hz. The subjects were asked to stop immediately the performance when hearing the “stop” command, and not to count the movements. The correct performance was trained for several minutes before data recordings. Additionally the subjects contracted both thumbs simultaneously for ~ 1 min with maximum possible strength (maximum voluntary contraction, MVC).

Motor imagery (kinesthetic): The subjects imagined the aforementioned thumb abductions (cf. “overt movements” condition). The subjects were asked to imagine continuous movements with a frequency of ~ 1 Hz. The subjects were instructed to perform motor imagery from the first person perspective and to concentrate only on kinesthetic aspects of the imagined movement, while avoiding its visualization or counting. The subjects performed a training of motor imagery (~ 20 min) of the thumb movements at home before coming to the lab for the experiment. Before data recordings the subjects familiarized themselves with the task again for several minutes while the researcher checked the EMG activity for being at baseline level.

Quasi-movements – A novel motor-cognitive skill: For details on the quasi-movement performance and EMG neurofeedback training please refer to Chapter 1.3.3. The subjects were instructed to perform quasi-movements also with a speed of ~ 1 Hz. The experimental procedures were approved by the Ethics Committee of Charité – University Medicine Berlin (Berlin, Germany).

4.2.3 Task ratings

Before EEG recordings the subjects were asked to fill out the “internal” (first-person perspective) subscale of the Vividness of Motor Imagery Questionnaire (VMIQ; Isaac et al., 1986) in order to assess general imagery abilities. Only this subscale was used (24 items) since the present study is only concerned with kinesthetic (first-person) motor imagery. In addition different task ratings were obtained for the “motor imagery” and “quasi-movements” conditions:

1) After each block (duration 15 min, including rest periods) the subjects were asked whether they switched their performance during the recordings (i.e., performing motor imagery instead of quasi-movements or vice versa). This rating was necessary in order to assess task compliance, since from the external viewpoint (i.e., observing EMG traces) the performance of both tasks looks similar.

2) After each block the subjects were asked to rate how many trials they performed with the required frequency of 1 Hz without strong deviations (e.g., 0.3 Hz or 3 Hz).

3) After each block the subjects were asked to rate the course of attention (“stable”, “decrease” or “increase”). If the subjects reported a decrease of attention they were asked for the time of decrease onset. Furthermore, the subjects gave report on the feeling of automatization (scale 0–5, 0 for “no automatization”, 1 for “very weak”, 3 for “medium”, and 5 for “very strong”), and if applicable the onset time of automatization.

4) After finishing the experimental recordings the subjects were asked for a final rating for their concentration during task performance, the task difficulty, and the “sense of movement” (i.e., the feeling of muscle contraction). All scales ranged from 1 to 5 (cf. labels see above).

4.2.4 EEG and EMG acquisition

EEG data were recorded by 62 Ag/AgCl electrodes positioned according to the 10–5 system (Oostenveld & Praamstra, 2001) with the reference placed on the nose. The surface EMG was recorded from the left and right abductor pollicis brevis muscles with Ag/AgCl electrodes. One electrode was positioned over the muscle belly and the other over the proximal base of the phalanx. EEG and EMG data were recorded by using BrainAmp amplifiers and BrainVision Recorder software (version 1.3; Brain Products GmbH, Munich, Germany). During data acquisition the EEG and EMG signals were band-pass filtered at 0.1–250 Hz and sampled at 1000 Hz. Offline analyses were carried out with Matlab (version 7; The MathWorks Inc., USA).

4.2.5 EMG data preprocessing

The EMG data were filtered with a notch filter (Butterworth filter, second order, band-stop 48–52 Hz) in order to decrease contamination by power socket frequency. However, power spectra density analysis revealed that the data were contaminated by higher harmonics of 50 Hz. Therefore, the data were additionally filtered with an IIR comb notch filter. Finally a high-pass filter at 10 Hz (Butterworth filter, second order) was applied and the data were rectified. Then the continuous data stream was visually inspected for occasionally remaining artifacts. If present, the contaminated samples were zero-padded. This approach was preferred over value substitution for instance by linear regression, since the true EMG activity is unknown in the contaminated intervals. Subsequently the data were segmented into epochs of 100 sec length, starting 20 sec before the stimulus onset and averaged (excluding zero-padded samples from the average).

4.2.6 EEG data preprocessing and artifact rejection

EEG data were decimated to 200 Hz and band-pass filtered at 0.5–40 Hz (Butterworth filter, second order). The data were cleaned by utilizing Fast Independent Component Analysis with kurtosis as contrast function (Hyvärinen & Oja, 2000) and filtered with a notch filter (48–52 Hz, Butterworth filter, second order). The Laplacian derivation was taken (Hjorth, 1975; Graimann & Pfurtscheller, 2006). For removing remaining physiological and technical outliers the Laplacian EEG data were zero-padded, as described above for the EMG data. Finally the EEG data were filtered in the individual alpha range (peak +/- 1–1.5 Hz) and in a fixed beta range (15–25 Hz) by obtaining the amplitude envelope of alpha and beta oscillations using the Hilbert transform (Clochon et al., 1996; Graimann & Pfurtscheller, 2006; Rosenblum & Kurths, 1998; Rosenblum et al., 2002), whereby the individual alpha range was determined on basis of the “rest” data (eyes open). Then the data were segmented into epochs of 100 sec length (starting 20 sec before the stimulus onset) and averaged separately for the left and right stimulus class (excluding zero-padded samples). Finally the amplitude dynamics were calculated (Pfurtscheller & Aranibar, 1977; Pfurtscheller & Lopes da Silva, 1999) for each channel by

$$ERD/ERS=((POST-PRE)/PRE)*100$$

where PRE is the averaged EEG activity in the pre-stimulus interval (-20–0 sec) and POST is the averaged activity in the post-stimulus interval (0–100 sec), including the task (0–60 sec) and subsequent rest-period (60–100 sec). ERD (i.e., negative values) indicates the amplitude decrease with respect to the baseline whereas ERS (i.e., positive values) indicate the amplitude increase, respectively.

4.2.7 Statistical analysis

Results are reported from the C3 and C4 Laplacian channels (i.e., representing the local average of the four neighboring channels), which are approx. located over the sensorimotor cortices and are usually reported for strongest responsiveness in overt and covert motor tasks (Carrillo-de-la-Peña et al., 2008; Nikulin et al., 2008; Pfurtscheller et al., 1997; Praamstra, 2007; Yuan et al., 2010). Multiple comparisons were done by ANOVA and repeated measures ANOVA, with Bonferroni post-hoc test and, if required, applying Greenhouse-Geisser correction. Analyses were performed with STATISTICA (version 6, StatSoft, Inc., USA). The recovery of ERD towards baseline was determined by a running t-test against zero for 16 bins (bin 1 = max. ERD in the range of 0–2 sec: bin 2:15 = mean ERD in 4 sec, i.e., 2:4:58 sec; bin 16 = mean ERD in 58–60 sec; bins were non-overlapping by 1 sample). The time point of “recovery”, i.e., ERD reaching baseline level, was defined as the time point where two consecutive bins did not significantly deviate from zero, so that the recovery time reported here is the last significant bin (e.g., 28 sec for a bin ranging from 26–30 sec). For indicating recovery differences the effect size was calculated (Cohen’s d; * denotes $d \geq 0.5 < 0.8$ [“medium” effect size], ** denote $d \geq 0.8$ [“large” effect size]; analysis was performed with G*Power, version 3.0.8, Faul et al., 2007). The relative change of ERD, when comparing start and end of task performance (the first and last 2 sec), was determined by (1-(bin16/bin1))*100. The significance level was set to $p = 0.05$. To control for the possible influence of EMG activity on oscillatory EEG within task performance (0–60 sec), the EMG amplitude was correlated with ERD in three subsequent bins (20 sec each; Pearson product-moment correlation, Bonferroni-corrected significant $p = 0.017$).

4.3 Results

Two subjects had to be excluded, since in one subject no alpha rhythm was observable and in the other subject the data were contaminated by excessive amounts of noise. The final data set consisted of thirteen subjects.

4.3.1 Task ratings

Vividness of motor imagery: On average the subjects reported “moderately clear and vivid” imagery abilities (mean = 3.2, SD = 0.35) on the “internal” subscale (kinesthetic motor imagery) of the VMIQ.

Intention: All subjects correctly performed the task and did not switch between imagery and quasi-movements. For the “motor imagery” condition all subjects reported intending to perform a “mental simulation of a movement (i.e., in the mind)”. For the “quasi-movements” condition all subjects reported intending to “perform a real movement (i.e., muscle contraction)”.

Frequency, task difficulty, concentration: In the majority of trials (~ 80%) the subjects reported to perform the task with a constant frequency in both conditions. The subjects reported “medium” task difficulty and “strong” concentration for both conditions alike (independent t-test, $p > 0.05$).

Attention, automatization, sense of movement: For the “motor imagery” condition 11 out of 13 subjects reported a decrease of attention across the 1 min of task performance, starting ~ 29 sec after stimulus onset (SD = 9 sec). And 8 out of 12 subjects reported to have a feeling of automatization (mean strength = 3, SD = 1) starting ~ 21 sec (SD = 13 sec) after stimulus onset. For the “quasi-movements” condition 12 out of 13 subjects reported a decrease of attention across the 1 min of task performance, starting ~ 30 sec after stimulus onset (SD = 11 sec). The same number of subjects reported to have a feeling of automatization (mean strength = 3, SD = 1) starting ~ 25 sec (SD = 12 sec) after stimulus onset. There were no significant differences (independent t-test, $p > 0.05$) between any comparisons within and between experimental conditions. Summarizing, after ~ 30 sec the attention decreases and the feeling of automatization starts.

For the “quasi-movements” condition the subjects reported a “strong” sense of movement (mean = 3.5, SD = 1.3), for “motor imagery” they reported to have a “medium” sense of movement (mean = 2.5, SD = 1.5). The sense of movement was stronger for quasi-movements than for motor imagery (independent t-test, p=0.04). Interestingly, when the subjects reported to have sensations of muscle contractions during motor imagery, the subjects spontaneously called this “quasi-movement“. Yet they negated producing these tiny muscle twitches during motor imagery by *conscious intention*. After this question the subjects refined their evaluation by reporting that the difference between motor imagery and quasi-movements is very clear to them: It might *feel* the same on basis of muscles, but still the action *intentions* were very different (i.e., *motor simulation* where muscle activity is not intended during motor imagery vs. *quasi-movements* where muscle activity is intended but the motor output is diminished up to zero).

4.3.2 EMG data

Overt movements: Figure 4.1 Panel A) shows the grand-average (n = 13) for overt movements, the values are averaged across both hands in bins of 10 sec each for the task performance of 1 min. The inter-movement-interval was ~ 0.9 Hz, without significant changes across the 1 min performance and without differences between the hands (repeated measures ANOVA; factor bin: $F_{5,120} = 0.975$, $p > 0.05$; factor bin*hand: $F_{5,120} = 1.419$, $p > 0.05$; factor hand: $F_{1,24} = 0.037$, $p > 0.05$). The amplitude of rectified EMG (max. values) was ~ 660 µV, without significant changes across the 1 min performance and without differences between the hands (repeated measures ANOVA; factor bin: $F_{5,120} = 0.474$, $p > 0.05$; factor bin*hand: $F_{5,120} = 1.628$, $p > 0.05$; factor hand: $F_{1,24} = 0.058$, $p > 0.05$). The movement duration was on average ~ 200 ms without differences between hands; a slight increase of duration by 30 ms (i.e., from ~ 170 ms to 200 ms) occurred after ~ 20 sec of task performance (repeated measures ANOVA; factor bin: $F_{5,120} = 8.290$, $p < 0.01$, post hoc: bin $p < 0.05$; factor bin*hand: $F_{5,120} = 0.682$, $p > 0.05$; factor hand: $F_{1,24} = 0.008$, $p > 0.05$). The average strength of maximum voluntary contraction (defined as max. peak in ~ 1 min of continuous thumb muscle contraction) was ~ 2 mV across both hands without significant differences between left and right hand performance (independent t-test, p>0.05). On average the subjects performed the “overt movements” task with ~ 50 %

of maximum voluntary contraction (calculated as mean of strongest EMG peaks across 10 sec task performance divided by the maximum voluntary contraction value), without significant differences between left and right hand performance (independent t-test, p>0.05). Summarizing, the results indicate that the subjects correctly performed the task with approx. 1 Hz frequency at ~ 50 % of maximum voluntary contraction, without strong variations of movement strength, inter-movement-interval or duration across the 1 min performance.

Motor imagery, quasi-movements: Figure 4.1 B) shows the grand-average (n = 13) of rectified EMG traces for imagined and quasi-movements for right-hand performance of 1 min (results for left hand performance were similar) as mean amplitude in bins of 6 sec each, including the mean amplitude in the pre-stimulus interval of 20 sec (altogether 11 bins). During task performance the average EMG amplitude was ~ 2 µV without significant differences between conditions (motor imagery vs. quasi-movements), between stimulus classes (left vs. right), and except the last bin between hands (active vs. inactive hand) (repeated measures ANOVA; factor bin*group: $F_{10,960} = 0.507$, $p > 0.05$; factor bin*class: $F_{10,960} = 1.843$, $p > 0.05$; factor bin*hand: $F_{10,960} = 4.054$, $p = 0.04$). Only in the last bin (50–60 sec) the active hand (~ 2.6 µV) is slightly more activated than the hand at rest (~ 1.5 µV) irrespective of the condition (post hoc p = 0.05). Very important is the result that the EMG activity in the pre-stimulus interval did not significantly differ from the EMG activity during task performance, neither for motor imagery nor for quasi-movements, as can be also seen in Figure 4.1 C) which shows the grand-average (n = 13) of rectified EMG for both covert conditions.

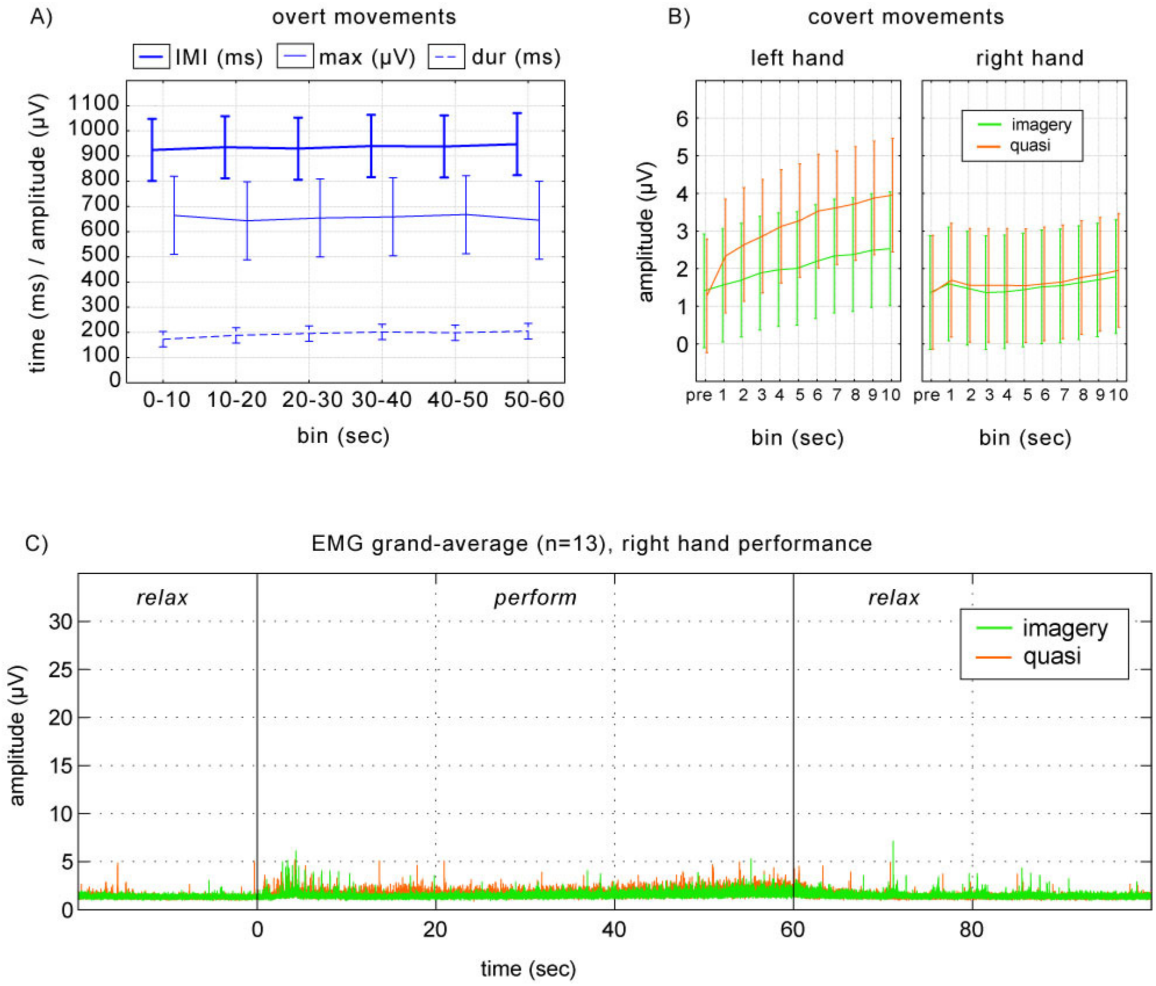


Figure 4.1 EMG results (APB muscle).
A) Grand-average (n = 13) for overt movement performance (1 min).
Values are averaged across left and right hand performance. Each value represents the mean in a window of 10 sec. IMI – inter-movement interval (onset); dur – duration of movement (onset vs. offset); max – maximum amplitude of rectified EMG. Error bars represent confidence intervals (95%).
B) Grand-average (n = 13) for motor imagery and quasi-movements, right hand performance (1 min).
Each value represents the mean amplitude of rectified EMG in a window of 6 sec. Error bars represent confidence intervals (95%).
C) Grand-average (n = 13) for motor imagery and quasi-movements, right hand performance.
The rectified EMG traces are shown for both covert movement conditions.

It is important to note that neither in motor imagery nor in quasi-movements the EMG activity was always at baseline level. It is well known that during motor imagery task-related muscle activation occurs (e.g., Guillot et al., 2007). In the training phase before data recordings all subjects managed to perform imagined and quasi-movements with muscular quiescence (EMG activity at baseline level) for periods of

~ 1 min. Yet during experimental recordings now and then occasional weak EMG activity occurred, either of the tonic or transient type with strength of ~ 30 µV, as can be seen in the single trials in Figure 4.2 – importantly, present in both motor imagery and quasi-movements alike. However, on average the EMG activity during task performance was at baseline level as reported above (cf. also Nikulin et al., 2008), without significant differences between both covert movement conditions, and the occasional weak EMG activation did not correlate with brain activity (reported below, cf. also extensive analysis in Nikulin et al., 2008).

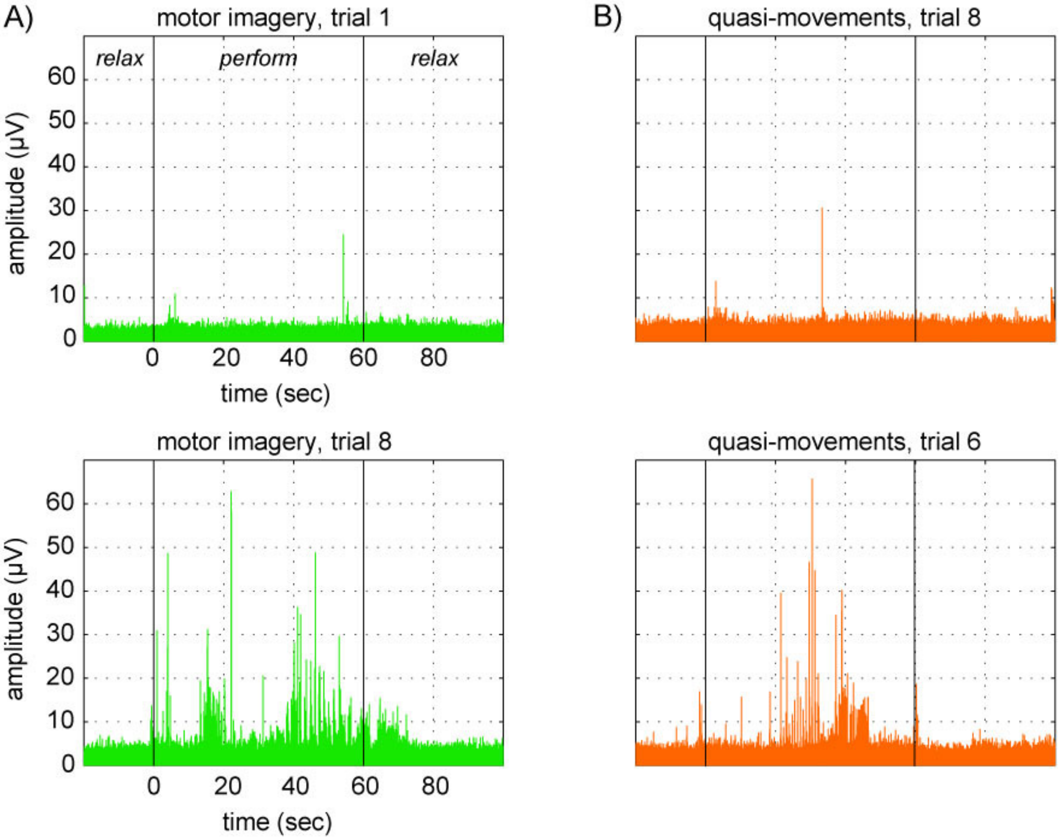


Figure 4.2. EMG single trials during left hand performance (APB muscle).
A) EMG of a single subject (S07), 2 trials, motor imagery.
B) EMG of a single subject (S07), 2 trials, quasi movements.
The two panels depict the rectified EMG activity in two separate trials during left hand performance, the thick lines indicate start and stop of performance, before and after which the subject relaxed the thumb muscle. Note that for overt thumb movements with medium strength the peak amplitudes are around ~ 600 µV.

4.3.3 EEG data

Figure 4.3 shows the grand-average (n = 13) curves for Laplacian transformed, stimulus-locked ERD in the individual alpha range (mean = 9–12 Hz, range = 8–14 Hz) and fixed beta range (15–25 Hz). The figure shows the contra- and ipsilateral hemispheres for right hand performance over sensorimotor cortices (channel C3 and C4, respectively). Results for left hand performance were similar.

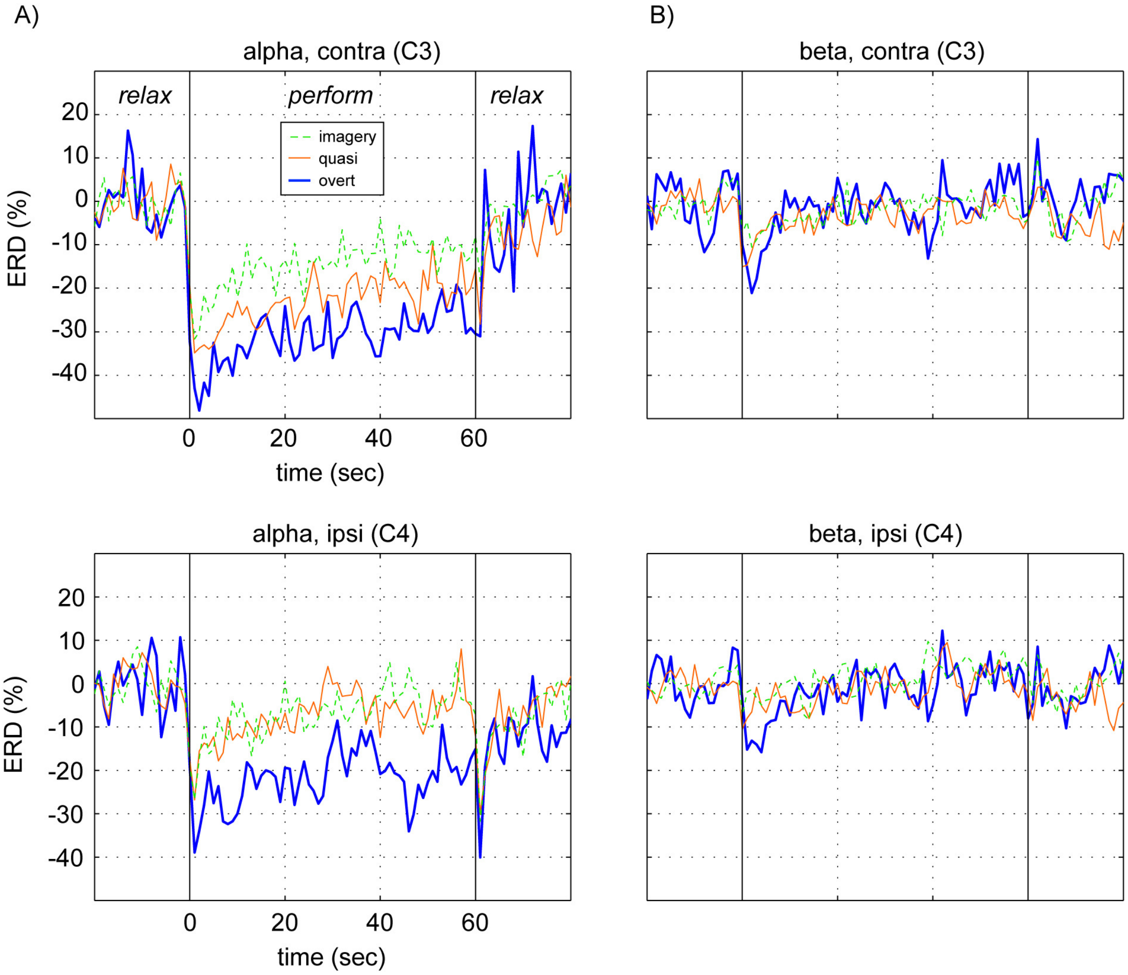


Figure 4.3 EEG results.
A) Alpha band (9–12 Hz), contra- and ipsilateral hemisphere.
B) Beta band (15–25 Hz), contra- and ipsilateral hemisphere.
The two panels depict the grand-average (n = 13) data for the EEG amplitude dynamics for right hand performance (thumb abduction). Imagery – motor imagery; overt - overt movements; quasi – quasi-movements. The data are smoothed (taking the mean value in windows of 1 sec). The thick lines indicate start and stop of performance, before and after which the subject relaxed the muscle.

