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**USER VARIATIONS IN ATTENTION
AND BRAIN-COMPUTER INTERFACE
PERFORMANCE**

**BY
SUSAN ALIAKBARYHOSSEINABADI**

DISSERTATION SUBMITTED 2017



AALBORG UNIVERSITY
DENMARK

USER VARIATIONS IN ATTENTION AND BRAIN-COMPUTER INTERFACE PERFORMANCE

Ph.D. Thesis

by

Susan Aliakbaryhosseinabadi



AALBORG UNIVERSITY
DENMARK

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PhD supervisor: Associate Prof. Natalie Mrachacz-Kersting,
Aalborg University

PhD committee: Associate Professor Parisa Gazerani
Aalborg University

Professor, Dr. Benjamin Blankertz
Technical University of Berlin

Associate Professor Preben Kidmos
Aarhus University

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CV



Susan Aliakbaryhosseinabadi received her Bachelor and Master degree in Electrical Engineering from Isfahan University of Technology, Iran in 2009 and 2012, respectively. She also worked as a research assistant at Aalborg University under the supervision of Associate Professor Natalie Mrachacz-Kersting from 2013-2014. In 2014, she was enrolled as a PhD student at the Center for Sensory Motor Interaction at Aalborg University under the supervision of Associate Professor Natalie Mrachacz-Kersting. In 2017, she was awarded first place for the International award for Brain-Computer Interface research. Her main research interests include brain-computer interfaces, signal processing, rehabilitation, motor and cognitive control.

PREFACE

The current PhD thesis was conducted at the Center for Sensory-Motor Interaction (SMI), Aalborg University, Denmark, from 2014 to 2017. This work is based on five studies that are detailed in the following chapters.

Study I:

Title: Detection of movement intention from single-trial movement-related cortical potentials using random and non-random paradigms

Authors: Susan Aliakbaryhosseinabadi, Ning Jiang, Aleksandra Vuckovic, Kim Dremstrup, Dario Farina and Natalie Mrachacz-Kersting

Journal: *Brain-Computer Interface*, vol.2, pp.29-39, 2015

Study II:

Title: Influence of attention alternation on movement-related cortical potentials in healthy individuals and stroke patients

Authors: Susan Aliakbaryhosseinabadi, Vladimir Kostic, Aleksandra Pavlovic, Sasa Radovanovic, Ernest Nlandu Kamavuako, Ning Jiang, Laura Petrini, Kim Dremstrup, Dario Farina and Natalie Mrachacz-Kersting

Journal: *Clinical Neurophysiology*, vol. 128, pp. 165-175, 2017

Study III:

Title: Influence of dual-tasking with different levels of attention diversion on characteristics of the movement-related cortical potential

Authors: Susan Aliakbaryhosseinabadi, Ernest Nlandu Kamavuako, Laura Petrini, Ning Jiang, Dario Farina and Natalie Mrachacz-Kersting

Journal: *Brain Research*, vol. 1674, pp. 10-19, 2017

Study IV:

Title: Classification of EEG signals to identify variations in attention during motor task execution

Authors: Susan Aliakbaryhosseinabadi, Ernest Nlandu Kamavuako, Ning Jiang, Dario Farina and Natalie Mrachacz-Kersting

Journal: *Neuroscience Methods*, vol.284, pp. 27-34, 2017

Study V:

Title: EEG-based identification of attention diversion during asynchronous motor tasks

Authors: Susan Aliakbaryhosseinabadi, Ernest Nlandu Kamavuako, Ning Jiang, Dario Farina and Natalie Mrachacz-Kersting

Journal: *IEEE Transaction on Biomedical Engineering*, 2nd review process

Other related publications:

N. Mrachacz-Kersting, M. Voigt, A.J.T. Stevenson, **S. Aliakbaryhosseinabadi**, N. Jiang, K. Dremstrup, D. Farina. “*The effect of type of afferent feedback timed with motor imagery on the induction of cortical plasticity*”. *Journal of Brain Research*, vol.1674, pp. 91-100, 2017.

N. Mrachacz-Kersting, **S. Aliakbaryhosseinabadi**, M. Pedersen, N. Jiang and D. Farina. “*Tactile Stimulation training to enhance MRCP detection in chronic stroke patients*”, *HCI2017*, vol. 10285, pp. 354-363, 2017.

S. Aliakbaryhosseinabadi, E. Nlandu Kamavuako, D. Farina and N. Mrachacz-Kersting, “*Effect of Attention division on movement detection and execution in dual-task conditions*”, 8th IEEE EMBS conference on Neural Engineering, pp. 552-555, Spring 2017.

S. Aliakbaryhosseinabadi, E. Nlandu Kamavuako, N. Jiang, D. Farina, and N. Mrachacz-Kersting, “*Detection of attention alteration of BCI users based on EEG analysis*”, Annual BCI meeting, Graz, Austria, 2017.

S. Aliakbaryhosseinabadi, V. Kostic, A. Pavlovic, S. Radovanovic, D. Farina, and N. Mrachacz-Kersting . “*Effect of Attention Variation in Stroke Patients: Analysis of Single Trial Movement-Related Cortical Potentials*” . Springer Publication, 3rd International Conference on NeuroRehabilitation (ICNR2016), pp. 983-987, Segovia, Spain, 2016.

N. Mrachacz-Kersting, A.J.T. Stevenson, **S. Aliakbaryhosseinabadi**, A.C. Lundgaard, H.R. Jørgensen, K.Eg. Severinsen, D. Farina. “*An associative Brain-Computer-Interface for acute stroke patients*”, Springer, 3rd International

Conference on NeuroRehabilitation (ICNR2016), pp. 841-845, Segovia, Spain, 2016.

S. Aliakbaryhosseinabadi, E. Nlandu Kamavuako, D. Farina, N. Mrachacz-Kersting, “*Effect of attention diversion on movement detection: analysis of movement related cortical potential*”, Submitted in 38th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC’16) will be hosted at Disney’s Contemporary Resort at Walt Disney World® Resort, Lake Buena Vista (Orlando), Florida USA on August 16-20.

S. Aliakbaryhosseinabadi, N. Jiang, L. Petrini, K. Dremstrup, D. Farina, N. Mrachacz-Kersting. “*Robustness of movement detection techniques from motor execution : single trial movement related cortical potential*” . IEEE Publication, 7th Annual International IEEE EMBS Conference on Neural Engineering, Montpellier, France, pp. 13-16, 2015.

N. Mrachacz-Kersting, N. Jiang, **S. Aliakbaryhosseinabadi**, R. Xu, L. Petrini, R. Lontis, M. Jochumsen, K. Dremstrup and D. Farina. “*The changing Brain: Bidirectional learning between algorithm and user*”, Book chapter in: Brain-Computer Interface Research: A State-of-the-Art Summary 4, pp. 115-125, 2014.

S. Aliakbaryhosseinabadi, N. Jiang, A. Vuckovic, R. Lontis, K. Dremstrup, D. Farina, N. Mrachacz-Kersting.(2014) . “*Detection of movement intention from movement-related cortical potentials with different paradigms*”. Springer Publication, Replace, Repair, Restore, Relieve : Bridging Clinical and Engineering Solutions in Neurorehabilitation: Proceedings of the 2nd International Conference on NeuroRehabilitation, ICNR2014, pp. 237-244, 2014.

S. Aliakbaryhosseinabadi, N. Jiang, L. Petrini, K. Dremstrup, D. Farina, N. Mrachacz-Kersting. “*Effect of Different Attentional Level and Task Repetition on Single-trial Movement-Related Cortical Potential.*” Paper presented at the Sixth International Brain-Computer Interface Conference, September 16-19, Graz, Austria, 2014.

ENGLISH SUMMARY

Brain-computer interface (BCI) systems translate brain signals into commands for external devices. In the area of neurorehabilitation, the main aim of these systems is to restore lost function. Since the original reports by Daly and colleagues (2009), several research groups have tested the efficacy of such BCIs in stroke patients. Most of these continue to be confined to the artificial laboratory setting likely as reliable detection of relevant brain signals remains difficult. In real-life conditions, attention diversion from a desired/target task is one of the most crucial factors that affect detection accuracy. Attention is defined as the ability to focus on the relevant/desired stimuli among various stimuli in our surrounding environment. It may be quantified by the size and latency of the event-related potential (ERP), one of the most common types of brain signal modalities used to study attention. Typically, when attending to a task, the P300 amplitude is increased and the latency decreased, while attention deterioration is characterized by a decrease in the P300 amplitude and an increment in the latency.

In the current thesis, the main aim was to design a robust and reliable real-time BCI system for restoration of lost motor function, under conditions where attention is varied. The BCI system implemented, uses the movement-related cortical potential (MRCP) as the control signal. The MRCP is a naturally occurring negative shift in the EEG that commences approximately 1-2 s prior to movement initiation, regardless if the movement is actually performed or only imagined. It is thus possible to detect movement intention at least 1 s prior to actual execution, making this an ideal control signal modality for BCIs. It is however not known how the MRCP is affected by shifts in attention of the user.

Through five studies of this thesis, the effect of the users' attention variation was investigated while they performed either cue-based (synchronous) or self-paced (asynchronous) movements. Regarding to the movement detection latency in Study I, an appropriate visual cue was selected to control the timing of motor movement execution (ankle dorsiflexion). Study II revealed that an imposed cognitive task between motor task executions can divert the attention particularly in the case of complex cognitive tasks. The effect of attention drift was greater in stroke patients. A significant finding was that a single channel could be used to reliably detect attention variations, while movement detection from a combination of channels was not deteriorated under attention drifts. It is well known that changes in attention significantly affect plasticity induction and thus restoration of lost motor function in patient populations. It therefore remains vital to detect attention changes within these BCIs to ensure that plasticity is induced effectively. The work in Study II was extended in Study III-V by the introduction of dual task conditions to alter the users' attention. Thus, participants were asked to attend to two tasks executed at the same time. Results revealed that movement preparation and thus movement execution

deteriorated in both levels of simple or complex dual-task conditions compared to the single-task. In addition, feature spaces of normal and diverted attention levels were distinguished and classified by using a global temporal model. Finally, it was shown that parietal and central channels were more affected under attention changes.

In conclusion, the findings of the work presented in the current thesis provide a source of information to detect the users' attentional state. This information is currently being used to implement a real-time neurofeedback BCI system that will focus the attention of the users on the main task of the BCI and thus optimize the induction of plasticity. It can also be used to improve the performance of assistive BCI devices such as wheelchairs or robotic prosthesis since the users' attention to the main task is controlled. Further, it has major implications for the design of BCIs in the area of neurorehabilitation for patient populations.

DANSK RESUME

Hjerne-computer-interface (brain-computer interface, BCI) systemer oversætter hjernesignaler til kommandoer, som kan afgives til eksterne enheder. Inden for neurorehabilitering er hovedformålet med disse systemer at genoprette tabt funktionsevne. Siden de første resultater fra Daly et al. i 2009 har flere forskningsgrupper testet effekten af BCI hos patienter, der har haft et slagtilfælde. De fleste af denne type forsøg når kun til laboratorierne, sandsynligvis fordi det stadig er vanskeligt at foretage pålidelige målinger af relevante hjernesignaler. Under virkelige forhold er opmærksomhedsafledning fra en opgave en af de mest afgørende faktorer, der påvirker detektionsnøjagtigheden. Opmærksomhed defineres som evnen til at fokusere på de relevante/ønskede stimuli blandt alle de forskellige stimuli i det omgivende miljø. Opmærksomheden kan kvantificeres ved hjælp af størrelsen og latensen af de event-relaterede potentialer (ERP), som er en af de mest almindelige typer hjernesignalmodalitet, der anvendes, når man studerer opmærksomhed. Når man udfører en opgave, forøges P300-amplituden typisk og latensen formindskes, mens opmærksomhedsforringelse karakteriseres ved et fald i P300-amplitude og en stigning i latens.

I denne afhandling er hovedformålet at designe et robust og pålideligt reeltids BCI-system til rehabilitering af tabt motorisk funktion under forhold, hvor opmærksomheden varieres. Det anvendte BCI-system bruger det bevægelsesrelaterede kortikale potentialer (movement-related cortical potential, MRCP) som styresignal. MRCP er den naturligt forekommende negative ændring i EEG, som indledes 1-2 s før en bevægelse initieres, uanset om personen faktisk udfører bevægelsen eller kun tænker på at udføre den. Det er således muligt at registrere igangsætningen af en bevægelse mindst 1 s før den aktuelle udførelse af bevægelsen, hvilket gør dette til en ideel styresignalmodalitet for BCI. Det er dog ikke kendt, hvordan MRCP påvirkes af ændringer i brugerens opmærksomhed.

Gennem de fem studier, der ligger til grund for denne afhandling, undersøgte variationer i brugernes opmærksomhed ved bevægelser udført efter signaler (synkrone) eller bevægelser ved en selvvalgt hastighed (asynkrone). Med hensyn til bevægelsesdetekteringslatensen i Studie I blev der valgt et passende visuelt signal til at kontrollere timingen af udførelsen af den motoriske bevægelse (dorsalfleksion af anklen). Studie I afslørede, at en pålagt kognitiv opgave mellem udførelsen af motoriske opgaver kan aflede opmærksomheden; særligt ved komplekse kognitive opgaver. Effekten af den afledte opmærksomhed var større hos patienter, der havde haft slagtilfælde. Et vigtigt resultat viste, at en enkelt EEG-kanal var anvendelig til at påvise ændringer i opmærksomheden, mens bevægelsesdetektion fra en kombination af kanaler ikke blev forringet under afledning af opmærksomheden. Det er velkendt, at ændringer i opmærksomheden signifikant påvirker plasticitetsinduktion og dermed rehabilitering af tabt motorisk funktion hos

-

patientpopulationer. Det er derfor afgørende, at opdage ændringer i opmærksomhed i BCI'er for at sikre, at plasticiteten induceres effektivt. Arbejdet i Studie II blev videreført i Studie III-V ved at introducere dobbelt-opgaver for at ændre brugerens opmærksomhed. Deltagerne blev således bedt om at udføre to opgaver samtidigt. Resultaterne viste, at forberedelsen af bevægelsen og dermed udførelsen af bevægelsen blev forringet ved både simple og komplekse dobbelt-opgaver sammenlignet med enkelt-opgaver. Derudover blev karakteristika ved normale og afledte opmærksomhedsniveauer udpeget og klassificeret ved hjælp af en global temporal model. Endelig blev det vist, at parietale og centrale kanaler blev påvirket mere under opmærksomhedsændringer.

De resultater, som præsenteres i afhandlingen, danner dermed basis for at kunne detektere brugerens opmærksomhedstilstand. Resultaterne anvendes i øjeblikket til at implementere et realtids BCI-system med neurofeedback, der fokuserer på brugernes opmærksomhed på BCI-systemets hovedopgave, og dermed optimere induktionen af plasticitet. Resultaterne kan også anvendes til at forbedre ydeevnen af BCI-enheder som fx rullestole og robot-proteser, idet brugernes opmærksomhed på hovedopgaven kontrolleres. Endvidere har resultaterne store konsekvenser for designet af BCI-systemer til neurorehabilitering af patientpopulationer.

