

MASTER

**Event-related synchronization in neurometric EEG data
a study in children with ADHD**

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Event-related synchronization in neurometric EEG data

- A study in children with ADHD -

by R.A.G. Vogels

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Event-related synchronization in neurometric EEG data

A study in children with ADHD

Master Thesis

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Preface

After graduating at the Fontys Hogeschool Elektrotechniek (Fontys University of Professional Education) in Eindhoven, I followed the master course Electrical Engineering at the Eindhoven University of Technology (TU/e).

This thesis contains the results of my graduation based upon studies conducted from September 2004 to September 2005 at the Signal Processing Systems (SPS) group of the Department of Electrical Engineering at the Eindhoven University of Technology, the Netherlands.

I would like to express my sincere gratitude to my supervisor dr. ir. P.J.M. Cluitmans for his time, guidance, input and discussions during this project. Further, I would like to thank my colleagues at floor 3 for the nice working atmosphere, especially René Schott and Sjoerd Diepen for their great co-operation, help and their comments on the thesis while writing.

Finally, I wish to express my thanks to my family and friends, who have supported me during my time on the TU/e and my graduation. Especially my parents for giving me the chance to continue my study at the University and their support in reaching this goal. And last but certainly not least Ciel for her patience and support.

Eindhoven, September 2005
Ronald Vogels.

Summary

Currently diagnosing of ADHD in children can only be done by means of a qualitative research on the psychological, psychiatric and social aspects using the criteria of the DSM-IV. The problem with this qualitative way of diagnosing is that, because of the sensitivity of the DSM-IV criteria to subjective influence introduced by for instance the parents or the psychiatrist, there is a considerable concern of miss diagnosis of ADHD which results in incorrect treatment and medication. Besides, the diagnosis time is long caused by the large amount of tests that have to be done.

During the past decades, numerous studies have been carried out in the area of event related synchronization (ERS)/event related desynchronization (ERD) in EEG signals. These phenomena can be described as an event-induced shift from a predominantly stochastic (desynchronous) EEG activity towards more regular, patterns or vice-versa. A relation with ERD/ERS and attention processes and the fact that ADHD is a neurological disorder might make it possible that EEG research can be used to diagnose or support the qualitative diagnosis of ADHD.

For the quantification of the ERD/ERS several methods are developed with each his own dis- and advantages. After investigating the different methods the Classical, Intertrial Variance and the Hilbert methods were implemented in a software application in MatLab. The ERD/ERS is highly frequency specific therefore, the EEG data was bandpass filtered using a FFT filter. The reactive frequency bands were determined individually on the basis of the Individual Alpha Frequency (IAF).

For the available data of ADHD and control children significant differences between the two groups were found within the IAF of both groups using 3 different ways of determining the IAF. The IAF of the ADHD and the control group showed that it was lower for the ADHD group than for the control group. Moreover the IAF determined from the frontal lobe were significant lower in the ADHD group than in the control group.

For lower frequency bands (up to the upper-alpha band) it is recommend to use the Intertrial Variance method because it eliminates the interference of evoked activity. For ERD/ERS computations of higher frequency bands the Hilbert method is recommend because of its ability to automatically adapt the time resolution to any frequency under investigation.

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List of abbreviations

ADHD	Attention-Deficit/Hyperactivity Disorder
CT	Computed Tomography
DFT	Discrete-time Fourier Transform
DSM-IV	The Diagnostic and Statistical Manual of Mental Disorders 4th edition
EEG	ElectroEncephaloGram
EC	Eyes Closed
ERBP	Event-Related Band Power
ERD	Event-Related Desynchronization
ERP	Event-Related Potential
ERS	Event-Related Synchronization
FFT	Fast Fourier Transform
FIR	Finite Impulse Response
IAF	Individual Alpha Frequency
IBP	Induced Band Power
IFFT	Inverse Fast Fourier Transform
IV	Intertrial Variance
M	Mean
MRI	Magnetic Resonance Imaging
PET	Positron Emission Tomography
S.D.	Standard Deviation
SNR	Signal-to-Noise Ratio
TF	Transition Frequency
TSE	Temporal-Spectral Evolution

Chapter 1

Introduction

It is estimated that about 2% of the children in the Netherlands, between the age of five and fourteen show severe symptoms of *Attention-Deficit/Hyperactivity Disorder* (ADHD). This corresponds with about forty thousand children of which boys outnumber girls by four to one. An additional 3% to 6% of the children of this age exhibit less serious or fewer symptoms of ADHD [Health Council of the Netherlands, 2000]. This means that statistically with a class size of 25 children, in half of the classrooms in the Netherlands at least one child is suffering from the effects of ADHD and in almost every classroom there is one child who shows less severe symptoms of ADHD!

At this time there is no quantitative way of diagnosing if a child has ADHD. Although the exact cause of ADHD is unknown, nowadays it is clear that it is a neurological related disorder. This suggests that electroencephalography (EEG), which provides a direct measure of the brain's functioning, could be an important tool for assisting the current way of diagnosing ADHD or even become a reliable quantitative method. Furthermore the EEG procedure is a non-invasive and relatively inexpensive medical examination. In practice the EEG technology is not (yet?!) suitable for diagnosing ADHD. The diagnosis of ADHD nowadays requires both medical (e.g. general practitioner, child neurologist) and psychosocial (e.g. child psychiatrist, developmental psychologist) expertise.

1.1 Problem definition

The current approach in diagnosing ADHD is almost exclusively based on observation and perception of the child's parents and in some cases the teachers. The medical and psychosocial specialist in diagnosing ADHD in children, compares the symptoms described by the child's parents to the criteria laid out by the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) [American Psychiatric Association, 1994].

There are a number of problems/difficulties regarding this present-day diagnosis of ADHD.

- The criteria given in the DSM-IV are qualitative (see section 2.2), which implies that specialists have to have a lot of experience and knowledge to come with a correct diagnosis;
- Specialists almost exclusively rely on the observations of the parents, which assumes that the parents have an accurate knowledge of the normal behavior of age related children, however this is not always the case;

- Because there is no quantitative way to diagnose ADHD, it takes a lot of examinations and time to come with a diagnosis from a psychosocial point of view. During this diagnostic process the child and the parents suffer from all the consequences of the disorder, e.g. social problems, repeating a year at school and losing friends;
- There is a considerable concern that with the current diagnostic approach there is an over-diagnosis in ADHD, which results in incorrect treatment and medication [Barry et al., 2003a];
- The long diagnosing time and wrong treatment will cost the government and the medical insurance companies a large amount of money each year.

These problems can be reduced or even solved by improving the diagnosis of ADHD. One way to accomplish this is to find a quantitative method to support the qualitative diagnosing of ADHD.

A relatively new method within EEG analysis, which in the last two decades is gaining popularity, is event-related desynchronization (ERD)/event-related synchronization (ERS) [Pfurtscheller and Aranibar, 1977]. A common hypothesis is that EEG desynchronization can be associated with an activation of the underlying cortical areas and synchronization is a sign of inactive nearby cortical areas. Also a relation with attention processes has been suggested. This last suggestion is the basis of the hypothesis that ERD/ERS may deviate or even be absent in children with attention deficits, such as ADHD. However, in literature no references were found by the author, that indicate that ERD/ERS has ever been used in any EEG research regarding ADHD.

1.2 Research objective

The objectives of this project are as follows:

- Comparing and analyzing the different algorithms/methods for the quantification of ERD/ERS, and determining which one(s) are suitable to use in this project;
- Implementing the algorithm in a software application, written in MatLab® (version 7.0.4) developed by “The MathWorks, Inc.”;
- Determining which values should be chosen for the variable settings (e.g. frequency bands, reference time, etc.);
- Evaluating EEG data collected during diagnostic research of ADHD and control subjects, with the implemented algorithm. The goal is to see if differences can be found between the two groups.

1.3 Report outline

This report is structured as follows:

- *Chapter 2:* Defines the ADHD-syndrome and the current way of diagnosing ADHD;
- *Chapter 3:* Describes the basics of EEG, the different frequency band and the meaning of Event-Related Potentials (ERP) and Event-Related Synchronization/Desynchronization (ERD/ERS);

- *Chapter 4*: Presents the basics of changes in the alpha and theta band, after which two methods of determining the different individual frequency bands needed for ERD/ERS quantification are explained;
- *Chapter 5*: Discusses the, most used, different methods to quantify ERD/ERS, together with their advantages and disadvantages;
- *Chapter 6*: Describes the implementation of the ERD/ERS algorithms in MatLab and the implementation of the FFT bandpass filter used in the ERD/ERS algorithms;
- *Chapter 7*: Presents the specifications of the used EEG data, Recording conditions of the subjects and the pre-processing of the data;
- *Chapter 8*: Presents the Results from the project;
- *Chapter 9*: Presents the conclusion and the recommendations for future work.

Chapter 2

ADHD-syndrome

2.1 Understanding ADHD

Attention-Deficit/Hyperactivity Disorder (ADHD) is a disorder related, in part, to the brain's chemistry and anatomy. Although the exact cause of ADHD remains unknown, it is believed to be genetic because a twins-research has shown that the heredity of ADHD has to be estimated on 70% to 80% [Health Council of the Netherlands, 2000]. Exposure to nicotine (smoking) and alcohol during pregnancy increases the chance of ADHD, probably in combination with hereditary factors.