Visual inspection shows that all three conditions (“motor imagery”, “quasi-movements”, “overt movements”) show a quick bilateral ERD after stimulus onset, where the initial ERD is stronger for the alpha band than for the beta band, and ERD is stronger for overt movements stronger than for covert movements. After the initial strong ERD both alpha and beta dynamics recover *towards* baseline (although not in all cases reaching it) and, importantly, for both overt and covert movements. Moreover, there are marked differences in the temporal dynamics:

1) Alpha band. In the alpha band the contralateral hemisphere is stronger activated than the ipsilateral hemisphere across the whole task performance. For both covert movements conditions there is even a quicker recovery towards baseline than for overt movements, yet quasi-movements seem to activate the sensorimotor system longer than motor imagery, especially in the contralateral hemisphere. Interestingly, the differences between the conditions (stronger and longer activation for overt than for covert movements) are more marked in the ipsilateral hemisphere. The spatial topography in the alpha band is shown in Figure 4.4 (Laplacian channels) for right hand performance (results for the left hand and beta band were comparable.

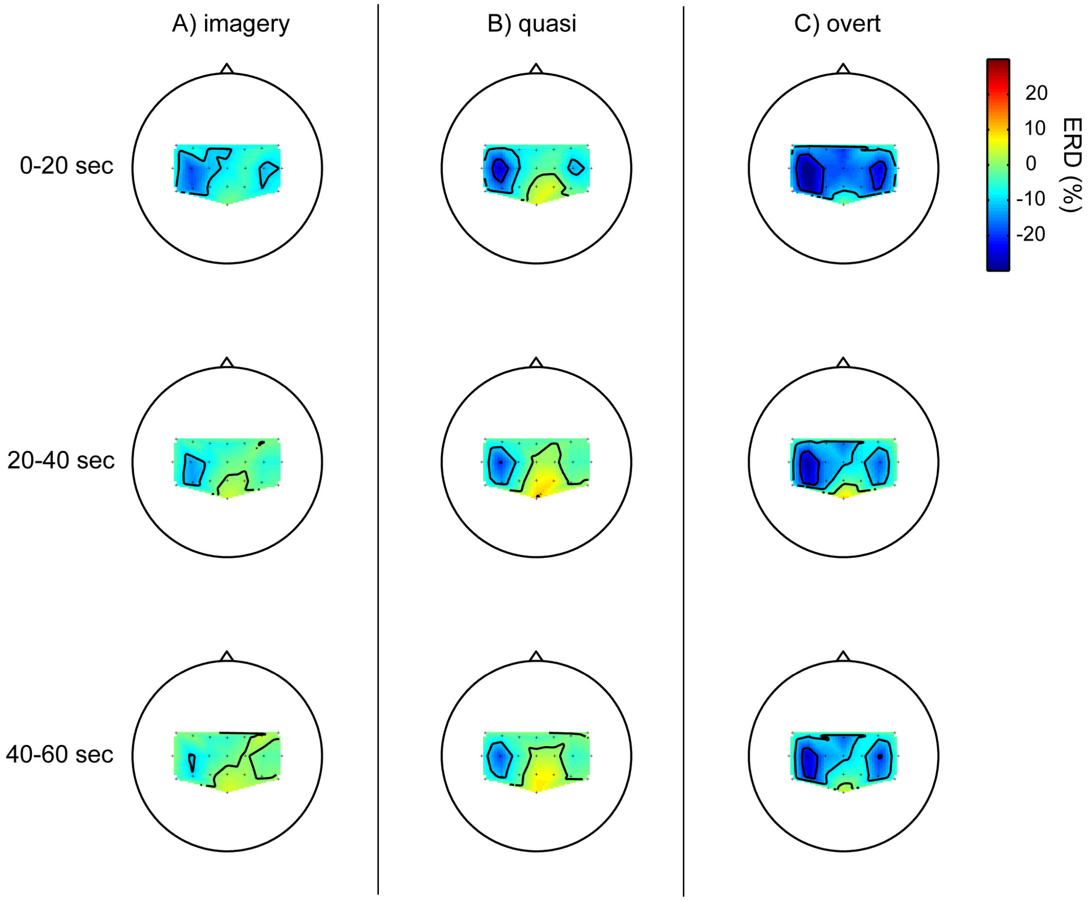


Figure 4.4. Alpha EEG scalp maps (Laplacian), right hand performance (total 1 min). A) Motor imagery. B) Quasi-movements. C) Overt movements.
The three panels depict the grand-average (n = 13) data for the EEG amplitude dynamics (alpha band, 9–12 Hz) for right hand performance. The data are smoothed (taking the mean value in windows of 20 sec).

2) Beta band. As can be seen in Figure 4.3, in the beta band after the initial ERD (stronger for overt than for covert movements) the ERD quickly return to baseline level after some seconds. This recovery is faster than in the alpha band and there are no obvious differences between the motor conditions.

Summarizing, the visual inspection shows an apparent modulation of the EEG dynamics over the course of the 1 min performance for overt and covert movements. The dynamics become weaker and return (partially) towards the baseline level. Main changes in the dynamics occur in the first 20 sec of the performance. The following analyses resolve the temporal ERD dynamics in more detail.

Initial alpha and beta ERD (0–2 sec): The strongest initial ERD (i.e., amplitude decrease within the first 2 sec after stimulus onset) was determined for each subject in each CONDITION ("motor imagery", "quasi-movements", "overt movements"), stimulus CLASS ("left hand", "right hand"), HEMISPHERE ("contralateral", "ipsilateral" regarding the Laplacian channels C3 and C4), and BAND ("alpha", "beta"). The data were subjected to a three-way ANOVA with the factors CONDITION, CLASS, and HEMISPHERE separately for each band, and to a four-way ANOVA for BAND comparison. The results are shown in Figure 4.5.

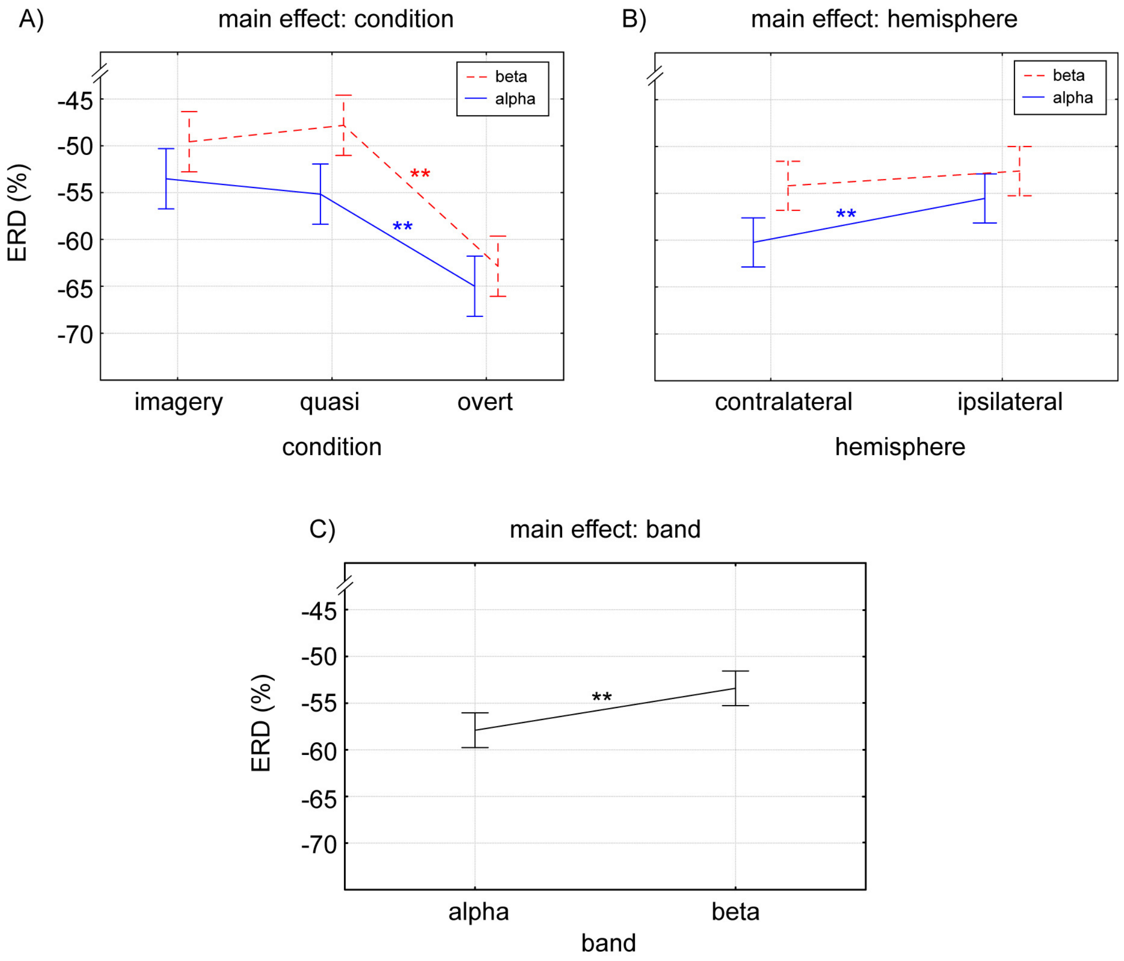


Figure 4.5 ANOVA results – initial ERD after stimulus onset.
A) ANOVA for max. ERD (0–2 sec) in alpha band (9–12 Hz).
B) ANOVA for max. ERD (0–2 sec) in alpha band (9–12 Hz).
C) ANOVA for max. ERD (0–2 sec) for alpha vs. beta band (15–25 Hz).
*ERD – event-related desynchronization. Error bars represent confidence intervals (95%); ** p < 0.01.*

In the alpha and beta bands the “overt movements” condition had a stronger ERD than both covert movements conditions, which did not differ in amplitude (Figure 4.5 Panel A; main effect CONDITION for alpha: $F_{2,144} = 11.357$, $p < 0.01$, post hoc $p < 0.01$ for both comparisons; for beta: $F_{2,144} = 34.831$, $p < 0.01$, post hoc $p < 0.01$). Only in the alpha band the contralateral hemisphere showed stronger ERD than the ipsilateral hemisphere (Figure 4.5 Panel B; main effect HEMISPHERE for alpha: $F_{1,144} = 4.885$, $p < 0.05$; for beta: $F_{1,144} = 0.953$, $p > 0.05$). Furthermore, the alpha-ERD was stronger than beta-ERD (Figure 4.5 Panel C; main effect BAND: $F_{1,288} = 11.308$, $p < 0.01$). The activation did not differ for the stimulus classes (left vs. right hand performance).

Summarizing, within the first 2 sec after stimulus onset the alpha and beta dynamics show strong ERD, with small but significant modulation by the task, hemisphere, and frequency band (differences are of approx. 10 %).

ERD during task performance (2–60 sec): In the time period of 2–60 sec during task performance the data were segmented in bins of 4 sec duration (n = 14) and a last bin with 2 sec duration. In these 15 bins the mean ERD was calculated, averaged, and subjected to a repeated measures ANOVA (four-way) with the factors CONDITION, CLASS, HEMISPHERE, and BIN (details see above), separately for each band. For band comparison a four-way ANOVA was calculated with the factors CONDITION, CLASS, HEMISPHERE, and BAND. Results are shown in Figure 4.6.

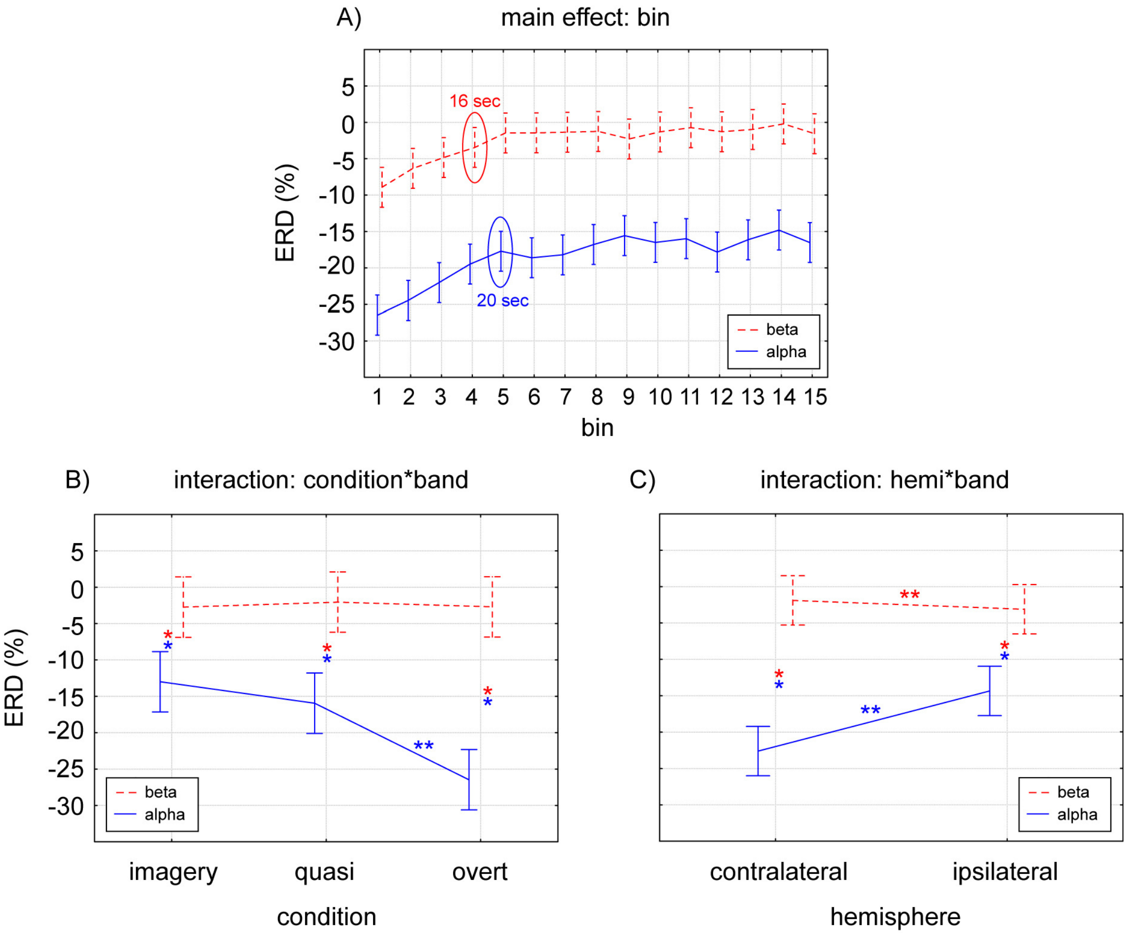


Figure 4.6. ANOVA results – ERD during task performance.
A) ERD during task performance (2–60 sec). Bin differences.
B) ERD during task performance (2–60 sec). Condition differences.
C) ERD during task performance (2–60 sec). Hemisphere differences.
*ERD – event-related desynchronization, hemi – hemisphere, imagery – motor imagery; overt – overt movements; quasi – quasi-movements. Error bars represent confidence intervals (95%); * p < 0.05, ** p < 0.01.*

For both the alpha and beta band the initial ERD recovered over the course of 1 min task performance towards zero baseline, stabilizing more or less after ~ 20 sec (Figure 4.6 Panel A; main effect BIN for alpha: $F_{14,2016} = 19.947$, $p < 0.01$; for beta: $F_{14,2016} = 13.127$, $p < 0.01$; post hoc for alpha: after bin 5 [18–22 sec] there are no significant differences to subsequent bins, except bin 6 vs. 14 with $p < 0.05$; post hoc for beta: after bin 4 [14–18 sec] there are no significant differences to subsequent bins). The alpha-ERD was stronger for overt movements than for motor imagery and quasi-movements, whereas both covert movement conditions did not differ. In the beta band there were no significant differences between the conditions (Figure 4.6 Panel B; main effect CONDITION, for alpha: $F_{2,144} = 8.547$, $p < 0.01$, post hoc $p < 0.01$; for beta: $F_{2,144} = 0.05$, $p > 0.01$). In the alpha band the ERD was stronger for the contra- than for the ipsilateral hemisphere, which was not the case in the beta band (Figure 4.6 Panel C; main effect HEMISPHERE, for alpha: $F_{2,144} = 8.726$, $p < 0.01$; for beta: $F_{2,144} = 0.373$, $p > 0.01$). The alpha-ERD was stronger than the beta-ERD in all conditions and both hemispheres (Figure 4.6 Panel B and C; interaction BAND*CONDITION: $F_{2,288} = 5.5$, $p < 0.01$, all post hoc $p < 0.01$; BAND*HEMISPHERE: $F_{1,288} = 7.603$, $p < 0.01$, all post hoc $p < 0.01$). Summarizing, after ~ 20 sec task performance the initial strong ERD recovers towards baseline and reaches a plateau, being still in the negative ERD range (alpha frequency) or around baseline level (beta frequency). Regarding the average ERD across the whole performance period, the amplitude dynamics are modulated by task (overt movements > motor imagery = quasi-movements), by hemispheric involvement (contralateral > ipsilateral), and by the frequency band (alpha > beta for all conditions and hemispheres), with differences of approx. 10–20 %.

Absolute ERD recovery towards baseline (0–60 sec): The apparent trend of ERD recovery towards baseline during task performance can be already seen in Figure 4.3. Also the running t-test (cf. Methods for details) revealed striking differences between task condition and frequency bands, as shown in Figure 4.7 (recovery times, i.e., time index of the last bin being significantly different from zero, were averaged across left and right stimulus classes).

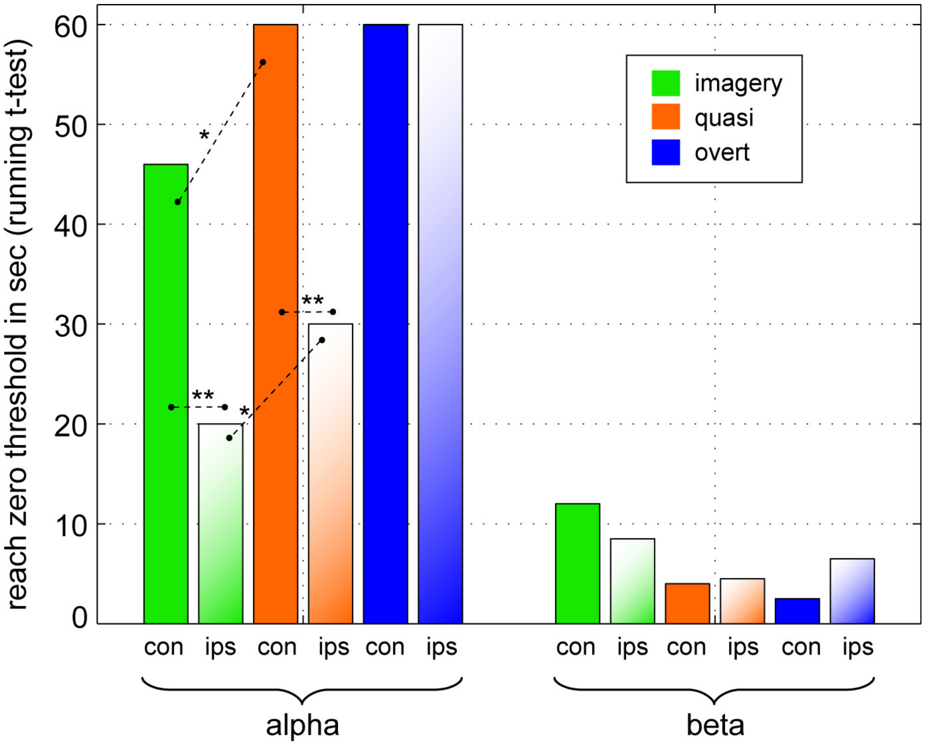


Figure 4.7. Recovery of EEG amplitude dynamics during task performance (0–60 sec).
The running t-test of ERD (Laplacian channels C3 and C4) revealed significant differences between overt and covert movement conditions and between contra- and ipsilateral hemispheres in the alpha band. The beta-ERD recovers much quicker than the alpha-ERD, without apparent differences between conditions or hemispheres. Con – contralateral hemisphere; ips – ipsilateral hemisphere; alpha – 9 to 12 Hz; beta – 15 to 25 Hz; ERD – event-related desynchronization.
** medium effect size (d ≥ 0.5 < 0.8), ** large effect size (d > 0.8).*

Alpha band: The ERD in the “overt movements” condition does not reach the zero baseline during task performance of 1 min (but importantly, there is a significant amplitude decrease comparing start vs. end of performance, see below, which is also the case in the other conditions). For quasi-movements the ERD recovers only in the ipsilateral hemisphere (after ~ 30 sec) but not in the contralateral hemisphere (effect size of the difference: d = **). For motor imagery the ERD recovers in both hemispheres (contralateral after ~ 46 sec, ipsilateral after ~ 20 sec; d = *). Importantly, the ERD in the “motor imagery” condition recovers earlier than for the “quasi-movements” condition (contralateral: 46 vs. 60 sec, d = **; ipsilateral 20 vs. 30 sec, d = *).

Beta band: The amplitude dynamics quickly recover to the baseline level (after 4–12 sec) without significant differences between the conditions or hemispheres. The recovery in beta was much quicker than in the alpha band (d = ** for all comparisons).

Summarizing, only in the alpha band there are significant differences in the ERD recovery between motor tasks. In the alpha band the recovery is quickest for motor imagery (mean across contra- and ipsilateral hemispheres ~ 33 sec), followed by quasi-movements (recovery only in the ipsilateral hemisphere after ~ 30 sec), whereas for overt movements the ERD did not recover back to baseline. The contralateral hemisphere remained longer activated than the ipsilateral hemisphere in covert movements, whereas for overt movements there were no such hemispheric differences. The beta-ERD almost immediately recovered to baseline after a few seconds in all three conditions without hemispheric differences.

Relative ERD recovery comparing start vs. end of task performance: The previous section clearly demonstrated that the amplitude dynamics dramatically change over task performance of 1 min, i.e., the running t-test revealed *when* the ERD values did not significantly differ from zero baseline. However, not reaching the baseline does not necessarily mean that there are no amplitude changes relative to the initial ERD. Therefore, the current section reports on *how much* the amplitude dynamics recover with respect to the initial ERD (i.e., the first 2 sec vs. the last 2 sec of performance, cf. Methods section for details).

The raw ERD values (mean across 58–60 sec) were subjected to a three-way ANOVA with the factors CONDITION, CLASS, and HEMISPHERE separately for each band, and for band comparison to a four-way ANOVA with the factors CONDITION, CLASS, HEMISPHERE, and BAND (cf. Results section of the initial ERD above). The results are shown in Figure 4.8. Similar to the initial ERD (0–2 sec) there was a significant CONDITION effect in the alpha band: the ERD in the “overt movements” condition was stronger than in both covert movement conditions (main effect CONDITION for alpha: $F_{2,144} = 5.701$, $p < 0.01$, post hoc $p < 0.01$). Furthermore, the alpha-ERD was also stronger for the contra- than for the ipsilateral hemisphere (main effect HEMISPHERE for alpha: $F_{1,144} = 5.839$, $p < 0.05$), whereas for beta there were no significant differences between conditions, hemispheres, or classes. The alpha-ERD was significantly stronger than beta-ERD but only in the “overt movements” condition (interaction CONDITION*BAND: $F_{2,288} = 5.878$, $p < 0.01$, also for post hoc).

Summarizing, after 58 sec of task performance the ERD in the alpha and beta bands resemble those at the beginning of the performance (after 2 sec), yet there are strong differences between the levels of activation, as shown by ANOVA below.

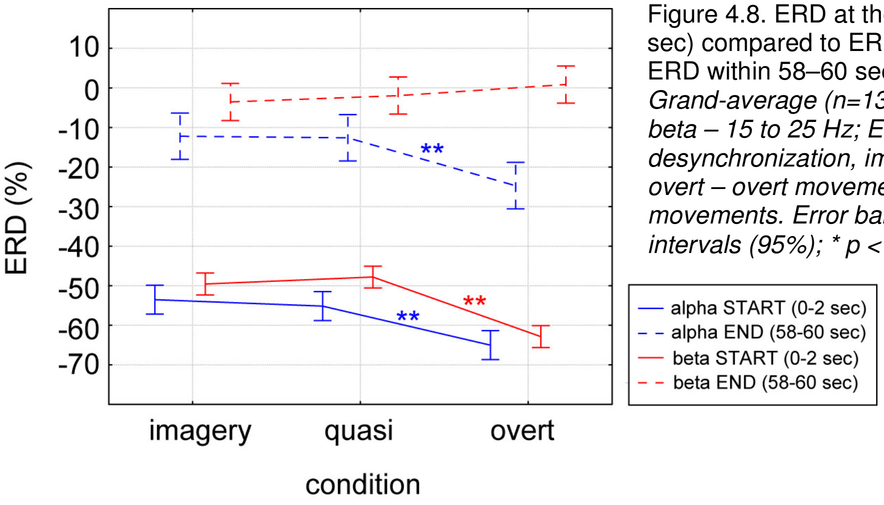


Figure 4.8. ERD at the start (max. within 0–2 sec) compared to ERD at the end (mean ERD within 58–60 sec) of task performance. *Grand-average (n=13). Alpha – 9 to 12 Hz; beta – 15 to 25 Hz; ERD – event-related desynchronization, imagery – motor imagery; overt – overt movements; quasi – quasi-movements. Error bars represent confidence intervals (95%); * p < 0.05, ** p < 0.01.*

In order to calculate the relative change of ERD the percentages were calculated of end-ERD with respect to the start-ERD (cf. Methods section). The values were subjected to a three-way ANOVA with the factors CONDITION, CLASS, and HEMISPHERE separately for each band, and for band comparison to a four-way ANOVA with the factors CONDITION, CLASS, HEMISPHERE, and BAND. The results are shown in Figure 4.9.