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LIST OF ABBREVIATIONS

AEP	Auditory evoked potential
ANOVA	Analysis of Variance
BCI	Brain Computer Interface
CAR	Common average reference
CNV	Contingent Negative Variation
CSP	Common spatial pattern
CST	Complex secondary task
DL	Detection latency
EEG	Electroencephalography
EMG	Electromyography
EOG	Electrooculography
ERD	Event related desynchronization
ERP	Event-related potential
ERS	Event related synchronization
ERSP	Event-related spectral perturbation
FES	Functional electrical stimulation
FMRI	Functional magnetic resonance imaging
FPR	False positive rate
ICA	Independent component analysis
ISI	Inter-stimulus interval
KNN	K nearest neighbor
LDA	Linear discriminant analysis
LF-ASD	Low frequency asynchronous switch design
LLSF	Large Laplacian spatial filter
LPP	Locality preserving projection
LTD	Long-term depression
LTP	Long-term potentiation
MCA	Middle cerebral artery

MEP	Motor evoked potential
MRCP	Movement related cortical potential
MRI	Magnetic resonance imaging
NIBS	Non-invasive brain stimulation techniques
OSF	Optimized spatial filter
PAS	Paired associative stimulation
PCA	Principle component analysis
PET	Positron emission tomographic
ROC	Receiver operating characteristic
RR	Rebound rate
RTMS	Repetitive transcranial magnetic stimulation
SCP	Slow cortical potential
SFS	Sequential forward selection
SMR	Sensory motor rhythm
SNR	Signal to noise ratio
SST	Simple secondary task
SVM	Support vector machine
TA	Tibialis anterior
tDCS	Transcranial direct current stimulation
TMS	Transcranial magnetic stimulation
TPN	Time of peak negativity
TPR	True positive rate
VEP	Visual evoked potential
VPN	Value of peak negativity

THESIS AT A GLANCE

	Question	Method	Answer
I	<p>a. Does prior knowledge of the task to be performed improve detection latency and accuracy of the MRCP?</p> <p>b. How is detection latency and accuracy of the MRCP affected when the cue to perform a task is separated into a preparation and execution phase?</p>	<p>8 healthy participants, two different visual cues, 28 EEG channels, ankle dorsiflexion timed to the visual cue</p>	<p>a. Yes, a non-random cue where participants have prior knowledge of the task to be performed resulted in a significantly higher accuracy and latency of movement intention detection when using MRCPs as the control signal of a BCI.</p> <p>b. Movement detection from MRCP parameters occurs earlier and with a higher accuracy.</p>
II	<p>a. What are the effects on MRCP parameters when attention of the user is artificially altered via an auditory oddball paradigm?</p> <p>b. Which EEG channel(s) is more affected under such attention variations?</p>	<p>20 healthy participants and 12 stroke patients, 9 EEG channels, ankle dorsiflexion timed to the visual cue, an auditory oddball</p>	<p>a. MRCP negativity and slope were significantly affected by artificial modifications of the user's attention, particularly during movement preparation.</p> <p>b. MRCPs obtained from the single channel Cz were significantly affected by attention variations. This was not the case for the Laplacian channel.</p>
	<p>a. What is the effect of dual-tasking on MRCP parameters and the execution of the main</p>	<p>24 healthy participants, 18 EEG channels, 2 EMGs, ankle</p>	<p>a. Dual tasking divided the attention between the motor and cognitive tasks. The MRCP was significantly decreased in amplitude during</p>

III	motor task?	dorsiflexion timed to a visual cue, two oddball paradigms with different levels of difficulty.	movement preparation. Increasing the difficulty of the secondary task lead to a decrease in attention and thus had a greater effect on the main motor task.
IV	<p>a. Is it possible to classify two different attention levels; focused and diverted attention?</p> <p>b. Can we distinguish feature distributions of two attention levels?</p>	<p>12 healthy participants, 18 EEG channels and 2 EMGs, ankle dorsiflexion timed to a visual cue, two oddball paradigms with different levels of difficulty</p>	<p>a. Yes, by using temporal features obtained from the MRCP, two attention levels were classified.</p> <p>b. Yes, the normal distribution of the temporal features have different means and StDs for two different attention levels. It was possible to develop a global model for attention distinction.</p>
V	<p>a. Can we detect the effect of attention variation on self-paced movement execution under various types of distractors?</p> <p>b. Which parts of the brain are more affected by attention variations?</p>	<p>27 healthy participants, 28 EEG channels and 2 EMGs, self-paced ankle dorsiflexion, Different types of oddball paradigms (Visual, auditory and combination of these two)</p>	<p>a. Yes, attention levels were classified by applying temporal and spectral features while a combination of these two groups of features showed the highest classification accuracy.</p> <p>b. Channels located over the parietal lobe revealed the highest classification accuracy when using tempo-spectral features. A combination of channels located over the parietal and central regions enhanced classification accuracy.</p>

CHAPTER 1. INTRODUCTION

Cerebral stroke is caused by a hemorrhage or blood clot in the brain. The ensuing partial or complete paralysis of part of the body reduces the mobility of the patient thereby directly affecting the quality of life. In Denmark, the prevalence of stroke is approximately 0.3% (15.500 cases) per year and 30.000-40.000 persons live with the consequences of a stroke. The direct costs are 2.7 billion DKK per year (corresponding to 4% of the annual, total health-care costs - <http://www.sst.dk/>).

Recovery of function following classical rehabilitation techniques, such as physical therapy, is scarcely predictable as individuals respond differently to the same treatment (Stinear, 2017). The Danish National Board of Health has recognized the urgent need to improve current rehabilitation strategies and to identify adequate markers for recovery. In an effort to enhance the recovery process, there have been increasing attempts over recent years to devise adjuvant therapies such as non-invasive brain stimulation (NIBS, for review see (Cirillo et al., 2017). The idea here is that any particular NIBS protocol ‘primes’ the motor cortex for subsequent learning, which then occurs during a period of increased excitability of the motor cortex. However, the benefits of such treatments on improved function or motor learning effects are relatively small (Rothwell, 2016), which is one reason they are not yet an integral part of the daily clinical routine.

Recently, brain-computer interface (BCI) systems have received increasing attention within the area of neuro-rehabilitation for stroke (Silvoni et al., 2011). BCIs use brain signals to train the users to learn new tasks and to control external devices. Since the seminal work of Daly (Daly et al., 2009), numerous studies have applied various types of such BCIs mainly in chronic stroke patients (Ang et al., 2009; Ang et al., 2010; Broetz et al., 2010; F. Cincotti et al., 2012; Li et al., 2014). While the initial results are promising, there remain several important areas to be addressed before such BCIs are relevant for the clinical setting. These may be divided into the following areas: (1) design of appropriate signal-acquisition hardware that can easily be used within the clinic, (2) validation of the various BCI systems available and (3) reliability (Shih et al., 2012). In this context, the body of work presented in the current thesis addresses the last area, reliability, and more precisely, how reliability may be affected by the various attention distractors during the use of an established BCI system. Following a brief overview of stroke, rehabilitation following stroke, plasticity, BCIs and attention, five studies are presented that have specifically addressed this issue.

1.1. NEUROREHABILITATION

1.1.1. STROKE

Stroke is classified into two main groups:

- Ischemic stroke: when a blood vessel is blocked and thus oxygen and nutrition cannot flow appropriately within the brain (figure 1-1). It is the more common type of stroke (about 85%).
- Haemorrhagic stroke: when a blood vessel is bleeding (figure 1-1). It can happen in the vessels inside or around the brain. This type of stroke is not as common as ischemic type (about 15%).

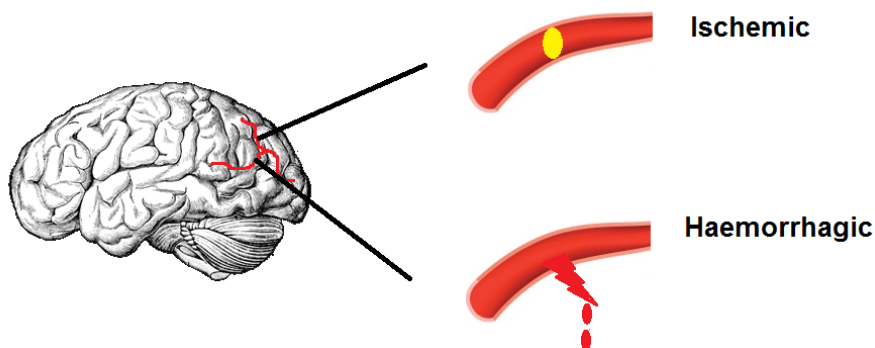


Figure 1-1 Illustration of the two stroke types of Ischemic (block of blood vessel) and Haemorrhagic (vessel bleeding).

Stroke can localize in each region of the brain however its location and volume have a significant effect on potential recovery (Ganguly et al., 2013). Consequences of right hemisphere stroke include decreased communication skills, decreased emotional understanding that induce indifference reactions to the environment and decreased visuospatial orientation causing problems in tracking or identifying visual orientations (Annett, 1975; Maaijwee et al., 2014). Left hemisphere stroke may cause aphasia, a disorder of language, apraxia, a disability in execution of voluntary movements and emotional disorders such as frustration or unconsciousness (Robinson et al., 1984).

1.1.2. REHABILITATION AFTER STROKE

Recovery following a stroke is divided into two main phases, the acute/subacute phase within the first three to six months and the chronic phase. The first phase is governed almost exclusively by spontaneous biological recovery processes (Krakauer & Marshall, 2015). According to this, most stroke survivors should attain

up to 70% of the maximum functionality as assessed by clinical scales within this time frame regardless of the type of rehabilitation procedure implemented. However, there remain exceptions to this rule, specifically for severely affected patients that do not reach this 70% (Krakauer & Marshall, 2015). This may be directly related to the size of the lesion, such that restoration of lost motor functions is greater if the lesion is small (Duncan et al., 2000; Kolb et al., 2011). Recent evidence suggests that tailoring rehabilitation during this critical phase according to clinical, neurophysiological and neuroimaging biomarkers may improve the outcome beyond 70% (Stinear, 2017). Most clinical trials for testing rehabilitation interventions have been conducted with chronic stroke patients. Rehabilitation interventions during the chronic phase, differ widely dependent on the country and often also region of where the patients are located. A recent review suggests that specifically for gait rehabilitation, positive outcomes depend on motivation and engagement of the patient and the family of the patient, attention to the task being trained, and variability of the task (e.g. training walking on different support surfaces) (Belda-Lois et al., 2011).

Aside from the time after stroke, age is a factor that significantly affects the efficiency of recovery (Jamrozik et al., 1999; Kugler et al., 2003; Nakayama et al., 1994). Thus, functional improvements are significantly greater for patients younger than 55 years of age. In addition, the speed of recovery is significantly greater for younger patients (Kugler et al., 2003).

Recovery of lost motor function in the clinical setting is typically quantified by clinical scales such as the Fugl-Meyer scale (Fugl-Meyer et al., 1975). Such recovery assumes that significant plasticity is being induced within the central nervous system.

1.2. PLASTICITY

Plasticity is defined as the ability of the central nervous system to change its structure and neuronal connections as a result of experience, learning new tasks and reorganizing after injury. Several mechanisms have been proposed to occur, such as changes in the efficacy of synapses, neuronal sprouting and the unmasking of existing but latent synapses (Cooke & Bliss, 2006). Of these, the most investigated has been the idea that synapses can alter their responsiveness depending on the specific inputs. This is often referred to as long-term potentiation (LTP) and long-term depression (LTD) (Cooke & Bliss, 2006). In one form of LTP and LTD, also termed associative LTP/LTD, if the presynaptic neuron is stimulated just prior to an action potential being generated in the postsynaptic neuron, the post-synaptic neuron's activation is increased (LTP) while if the pre-synaptic neuron is activated after the post-synaptic neuron has fired an action potential, LTD is induced (Bliss & Collingridge, 1993). These processes are based on the Hebbian principle which claims that "*neurons that fire together, wire together*" (Clark, 1950). The idea that

associative LTP and LTD may be the mechanisms behind memory formation and learning was tested non-invasively in humans in 2000 by the group of Stefan (Stefan et al., 2000). Briefly, a peripheral nerve stimulus was applied to the nerve innervating the target muscle. When the afferent signal so generated had reached the motor cortex, that part of the motor cortex that has direct projections to the target muscle was stimulated by non-invasive transcranial magnetic stimulation (TMS). This intervention is commonly referred to as paired associative stimulation (PAS). By continuously pairing these two artificial stimuli, significant plasticity was induced in the motor cortex (LTP-like plasticity) as assessed by the increase in the motor evoked potential (MEP). If the TMS stimulus was applied prior to the afferent signal arriving at the motor cortex, a significant decrease in the MEP was attained (LTD-like plasticity). Interestingly, if LTP-like PAS is applied immediately following the learning of a motor skill, the effects of PAS are diminished, supporting the view that learning in human motor cortex occurs through LTP-like mechanisms (Ziemann et al., 2004).

1.2.1. PLASTICITY AND REHABILITATION

Functional recovery through rehabilitation techniques following stroke is accompanied by significant reorganization and induction of plasticity (for review see Pekna et al., 2012). For example, functional imaging such as functional magnetic resonance imaging (fMRI) or positron emission tomographic (PET) have shown reorganization of the contralesional hemisphere in somatosensory cortex after stroke as a result of rehabilitation that rewires surviving neural networks to make new response routes for lost abilities (Butefisch et al., 2006; Calautti & Baron, 2003; Chollet et al., 1991). The main sites for the reorganization are thus not limited to the lesioned hemisphere but include the involvement of the hemisphere contralateral to the stroke site as well as the spinal cord (Nudo, 2006; Pekna et al., 2012).

In an effort to enhance the natural neuro-restorative processes within the brain following a stroke and thus promote functional recovery, several strategies have been proposed to promote plasticity. These include, exogenous pharmacological and cell-based treatments (for review see (Hermann & Chopp, 2012) and novel non-invasive brain stimulation techniques (NIBS) such as TMS, repetitive TMS (rTMS) and transcranial direct current stimulation (tDCS) (for review see (Edwardson, 2013). In particular the latter have been shown to exert three main effects to increase brain plasticity: Increment of cortical excitability, enhancement of contralesional hemisphere activity and somatotopic reorganization which leads to improved motor, language, cognitive and visual functions (Byrnes et al., 2001; Cramer, 2008; Seitz et al., 1998; Weiller et al., 1993).

However, the overall effects on changes in functionality remain unclear specifically for such techniques as NIBS (Rothwell, 2016). This is likely as responses to NIBS are variable between individuals and from application to application in a single

individual. A recent review on PAS protocols (Suppa et al., 2017) suggests that a novel approach to NIBS that uses a BCI approach where stimulation occurs during endogenous activation of the motor cortex may be the future in enhancing plasticity induction for stroke rehabilitation.

CHAPTER 2. BRAIN COMPUTER INTERFACES

Brain-computer interface (BCI) systems have different applications. Although they can be used for entertainment and communication, they are widely used for neuro-rehabilitation. In this application area, BCIs aim to translate brain signals into commands that control external devices. They thus make a connection between the brain and the external environment without using nerve or muscle activity to help disabled people to manage their responses to the surrounding environment.

2.1. STRATEGY OF BRAIN COMPUTER INTERFACES

BCIs require five main steps, 1. signal acquisition, 2. signal processing, 3. feature extraction, 4. classification and 5. providing control feedback (Khalid et al., 2009) as illustrated in figure 2-1. The output of this procedure may then be applied in five categories included to replace, restore, enhance, supplement or improve function as presented in figure 2-1.

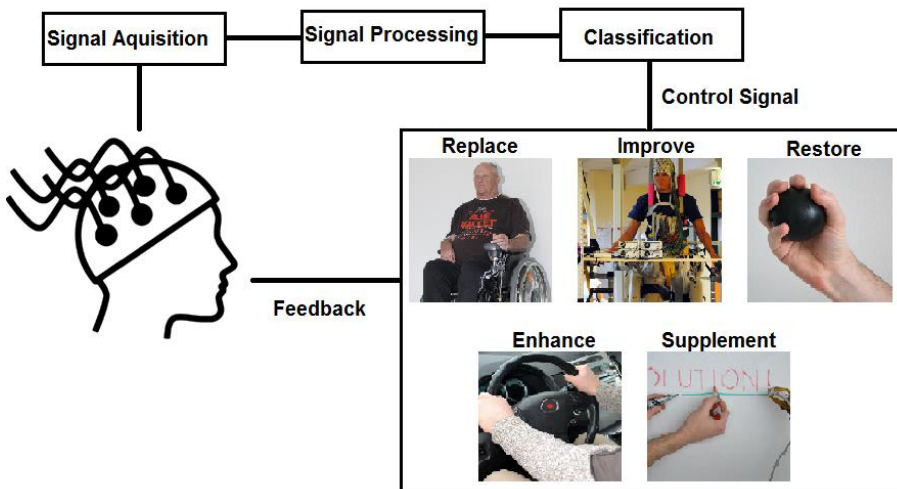


Figure 2-1 Illustration of BCI components and applications. BCI systems are designed based on five steps, signal acquisition, signal processing, classification, providing control signals and feedback between the controlled device and the user. BCIs can be used for replacement, improvement, restoration, enhancement and supplementary goals.

Input signals that represent the activity of the brain can be based on electrophysiological and hemodynamic measures. The first type is generated by ionic current flow within neurons and may be recorded invasively (intracortical

recordings and subdural recordings (Leuthardt et al., 2004; Schalk & Leuthardt, 2011)) or non-invasively. The latter is related to the blood flow within the brain and may include methods such as fMRI, (Weiskopf et al., 2003), near infrared spectroscopy (NIRS, (Sitaram et al., 2009)) and PET (Van Mier et al., 1998). These latter methods are not ideal for BCI control as some (fMRI and PET) require expensive equipment where the user is often confined to a static state and all have long response latencies making them inappropriate for real-time control. Techniques based on electrophysiology have by far been the most exploited for BCI use. Invasive techniques have an excellent signal to noise ratio but the disadvantage that invasive surgery has to be conducted to place the recording electrode(s) into position. For applications such as neurorehabilitation following stroke, non-invasive electroencephalography (EEG) is to date the most optimal signal recording technique. However, since the signals are collected from the surface of the skull they are prone to noise from the surrounding environment. Nevertheless, with advancement in technologies, the low cost, ease of application and excellent temporal resolution their performance has become acceptable.

2.1.1. TYPES OF BRAIN COMPUTER INTERFACES

A BCI can be classified into two groups with regards to the control procedure. The first group encompasses synchronous (cue-based) BCIs where an external cue is used to control the start of the task (e.g. P300 speller (a time-locked BCI)) (Xu et al., 2013). The second group are asynchronous (self-paced) BCIs where the brain signals are continuously analyzed as to the users' state which can change at any moment (Diez et al., 2011; Sadeghian & Moradi, 2007). Synchronous BCIs are more applicable for neuro-rehabilitation following stroke, since it applies a cue as a source of information for movement execution. In addition, patients tend to respond better when provided with a cue (Heremans et al., 2009). However asynchronous systems represent the natural way we move though they are more complex from an analysis point of view as there is no special window time for the movement. These are better suited for replacement of lost motor function such as robotic systems as users can start the movement at their self-selected pace.

2.2. CONTROL SIGNAL MODALITIES IN BRAIN COMPUTER INTERFACE

In EEG-based BCIs, different signal modalities extracted from EEGs have been used as control signals. A sample of these signals is illustrated in figure 2-2. These may be divided into two main categories, evoked control signals where an external stimulus is provided to the user (this may be visual, auditory or sensory) that produces an evoked potential which is then detected by the BCI algorithm, and induced control signals where the user voluntarily performs or imagines a task and the alterations in the EEG signal are detected by the algorithm. Different types of signal modalities have been used in BCI applications, such as steady-state evoked

potentials (Pokorný et al., 2016) and event-related (de)synchronization (ERD/ERS) (Aftanas et al., 2004). In the following, only those signals that have been implemented in a BCI for neurorehabilitation of stroke patients will be further discussed. These include the event-related potential, sensorimotor rhythms and slow cortical potentials.