ADHD in general is a limitation of behavioral inhibition. Behavioral-inhibition is the power to suppress, delay or stop stimuli of internal or external nature. Children with ADHD develop the weakness around their first year and is based on the functioning of the frontal cerebral cortex and the basal cerebral kernels.

The symptoms of ADHD are usually recognized in the earliest childhood. The three key symptoms of the ADHD-syndrome are hyperactivity, impulsiveness and attention weakness. Other symptoms are education-disorders, behavioral problems and some children do not learn of their experiences. [Health Council of the Netherlands, 2000]

In most cases ADHD is accompanied by other psychopathological conditions like depression, conduct disorder and anxiety disorder. In roughly one third of the cases, the symptoms persist into adulthood.

2.2 Classification

According to The Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) [American Psychiatric Association, 1994], the symptoms of ADHD fall into three categories [Temmink and Merkelbach, 2000]:

- **Inattention**

Children of this type mainly show disorders in the selective functions of the brain. This expresses itself in sustained attention and selective attention disorders.

Some symptoms of *inattention* a child may be exhibit are:

- Problems with sustaining attention in work or play;
- Ignoring details; Making careless mistakes;
- He/she does not seem to listen when directly addressed;
- He/she does not follow through on instructions;
- Difficulty organizing tasks and activities;

- He/she gets distracted by extraneous noise and activities;
- Is forgetful in daily activities;

This type occurs in about 20% of the ADHD-cases and of which boys outnumber girls with 2:1 [Temmink and Merkelbach, 2000].

- **Hyperactivity/Impulsivity**

In this type symptoms can be related to a poor control function of the brain. The symptoms are related to movement, observance, impulses and emotions.

Some symptoms of *hyperactivity* a child may exhibit are:

- Often fiddle with hands or feet;
- Runs or climbs when he or she shouldn't;
- Has difficulty with quiet leisure activities;
- Talks excessively;
- Has to get up if sitting on a chair;

Some symptoms of *impulsivity* a child may exhibit are:

- Blurs out answers before questions have been complemented;
- Has difficulty waiting his or her turn;
- Interrupts or intrudes on others;

This type occurs in about 25% of children with ADHD and of which boys outnumber girls with 5:1 [Temmink and Merkelbach, 2000].

- **A combination of the two**

These children show phenomena of equal proportions of both hyperactivity/impulsivity and inattention. With these children we often see a lack of visually and auditory storage in their memory. With this, the storage of information coming from the ears or eyes in the brain, is meant. This type of ADHD is the most common one, it occurs in 55% of the ADHD-cases and of which boys outnumber girls with 3:1 [Temmink and Merkelbach, 2000].

2.3 Diagnosis

Parents and/or teachers of a child are the first to notice that a child is showing strange behaviors compared to the other children of his/her age. For example the child has trouble sustaining attention in work or play, has difficulty with quiet leisure activities and has difficulty waiting his/her turn. These symptoms mostly results in, for instance education-disorders and behavioral problems, which forces the parents to find help. In most cases the general practitioner is the first specialist the family turns to for help and advise. Knowledge about the child's family circumstances and school environment should be taken into account when considering the diagnosis of ADHD; use of information from more than one source is crucial. In addition, the presence of comorbidity¹ should be carefully investigated. Because the diagnosis of the condition requires both medical and psychosocial expertise, it is of great interest that there is a good cooperation between different disciplines. The core-professionals involved should also be experienced in diagnosing ADHD.

¹having two or more diagnosable conditions at the same time

Extensive research is necessary to diagnose ADHD. This research is mostly done in the following order:

1. An interview focusing on patient history, including illness and development, his or her behavior, contact with contemporaries and adults, school development and motoric development. (anamnesis)
2. A general physical examination, e.g. blood pressure, posture, sense functions.
3. A psychological examination, e.g. attention- and memory investigation.
4. An EEG and imaging examination (CT-scan, MRI-scan, PET-scan) to prove or exclude neurological disorders that are coupled with ADHD.

The goal is that EEG analysis in the future becomes a reliable method to assist in diagnosing ADHD. A great amount of research has already been performed on the effects of ADHD on the EEG signal compared to healthy subjects. For instance researchers looked at the difference of absolute and relative band power and event-related potentials (ERP) (Section 3.3) between ADHD and normally developed children. For a review of research on ADHD see Barry et al. [2003a] and Barry et al. [2003b].

Chapter 3

Rhythmic EEG activity

3.1 A look in history

EEG stands for *electroencephalogram*, the electrical activity of the human brain. The first description of the electroencephalogram was reported by the English physiologist Richard Caton in February 1875 in a brief abstract of about 10 sentences.

Several years later Adolf Beck, who was not aware of Caton's work, explored the electrical brain activity in greater detail than Caton did. He provided important contributions to the nature of electrical brain activity. He discovered the spontaneous oscillations of the brain potentials and showed that these fluctuations were not related to heart and breathing rhythms. Moreover, he observed a discontinuation in the fluctuations of the electrical waves as a consequence of afferent stimulation. Thus he was the first to describe the desynchronization in the EEG.

On 14 October 1927 a new breakthrough was made by Hans Berger who was the first to record the electrical brain activity from an intact skull of a human (of his son Klaus). He also described changes in the EEG during sleep and narcosis, and recorded deviant patterns during epileptic attacks in humans. This is the moment that the EEG became not only important in basic neuroscience, but also became important for clinical practice.

For further details of the history of desynchronization of the EEG the article of Coenen et al. [1998] can be consulted.

3.2 EEG recording

The brain continuously processes information. The EEG measured during no controlled conditions is called *spontaneous EEG* activity. This spontaneous EEG may be recorded at all times even when the person is at sleep.

To record spontaneous EEG signals, electrodes are placed on the skull. The most widely used method of electrode placements is the international 10-20 system, Fig. 3.1(b). With this method the electrodes are placed at specific distance across the scalp. Each position has prefix letter(s) to identify the lobe (Fig. 3.1(a)): Fp for FrontoPolar (or prefrontal), F for Frontal, C for Central, T for Temporal, P for Parietal, O for Occipital. The letters are followed by an even number to refer to the right hemisphere, odd numbers to refer to the left hemisphere or "z" (zero) to refer to the midline. The numbers increase if the distance between the midline increases.

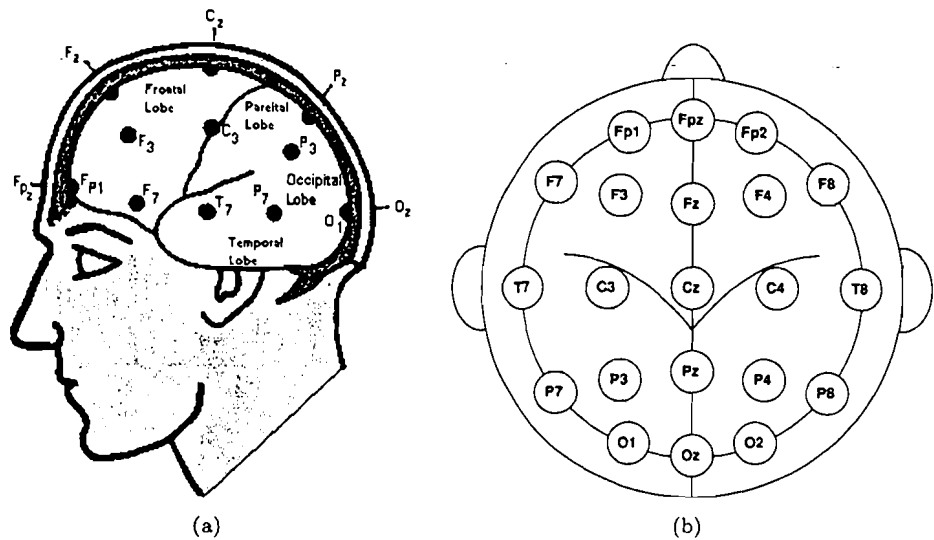


Figure 3.1: (a) International (left side) 10-20 system with underlying lobes. (b) Electrode positions according to the international 10-20 system. Electrode positions are named according to Oostenveld and Praamstra [2001].

The amplitude of the measured EEG activity lies between 10 and $100\mu\text{V}$ in children and 10 to $50\mu\text{V}$ in adults [Niedermeyer, 1999]. If the amplitude is lower than $10\mu\text{V}$ during a prolonged period it must be considered as abnormal. The frequencies of the EEG activity, range from 0.5 up to about 70Hz . In electroencephalography this frequency range is divided into the following bands [Cluitmans, 2003]:

Delta (δ) 0.5-4 Hz Normally this activity is only recorded during sleep.

Theta (θ) 4-8 Hz In normal conditions the recording of an awake adult a small amount of theta frequencies can be detected. However, it plays an important role in the recordings of children in drowsiness, sleep and wakefulness. [Niedermeyer, 1999]

Alpha (α) 8-13 Hz The alpha rhythm has a maximum amplitude at the occipital and parietal areas, see Fig. 3.1(a) for the location of the areas. The mean frequency of the alpha rhythm increases with age.