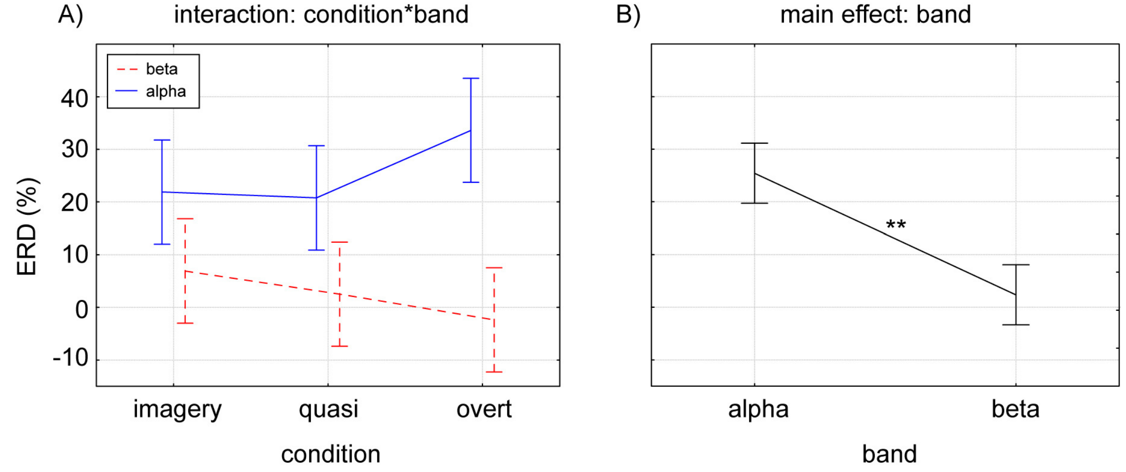


Figure 4.9. Relative ERD change comparing start vs. end of task performance (first vs. last 2 sec).
A) Relative change in the motor conditions and frequency bands.
B) Relative change in the frequency bands (main effect).
*Grand-average (n=13). Alpha – 9 to 12 Hz; beta – 15 to 25 Hz; ERD – event-related desynchronization. For instance, a relative value of 20 % indicates that after 58 sec of task performance 20 % of the initial ERD remained.In Panel A the values represent the average across hemispheres and stimulus classes, in Panel B the average across conditions, hemispheres, and stimulus classes. Error bars represent confidence intervals (95%); * p < 0.05, ** p < 0.01.*

As shown in Figure 4.9 Panel A, after 58 sec only ~ 22 % of the initial ERD remained at the end of the task performance for motor imagery, ~ 21 % for quasi-movements, and ~ 34 % for overt movements in the alpha band. In the beta band only 7 % remained for motor imagery, 3 % for quasi-movements, and -2 % for overt movements. Please note that positive values indicate here that there was still ERD at the end of task performance, while negative values indicate that there was ERS (i.e., overshooting the baseline).

The ANOVA did not reveal significant differences between conditions or hemispheres within each frequency band; however, there was a significant main effect of BAND (Figure 4.9 Panel B): on average the relative recovery of beta-ERD was stronger than for alpha (main effect BAND, $F_{1,288} = 31.610$, $p < 0.01$), i.e., for alpha only 25 % of the initial ERD remained and only 2 % for beta-ERD (averaged values across conditions); there were no significant differences between conditions, hemispheres or stimulus classes.

Correlation of EMG activity with ERD in covert movements: There were no significant correlations between EMG amplitude and ERD for the alpha and beta band, as shown exemplarily in Figure 4.10. Specifically, there was no significant correlation for the comparisons in alpha and beta: left hand performance (EMG left vs. EEG channel C4; EMG left vs. EEG channel C3) and right hand performance (EMG right vs. EEG channel C3; EMG left vs. EEG channel C4) neither for the “motor imagery” nor for the “quasi-movements” condition, respectively.

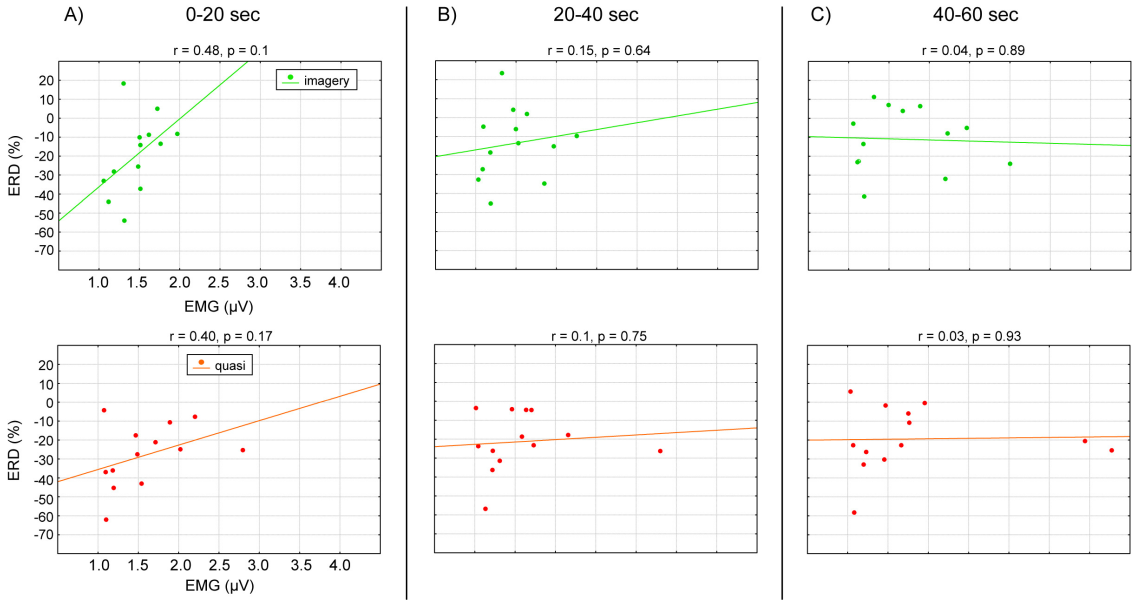


Figure 4.10. No significant correlation between EMG and alpha ERD during task performance (0–60 sec).

ERD – event-related desynchronization; imagery – motor imagery; quasi – quasi-movements; r = Pearson correlation.Dots represent individual subjects (n = 13) for right hand performance (EMG right hand, EEG contralateral channel C3 Laplace, alpha). Green dots represent values for the "motor imagery" condition (upper row), orange dots represent values for the "quasi-movements" condition (lower row).

Results for the left hand, ipsilateral hemisphere, and beta frequency band were similar and also not significant. Broken lines represent least squares trend.

4.4 Discussion

Summarizing, in contrast to previous studies we investigated for the first time the question whether repetition suppression (RS) can also be present without external sensory stimuli during the performance of repeated cognitive tasks (referred to as “internally-driven” RS), such as covert movements which are assumed to involve negligible proprioception.

Our results demonstrate during the repeated performance of covert movements (i.e., motor imagery, quasi-movements) and overt movements (unilateral thumb movement; target muscle APB) the task-related EEG activation over sensorimotor cortices gradually decreases over the course of the 1 min performance. In contrast to a previous study (Erbil & Ungan, 2007) RS is present in both the alpha *and beta* frequencies: The remaining ERD after 1 min was in the alpha range ~ 20 % for covert movements and 34 % for overt movements, and in the beta range ~ 5 % for covert and full recovery for overt movements.

According to statistical testing against baseline level (zero threshold), the beta oscillations recover back to baseline level after ~ 10 sec, while in the alpha band there were pronounced differences: motor imagery (~ 33 sec) < quasi-movements (~ 45 sec) < overt movements (60 sec; values averaged across the contra- and ipsilateral hemisphere); and for the ipsilateral hemisphere (~ 37 sec) < contralateral hemisphere (~ 55 sec; values averaged across conditions). There was no significant correlation between EEG and EMG amplitudes (EMG: on average ~ 2 µV both in pre-stimulus and task intervals and for both motor imagery and quasi-movements).

Notably, the neural dynamics are remarkably similar for overt and covert movements despite extreme differences regarding the motor intention and presence/absence of reafferent sensory feedback. On the basis of our results we might tentatively suggest that movement-related RS could be primarily internally-driven (in agreement with Erbil & Ungan, 2007; Freude & Ullsperger, 1987; Hamilton & Grafton, 2009; Schillings et al., 2006).

4.4.1 Repetition suppression in covert movements

The main finding of our study is the evidence of RS in sensorimotor cortices for covert movements, i.e., motor imagery and quasi-movements, as demonstrated by full (motor imagery: contra- and ipsilateral hemisphere) or partial recovery (quasi-movements: only ipsilateral hemisphere) of the neural oscillations towards baseline, depending on the hemispheric involvement and frequency band. Since during covert movements the muscles usually remain at rest, there is negligible contribution of reafferent sensory feedback to RS. The presence of neural activity decrase over the repeated performance of covert movements is compatible with the view of movement-related RS being a primarily internally-driven phenomenon (cf. references above). We will discuss the implications with respect to (1) the "continuity" assumption between overt and covert movements, (2) potential cognitive correlates to RS, (3) patient data, and (4) crucial differences between motor imagery and quasi-movements.

Continuity between overt and covert movements: It is generally assumed that a common neural network is activated when performing overt and covert movements on cortical and subcortical levels, with less activation in the case of covert movements (Decety, 1996; Lotze & Halsband, 2006; Munzert et al., 2009). Furthermore, decreasing movement force scales with decreasing neural activation in sensorimotor areas (e.g., Dettmers et al., 1995; Dettmers et al., 1996; Mima et al., 1999; Romero et al., 2000) which implies a continuity of activation such that imagined movements can be conceived basically as "scaled-down" version of an overt movement (Jeannerod, 2001).

In line with this assumption we observed that after 1 min of task performance the relative ERD differences between the conditions remain approximately the same (~ 10–20 %; cf. Figure 4.8). However, there are pronounced differences in the temporal dynamics *between* the start and end state: We demonstrate significant differences in the early vs. late onset of repetition suppression in the EEG alpha oscillations: (early) motor imagery < quasi-movements < overt movements (late). Accordingly, regarding the longer sustained central neural activation associated with quasi-movements, one might argue that on the continuum quasi-movements lie further towards the "overt movements" pole. However, it is important to note that although comparatively late stages of neural processing (i.e., some 300 ms to tens of seconds or minutes with respect to stimulus onset) appear to be a scaled version of each other, very early stages of neural processing strongly differ (~ 120 ms, cf. Study 1). The latter result might imply for instance the preemptive routing of early stimulus-processing depending on the prior action intention.

RS and potential cognitive correlates: Interestingly, the subjects reported a feeling of “attention decrease” and “automatization” after ~ 30 sec while the EEG dynamics reach a “plateau” shape after ~ 20 sec. This might suggest that the subjective experience of attention decrease and automatization is related to RS in neural networks. Since in the present study the subjects did the task rating after the whole performance block, there is no data for trial-to-trial correlation of subjective measures with EEG, which might be addressed by future studies. However, there is interesting evidence showing that attentional lapses are related to increased alpha band activity up to 20 sec before the occurrence of the lapse (O’Connell et al., 2009) and for ~ 6 sec (trends for up to 30 sec) by decreased central/premotor activity as well as increased hemodynamic activity in the “default mode network” (e.g., precuneus, posterior cingulate cortex, frontal cortices) which is usually indicative for passive resting (Eichele et al., 2008; Raichle et al., 2001; Raichle & Schneider, 2007). Moreover, movement automaticity is associated with decreased activation in various cortical and subcortical regions (e.g., premotor, parietal, and prefrontal cortices; cerebellum; Wu et al., 2004) whereas connectivity increases in motor regions (e.g., supplementary motor area, cerebellum), but decreases in the precuneus which is part of the resting state “default mode network” (Wu et al., 2008). Importantly, there were no differences between motor imagery and quasi-movements regarding the subjective ratings of task difficulty and concentration. Therefore, the apparent differences in RS might arise as a complex interplay between general slowly changing arousal levels and specific engagement of sensorimotor systems by motor imagery and quasi-movements.

Evidence from patient data: The evidence of the present study, i.e., the presence of RS also in covert movements without significant contribution of reafferent sensory feedback since the limbs remain at rest, suggest that repetitive central activation of sensorimotor networks suffices to trigger RS. This notion is further strengthened by patient data with deafferentation (Patino et al., 2006) and from a healthy subject with transient ischemia (Schnitzler et al., 1997). In these cases the movement control is achieved without reafferent sensory feedback from the moving limbs. Interestingly, for patient GL with chronic deafferentation up to the nose there is a larger ERD during movement performance compared to the healthy control group, interpreted as effort-related effect since it should be more difficult to perform a movement without sensory feedback (Patino et al., 2006). Importantly, this increased negativation is only present in the EEG alpha dynamics, whereas the beta dynamics remain unaffected after chronic deafferentation and in transient ischemia (Schnitzler et al., 1997). Although in these studies it is not possible to distinguish whether the increased alpha negativation is due to increased effort or due to the removal of the expected sensory input (i.e., larger prediction error requiring increased neural processing, see below), it is shown that the removal of reafferent feedback does not significantly influence the strength of beta dynamics and at least does not weaken the alpha dynamics.

Modulation of alpha-EEG during covert movements: Intention or somatosensory error? The results from patient data above are in line with neuroimaging studies locating the origin of beta oscillations primarily in the precentral gyrus (primary motor cortex, MI) and the origin of alpha oscillations primarily in the postcentral gyrus (primary somatosensory cortex, SI) as evidenced in MEG and EEG-fMRI data (Ritter et al., 2009; Salmelin & Hari, 1994; Salmelin et al., 1995). While both rhythms are susceptible to motor performance, according to experimental evidence the rolandic EEG beta rhythm has been often interpreted to be rather associated with executive motor control and termination of movement (Erbil & Ungan, 2007; Pfurtscheller et al., 1998), whereas the rolandic alpha rhythm rather relates to somatosensory processing (e.g., Chatrian et al., 1959; Nikouline, Linkenkaer-Hansen et al., 2000; Stancák, 2006) and to motor attention/intention, since frequent studies demonstrated the modulation of alpha oscillations during covert movements, e.g., motor imagery (review: Lotze & Halsband, 2006; Munzert et al., 2009) or quasi-movements (Nikulin et al., 2008).

In the case of covert movements it is tempting to interprete the variations of alpha-ERD being primarily related to motor attention/intention, since usually no or only negligible no somatosensory processing is involved when the limb remains at rest. However, given the assumption that the rolandic alpha rhythm most likely originates in S1, an alternative explanation for alpha-ERD during covert movements could be that it actually might reflect *sensory error*. Covert movements are assumed to involve the activation of inverse/forward models, i.e., motor and sensory simulators, respectively (Grush, 2004), without the activation of the executive efferent motor pathways (Jeannerod, 2001). However, if the forward model constantly predicts sensory consequences (experienced as “sense of movement”) but there are no reafferences, the comparator gives a prediction error signal (Wolpert & Gharahmani, 2000). This might be reflected in the suppression of rolandic alpha oscillations. Indeed it has been argued that evoked cortical responses actually express prediction errors (cf. Friston, 2005 and discussion below in the BCI context).

Differences between motor imagery and quasi-movements: At the first glance imagined and quasi-movements seem to be very similar: recruitment of sensorimotor networks and absence of measurable muscle responses in EMG, since movements should be performed only “in the head” and not by the muscles. However, there are fundamental differences between both tasks (cf. present results and Nikulin et al., 2008), namely on the level of action intention (motor *simulation* vs. motor *execution with effectively zero muscular output*, see also the Results section), on the level of subjective experience (higher “sense of movement” in quasi-movements), and on the level of brain dynamics in sensorimotor networks (stronger engagement by quasi-movements).

Our previous study demonstrated a stronger modulation of EEG alpha dynamics in the case of unilateral quasi-movements (i.e., stronger ERD and more pronounced lateralization of activation patterns over sensorimotor cortices) compared to motor imagery ~ 1 sec after stimulus onset (Nikulin et al., 2008). However, in the present study there was no significant difference in the ERD strength for imagined and quasi-movements across 1 min, although such trend was visible on the grand-average level (cf. Figure 4.3). This result might be due to the fewer amount of trials in the present study (8 vs. 54 trials), a potential disadvantage of the present study due to the experimental setup comparing three conditions with trials of 1 min length.

Yet when comparing the ERD to the zero baseline (running t-test) the differences between both covert movement tasks became significant in the long-term perspective: For quasi-movements the alpha-ERD are longer sustained (by ~ 10–15 sec) than for motor imagery – a finding with important implications for brain-computer interfacing, as discussed below.

Furthermore, another crucial difference between motor imagery and quasi-movements, on the level of action intention and possible neural substrates, becomes clear when recapitulating the definition of mental imagery: Mental imagery is a quasi-perceptual experience in absence of adequate sensory stimuli (Richardson, 1969).

Accordingly, motor imagery involves “kinesthetic images; that is, … somatosensory feelings that a participant experiences when performing a movement him- or herself” (Munzert et al., 2009, p. 307). Therefore, during motor imagery the subjects are instructed to simulate *proprioception*, they do not intend to simulate the movement/motor command itself (Jeannerod, 1994; Kosslyn et al., 2001; Moulton & Kosslyn, 2009; Nikulin et al., 2008 and Results section above). In contrast, during quasi-movements the subjects intend to perform an overt movement, yet they have learned by EMG neurofeedback to control motor output, i.e., decrease and finally inhibit the muscular contraction.

Summarizing, we have argued that the current finding, i.e., RS in covert movements, is congruent with the notion of a continuity between overt and covert movements, that RS might be related to the subjective reports of attention decrease and automatization, and finally that the present results and patient data support the notion of movement-related RS being primarily internally-driven.

4.4.2 Muscular activity in covert movements: A potential confound to RS?

The “simulation” theory defines motor imagery as a mental simulation of a movement without muscular activation (Finke, 1979; Jeannerod, 2001). Subjective reports are in line with this definition (e.g., Nikulin et al., 2008), as well as studies showing the absence of EMG activity during motor imagery and quasi-movements (Lotze et al., 1999; Nikulin et al., 2008). However, it is also well-documented that motor intentions and motor imagery *can* be accompanied by occasional, task-related subliminal muscular activity, usually being a small fraction of it’s “real” counterpart (Gandevia et al., 1997; Guillot & Collet, 2005; Guillot et al., 2007; Hashimoto & Rothwell, 1999; Jacobson, 1932; Lebon et al., 2008; Shaw, 1938). Therefore, it is important to note that the requirement “without muscular activation” is not always met for motor imagery. This is also in line with the so-called ideomotor principle, actions are initiated by the anticipation of their consequences (also termed “psychoneuromuscular theory”: James, 1890; Knuf et al., 2001; A. Stock & C. Stock, 2004; cf. inverse modeling: Wolpert & Gahramani, 2000; Wolpert et al., 2001). The “anticipation”, i.e., movement intention or motor imagination, can induce weak EMG activation resulting from incomplete inhibition of the efferent motor command, since motor imagery and overt movements are assumed to share neural networks in the motor system (Jeannerod, 2001; Jeannerod & Frak, 1999). Given that, how to discuss the present results of RS in covert movements regarding (1) possible peripheral confounds by residual EMG activity? (2) To what extent does RS depend on stimulus regularity?

Residual EMG in covert movements: In the present study we cannot exclude a possible influence of reafferent proprioceptive feedback on brain dynamics, since in single trials *occasional and subliminal* (~ 1–2 % of max. voluntary contraction) EMG activity was present. However, we have evidence that on average there was no significant muscular contribution:

a) The EMG activity between the pre-stimulus interval and task-performance did not differ significantly.

b) The “motor imagery” and “quasi-movements” conditions also did not significantly differ in EMG amplitude (mean activation between pre- and task-interval ~ 2 µV) and there was no significant difference of EMG amplitude between early and late time bins during task performance.

Furthermore, as we have demonstrated in depth in our previous study (Nikulin et al., 2008) even if there were residual small EMG activations they did not contribute to the modulation of EEG alpha dynamics. c) There was no significant correlation between EMG and EEG amplitudes in the alpha and beta frequency bands. Furthermore, a non-physiological reason for transient EMG responses and accompanying EEG positivation (i.e., which would appear as RS) can be head and body movements of the subjects, thus shifting wires of EMG and simultaneously affecting EEG.

RS and stimulus regularity: Important for the discussion of possible EMG confounds for RS during covert movements is the finding that the degree of RS depends on the regularity of external stimulus presentation (Gruber et al., 2004; Henson et al., 2000; Summerfield et al., 2008). Deviations in the externally presented stimulation pattern, for instance, by timing (“omission”) or stimulus type (“standard” vs. “deviant”), usually *increase* neural activation, indicating a larger computational demand for unexpected stimulus features (“novelty” or “prediction error”; Friston, 2005). If we assume that peripheral EMG feedback is the major factor contributing to movement-related RS, then we would not expect to observe RS during covert movements, since any sporadic, weak muscle activation is highly irregular in time (see also Figure 4.2 for single trial examples). However, the present study demonstrates robust RS in the case of covert (and overt) movements in EEG alpha and beta oscillations, speaking for a central triggering (top-down) of RS. Summarizing, the present results do not suggest a significant contribution of occasional, weak EMG activation to RS during covert movements.

4.4.3 Overt movements: Repetition suppression in alpha and beta oscillations

The only previous study on long-term dynamics of EEG oscillations during overt movements (Erbil & Ungan, 2007) reported that during a 30-sec performance alpha oscillations gradually (but not fully) recover towards baseline, whereas for beta oscillations there was no such recovery since the amplitude suppression was sustained until the end of the trial. Importantly, in the present study we demonstrated an amplitude recovery towards baseline not only for alpha but also for beta oscillations within 1 min of performing overt movements. The beta dynamics showed a full recovery back to baseline after ~ 10 sec for both overt and covert movements, and there were no differences between the contra- and ipsilateral hemisphere. The alpha dynamics showed a partial recovery towards baseline, i.e., ~ 34 % remaining ERD for overt movements at the end of performance.

Importantly, the increase of oscillatory power (i.e., ERD towards zero baseline or even ERS overshooting the baseline) is often assumed to relate to cortical idling and a reduced excitability of the respective area (e.g., Neuper et al., 2006; Pfurtscheller & Neuper, 1994; also see below). This assumption, together with the hypothesized differences between the functional roles of rolandic alpha and beta rhythms (cf. discussion above), we would have expected in our study: (a) no RS in the beta band for overt movements, since executive motor processing should remain unaffected due to the continuous performance of the movements (cf. also Erbil & Ungan, 2007), and (b) RS in alpha due to habituation of afferences and the decrease of motor attention across task performance.

However, while (b) was confirmed by the present findings, we demonstrate the quick recovery of beta oscillations after a few seconds, similarly to previous results showing beta recovery in isolated or sustained movements (Cassim et al., 2000; Doyle et al., 2005; Jasper & Penfield, 1949; Stancák & Pfurtscheller, 1995; Stancák & Pfurtscheller, 1996). Thus the present findings do not replicate the findings from Erbil and Ungan (2007).

Our unexpected result of RS in beta oscillations suggests the following questions: (1) Beta recovery (ERS) is often interpreted as being indicative for cortical idling (deactivation, reduced excitability; cf. references above). How can this interpretation be reconciled with the present finding of beta-ERS back to baseline during the *ongoing* movement performance, where the motor cortex cannot be in a "deactivated" state? (2) To which extent do movement parameters influence RS? (3) How can the present results of *decreased* oscillatory power be reconciled with the findings of an *increased* negativity in Readinesspotentials for repeated movements (Freude & Ullsperger, 1987; Johnston et al., 2001; Schillings et al., 2006)?

Beta dynamics and cortical idling: According to experimental evidence it is often assumed that the decrease of oscillatory EEG amplitude (i.e., amplitude negativation with respect to a prior baseline) or "blocking" of sensorimotor rhythms, indicates the activation of neural networks which might be reflected in the event-related desynchronization of the oscillatory neural activity in the population (Pfurtscheller & Lopes da Silva, 1999; Pfurtscheller, 2001; although other scenarios are conceivable, cf. Introduction). In contrast, an increase in amplitude of oscillatory EEG rhythms (i.e., returning towards or overshooting the prior baseline) is assumed to reflect an inhibitory or deactivated "idling" state of the neural population with low excitability and little information processing capacity (Adrian & Matthew, 1934; Chase & Harper, 1971; Jasper & Penfield, 1949; Klimesch et al., 2007a; Pfurtscheller, 2001; Pfurtscheller & Neuper, 1994; Pfurtscheller et al., 1996).

Thus at first glance it seems to be plausible to interpret the RS demonstrated in our study (i.e., gradual reappearance of sensorimotor rhythms) by cortical "idling". However, the "idling" sensorimotor cortex is highly active since the movements were continuously performed for 1 min. Although motor networks partially adapt, as indicated by RS, the "idling" notion might not be feasible since it has been discussed "that even if only a small fraction of the total population of neurons is synchronized, the resulting output may well overweigh the rest of the not-synchronized neural populations. It was estimated that "even if only 10% of a population of neurons are synchronized, the amplitude is 10-fold the activity of the 90% of not-synchronized neurons" (Pfurtscheller, 2001, pp. 1257–1258).

RS and movement parameters: Compared to the previous study we utilized a much simpler motor task (i.e., thumb movement instead of the flexion of four fingers), higher movement frequency (1 Hz instead of 2 Hz), and a longer duration of performance (1 min instead of 30 sec). Usually, higher movement frequencies are related to increased neural activity (Rao et al., 1996; Romero et al., 2000; Yuan et al., 2010) as it is the case for more complex movements (Kranczioch et al., 2010; Kuhtz-Buschbeck et al.,2003). Given the present results (RS in beta band) and the previous study (no RS in beta band: Erbil & Ungan, 2007) we might only speculate that RS in beta oscillations depends on movement parameters which modulate neural activation strength in the motor networks. In the case of simple movements fewer resources are needed to maintain executive motor control, such that after an initial stage of establishing motor routines the neural networks quickly adapt after a few seconds. Importantly, we can exclude the influences from muscular fatigue on RS, since there were no significant differences in EMG movement speed and strength (~ 50 % of MVC) across the 1 min performance. In such scenario other authors have suggested that RS might be modulated by cognitive and neural fatigue in central sensorimotor networks (Freude & Ullsperger, 1987; Schillings et al., 2006).