2.2.1. EVENT RELATED POTENTIALS

Event-related potentials (ERPs) are a group of positive or negative peaks obtained in response to a sensory stimuli or event. To enhance signal to noise ratio, different trials of ERP, which are locked to the stimulus onset, are averaged. In most of the ERP based BCIs, the P300 component was used as the control signal, but other components such as the N400 have also been employed to improve BCI performance (Kaufmann et al., 2011).

The P300 is a positive peak induced 300-400 ms after the stimulus onset (visual, auditory or somatosensory). The amplitude and latency of the P300 represents the response level to the specific event such as the level of attention (Ramirez et al., 2005; Sangal et al., 1995). The P300 is mostly induced in experiments using an ‘oddball paradigm’. The Oddball may contain two or more types of stimuli; one of these is the so called rare stimulus, while the others may also be referred to as the common stimulus. This latter type of stimulus is provided more frequently. The P300 is then evoked when participants attend to the rare stimuli.

Visual evoked potentials (VEPs) and auditory evoked potentials (AEPs) are two signal modalities in response to either visual or auditory stimuli and induced by activity within the visual cortex (occipital lobe) and auditory cortex (temporal lobe) (De Vlieger et al., 1981). VEP based BCIs use the users’ gaze to flashing letters or digits to provide a string for communication (Lee et al., 2008). One of the applications of AEPs in BCI systems is for detection of attention direction in response to different auditory stimuli (Ebisawa et al., 2011).

2.2.2. SENSORIMOTOR RHYTHMS

Sensorimotor rhythms (SMR) contain information within two frequency bands, alpha (7-13 Hz) and beta (13-30 Hz). The amplitude suppression and enhancement of SMR in sensory motor cortex occurs around movement onset (Derambure et al., 1999). SMRs are generated in real and imagined movements by the intent of the users (He et al., 2013). These can be obtained from both healthy individuals and patients with spinal-cord injury, amyotrophic lateral sclerosis and stroke (He et al., 2013; He et al., 2015). The main advantage of this signal modality is usability in control applications with a high degree of freedom (Royer et al., 2010; Lafleur et al., 2013). This signal modality is evoked independent of any external stimulus and can

thus be applied in several BCI applications (He et al., 2015) compared to signal modalities such as steady-state potentials or ERPs (Gao et al., 2003).

ERD is the decrement of the amplitude or power of SMRs in low frequency components of the alpha/beta band in relation to task performance (Pfurtscheller & Lopes da Silva, 1999). ERS is when the power or amplitude of SMRs is increased (Pfurtscheller & Lopes da Silva, 1999). Modulation of SMRs in the beta and alpha band can be used to obtain information about planning and execution of different types of movements (Pfurtscheller et al., 1997).

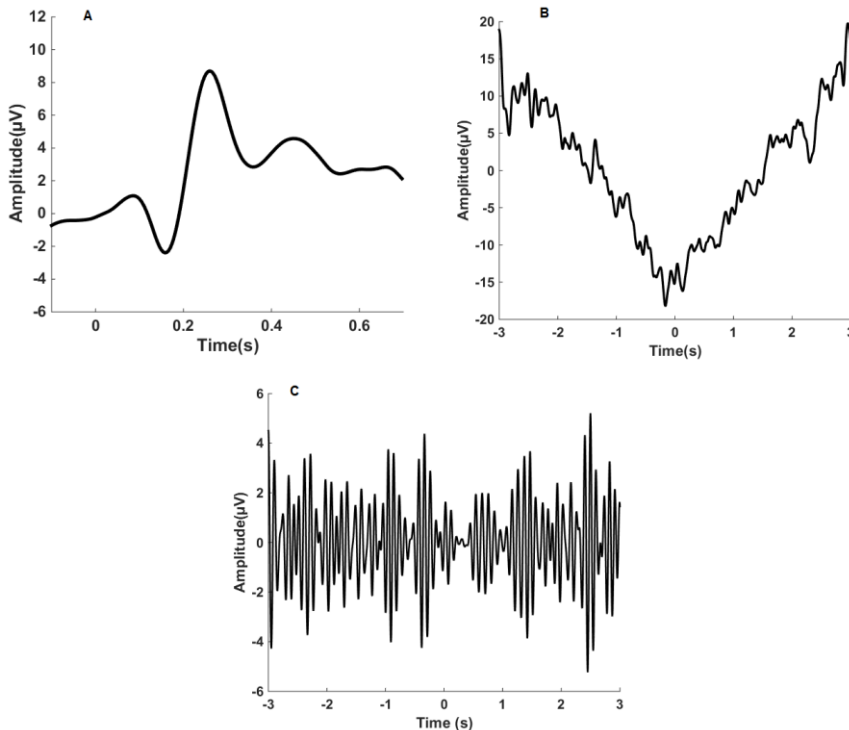


Figure 2-2 Illustration of different control signal modalities used for BCIs. (A) ERP, (B) MRCP and (C) SMR.

2.2.3. SLOW CORTICAL POTENTIALS

The slow cortical potential (SCP) is a voltage positive or negative drift in the EEG signal. A negative drift shows enhancement in brain activity while a positive shift represents a decrement in cortical excitability. These signals can be generated by healthy and paralyzed patients and used as the control signal within a BCI (Birbaumer et al., 1990; Kübler et al., 1999).

The movement related cortical potential (MRCP) is one type of SCPs that appears approximately 2 s prior to movement onset for both real or imaginary movements (Shibasaki et al., 1978). The MRCP provides information about either cue-based or self-paced movement preparation/execution (Jankelowitz & Colebatch, 2002; Walter et al., 1964). In the standard cue-based paradigm, two stimuli, a warning (S1) and an execution (S2) stimulus are used to indicate to the user when to prepare and commence the movement. The negative drift observed in the EEG signal occurs between S1 and S2 with the peak negativity around the time of S2. This is often referred to as the Contingent Negative Variation (CNV) (Walter et al., 1964). In self-paced (voluntary) movements, the MRCP commences approximately 2s before movement onset and has a peak negativity at the time of movement onset. It is also termed the 'Bereitschaftspotential' (Hallett, 1994). Temporal or spectral features obtained from the MRCP can be used to classify movement types such as hand/foot movement, movement properties like force level and the users' mental state like attention or learning (Dirnberger et al., 2000; Jochumsen et al., 2013; Jochumsen et al., 2016).

2.2.3.1. Signal processing of SCPs

The SCP represents the lowest frequency component of the EEG signal, very close to the DC offset in EEG recording devices. To obtain any type of SCP, it is essential to use a band-pass filter on raw EEG signals before any further processing. The range of this filter is mainly defined between [0.05 5] Hz (Birbaumer et al., 1990). Low signal to noise ratio (SNR) of SCP signals can be improved by using weighted average spatial filters. Based on the comparison among four common spatial filters, the large Laplacian spatial filters (LLSF), common average reference (CAR), common spatial pattern (CSP) and optimize spatial filters (OSF), LLSF had the best accuracy for detection of real, imagined and attempted movement intention (~80%) (Jochumsen et al., 2015). Laplacian filters have also been used in previous studies to increase the SNR level (McFarland et al., 1997; Mrachacz-Kersting et al., 2012; Niazi et al., 2011).

MRCP signals can be used for detection of movement intention. In the template matching technique, movement onset is found by the correlation of continues EEG signals with an extracted template from the initial negative part of MRCPs. Self-paced movements have been detected with an average accuracy of 80% and latency of 100 ms before the task onset (Lew et al., 2012; Niazi et al., 2011). In a recent method proposed by Xu et al. (2014), a wider range of EEG signals corresponding to the movement onset are projected into a lower dimension space by locality preserving projection (LPP) method followed by Linear Discriminant Analysis (LDA). The accuracy of this method in online applications was around 80% with a delay of 300 ms after the movement onset (Xu et al., 2014).

MRCP signals can be classified with regards to the types of movements or movement characteristic such as force level with two common types of LDA and Support Vector Machine (SVM) classifiers (Jochumsen et al., 2015). Although the performance of SMV can be enhanced by selecting various kernels, it is not easy to define the appropriate kernel (Gokcen & Peng, 2002). In addition, classification of the feature extracted using the LDA method was superior to Independent Component Analysis (ICA) and Principle Component Analysis (PCA) techniques (Subasi & Gursoy, 2010). The average accuracy obtained from the LDA method in classification of different rest conditions was around 99% while it was lower in the other types of classifiers (Subasi & Gursoy, 2010).

2.3. BRAIN COMPUTER INTERFACES FOR STROKE REHABILITATION

Daly (Daly et al., 2009) was the first to suggest that BCIs may be used for stroke rehabilitation. In her seminal study, she showed that by modulating the brain signal power in a selected frequency band from pre-selected electrode locations, during cue based index finger movements, the patient was able to trigger an functional electrical stimulation (FES) device. This induced the artificial activation of the index finger extensors. Following nine sessions, the patient recovered some of the ability to produce isolated finger extension.

Since that time, numerous clinical studies have demonstrated that BCIs may be used in stroke rehabilitation to improve upper limb and hand function (Ang et al., 2010; Broetz et al., 2010; Daly et al., 2009; M. Li et al., 2014; Shindo et al., 2011). The control signals used in these has been the modulation of the sensory-motor rhythm and the feedback provided has been either proprioceptive/haptic (Ang et al., 2009; Ang et al., 2010; Broetz et al., 2010; Buch et al., 2008; Caria et al., 2011; Ono et al., 2014; Ramos-Murguialday et al., 2013; Shindo et al., 2011), FES (Young et al., 2014) or visual (Pichiorri et al., 2015; Prasad et al., 2010). To date only two studies have used BCIs to target lower limb function (Takahashi et al., 2012) combined modulation of the sensory-motor rhythm with feedback provided by FES and Mrachacz-Kersting et al. (2016) used the MRCP to provide proprioceptive feedback via a single electrical stimulus to the target nerve.

Aside from the last study where only three short BCI sessions led to significant functional improvements in chronic stroke patients, all previous studies required numerous training sessions to induce a significant effect. This may be directly related to the associative nature of the BCI used in Mrachacz-Kersting et al (2016).

2.3.1. A NOVEL ASSOCIATIVE BCI FOR STROKE REHABILITATION

As has been suggested in the section on plasticity, one of the prime mechanisms for plasticity induction requires the precise timing between two inputs to the post-

synaptic neuron. The associative BCI developed by Mrachacz-Kersting et al. (2012) combines precisely in time, the endogenous activation of the motor cortex with an afferent signal produced artificially by an electrical stimulation of the peripheral nerve that innervates the target muscle. In the first phase of this BCI, the patient is asked to attempt to perform a ballistic dorsiflexion task timed to a cue for 30-50 repetitions, as continuous EEG activity is monitored. This motor task produces a MRCP, the peak negative phase of which indicates the activation of the motor cortex. In the subsequent intervention phase, the patient again performs the motor task while the electrical stimulus is applied so that the induced afferent signal arrives precisely at the time of the peak negative phase of the MRCP. Chronic stroke patients exposed to this intervention that lasts approximately 10 minutes, over three consecutive sessions showed significant functional improvements (e.g., they were able to walk faster and exhibited a higher foot tapping frequency) (Mrachacz-Kersting, 2016).

One disadvantage of this associative BCI is that the EEG signals are not monitored in real-time during the intervention phase. Thus, the time of the peak negativity is extracted from a training set established in the first phase. If this associative BCI is to be applied successfully in the acute/subacute phase of stroke, where patients tire more easily and have a decreased ability to concentrate on the task for prolonged periods of time, it is necessary to monitor their level of attention. Attention is known to significantly affect plasticity induction even in PAS protocols where the pre and post-synaptic neurons are activated artificially (Stefan et al., 2004).

CHAPTER 3. ATTENTION

Attention is a cognitive task that allocates processing resources to a particular sensory stimulus, memory, thoughts or any other mental task (Esghaei & Daliri, 2014; Treder et al., 2014). Attention can be based on external sensory stimuli such as sounds, images or smells (exogenous attention) or based on internal events such as memories or thoughts (endogenous attention). In the nineteenth century the psychologist William James claimed that (James, 1891):

“Everyone knows what attention is. It is the taking possession of the mind, in clear and vivid form, of one out of what seem several simultaneously possible objects or trains of thoughts. Focalization, concentration, of consciousness are of its essence. It implies withdrawal from some things in order to deal effectively with others.”

The amount of attention to a particular task plays a key role in task behavior such as reaction time or accuracy of movement detection. Different allocation of processing resources to various tasks based on the level of attention is the main reason for variations in the execution of tasks (Purves, 2008).

3.1. ATTENTION TYPES

As illustrated in figure 3-1, attention may be divided into four main categories. Sustained attention is defined as the ability to focus on a specific task for a prolonged period of time in the absence of any distractor. Examples include reading a book or playing a video game. Training of sustained attention such as meditation improves attentional processing and reduces reaction time to the target stimuli (Lutz et al., 2009).

Alternative attention is an indicator of mental flexibility. An example is reading a recipe (learning task) and performing the task based on the recipe (execution task). It refers to the ability to move the attention concentration between two tasks with different cognitive demands. An impairment in alternative attention is correlated to increased mental fatigue (Kawatani et al., 2011; Mizuno et al., 2011).

Selective attention is the ability to select desired stimuli/tasks among various stimuli in the surrounding environment. Attending to a particular voice in a noisy room is one example of selective attention (cocktail party effect). Selection of the target signal among different signals decreases the reaction time and improves the task judgment because of the enhancement in prediction of time or place of that target stimulus (Spence & Driver, 1997; Spence et al., 2001).

The last type of attention is divided attention which refers to the ability to perform two or more tasks concurrently, so attention is split among these tasks. Dual-task

conditions are examples of divided attention where attentional resources and processing information are allocated differently between the tasks (Shapiro et al., 2006). These involve functional costs such as increments in the reaction time in comparison to performing only one task (Han & Marois, 2013).

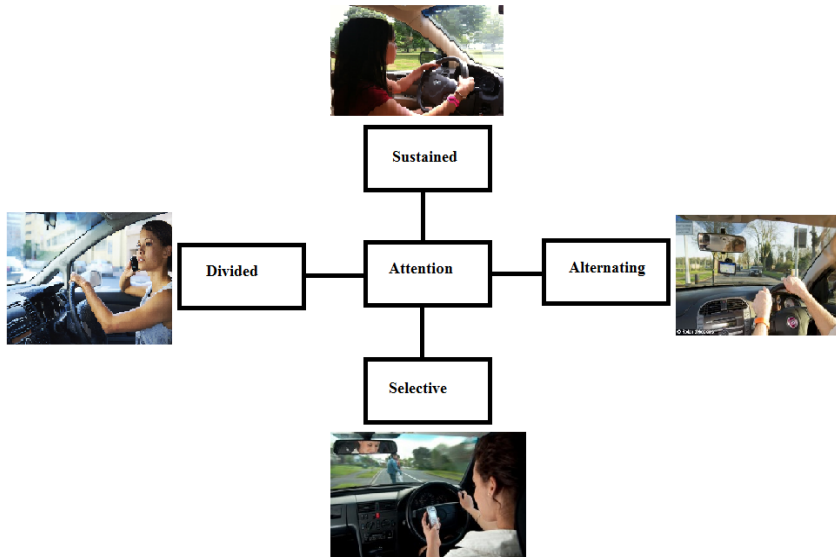


Figure 3-1 Four main types of attention, sustained, alternating, selective and divided attention. Driving is a good example to show various types of attention. When the majority of our focus is used for driving, sustained attention is used while considering the other tasks such as talking on the phone at the same time as driving divides the attention between these two (or more) tasks. Checking the car mirrors is an example of alternative attention. Selective attention allows deciding for attention allocation to the driving or the other tasks such as phones or the environment of the road.

3.1.1. ATTENTION PROCESSING IN THE BRAIN

Psychologists believe that there are two different levels for information processing under attention effect (see details in figure 3-2). In the first model referred to as 'early selection', only the target stimulus is selected based on its properties and sent for further analysis. However, in the 'late selection' model, the target stimulus is selected after pre-processing and thus requires a greater amount of working memory.

In the 'early selection' model, defined by Donald Broadbent in 1958 (Broadbent, 1958), incoming information can be selected after some basic processing based on some physical features such as color, pitch, loudness and direction. However, according to this model, participants cannot remember unattended stimuli.

In 1963, Deutsch and Deutsch (Deutsch & Deutsch, 1963) proposed the ‘late selection’ model where all incoming stimuli are processed according to their semantic properties. The attention influence occurs prior to working memory. This theory seems inappropriate since all information has to be analyzed prior to selection of attention to the relevant stimuli.

In 1980, Anne Treisman (Treisman & Gelade, 1980) provided the ‘middle selection’ model where all stimuli are processed initially and in the following step (the attention stage), individual features are combined to make a final response. Participants can remember all stimuli but the level of information they recall is depended on the level of attention to that stimulus. This theory is often referred to as the ‘attenuation theory’.