The amplitude of the alpha rhythm can be up to $50\mu\text{V}$ and occurs during sleep and wakefulness. One important property of the alpha rhythm is that it is blocked or attenuated by attention, especially by visual and mental effort. [Niedermeyer, 1999]

In the case of desynchronization the high theta and alpha bands are mostly divided in three smaller bands, namely the lower1-alpha ($6-8\text{Hz}$), lower2-alpha ($8-10\text{Hz}$) and the upper-alpha ($10-13\text{Hz}$) band. More information about the alpha and the theta band can be found in Section 4.1.

Beta (β) 13-30 Hz The rhythmic beta activity is usually of low amplitude ($\pm 35\mu\text{V}$) and is distributed maximal over frontal and central regions of the skull [Niedermeyer, 1999]. These beta rhythms can be blocked by movement or intention to move and tactile stimulation. A widespread beta activity (i.e. occurs over all electrode positions) are not blocked by any stimulus. The

beta rhythm occurs in all individuals and mainly over the frontal and central regions [Niedermeyer, 1999].

Gamma (γ) >30 Hz The gamma rhythm has about the same properties as the beta rhythm. The reason that the high frequency band is divided into a beta and a gamma band is because the range is too large for research on induced activity. See the following Sections for a detailed review about induced activity.

Another rhythm that can be distinguished is the Rolandic¹ (Central) **Mu** Rhythm. The frequency and amplitude are similar to the alpha rhythm, but its topography and physiological significance is different. The mu rhythm is blocked by movement that is either active (voluntary), passive or reflexive². The rhythm is present at the electrode positions C3 and C4 (Fig. 3.1(b)) and can be detected by the use of frequency analysis like event-related desynchronization (Section 3.4). [Niedermeyer, 1999]

3.3 Event-Related Potentials

In the previous section the spontaneous EEG was described in terms of different rhythms. However, not only spontaneous EEG signals can be measured from the scalp. Under certain circumstances it is possible to extract potential fluctuations that are related to sensory processing, thought processes and motor behavior. These potential fluctuations can be elicited by means of an external stimulus or an event, for instance by moving a finger in response to a certain type of stimulus.

The problem of this potential fluctuation is that it is difficult to detect it within the EEG because the electrical activity of the spontaneous EEG is usually much higher. The spontaneous activity in this case can be seen as "noise", and thus that the signal-to-noise ratio is extremely poor. It is possible to improve the signal-to-noise ratio (SRN) by using an averaging technique. In order to do this, a number of distinct periods of the EEG signal are required. These periods are event-related EEG periods which means that they are triggered by a certain event (e.g. stimulus or movement). In EEG research these periods are denoted as event-related EEG *trials*. These trials are averaged over each other, this way the noise is averaged out. [Cluitmans, 2003]

This technique is called *Event-Related Potential* (ERP) and relies on two assumptions:

1. The background (spontaneous) EEG is a stochastic, zero-mean and stationary signal.
2. The ERP signal (response) remains constant in each trial. This implies that the signal is stationary as to phase, morphology, latency and amplitude.

However there is more and more evidence that the ERP response may vary in each trial. This means that the second assumption is incorrect. This way, if the averaging technique is used to process the ERP, there is a considerable loss of information. This has led to the development of (near) *single-trial* ERP processing methods [Britton et al., 2000]. In these methods just a single trial or a small ensemble of trials (<10) are needed. Because ERP is not a main subject for this thesis these methods are not discussed further.

An important characteristic of ERPs is that they are time-locked and phase-locked (evoked) to an event. See Section 3.5 for further explanation of evoked signals.

¹Rolandic refers to a part of the brain under the "central-temporal" electrodes C3 and C4

²Involuntary response to a stimulus

3.4 Event-Related (De-)Synchronization

Event-related Potentials are not the only phenomena that occur during an internal or external event³. Another phenomenon that occurs is known as *Event-Related Desynchronization* (ERD) and *Event-Related Synchronization* (ERS) [Pfurtscheller and Aranibar, 1977]. The ERD/ERS are, in contrast to the ERP, also time-locked but NON-phase-locked (induced) to an event. These activities represent highly frequency-specific changes of the ongoing EEG activity, and results in a decrease (ERD) or increase (ERS) of power in given frequency bands. A classical example of this is the decrease of alpha band (8-12Hz) activity when opening the eyes as first described by Berger [1929].

An event-related desynchronization (ERD) represents an amplitude *decrease* of rhythmic activity. This means that in the underlying neural network or neuronal circuitry, small patches of neurons or neuronal assemblies work in a relative independent or desynchronized manner. An event-related synchronization (ERS) however, is the opposite and represents an amplitude *increase* of rhythmic activity.

The functional meaning of ERD is that the underlying cortical area is activated ("working"), for instance processing information or preparing a movement. In the case of ERS the functional meaning is that the underlying cortical area is in a resting or idling⁴ state in which, at a specific moment of time, no information is processed.

The size and magnitude of ERD reflect the mass of neural networks involved in the performance of a specific task at a specific moment in time [Pfurtscheller et al., 1996]. In ERS the size and magnitude represent the state of relaxation and idling.

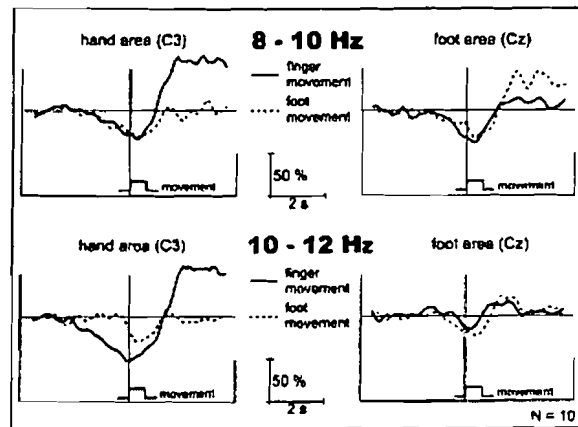


Figure 3.2: Average ERD/ERS curves recorded at electrode location C3 and Cz during voluntary hand (full line) and foot (stippled line) movement. (From Pfurtscheller et al. [2000])

An example of ERD/ERS is given in Fig. 3.2. The horizontal line in each group marks the level of reference band power and the vertical line the onset of movement. A downward deflection indicates a band power decrease or ERD, an upward deflection indicates a band power increase or ERS.

³Internal event is an event generated by the subject itself, e.g. if an subject is memorizing words. An external event is generated by a stimulus presented to a subject, e.g. pressing a response button at a specific trigger.

⁴'an area that has nothing to do' [Adrian and Matthews, 1934]

The ERD/ERS are both short lasting (several seconds), localized and can be characterized by the following parameters [Pfurtscheller and Lopes da Silva, 1999]:

- Spatial localization
- Magnitude
- Latency
- Reactive frequency band

3.5 Evoked and induced rhythms

Because the ERD/ERS is non-phase-locked (induced) to an event, the averaging technique applied on the ERP which is phase-locked (evoked), can not be used.

To explain this, a schematic representation of an evoked and an induced activity is given in Fig. 3.3. Here we can see that if evoked signals are averaged over the total number of signals, the remaining signal will be enhanced because they are in phase to each other. However, if we apply this technique to induced signals, which are not in phase, the signal will deteriorate or can even be almost averaged out.

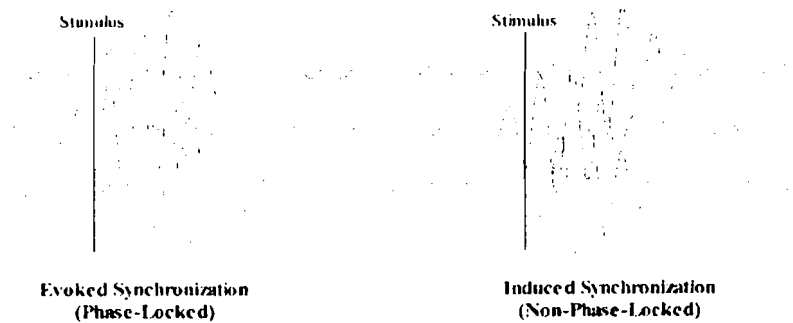


Figure 3.3: Schematic description of evoked and induced activity in EEG.

An event-related EEG signal consists of both evoked and induced activity, which means that by the averaging technique only the evoked activity (ERP) will remain. Consequently, this technique can not be applied to compute the ERD/ERS. In Chapter 5 several methods to compute the induced activity (ERD/ERS) will be discussed.

Chapter 4

Determination of reactive frequency band

The first step in quantifying the ERD/ERS is bandpass filtering the EEG data. The choice for the lower and upper limit of the bandpass filter is one of the difficulties in ERD/ERS analysis. One way is to use the predefined theta, lower alpha, higher alpha and beta bands, as referred to in Section 3.2. The problem with these predefined bands is that the frequency bands of interest are not always the same but can vary from every individual.

In this chapter two methods are described to individually determine the reactive frequency band(s) [Pfurtscheller, 1999b]. To explain these methods first some basic aspects of theta and alpha activity are described [Klimesch, 1999].