RS in EEG oscillatory dynamics vs. EEG event-related potentials: While RS in ERD refers to an amplitude positivation (i.e., recovery towards baseline or even overshooting it; the latter is referred to as ERS), it has been reported that the Readinesspotential shows increased negativity for fatiguing movements (i.e., for 80% and 20% of max. voluntary contraction, where either muscular or attentional load is high), which was interpreted as compensatory mechanism in central motor processing (Freude & Ullsperger, 1987; Johnston et al., 2001; Schillings et al., 2006). However, for simple repeated movements without muscular fatigue, i.e., 50% of max. voluntary contraction or simple button presses, the Readinesspotential shows decreased negativity (Freude & Ullsperger, 1987; Dirnberger et al., 2004a; Dirnberger et al., 2004b), which is similar to the results of the present study. However, it is important to keep in mind that the movement-locked Readinesspotential reflects preparatory motor processes a few seconds before and after movement onset, in contrast to the stimulus-locked oscillatory dynamics of the present study which indicate ongoing motor control over a period of 1 min. In principle we could have analyzed movement-locked Readinesspotentials, but since the main interest of our study was RS in *covert* movements (i.e., no muscular contraction) it was reasonable to analyze stimulus-locked data in all three experimental conditions.

Summarizing, we found significant RS in alpha and beta dynamics for movements executed with ~ 50 % of max. voluntary contraction, which suggests the adaptation and optimization of neural networks in the case of self-paced automatic movements without muscular fatigue as evidenced by EMG data (i.e., no significant changes of movement strength or inter-movement-intervals during a trial).

4.4.4 Repetition suppression in the ipsilateral sensorimotor cortices

The striking difference between alpha-RS in the contra- and ipsilateral hemispheres in covert movements (ipsilateral hemisphere recovers back to baseline ~ 28 sec earlier than the contralateral hemisphere) but not in overt movements (no recovery to baseline, yet only 34 % of remaining alpha-ERD after 58 sec in both hemispheres) might be explained (1) by a quicker adaptation of the ipsilateral hemispheres during covert movements ("active" role). We might also hypothesize that (2) the ipsilateral excitability (or decrease of it) depends on a critical activation level in the contralateral hemisphere ("passive" role).

"Active" role of ipsilateral hemispheres: In general, it is assumed that motor programs are stored in a "bilateral" mode and the execution of unimanual movements in healthy adults result from the active inhibition of simultaneous "mirror movements" in the ipsilateral hemisphere. The occurrence of mirror movements is more likely with increasing movement complexity, fatigue or attentional demands (Carson, 2005; Chan & Ross, 1988; Cincotta & Ziemann, 2008). In agreement with this notion it has been also demonstrated that for high force movements there is an increased excitability for the ipsilateral motor cortex, whereas excitability was decreased for low force movements (i.e., 1–2 % of max. voluntary contraction; Liepert et al., 2001), whereas the former seems to be mediated by the ipsilateral cortico-spinal sensorimotor pathways and the latter by interhemispheric transcollosal connections (Rau et al., 2003; Sohn et al., 2003). Since covert movements are generally believed to share many cognitive and neural aspects with overt movements (review: Jeanneord, 2001; Lotze & Halsband, 2006; Munzert et al., 2009), it might be the case that during covert movements bilateral motor programs are activated and a similar active suppression of ipsilateral mirror movements occurs.

"Passive" role of ipsilateral hemispheres: However, in the case of covert movements it is unclear whether the inhibition of "mirror movements" is involved at all – it might be also the case that only the unilateral motor program is activated. An interesting study (Liang et al., 2008) utilized transcranial magnetic stimulation over the *ipsilateral* hemisphere and demonstrated increased motor evoked potentials in the target muscle for both overt and imagined movements. They interpreted "that the excitability changes in M1 are induced by motor overflows of voluntary drive given to the ipsilateral limb" (Liang et al., 2008, p. 138). Therefore, we might speculate that the ipsilateral excitability depends on a critical activation level in the contralateral hemisphere: both hemispheres show gradual amplitude decrease (indicating repetition suppression), but they start from different activation levels in the alpha band (contra- stronger negativation than ipsilateral hemisphere). If the ipsilateral hemisphere in the case of covert movements shows "passive" and weaker co-activation, it is conceivable that the activation decreases faster.
Summarizing, the modulation of ipsilateral hemispheric activation during covert movements, i.e., initial bilateral negativation after stimulus onset and faster decrease of activation than in the contralateral hemisphere, might be due to different accounts: *active* inhibition of mirror movements or *passive* interhemispheric cross-talk, e.g., receiving efference copy from the contralateral hemisphere or inhibitory inputs. However, a distinction between both accounts is not feasible on basis of the current data. Regarding the sustained ipsilateral activation during overt movements this might be due to a combination of passive interhemispheric flow, active suppression of mirror movements, and the reafferent sensory input projecting also to the ipsilateral hemisphere via uncrossed fiber tracts (Korvenoja et al., 1995).

4.4.5 Neural basis of repetition suppression

Repetition suppression, i.e., the *decrease* of neural activity to repeated stimulation, is usually accompanied with an *increase* of speed and accuracy in stimulus processing as well as increased sensitivity to novel input (behaviorally manifested as "priming": decreased reaction time, error reduction). This suggests the short- and long-term plasticity of neural networks, resulting in the optimization of response rates and reduced energy consumption. The neural plasticity can be achieved by different mechanisms: firing rate adaptation, lateral inhibition or changes in synaptic efficacy (e.g., short-term synaptic depression, long-term depression/potentiation), as depicted by different RS models (Desimone, 1996; Friston, 2005; Grill-Spector et al., 2006):

Fatigue model: All initially responsive neurons equally reduce their firing rate (firing rate adaptation), both the optimally tuned and suboptimally tuned neurons.

Sharpening model: From the initially responsive neurons only a part shows RS, specifically, those neurons representing irrelevant stimulus features reduce their firing rate (e.g., by lateral inhibition). Thus only the optimally tuned neurons stay active, resulting in sharpened tuning curves.

Facilitation model: Repeated stimulation facilitates subsequent processing by shorter duration/latency of neural firing (e.g., synaptic potentiation), thus increasing the processing speed.

However, there is no consensus on which of these models is accurate; it is more likely that the applicability of RS models depends on different factors: the brain region under investigation, the network size (single cell vs. population), time scales (RS effects measured on millisecond’s range, hours, days or years), stimulus features, lag between repetitions, and the amount of repetitions (short vs. long-term adaptation effects). Although the present data do not allow unequivocal conclusion about either of the models, the current study adds an important factor to the discussion of RS, namely the dimension of external vs. internal elicitation. All models discussed so far were based on data from repeated *external* sensory stimulation. In contrast, the results of the present study investigated RS in the absence of or with minimized sensory input, i.e., during the performance of repetitive cognitive tasks (in our case covert movements) and we did not present repetitive external stimuli to which neural activity was locked (e.g., repeated presentation of visual objects; cf. Grill-Spector et al., 2006). Since we nevertheless observed RS in covert movements, where the reafferent proprioceptive input is minimal (i.e., no significant differences between EMG activity in pre- compared to post-stimulus intervals, and no significant correlation of EMG and EEG activity), we might very hypothetically assume that RS might occur for *any* repeated activity in the brain, cf. also Hamilton & Grafton, 2009). Accordingly, RS probably reflects the adaptation and optimization of neural processes during stereotyped, automatized activation regardless of the internal or external elicitation.

4.4.6 Action intention and brain-computer interfacing

The present study demonstrated significant RS in the case of self-paced, repeated internal stimulation by performing covert movements. This adaptive mechanism, i.e., reduction of neural responses for increased predictability, has the benefit of reducing energy costs in the sensorimotor system. However, this has crucial implications for the long-term usage of methods relying on the detection of neural correlates of action intentions by utilizing a brain-computer interface (BCI). “A BCI is a communication system in which messages or commands that an individual sends to the external world do not pass through the brain’s normal output pathways of peripheral nerves and muscles” (Wolpaw et al., 2002, p. 769), enabling the “control of computers or external devices with regulation of brain activity alone” (Birbaumer, 2006, p. 517). This makes BCI technology a valuable tool for restoring communication and mobility in patients suffering from paralysis, e.g., due to amyotrophic lateral sclerosis, spinal cord injury or amputation (Birbaumer et al., 1999; Blankertz et al., 2007; Dornhege et al., 2007; Hochberg et al., 2006; Kübler et al., 2001; Pfurtscheller et al., 2006). Furthermore, BCI is applicable in healthy subjects in order to monitor cognitive states, e.g., error detection (Blankertz et al., 2002; Schalk et al., 2000) or detection of attentional lapses during security surveillance (Müller et al., 2008).

BCI relies on the accurate classification of the user’s intention-related brain states, which are usually translated into simple commands such as “yes/no”, “up/down” or “left/right”, or in more complex outputs utilizing for instance text spelling programs (Hinterberger et al., 2004; Müller et al., 2008). The neural activity is usually measured by EEG, e.g., utilizing the P300, slow cortical potentials, or the modulation of sensorimotor rhythms in the alpha and beta frequency range by motor imagery (Blankertz et al., 2007; Neuper et al., 2006). EEG-based BCI is often preferred over other methods (e.g., fMRI) because of its mobility, high temporal resolution allowing rapid communication, and relative low costs (Wolpaw et al., 2002).

Neural repetition suppression vs. continuous cognitive control: Given a running BCI system and sufficient control on behalf of the subject, it requires many repeated cognitive commands, translated by the BCI, in order to write a letter or navigate a wheelchair, as it would be the case with “real” motor control. As we have demonstrated in our present study the repeated, self-paced internal stimulation is associated with RS. Thus, the more trials the user performs the stronger should be the decrease of neural responses, which is problematic for the stability of the interface, as reflected by increasing classification errors with increasing number of sessions (Blankertz et al., 2010; Kotchoubey et al., 1997; Pfurtscheller et al., 2008). Therefore, algorithms must take into account the neural long-term dynamics, where the activation decrease is in contrast to prevailing strong action intentions. This discrepancy between low-level neural response optimization and high-level cognitive control is not easy to address: In early BCI systems the algorithms were fixed and the subject had to train over weeks and months to control their own brain activity in order to produce strong and reliably classifiable signals (Kübler et al., 2001; Pfurtscheller et al., 2000).

Recent BCI systems rely on sophisticated machine learning techniques, where the classifiers quickly adapt to the user’s brain, thus reducing the training time to less than half an hour or only some minutes, with continuous adaptation during the subsequent BCI control (Krauledat et al., 2008; Wolpaw et al., 2002). However, the adaptation is twofold: the BCI adapts to the brain and the brain adapts to the BCI. Here the important notion is that BCI control can be considered as a skill, with the only difference that the subject learns to modulate brain signals directly and that the normal muscular output is replaced by the electronic application. Therefore, as it is the case with learning a new motor skill, the brain adapts to this new performance as reflected by reduced energy costs once the skill is learned (Wolpaw et al., 2002; Wolpert, 2007). This adaptive learning is reflected in, for instance, repetition suppression in the cortical sensorimotor areas and transfer of activation to subcortical motor circuits (Erbil & Ungan, 2007; Floyer-Lea & Matthews, 2004). Therefore, the signal strength decreases which is detrimental for the BCI classifier, since even the best classifier is limited by the signal-to-noise-ratio.

Protocols for optimizing long-term usage of brain-computer interfacing: As discussed in the previous section, optimizing BCI control comprises advantages and disadvantages of a learning brain: On the one hand the brain quickly adapts to a completely new and artificial situation (i.e., executive control bypassing muscular output pathway), but on the other hand the brain adapts so well to this task, by reducing energy consumption and thus signal strength, such that BCI performance is decreased. The results of the present study have important implications regarding the design of experimental protocols for the long-term usage of a BCI (i.e., many repeated trials over hours, weeks or years) in order to deal with the issue of signal decrease due to repetition suppression and skill learning. It might be the case that for optimal long-term BCI usage it is necessary to keep a balance between adaptation (of the classifiers and the user's brain) and excitation, i.e., variability which induces re-adaptation of the user's brain, thereby increasing neural signal strength.

(a) Task variation. The results of the present study as well as our previous study (Nikulin et al., 2008) clearly demonstrate that quasi-movements might be a beneficial paradigm for BCI compared to motor imagery, due to the stronger and more sustained activation of sensorimotor areas and the increased classification accuracy of neural activation patterns. In order to maintain a necessary level of excitation during long-term usage, i.e., counter-acting the repetition suppression effect, monotonous experimental protocols should be avoided. This might be achieved, for instance, by changing inter-stimulus intervals or session durations. Another possibility might be the variation of the motor task: non-stereotyped movements (e.g., rhythm variation, different limbs) avoid quick automatization of the performance and thus might alleviate the RS effect. This assumption is supported by studies showing that RS depends on stimulus regularity (Gruber et al., 2004; Henson et al., 2000; Summerfield et al., 2008), as discussed above. Deviations from the regular, stereotyped pattern increase neural activity (in the sense of a “mismatch” or “oddball” effect; cf. Duncan et al., 2009). Therefore, given the frequent reports on similar neural activation during overt and covert movements, it is likely that non-stereotyped *covert* movements might counteract RS in a similar way. In this sense one might vary covert task performance, for instance, by performing quasi-movements with different body parts (e.g., left hand vs. left foot), variation of the movement speed or variation of the motor sequence (e.g., different finger order).

(b) Limiting adaptability of BCI classifiers. Although a certain adaptation of the interface to the user's brain is beneficial as many studies have demonstrated (review: Wolpaw et al., 2002), the "perfect" adaptation (e.g., continuous adaptive classifiers) might actually be counter-productive. The brain is a learning system, continuously processing information and reorganizing neural responses due to changing inputs and different output requirements, trying to reduce free energy (i.e., prediction error). In this sense it has been suggested "that evoked cortical responses can be understood as transient expressions of prediction error" (Friston, 2005, p. 816). Therefore, the ideal classifier, fitting the brain's activity like a glove, would make it too easy for the brain. There would be only few/none prediction errors and thus only small neural activation, maybe decreasing the signal-to-noise ratio under a critical threshold for being detectable by macroscopic EEG. Therefore, increasing classification accuracy further and further might not be optimal, since a certain amount of noise/prediction error might be a necessity for successful BCI: Interestingly, it has been shown that prototypical classifiers, based on the subject's brain signals from previous BCI sessions or being even subject-independent, allow the immediate BCI control without "optimal" adaptation to the current state of the subject's brain (Fazli et al., 2009; Krauledat et al., 2008; Krauledat et al., 2007). This suggests that also in the unnatural situation of controlling external devices by brain activity alone, the brain tolerates certain amounts of noise in the interface, e.g., prediction error due to a suboptimal classifier (i.e., the "artificial muscle"). It might also suggest that this noise is essential for BCI to work and that the neural signals utilized for BCI control actually reflect to a major extent prediction errors.

In sum, the presence of repetition suppression in the sensorimotor system during the performance of continuous covert movements (motor imagery, quasi-movements) has important implications when designing protocols utilizing covert movements for the long-term operation of brain-computer interfaces. We argue that successful BCI (i.e., good discrimination of intention-related brain signatures by algorithmic classifiers) depends on strong neural signals, which seem to a large extent reflect prediction errors. Therefore, minimizing such prediction errors by designing the "perfect" classifier might be detrimental for the signal-to-noise-ratio. This might be avoided by inducing an optimal balance between adaptation/automatization (well-defined task, subject-training, using brain-state classifiers) and excitation/variability (e.g., by inducing variable experimental schedules, non-stereotyped motor tasks, or limiting the adaptability of BCI classifiers).

4.4.7 Outlook

The results of the present study demonstrate for the first time that the well-known phenomenon of repetition suppression, i.e., the decrease if neural activity over time in the case of repeated external stimulation, is also present in the absence of repeated exernal sensory stimuli during the performance of a repeated cognitive task, e.g., covert movements. We show that the performance of covert movements over a period of 1 min is associated with the progressive recovery of EEG alpha and beta oscillations towards baseline level over sensorimotor cortices, which has important implications for designing experimental paradigms for BCI.

Based on these results we might tentatively hypothesize that movement-related RS is primarily internally-driven. Importantly, in the case of EEG the RS is reflected in the decreased amplitude of event-related potentials and in the reappearance of oscillatory rhythms after initial stimulus-induced blocking. Clearly more research is needed on the unfolding and long-term dynamics of neural activity during continuous task performance (i.e., trial lengths > 1 min), since repetitive cognitive and motor activities belong to the daily repertoire. For this purpose the high temporal resolution of data recordings is necessary, which is provided by EEG. However, given the limited spatial resolution of macroscopic EEG, a complementary approach could be the assessment of invasive intracortical or electrocorticographic data with higher spatial resolution (yet with the limitation of being restricted to patient data and impaired motor functioning).

Another interesting feature regarding repetitive information processing is the interplay between attention and neural activity. The present study suggests a relation between the subjective attention decrease and feeling of automatization and the time course of EEG oscillations showing decreased activation (i.e., after 20–30 sec in both domains). However, these data are on grand-average level and do not allow conclusions on the level of single subjects/trials. Therefore, a study focussing on the correlation between single-trial amplitude dynamics and single-trial measures of attention and automatization during long trials of repetitive performance/perception could reveal interesting divergence or convergence of neural and cognitive activities.

Acknowledgements

FH is supported by the Berlin School of Mind and Brain. VVN and GC are partially supported by the Berlin Bernstein Center for Computational Neuroscience.

Chapter 5

V. GENERAL DISCUSSION

“The seat of the soul and the control of voluntary movement
– in fact, of nervous functions in general – are to be sought in the heart.
The brain is an organ of minor importance”
(Aristotle, 384–322 BC)

“The brain is the seat of consciousness”
(Clifford, 2010)

“There is no fundamental obstacle to modelling the brain
and it is therefore likely that we will have detailed models of mammalian brains,
including that of man, in the near future”
(Blue Brain Project: Markram, 2006)

5.1 Summary of results and implications

The present thesis focused on neural correlates of action intention (covert and overt movements) by investigating short- and long-term dynamics of EEG alpha/beta oscillations and event-related potentials. The results of the three studies are discussed with respect to a basic neurophysiological understanding of action intention and motor inhibition in covert movements (i.e., motor imagery, quasi-movements) and potential application for clinical rehabilitation.

Another main focus of my thesis concerns the optimization of brain-computer interfacing (BCI) from neurophysiological and cognitive viewpoints: BCI relies on neurofeedback methods and the effectiveness of neurofeedback learning relies on the cognitive states of the subject, i.e., the strategy which the subject employs in order to modulate the own brain dynamics.

In this chapter I will discuss the implications of the present results regarding representative assumptions from the research community. In each section quotations will be given from representative studies and subsequently I will briefly discuss the novelty of our findings and how they fit into current views in the field. Please also refer to the discussion sections of the individual study chapters for more details. A summary of the results in table format can be found in the Appendix below.

5.1.1 Implications from Study 1

"Covert actions [e.g., motor imagery, prepared movements] are neurally simulated actions" (Jeannerod, 2001, p. 103)

Already 120 ms after the onset of an instructive stimulus the contralateral sensorimotor cortex is stronger activated than the ipsilateral cortex in the case of upcoming overt movements. However, there was no significant lateralized EEG activation for covert movements (i.e., motor imagery, quasi-movements). In contrast to the "simulation" assumption, our results are more in line with the notion that already the prior action intention (overt vs. covert) differentially routes early stimulus-processing into the sensorimotor system, thus possibly contributing to significantly different behavioral outcomes, i.e., movement generation or (preemptive) inhibition.

The novel motor-cognitive skill of quasi-movements has been recently introduced (Nikulin et al., 2008). Although at a first glance both motor imagery and quasi-movements seem to be very similar, since both tasks activate sensorimotor networks in the brain while there are no detectable motor responses, there are clear differences between both tasks, as the present studies demonstrate: (1) on the level of the action intention (motor/proprioceptive *simulation* vs. motor *execution with effectively zero muscular output*), (2) on the level of subjective experience (i.e., higher "sense of movement" for quasi-movements than for motor imagery), and (3) on the level of brain dynamics in sensorimotor networks (i.e., stronger and more sustained engagement by quasi-movements).

Furthermore, we discuss the idea that quasi-movements could represent an intermediate stage in a continuum (cf. Jeannerod, 1994, 2001) between overt and covert stages of action/perception in terms of neural processing (generally: motor imagery < quasi-movements < overt movements), which poses the question of whether early stimulus-processing is scaled in a similar way (as discussed below). However, the present results provide converging evidence that early stimulus-processing in the motor system is unique for subsequently executed movements.

"The LRP is an electrophysiological indicator of unimanual response activation in primary motor cortex, reflected by an enhanced negativity over the motor cortex contralateral to the side of the activated response" (Eimer et al., 2005, p. 959)

In the present study we have introduced a novel calculation of the LRP, based on the calculation from *rectified* EEG signals (LRPrect): Importantly, the enhanced activity of the contralateral motor cortex in the case of unimanual overt/covert movements is not necessarily reflected by a *negativation* of EEG signals, it might also be a positivation. As we also demonstrate by dipole simulations, this contra-intuitive result might simply be explained by anatomical variations of source orientation in the motor cortex, and by differential electrode positioning or superposition of local and global source activity. Therefore, much like the calculation of the EEG Global Mean Power based on rectified/squared values, we demonstrated the utility of LRPrect as complementary measure to the classic LRP, both emphasizing different aspects: LRP indicates the relative negativation difference between the contra- and ipsilateral hemisphere, and LRPrect indicates the absolute activation difference regardless of the signals' polarity (cf. discussion and appendix in Study 1).

5.1.2 Implications from Study 2

"A BCI is a communication system in which messages or commands that an individual sends to the external world do not pass through the brain's normal output pathways of peripheral nerves and muscles. For example, in an EEG-based BCI the messages are encoded in EEG activity." (Wolpaw et al., 2002, p. 769)

In many BCI systems users modulate their own EEG activity by performing covert movements, e.g., motor imagery, which should not involve muscular activation. More precisely, we introduced the distinction between two types of neural activity, which in principle can serve as signal for BCI: *Type 1)* denotes modulations of neural brain activity which *cannot* be predicted on the basis of external events occurring outside of the brain (e.g., associated with mental/motor imagery). *Type 2)* denotes modulations of neural brain activity which are predictable on the basis of external events associated with sensory input. Ideally a "genuine" BCI should only rely on Type 1 neural activity which is challenged by the fact that in healthy subjects there are occasional EMG responses during the performance of motor imagery. Therefore, it is practically challenging to distinguish between Type 1 and Type 2. This discussion makes clear why EMG monitoring of muscle activity is crucial for BCI and, in general, for studies involving covert movements. In our analysis we showed that extensive analysis of EMG and accelerometer data of different muscles contributing to the thumb movement (single trial analysis: visual inspection, machine learning techniques, statistical comparisons) demonstrated the absence of detectable motor responses during the performance of quasi-movements and motor imagery in the majority of trials. Notably, we demonstrate the superior recording sensitivity of the abductor pollicis brevis (APB) muscle for EMG monitoring of thumb movements.

“The visual method is subjective, dependent on the experience of the person performing the EMG-onset detection (Micera et al., 2001), and cannot be automated. To overcome these shortcomings, numerous onset detection algorithms have been proposed, but there is no standardized method for EMG-onset detection (Hodges and Bui, 1996).” (Vaisman et al., 2010, p. 750)

Our results suggest that visual EMG inspection is an advantageous strategy compared to automatic procedures for the detection of weak and transient motor responses occasionally present in covert movements: indeed, we show a higher detection rate by visual inspection than for automatic/statistical methods.

5.1.3 Implications from Study 3

“Following a bilateral alpha and beta suppression at the movement onset, alpha amplitude gradually but not fully recovered towards the baseline… . Habituation of afferences and transfer of the cortical function were discussed as the two alternative explanations for this gradual recovery. Beta amplitude, however, displayed no recovery as long as the movement continued.” (Erbil & Ungan, 2007, p. 44)

Importantly, in the case of EEG repetition suppression (RS) is reflected in the decreased amplitude of event-related potentials and in the reappearance of oscillatory rhythms (i.e., power increase) after initial stimulus-induced blocking (i.e., power decrease). Our results clearly demonstrate RS in oscillatory EEG dynamics (i.e., recovery of oscillations after initial suppression) in the alpha and beta frequency ranges for both overt and covert movement conditions (motor imagery, quasi-movements). We show differential recovery of the EEG dynamics:

covert movements	faster recovery than overt movements
ipsilateral hemisphere	recovers faster than contralateral hemisphere
beta dynamics	recover faster and stronger than alpha.

Differences between condition and hemisphere were only expressed in the alpha band. The amplitude dynamics recover faster for motor imagery than for quasi-movements.

Given the pronounced RS effect in covert movements, we might tentatively assume that movement-related RS (involving thumb movements in the present study) could be primarily internally-driven. It is possible to generalize this result to other muscles and hypothetically speaking, it is not entirely unlikely that *any* repeated stimulation of the brain, externally- or internally-driven, could be associated with RS (also discussed by Hamilton & Grafton, 2009), which possibly reflects adaptation and response optimization in neural networks to stereotyped activation.

"In repetition suppression, repeated experience with the same visual stimulus leads to both short- and long-term suppression of neuronal responses in subpopulations of visual neurons." (Desimone, 1996, p. 13494)
This classical definition of repetition suppression restricted the phenomenon to external (here visual) sensory input (cf. also recent reviews, e.g., Grill-Spector et al., 2006). Based on our findings we might suggest an extended version of the definition: Repetition suppression is defined as a) the reduction of neural activity to repeated external sensory stimulation and b) the reduction of neural activity to the repeated performance of cognitive tasks in the absence of repetitive external sensory stimulation.