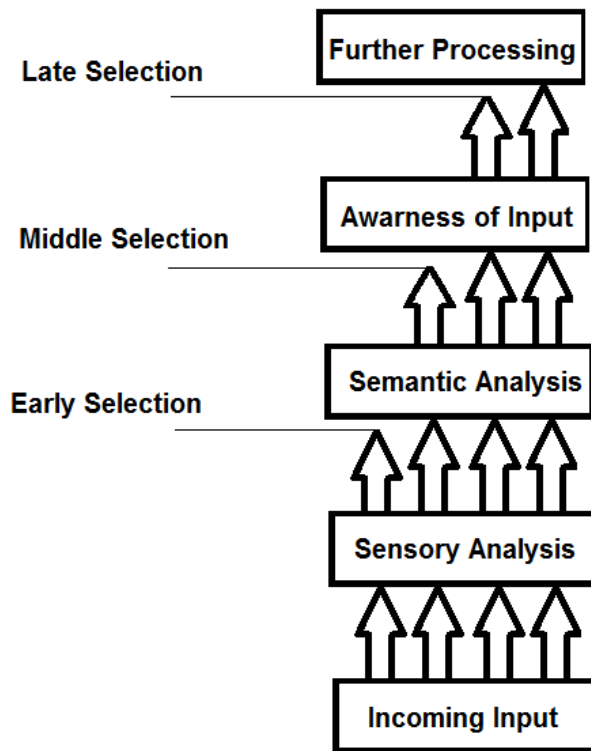


Figure 3-2 Early, middle and late stage selection of the incoming stimuli by attention direction. The early stage is just after the processing of sensory information, the middle stage follows the semantic analysis and the late stage selection is based on the awareness of the new data.

3.2. ATTENTION DISTRACTORS

Distraction is a process to divert attention from the desired (attended) goal by an interference which can have external or internal sources. External factors include distractors from the surrounding environment such as auditory and visual variations in the environment. Internal distractors include feelings and thoughts such as fear, anger, fatigue and boredom.

Any kind of distraction causes some costs for the attended task (Paul et al., 2016) mainly for movement preparation and detection of movement intention. Thus, it is vital to detect and compensate any attention drifts from a main task.

3.2.1. DUAL TASKING

Dual tasking refers to the execution of two tasks simultaneously when attention is divided between these tasks to control the performance of both tasks simultaneously (Newman et al., 2007; Vaportzis et al., 2014). Attention allocation to each task (prioritization) is obtained by a tradeoff between each task expense (cost) described by the performance operating characteristics curve (Gopher & Navon, 1980; Jansen et al., 2016; Norman, 1976). An increment in performance of one task corresponds to a decrement in the other task execution as illustrated in figure 3-3. Thus, a tradeoff is required between two tasks to accomplish the appropriate performance accuracy for each task. In the same condition of multi-tasking, task preference can be different among different people. For example, two police officers within the same environment will be exposed to the same distractors but have different tasks to perform. They will thus allocate different priorities to the same distractors to be able to execute their respective tasks. The first police officer has to drive the car and will thus have more focus on the road conditions and the act of driving. The second officer is the passenger and may thus focus on the messages from the radio such as eventual crimes and dangers (Jansen et al., 2013). In dual-tasking one of the tasks plays the role of interference (secondary task) for the other task (main task) and degrades the performance of the main task in comparison to single-task conditions.

To measure the dual-tasking cost, increments in response time and error rate of task execution may be quantified (Cecotti et al., 2011). In dual-task conditions, the cortical sites corresponding to each task are activated (Salo et al., 2013) without significant expansion to other cortical sites. However, the competition between task-specific resources degrades the performance of both tasks as compared to only performing a single-task (Bunge et al., 2000; Nijboer et al., 2014). This explanation is based on rapid switching between simultaneous tasks for information analysis (Salvucci & Taatgen, 2008). For instance, if a motor task execution (walking) is contaminated with a cognitive task (counting), the cost will increase because the motor task preparation is reduced as attention is divided between two concurrent

tasks and thus the level of task processing deteriorates compared to single task conditions (Halvorson, 2013; Kodesh & Kizony, 2014; Strobach et al., 2012).

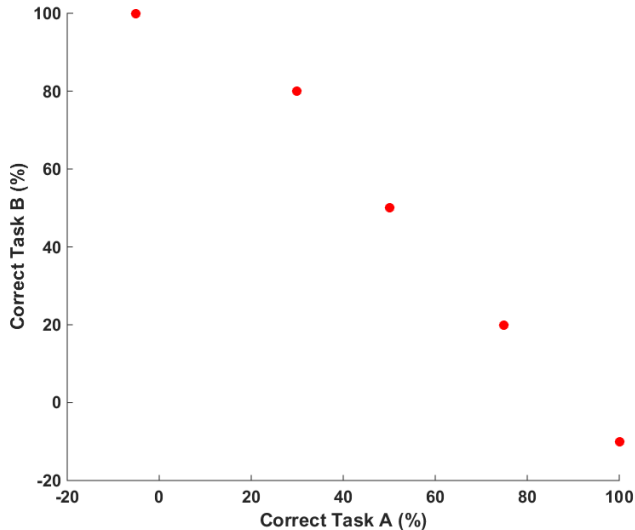


Figure 3-3 Sample of an operating characteristic curve. It displays the tradeoff between task expenses. If accuracy of one task is increased, the other task accuracy will be reduced.

This is a particular problem in the elderly population, where walking while talking at the same time may increase the possibility of falling (Beauchet et al., 2009). Thus, in addition to the resource competition, aging increases the reaction time and error rates for dual-tasks as compared to single-tasks (Asai et al., 2013; Tsang et al., 2013). Although it is possible to improve elderly dual-task performance by increasing their skills through practice of specific dual-tasks (Allen et al., 2002; Allen et al., 2009). Here, the compatibility between tasks plays a key role in improving performance (Grabbe & Allen, 2012). If the two tasks require similar responses (e.g. pressing the same button) but use different stimuli to cue the task, performance is enhanced. Interestingly, if the stimuli are compatible, (have the same color or shape) but the response required for each task differs (e.g. pressing one button (task one) versus pressing a different button (task 2)), performance is decreased (Grabbe & Allen, 2012). In general, incompatibility between two tasks both in terms of the required response or the stimuli that trigger the response decreases performance of the task(s).

Patients that have suffered a stroke are generally within the elderly age range and as outlined above, will likely have a decreased ability to perform dual tasks. In

addition, stroke patients, specifically in the acute and subacute phase, will experience fatigue more rapidly than age matched controls thus affecting their ability to attend to the rehabilitation task. In an effort to compensate for this, a BCI for neurorehabilitation should be designed to monitor attention in real time. In this vision of a BCI, attention shifts detected on a single trial basis may be used to alert the therapist (or indeed the patient) who may then take the appropriate steps to focus the attention of the patient back on the main task. This may be as simple as closing the door to the therapy room if outside distractors increase during a session, or providing verbal feedback to the patient. In the extreme case, the session may be stopped prematurely to avoid a bad BCI training session. Thus signal processing algorithms need to be developed to monitor attention level to the target task.

CHAPTER 4. AIMS AND HYPOTHESES

The overall objective of this thesis was to investigate the effects of attention on the control signal, the MRCP, of an associative BCI designed for neurorehabilitation of stroke patients. Attention was artificially modulated using either an auditory or visual oddball task or a combination of these two. The main task was comprised of a simple ballistic dorsiflexion movement of the dominant foot that generated the MRCP. The main focus of this work was on signal processing to establish if it is possible to separate the feature space of normal attention and diverted attention conditions. There were three major aims of this Ph.D. project:

1. To investigate the effect of attention variations on the movement preparation phase of the MRCP generated during motor task execution – in the established associative BCI this is the phase for detection.
2. To localize which areas of the brain are affected by attention alterations by quantifying MRCP features extracted from different channel locations during motor task execution.
3. To classify normal and diverted attention levels using temporal and spectral features extracted from EEG signals both offline and online during motor task execution.

Five studies were performed to fulfill these aims:

Study I:

The primary aim of Study I was to establish an appropriate cue based paradigm for early and accurate detection of the MRCP generated by an imaginary motor task. Two different visual paradigms, one where the participant had prior knowledge of the motor task to be performed (non-random paradigm) and one where this information was presented only at the time when the movement had to be executed (random paradigm) were investigated. A semi-random paradigm was implemented to investigate if the time phase (preparation or execution phase) where knowledge on the type of task to be performed, had an influence on detection latency and accuracy of the MRCP. It was hypothesized that the cue that provides prior information about the type of motor imagery task would result in earlier detection latency and a higher detection of the MRCP. The cue with the highest accuracy and shortest detection latency was selected for all subsequent studies.

Study II:

The primary aim of Study II was to quantify the effect of attention variations using an auditory oddball task on extracted MRCP parameters. Further to establish which EEG channel is most affected. The optimal cue-based paradigm selected in Study I, was used by healthy participants and stroke patients to perform cue-based motor

movement executions. Two conditions were examined, cue-based motor movement executions with an auditory oddball task imposed between two sets of 30 trials (experimental group) or a rest time of the same duration (control group). It was hypothesized that the MRCP parameters would be significantly affected only in the experimental group.

Study III:

The major aim of Study III was to investigate the effect of divided attention on MRCP parameters and main task performance. Participants were asked to perform two concurrent tasks (dual-tasking). The main task was cue-based motor movement executions and the secondary task was an auditory oddball task with two levels of complexity. It was hypothesized that MRCP parameters will be significantly affected in dual task conditions and that this will be further enhanced with increases in the dual task complexity.

Study IV:

The aim of Study IV was to classify different attention conditions using time and time-frequency features. The data of Study III was used to extract features from channels located in frontal, fronto-central and central cortex. It was hypothesized that the feature distributions for the two attentional levels can be distinguished

Study V:

The aim of this study was to classify different attention levels while executing self-paced movements. Three modalities of the oddball task (auditory, visual and audiovisual) were used to influence attention levels during movement execution in healthy participants. For each modality, the performance of the classifier was compared with regards to the type of the feature (temporal, spectral and tempo-spectral) and different channel locations. It was hypothesized that tempo-spectral features in movement-related channels will have the highest classification accuracy.

CHAPTER 5. METHODS

5.1. PARTICIPANTS

Table 4-1 presents the number and mean age of the participants that took part in each study. Healthy participants were without any neurological disease and hearing or visual abnormality. Stroke patients were also without any hearing or visual problems. Inclusion criteria encompassed patients aged over 18 years having suffered from superior division middle cerebral artery (MCA) stroke in a period 3-24 months before the recruitment in the study; able to follow commands (no or limited cognitive impairment). Patients were excluded if they also presented with concomitant neurological or other severe medical problems, seizure history, cognitive impairments, treatment with drugs that act on central nervous system, complete paralysis of legs, cardiovascular or respiratory symptoms contraindicative of walking, contraindications to magnetic resonance imaging (MRI), cardiovascular or respiratory symptoms contraindicative of walking and any other significant non-stroke-related impairment affecting walking.

In Study II and III, healthy participants were divided into two groups with an equal number of subjects since the type of distractor was different between groups. In Study V, they were divided into three groups with the same number of participants.

Table 5-1 Number, gender, mean age and health conditions of the participants for all five studies.

	Number of population	Type	Age	Females	Males
Study I	8	Healthy	28.2±4.2	2	6
Study II	20	Healthy	24.33± 8.7	8	12
Study II	12	Stroke	57.4±10.1	2	10
Study III	24	Healthy	23.87±3.5	12	12
Study IV	12	Healthy	23.87±3.5	6	6
Study V	27	Healthy	27.1±3.4	13	14

5.2. EXPERIMENTAL SETUP

EEG signals were recorded using an active EEG electrode system (g. GAMMAcap², Austria) and g.USBamp amplifier (gTec, GmbH, Austria). The number and placement of EEG channels analyzed in each study are indicated in table 4-2. In all studies, the ground and reference electrode were placed on FP_z and the right ear lobe respectively. In addition, two electromyography (EMG) channels were placed on the tibialis anterior (TA) muscle to control real movement onset by the participants in Study II-V. All signals were sampled at a frequency of 256 Hz with 16 bits accuracy.

Table 5-2 Number and placement of EEG channels in five studies. Channel location was based on International 10-20 system.

	Number of Channels	Channel Placement
Study I	28	F5, F3, F1, Fz, F2, FC5, FC3, FC1, FCz, FC2, FC4, C5, C3, C1, Cz, C2, C4, CP5, CP3, CP1, CPz, CP2, CP4, P5, P3, P1, Pz, P2
Study II	9	Fz,FC1,FC2,C3,Cz,C4,CP2,CP1,Pz
Study III	18	AF3, AFz, AF4, F3, F1, Fz, F2, F4, FC3, FC1, FCz, FC2, FC4, C3, C1, Cz, C2, C4
Study IV	18	AF3, AFz, AF4, F3, F1, Fz, F2, F4, FC3, FC1, FCz, FC2, FC4, C3, C1, Cz, C2, C4
Study V	28	AF3, AFz, AF4, F3, F1, Fz, F2, F4, FC3, FC1, FCz, FC2, FC4, C3, C1, Cz, C2, C4, CP3, CP1, CPz, CP2, CP4, P3, P1, Pz, P2,P4

5.3. EXPERIMENTAL PARADIGMS AND TASKS

5.3.1. VISUAL PARADIGMS

In all studies, participants were asked to sit on a comfortable chair placed one meter away from a digital screen with the ankle and knee joint at approximately neutral and 120° respectively. Visual paradigms were shown on the screen while auditory stimuli were played via a conventional headphone.

In Study I, three different visual stimuli were used to cue participants to commence movement imagery. The main difference between paradigms relates to the amount of prior information as to the type of the movement to be imagined. In the non-random paradigm, five time slots of focus, preparation, execution, hold and rest phase were shown (Figure 4-1b). After 2-3 s of focus time, a visual schematic appeared on the screen while a cursor moved along a ramp. Participants were asked to imagine the pre-defined movement when the cursor reached the upward turn and to hold this for 2s during the hold phase. 3-5 s of rest time were imposed between two consecutive trials. Each experimental block included 60 trials where the participant had to perform the exact same motor imagery (ballistic dorsiflexion or ballistic right wrist extension). Block order was randomized between participants.

The random paradigm included four main phases of preparation, execution, hold and rest phase (Figure 4-1a). After 2 s of the preparation phase with a cross sign on the screen, an arrow with a random direction was shown to indicate the type of the imagination: ballistic right wrist extension (right arrow), ballistic left wrist extension (left arrow) and ballistic dorsiflexion (downward pointing arrow). The arrow disappeared after 1.25 s however participants had to continue their imagination for 3 s until the end of the hold phase. A rest time of 3-5 s was imposed between movement trials. Each experimental block consisted of 60 trials with the same probability of all three types of movements (20 trials for each movement type). So, three blocks with 60 trials were performed for a total of 60 trials for each movement type.

A control experiment consisted of using a semi-random paradigm. The only difference between the semi-random and non-random paradigm was that each block could contain two types of motor imagery. Thus, in this control experiment, a text appeared during the preparation phase that indicated the type of the imagined movement the participant had to perform in that trial when the cursor reached the upward turning ramp Figure 4-1c). The text was ‘Foot’ indicating ballistic dorsiflexion, ‘Right Hand’ for ballistic right wrist extension and ‘Left Hand’ for ballistic left wrist extension.

In Study II-IV, the non-random visual paradigm was used to indicate to the participants to perform a ballistic ankle dorsiflexion movement.

5.3.2. ODDBALL PARADIGMS

Three different types of oddballs paradigms were used in the various studies of this thesis to artificially alter the attention of the participants. These could be either auditory, visual or a mix of these two.

Two tone oddball paradigm: In the simple auditory oddball paradigm, a 500 Hz tone with a probability of 80% (low pitch) was randomized with a 1200 Hz tone (middle

pitch) with a probability of 20%. All auditory stimuli had the same loudness of 75 dB with duration of 200 ms and a randomized inter-stimulus interval (ISI) of 1.5-2.5 sec.

Three tone oddball paradigm: In the complex auditory oddball paradigm, an additional 1900 Hz tone (high pitch) was added to the previous low and middle pitches. In this case the probability of low, middle and high pitch was 60%, 20% and 20% respectively with the same loudness, duration and ISI as the simple auditory oddball.

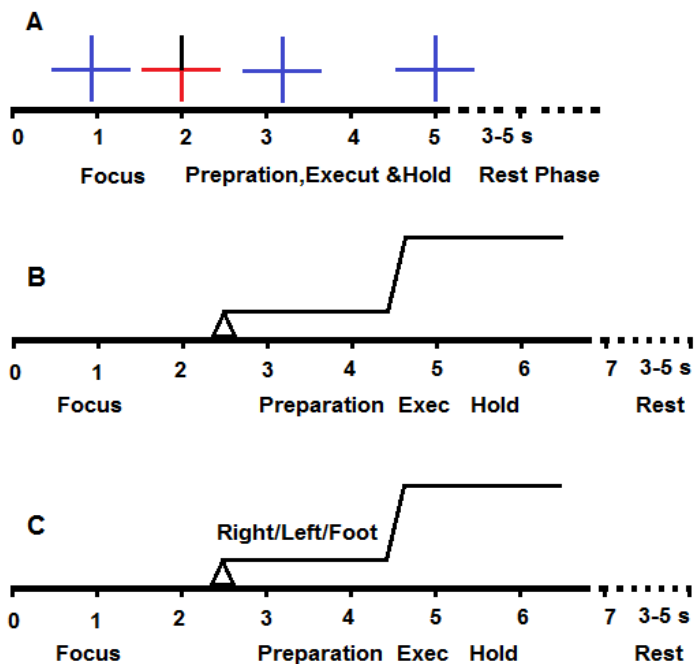


Figure 5-1 Illustration of three types of visual paradigms. (A) A random paradigm composed of five main phases where the preparation and execution phase are not separated (B) Non-random paradigm composed of five separated parts including focus, preparation, execution, hold and rest phases and (C) Semi-random paradigm with five separated sections and a non-specific movement cue until the preparation phase.