4.1 Changes in Alpha and Theta frequency range: basic aspects

Changes in alpha and theta frequency bands can be divided in Phasic and Tonic changes. *Tonic* changes occur over a life cycle and in response to for instance circadian rhythms¹, growing age, neurological disorders, etc. *Phasic* (or event-related) changes are under volitional control and occur in a rapid rate (e.g. ERP and ERD).

4.1.1 Tonic changes in EEG

The brain develops itself until a person reaches the age of about 16 (e.g. brain volume and learning). This development can be seen in the EEG signal by looking at the peak frequency in the power spectra of the alpha band. At the age of 1 year the peak alpha frequency is around 5.5 Hz, 8 Hz at the age of 3 years and 9 Hz at the age of 9. When the age of 15 years is reached the mean alpha frequency raised to about 10 Hz [Hughes, 1987; Klimesch, 1999]. There is no linear relation in this increase of alpha peak frequency because they occur in several grow spurts.

The opposite applies to a person of 20 years old growing older, here the alpha peak frequency decreases from about 11 Hz for a young adult of the age of 20 to 8 Hz of 70 year old person, following a linear relation between age and alpha peak frequency, $alpha_peak_frequency = 11.95 - 0.053 \times age$, as found by Köpruner et al. [1984]. The cause of the increase and decrease of alpha peak frequency is

¹ A daily rhythmic activity cycle, based on 24-hour intervals.

not always age related but can also be related to neurological disease or lack of education.

Not only the alpha peak frequency changes during a lifespan but also the total power of the delta, theta and alpha band varies. There is a strong increase in alpha power (especially in the upper alpha band) and a decrease in delta and theta power from early childhood until adulthood. Also in children with poor education, reading/writing/spelling disabilities or with other types of neurological disorders the delta and theta power are significantly higher than power in the alpha band [Klimesch, 1999]. Because ADHD is a neurological disorder and is almost always detectible in early childhood, these facts are an important factor in EEG frequency analysis on the study of ADHD children.

4.1.2 Phasic changes in EEG

A typical phasic (event-related) change in EEG is the desynchronization (ERD) of the alpha band during the presentation of a warning signal before a task has to be performed. An example of such a task related experiment is that a subject has to respond with 'yes' if a word of a living object appears on a screen and 'no' if the word is a non-living object, but before the word appears the subject gets a warning signal [Klimesch, 1999]. This cycle will repeatedly be presented to a subject. After each response on the task the subject becomes in a relaxed but alert state which results in a pronounced alpha activity (synchronization), which is mostly taken as reference period. However, just before the warning signal appears the alpha activity becomes suppressed (desynchronization) because the subject anticipates the appearance of the warning signal.

There are also differences in the phasic reaction of the alpha power compared to the theta power. If the EEG power during resting period is compared to one during an active period where a subject has to perform some kind of task, alpha power decreases (desynchronizes) but theta power increases (synchronizes). The transition between alpha desynchronization and theta synchronization (Fig. 4.1) is marked by TF (Transition Frequency), of which the value lies in the range of 4 to 7 Hz depending the individual. This means that alpha and theta responses tend to oppose each other and that if the TF point lies within a chosen frequency band, the theta and alpha reaction can partly or completely mask each other. The key problem here, is that the alpha frequency varies to a large extent as a function of age, neurological diseases, memory performance, brain volume and task demands. This is why the use of fixed predefined frequencies in ERD/ERS research is not advisable.

Klimesch and coworkers found that the changes in alpha activity can be divided in 3 separate frequency bands that each react on different states of mind [Klimesch et al., 1992, 1998a]:

- Lower1-Alpha: reflects alertness;
- Lower2-Alpha: reflects expectation;
- Upper-Alpha: reflects on sensory-semantic processing or task specific effects;

4.2 Peak frequency

One way of determining individual frequency bands was suggested by Klimesch et al. [1998b]. Klimesch found that the theta frequency varies as a function of alpha frequency and suggested that the alpha frequency is taken as a common reference point for determining the individual alpha and theta bands.

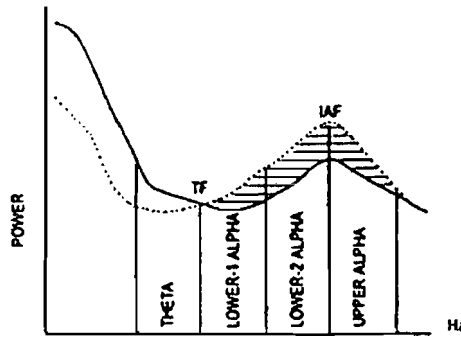


Figure 4.1: Individual Alpha Frequency (IAF) and Transition Frequency (TF). The dotted line represents a reference period in which a subject is in a state of alert wakefulness and the bold line is an active period in which the subject performs an specific task (e.g. memorizing visual presented words). During the active period the alpha power becomes suppressed (decreases) while theta power increases in comparison to the reference period. From Klimesch [1999]

Apart from the delta frequencies the human scalp EEG contains predominantly alpha activity. When a spectral analysis is made of an EEG signal taken from a healthy, wakefulness and alert subject, one can find a peak frequency (the spectral component with shows the largest power) in the alpha range (8-13Hz) that for an young adult lies around 10 Hz (see Chapter 3.2). In the literature the term *Individual Alpha Frequency* (IAF) is used by Klimesch and coworkers to indicate that this is the peak frequency of only the alpha rhythm and not of the whole signal, see Fig. 4.1. It is possible, due to for instance neurological disorders, that there is no adequate peak frequency detectable in the power spectrum. The spectrum could be virtually peak-less or contain multiple peaks with almost the same power. In that case one can chose to calculate the gravity (or mean) frequency within the alpha band. The gravity frequency is the weighted sum of the spectral power, divided by the total alpha power

$$\text{Gravity IAF} = \frac{\sum(P_{(f)} \times f)}{\sum P_{(f)}} , \quad (4.1)$$

where $P_{(f)}$ is the power of frequency f and f contains the frequencies within the alpha range.

In Fig. 4.2 two examples of two different subjects are given of a power spectrum computed from 1 second EEG resting period during which the subjects are in a state of alert wakefulness (dotted line) and a 1 second active period in with the subjects had to perform some kind of task. In Fig. 4.2(a) it is clear that there is a peak frequency at 9.8 Hz so there is no necessity to use the gravity frequency. But in Fig. 4.2(b) no distinguished peak frequency is detectable in the alpha range, so the use of the gravity frequency in this case is a very useful method to determine the IAF.

Klimesch and coworkers (see Klimesch [1999] for a review) suggested the use of the IAF as an anchorpoint to individually adjust the alpha and theta band. They defined 4 frequency bands with a width of 2Hz as follows:

- Theta = (IAF - 6Hz) to (IAF - 4Hz);
- Lower1-Alpha = (IAF - 4Hz) to (IAF - 2Hz);
- Lower2-Alpha = = (IAF - 2Hz) to (IAF);

- Upper-Alpha = (IAF) to (IAF + 2Hz).

There is no clear definition of the beta/gamma band based on individual spectral peaks.

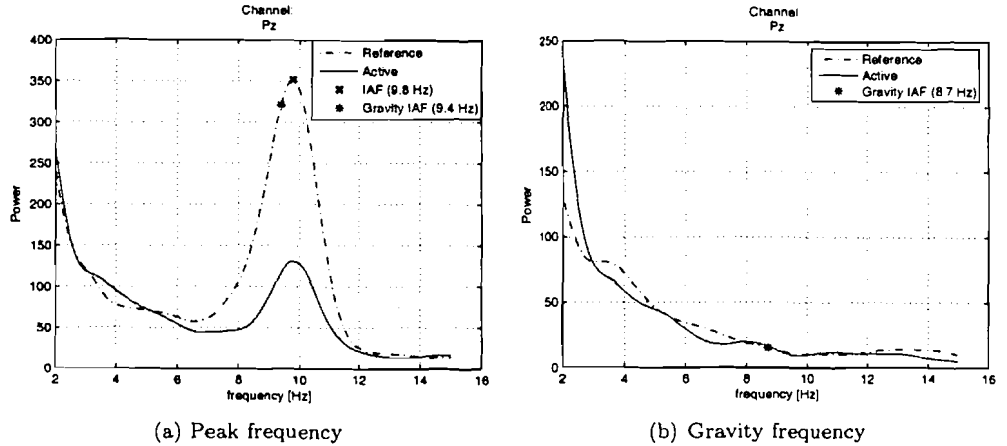


Figure 4.2: Example of determining the individual alpha frequency (IAF) between the alpha range 6-19 Hz. The two graphs are taken from 2 different subjects. The dotted lines are the power spectrum of a subject in a state of alert wakefulness and the bold lines are the power spectrum of the same subject performing some kind of task. In (a) the IAF is easy to determine because there is a clear peak at 9.8 Hz. But in (b) there is no clear peak in the range of 6-13 Hz, here the use of computing the gravity frequency is necessary for determining the IAF.