5.2 Neural correlates of action intention

5.2.1 Short- and long-term neural dynamics of action intention

One of the main interests of my thesis concerns the neural correlates of overt and covert action intentions on different time scales: does it matter for the brain whether a "real" movement is executed or whether it is merely a "movement in the mind", given the beneficial effects of motor imagery training on physical performance of sportsmen or for rehabilitation after stroke?
Integrating the present results, the answer might be: yes it matters, depending on the *when*. Very early stimulus-processing in the sensorimotor system clearly differs between overt and covert movements (~ 120 m after stimulus onset; Study 1 Figure 2.4), while later processes (2–60 sec) seem to be a scaled version of each other in terms of activation strength (cf. Study 3 Figure 4.8). The latter notion is generally accepted in the research community, also often subsumed under the notion "motor imagery as movement simulation" (cf. Jeannerod, 2001; Munzert et al., 2009). However, apart from a few behavioral studies (Gabbard et al., 2009; Rodriguez et al.,

2008; Rodriguez et al., 2009) there has not been direct neural evidence that covert movements might not merely be a scaled-down version of overt movements, at least not from the very beginning. Usually a covert movement is considered as basically a prepared overt movement, minus the motor command (Jeannerod, 1994; Pfurtscheller et al., 2008). The mechanism of how the motor command is inhibited is under scrutiny, but it is generally assumed that there is such a “reactive” inhibitory mechanism (Jeannerod, 2001). However, in contrast to previous studies we formulated the hypothesis of “preemptive” inhibition, with which our results from high-temporal resolution EEG are more compatible: already the prior action intention differentially primes early stimulus-processing in the motor system, thereby contributing to later movement generation/inhibition (for alternative interpretations cf. Discussion of Study 3 in Chapter 4). For illustration purposes I will reconcile our findings by extending the “What, When, Whether Model of Intentional Action” from Brass and Haggard (2008) and I include the distinction between overt and covert modes of action into this model:

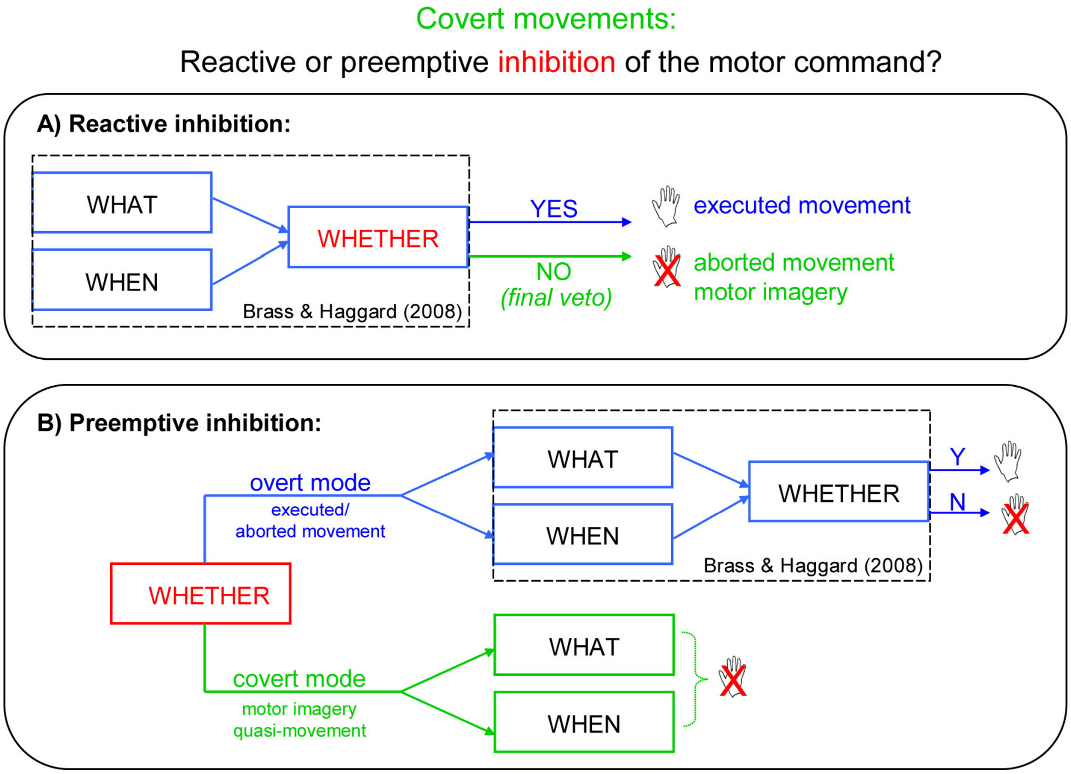


Figure 5.1. Extending the “What, When, Whether Model of Intentional Action” (Brass & Haggard, 2008, p. 320).

Figure 5.1 Panel A "Reactive" inhibition model: According to Brass and Haggard (2008), the "what" component determines details of the action, e.g., choosing between action alternatives such as grasping the glass with the left or right hand, or choosing to grasp the glass with all fingers of the hand or only by using the thumb and index finger. The "when" component refers to the self-paced timing of voluntary actions (in contrast to the fixed timing of involuntary reflexes). Then the prepared action (specified by the "what" and "when" components), is subjected to a final check, i.e., the "whether" component. At this stage the prepared action can be intentionally inhibited by a final "veto". This veto is a vital component of daily actions, e.g., when refraining from crossing a busy street in the very last moment.

However, covert movements (e.g., motor imagery or a prepared but aborted movement) would then result from the whether-veto, such that the final motor command is inhibited. This notion is in line with classic accounts of motor imagery (Jeannerod, 1994, 2001). In the case of aborted movements the inhibition is rather intentionally controlled, while in the case of motor imagery the inhibition is probably rather automatic since the subjects imagine "how a movement feels like" without the intention to actually execute a movement. However, in neural terms it is assumed that in any case the movement is completely prepared in the overt mode and finally vetoed – in this sense the inhibition is "reactive".

Figure 5.1 Panel B "Preemptive" inhibition model: In contrast to previous accounts we suggest a preemptive inhibition model with which our results are more compatible: The prior action intention specifies in an early "whether component" the overt or covert operational mode of the to-be-performed movement. Thus the prior action intention puts the brain into a covert or overt movement mode (default modes of brain functioning: Jaffard et al., 2008; Raichle & Snyder, 2007; Raichle et al., 2001) which influences all stages of the information and motor processing, thereby contributing to the motor inhibition. Notably, an early "whether component" was also discussed by Haggard (2008, p. 938, Figure 2), but it was not included in the WWW-model and it was also not related to the selection between overt/covert modes of action.

Regarding neural evidence, the "reactive inhibition model" would predict that very early stages of sensorimotor information processing (e.g., hand selection) do not differ between overt and covert movements, since at this stage (< 150 ms) no motor command is generated yet. In contrast, the “preemptive inhibition model” predicts differences between very early stages of information processing since the prior action intention differentially primes the sensorimotor system. This prediction is supported by the present EEG data.

Differences between motor imagery and quasi-movements – motor control:

After conceptually discussing how a covert movement can become “covert”, i.e., that there is no movement generated, another question should be discussed: Are motor imagery and quasi-movements actually not one and the same thing? Importantly, both phenomena crucially differ in subjective, behavioral, and neural terms, as I have already discussed in Chapter 5.1.1. I will now consider this with respect to a model of motor control, see Figure 5.2 below.

Movements are vital for an organism to communicate with the environment. From this viewpoint the brain can be conceived as a processing system converting sensory and internal inputs into motor outputs (perception/intention → action). In addition to this “overt” operational mode another mode developed during evolution, namely a “covert” mode where no action is executed by the muscles (cf. Currie & Ravenscroft, 1996): motor planning, preparation, imagination, thinking about movements. Probably the covert mode had evolutionary advantages, e.g., mentally preparing how to hunt down the animal while waiting for the right moment in the hideout. In modern terms, the ability to observe and internally predict an action of another being is a prerequisite for action understanding: We understand others by internally acting in the same way and simulating the sensory/emotional consequences, which is realized by a common neural sensorimotor network which can operate in both overt and covert modes (mirror neuron theory: Rizzolatti et al., 2001).

This simulation of movements and sensory consequences is achieved by so-called internal models, i.e., “neural mechanisms that can mimic the input/output characteristics, or their inverses, of the motor apparatus” (Kawato, 1999, p. 718). Two main types of internal models are assumed, inverse and forward models, which are organized in multiple, linked pairs (Miall, 2002). Given the current and desired state in terms of sensory input (proprioceptive, visual), inverse models predict motor commands necessary to move the body until the updated current state matches the desired state. The predicted motor commands are then realized by the executive motor control center. Based on the efference copy of the issued motor command, forward models predict its sensory consequences and the comparison between the predicted state and the current state results in a prediction error. This error constitutes a training signal for motor learning and is also forwarded to the inverse model. Figure 5.2 illustrates these notions, modified and extended from Miall and Wolpert (1996, p. Figure 3) and Miall (2002, Figure 1), please refer also to Blakemore et al. (2002).

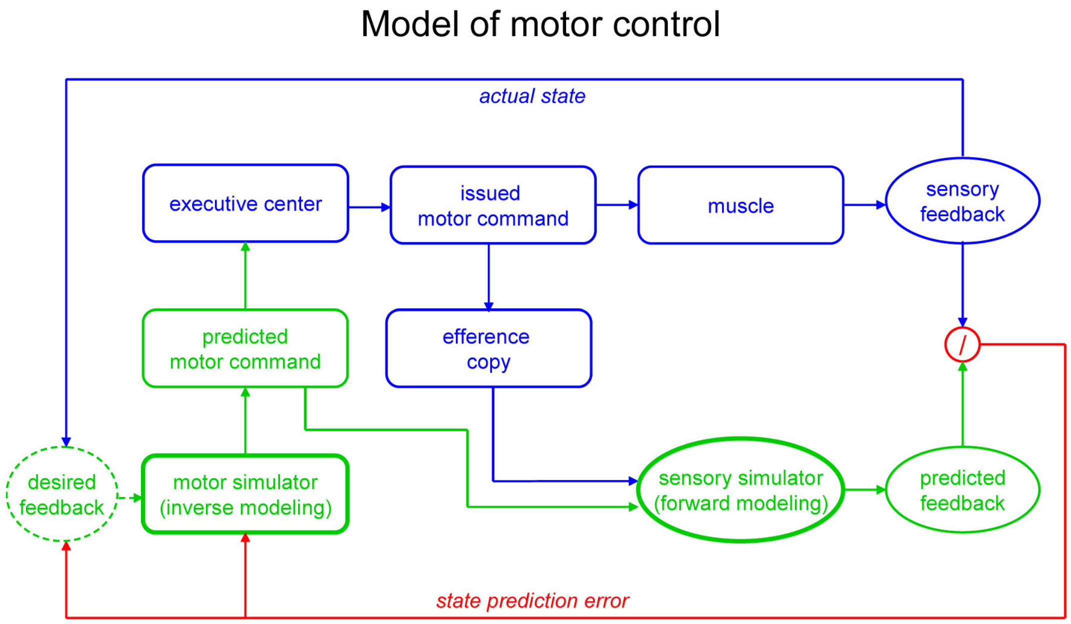


Figure 5.2. A model of motor control (modified from Miall & Wolpert, 1996, Figure 3 p. 1267; Miall, 2002, Figure 1 p. 2).

Utilizing the introduced vocabulary we might refer to covert movements as motor processing involving internal models, i.e., inverse/forward modeling (in other words: motor/sensory simulators), without activating the target muscle. The absence of muscle activation might be achieved by inhibition of a motor command or/and the command is not generated at all (subliminal activation of the executive center). Importantly, per definition covert movements do not implicate the intentional generation of a motor command by the subject – accordingly, the executive motor center should be "offline" but both simulator modules should be still active, predicting motor commands/sensory consequences by inverse/forward modeling, respectively (cf. Figure 5.2). Under this prerequisite we can hypothesize:

During motor imagery the forward model is intentionally activated, since motor imagery requires “the internal simulation of the predicted sensory consequences of actual task performance in the absence of stimuli input” (Stinear et al., 2006, p. 162). However, the inverse model might be automatically co-activated since both modules are paired (cf. Miall, 2002) – for a sensory simulation the forward model needs input in form of a motor command equivalent (motor prediction) from the inverse model (Kawato, 1999).

During quasi-movement performance the inverse model is intentionally activated, since quasi-movements are defined as volitional movements which are minimized by the subject to such an extent that finally they become undetectable by objective measures of muscular activity. Thus the subjects might learn to voluntarily shut down the executive efferent motor modules while keeping the inverse module active, resulting in the automatic co-activation of the forward model simulating proprioceptive feedback. Importantly, this fine-graded balance between excitatory and inhibitory control of the efferent motor pathways is essential to achieve a peripheral zero net outcome, which in the case of quasi-movements is achieved by conscious, intentional control. However, during motor imagery the zero outcome is rather an automatic byproduct.

After discussing the ideal case of the executive motor systems being completely “offline”, we now discuss the more frequently reported case of residual EMG activation in covert movements from a dynamical systems viewpoint of motor control (cf. also the reactive-preemptive inhibition discussion above, and neural inhibitory mechanisms in Chapter 1.3.2.4).

Differences between motor imagery and quasi-movements – continuity assumption: Our initial results (Nikulin et al., 2008) showed that neural activation strength over sensorimotor cortices follows the order: motor imagery < quasi-movements < overt movements at a latency of ~ 1 sec after visual stimulus onset. This result suggested a continuity of neural activation between overt and covert stages of action (cf. Jeannerod, 2001). In agreement with this interpretation were results from Study 3 with earliest repetition suppression onset in the alpha band for motor imagery (~ 33 sec after stimulus onset, averaged across hemispheres), later for quasi-movements (~ 45 sec) and latest for overt movements (not reaching baseline level within 60 sec). However, in Study 1 we clearly demonstrated that very early stimulus-processing (120 ms) is not scaled in a similar way – only in the “overt movements” condition there is significant LRPrect activation. Therefore, our initial “continuity” interpretation has to be modified by taking into account the time scale of neural dynamics in the sensorimotor networks: Early stages (~ 120 ms) after stimulus onset (e.g., stimulus identification, stimulus-response mappings) are unique for subsequent overt movements (“openness” of motor cortex, cf. Study 1), but similar for different types of covert movements which do not imply muscle responses. However, later processing stages some few hundred milliseconds up to minutes after stimulus onset (e.g., related to continuous task performance, motor attention) reveal differential neural activity also between imagined and quasi-movements. Since the movement type is the same for all conditions, such difference might rather relate to motor *cognition* (e.g., attention). Supporting this assumption are data showing that motor routines (e.g., sequence, rhythm) during motor learning are quickly established (e.g., Karni et al., 1995, 1998), while neural correlates of motor cognition might vary as a function of task or performance duration (e.g., Pascual-Leone et al., 1995).

Residual EMG in covert movements – dynamical systems view: Covert movements involve occasional subliminal muscle activation. In terms of the motor control model above (Figure 5.2) this would refer to the generation of a motor command by the “online” executive control center and the failure to inhibit the command. This might be explained by the fact that the motor system is naturally designed for and used to the execution of overt movements, i.e., the executive subsystems and inverse/forward simulator subsystems usually work hand in hand. However, in the covert mode the executive subsystem is “shut down”, thus enabling conscious motor planning or motor imagery. Yet the covert mode is much less frequently used in daily life – indeed it might be evolutionarily younger than the overt mode (cf. Currie & Ravenscroft, 1996) – and therefore it is a rather “unnatural” state for the motor system. It requires more energy/resources (e.g., neural, attention, concentration) to maintain the covert state, and the motor system might have a natural strife to quickly return into the more economically overt mode, either passively (e.g., distracted attention) or actively (e.g., by the subject’s intention).
Furthermore, the motor system is used to the coordinated activity of the executive and simulator subsystems and constantly minimizes the prediction error resulting from the comparison of the forward model’s output and the reafferent input.

Summarizing, there appears to be an intricate balance between the activity of the three interacting subsystems (executive, simulator, and comparator), which is more or less re-established after disturbance, e.g., when during motor imagery the forward model predicts sensory input while there is no proprioception since the executive subsystem is offline, this might in turn activate the executor in order to self-produce the expected sensory feedback.

This shift between overt or covert modes of action might also be described in terms of a phase transition in the neural dynamics. The phase transition is a common notion in theories of motor control: For instance it has been demonstrated that bimanual movements in anti-phase switch to the in-phase state when increasing the movement frequency, i.e., the order parameter, beyond a critical threshold (Haken et al., 1985¸ Kelso et al., 1984). Importantly, the critical transition frequency differed across subjects, but it was a constant value when expressed in units of the individually preferred movement frequency of the subject, similar to gait transitions in animals (Kelso et al., 1984). Furthermore, the transition behavior, depending on critical levels of the order parameter, is very similar in complex biological and physical systems, suggesting a similar mechanism for the transition between different cognitive or neural states (Bressler & Kelso, 2001).

Accordingly, one might argue that there are similar order parameters controlling the transition between covert and overt modes of action, in the sense of the HKB model for bimanual coordination (see above; Haken et al., 1985; Kelso, 2010): In the case of low movement frequency there are two stable states, the overt and covert mode (comparable to the in-phase and anti-phase state, respectively). When increasing the frequency of covert movements, the covert state becomes instable and beyond a critical fatigue level it turns into a repellor and the system switches to the overt state. Other order parameters could be for instance attention or mental/neural fatigue.

In this respect it would be interesting to identify neural/mental correlates of order parameters and to quantify the transition dynamics between overt and covert modes of action. For this purpose quasi-movements might be a suitable paradigm, since it involves subjects to learn the overt-covert transition in a self-paced manner with neurofeedback by gradually decreasing movement strength. Furthermore, once the quasi-principle is learned the subjects report to intend real movements, but on the other hand they are aware of simultaneously inhibiting the movement (“I do a movement without doing it”). When there is a disturbance, for instance, distracted attention, motor responses occur in an all-or-nothing manner: either muscular quiescence in EMG or occasional peaks with a typical strength of ~ 20–50 µV. This might be indicative for the motor system being in a critical state where abrupt transitions between covert and overt states can occur, especially in early performance stages since the quasi-performance improves with training similar to other motor skills. Given these characteristics the quasi-movements paradigm might represent a window into the neural coordination in the motor system for realizing different performance modes.

Interestingly to note in this respect: In contrast to the bimanual coordination experiments (HBK model, see above), where subjects did not switch back into the energetically more demanding anti-phase state when decreasing movement frequency again (asymmetry principle; Haken et al., 1985). However, in the case of quasi-movements/motor imagery the motor system usually switches back to the energetically more demanding covert mode, even if there was a period of "more convenient" overt responses. This aspect might suggest different symmetric or asymmetric transition models depending on the context: motor transitions (e.g., in-phase and anti-phase movements), cognitive transitions (e.g., attentive and not-attentive), or motor-cognitive transitions (quasi-movements or motor imagery).

5.2.5 Clinical application of quasi-movements

A growing body of research suggests motor imagery as a beneficial tool in rehabilitation therapy of patients with neuromotor impairments, for instance after stroke (Jackson et al., 2001; Sharma et al., 2006). The therapeutic application of motor imagery is based on frequent reports that mental practice enhances motor skill learning and performance in athletes and on the strong similarities between imagined and "real" movements regarding the activation of the sensorimotor networks in the central nervous system, including cortico-spinal motor pathways (Decety, 1996; Guillot & Collet, 2005; Lotze & Halsband, 2006; Munzert et al., 2009; Stinear et al., 2006). If the patient's limb is paralyzed motor imagery training can serve as a substitute to executed movements in order to activate the affected central motor networks for inducing neural re-organization and recovery, especially in early phases after stroke. However, as frequently demonstrated, the activation of sensorimotor networks during motor imagery is much smaller than in overt execution (cf. reviews cited above), and, as shown in the present study, the activation is less sustained over time with many repetitions. But importantly, repetition is the essential part of the imagery training for rehabilitation. Given the stronger and more sustained sensorimotor activation during quasi-movements as compared to motor imagery (present results and Nikulin et al., 2008), could quasi-movements serve as alternative, beneficial strategy for neurorehabilitation?

At first glance, quasi-movements do not seem to be a therapeutic strategy when the limb is paralyzed due to brain lesions after stroke, since muscular neurofeedback is essential for learning quasi-movement performance: how should the patient learn to minimize movement strength down to baseline level, if the limb is already paralyzed? However, the patient could initially learn to perform quasi-movements with the *intact* limb in order to learn the principle. Then the patient tries to perform quasi-movements with the paralyzed limb, which is clearly conceivable since the intermanual transfer of motor practice from the trained to the untrained hand has been demonstrated (Schulze et al., 2002). Importantly, the performance of quasi-movements might also be more beneficial than rehabilitation training with attempted movements. Attempted movements, which cannot (or only partially) be executed with the impaired limb, naturally induce frustration and fatigue in the patient (Sharma et al., 2006), since there is a strong mismatch between the patient's intention/expectation (i.e., motor command/proprioceptive feedback) and the outcome (i.e., paralysis).
However, performing quasi-movements might be less frustrating when instructed to the patient as "attempted movements with minimized/zero strength" or "attempt infinitively small movements" – thus there is only little/no mismatch between the patient's intention and the experienced null-effects. Summarizing, in addition to beneficial cognitive and emotional effects our results suggest possible long-term beneficial rehabilitative effects in the affected sensorimotor networks of quasi-movements.

Furthermore, quasi-movements might be a helpful strategy for detecting early signs of motor disorders, e.g., in Parkinson disease. Usually the disease is diagnosed in already advanced stages where comparatively gross symptoms such as tremor or bradykinesia manifested. Yet the preclinical periods last many years (Savica et al., 2010), so that one might hypothesize that motor disorders manifest much earlier on a very small scale: One example might be an impedence in learning/performing movements with extremely small and fine-graded force levels, as can be assessed by EMG. Importantly, EMG is highly sensitive to electrical muscle activity, possibly even on the single motor unit level (Roeleveld & Stegeman, 2002; Roeleveld et al., 1997). A task involving very fine-graded control of movement force is represented in the skill of quasi-movements, which therefore could suggest quasi-movements as a useful strategy for screening early signs of motor disorders, especially in people with hereditary risks.

5.3 Future research

5.3.1 The paradoxical nature of quasi-movements: Open research questions

One of the main interests of my thesis was the behavioral and neurophysiological investigation of the novel motor-cognitive skill quasi-movements (Nikulin et al., 2008). As we discussed, the quasi-movements paradigm allows studying the organization and functioning of the motor system with minimized contamination by peripheral reafferent feedback. Another important aspect in this respect is the intentionally controlled motor inhibition, which the subjects employ in order to minimize movement strength down to baseline level.

After the first three studies we are just beginning to understand the paradoxical nature of quasi-movements – “doing a movement without doing it” – and further research is necessary to investigate neural and cognitive correlates, and to evaluate effective application in the area of brain-computer interface research and rehabilitation.

Residual EMG – neural correlates of inhibitory failure in the brain? Movement inhibition is an essential aspect of daily performance, e.g., aborting a movement due to changed intention (e.g., changing lanes in the last moment to bypass the traffic jam further ahead) or changed environmental context (e.g., releasing the grasp from the hot coffee mug) which is especially important in emergency situations. In this respect it is not only important to study how movement inhibition works but also to understand how inhibition might fail, and to assess possible neural predictors for subsequent inhibitory failure.

One way to study movement inhibition are GO/No-GO paradigms (e.g., Galdo-Álvarez & Carrillo-de-la-Peña, 2004; Hughes et al., 2009; Naito & Matsumura, 1994), where a prepared movement (S1 stimulus) is executed or aborted (S2 stimulus) – here one could speak of *phasic* inhibition, and can study No-GO trials where the movement is erroneously not aborted (Boehler et al., 2010). Yet this does not completely apply to the situation of residual EMG in covert movements, where *tonic* inhibition is rather the case, as our results imply (cf. Study 1), accompagnied by occasional suprathreshold activation of the efferent motor pathways. Therefore, another possibility to study movement inhibition and its failures would be investigating response-locked EEG dynamics to the occasional EMG responses in covert movements, e.g., quasi-movements or motor imagery. It would be interesting to (a) investigate readiness potentials or oscillatory dynamics *before* a movement occurs in covert mode (e.g., attentional lapse, supra-threshold activation?), and (b) movement-locked potentials *after* the movement (e.g., larger error potentials, relation between post-failure neural dynamics at t1, and the next failure at t2 in terms).

Residual EMG – comparing invasive and surface recordings: Another main question is the adequate monitoring of muscle activity during the quasi-movement performance. We showed in our analyses that in the majority of trials there are no detectable motor responses (visual, statistical, machine learning methods) and the surface EMG activity is at baseline level of the muscle at rest. Another approach might be invasive EMG from the target muscle in order to increase spatial resolution and measure single motor units activity. Ideally it would be combined with surface EMG, since when recording single units activity there is always the chance of missing others. In any case the quasi-movement training (neurofeedback to the subject, visual monitoring only by the researcher) is essential for subsequent successful performance. So far we employed ~ 30 min of training and we observed occasional EMG responses especially in longer trials, and less EMG responses in experienced than in novice performers, suggesting the extension of the training period to 1–2 hours, possibly on different days.

Further investigation of differences between quasi-movements and motor imagery: In addition to the present studies, another possibility would be a simple behavioral study, namely performing both tasks with different frequencies. Although a recent study showed EEG data for imagined movements with a frequency up to 3.5 Hz, the authors did not quantify task compliance (Yuan et al., 2010). From our observations and interrogations higher frequencies than 2 Hz are quite difficult to imagine, if not even impossible. However, performing quasi-movements at high speed is very easy, similar to a normal overt movement. This divergence might be quantified by task ratings and also by neurophysiological evidence: usually the neural activity increases with increasing movement frequency in EEG or fMRI (Rao, 1996; Yuan et al., 2010), and therefore one would expect a positive correlation between the signal difference quasi-imagery and frequency.