Visual oddball paradigm: This contained three different Gabor masks with various orientations (90°, 60°, 30°). The probability of the 90° Gabor was 50% while that of the two others was 25% each. The ISI was randomized between 1-2 sec.

Mixed Oddball paradigm: This encompassed two types of visual and auditory stimuli. Two Gabor masks with an orientation of 30° and 60° with the probability of 25% each (visual oddball) and middle and high pitch tone (1200 and 1900 Hz) with a probability of 25% for each tone (auditory oddball).

5.3.3. ODDBALL TASKS

Participants were asked to do a cognitive task with regards to the oddball paradigms (considered the secondary task), to ensure their performance of attending to the oddball task was maintained while they performed the main task. In Study II, they were asked to press a button with their right index finger if the target tone (middle pitch) was played. In Study III, the auditory oddball paradigm contained three different tones while the oddball task differed between the two groups of participants. Participants in one group were asked to count the number of one of the three tones played during the experiment. The task of the other group that was the same in Study IV and V, was to count the number of a special sequence of tones. The target sequence could be the number of times that the middle pitch played after the low pitch, or the high pitch played after the low pitch or the low pitch was heard after the low pitch.

Visual and mixed oddball paradigms were only used in Study V. Participants working with the visual oddball only had to count the number of a target sequence that could be either Gabor 60° appearing immediately after Gabor 90° or Gabor 30° appearing immediately after Gabor 90°. Those participants exposed to the mixed oddball had to count the number of one of the target sequences that could be either Gabor 30° shown after the occurrence of the middle pitch or the high pitch played after Gabor 60°.

5.3.4. COMBINATION OF VISUAL AND ODDBALL TASKS

In Study II-V, two tasks had to be completed by the participants, where one consisted of a motor movement (ballistic ankle dorsiflexion) performed either to the non-random cue (Study II-IV) or at a self-paced mode (Study V). In addition, oddball tasks were applied to artificially alter the users' attention level. In all cases, there was one common level with two or three blocks of dorsiflexion called 'Control condition', 'Control level' or 'Control task'. The control condition in Study II and III contained 90 trials of cue-based dorsiflexion divided into three blocks with 30 trials in each. Movement blocks were separated with a minimum of four minutes rest time. In Study III and IV, the auditory oddball was also played during this control condition but the subjects were asked to ignore this by only concentrating on the dorsiflexion task. However, two blocks each with 30 trials of self-paced dorsiflexion were performed by the participants.

The other level of these studies was the diverted attention level. In Study II, each healthy subject had to complete a low attention condition or a high attention condition as described below:

Low attention condition: Participants had to execute 90 trials of dorsiflexion in three sets of 30 trials. In-between each set, the two tone auditory oddball task was played.

High attention condition: Participants had to execute 90 trials of dorsiflexion in three sets of 30 trials. In-between each set, the three tone auditory oddball task was played.

Stroke patients had to only perform the control and high attention condition and 60 trials of dorsiflexion divided into two sets.

In the attention level of Study III, the visual and auditory oddball tasks were combined in three sets, each containing 30 trials of dorsiflexion. The oddball tasks had two levels of complexity:

Simple Secondary Task (SST): In this group, subjects had to perform dorsiflexion based on the visual paradigm and simultaneously focus on the sounds heard from the headphone. They were asked to count the number of one particular tone. The tone was changed after each block to avoid habituation.

Complex Secondary Task (CST): The participants of this group were asked to perform ankle dorsiflexion timed with the visual cue and attend to the tones to count the number of defined target sequences. The sequence contained two particular tones.

The oddball task of the CST level was also applied in Study IV and V.

5.4. SIGNAL ANALYSIS

To quantify and thus control for attention to the oddball task, the amplitude of the P300 was extracted. Generally, if attention to the oddball task is low then the P300 amplitude will decrease. EEG signals were band-pass filtered in the range of 3-30 Hz and then divided into single trials in a time slot of [-0.1 0.7] s where 0 marks the onset of the auditory or visual oddball. The P300 was defined as the maximum point in the chosen time slot.

To obtain MRCP signals, continuous EEG signals were filtered with a 2nd order Butterworth filter in the frequency range of [0.05 3] Hz and movement trials were obtained in the range of [-3 3] sec with respect to the movement onset calculated from EMG signals. Trials contaminated by electrooculogram (EOG) artifacts were removed using a threshold of 120 μ V. MRCPs were obtained from channel Cz as

previous studies have demonstrated that Cz is the optimal channel for analysis and detection of simple dorsiflexion (Xu et al., 2014). In addition, the Large Laplacian filter was used to increase the SNR (McFarland et al., 1997; Niazi et al., 2011). In this method, a linear combination of surrounding channels of Cz were applied to reduce the noise level in the signal and thus increase SNR.

5.4.1. MRCP FEATURES

Nine temporal features as illustrated in figure 4-2 were extracted from single trials of the MRCP. Value and Time of peak negativity (VPN and TPN), pre-movement slopes computed with linear regression in the time ranges of: $[-2 -1]$ s, $[-1 0]$ and $[-2 0]$ s where 0 indicates TPN. In addition, the Rebound Rate (RR) was quantified in the time range of TPN to 1 sec after this point.

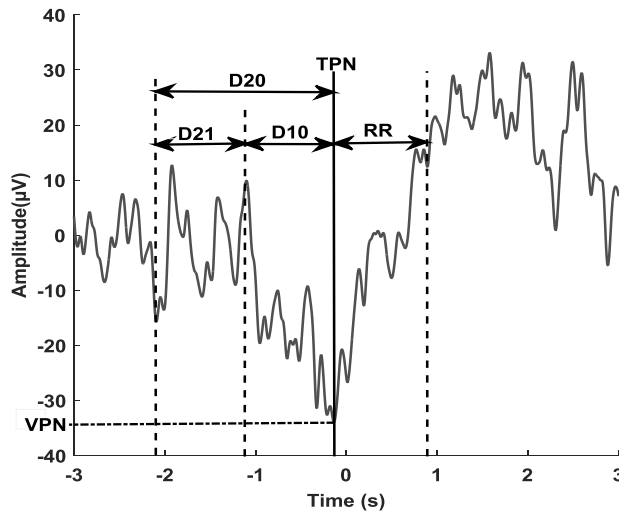


Figure 5-2 Temporal features extracted from a single trial of the MRCP. Three pre-movement time domains indicated by D20 for $[2 0]$ s prior to peak negativity, D21 corresponding to $[2 1]$ s before peak negativity and D10 for $[1 0]$ s in relation to the negative peak of the MRCP. The rebound Rate (RR) is computed in the range of $[0 1]$ s where 0 is the time of peak negativity.

Pre-movement variability was defined as the standard deviation of single trials in the same time range as for the slopes described above. The number of features was increased for the classification approaches of Study IV and V by computing slopes, variability and mean amplitudes in three additional time domains of $[-1 -0.5]$ s, $[-0.5 0]$ s and $[0 1]$ s.

Event-related spectral perturbation (ERSP) was computed by the time-frequency analysis of the MRCP signals. ERSP are the variations of the EEG power spectrum amplitude. A wavelet transformation was used with a Gaussian-windowed sinusoidal moving Morlet wavelet when the number of cycles increases linearly with the frequency. ERSP values were extracted in the time slots of [-1 -0.5], [-0.5 0] and [0 0.5] s where 0 is the movement onset, as well as in five main frequency bands of Delta (0-4 Hz), Theta (4-8 Hz), Alpha (8-13 Hz), Beta (15-30 Hz) and Gamma (30-60 Hz).

Spectral features were obtained from the Welch power spectral density within five frequency domains of Delta (0-4 Hz), Theta (4-8 Hz), Alpha (8-13 Hz), Beta (15-30 Hz) and Gamma (30-60 Hz) and four time intervals of [-2 0] s, [-2 -1] s, [-1 0] s and [0 1] s. A combination of these features named tempo-spectral features was also used for attention classification.

5.4.2. DETECTION TECHNIQUES

To detect the intention of movement execution two methods were used. The first method ‘template matching’, was only used in the first study. In the first step of this technique, the data was divided into training and test sets based on a 10-fold cross validation. A template was extracted from the initial 2 s of the training data set and then correlated with a 2 s sliding windows shifted by 100 ms in EEG trials of the test set. Movement was detected if two of the three tandem correlation results were more than a defined threshold. The threshold was selected to maximize the true positive rate (TPR, the number of true imaginary detections divided by the number of all trials), and to minimize the false positive rate (FPR, the number of false detections divided by the number of all movements). Detection latency (DL), defined as the difference between detection time to the onset of the execution cue, served as an additional criteria for detection accuracy.

In Studies II-V, movement intention was detect using the Locality preserving projection (LPP) method followed by a linear discriminant analysis (LDA). In this method as described in (Xu et al., 2014), both the signal and noise part of the EEG trials were extracted with regards to the movement onset and used as features of two classes. After projecting these features into a new feature space with lower dimension using the LPP method, a LDA classifier was applied to classify two classes of the signal. If two consecutive classification outputs showed a signal group, a movement was detected. Similar to the previous method, TPR and FPR as well as DL were considered as the detection outputs.

5.4.3. CLASSIFICATION METHOD

5.5.3.1. *Single subject classification*

Study IV and V focused on the classification of two different attention levels by using EEG features defined in section 4.5.1. For classification at a single subject level (Study IV and V) as well as for a global classification (Study IV), a ten-fold test procedure was used (Kamavuako et al., 2015). Each group of features was divided into ten-folds while nine of them were used for cross-validation and one remaining was used to test the classifier. Nine folds were used to design the best LDA classifier in the validation step and the remaining fold tested the classifier. After ten permutations, the classification accuracy was computed from the average TPR and FPR obtained from the LDA classifier. Prior to classification, the number of temporal, time-frequency and spectral features obtained from each subject were reduced by using the Principle Component Analysis (PCA) method.

5.5.3.2. *Global classification*

The aim of the second phase of Study IV was to investigate a global threshold for attention discrimination using features from all participants. Fifteen time-frequency features from all participants were combined as they showed the highest single-subject classification accuracy and then the PCA method was applied to reduce the feature space dimension. First, normality of the features was ascertained using the Shapiro-Wilk test. Then, the distribution parameters including the mean and standard deviation were computed for each feature from each separate channel to design a multivariate Gaussian distribution. Finally, a global feature distribution was evaluated by the Likelihood ratio method that classifies two groups of hypotheses of normal attention (H_0) and diverted attention level (H_1).

5.5.3.3. *Channel selection*

Study V was designed to establish the appropriate channel locations for attention classification. After establishing the best channels according to their locations within a particular brain lobe and hemisphere within each group of features for attention classification, a sequential forward selection (SFS) was applied to add more channels to increase the discrimination accuracy. This provided a combination of channels with the highest ability for attention separation.

5.4.4. STATISTICS

In Study I, Paired t-test was applied to reveal the effect of cue type (random, non-random and semi-random) on three classification performance parameters of TPR, FPR and DL. The normality of the data was ascertained by Lilliefors test ($P < 0.05$).

In Study II, the P300 amplitude was compared between two attention levels (Low attention and High attention condition) by an independent paired t-test. To investigate the influence of task repetition on the P300 amplitude, a one-way

analysis of variance (ANOVA) with the main factor of 'Block' with three levels was used. MRCP features of each group of healthy participants were compared between two attention conditions (Control- Low attention or Control- High attention) by a two-way ANOVA with the independent factors 'movement block' with three levels of first, second and third block and 'attention status' with two levels of control and shifted attention. MRCP features for the stroke group were also compared using a two-way ANOVA with the main factors of 'movement block' with two levels (first and second block) and 'attention status' with two levels (control and drifted attention).

In Study III, a two-way ANOVA was applied in each group of participants to compare the P300 amplitude and MRCP features among three 'movement blocks' (first, second and third block) and two 'task demands' (Control- SST or Control- CST). An independent t-test was also used to compare the P300 amplitude between the two dual-task conditions of the two groups of subjects (SST and CST). Normality of the features was ascertained based on the Shapiro-Wilk test ($P < 0.05$).

In Study IV, the Mann-Whitney U-test was used for comparison of classification accuracies between two groups of features (temporal and time-frequency). To determine the influence of channel locations on classification accuracy, the Kruskal-Wallis test was applied where 'channel hemisphere' with three levels of right, midline and left hemisphere and 'channel lobe' with four cases of antero-frontal, frontal, fronto-central and central lobes were the two independent factors.

Study V used a two-way ANOVA for the comparison of classification accuracy in each groups of features (temporal, spectral and tempo-spectral) where 'channel hemisphere' with three levels (right and left hemispheres and midline) and 'channel lobes' with six levels (Antero-frontal, frontal, fronto-central, central, centro-parietal and parietal lobe) were the independent factors. Accuracy was compared between three feature types based on an independent paired t-test.

Significance was set to $p \leq 0.05$.

CHAPTER 6. MAIN FINDINGS OF THE THESIS

6.1. STUDY I

Figure 5-1 illustrates the template sample for the three types of paradigms (random, non-random and semi-random). The initial negative amplitude with the random paradigm (10.1 and 9.2 μV for foot and right hand movement) is smaller compared to the non-random (17.6 and 16.8 μV for foot and right hand) and the semi-random paradigms (18.2 and 16.4 μV for foot and right hand).

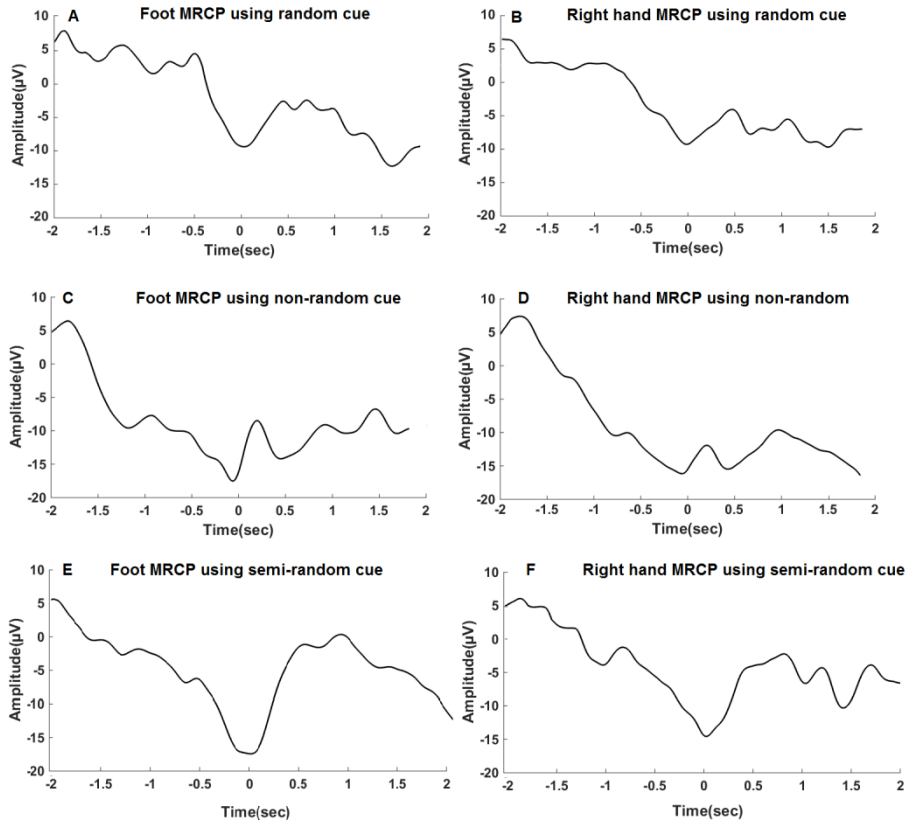


Figure 6-1 Illustration of templates obtained for each paradigm. A and B represent the template extracted by using a random cue. The amplitude of the peak negativity is -11.7 and -

10.9 μV and occurred at -12 ms and -20 ms for foot and dominant hand movement. In C and D the non-random cue was implemented and the peak negativity had an amplitude of -18.6 and -17.5 measured at -72 and -71 ms with respect to the foot and dominant hand movement. E and F illustrate the results for the semi-random paradigm, where peak negativity occurred at -12.1 and -18.4 ms for foot and dominant hand movement with an amplitude of -18.4 and -16.2 μV respectively.

Figure 5-2 shows examples of single MRCP trials and the corresponding output of the matched filter. The vertical line indicates the movement onset and the horizontal line corresponds to the threshold obtained from the receiver operating curve (ROC) curve. The detection time was computed from the intersection of the horizontal line with the output of the matched filter.