4.3 Power spectra comparison

A different approach of defining EEG frequency bands is to compare the power spectra of two 1 second EEG periods over the available trials from a specific electrode position and finding statistically significant differences between the two. One period (R) is taken some seconds before an event occurs and is defined as the reference period that is used in the ERD computation (Section 3.4). The other period (A) lies in the active period. This active period can be before an event (planning phase), on an event (during execution) or after an event occurred (recovery phase). From these two periods the power spectra P are computed. The power spectra are then converted to a logarithmic scale because it makes it easier to observe large and small amplitude signals at the same time. The difference between the two logarithmic power spectra is computed together with the 95% confidence interval.

This 95% confidence interval contains the upper and lower limits of which it is for 95% sure that the estimate mean of the samples (μ) lies between these boundaries. The formula for the 100(1- α)% Confidence Interval (CI) of a normal mean and an unknown variance is as follows

$$CI = \left(\bar{x} - t_{\alpha/2, n-1} \cdot \frac{s}{\sqrt{n}}, \bar{x} + t_{\alpha/2, n-1} \cdot \frac{s}{\sqrt{n}} \right), \quad (4.2)$$

with s the standard deviation

$$s = \frac{1}{n-1} \sum_{i=1}^n (x_i - \bar{x})^2, \quad (4.3)$$

where \bar{x} is the mean of all samples, n the number of samples, and $t_{\alpha/2, n-1}$ is the t -distribution or Student's distribution, a variable defined by the t -density function

and of which the value can be found in tables, e.g. Table 4.1 for $t_{0.025,n-1}$ [Ross, 2000].

Table 4.1: *t*-distribution table for 95% CI.

n-1	$t_{0.025,n-1}$
2	4.303
4	2.776
8	2.306
10	2.228
20	2.086
50	2.009
100	1.984
500	1.965
∞	1.960

The difference between the reference and active power spectra either displays a power increase which indicates an ERS or a power decrease which indicates an ERD. The 95% CI can be used to determine the corresponding frequency band.

An example of optimizing individual frequency bands using power spectra comparison is given in Fig. 4.3. In this case an ERS is detectable within the frequency band 1-7Hz and an ERD within 9-13Hz.

4.4 Conclusion

Klimesch and coworkers divided the alpha band in three separate bands that reflects alertness, expectation and task specific aspects effects. They also found a way to define these bands individually with the use of the Individual Alpha Frequency.

With the power spectrum comparison method one is able to find the frequency bands in which an event-related Desynchronization or Synchronization occurs. However, this method gives no background information of what caused this ERD or ERS to evolve.

Most of the symptoms of ADHD are directly or indirectly involved with alertness (see Chapter 2) with are reflected by the lower1-alpha band using the method of Klimisch and coworkers. Furthermore, this method is well investigated and used in several other projects regarding alertness. Therefore the use of the Individual Alpha Frequency method for determining the reactive frequency bands is used for this project.

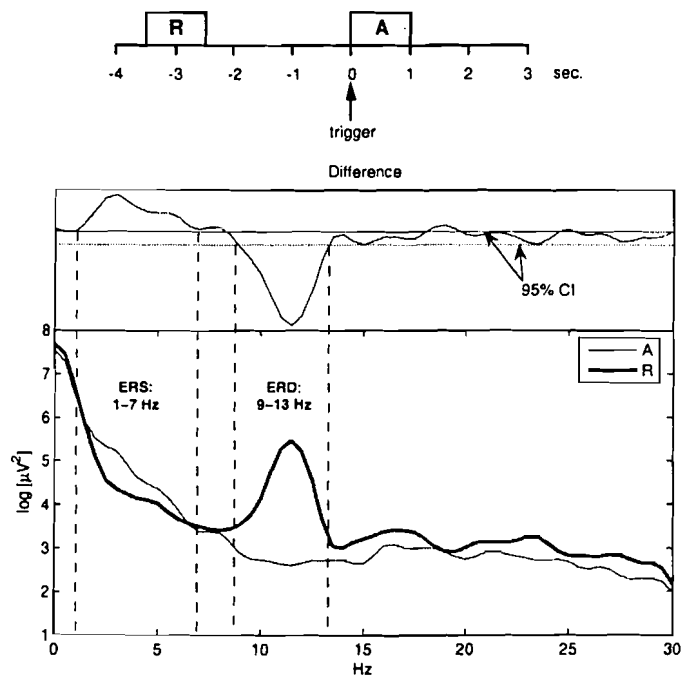


Figure 4.3: Principle for optimizing frequency bands using power spectra comparison. The data is taken from electrode position C3 (10-20 system). The bold line represents the power spectrum of the reference period (R) and the thin line represents the power spectrum of the active period (A; movement of a right hand finger at the trigger). Above the difference between both spectra with 95% confidence limits are given.

Chapter 5

Quantification methods

For a reliable quantification of ERD¹ the number of event-related EEG trials should at least be 30 trials that are synchronously triggered to an event [Pfurtscheller, 1999b]. The time between two consecutive trials must be several seconds to have no interference between the different trials. Because event-related changes in the EEG need time to develop and recover, these trials must have a length of at least some seconds before and after the trigger. In the case of voluntary movement for instance, the used trials could be at least 10 seconds long.

Over the years a number of different methods have been developed for the quantification of ERD as a function of time. In this chapter an overview is given of the most used methods and their properties.

5.1 Classical ERD

In section 3.5 it became clear that when averaging an EEG signal the induced (non-phase locked; ERD) activity deteriorated. However the averaging technique, used for ERP, is a good technique to improve the poor SNR, as explained in section 3.3. One way to solve the problem of deterioration of the non-phase-locked signal and still use the averaging technique is to first square the signal. This way the negative component is set positive and the signal is enhanced when averaged over trials.

The common method to compute the ERD from event-related EEG trials in literature is referred to as the “Classical” method and was first described by Pfurtscheller and Aranibar [1977] and involves the following steps [Pfurtscheller, 1999a]:

1. The trials are bandpass filtered by a selected frequency band of interest. (e.g. lower alpha (8-10Hz))
2. Each sample, from the bandpass filtered trials, is squared to obtain power samples.
3. The power samples are averaged over the total number of trials to improve the SNR.
4. The mean power samples are averaged over a number of samples (interval) to smooth the data and reduce the variability.

¹In this chapter ERD/ERS is referred to as ERD

5. The power samples of each interval will be expressed as a percentage and a reference interval chosen a few seconds before the trigger will be set to zero

$$ERD_{(j)} = \frac{A_{(j)} - R}{R} \times 100\% , \quad (5.1)$$

with

$$R = \frac{1}{k} \sum_{j=n_0}^{n_0+k} A_{(j)} , \quad (5.2)$$

where $A_{(j)}$ is the power at the j -th sample and R is the average power in the reference interval ($n_0, n_0 + k$), averaged over k samples.

The steps 2 and 3 of the classical method can be summarized with the following formula

$$P_{(j)} = \frac{1}{N} \sum_{i=1}^N x_{f(i,j)}^2 , \quad (5.3)$$

where N is the total number of trials and $x_{f(i,j)}$ is the j -th sample of the i -th trial of the bandpass filtered EEG data.

In Fig. 5.1 the steps of the above mentioned procedure are visualized with real EEG data.

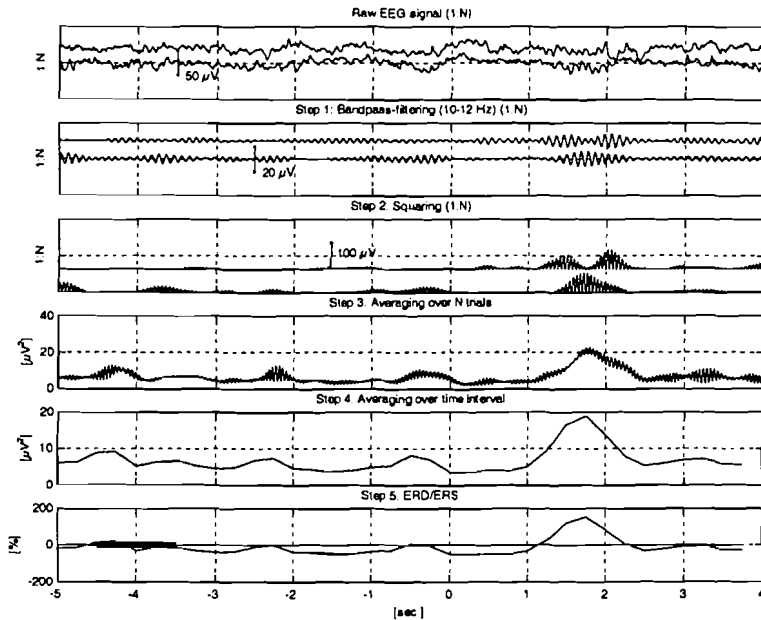


Figure 5.1: Principle of ERD/ERS quantification. The used data is from position C_4 , of the 10-20 system, and the trigger ($t=0s$) is a movement of a right hand finger. In step 1 through 3 only two of the total number of trials (N) taken from one recording session and one electrode position are visualized underneath each other. The signal between the bold-faced line in step 5 is the data with which the reference interval is defined. As can be seen in the last step, there is an increase of bandpower with indicates an event-related synchronization (ERS).