Neurophysiology of quasi-movements performance: Given the low spatial resolution of EEG recordings, an fMRI study would reveal differences in brain activation compared to overt movements and motor imagery. Indeed, in a pilot fMRI experiment (3 T, TRIO, Siemens, Erlangen, Germany) we found that during quasi-movements there is a pronounced activity in primary and supplementary motor cortices, and in the parietal cortex and cerebellum. Interestingly, quasi-movements showed stronger blood-oxygen-level dependent (BOLD) responses than motor imagery in the ventral primary motor cortex (BA 4p) and in the cerebellum. Furthermore, there was a stronger activation in the inferior parietal cortex (BA 40) for quasi-movements than for overt movements.

Notably, the 4p area in the primary motor cortex has recently been suggested to relate to cognitive motor processing and attention to action, while 4a rather relates to executive motor processing (Binkofski et al., 2002; Sharma et al., 2008). In fact, in our pilot experiment the BOLD signal was stronger for overt than for both covert movement conditions in area 4a.

Furthermore, the cerebellum is associated with movement timing, motor learning, and storage of motor plans (Raymond et al., 1996). The inferior parietal cortex is associated with selective/spatial attention, motor planning and inhibition, visuo-motor integration (Fogassi & Luppino, 2005; Gottlieb, 2007; Wheaton et al., 2009), and also with the Gerstmann syndrome (i.e., finger agnosia; Rusconi et al., 2010). The results suggest that quasi-movements might be associated with an increased activation in motor centers responsible for executive control and learning (primary motor cortex, cerebellum) compared to motor imagery, and with an increased activation in associative motor networks (parietal cortex) compared to overt movements.

However, these initial results need to be investigated by future fMRI studies, ideally in combination with simultaneous EMG monitoring.

Neural correlates of the sense of movement: The quasi-movements paradigm represents an interesting alternative to current approaches studying the neural correlates of the “sense of movement”. Namely, TMS stimulation of the contralateral primary motor cortex (M1) elicits sensations of muscle contractions in the completely paralyzed (healthy subjects: induced transient ischemia) or absent limb (phantom limb of amputees). These studies strongly suggest that the sense of movement can be elicited by central motor activation alone (Amassian et al., 1989; Bestmann et al., 2006; Gandevia et al., 1990; Gandevia & McCloskey, 1977; Walsh et al., 2010), since there are no proprioceptive reafferences from the paralyzed or amputated limb. However, these studies cannot be generalized to *normal* motor functioning in healthy subjects, and furthermore, methods utilizing transient ischemia, curare or TMS are invasive or induce discomfort or even pain in the subjects.

The non-invasive, painless alternative for healthy subjects would be quasi-movements, since this strategy preserves the voluntary intention to move while minimizing reafferent sensory feedback, yet the subjects report having a vivid sense of movement (which is stronger than during motor imagery). By itself this result is congruent with the central-hypothesis of movement sensation (see above), and it would be interesting to investigate the neural correlates in fMRI during quasi-movement performance, since studies involving overt movements are always challenged by the fact that the recorded signals represent a mixture between motor efferences and sensory afferences.

Relation between brain activity and movement force: Although the relation between brain activity and movement force was already investigated previously (cf. references below), very little is known about the production of very weak movement forces, i.e., ~ 1 % of max. voluntary contraction (MVC), which would approx. correspond to < 20 µV of surface EMG amplitude (for APB muscle in the thumb). However, fine-graded force production is essential for daily motor routines, especially in grip control – yet the *voluntary* generation of these very weak forces usually is not possible for the subject (before EMG neurofeedback training, as we consistently observed in our quasi-movement studies).

How are weak movements initiated and controlled by the motor system, why is it more difficult to maintain a weak force level (say 1 %) compared to a strong level (say 80 %) in repeated trials? Some studies involve forces as small as 4–10 % MVC but often do not report corresponding EMG amplitudes (Chakarov et al., 2009; Mima et al., 1999; Witte et al., 2007; except: Dettmers et al., 1995). Interestingly, alpha power is negatively correlated with force from 10–60 % MVC, while at 80 % there is a power increase (Mima et al., 1999), but how is the relationship at lower levels of force production? Investigating this relationship would throw more light on the compensatory nature of attentional and motor processes, as reflected in ERD: if low level force (~ 1 %) were associated with a similar alpha power than ~ 10 %, this would suggest that the increased motor attentional demands compensate for the decreased executive motor activation.

Quasi-movements – effective BCI control: Our first study (Nikulin et al., 2008) successfully demonstrated the increased classification accuracy of brain states by ~ 50–80 % compared to standard motor imagery. In this offline classification we demonstrated the applicability of the quasi-movements strategy for BCI, and in subsequent pilot experiments we already observed the successful online BCI control with quasi-movements while there was no observable EMG activity. However, a systematic study is needed to test whether the increased brain state classification during quasi-movements also translates to the online feedback situation (in a non-negligible number of subjects the performance of the classifiers degrades; Shenoy et al., 2006).

Another important aspect is the long-term usage of BCI with quasi-movements, as our results (Study 3) demonstrate the more sustained activation of motor networks compared to motor imagery, which showed a quicker relaxation of neural activity towards baseline level. BCI research nowadays is challenged by the development of novel experimental paradigms, since very sophisticated methods for feature extraction and classification have already been developed. What is needed is an effective strategy to induce voluntary changes of the subject’s brain activity, addressing the non-trivial problem of BCI “illiteracy”. This challenge has been met with the quasi-movements paradigm. Furthermore, the combination of this strategy with the utilization of the novel miniaturized surface-EEG electrodes (diameter 2–3 mm, wires thinner than a human hair) would provide a high degree of subject comfort over many hours and a powerful signal detection and discrimination for BCI purposes, as it was demonstrated by Nikulin et al. (2010).

5.3.2 Neurofeedback and BCI: Cognition matters

Neurofeedback can be utilized to make neural processes accessible to one's own awareness and voluntary control. In turn, the voluntary control of brain activity can serve as a technical signal for operating external devices or textspelling programs. Accordingly, BCI could also be conceived as a "bridge" between the mind and the brain, since naturally direct correlates of the own neural activity is not available to the senses.

When Prinz (1992) asked "Why don't we perceive our brain states?", one possible answer could have been: The brain does not have its own sensors, but you could use neurofeedback methodology. Of course, even neurofeedback relies on the sensory processing of visual/auditory/tactile correlates of the monitored brain activity which are fed back to the subject – therefore neurofeedback can never enable a *direct* perception of the brain's activity. However, it represents a more direct window than is possible by mere introspection or by perceiving delayed sensory feedback, for instance as compared to the high temporal and spatial resolution of local field potential recordings in the motor cortex (review: Lebedev & Nicolelis, 2006).

Putting this thought to a hypothetical extreme, neurofeedback of patch-clamp recordings might enable a subject to control even the activity of a single neuron in the brain. In general, neurofeedback demonstrates the flexible borders between "unconscious" and "conscious" states (for precise terminology, which is beyond the scope of the current discussion: see, e.g., Block, 2005; Dehaene et al., 2006; Lamme, 2003) – given the appropriate method basically anything could become subject to attentional monitoring and conscious control (e.g., single motor unit control: Gandevia & Rothwell, 1987).

Summarizing, neurofeedback-based methods such as BCI enable the association between cognitive states and neurophysiological states with high temporal and spatial resolution. Current and future studies are challenged to find an effective match between the cognitive level and the neurophysiological level in order to optimize BCI development and practical application. In a long-term perspective the BCI improvement, especially from the psychological perspective, contributes to the study of the mind-brain relationship in general. Moreover, it has fundamental implications for the effective application of BCI methods in clinical contexts (Kübler & Kotchoubey, 2007; Owen et al., 2006):

> *"Patients with disorders of consciousness may also be able*
> *to communicate their thoughts to those around them*
> *by simply modulating their own neural activity."*
> (Owen et al., 2009, p. 403)

Acknowledgements

The most exciting phrase to hear in science,
the one that heralds the most discoveries,
is not "Eureka!" but "That's funny..."
(Prof. Dr. Isaac Asimov)

The human brain has provided neuroscientists, psychologists, and philosophers with "funny" moments throughout all decades. However, resolving a "funny" to "Eureka!" can be best achieved by joined efforts of both, the brain and the mind sciences. In this sense I would like to thank my supervisors, Prof. Dr. Gabriel Curio and Prof. Dr. Arthur M. Jacobs, for your invaluable support, profound discussions, and "mind-brain" food for thought.
Furthermore, I would like to thank the Neurophysics Group at Charité, especially Dr. Vadim V. Nikulin, for representing this very collaborative, inspiring working environment throughout all these years. My Ph.D. research was funded by the Berlin School of Mind and Brain, I am very grateful for your support and the wonderful graduate program. To my family: Thank you.

Appendix

The following tables summarize the results of the three studies:

Table 5.1. Summary of the results from task ratings.
Note: Differences between the sense of movement were significant but not for the other quantitative measures (i.e., concentration, task difficulty, attention decrease, automatization onset/strength).

TASK RATINGS	**quasi-movements**	**motor imagery**	**overt movements**
action intention	movement execution with minimized strength (i.e., zero output)	mental simulation	movement execution
sense of movement	medium	small	strong
concentration	strong	strong	
task difficulty	medium	medium	
attention decrease during task performance	after ~ 29 sec	after ~ 30 sec	
automatization onset	after ~ 21 sec	after ~ 25 sec	
strength of feeling of automatization	medium	medium	

Table 5.2. Summary of testing the presence of motor responses in covert movements.
Note: On average the EMG amplitude was ~2–5 µV both in pre- and task-intervals in APB muscle, without significant modulation by the task performance. There were no significant differences between EMG/ACC activity of the left and right hand performance.

EMG and ACC recordings	**quasi-movements**	**motor imagery**
pre-stimulus vs. task (statistics)	not significant	not significant
automatic classification (machine learning)	not significant	not significant
visual inspection (detection rate)	3 % (averaged across EMG and ACC)	3 % (averaged across EMG and ACC)

Table 5.3. Summary of the EEG results.
LRPrect – lateralized readiness potentials from rectified EEG signals; ERD – event-related desynchronization; contra – contralateral hemisphere; ipsi – ipsilateral hemisphere. Time is given with respect to stimulus onset. LRPrect and ERD values represent activity from C3 and C4 electrodes (Laplacian transformed) over sensorimotor cortices.

EEG	**quasi-movements**	**motor imagery**	**overt movements**
LRPrect ~ 120 ms	no significant lateralization	no significant lateralization	significant lateralization: contralateral sensorimotor hemisphere stronger activated than ipsilateral hemisphere
ERD ~ 1 sec (Nikulin et al., 2008)	overt > quasi > imagery in alpha (mu) frequency band (8–13 Hz)		
ERD mean across 60 sec	overt > quasi = imagery (alpha) overt = quasi = imagery (beta)		
ERD repetition suppression – speed: **How long is ERD significantly different from zero baseline?**	alpha: ipsilateral hemisphere at baseline after ~ 30 sec; contralateral not reaching baseline within 60 sec beta: at baseline after ~ 5 sec (contra + ipsi)	alpha: ipsilateral hemisphere at baseline after ~ 20 sec; contralateral after ~ 46 sec beta: at baseline after ~ 8 sec (contra + ipsi)	alpha: not reaching baseline within 60 sec (contra and ipsi hemi) beta: at baseline after ~ 5 sec (contra + ipsi)
ERD repetition suppression – strength: **How much of the initial ERD (~ 1 sec after stimulus onset) remains after 58 sec of task performance?**	alpha: ~ 21 % beta: ~ 3 % (no significant differences between contra and ipsi)	alpha: ~ 22 % beta: ~ 7 % (no significant differences between contra and ipsi)	alpha: ~ 44 % beta: 0 % (no significant differences between contra and ipsi)

References

Abbink, J. H., van der Bilt, A., & van der Glas, H. W. (1998). Detection of onset and termination of muscle activity in surface electromyograms. *Journal of Oral Rehabilitation*, *25*(5), 365–369.

Adams, R., Bahr, G. S., & Moreno, B. (2008). Brain computer interfaces: Psychology and pragmatic perspectives for the future. Paper presented on the AISB 2008 Convention Communication, Interaction and Social Intelligence, Aberdeen, Scotland.

Adrian, E. D., & Matthews, B. H. (1934). The interpretation of potential waves in the cortex. *Journal of Physiology*, *81*(4), 440–471.

Alegre, M., Labarga, A., Gurtubay, I. G., Iriarte, J., Malanda, A., & Artieda, J. (2002). Beta electroencephalograph changes during passive movements: Sensory afferences contribute to beta event-related desynchronization in humans. *Neuroscience Letters*, *331*(1), 29–32.

Alegre, M., Gurtubay, I. G., Labarga, A., Iriarte, J., Malanda, A., & Artieda, J. (2003). Alpha and beta oscillatory changes during stimulus-induced movement paradigms: Effect of stimulus predictability. *NeuroReport*, *14*(3), 381–385.

Alho, K. (1992). Selective attention in auditory processing as reflected by event-related brain potentials. *Psychophysiology*, *29*(3), 247–263.

Amassian, V. E., Cracco, R. Q., & Maccabee, P. J. (1989). A sense of movement elicited in paralyzed distal arm by focal magnetic coil stimulation of human motor cortex. *Brain Research*, *479*(2), 355–360.

Andersen, R. A., & Buneo, C. A. (2002). Intentional maps in posterior parietal cortex. *Annual Review of Neuroscience*, *25*, 189–220.

Bastian, A., Riehle, A., Erlhagen, W., & Schöner, G. (1998). Prior information preshapes the population representation of movement direction in motor cortex. *NeuroReport , 9*(2), 315–319.

Bartolomeo, P. (2008). The neural correlates of visual mental imagery: An ongoing debate. *Cortex*, *44*(2), 107–108.

Bear, M., Paradiso, M., & Connors, B. W. (2007). *Neuroscience: Exploring the brain (3rd Edition)*. Baltimore, MD: Lippincott Williams & Wilkins.

Berger, H. (1929). Über das Elektrenkephalogramm des Menschen. *Archiv für Psychiatrie und Nervenkrankheiten*, *87*, 527–570.

Bestmann, S., Oliviero, A., Voss, M., Dechent, P., LopezDolado, E., Driver, J., & Baudewig, J. (2006). Cortical correlates of TMS-induced phantom hand movements revealed with concurrent TMS--fMRI. *Neuropsychologia*, *44*(14), 2959–2971.

Betts, G. H. (1909). *The distribution and functions of mental imagery*. New York: Columbia University.

Bigman, Z., & Pratt, H. (2004). Time course and nature of stimulus evaluation in category induction as revealed by visual event-related potentials. *Biological Psychology*, *66*(2), 99–128.

Binkofski, F., Fink, G. R., Geyer, S., Buccino, G., Gruber, O., Shah, N. J., Taylor, J. G., et al. (2002). Neural activity in human primary motor cortex areas 4a and 4p is modulated differentially by attention to action. *Journal of Neurophysiology*, *88*(1), 514–519.

Birbaumer, N., Ghanayim, N., Hinterberger, T., Iversen, I., Kotchoubey, B., Kübler, A., Perelmouter, J., et. al. (1999). A spelling device for the paralysed. *Nature*, *398*(6725), 297–298.

Birbaumer, N. (2006). Breaking the silence: Brain-computer interfaces (BCI) for communication and motor control. *Psychophysiology*, *43*(6), 517–532.

Blakemore, S., Wolpert, D. M., & Frith, C. D. (2002). Abnormalities in the awareness of action. *Trends in Cognitive Sciences*, *6*(6), 237–242.

Blankertz, B., Dornhege, G., Krauledat, M., Müller, K., & Curio, G. (2007). The non-invasive Berlin Brain-Computer Interface: Fast acquisition of effective performance in untrained subjects. *NeuroImage*, *37*(2), 539–550.

Blankertz, B., Losch, F., Krauledat, M., Dornhege, G., Curio, G., & Müller, K. (2008). The Berlin Brain-Computer Interface: Accurate performance from first-session in BCI-naïve subjects. *IEEE Transactions on Biomedical Engineering*, *55*(10), 2452–2462.

Blankertz, B., Schäfer, C., Dornhege, G., & Curio, G. (2002). Single trial detection of EEG error potentials: A tool for increasing BCI transmission rates. *Artificial Neural Networks — ICANN 2002* (p. 138).

Block, N. (2005). Two neural correlates of consciousness. *Trends in Cognitive Sciences*, *9*(2), 46–52.

Boehler, C. N., Appelbaum, L. G., Krebs, R. M., Hopf, J. M., & Woldorff, M. G. (2010). Pinning down response inhibition in the brain--conjunction analyses of the Stop-signal task. *NeuroImage*, *52*(4), 1621–1632.

Brass, M., & Haggard, P. (2008). The what, when, whether model of intentional action. *Neuroscientist*, *14*(4), 319–325.

Bressler, S. L., & Kelso, J. A. (2001). Cortical coordination dynamics and cognition. *Trends in Cognitive Sciences*, *5*(1), 26–36.

Brown, G. D., Yamada, S., & Sejnowski, T. J. (2001). Independent component analysis at the neural cocktail party. *Trends in Neurosciences*, *24*(1), 54–63.

Budzynski, T. H. (1999). From EEG to neurofeedback. In J. R. Evans & A. Arbabanel (Eds.), *Introduction to quantitative EEG and neurofeedback* (pp.65–79). San Diego: Academic Press.

Burde, W., & Blankertz, B. (2006). Is the locus of control of reinforcement a predictor of brain-computer interface performance? *Proceedings of the 3rd International Brain-Computer Interface Workshop and Training Course 2006, Verlag der Technischen Universität Graz*, 76–77.

Carrillo-de-la-Peña, M. T., Galdo-Alvarez, S., & Lastra-Barreira, C. (2008). Equivalent is not equal: Primary motor cortex (MI) activation during motor imagery and execution of sequential movements. *Brain Research*, *1226*, 134–143.

Carrillo-de-la-Peña, M. T., Lastra-Barreira, C., & Galdo-Alvarez, S. (2006). Limb (hand vs. foot) and response conflict have similar effects on event-related potentials (ERPs) recorded during motor imagery and overt execution. *European Journal of Neuroscience*, *24*(2), 635–643.

Carson, R. G. (2005). Neural pathways mediating bilateral interactions between the upper limbs. *Brain Research. Brain Research Reviews*, *49*(3), 641–662.

Cassim, F., Szurhaj, W., Sediri, H., Devos, D., Bourriez, J., Poirot, I., Derambure, P., et al. (2000). Brief and sustained movements: Differences in event-related (de)synchronization (ERD/ERS) patterns. *Clinical Neurophysiology*, *111*(11), 2032–2039.

Castellini, C., Fiorilla, A. E., & Sandini, G. (2009). Multi-subject/daily-life activity EMG-based control of mechanical hands. *Journal of Neuroengineering and Rehabilitation*, *6*, 41.

Chakarov, V., Naranjo, J. R., Schulte-Mönting, J., Omlor, W., Huethe, F., & Kristeva, R. (2009). Beta-range EEG-EMG coherence with isometric compensation for increasing modulated low-level forces. *Journal of Neurophysiology*, *102*(2), 1115–1120.

Chan, J. L., & Ross, E. D. (1988). Left-handed mirror writing following right anterior cerebral artery infarction: Evidence for nonmirror transformation of motor programs by right supplementary motor area. *Neurology*, *38*(1), 59–63.

Chase, M. H., & Harper, R. M. (1971). Somatomotor and visceromotor correlates of operantly conditioned 12-14 C-SEC sensorimotor cortical activity. *Electroencephalography and Clinical Neurophysiology*, *31*(1), 85–92.

Chatrian, G. E., Petersen, M. C., & Lazarte, J. A. (1959). The blocking of the rolandic wicket rhythm and some central changes related to movement. *Electroencephalography and Clinical Neurophysiology*, *11*(3), 497–510.

Chen, X., Zhu, X., & Zhang, D. (2010). A discriminant bispectrum feature for surface electromyogram signal classification. *Medical Engineering & Physics*, *32*(2), 126–135.

Cincotta, M., & Ziemann, U. (2008). Neurophysiology of unimanual motor control and mirror movements. *Clinical Neurophysiology*, *119*(4), 744–762.

Cisek, P. (2007). Cortical mechanisms of action selection: the affordance competition hypothesis. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences, 362*(1485), 1585–1599.

Cisek, P., & Kalaska, J. F. (2005). Neural correlates of reaching decisions in dorsal premotor cortex: Specification of multiple direction choices and final selection of action. *Neuron, 45*(5), 801–814.

Clochon, P., Fontbonne, J., Lebrun, N., & Etévenon, P. (1996). A new method for quantifying EEG event-related desynchronization: Amplitude envelope analysis. *Electroencephalography and Clinical Neurophysiology*, *98*(2), 126–129.

Coles, M. G. H. (1989). Modern mind-brain reading: Psychophysiology, physiology, and cognition. *Psychophysiology*, *26*(3), 251–269.

Corradi-Dell'Acqua, C., Tomasino, B., & Fink, G. R. (2009). What is the position of an arm relative to the body? Neural correlates of body schema and body structural description. *Journal of Neuroscience*, *29*(13), 4162–4171.

Craver-Lemley, C., & Reeves, A. (1992). How visual imagery interferes with vision. *Psychological Review*, *99*(4), 633–649.

Decety, J. (1996). The neurophysiological basis of motor imagery. *Behavioural Brain Research*, *77*(1–2), 45–52.

Dehaene, S., Changeux, J., Naccache, L., Sackur, J., & Sergent, C. (2006). Conscious, preconscious, and subliminal processing: A testable taxonomy. *Trends in Cognitive Sciences*, *10*(5), 204–211.

Desimone, R. (1996). Neural mechanisms for visual memory and their role in attention. *Proceedings of the National Academy of Sciences of the United States of America*, *93*(24), 13494–13499.

Desmurget, M., Reilly, K. T., Richard, N., Szathmari, A., Mottolese, C., & Sirigu, A. (2009). Movement intention after parietal cortex stimulation in humans. *Science*, *324*(5928), 811–813.

Dettmers, C., Fink, G. R., Lemon, R. N., Stephan, K. M., Passingham, R. E., Silbersweig, D., Holmes, A., et al. (1995). Relation between cerebral activity and force in the motor areas of the human brain. *Journal of Neurophysiology*, *74*(2), 802–815.

Dettmers, C., Ridding, M. C., Stephan, K. M., Lemon, R. N., Rothwell, J. C., & Frackowiak, R. S. (1996). Comparison of regional cerebral blood flow with transcranial magnetic stimulation at different forces. *Journal of Applied Physiology*, *81*(2), 596–603.

Dewan, E. M. (1967). Occipital alpha rhythm eye position and lens accommodation. *Nature*, *214*(5092), 975–977.

Dinstein, I., Gardner, J. L., Jazayeri, M., & Heeger, D. J. (2008). Executed and observed movements have different distributed representations in human aIPS. *Journal of Neuroscience*, *28*(44), 11231–11239.

Dirnberger, G., Duregger, C., Lindinger, G., & Lang, W. (2004). Habituation in a simple repetitive motor task: A study with movement-related cortical potentials. *Clinical Neurophysiology*, *115*(2), 378–384.

Dirnberger, G., Duregger, C., Trettler, E., Lindinger, G., & Lang, W. (2004). Fatigue in a simple repetitive motor task: A combined electrophysiological and neuropsychological study. *Brain Research*, *1028*(1), 26–30.

Donoghue, J. P. (2002). Connecting cortex to machines: Recent advances in brain interfaces. *Nature Neuroscience*, *5 Suppl*, 1085–1088.

Dornhege, G., Millán, J. D. R., Hinterberger, T., McFarland, D. J., & Müller, K. (2007). *Toward Brain-Computer Interfacing*. Cambridge, Massachusetts: MIT Press.

Doyle, L. M., Yarrow, K., & Brown, P. (2005). Lateralization of event-related beta desynchronization in the EEG during precued reaction time tasks. *Clinical Neurophysiology*, *116*(8), 1879–1888.

Duncan, C. C., Barry, R. J., Connolly, J. F., Fischer, C., Michie, P. T., Näätänen, R., Polich, J., et al. (2009). Event-related potentials in clinical research: Guidelines for eliciting, recording, and quantifying mismatch negativity, P300, and N400. *Clinical Neurophysiology*, *120*(11), 1883–1908.

Ehrsson, H. H., Geyer, S., & Naito, E. (2003). Imagery of voluntary movement of fingers, toes, and tongue activates corresponding body-part-specific motor representations. *Journal of Neurophysiology*, *90*(5), 3304–3316.

Eichele, T., Debener, S., Calhoun, V. D., Specht, K., Engel, A. K., Hugdahl, K., von Cramon, D. Y., et al. (2008). Prediction of human errors by maladaptive changes in event-related brain networks. *Proceedings of the National Academy of Sciences of the United States of America*, *105*(16), 6173–6178.

Eimer, M. (1998). The lateralized readiness potential as an on-line measure of central response activation processes. *Behavior Research Methods, Instruments, & Computers*, *30*(1), 146–156.

Eimer, M., Forster, B., Van Velzen, J., & Prabhu, G. (2005). Covert manual response preparation triggers attentional shifts: ERP evidence for the premotor theory of attention.

Neuropsychologia, *43*(6), 957–966.

Eimer, M., & Schlaghecken, F. (2003). Response facilitation and inhibition in subliminal priming. *Biological Psychology*, *64*(1–2), 7–26.

Elbert, T., Rockstroh, B., Lutzenberger, W., & Birbaumer, N. (1980). Biofeedback of slow cortical potentials. I. *Electroencephalography and Clinical Neurophysiology*, *48*(3), 293–301.

Erbil, N., & Ungan, P. (2007). Changes in the alpha and beta amplitudes of the central EEG during the onset, continuation, and offset of long-duration repetitive hand movements. *Brain Research*, *1169*, 44–56.

Farah, M. J. (1988). Is visual imagery really visual? Overlooked evidence from neuropsychology. *Psychological Review*, *95*(3), 307–317.