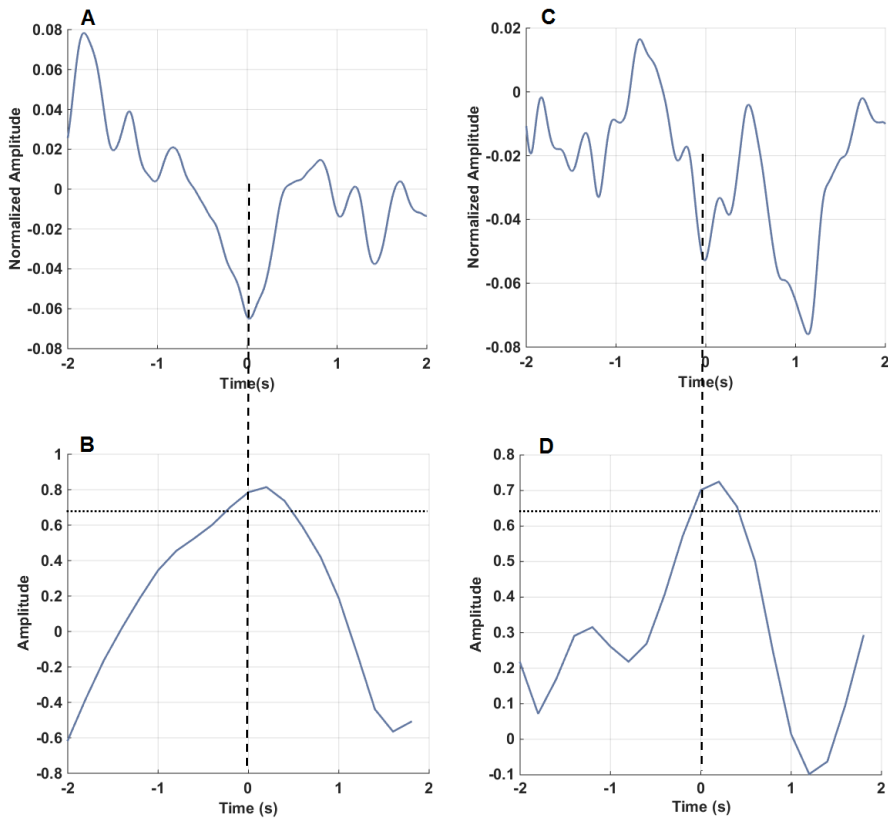


Figure 6-2 Illustration of the template matching procedure when using the non-random (A and B) and random paradigms (C and D). A and C represent one sample of single trials for the non-random and random visual paradigms while B and D are the outputs from the template matching method for the non-random and random paradigms. Vertical lines

represent the time of peak negativity and the horizontal line the selected threshold. The place of intersection between the threshold and output of the template matching indicates the estimated movement onset. In this example, movement detection occurred at 208 ms and 125 ms prior to peak negativity for the non-random and the random paradigm respectively.

Table 5-1 contains a summary of the TPR, FPR and DL of movement detection for the three types of visual paradigms. TPR of foot and right hand movement detection was significantly higher using the semi-random and non-random paradigm in comparison with the random paradigm ($p < 0.05$). DL was also significantly lower for the non-random and semi-random paradigm in comparison with the random paradigm ($p < 0.05$).

Table 6-1 TPR, FPR and DL obtained from template matching methods in the various paradigms.

Paradigm type	Movement type	TPR	FPR	DL
Random	Foot	63.5±5.9	25.5±7.6	-102.8±119.3
	Right hand	61±6.5	28.7±10.6	-112.2±104
Non-random	Foot	75.3±5.5	21.7±7.7	-198±147.3
	Right hand	70.2±6.1	19.1±9.4	-206±134.2
Semi-random	Foot	72.1±3.8	22.1±4.2	-197±118
	Right-hand	71.4±4.1	22.4±5.2	-201±104

6.2. STUDY II

The P300 amplitude induced by the complex oddball was significantly lower than the P300 obtained from the simple oddball task ($5.9 \pm 2.8 \mu\text{V}$ and $4.4 \pm 2.6 \mu\text{V}$ respectively; $F_{(1,28)}=6.1$, $P=0.02$). According to Bonferroni *post-hoc* test however, the P300 amplitude was not significantly different between the two sets of the auditory oddball task ($P > 0.05$).

6.2.1. HEALTHY GROUP

None of the MRCP features were significantly different between the two levels of control versus low attention condition or among the three sets of movement

execution. However, the two-way ANOVA demonstrated that VPN was significantly decreased in the control level compared to the high attention level ($F_{(1,42)}= 4.7, p=0.03$) and among movement sets ($F_{(2,42)}= 3.9, p= 0.03$, figure 5-3). The pre-phase variability in the range of two to one seconds prior to TPN ($F_{(2,42)}=4.3, p= 0.02$) was significantly increased based on the movement sets. The first and second set of the complex oddball task revealed significant differences (Bonferroni Post-hoc test, $p=0.02$). Table 5-2 shows the values of these parameters between the control and the attention levels and also among the three movement sets.

The two-way ANOVA revealed that DL, TPR and FPR were not changed significantly between the control and low/high attention condition but movement set had a statistical effect on these parameters as shown in table 5-2. DL was significantly different among sets for the high attention condition ($F_{(2,21)}=4.1, p=0.03$) while *post-hoc* analysis revealed that the first and second set had significantly different DL ($P=0.04$). TPR changed significantly between sets only for the high attention condition ($F_{(2,21)}=5.3, p=0.01$; $77.1\pm3.9, 67.1\pm5.1, 71.1\pm7.1$) in relation to the three movement sets where the *post-hoc* test revealed significant differences between the first and second set of movement ($p=0.01$). As for TPR and DL, FPR was also increased significantly only amongst sets in the high attention condition ($F_{(2,21)}= 5.2, p= 0.01$) and only between the first and second movement sets ($P<0.05$).

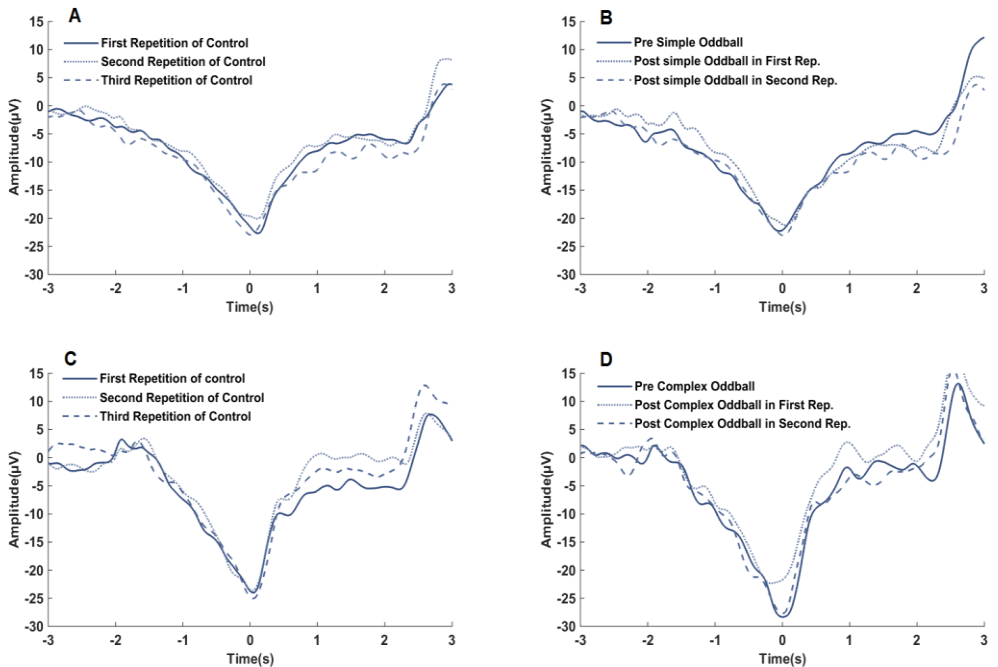


Figure 6-3 Grand average of the MRCP in the control and different diverted attention levels conditions. A shows the output of the three control blocks in the first group of healthy participants. The amplitude of the peak negativity is -23.6, -24.1 and -19.8 μV for the first, second and third blocks. B represents the MRCP for the low attention conditions. The amplitude of the peak negativity is -22.9, -24.3 and -21.1 with respect to the first, second and third movement blocks. C illustrates three MRCPs for the control level in the high attention condition group. MRCP amplitudes are -24.3, -23.9 and -25.1 μV . D shows three MRCPs during the complex oddball task. MRCP amplitudes are -28.2, -21.9 and -26.8 μV respectively.

In spite of the results obtained from the analysis of the MRCP of the single channel Cz, the Laplacian output was not changed statistically by attention variations according to the movement sets or attention levels.

6.2.2. STROKE PATIENTS

Among nine temporal features extracted from the MRCP trials, VPN, pre-movement slopes and pre-movement variability were significantly affected by attention alterations. The two-way ANOVA revealed that VPN decreased significantly between the control and high attention conditions ($F_{(1,40)} = 5.1$, $p = 0.03$) and also between the two movement sets ($F_{(1,40)} = 4.9$, $p = 0.03$). Figure 5-4a and 5-4b demonstrate that VPN in the control level was higher than in the high attention level. In addition, pre-movement slopes in the time range of two seconds prior to peak negativity up to this point were statistically different based on the attention condition ($F_{(1,40)} = 5.5$, $p = 0.02$; -11.6 ± 4.8 and -8.7 ± 3.3 for the control and attention conditions respectively) and movement sets ($F_{(1,40)} = 5$, $p = 0.03$; -11.6 ± 4.5 in first set and -8.7 ± 3.9 in the second set of the movement task). Slopes in the time slot of one second prior to movement onset up to this point were significantly different based on attention conditions ($F_{(1,40)} = 6.2$, $p = 0.02$) and movement sets ($F_{(1,40)} = 5$, $p = 0.03$). Variability in the range of two to one second prior to peak negativity was increased significantly in the control versus the high attention condition ($F_{(1,40)} = 14$, $p = 0.001$) and also from the first to the second set of movement execution ($F_{(1,40)} = 6.6$, $p = 0.01$). The values of these parameters are shown in table 5-2.

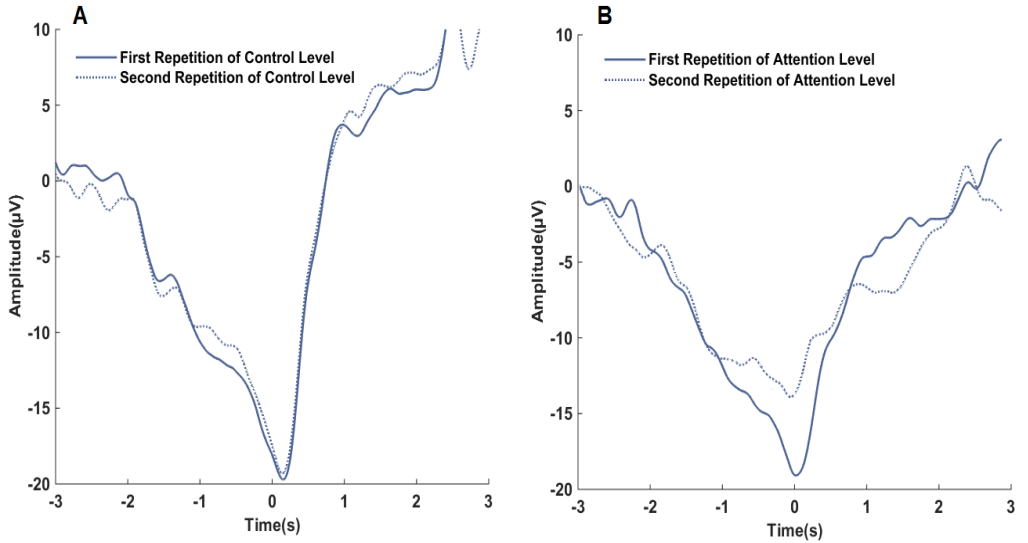


Figure 6-4 Grand average of the MRCP obtained from stroke patients. A represents the MRCP for two blocks of movement execution. The peak negativity occurred at 81 ms and 76 ms after movement onset and had an amplitude of $-19.4 \mu\text{V}$ and $-18.1 \mu\text{V}$. B illustrates the MRCP for two blocks in the diverted attention task. The time of peak negativity was 48 ms (block 1) and 54 ms (block 2) after movement onset attaining amplitudes of $18.7 \mu\text{V}$ and $-13.5 \mu\text{V}$ respectively.

DL was increased significantly in the high attention as compared to the control condition ($F_{(1,40)}=7.1$, $p=0.01$) and also in the second compared to the first set of movements ($F_{(1,40)}=12.6$, $p=0.001$). Similarly, FPR values were higher in the second movement set in comparison with the first set ($F_{(1,40)}=4.8$, $p=0.03$). TPR was also changed significantly between the control and the drifted attention level ($F_{(1,40)}=4.9$, $p=0.03$) and also among the movement blocks ($F_{(1,40)}=5.6$, $p=0.01$)

As for the healthy group, Laplacian outputs were not changed significantly under attention drifts.

Table 6-2 Value of different MRCP features in two attention levels and three movement blocks for the healthy subjects and stroke patients performing the complex oddball task.

	Control Condition	High Attention Condition	Block 1	Block 2	Block 3
Healthy	-26.3 ± 3.2	-20.6 ± 4.6	-26.4 ± 5.1	-21.6 ± 4.8	-25.8 ± 3.6

VPN	Patient	-18.8±8.7	-14.5±7.1	-19.1±7.6	-11.1±9.2	-----
	Healthy	-12.2±7.1	-11.4±7.5	-13.7±6.2	-10.1±5.4	-14.5±6
S20	Patient	-6.5±.78	-2.8±.73	-7.1±1.2	-3.8±1.6	-----
	Healthy	-14.5±5.3	-15.9±5.5	-15.5±5.7	-14.3±6.2	-14.8±4.9
S10	Patient	-6.2±5.1	-3.6±3.4	-5.9±6.3	-4±3.9	-----
	Healthy	13.5±4.3	16.9±6	12.8±5.5	18.1±6.3	13.6±5.7
Var21	Patient	15.7±7.2	20.4±8.7	16.1±6.9	21.7±7.1	-----
	Healthy	243±102.6	298±124.5	220±113.6	304±106.5	285±109.7
DL	Patient	257±112.7	357±134.1	265±184.1	382±145.8	-----
	Healthy	74±7.8	67±8.1	76±8.3	65±9.4	70±7.4
TPR	Patient	71±7.1	60±8.3	70±13	57±14.2	-----
	Healthy	17±7.4	22±8.2	10±5.8	25±5.7	27±6.9
FPR	Patient	24±8.4	29±9.2	21±9.5	31±13.4	-----

6.3. STUDY III

Figure 5-5 illustrates the visual and auditory P300 in single and dual task conditions for both the simple and the complex oddball tasks. The auditory P300 amplitude was significantly different between the two complexity conditions ($t(70) = 2, P = 0.04$) being lower for the simple auditory oddball task. The auditory P300 amplitude was also significantly increased for the control versus the CST ($F(1,48) = 4.6, P = 0.04$) and the control versus the SST ($(F(1,48) = 4.8, P = 0.04)$). The visual P300 amplitude was significantly decreased only from the control to CST level ($F(1,66) = 4.1, P = 0.04$).

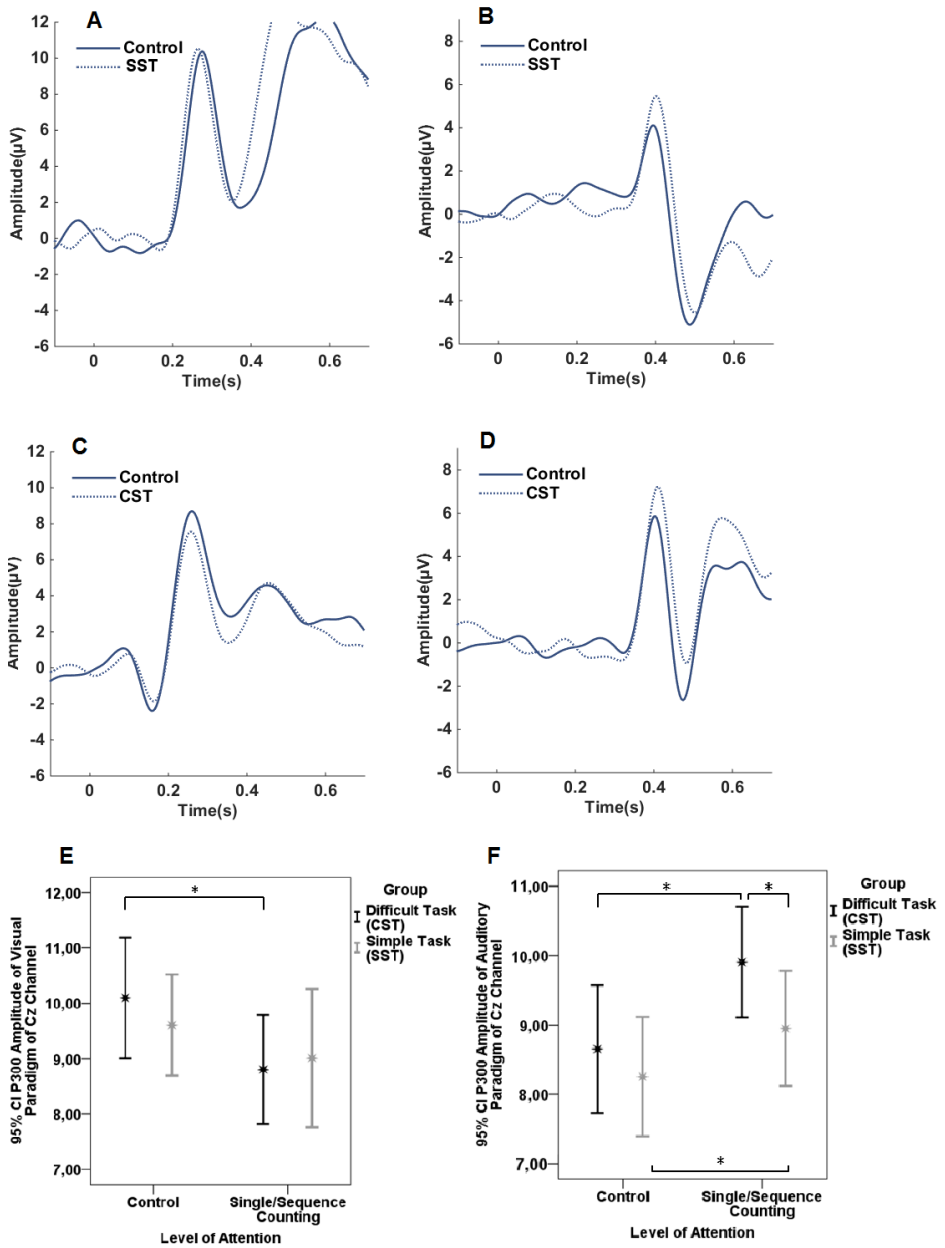


Figure 6-5 Event-related potential at channel Cz for the auditory or visual stimuli. A and C show the P300 elicited by the visual stimuli in the control-SST and control-CST group. B and D show the P300 component elicited by the auditory stimuli in both groups of task difficulty.