A disadvantage of this ERD technique is the poor temporal resolution of the ERD because the signal has to be averaged over predefined time intervals (step 4) to get statistically reliable responses. Besides, if these intervals are chosen too brief (Fig. 5.2(a)) this results in an oscillating and unstable ERD, if chosen

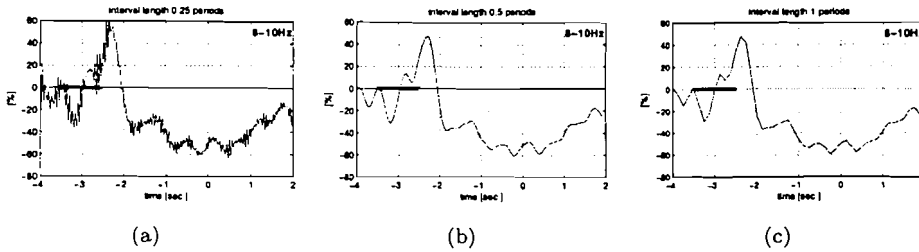


Figure 5.2: Examples of different interval length using 'classic' ERD. The ERD is computed from electrode Pz with an interval length of 0.25 (a) 0.5 (b) and 1 (c) times the period of 8 Hz. The sample frequency equals 512 samples/sec., so the interval length are respective 16, 32 and 64 samples long.

too long (Fig. 5.2(c)) it results in unnecessary reduction of temporal resolution. Knösche and Bastiaansen [2002] have found that the ideal time interval should be half the period of the slowest frequency under study (Fig. 5.2(b)). See Section 5.2 for more information.

Sterman et al. [1996] and Klimesch et al. [1998b] also use the classical method only they use z-transformed power values to quantify the ERD instead of percentage as in the classical method. Klimesch et al. [1998b] termed this method Event-Related band power (ERBP).

There are two variations on the above mentioned ERD computation, namely the Intertrial Variance (IV) and the Temporal-Spectral Evolution (TSE) methods. The difference between these methods can be found in step 2 of the computation. In the block scheme of Fig. 5.3 the difference between the three methods of quantifying ERD are visualized together with the process of ERP.

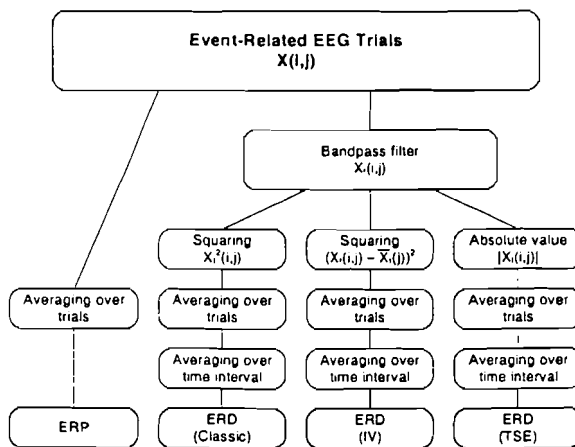


Figure 5.3: Methods for event-related EEG trial processing. The block scheme shows the steps of the classical , intertrial variance (IV) and the temporal-spectral evolution (TSE) methods compared to the event-related potential (ERP).

5.1.1 Intertrial Variance (IV)

With the classical method both phase-locked (evoked, ERP) and non-phase-locked (induced, ERD) activities contribute to the bandpower changes. So it is possible, especially in the lower alpha and/or theta band, where the majority of the ERP power occurs, that an ERP masks an ERD.

The Intertrial Variance method, developed by Kalcher and Pfurtscheller [1995], also uses squaring but with subtraction of the average across trials. The formula of this method is as follows:

$$IV_{(j)} = \frac{1}{N-1} \sum_{i=1}^N \{x_{f(i,j)} - \bar{x}_{f(j)}\}^2, \quad (5.4)$$

with

$$\bar{x}_{f(j)} = \frac{1}{N} \sum_{i=1}^N x_{f(i,j)}, \quad (5.5)$$

where N is the total number of trials, $x_{f(i,j)}$ is the j -th sample of the i -th trial of the bandpass filtered EEG data and $\bar{x}_{f(j)}$ is the mean of the j -th sample average over all bandpass filtered trials.

If we go back to Section 3.3 we can see that $\bar{x}_{f(j)}$ is equal to the calculation of the ERP.

Thus the IV method (Eq. 5.4) is equal to the classical method (Eq. 5.3) except for the fact that in the IV method the ERP component is subtracted from the ERD component.

The advantage of this method compared to the classical method is that only the non-phase-locked activities contribute to the bandpower changes and therefore is more accurate, specially in the lower alpha and/or theta band, than the classical method.

This method is also termed induced band power (IBP; Klimesch et al. [1998b]) method. The difference is that the IBP (like the ERPB, Section 5.1) uses z-transformation of the power values in stead of percentage to quantify the ERD/ERS.

5.1.2 Temporal-Spectral Evolution (TSE)

An other variation on the computation of the ERD as described in step 2 of the procedure in Section 5.1 is the Temporal-Spectral Evolution (TSE) method as proposed by Salmelin and Hari [1994].

Instead of squaring (bandpower) this method uses absolute values of the bandpass filtered EEG data,

$$TSE_{(j)} = \frac{1}{N} \sum_{i=1}^N |x_{f(i,j)}|, \quad (5.6)$$

where N is the total number of trials and $x_{f(i,j)}$ is the j -th sample of the i -th trial of the bandpass filtered EEG data.

The advantage of this method is that the amplitude of the ERD samples are expressed in the same units as the original response so they are directly comparable to, for instance an ERP.

5.2 Hilbert transformation

In an article of Clochon et al. [1996] the use of amplitude modulation (AM) was proposed to quantify the ERD. In this method the envelope of the bandpass filtered event-related EEG signal is estimated based on the *Hilbert Transformation*.

The Hilbert transform of a given signal $s(t)$ is defined as

$$h(t) = \frac{1}{\pi} \int_{-\infty}^{\infty} \frac{s(\tau)}{t - \tau} d\tau = \int_{-\infty}^{\infty} s(\tau) \frac{1}{\pi(t - \tau)} d\tau. \quad (5.7)$$

If Equation 5.7 is compared to the convolution integral

$$s(t) * f(t) = \int_{-\infty}^{\infty} s(\tau) f(t - \tau) , \quad (5.8)$$

the following comparison between the Hilbert transform (Eq. 5.7) and the convolution integral (Eq. 5.8) can be found

$$f(t - \tau) = \frac{1}{\pi(t - \tau)} \quad \{t=t-\tau\} \quad f(t) = \frac{1}{\pi t}. \quad (5.9)$$

This way the Hilbert transform can be written as the convolution

$$h(t) = f(t) * s(t) = \frac{1}{\pi(t)} * s(t). \quad (5.10)$$

The Fourier Transform (frequency domain) of this equation is defined as

$$H(f) = -j \cdot \text{sgn}(f) \cdot S(f) = \begin{cases} -jS(f) & \text{for } f > 0 \\ 0 & \text{for } f = 0 \\ jS(f) & \text{for } f < 0 \end{cases} \quad (5.11)$$

This means that the Hilbert transform can be considered as a filter which simply shifts phases of negative frequencies components by $+90^\circ$ and positive frequencies by -90° . The reason for this conversion is that this way the Hilbert transform is much easier to compute in a software environment.

Now an analytic signal can be constructed from the original signal $s(t)$ and the Hilbert signal $h(t)$

$$s_+(t) = s(t) + jh(t) = m(t)e^{j\omega_0 t} , \quad (5.12)$$

where $m(t)$ is the complex envelope of the absolute value of signal $s_+(t)$

$$m(t) = |s_+(t)| = \sqrt{s_f^2(t) + h_f^2(t)}. \quad (5.13)$$

In Fig. 5.4 the steps of the method based on the Hilbert Transform applied on event-related EEG signals is visualized in a block scheme.

Finally, the ERD referred to as AM-ERD (Amplitude Modulation ERD), is obtained by averaging the amplitude envelope synchronized by repetitive stimulations (trials) and normalized the same way as in the classical method (Eq. 5.1)

$$AM - ERD = \frac{m(t) - m_{ref}}{m_{ref}} \times 100\% , \quad (5.14)$$

where m_{ref} is the average amplitude in a reference interval. In Fig. 5.5, an example of ERD quantification with the use of the Hilbert method is given.

According to Clochon et al. [1996] the Hilbert transform compared to the classical method produces statistically significant results, but the Hilbert method has a much better time resolution. This was contradicted by Knösche and Bastiaansen [2002], who compared the classical ERD with ERD based on the Hilbert transform. In order to compare the time resolution of the different methods they

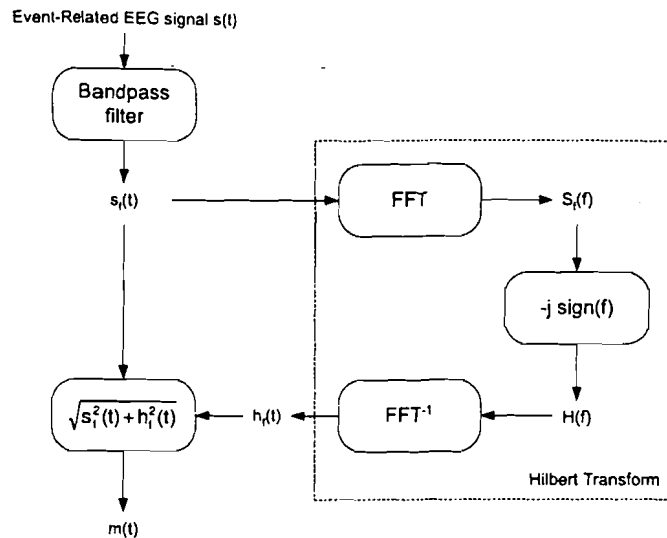


Figure 5.4: Computation of amplitude modulation using the Hilbert Transform. The event-related EEG signal is bandpass filtered and the Fast Fourier Transform is computed, then the real and imaginary parts are inverted and the inverse FFT is computed to obtain the analytic signal $h_f(t)$. Finally, the envelope $m(t)$ is calculated by computing the absolute value of the complex signal ($s_f(t), h_f(t)$).