Farwell, L. A., & Donchin, E. (1988). Talking off the top of your head: Toward a mental prosthesis utilizing event-related brain potentials. *Electroencephalography and Clinical Neurophysiology*, *70*(6), 510–523.

Faul, F., Erdfelder, E., Lang, A.-G., & Buchner, A. (2007). G*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behavior Research Methods*, *39*, 175–191.

Fazli, S., Popescu, F., Danóczy, M., Blankertz, B., Müller, K.-R., & Grozea, C. (2009). Subject-independent mental state classification in single trials. *Neural Networks*, *22*(9), 1305–1312.

Finke, R. A. (1979). The functional equivalence of mental images and errors of movement. *Cognitive Psychology*, *11*(2), 235–264.

Finke, R. A. (1980). Levels of equivalence in imagery and perception. *Psychological Review*, *87*(2), 113–132.

Fisher, R. A. (1936). The use of multiple measurements in taxonomic problems. *Annals of Eugenics*, *7*, 179–188.

Fitts, P. M. (1954). The information capacity of the human motor system in controlling the amplitude of movement. *Journal of Experimental Psychology*, *47*(6), 381–391.

Fleming, M., Stinear, C., & Byblow, W. (2010). Bilateral parietal cortex function during motor imagery. *Experimental Brain Research*, *201*, 499–508.

Floyer-Lea, A., & Matthews, P. M. (2004). Changing brain networks for visuomotor control with increased movement automaticity. *Journal of Neurophysiology*, *92*(4), 2405–2412.

Fogassi, L., & Luppino, G. (2005). Motor functions of the parietal lobe. *Current Opinion in Neurobiology*, *15*(6), 626–631.

Formaggio, E., Storti, S. F., Avesani, M., Cerini, R., Milanese, F., Gasparini, A., Acler, M., et al. (2008). EEG and FMRI coregistration to investigate the cortical oscillatory activities during finger movement. *Brain Topography*, *21*(2), 100–111.

Freeman, W. J., & Holmes, M. D. (2005). Metastability, instability, and state transition in neocortex. *Neural Networks*, *18*(5–6), 497–504.

Freude, G., & Ullsperger, P. (1987). Changes in Bereitschaftspotential during fatiguing and non-fatiguing hand movements. *European Journal of Applied Physiology and Occupational Physiology*, *56*(1), 105–108.

Friedman, J. H. (1989). Regularized discriminant analysis. *Journal of the American Statistical*, *84*, 165–175.

Friston, K. (2005). A theory of cortical responses. *Philosophical Transactions of the Royal Society B: Biological Sciences*, *360*(1456), 815–836.

Friston, K. J. (2009). Modalities, modes, and models in functional neuroimaging. *Science*, *326*(5951), 399–403.

Gabbard, C., Cordova, A., & Lee, S. (2009). A question of intention in motor imagery. *Consciousness and Cognition*, *18*(1), 300–305.

Galdo-Álvarez, S., & Carrillo-de-la-Peña, M. T. (2004). ERP evidence of MI activation without motor response execution. *NeuroReport*, *15*(13), 2067–2070.

Gallese, V., Fadiga, L., Fogassi, L., & Rizzolatti, G. (1996). Action recognition in the premotor cortex. *Brain*, *119*(2), 593–609.

Gallese, V., Keysers, C., & Rizzolatti, G. (2004). A unifying view of the basis of social cognition. *Trends in Cognitive Sciences*, *8*(9), 396–403.

Galton, F. (1880). Statistics of mental imagery. *Mind*, *5*, 301–318.

Gandevia, S. C., Macefield, G., Burke, D., & McKenzie, D. K. (1990). Voluntary activation of human motor axons in the absence of muscle afferent feedback. The control of the deafferented hand. *Brain*, *113 (5)*, 1563–1581.

Gandevia, S. C., & McCloskey, D. I. (1977). Sensations of heaviness. *Brain*, *100*(2), 345–354.

Gandevia, S. C., Wilson, L. R., Inglis, J. T., & Burke, D. (1997). Mental rehearsal of motor tasks recruits alpha-motoneurones but fails to recruit human fusimotor neurones selectively. *Journal of Physiology*, *505*(1), 259–266.

Gandevia, S. C., & Rothwell, J. C. (1987). Knowledge of motor commands and the recruitment of human motoneurons. *Brain*, *110*, 1117–1130.

Ganis, G., Thompson, W. L., & Kosslyn, S. M. (2004). Brain areas underlying visual mental imagery and visual perception: An fMRI study. *Cognitive Brain Research*, *20*(2), 226–241.

García-Larrea, L., Lukaszewicz, A. C., & Mauguière, F. (1995). Somatosensory responses during selective spatial attention: The N120-to-N140 transition. *Psychophysiology*, *32*(6), 526–537.

Gastaut, H., Naquet, R., & Gastaut, Y. (1965). Étude d'une activité éctroencéphalographique méconnue: "Le rhythme rolandique en arceau.". *Marseille Médicine*, *18*, 720–721.

Georgopoulos, A. P., Kalaska, J. F., Caminiti, R., & Massey, J. T. (1982). On the relations between the direction of two-dimensional arm movements and cell discharge in primate motor cortex. *Journal of Neuroscience, 2*(11), 1527–1537.

Gerloff, C., Richard, J., Hadley, J., Schulman, A. E., Honda, M., & Hallett, M. (1998). Functional coupling and regional activation of human cortical motor areas during simple, internally paced and externally paced finger movements. *Brain*, *121*(8), 1513–1531.

Goodale, M. A., Króliczak, G., & Westwood, D. A. (2005). Dual routes to action: Contributions of the dorsal and ventral streams to adaptive behavior. *Progress in Brain Research*, *149*, 269–283.

Gottlieb, J. (2007). From thought to action: The parietal cortex as a bridge between perception, action, and cognition. *Neuron*, *53*(1), 9–16.

Graimann, B., & Pfurtscheller, G. (2006). Quantification and visualization of event-related changes in oscillatory brain activity in the time-frequency domain. *Progress in Brain Research*, *159*, 79–

97.

Gratton, G., Coles, M. G., Sirevaag, E. J., Eriksen, C. W., & Donchin, E. (1988). Pre- and poststimulus activation of response channels: A psychophysiological analysis. *Journal of Experimental Psychology. Human Perception and Performance*, *14*(3), 331–344.

Grill-Spector, K., Henson, R., & Martin, A. (2006). Repetition and the brain: Neural models of stimulus-specific effects. *Trends in Cognitive Sciences*, *10*(1), 14–23.

Gruber, T., Malinowski, P., & Müller, M. M. (2004). Modulation of oscillatory brain activity and evoked potentials in a repetition priming task in the human EEG. *European Journal of Neuroscience*, *19*(4), 1073–1082.

Grush, R. (2004). The emulation theory of representation: Motor control, imagery, and perception. *Behavioral and Brain Sciences*, *27*(3), 377–396; discussion 396–442.

Gruzelier, J., Egner, T., & Vernon, D. (2006). Validating the efficacy of neurofeedback for optimising performance. In C. Neuper & W. Klimesch (Eds.), *Progress in Brain Research* (Vol. 159, pp. 421–431). Amsterdam: Elsevier.

Guillot, A., & Collet, C. (2005). Duration of mentally simulated movement: A review. *Journal of Motor Behavior*, *37*(1), 10–20.

Guillot, A., Lebon, F., Rouffet, D., Champely, S., Doyon, J., & Collet, C. (2007). Muscular responses during motor imagery as a function of muscle contraction types. *International Journal of Psychophysiology*, *66*(1), 18–27.

Hackley, S., & Valle-Inclan, F. (1998). Automatic alerting does not speed late motoric processes in a reaction-time task. *Nature*, *391*(6669), 786–788.

Haggard, P. (2005). Conscious intention and motor cognition. *Trends in Cognitive Sciences*, *9*(6), 290–295.

Haggard, P. (2008). Human volition: Towards a neuroscience of will. *Nature Reviews Neuroscience*, *9*(12), 934–946.

Haken, H., Kelso, J. A., & Bunz, H. (1985). A theoretical model of phase transitions in human hand movements. *Biological Cybernetics*, *51*(5), 347–356.

Hall, C. R., & Martin, K. A. (1997). Measuring movement imagery abilities: A revision of the movement imagery questionnaire. *Journal of Mental Imagery*, *21*, 143–154.

Hamilton, A. F. D. C., & Grafton, S. T. (2009). Repetition suppression for performed hand gestures revealed by fMRI. *Human Brain Mapping*, *30*(9), 2898–2906.

Hashimoto, R., & Rothwell, J. C. (1999). Dynamic changes in corticospinal excitability during motor imagery. *Experimental Brain Research*, *125*(1), 75–81.

Hatem, S. M., Plaghki, L., & Mouraux, A. (2007). How response inhibition modulates nociceptive and non-nociceptive somatosensory brain-evoked potentials. *Clinical Neurophysiology*, *118*(7), 1503–1516.

Henson, R., Shallice, T., & Dolan, R. (2000). Neuroimaging evidence for dissociable forms of repetition priming. *Science*, *287*(5456), 1269–1272.

Henson, R. N. A. (2003). Neuroimaging studies of priming. *Progress in Neurobiology*, *70*(1), 53–81.

Hesse, M. D., Thiel, C. M., Stephan, K. E., & Fink, G. R. (2006). The left parietal cortex and motor intention: An event-related functional magnetic resonance imaging study. *Neuroscience*, *140*(4), 1209–1221.

Hinterberger, T., Schmidt, S., Neumann, N., Mellinger, J., Blankertz, B., Curio, G., & Birbaumer, N. (2004). Brain-computer communication and slow cortical potentials. *IEEE Transactions on Bio-Medical Engineering*, *51*(6), 1011–1018.

Hjorth, B. (1975). An on-line transformation of EEG scalp potentials into orthogonal source derivations. *Electroencephalography and Clinical Neurophysiology*, *39*(5), 526–530.

Hochberg, L. R., Serruya, M. D., Friehs, G. M., Mukand, J. A., Saleh, M., Caplan, A. H., Branner, A., et al. (2006). Neuronal ensemble control of prosthetic devices by a human with tetraplegia. *Nature*, *442*(7099), 164–171.

Hodges, P. W., & Bui, B. H. (1996). A comparison of computer-based methods for the determination of onset of muscle contraction using electromyography. *Electroencephalography and Clinical Neurophysiology*, *101*(6), 511–519.

Hohlefeld, F. U. (2006). *Introducing quasi-movements: An EEG/EMG study with special emphasis on brain-computer interfacing* (unpublished diploma thesis). Berlin: Free University Berlin, Germany.

Hohlefeld, F. U., Nikulin, V. V., & Curio, G. (in press). Visual stimuli evoke rapid activation (120 ms) of sensorimotor cortex for overt but not for covert movements. *Brain Research*. http://dx.doi.org/10.1016/j.brainres.2010.10.035

Hohlefeld, F. U., Nikulin, V. V., & Curio, G. (submitted). Covert movements trigger repetition suppression of EEG in sensorimotor cortex. http://dx.doi.org/10.1097/WNR.0b013e3283436d84

Huettel, S. A., Song, A. W., & McCarthy, G. (2009). *Functional Magnetic Resonance Imaging (2nd Edition)*. Sunderland, MA: Sinauer Associates.

Hughes, G., Velmans, M., & De Fockert, J. (2009). Unconscious priming of a no-go response. *Psychophysiology*, *46*(6), 1258–1269.

Hyvärinen, A., & Oja, E. (2000). Independent component analysis: Algorithms and applications. *Neural Networks*, *13*(4–5), 411–430.

Isaac, A., Marks, D. F., & Russell, D. G. (1986). An instrument for assessing imagery of movement. The Vividness of Movement Imagery Questionnaire. *Journal of Mental Imagery*, *10*(4), 23–30.

Jackson, P. L., Lafleur, M. F., Malouin, F., Richards, C., & Doyon, J. (2001). Potential role of mental practice using motor imagery in neurologic rehabilitation. *Archives of Physical Medicine and Rehabilitation*, *82*(8), 1133–1141.

Jacobs, A. M. (2006). Messung der Hirnaktivität. In *J. Funke & P. Frensch (Eds.), Handbuch der Allgemeinen Psychologie, Kognition* (pp. 697–704). Göttingen: Hogrefe.

Jacobson, E. (1932). Electrophysiology of mental activities. *American Journal of Psychology*, *44*, 677–694.

Jaffard, M., Longcamp, M., Velay, J., Anton, J., Roth, M., Nazarian, B., & Boulinguez, P. (2008). Proactive inhibitory control of movement assessed by event-related fMRI. *NeuroImage*, *42*(3), 1196–1206.

James, W. (1890). *The principles of psychology (2 Volumes)*. New York: Holt. Retrieved August 30, 2010, from http://psychclassics.yorku.ca/James/Principles/index.htm.

Jankelowitz, S. K., & Colebatch, J. G. (2002). Movement-related potentials associated with self-paced, cued and imagined arm movements. *Experimental Brain Research*, *147*(1), 98–107.

Jasper, H., & Penfield, W. (1949). Zur Deutung des normalen Elektrencephalogramms und seiner Veränderungen. [Electrocorticograms in man: Effect of voluntary movement upon the electrical activity of the precentral gyrus]. *Archiv für Psychiatrie und Nervenkrankheiten*, *183*(1–2), 163–174.

Jeannerod, M. (1994). The representing brain: Neural correlates of motor intention and imagery. *Behavioral and Brain Sciences*, *17*, 187–245.

Jeannerod, M. (1995). Mental imagery in the motor context. *Neuropsychologia*, *33*(11), 1419–1432.

Jeannerod, M. (2001). Neural simulation of action: A unifying mechanism for motor cognition. *NeuroImage*, *14*, 103–109.

Jeannerod, M., & Frak, V. (1999). Mental imaging of motor activity in humans. *Current Opinion in Neurobiology*, *9*(6), 735–739.

Johnston, J., Rearick, M., & Slobounov, S. (2001). Movement-related cortical potentials associated with progressive muscle fatigue in a grasping task. *Clinical Neurophysiology*, *112*(1), 68–77.

de Jong, R., Wierda, M., Mulder, G., & Mulder, L. J. (1988). Use of partial stimulus information in response processing. *Journal of Experimental Psychology. Human Perception and Performance*, *14*(4), 682–692.

Jung, T. P., Makeig, S., Westerfield, M., Townsend, J., Courchesne, E., & Sejnowski, T. J. (2001). Analysis and visualization of single-trial event-related potentials. *Human Brain Mapping*, *14*(3), 166–185.

Kalcher, J., & Pfurtscheller, G. (1995). Discrimination between phase-locked and non-phase-locked event-related EEG activity. *Electroencephalography and Clinical Neurophysiology*, *94*(5), 381–384.

Kamiya, J. (1968). Conscious control of brain waves. *Psychology Today*, *1*, 56–60.

Karni, A., Meyer, G., Jezzard, P., Adams, M. M., Turner, R., & Ungerleider, L. G. (1995). Functional MRI evidence for adult motor cortex plasticity during motor skill learning. *Nature*, *377*(6545), 155–158.

Karni, A., Meyer, G., Rey-Hipolito, C., Jezzard, P., Adams, M. M., Turner, R., & Ungerleider, L. G. (1998). The acquisition of skilled motor performance: Fast and slow experience-driven changes in primary motor cortex. *Proceedings of the National Academy of Sciences of the United States of America*, *95*(3), 861–868.

Kawato, M. (1999). Internal models for motor control and trajectory planning. *Current Opinion in Neurobiology*, *9*(6), 718–727.

Kelso, J. A. S. (1984). Phase transitions and critical behavior in human bimanual coordination. *American Journal of Physiology*, *246*, R1000–R1004.

Kelso, J. A. S. (2010). Instabilities and phase transitions in human brain and behavior. *Frontiers in Human Neuroscience*, *4*, 23.

Klimesch, W., Sauseng, P., & Hanslmayr, S. (2007a). EEG alpha oscillations: The inhibition-timing hypothesis. *Brain Research Reviews*, *53*(1), 63–88.

Klimesch, W., Sauseng, P., Hanslmayr, S., Gruber, W., & Freunberger, R. (2007b). Event-related phase reorganization may explain evoked neural dynamics. *Neuroscience and Biobehavioral Reviews*, *31*(7), 1003–1016.

Knuf, L., Aschersleben, G., & Prinz, W. (2001). An analysis of ideomotor action. *Journal of Experimental Psychology. General*, *130*(4), 779–798.

Kornhuber, H. H., & Deecke, L. (1965). Hirnpotentialänderungen bei Willkürbewegungen und passiven Bewegungen des Menschen: Bereitschaftspotential und reafferente Potentiale [Changes in the brain potential in voluntary movements and passive movements in man: Readiness potential and reafferent potentials]. *Pflügers Archiv für die gesamte Physiologie des Menschen und der Tiere*, *284*, 1–17.

Korvenoja, A., Wikstrom, H., Huttunen, J., Virtanan, J., Laine, P., Aronen, H. J., Seppalainen, A. M., et al. (1995). Activation of ipsilateral primary sensorimotor cortex by median nerve stimulation. *NeuroReport*, *6*(18), 2589–2593.

Kosslyn, S. M. (1973). Scaning visual images: Some structural implications. *Perception and Psychophysics*, *14*, 90–94.

Kosslyn, S. M., Ganis, G., & Thompson, W. L. (2001). Neural foundations of imagery. *Nature Reviews. Neuroscience*, *2*(9), 635–642.

Kosslyn, S. M., Thompson, W. L., Kim, I. J., & Alpert, N. M. (1995). Topographical representations of mental images in primary visual cortex. *Nature*, *378*(6556), 496–498.

Kosslyn, S. M., Thompson, W. L., Sukel, K. E., & Alpert, N. M. (2005). Two types of image generation: Evidence from PET. *Cognitive, Affective & Behavioral Neuroscience*, *5*(1), 41–53.

Kotchoubey, B., Schneider, D., Schleichert, H., Strehl, U., Uhlmann, C., Blankenhorn, V., Fröscher, W., et al. (1996). Self-regulation of slow cortical potentials in epilepsy: A retrial with analysis of influencing factors. *Epilepsy Research*, *25*(3), 269–276.

Kotchoubey, B., Schneider, D., Uhlmann, C., Schleichert, H., & Birbaumer, N. (1997). Beyond habituation: Long-term repetition effects on visual event-related potentials in epileptic patients. *Electroencephalography and Clinical Neurophysiology*, *103*(4), 450–456.

Kotchoubey, B., Kübler, A., Strehl, U., Flor, H., & Birbaumer, N. (2002). Can humans perceive their brain states? *Consciousness and Cognition*, *11*(1), 98–113.

Kranczioch, C., Mathews, S., Dean, P. J. A., & Sterr, A. (2009). On the equivalence of executed and imagined movements: Evidence from lateralized motor and nonmotor potentials. *Human Brain Mapping*, *30*(10), 3275–3286.

Kranczioch, C., Mathews, S., Dean, P., & Sterr, A. (2010). Task complexity differentially affects executed and imagined movement preparation: Evidence from movement-related potentials. *PloS One*, *5*(2), e9284.

Krauledat, M., Schröder, M., Blankertz, B., & Müller, K. (2007). Reducing calibration time for brain-computer interfaces: A clustering approach. *Advances in Neural Information Processing Systems*, *19*, 753–760.

Krauledat, M., Tangermann, M., Blankertz, B., & Müller, K. (2008). Towards zero training for brain-computer interfacing. *PLoS ONE*, *3*(8), e2967.

Kübler, A., Kotchoubey, B., Kaiser, J., Wolpaw, J. R., & Birbaumer, N. (2001). Brain-computer communication: Unlocking the locked in. *Psychological Bulletin*, *127*(3), 358–375.

Kübler, A., & Kotchoubey, B. (2007). Brain-computer interfaces in the continuum of consciousness. *Current Opinion in Neurology*, *20*(6), 643–649.

Kühn, S., Haggard, P., & Brass, M. (2008). Intentional inhibition: How the "veto-area" exerts control. *Human Brain Mapping*, *30*(9), 2834–2843.

Kuhtz-Buschbeck, J. P., Mahnkopf, C., Holzknecht, C., Siebner, H., Ulmer, S., & Jansen, O. (2003). Effector-independent representations of simple and complex imagined finger movements: A combined fMRI and TMS study. *European Journal of Neuroscience*, *18*(12), 3375–3387.

Kutas, M., & Donchin, E. (1974). Studies of squeezing: Handedness, responding hand, response force, and asymmetry of readiness potential. *Science*, *186*(4163), 545–548.

Kutas, M., & Donchin, E. (1980). Preparation to respond as manifested by movement-related brain potentials. *Brain Research*, *202*(1), 95–115.

Kwan, H. C., MacKay, W. A., Murphy, J. T., & Wong, Y. C. (1985). Properties of visual cue responses in primate precentral cortex. *Brain Research, 343*(1), 24–35.

Lamme, V. A. F. (2006). Towards a true neural stance on consciousness. *Trends in Cognitive Sciences*, *10*(11), 494–501.

Laureys, S. (2005). The neural correlate of (un)awareness: Lessons from the vegetative state. *Trends in Cognitive Sciences*, *9*(12), 556–559.

Lebedev, M. A., & Nicolelis, M. A. L. (2006). Brain-machine interfaces: Past, present and future. *Trends in Neurosciences*, *29*(9), 536–546.

Lebedev, M. A., & Wise, S. P. (2002). Insights into seeing and grasping: Distinguishing the neural correlates of perception and action. *Behavioral and Cognitive Neuroscience Reviews*, *1*(2), 108–129.

Lebon, F., Rouffet, D., Collet, C., & Guillot, A. (2008). Modulation of EMG power spectrum frequency during motor imagery. *Neuroscience Letters*, *435*(3), 181–185.

Lehmann, D., & Skrandies, W. (1980). Reference-free identification of components of checkerboard-evoked multichannel potential fields. *Electroencephalography and Clinical Neurophysiology*, *48*(6), 609–621.

Leins, U., Goth, G., Hinterberger, T., Klinger, C., Rumpf, N., & Strehl, U. (2007). Neurofeedback for children with ADHD: A comparison of SCP and Theta/Beta protocols. *Applied Psychophysiology and Biofeedback*, *32*(2), 73–88.

Leuthardt, E. C., Freudenberg, Z., Bundy, D., & Roland, J. (2009). Microscale recording from human motor cortex: Implications for minimally invasive electrocorticographic brain-computer interfaces. *Neurosurgical Focus*, *27*(1), E10.

Li, S., Kamper, D. G., Stevens, J. A., & Rymer, W. Z. (2004). The effect of motor imagery on spinal segmental excitability. *Journal of Neuroscience*, *24*(43), 9674–9680.

Li, X., Zhou, P., & Aruin, A. S. (2007). Teager-Kaiser energy operation of surface EMG improves muscle activity onset detection. *Annals of Biomedical Engineering*, *35*(9), 1532–1538.

Liang, N., Murakami, T., Funase, K., Narita, T., & Kasai, T. (2008). Further evidence for excitability changes in human primary motor cortex during ipsilateral voluntary contractions. *Neuroscience Letters*, *433*(2), 135–140.

Liepert, J., Dettmers, C., Terborg, C., & Weiller, C. (2001). Inhibition of ipsilateral motor cortex during phasic generation of low force. *Clinical Neurophysiology*, *112*(1), 114–121.

Liguori, R., Dahl, K., & Fuglsang-Frederiksen, A. (1992). Turns-amplitude analysis of the electromyographic recruitment pattern disregarding force measurement. I. Method and reference values in healthy subjects. *Muscle & Nerve*, *15*(12), 1314–1318.

Lotze, M., Montoya, P., Erb, M., Hülsmann, E., Flor, H., Klose, U., Birbaumer, N., et al. (1999). Activation of cortical and cerebellar motor areas during executed and imagined hand movements: An fMRI study. *Journal of Cognitive Neuroscience*, *11*(5), 491–501.

Lotze, M., & Halsband, U. (2006). Motor imagery. *Journal of Physiology*, *99*(4–6), 386–395.

Loveless, N. E. (1977). Event-related brain potentials in selective response. *Biological Psychology*, *5*(2), 135–149.

Lubar, J. F. (1998). Electroencephalographic biofeedback methodology and the management of epilepsy. *Integrative Physiological and Behavioral Science*, *33*(2), 176–207.

Lulé, D., Zickler, C., Häcker, S., Bruno, M. A., Demertzi, A., Pellas, F., Laureys, S., u. a. (2009). Life can be worth living in locked-in syndrome. *Progress in Brain Research*, *177*, 339–351.

Lynn, M. T., Berger, C. C., Riddle, T. A., & Morsella, E. (in press). Mind control? Creating illusory intentions through a phony brain-computer interface. *Consciousness and Cognition*.

Majdandzić, J., Grol, M. J., van Schie, H. T., Verhagen, L., Toni, I., & Bekkering, H. (2007). The role of immediate and final goals in action planning: An fMRI study. *NeuroImage*, *37*(2), 589–598.

Makeig, S., Debener, S., Onton, J., & Delorme, A. (2004). Mining event-related brain dynamics. *Trends in Cognitive Sciences*, *8*(5), 204–210.

Masaki, H., Wild-Wall, N., Sangals, J., & Sommer, W. (2004). The functional locus of the lateralized readiness potential. *Psychophysiology, 41*(2), 220–230.

McFarland, D. J., Sarnacki, W. A., Vaughan, T. M., & Wolpaw, J. R. (2005). Brain-computer interface (BCI) operation: Signal and noise during early training sessions. *Clinical Neurophysiology*, *116*(1), 56–62.

Miall, C. (2002). Modular motor learning. *Trends in Cognitive Sciences*, *6*(1), 1–3.

Miall, R., & Wolpert, D. (1996). Forward models for physiological motor control. *Neural Networks*, *9*(8), 1265–1279.

Michelon, P., Vettel, J. M., & Zacks, J. M. (2006). Lateral somatotopic organization during imagined and prepared movements. *Journal of Neurophysiology*, *95*(2), 811–822.

Mima, T., Simpkins, N., Oluwatimilehin, T., & Hallett, M. (1999). Force level modulates human cortical oscillatory activities. *Neuroscience Letters*, *275*(2), 77–80.