E and F show the P300 amplitude in two different attention conditions (control and diverted attention level (SST/CST)). Significant differences are indicated by ().*

The number of errors in counting oddball was significantly lower in the SST compared to the CST group ($F_{(1,66)}=27.6$, $P<0.01$; SST: $6.4\pm 6.8\%$, CST: 28.5 ± 24.1). The reaction time was increased from the control level to both SST ($F_{(1,66)}=4.3$, $P=0.04$; control: 198 ± 11.6 , SST: 218 ± 14.4) and CST level ($F_{(1,66)}=6$, $P=0.02$; control: 212 ± 12.6 , CST: 254 ± 16.5) while the reaction time of the CST was significantly higher compared to that for the SST group ($t(70)= 2.7$, $p=0.01$).

The two-way ANOVA indicated that the EMG correlation was not changed significantly between the control versus CST level (CST ($F_{(1,66)}= 2.4$, $P> 0.05$) or the control and SST level ($F_{(1,66)}= 0.6$, $P> 0.05$). Although, it was different between the two dual-task condition of the SST and CST ($t(35)= -5.6$, $P<0.001$).

Figure 5-6 displays the MRCP obtained from channel Cz and its surrounding channels for one subject in each group (SST and CST) and the associated control condition. The motor cortex and fronto-midline channels show greater differences during variations in task demands and thus attention alteration. The two-way ANOVA revealed a statistically significant difference between the VPN of the control and CST levels in channels FCz ($F_{(1,54)}=4.7$, $P = 0.034$), Cz ($F_{(1,54)}=4.2$, $P = 0.043$) and C4 ($F_{(1,66)}=4.3$, $P = 0.044$). This was similar for the control versus the SST level in channels FCz ($F_{(1,60)}=5.4$, $P = 0.023$), Cz ($F_{(1,60)}=4.2$, $P = 0.045$) and C2 ($F_{(1,60)}=4.6$, $P = 0.039$). The slope in the range of 2 seconds prior to TPN up to this point was significantly reduced only from control to CST level in channels FCz ($F_{(1,54)}=4.4$, $P = 0.04$), C1($F_{(1,54)}=5.1$, $P = 0.028$), Cz ($F_{(1,54)}=4.7$, $P = 0.035$) and C4 ($F_{(1,54)}=4.2$, $P = 0.043$).

Based on the statistical analysis, DL was significantly increased from control to CST level in channels Fz ($F_{(1,54)}=4.3$, $P = 0.044$), C3 ($F_{(1,54)}=4.8$, $P = 0.033$), C1($F_{(1,54)}=4.7$, $P = 0.038$), Cz ($F_{(1,54)}=4.1$, $P = 0.048$), C2 ($F_{(1,54)}=4.7$, $P = 0.033$) and CPz ($F_{(1,54)}=4.1$, $P = 0.048$). This was similar for the control versus SST level in channels C1($F_{(1,66)}=4.2$, $p = 0.046$) and C2 ($F_{(1,66)}=5.4$, $P = 0.023$). The TPR values were lower for the CST level in comparison to the control level in channels C3 ($F_{(1,66)}=5.3$, $P = 0.025$), C1 ($F_{(1,66)}=4.8$, $p = 0.034$), Cz ($F_{(1,66)}=4.8$, $P = 0.034$), C2 ($F_{(1,66)}=4.9$, $P = 0.032$) and C4 ($F_{(1,66)}=4.6$, $P = 0.038$). In the control-SST experiment, TPR was reduced statistically in channels FCz ($F_{(1,66)}=4.5$, $P = 0.038$), Cz ($F_{(1,66)}=5.1$, $P = 0.027$) and C2 ($F_{(1,66)}=4.5$, $P = 0.038$).

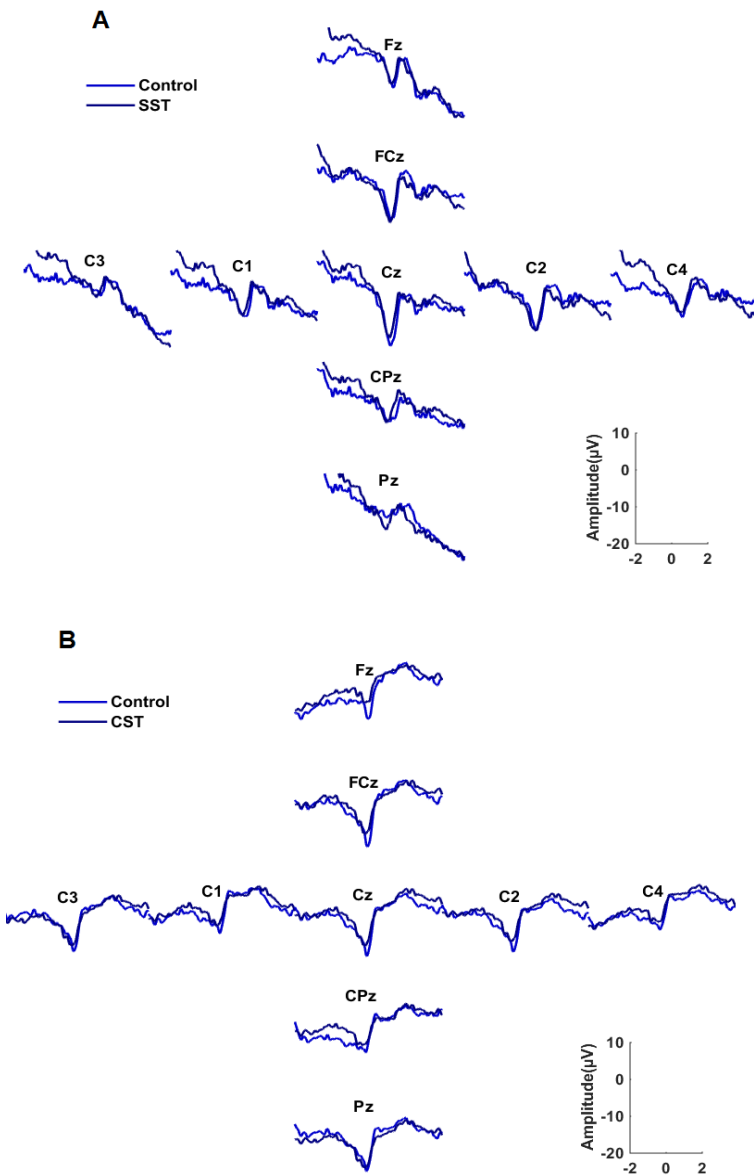


Figure 6-6 Illustration of the MRCP from one subject for each task difficulty group and nine single EEG channels. A shows the MRCPs during the single task level and the simple dual-task condition while B shows the MRCP during the single task level and the complex dual-task condition.

6.4. STUDY IV

By comparing the accuracy of two groups of features in the single-subject classification, the time-frequency features had a higher accuracy as compared to the temporal features ($U=30.7$, $p<0.001$) (figure 5-7a).

The accuracy of the two groups of features was not changed significantly based on channel hemisphere although midline and right hemisphere channels showed a higher accuracy compared to the left hemisphere channels (figure 5-7b). However, accuracy obtained from the time-frequency features was significantly different based on lobe location of EEG channels ($H(3) = 8.4$, $p = 0.04$). There was a significant difference between central and antero-frontal lobe ($P=0.03$), central and frontal lobe ($P=0.04$) and fronto-central and antero-frontal lobe ($P= 0.04$) channels. The average accuracies from different lobes are shown in figure 5-7c.

The accuracy obtained from the global classification was significantly different based on channel location as central channels showed the highest accuracy ($F_{(3,212)}= 16.2$, $p<0.001$). Post-hoc analysis demonstrated that the classification accuracy of central channels was significantly higher than antero-frontal ($p<0.001$) and frontal lobe channels ($p<0.01$).

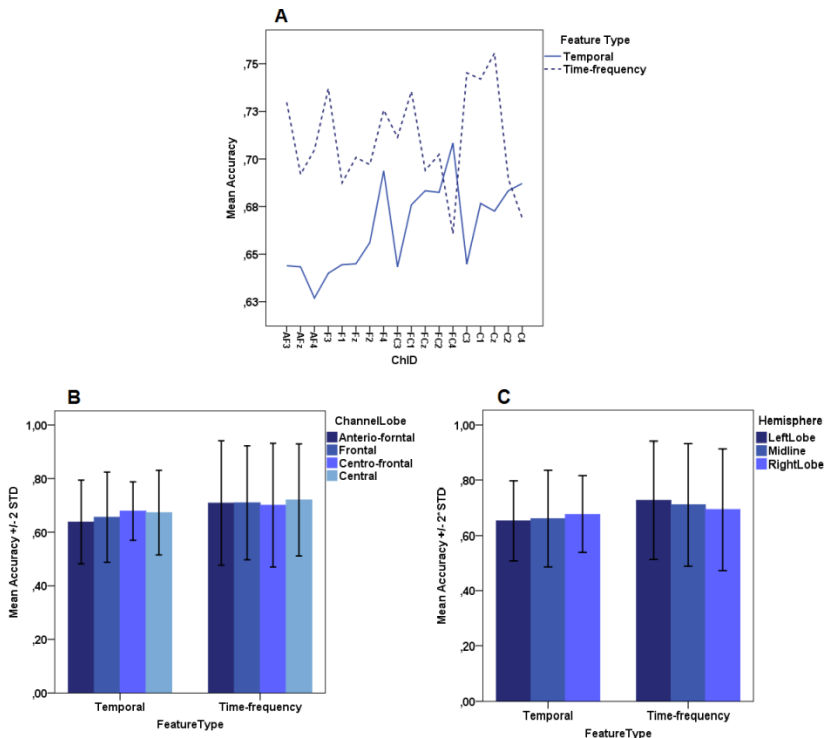


Figure 6-7 Accuracy of different channel placements by two groups of features. A time-frequency features performed better than temporal group in most of the channels. B and C illustrate classification accuracy regarding to four channel lobes and three hemispheres.

6.5. STUDY V

For the auditory attention diversion, the two-way ANOVA demonstrated that channel lobe had a significant effect on classification accuracy using temporal ($F_{(5,206)}=2.5$, $p=0.03$), spectral ($F_{(5,206)}=2.5$, $p=0.04$) and tempo-spectral ($F_{(5,206)}=2.6$, $p=0.03$) features. Although central lobe channels had the best accuracy for the temporal features, parietal lobe channels were superior for the spectral and tempo-spectral features (table 5-3). Among the three groups of features, tempo-spectral and spectral features had significantly higher accuracies compared to temporal features (spectral features: $t_{(223)}=-10.8$, $p<0.001$; tempo-spectral: $t_{(223)}=-16$, $p<0.001$). Tempo-spectral features had a significantly better detection accuracy than spectral features ($t_{(223)}=-3.5$, $p<0.001$).

When the visual oddball was implemented as the attention distractor, the accuracy of tempo-spectral features were significantly higher than spectral ($t_{(223)}=-3.2$, $p=0.002$) and temporal features ($t_{(223)}=-15$, $p<0.001$). The channels located in the parietal lobe were significantly better for attention classification when using spectral ($F_{(5,206)}=2.3$, $p=0.04$) and tempo-spectral ($F_{(5,206)}=2.4$, $p=0.03$) features while channels located in the central lobe had a significantly higher accuracy when temporal features ($F_{(5,206)}=2.6$, $p=0.03$) were used for attention classification (table 5-3).

A combination of visual and auditory distractors (mixed distractor) revealed that tempo-spectral features had a significantly higher accuracy than temporal ($t_{(223)}=-14.8$, $p<0.001$) and spectral features ($t_{(223)}=-5.8$, $p<0.001$). Similar to other distractor types, the central lobe channels outperformed other locations for attention classification using temporal features ($F_{(5,206)}=2.7$, $p=0.02$) while parietal lobe channels were superior when using spectral ($F_{(5,206)}=2.4$, $p=0.04$) and tempo-spectral ($F_{(5,206)}=2.4$, $p=0.04$) features.

Table 6-3 Classification accuracy with three feature groups and three types of oddballs (attention distractors) obtained from channels located over various brain lobes and hemispheres.

	Anterio- Frontal	Frontal	Fronto- central	Central	Centro- parietal	Parietal
Temporal	66.9±7.9	67.6±8.5	68.5±8	71.2±5.5	66.7±8	65.5±7.5

Auditory	Spectral	78.6±11.4	77.5±11	79.8±12.7	79.4±12.3	77.1±13.2	83.5±9.9
	Tempo-spectral	79.4±14.5	80.5±12	81.7±12.7	84.1±9.8	78.6±14.7	87.5±9.4
	Temporal	66±4.7	68.9±7.1	69.4±8.8	72.8±5.5	69.4±8.5	70.4±8.8
Visual	Spectral	77.8±9.5	81.7±7.1	80.6±14.4	81.1±14	80±13.5	85.1±8.7
	Tempo-spectral	78.6±10.9	80.7±9.6	84.9±12.1	83.6±13.8	80.2±15.3	86.7±8.9
	Temporal	67.4±12	68±10.6	71.8±5.3	73.2±6	68.6±8.2	69.6±7.6
Mix	Spectral	78.6±8.9	78.7±10.7	81.3±10.9	81.8±11.4	77.5±15.3	86±8.3
	Tempo-spectral	82.9±10.1	81.3±14.8	82±14	86.2±12.7	80.1±17	88.1±9.5

		Right	Midline	Left
Auditory	Temporal	67.4±7.7	67.9±7.4	66.3±8.2
	Spectral	80.5±11.1	79.7±11.6	78.7±13
	Tempo-spectral	83.1±12.3	81.7±12.9	81.1±12.2
Visual	Temporal	69.8±8.5	70.8±6.3	70.2±7.8
	Spectral	81.1±11.9	82.4±10.2	81.2±12.8
	Tempo-spectral	82.7±13	84±12.1	82.5±11.8
Mix	Temporal	69.6±8.7	70±9.2	70.8±7.9
	Spectral	82.4±12.2	79.5±10.6	81.6±11.1

Tempo-spectral	85.6±14.3	83.1±15.2	85.4±12.1
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6.5.1. CHANNEL COMBINATION

As mentioned in the previous section, central channels when using temporal features and parietal lobe channels when using spectral and tempo-spectral features showed the highest attention classification. These channel placements were combined with other channels to increase accuracy. The results showed that accuracy of tempo-spectral features was significantly increased by adding channels Cz, C2 and C4 to the parietal channels for both auditory ($t(7)= 2.5, P= 0.04$) and visual distractors ($t(7)= 2.6, P= 0.03$). Discrimination accuracy of the temporal features was also improved by adding FC1, FCz and FC2 to the central channels ($t(7)= 3.9, P= 0.006$).

CHAPTER 7. DISCUSSION

This chapter will focus on the discussion of the main findings of the current thesis. The main aim of this series of studies was to use MRCP signals for detection of the users' attention level and then implement this into the design of a robust and reliable BCI system able to cope with the changes in the users' attention status. Initially, a cue based paradigm was established able to produce MRCPs that could reliably be detected prior to movement execution (Study I). This paradigm was implemented in subsequent studies (II-IV) to quantify the effect on MRCP parameters under conditions of different types of attention diversion. The influence of alternating attention which shows the ability of the brain to switch between two tasks with different demands on the MRCP was investigated in Study II while the effect of divided attention, which represents the ability of the brain to perform two tasks concurrently on MRCP parameters was quantified in Study III. The possibility for attention discrimination from MRCP parameters was investigated in Study IV and V for either synchronous or asynchronous movements.

7.1. OPTIMAL PARADIGM FOR CUE-BASED BCI

As suggested in the introduction, the established associative BCI for neuromodulation requires that the MRCP is detected prior to the peak negative phase. In this way, the artificially generated afferent feedback may be timed to arrive at precisely the peak negativity of the MRCP. Only then will the Hebbian principle of associativity be satisfied (Hebb, 1949) and plasticity be induced (Mrachacz-Kersting et al., 2012). In principle, any cue may be implemented to indicate to the participant when to perform the movement. The results from Study I suggest that movement intention can be reliably detected prior to the occurrence of the peak negativity using various types of cued paradigms. However, if the cue is designed so that participants were only required to perform one type of movement, and if the preparation and execution phase were separated, movement detection was more reliable and occurred earlier. In this way, a non-random cue may be more appropriate for a BCI for neuromodulation. On the other hand, a cue that requires different types of movements to be performed in a random manner affords for variability of practice. Random and semi-random paradigms may also prevent fatigue of a particular muscle group since each trial requires a different type of movement to be performed. Fatigue is known to deteriorate BCI performance (van Duinen et al., 2007), causing increments in force variability and muscle activity as well as a decrease in the activation of the supplementary motor area.