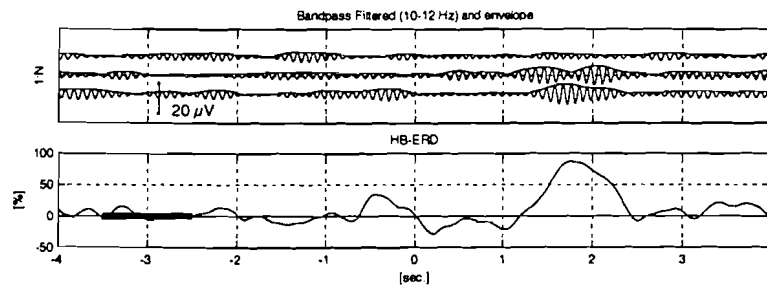


Figure 5.5: Example of Hilbert Transform applied on event-related EEG data (same data as used in Fig. 5.1). In the upper plot bandpass filtered signals with their envelope (computed with the Hilbert Transform) are given. In the lower plot the ERD is computed by averaging the envelope over N trials and applying Eq. 5.14. The signal between the bold-faced line is the reference interval for m_{ref} .

investigated 3 basic dimensions of the methods (accuracy, step response and sensitivity) using simulated data. They concluded that if the time interval (step 4 in Section 5.1) is set to half a period of the slowest frequency component under study, the classical ERD results are in the same range as those of the Hilbert ERD with almost the same time resolution (Fig. 5.6). Only if high sampling frequencies ($>10\text{kHz}$) are used the Hilbert method has a better time resolution.

In spite of this the advantages of this method in comparison with the above described classical, IV and TSE methods is the fact that the Hilbert method automatically adapts the time resolution to any frequency under investigation, and is therefore easier to use.

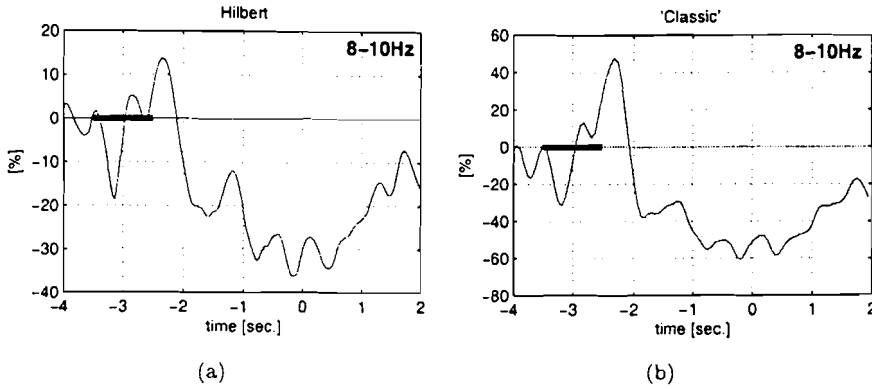


Figure 5.6: (a) Hilbert ERD and (b) classical ERD of position Pz with a bandwidth of 8-10Hz and a sampling frequency of 512 samples/sec.. The classical ERD has an interval length of 0.5 times the period of 8Hz. The amplitude difference between the two is due to the squaring technique applied in the classical method.

5.3 Autoregressive model

To use an autoregressive (AR) model, the event-related EEG trials (which are non-stationary stochastic signals) have to be stationary. To overcome this problem the concept of local stationarity can be used. This concept says that:

”A stochastic process is defined as locally stationary if, within short intervals of time, it behaves very much like a stationary process, although its global characteristics may vary over time” [Pfurtscheller, 1999b].

Therefore the EEG trials have to be divided into segments of the same length, so that within each segment the data is stationary.

If $x(n)$ is the n -th sample of a segment, the AR-model of order p is given by

$$x(n) = \sum_{i=1}^p a_i \cdot x(n-i) + e(n) , \quad (5.15)$$

where a_i are the AR parameters and $e(n)$ is a white noise process with variance σ^2 . The AR parameters can be estimated from the *autocovariance function* by solving the *Yule-Walker* equations. [Florian and Pfurtscheller, 1995]

Once the AR model is estimated, the power spectrum within a segment of the event-related EEG signal can be computed as:

$$S(\omega) = \frac{\sigma^2}{2\pi} \frac{1}{|1 - a_1 e^{-j\omega} - \dots - a_p e^{-j\omega p}|^2} , \quad -\pi \leq \omega \leq \pi , \quad (5.16)$$

where σ^2 is the variance of the white noise $e(n)$.

To analyze event-related EEG data trails with an AR-model, the steps are as follows [Florian et al., 1998]:

1. Trials are divided into segments;
2. For a given segment the autocovariance function is estimated for all trials;
3. These estimates are averaged across trials, giving an average covariance matrix function;

4. Solving the Yule-Walker equations based on the average covariance matrix function.
5. The spectral matrix function is estimated using the autoregressive model. (Eq. 5.15)
6. By repeating steps 1-4 for the sequence of segments chosen in step 1, time courses of power spectra are obtained. (Eq. 5.16)

An example of the time course of a power spectrum of event-related EEG signals computed with the use of an AR-method is given in Fig. 5.7.

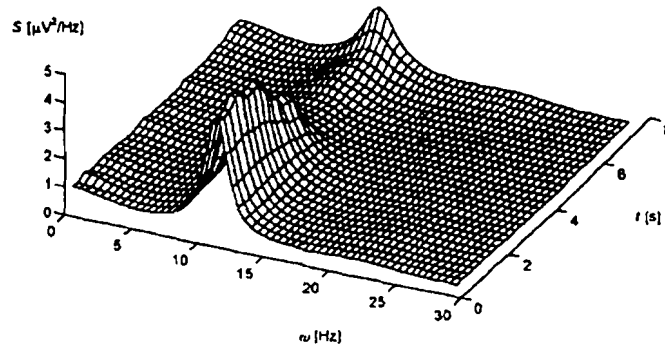


Figure 5.7: Example of power spectra of event(movement)-related EEG data. The signal is taken from position C3 (10-20 system) where at time $t=5$ a movement of the right finger was performed. In the frequency band from 5-15Hz a decrease of power starts at about 2 seconds prior to movement, indicating an ERD (From Florian and Pfurtscheller [1995]).

The advantage of the AR method is that it has a better spectral resolution than the above described methods. The disadvantages of this method, beside the fact that the AR method is computationally very expensive, are that two parameters have to be chosen to get a reliable and correct computation of the ERD. These parameters are:

- The length of the data segments.
If long segments are chosen the time resolution is low but the reliability is poor (poor biased) because of the locally stationary criteria. If the segments are short the reliability is good (unbiased) but the time resolution is high. This means a balance must be found between time resolution and reliability.
- The order of the AR-model.
In general, if the order for the AR-model is chosen to low the spectral components that are too close to each other are smeared together, while too high will cause fake peaks in the spectrum.

5.4 Conclusion

With the classical method the time resolution of the ERD depends on the length of the time interval. The advantage of the Hilbert method is that it automatically adapts the time resolution to any frequency under investigation. So this way there is no need for manual adjustment of settings, which is a time consuming activity. Still the classical method has the advantage that it is very easy to compute and

in literature this method is a common used technique, so the results could be compared with earlier findings.

As mentioned in the introduction, attention process is an important aspect within ERD research of ADHD. The fact that attention processes are reflected by the ERD computed within the lower alpha frequency range, in which it is likely to get interference of ERP's, the use of the intertrial variance method is advisable.

As can be seen all these three methods have there own advantage that could make it useful within the ERD study of ADHD. Therefore the quantification methods classical, intertrial variance and Hilbert are used for the implementation of the ERD software in MatLab. Another reason for using more than one method is that this way the results form the different methods can be compared to each other. The Temporal-Spectral Evolution (rarely used so not comparable) and the Autoregressive method (intensive computation and 2 settings) are not used in the implementation.

The choices for the used methods are made after discussions with my supervisor dr. ir. P. Cluitmans.

Chapter 6

Implementation ERD/ERS Algorithm (MatLab)

For the computation of an ERD/ERS a software application (ERDtool) has been designed in MatLab that uses the Classical, Intertrial Variance and Hilbert methods. This tool is based on the data that is available for this project and is used for the ADHD research described in Chapter 7 and 8. In Appendix A the different options and panels of this tool are described.