Morton, A. (1994). Motor simulation. *Behavioral and Brain Sciences*, *17*(2), 215–215.

Moulton, S. T., & Kosslyn, S. M. (2009). Imagining predictions: Mental imagery as mental emulation. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences*, *364*(1521), 1273–1280.

Müller, K.-R., Tangermann, M., Dornhege, G., Krauledat, M., Curio, G., & Blankertz, B. (2008). Machine learning for real-time single-trial EEG-analysis: From brain-computer interfacing to mental state monitoring. *Journal of Neuroscience Methods*, *167*(1), 82–90.

Müller-Gerking, J., Pfurtscheller, G., & Flyvbjerg, H. (2000). Classification of movement-related EEG in a memorized delay task experiment. *Clinical Neurophysiology, 111*(8), 1353–1365.

Munzert, J., Lorey, B., & Zentgraf, K. (2009). Cognitive motor processes: The role of motor imagery in the study of motor representations. *Brain Research Reviews*, *60*(2), 306–326.

Murray, M. M., Brunet, D., & Michel, C. M. (2008). Topographic ERP analyses: A step-by-step tutorial review. *Brain Topography*, *20*(4), 249–264.

Naito, E., & Matsumura, M. (1994). Movement-related slow potentials during motor imagery and motor suppression in humans. *Cognitive Brain Research*, *2*(2), 131–137.

Neumann, N., Kübler, A., Kaiser, J., Hinterberger, T., & Birbaumer, N. (2003). Conscious perception of brain states: Mental strategies for brain-computer communication. *Neuropsychologia*, *41*(8), 1028–1036.

Neuper, C., Müller-Putz, G. R., Scherer, R., & Pfurtscheller, G. (2006). Motor imagery and EEG-based control of spelling devices and neuroprostheses. *Progress in Brain Research*, *159*, 393–409.

Neuper, C., Scherer, R., Reiner, M., & Pfurtscheller, G. (2005). Imagery of motor actions: Differential effects of kinesthetic and visual-motor mode of imagery in single-trial EEG. *Cognitive Brain Research*, *25*(3), 668–677.

Neuper, C., Wörtz, M., & Pfurtscheller, G. (2006). ERD/ERS patterns reflecting sensorimotor activation and deactivation. *Progress in Brain Research*, *159*, 211–222.

Nicolelis, M. A. (2001). Actions from thoughts. *Nature*, *409*(6818), 403–407.

Niedermeyer, E., & Lopes da Silva, F. H. (2004). *Electroencephalography. Basic principles, clinical applications, and related fields (fifth edition)*. Baltimore, MD: Lippincott Williams & Wilkins.

Nikouline, V. V., Linkenkaer-Hansen, K., Wikström, H., Kesäniemi, M., Antonova, E. V., Ilmoniemi, R. J., & Huttunen, J. (2000). Dynamics of mu-rhythm suppression caused by median nerve stimulation: A magnetoencephalographic study in human subjects. *Neuroscience Letters*, *294*(3), 163–166.

Nikouline, V. V., Wikström, H., Linkenkaer-Hansen, K., Kesäniemi, M., Ilmoniemi, R. J., & Huttunen, J. (2000). Somatosensory evoked magnetic fields: Relation to pre-stimulus mu rhythm. *Clinical Neurophysiology*, *111*(7), 1227–1233.

Nikulin, V. V., Hohlefeld, F. U., Jacobs, A. M., & Curio, G. (2008). Quasi-movements: A novel motor-cognitive phenomenon. *Neuropsychologia*, *46*(2), 727–742. http://dx.doi.org/10.1016/j.neuropsychologia.2007.10.008

Nikulin, V. V., Linkenkaer-Hansen, K., Nolte, G., Lemm, S., Müller, K. R., Ilmoniemi, R. J., & Curio, G. (2007). A novel mechanism for evoked responses in the human brain. *European Journal of Neuroscience*, *25*(10), 3146–3154.

O'Connell, R. G., Dockree, P. M., Robertson, I. H., Bellgrove, M. A., Foxe, J. J., & Kelly, S. P. (2009). Uncovering the neural signature of lapsing attention: Electrophysiological signals predict errors up to 20 s before they occur. *The Journal of Neuroscience*, *29*(26), 8604–8611.

Oldfield, R. C. (1971). The assessment and analysis of handedness: The Edinburgh inventory. *Neuropsychologia*, *9*(1), 97–113.

Oostenveld, R., & Praamstra, P. (2001). The five percent electrode system for high-resolution EEG and ERP measurements. *Clinical Neurophysiology*, *112*(4), 713–719.

Oostenveld, R., Stegeman, D. F., Praamstra, P., & van Oosterom, A. (2003). Brain symmetry and topographic analysis of lateralized event-related potentials. *Clinical Neurophysiology*, *114*(7), 1194–1202.

Osman, A., & Moore, C. M. (1993). The locus of dual-task interference: Psychological refractory effects on movement-related brain potentials. *Journal of Experimental Psychology. Human Perception and Performance*, *19*(6), 1292–1312.

Owen, A. M., Coleman, M. R., Boly, M., Davis, M. H., Laureys, S., & Pickard, J. D. (2006). Detecting awareness in the vegetative state. *Science*, *313*(5792), 1402.

Owen, A. M., Schiff, N. D., & Laureys, S. (2009). A new era of coma and consciousness science. *Progress in Brain Research*, *177*, 399–411.

Pacherie, E. (2008). The phenomenology of action: A conceptual framework. *Cognition*, *107*(1), 179–217.

Pascual-Leone, A., Nguyet, D., Cohen, L. G., Brasil-Neto, J. P., Cammarota, A., & Hallett, M. (1995). Modulation of muscle responses evoked by transcranial magnetic stimulation during the acquisition of new fine motor skills. *Journal of Neurophysiology*, *74*(3), 1037–1045.

Patino, L., Chakarov, V., Schulte-Mönting, J., Hepp-Reymond, M., & Kristeva, R. (2006). Oscillatory cortical activity during a motor task in a deafferented patient. *Neuroscience Letters*, *401*(3), 214–218.

Penfield, W. (1958). The state of consciousness and central encephalic organization [Article in French]. *Laval Médical*, *26*(4), 469–481.

Perky, C. W. (1910). An experimental study of imagination. *American Journal of Psychology*, *21*(3), 422–452.

Pfurtscheller, G. (1981). Central beta rhythm during sensorimotor activities in man. *Electroencephalography and Clinical Neurophysiology*, *51*(3), 253–264.

Pfurtscheller, G. (2001). Functional brain imaging based on ERD/ERS. *Vision Research*, *41*(10–11), 1257–1260.

Pfurtscheller, G., & Aranibar, A. (1977). Event-related cortical desynchronization detected by power measurements of scalp EEG. *Electroencephalography and Clinical Neurophysiology*, *42*(6), 817–826.

Pfurtscheller, G., & Lopes da Silva, F. H. (1999). Event-related EEG/MEG synchronization and desynchronization: Basic principles. *Clinical Neurophysiology*, *110*(11), 1842–1857.

Pfurtscheller, G., & Neuper, C. (1994). Event-related synchronization of mu rhythm in the EEG over the cortical hand area in man. *Neuroscience Letters*, *174*(1), 93–96.

Pfurtscheller, G., Neuper, C., Ramoser, H., & Müller-Gerking, J. (1999). Visually guided motor imagery activates sensorimotor areas in humans. *Neuroscience Letters, 269*(3), 153–156.

Pfurtscheller, G., Scherer, R., Müller-Putz, G. R., & Lopes da Silva, F. H. (2008). Short-lived brain state after cued motor imagery in naive subjects. *European Journal of Neuroscience*, *28*(7), 1419–1426.

Pfurtscheller, G., Zalaudek, K., & Neuper, C. (1998). Event-related beta synchronization after wrist, finger and thumb movement. *Electroencephalography and Clinical Neurophysiology*, *109*(2), 154–160.

Polich, J. (2007). Updating P300: An integrative theory of P3a and P3b. *Clinical neurophysiologyysiology*, *118*(10), 2128–2148.

Prinz, W. (1992). Why don’t we perceive our brain states? *European Journal of Cognitive Psychology*, *4*(1), 1–20.

Raichle, M. E., MacLeod, A. M., Snyder, A. Z., Powers, W. J., Gusnard, D. A., & Shulman, G. L. (2001). A default mode of brain function. *Proceedings of the National Academy of Sciences of the United States of America*, *98*(2), 676–682.

Raichle, M. E., & Snyder, A. Z. (2007). A default mode of brain function: A brief history of an evolving idea. *NeuroImage*, *37*(4), 1083–1090.

Rao, S. M., Bandettini, P. A., Binder, J. R., Bobholz, J. A., Hammeke, T. A., Stein, E. A., & Hyde, J. S. (1996). Relationship between finger movement rate and functional magnetic resonance signal change in human primary motor cortex. *Journal of Cerebral Blood Flow and Metabolism*, *16*(6), 1250–1254.

Rau, C., Plewnia, C., Hummel, F., & Gerloff, C. (2003). Event-related desynchronization and excitability of the ipsilateral motor cortex during simple self-paced finger movements. *Clinical Neurophysiology*, *114*(10), 1819–1826.

Raymond, J. L., Lisberger, S. G., & Mauk, M. D. (1996). The cerebellum: A neuronal learning machine? *Science*, *272*(5265), 1126–1131.

Reaz, M., Hussain, M., & Mohd-Yasin, F. (2006). Techniques of EMG signal analysis: Detection, processing, classification and applications. *Biological Procedures Online*, *8*, 11–35.

Requin, J., & Riehle, A. (1995). Neural correlates of partial transmission of sensorimotor information in the cerebral cortex. *Acta Psychologica, 90*(1–3), 81–95.

Richardson, A. (1969). *Mental Imagery*. New York: Springer Publishing Company, Inc.

Riehle, A. (1991). Visually induced signal-locked neuronal activity changes in precentral motor areas of the monkey: Hierarchical progression of signal processing. *Brain Research, 540*(1–2), 131–137.

Riehle, A., & Requin, J. (1995). Neuronal correlates of the specification of movement direction and force in four cortical areas of the monkey. *Behavioural Brain Research, 70*(1), 1–13.

Ritter, P., Moosmann, M., & Villringer, A. (2009). Rolandic alpha and beta EEG rhythms' strengths are inversely related to fMRI-BOLD signal in primary somatosensory and motor cortex. *Human Brain Mapping*, *30*(4), 1168–1187.

Rizzolatti, G., Fogassi, L., & Gallese, V. (2001). Neurophysiological mechanisms underlying the understanding and imitation of action. *Nature Reviews. Neuroscience*, *2*(9), 661–670.

Rockstroh, B., Birbaumer, N., Elbert, T., & Lutzenberger, W. (1984). Operant control of EEG and event-related and slow brain potentials. *Biofeedback and Self-Regulation*, *9*(2), 139–160.

Rodrigues, J. P., Mastaglia, F. L., & Thickbroom, G. W. (2009). Rapid slowing of maximal finger movement rate: Fatigue of central motor control? *Experimental Brain Research*, *196*(4), 557–563.

Rodriguez, M., Llanos, C., Gonzalez, S., & Sabate, M. (2008). How similar are motor imagery and movement? *Behavioral Neuroscience*, *122*(4), 910–916.

Rodriguez, M., Llanos, C., & Sabate, M. (2009). The kinematics of motor imagery: Comparing the dynamics of real and virtual movements. *Neuropsychologia*, *47*(2), 489–496.

Roeleveld, K., & Stegeman, D. F. (2002). What do we learn from motor unit action potentials in surface electromyography? *Muscle & Nerve*, *Suppl 11*, S92–S97.

Roeleveld, K., Stegeman, D. F., Falck, B., & Stålberg, E. V. (1997). Motor unit size estimation: Confrontation of surface EMG with macro EMG. *Electroencephalography and Clinical Neurophysiology/Electromyography and Motor Control*, *105*(3), 181–188.

Rohrbaugh, J. W., Syndulko, K., & Lindsley, D. B. (1976). Brain wave components of the contingent negative variation in humans. *Science*, *191*(4231), 1055–1057.

Romero, D. H., Lacourse, M. G., Lawrence, K. E., Schandler, S., & Cohen, M. J. (2000). Event-related potentials as a function of movement parameter variations during motor imagery and isometric action. *Behavioural Brain Research*, *117*(1–2), 83–96.

Rosenblum, M., & Kurtz, J. (1998). Analysing synchronization phenomena from bivariate data by means of the Hilbert transform. In H. Kantz, J. Kurths, & G. Mayer-Kress (Eds.)*, Nonlinear Analysis of physiological data* (pp. 91–99). Berlin: Springer.

Rosenblum, M. G., Pikovsky, A. S., Kurths, J., Osipov, G. V., Kiss, I. Z., & Hudson, J. L. (2002). Locking-based frequency measurement and synchronization of chaotic oscillators with complex dynamics. *Physical Review Letters*, *89*(26), 264102.

Rusconi, E., Pinel, P., Dehaene, S., & Kleinschmidt, A. (2010). The enigma of Gerstmann's syndrome revisited: A telling tale of the vicissitudes of neuropsychology. *Brain*, *133*(2), 320–332.

Rushworth, M. F., Johansen-Berg, H., Gobel, S. M., & Devlin, J. T. (2003). The left parietal and premotor cortices: Motor attention and selection. *NeuroImage*, *20*, S89–S100.

Salmelin, R., Hämäläinen, M., Kajola, M., & Hari, R. (1995). Functional segregation of movement-related rhythmic activity in the human brain. *NeuroImage*, *2*(4), 237–243.

Salmelin, R., & Hari, R. (1994). Spatiotemporal characteristics of sensorimotor neuromagnetic rhythms related to thumb movement. *Neuroscience*, *60*(2), 537–550.

Sauseng, P., Klimesch, W., Gruber, W. R., Hanslmayr, S., Freunberger, R., & Doppelmayr, M. (2007). Are event-related potential components generated by phase resetting of brain oscillations? A critical discussion. *Neuroscience*, *146*(4), 1435–1444.

Savica, R., Rocca, W. A., & Ahlskog, J. E. (2010). When does Parkinson disease start? *Archives of Neurology*, *67*(7), 798–801.

Schalk, G., Wolpaw, J. R., McFarland, D. J., & Pfurtscheller, G. (2000). EEG-based communication: Presence of an error potential. *Clinical Neurophysiology*, *111*(12), 2138–2144.

Schillings, M. L., Kalkman, J. S., van der Werf, S. P., Bleijenberg, G., van Engelen, B. G. M., & Zwarts, M. J. (2006). Central adaptations during repetitive contractions assessed by the readiness potential. *European Journal of Applied Physiology*, *97*(5), 521–526.

Schlaug, G., Sanes, J. N., Thangaraj, V., Darby, D. G., Jancke, L., Edelman, R. R., & Warach, S. (1996). Cerebral activation covaries with movement rate. *NeuroReport*, *7*(4), 879–883.

Schnitzler, A., Salenius, S., Salmelin, R., Jousmäki, V., & Hari, R. (1997). Involvement of primary motor cortex in motor imagery: A neuromagnetic study. *NeuroImage*, *6*(3), 201–208.

Schulze, K., Lüders, E., & Jäncke, L. (2002). Intermanual transfer in a simple motor task. *Cortex*, *38*(5), 805–815.

Schwägerl, C. (2004). Ich bin ein Cursor [I am a cursor]. *FAZ*, *66*, 44.

Schwoebel, J., Boronat, C. B., & Branch Coslett, H. (2002). The man who executed "imagined" movements: Evidence for dissociable components of the body schema. *Brain and Cognition*, *50*(1), 1–16.

Segal, S. J., & Fusella, V. (1970). Influence of imaged pictures and sounds on detection of visual and auditory signals. *Journal of Experimental Psychology*, *83*(3), 458–464.

Shapiro, D. (1979). Biofeedback and behavioral medicine in perspective. *Biofeedback and Self-Regulation*, *4*(4), 371–381.

Shah, A. S., Bressler, S. L., Knuth, K. H., Ding, M., Mehta, A. D., Ulbert, I., & Schroeder, C. E. (2004). Neural dynamics and the fundamental mechanisms of event-related brain potentials. *Cerebral Cortex*, *14*(5), 476–483.

Sharma, N., Jones, P. S., Carpenter, T. A., & Baron, J. (2008). Mapping the involvement of BA 4a and 4p during motor imagery. *NeuroImage*, *41*(1), 92–99.

Sharma, N., Pomeroy, V. M., & Baron, J. (2006). Motor imagery: A backdoor to the motor system after stroke? *Stroke*, *37*(7), 1941–1952.

Shaw, W. A. (1938). The distribution of muscular action potentials during imaging. *Psychological Record*, *2*, 195–216.

Shenoy, P., Krauledat, M., Blankertz, B., Rao, R. P. N., & Müller, K. (2006). Towards adaptive classification for BCI. *Journal of Neural Engineering*, *3*(1), R13–23.

Shepard, R. N., & Metzler, J. (1971). Mental rotation of three-dimensional objects. *Science*, *171*(972), 701–703.

Shmuelof, L., & Zohary, E. (2007). Watching others' actions: Mirror representations in the parietal cortex. *Neuroscientist*, *13*(6), 667–672.

Sirigu, A., Duhamel, J. R., Cohen, L., Pillon, B., Dubois, B., & Agid, Y. (1996). The mental representation of hand movements after parietal cortex damage. *Science*, *273*(5281), 1564–1568.

Sirigu, A., Zalla, T., Pillon, B., Grafman, J., Dubois, B., & Agid, Y. (1995). Planning and script analysis following prefrontal lobe lesions. *Annals of the New York Academy of Sciences*, *769*, 277–288.

Smulders, F. T., Kok, A., Kenemans, J. L., & Bashore, T. R. (1995). The temporal selectivity of additive factor effects on the reaction process revealed in ERP component latencies. *Acta Psychologica*, *90*(1–3), 97–109.

Sohn, Y. H., Jung, H. Y., Kaelin-Lang, A., & Hallett, M. (2003). Excitability of the ipsilateral motor cortex during phasic voluntary hand movement. *Experimental Brain Research*, *148*(2), 176–185.

Solodkin, A., Hlustik, P., Chen, E. E., & Small, S. L. (2004). Fine modulation in network activation during motor execution and motor imagery. *Cerebral Cortex*, *14*(11), 1246–1255.

Stancák, A., & Pfurtscheller, G. (1995). Desynchronization and recovery of beta rhythms during brisk and slow self-paced finger movements in man. *Neuroscience Letters*, *196*(1-2), 21-24.

Stancák, A., & Pfurtscheller, G. (1996). Mu-rhythm changes in brisk and slow self-paced finger movements. *NeuroReport*, *7*(6), 1161–1164.

Stancák, A. (2006). Cortical oscillatory changes occurring during somatosensory and thermal stimulation. *Progress in Brain Research*, *159*, 237–252.

Stinear, C. M., & Byblow, W. D. (2003). Role of intracortical inhibition in selective hand muscle activation. *Journal of Neurophysiology*, *89*(4), 2014–2020.

Stinear, C. M., Byblow, W. D., Steyvers, M., Levin, O., & Swinnen, S. P. (2006). Kinesthetic, but not visual, motor imagery modulates corticomotor excitability. *Experimental Brain Research*, *168*(1–2), 157–164.

Stippich, C., Ochmann, H., & Sartor, K. (2002). Somatotopic mapping of the human primary sensorimotor cortex during motor imagery and motor execution by functional magnetic resonance imaging. *Neuroscience Letters*, *331*(1), 50–54.

Stock, A., & Stock, C. (2004). A short history of ideo-motor action. *Psychological Research*, *68*(2-3), 176-188.

Summerfield, C., Trittschuh, E. H., Monti, J. M., Mesulam, M., & Egner, T. (2008). Neural repetition suppression reflects fulfilled perceptual expectations. *Nat Neurosci*, *11*(9), 1004–1006.

Tallon-Baudry, C., & Bertrand, O. (1999). Oscillatory gamma activity in humans and its role in object representation. *Trends in Cognitive Sciences*, *3*(4), 151–162.

Thoenissen, D., Zilles, K., & Toni, I. (2002). Differential involvement of parietal and precentral regions in movement preparation and motor intention. *Journal of Neuroscience*, *22*(20), 9024–9034.

Thomas, N. J. T. (1999). Are theories of imagery theories of imagination? An active perception approach to conscious mental content. *Cognitive Science*, *23*, 207–245.

Thomas, N. J. T. (2010). *Mental imagery [Online document]*. Abgerufen von Retrieved August 30, 2010, from http://plato.stanford.edu/entries/mental-imagery/

Tye, M. (1991). *The imagery debate.* Cambridge, MA: MIT Press.

Vaisman, L., Zariffa, J., & Popovic, M. R. (2010). Application of singular spectrum-based change-point analysis to EMG-onset detection. *Journal of Electromyography and Kinesiology*, *20*(4), 750–760.

Vaughan, T. M., Miner, L. A., McFarland, D. J., & Wolpaw, J. R. (1998). EEG-based communication: Analysis of concurrent EMG activity. *Electroencephalography and Clinical Neurophysiology*, *107*(6), 428–433.

Vidal, J. J. (1973). Toward direct brain-computer communication. *Annual Review of Biophysics and Bioengineering*, *2*, 157–180.

Vidal, J. (1977). Real-time detection of brain events in EEG. *Proceedings of the IEEE*, *65*(5), 633–641.

Vidaurre, C., & Blankertz, B. (2010). Towards a cure for BCI illiteracy. *Brain Topography*, *23*(2), 194–198.

Walsh, E., Kühn, S., Brass, M., Wenke, D., & Haggard, P. (2010). EEG activations during intentional inhibition of voluntary action: An electrophysiological correlate of self-control? *Neuropsychologia*, *48*(2), 619–626.

Wascher, E., & Wauschkuhn, B. (1996). The interaction of stimulus- and response-related processes measured by event-related lateralizations of the EEG. *Electroencephalography and Clinical Neurophysiology, 99*(2), 149–162.

Wheaton, L., Fridman, E., Bohlhalter, S., Vorbach, S., & Hallett, M. (2009). Left parietal activation related to planning, executing and suppressing praxis hand movements. *Clinical Neurophysiology*, *120*(5), 980–986.

White, T. D., Asfaw, B., DeGusta, D., Gilbert, H., Richards, G. D., Suwa, G., & Howell, F. C. (2003). Pleistocene Homo sapiens from Middle Awash, Ethiopia. *Nature*, *423*(6941), 742–747.

Wilson, M. (2003). Imagined movements that leak out. *Trends in Cognitive Sciences*, *7*(2), 53–55.

Witte, M., Patino, L., Andrykiewicz, A., Hepp-Reymond, M., & Kristeva, R. (2007). Modulation of human corticomuscular beta-range coherence with low-level static forces. *European Journal of Neuroscience*, *26*(12), 3564–3570.

Wolpaw, J. R., McFarland, D. J., Neat, G. W., & Forneris, C. A. (1991). An EEG-based brain-computer interface for cursor control. *Electroencephalography and Clinical Neurophysiology*, *78*(3), 252–259.

Wolpaw, J. R. (2007). Brain-computer interfaces as new brain output pathways. *Journal of Physiology*, *579*(3), 613–619.

Wolpaw, J. R., Birbaumer, N., McFarland, D. J., Pfurtscheller, G., & Vaughan, T. M. (2002). Brain-computer interfaces for communication and control. *Clinical Neurophysiology*, *113*(6), 767–791.

Wolpert, D. M., & Ghahramani, Z. (2000). Computational principles of movement neuroscience. *Nature Neuroscience*, *3 Suppl*, 1212–1217.

Wolpert, D., Ghahramani, Z., & Flanagan, J. (2001). Perspectives and problems in motor learning. *Trends in Cognitive Sciences*, *5*(11), 487–494.

Wu, T., Chan, P., & Hallett, M. (2008). Modifications of the interactions in the motor networks when a movement becomes automatic. *Journal of Physiology*, *586*(17), 4295–4304.

Wu, T., Kansaku, K., & Hallett, M. (2004). How self-initiated memorized movements become automatic: A functional MRI study. *Journal of Neurophysiology*, *91*(4), 1690–1698.

Yuan, H., Perdoni, C., & He, B. (2010). Relationship between speed and EEG activity during imagined and executed hand movements. *Journal of Neural Engineering*, *7*(2), 26001.

Zacks, J. M. (2008). Neuroimaging studies of mental rotation: A meta-analysis and review. *Journal of Cognitive Neuroscience*, *20*(1), 1–19.

Erklärung

Hiermit versichere ich, dass ich die vorgelegte Arbeit selbständig verfasst habe. Andere als die angegebenen Hilfsmittel habe ich nicht verwendet. Die Arbeit ist in keinem früheren Promotionsverfahren angenommen oder abgelehnt worden.

Berlin, der 26.10.2010

Friederike Hohlefeld

Aus dieser Dissertation hervorgegangene Veröffentlichungen

Kapitel 2 (Study 1) wird veröffentlicht in *Brain Research*:

> Hohlefeld, F.U., Nikulin, V.V., & Curio, G. (in press). Visual stimuli evoke rapid activation (120 ms) of sensorimotor cortex for overt but not for covert movements. *Brain Research*. http://dx.doi.org/10.1016/j.brainres.2010.10.035

Eine modifizierte Version von Kapitel 3 (Study 2) ist erschienen in *Neuropsychologia*:

> Nikulin, V.V., Hohlefeld, F.U., Jacobs, A.M., & Curio, G. (2008). Quasi-movements: A novel motor-cognitive phenomenon. *Neuropsychologia 46*, 727–742. http://dx.doi.org/10.1016/j.neuropsychologia.2007.10.008

Eine gekürzte Version von Kapitel 4 (Study 3) wurde eingereicht:

> Hohlefeld, F.U., Nikulin, V.V., & Curio, G. (submitted). Covert movements trigger repetition suppression of EEG in sensorimotor cortex. http://dx.doi.org/10.1097/WNR.0b013e3283436d84

Curriculum Vitae – Friederike U. Hohlefeld

… aus Gründen des Datenschutzes in der Online-Version nicht enthalten …