Random cued paradigms resulted in a significant delay of the detection latency, as compared to either the semi-random or non-random cue, though detection still occurred prior to movement execution. Afferent feedback would thus nonetheless arrive at the appropriate time in relation to the PN of the MRCP. However, detection accuracy was significantly reduced so that the number of pairings of the afferent

inflow and the PN of the MRCP would be reduced. This reduced detection accuracy is the direct result of the significantly higher variability of the initial negative part of the MRCP signals. In addition, the PN amplitude was significantly smaller. This is in contrast to previous studies that have shown an increase in the MRCP amplitude when participants were asked to perform different movements as compared to the same movement over many repetitions at a self-selected pace (Dirnberger et al., 2000). The reasons for this discrepancy are unclear but may be related to the differences in the activation of specific brain areas between cued versus self-paced movements. Thus, it is known that the supplementary motor area is involved in the preparation of self-paced movements, while the pre-motor cortex has a greater contribution during cue based movements (Lu et al., 2012). Another reason may be related to the amount of prior information available. Thus, if the amount of information about the impending task is increased (as is the case for the non-random and to a lesser extent the semi-random cue used here), the MRCP amplitude is increased (Jentzsch & Leuthold, 2002). In line with that study, results presented in the current thesis, show that when the preparation and execution phases were separated (as for the non-random and semi-random cue), the MRCP attained the largest amplitudes as opposed to when they were combined (as for the random cue).

7.1.1. MOVEMENT DETECTION

Detection of movement intention onset is an important parameter in the design of BCI systems to provide a trigger for external devices such as an electrical stimulation or an orthosis. Inappropriate movement detection (more than 50 ms) cannot induce brain plasticity based on the Hebbian theory (Mrachacz-Kersting et al., 2012; Xu et al., 2014) and thus cannot be applied in BCI for neuro-rehabilitation applications. Movement detection can be altered under different conditions such as the type of the paradigm used to make instructions for movement execution and also the users' state like fatigue, learning or attention level.

Movement intention can be detected using various techniques which differ in terms of the movement intention detection latencies and accuracies. A low frequency asynchronous switch design (LF-ASD) was one of the initial attempts for movement detection, that was later extended to three and four state systems. These studies applied supervised methods such as LDA, K nearest neighbor (KNN) and SVM to classify different types of hand movements from the idle (resting) state of EEG signals (Bashashati et al., 2007; Birch et al., 2003; Sadeghian & Moradi, 2007b). In the best case, the average TPR of classification was around 75% with a FPR of 20%. In Awwad Shiekh Hasan et al. (2010), an unsupervised system was defined for detection of a transient phase from the idle state to the movement execution phase. This method may be more useful for asynchronous movement detection as there is no EMG to show true movement labels. In this method, self-paced hand movements were detected with an average true false rate of 80% while the average true positive rate was low (~50%).

MRCP have also been used for the classification of different movements like foot, hand and tongue movements since characteristics of the tasks are modulated in the MRCP features such as in the amplitude and time of peak negativity (Gu et al., 2009; Käthner et al., 2014; Morash et al., 2008; Niazi et al., 2012). This signal modality also contains useful information with regards to the movement preparation phase that may be implemented for fast and reliable movement detection (Niazi et al., 2011; Xu et al., 2014) when the MRCP template was used for detection of real or imagined movements. In recent years two techniques, template matching and LPP-LDA, have been applied for movement detection based on MRCP analysis [more details in section 2.2.3.1]. The TPR obtained from these methods is higher than for the previous techniques (~80%) while these also have a lower FPR (~15%). Detection latency of the MRCP may be influenced by several factors such as the timing of the paradigm if a cue is used and attention distraction from the main movement. The following two sections provide details about the influence of detection parameters in these two conditions.

7.2. ATTENTION AND BCI SYSTEMS

Following Study I, the current thesis, centered on quantifying the influence of artificially imposed attention shifts on the performance of the main (BCI) motor task and various MRCP parameters typically used for detection (Study II-V). Many previous studies have attempted to identify EEG signal characteristics under various types of attention distractors (visual, auditory, audiovisual) while participants had to perform a main task. These past studies used EEG signals from different parts of the brain as a control signal to show different attention states such as ERPs and fMRI (Kulke et al., 2016; Praamstra et al., 2005; Serences, 2015).

However, the work reported in the current thesis aimed to control the attention level of the user to a motor task and to recognize attention distraction. The goal is to then use this information to provide feedback to the users to guide their attention back to the main BCI task. Mental states such as fatigue and attention alter BCI performance (Myrden & Chau, 2015). Although frustration and fatigue have been shown to have a greater effect on BCI performance (Myrden & Chau, 2015; Wijesuriya et al., 2008), there are some other BCI designs that specifically use the users control of his/her attention level (Iturrate et al., 2009; Nijboer et al., 2008). According to this, there is no doubt that attention levels need to be controlled in BCI systems. This plays a key role in the BCI design for neuromodulation since if attention to a task is low, no plasticity will be induced, regardless to the acceptable timing between the movement intention and external trigger (Stefan et al., 2004; Ziemann et al., 2008). Although, there are few previous studies that have quantified attention distraction with different methods such as analyzing event-related potentials and EEG frequency bands (Markman et al., 2013; Ponjavic-Conte et al., 2012), no prior studies have used the MRCP for this purpose.

As outlined in Chapter 3, there are several different types of attention, *sustained*, where no distractors arise, *alternate*, where participants switch between two tasks, *selective*, where participants concentrate on selecting specific stimuli from the surrounding environment, and *divided*, where participants have to perform several tasks concomitantly. Of these four, alternate and divided attention is of particular relevance for BCIs used in the clinical setting. For example, patients may be required to perform a specific set of exercises and during the rest periods, the therapist may engage them in conversation not directly related to the exercise (alternate attention). Alternatively, while the patient is performing a particular set of exercises, distractors in the form of noise from the surrounding environment may occur (divided attention) such as a fellow patient coming into the training room wishing to say hello. Study II was performed to assess the effects of alternate attention on the main BCI task, while in Studies III-V, divided attention was investigated. The results will be discussed in the following sections.

7.3. ALTERNATIVE ATTENTION

In Study II, the attention of the participants was shifted between two tasks (a motor task and a cognitive task). One of the important findings of Study II was that specific MRCP features vary when the state of attention of the user was altered. As suggested in section 6.1.2, the initial negative drift of MRCP signals contains information about the preparation for the impending movement execution. It is in this phase where detection of movement intent is made for the associative BCI. Significant reductions in the users' attention were quantified which had a direct consequence for MRCP features in the movement preparation and execution phases, particularly in the complex tasks which required more focus and analysis of resources. Thus, the amplitude of the negative peak of MRCP signals reduced significantly which is supported by previous studies that have shown a positive and monotonic relation between attention and the MRCP negativity amplitude (McCallum et al., 1968; Tard et al., 2014; Tecce et al., 1976). Attention is a main factor affecting the processing of task resources and in motor learning. For example, attending to the target hand during the application of rTMS (a technique to induce cortical plasticity) results in larger changes in the output of the motor cortex to the target muscle compared to non-attendance to the target hand (distracted condition) (Purves, 2008; Ziemann et al., 2008).

The most important finding of Study II was that the MRCP extracted from only a single channel (Cz) sufficed in monitoring the attention drift as movement detection was significantly delayed in this single channel. However, movement detection latency obtained from the large Laplacian method was not affected by attention variations. This suggests that to have a robust and reliable BCI system under attention changes, a multi-modal BCI is imperative: movement intention is reliably detected from Laplacian output that is not altered by attention variations and the single channel Cz is used to indicate attention variations. Thus, the output from Cz

may be used to provide feedback to the users during attention diversion from the main movement.

In order to verify that attention changes using MRCP features are comparable to the typical measures of ERP components such as the P300 and N100, the P300 was also used as a measure of attention in the current thesis. Thus, it is well known that the P300 and N100 latency are increased and their amplitudes decreased when attention to a particular task or stimulus is decreased (Näätänen & Michie, 1979; Trujillo et al., 2009). In line with this, results presented here showed lower P300 amplitude and a later P300 peak during conditions of attention reduction.

The findings of Study II showed smaller P300 amplitude as task complexity increased. This is in line with previous studies where the effect of task complexity was also monitored by changes in the P300 (Barkaszi et al., 2013; Wei et al., 2002; Wilson et al., 2012). The amplitude of the P300 was shown to decrease for more difficult tasks (Hoffman et al., 1985; Kida et al., 2012) and the corresponding latency increased (Wilson et al., 2012; Wintink et al., 2001).

7.4. DUAL TASKING

In Study III-V, two tasks with different demands were combined (motor and cognitive tasks) to provide dual-tasking conditions. Participants were asked to perform one motor task in a single task level while in dual-task conditions they were asked to concentrate and respond to two tasks at the same time. This diverted their visual attention on the cue for the main task, to the auditory cue. Motor movement preparation and execution were significantly diminished by performing two concurrent tasks in comparison with single task execution.

Pre-movement slopes and the amplitude of the peak negativity of the MRCP decreased with increments in the task demand in dual-task conditions. This suggests that more information needs to be processed particularly in complex task conditions (Montani et al., 2014). Non-significant changes of the EMG envelopes between single and dual-task levels indicate that the level of contraction and performance of the main BCI task of dorsiflexion was not affected. The increment in the reaction time as quantified by the difference between EMG onset and cue onset is likely a result of a delay in movement preparation/execution.

According to the results of different channel locations in Study III, motor cortex and fronto-motor channels were more influenced by dual-tasking. Information competition between two task demands in dual-task conditions can alter movement planning in the brain regions responsible to control and process the movement resources (Lin et al., 2011; Stopford et al., 2012). Based on this, the motor cortex is likely the first possible candidate to illustrate properties of motor movement preparation/execution.

The amplitude of the visually evoked P300 decreased significantly in dual-task versus the single task condition. It may be that the attention level in the dual-task condition was decreased for the visual stimulus (since this cued the main task which was a simple ballistic dorsiflexion) and diverted to the auditory oddball task. The auditory P300 was thus increased for more complex dual task conditions. Since the auditory oddball task was only performed in the dual task conditions, it was also the novel task and thus required more attention resources. This is in line with Kok (2001) who showed that task difficulty causes decrements of the P300 amplitude particularly if the subjects' attention was diverted away from the response stimulus. Montani et al. (2014) investigated both alternative and divided attention in different trials of a videogame and showed that training decreased the dual-task and task switching costs. They did not quantify the ERP components but rather measured the success rate in a game which was decreased by increments in the game difficulty.

In Study IV, classification of attention was performed using different types of MRCP features extracted from different channel locations. The time-frequency feature (ERSP) components attained a higher accuracy compared to temporal features. Time-frequency features contain information about different frequency bands from various time domains and thus are more informative than a single group of temporal features. They thus allow for improved movement detection performance when the goal was to classify dorsiflexion with different levels of voluntary contraction (Jochumsen et al., 2015; Kamavuako et al., 2015). However, these MRCP features have not been extensively used for attention classification. Results presented here reveal a classification of attention with an accuracy of ~ 75%. This is comparable with the performance of BCI systems that provide feedback based on attention classification using ERPs and steady state auditory evoked potentials (classification accuracy was reported to be ~ 70%) (Hill & Schölkopf, 2012; Kim et al., 2011). It is also in line with the accuracy of movement classification under variations of task related parameters like force level (70-80%) (Farina et al., 2007; Gu et al., 2009).

Among different channel locations, those placed over the motor cortex showed the best classification output. However, this is in contrast to reports suggesting that frontal lobe activation is increased to a greater extent in dual-task conditions (Contreras-Rodríguez et al., 2015; Mirelman et al., 2014). However, it may be that the type of the task is an important factor (Wu et al., 2013). Central channels are known to be most active during a dorsiflexion task (Fall & de Marco, 2008; Kleim et al., 2003) and by combining this with a cognitive task, motor cortex activation was more influenced than the other locations. Thus, in these cases where motor and cognitive tasks are combined, the frontal lobe activation may not increase significantly due to the cognitive task.

7.5. SELF-PACED MOVEMENTS AND DUAL-TASKING

In Study V, the effect of dual-tasking on EEG features was investigated during self-paced movements. While in previous chapters, cue based motor movements have been suggested to be more suited for BCI applications in stroke rehabilitation, self-paced movements have the advantage that the user can decide when to perform the movement and thus have wider applications within the BCI field. The distractors used in Study V encompassed three different modalities (visual, auditory and a combination of the visual and auditory oddball) to divert the attention away from the main task (dorsiflexion). The aim of using different modalities as distractors was to increase the compatibility of our findings with the real-life conditions as in the surrounding environment there are various types of distractors. In the same direction with Study IV, it was shown that a combination of temporal and spectral features obtained from movement-related EEG signals are more reliable for attention discrimination as this feature type revealed a higher accuracy in attention classification compared to only temporal and spectral features. Previous studies have used spectral features from EEG signals to monitor attention variations, alertness and workload (Berka et al., 2007; Lin et al., 2013). Classification of attentional state to a motor task attained values of only 61-68% (Melinscak et al., 2016; Myrden & Chau, 2017). The classification accuracies presented in the current work were higher than the results presented in the latter study (on average ~84%) in spite of the methodological differences.

In self-paced movements, the parietal lobe was the best channel placement for spectral and tempo-spectral features in attention classification for both auditory and visual distractors. Processing of visual information is mainly confined to the parietal and occipital lobes (Li et al., 2012) and auditory to the temporal regions (Potts et al., 1998). The reason why parietal channels were most suited for classification irrespective of the type of distractor may be explained by the effect of attention on the channels localized in this lobe. For example, Moores et al., (2003) investigated that during execution of a visual-verbal oddball task superior parietal lobe was activated in relation to the attention process. In addition, Tenke et al. (2008) showed that channels located over the left hemisphere were superior to distinguish between target and non-target stimuli. In this work, healthy subjects and patients performed an auditory oddball played to the right or left ear alternatively while they were asked to find a target tone by pressing a right or left button. P300 analysis revealed significantly larger amplitudes over left hemisphere in both conditions.

7.6. EFFECT OF TASK REPETITION ON ATTENTION DETECTION

Significant differences in MRCP features (value of peak negativity, pre-phase slopes and variability) were obtained between the first and second block of motor movement execution in Study II. However, this was not the case for Study III.

Repetition of a stimulus helps to learn and to strengthen the routes among activated neurons to induce plasticity (Hebb, 1994) and consequently improve the performance of a task conducted with that particular stimulus (Grill-Spector et al., 2006). In Study II after the first block of the auditory oddball task, participants may have been habituated to the stimuli and this may be the main reason why the effects of the second oddball block on movement execution (MRCP features) were reduced (Ritter et al., 1968). Another possible reason for the less affected MRCP features in the second block may be a reduction of the memory load and facilitation in resource processing. If the amount of new information is reduced, participants recognize the sounds easier (Brown & Xiang, 1998) particularly if the task is not so complex (Jordan & Rabbitt, 1977).

The fact that no difference on MRCP parameters among movement blocks were quantified in Study III may be due to a longer time being required to learn the new oddball task. By increasing the task difficulty, more time (task repetition) may be needed to learn and control task requirements. In Pineda et al., (2003), subjects trained for 10 h to learn how to manage left or right movements in a videogame. Mu power analysis in the sensorimotor cortex revealed linear increments during this learning process. In addition, if two tasks are performed simultaneously, more repetitions are required to simplify task execution since the timing and information processing of the primary task is disrupted by the secondary one in the initial blocks of dual-tasking (Taatgen et al., 2007).

7.7. METHODOLOGICAL CONSIDERATIONS

All of the experiments were done in a controlled laboratory set up either at the University or the rehabilitation clinic to minimize the number of the other distractors arriving from the surrounding environment. However, attention can be diverted either endogenously (voluntary attention) or exogenously (involuntary stimulus-driven attention) (Chun et al., 2011). So, BCI users attend to more than two tasks and this can degrade BCI performance. On the other hand, it is not easy to control all types of distractors particularly those controlled by the users (internal distractor).

The results obtained from the different studies were based on offline analysis. However, in the real-life situation we need to have online (real-time) systems to provide a feedback when the user's attention is changed. In addition, it is possible that performance of the system reduces in the online mode and thus more temporal or spectral features may be required to compensate for this deterioration.

Except for Study II, the other parts of the thesis were conducted in healthy participants. The next step is to include patients as these are the main end users of BCIs for neurorehabilitation. It is clearly predictable that performance of patients differs from the healthy group as indicated by the results from Study II. It should also be considered that healthy participants used in this thesis were young adults but

most of the patients are older than these groups. Age is a factor that may affect MRCP features.

7.8. FUTURE PERSPECTIVES

Previously different BCI systems have been designed that use attention as a way to provide feedback to the user, but the effect of attention drift on BCI performance is a new topic in the area of neuro-rehabilitation. The main aim of this thesis was to decode attention variations and to classify two attention levels of normal and diverted conditions using movement-related EEG features in both synchronous and asynchronous BCIs. All of the studies were conducted in the offline mode to get an overview about attention alteration, so the next step is to implement an online BCI that can adapt with attention variations. Preliminary results in healthy participants and a small cohort of stroke patients show the feasibility of this approach. In addition, these systems need to be applied in real-life conditions with different types of distractors (the same as Study V) to make them more robust and reliable for general attention changes. Furthermore, the performance of these systems should be evaluated with the actual end users, i.e. neurological patients such as those that have suffered a stroke. As was shown in the second study, controlling of attention is more critical for stroke patients. The classification performance can be increased by using different classifiers or larger sample sizes. The size and variability of the training data is also another factor that will likely affect classification performance and thus needs to be further investigated.

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