The first section of this chapter focuses on bandpass filtering of EEG data in a MatLab environment used in the computation of the ERD/ERS. In the second section the steps of the implemented algorithms are described.

6.1 Bandpass filtering

One important feature of ERD/ERS is that it is highly frequency specific. Therefore the event-related EEG signals have to be bandpass filtered in different frequency bands. This is done by using a Fast Fourier Transform (FFT) filter instead of a more common used and faster, Finite Impulse Response (FIR) filter. The reason for this is that a FIR filter changes the phase of the signal, whereas a FFT filter leaves the phase information unchanged. This means that if a FIR filter is used on an event-related EEG signal, which is non-phase-locked to the event, it would change the phase information of the signal and make the signal unusable. Besides, the FFT is also used to compute the envelop using the Hilbert method thus it is logical to filter the EEG signal and compute the envelop both in the frequency domain.

6.1.1 Fast Fourier Transform

By using the Fourier Transformation, a time continuous signal in time domain can be transformed to the frequency domain. This is accomplished by decomposing the original time-based signal into a series of sinusoidal terms, each with a unique magnitude, frequency and phase. Since, the event-related EEG data used in this project is a time-discrete (sampled) signal, the *Discrete-time Fourier Transform* (DFT) is used.

If the signal has a segment duration of T_0 and is sampled at a frequency f_s ,

the number of samples within the signal is equal to N:

$$N = T_0 \cdot f_s. \quad (6.1)$$

Given a sequence of N samples $x[n]$ ($0 \leq n \leq N - 1$), the DFT is defined as $X[k]$:

$$X[k] = \sum_{n=0}^{N-1} x[n] e^{(-j2\pi kn/N)}, \quad 0 \leq k \leq N - 1. \quad (6.2)$$

The index k defines the different frequencies (f_k) associated with the spectral component $X[k]$:

$$f_k = \frac{k}{T_0}, \quad 0 \leq k \leq N - 1. \quad (6.3)$$

To reconstruct the original signal the *inverse DFT* or *IDFT* is used:

$$x[n] = \frac{1}{N} \sum_{k=0}^{N-1} X[k] e^{(j2\pi kn/N)}. \quad (6.4)$$

The lowest frequency defined by the length of the data set, sample length N, is called the *fundamental frequency*. It has exactly one cycle per total number of samples (N).

The disadvantage of the DFT transform given by Equation 6.2, is that in practice for large signals it can take considerable time to compute the result. A much faster algorithm is the *Fast Fourier Transform* (FFT). This FFT algorithm reduces the number of calculations of a n-point fourier transform. For instance, it reduces the number of multiplications to about $(n/2) \log_2(n)$. In comparison, if a DFT is computed on a signal of 1024 samples it needs 1,048,576 multiplications. If the same signal is computed with a FFT the number of multiplications will be reduced to 5,120. This is a factor 200 improvement. The only difference between FFT and DFT is that FFT decomposes the N-point DFT computation into computations of smaller-size DFTs and takes advantage of the periodicity and symmetry of the complex number $e^{(-j2\pi kn/N)}$. One of the requirements to use the FFT is that it requires a total number of data points (samples) that is equal to 2^n (eg. 512, 1024, 2048, etc.). If the signal contains less samples than required by the FFT, samples of the value zero will be added, to the signal until it has the desired length. This is called zero padding and is also used by the `fft.m` function in MatLab.

6.1.2 The FFT filter

Filtering of data using an FFT filter is accomplished as follows: first the FFT of a signal is computed and, within the frequency domain, all spectral coefficients outside the desired frequency band are set to zero. The filtered data is then transformed back to the time domain with the *Inverse FFT* or *IFFT*. What remains is a bandpass filtered signal of the original data.

However, a disadvantage of FFT (and the DFT) is, that if the FFT is applied to a data set that contains non-harmonic components an error known as spectral leakage occurs. An example of this phenomenon is shown in Fig. 6.1(b), where the top graph shows a section (between 2 and 5 sec.) of the signal $s[n] = \sin(\frac{2\pi n}{512} \cdot 3.7) + \sin(\frac{2\pi n}{512} \cdot 5.5) + \sin(\frac{2\pi n}{512} \cdot 7.1)$. The signal is sampled at 512 Hz and visualized in Fig. 6.1(a). If a FFT of this section of the signal is computed a peak at 3.7, 5.5 and 7.1 Hz is expected in the spectrum. However because the signal contains non-harmonics there is a wide area of peaks around the 3.7, 5.5 and 7.1

6.1. Bandpass filtering

Hz as can be seen in the FFT graph of Fig. 6.1(b). If this signal is bandpass filtered between 5 and 6 Hz and transferred back to the time domain one would expect to retrieve a 5.5 Hz sine wave. However, because of the leakage there is a disturbance in the 5.5 Hz retrieved signal. This is shown in the two bottom graphs of Fig. 6.1(b).

Spectral leakage occurs because the DFT actually finds the frequency components of a signal which consists of endlessly repeated copies of the sampled signal with infinite width. For frequency components of the signal for which there is a "pattern match" at the two ends (i.e. harmonics of the fundamental frequency with complete periods), there is no problem and the spectrum will show a nice peak. However, for the non-harmonic components there is a mismatch where adjacent sections join. The sudden jump or discontinuity created by the pattern mismatch gives rise to spurious components in the spectrum of the signal, causing a particular frequency component of the signal to appear not as a single sharp line but as a spread of frequencies, roughly centered around where the frequency component should be located, somewhere between the two nearest frequency channels on either side.

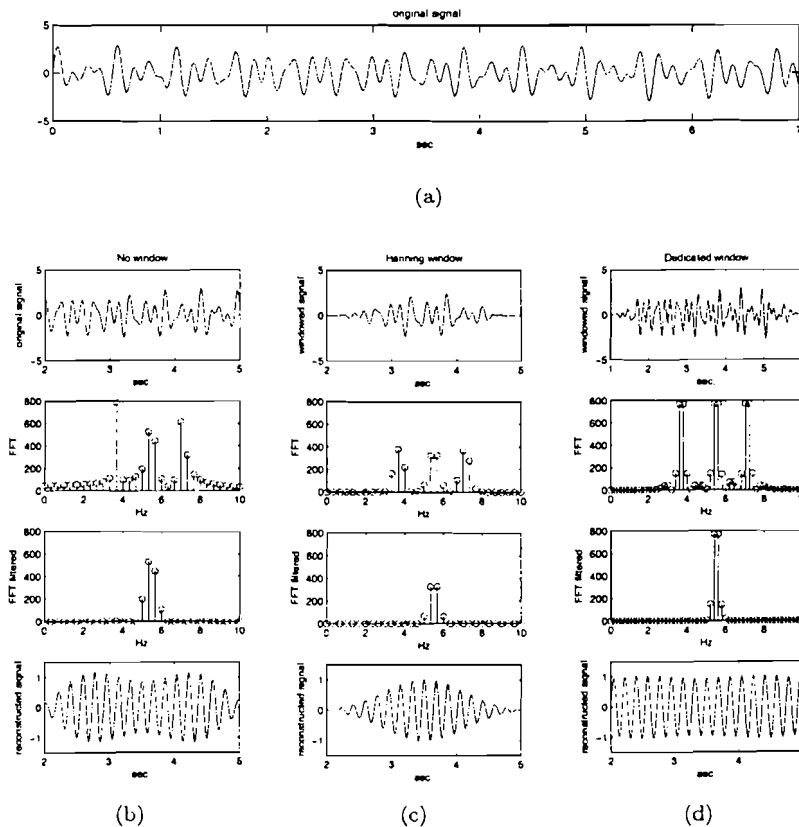


Figure 6.1: Example of different windows. The original signal (a) is $s[n] = \sin(\frac{2\pi n}{512} \cdot 3.7) + \sin(\frac{2\pi n}{512} \cdot 5.5) + \sin(\frac{2\pi n}{512} \cdot 7.1)$ and sampled at a frequency of 512 Hz. The bandpass filter was set to filter between 5 and 6 Hz. (b) The original signal between 2 and 5 sec. and (c) the same signal multiplied with a Hanning window with their FFT, filtered FFT and IFFT of the filtered FFT. (d) The original signal between 1 and 6 sec. multiplied with the dedicated window with its FFT, filtered FFT and the IFFT of the filtered FFT between 2 and 5 sec.

The event-related EEG data is stochastic, which means that it always contains frequencies that are not exact harmonics of the fundamental frequency. This introduces spectral leakage which has to be reduced. This is done by using a window technique. These windows are data blocks that are shaped in a way to be exactly or approximately zero at the beginning and end of the data block and have special designed shapes in between. Such a window is multiplied with the original signal so that the sampled signal, "fades" in and out rather than starting and stopping abruptly. This reduces the effect of the discontinuities where the mismatched sections of the signal join up, and hence also the amount of leakage. An example of such a window, called the Hanning window, is given in Fig. 6.2(a). In Fig. 6.1(c) the top graph is the result of a multiplication of the original (non-harmonic) signal between 2 to 5 sec of the signal given in Fig. 6.1(a) with a Hanning window. This way the spectral leakage of the FFT of this signal (second graph of Fig. 6.1(c)) has been reduced.

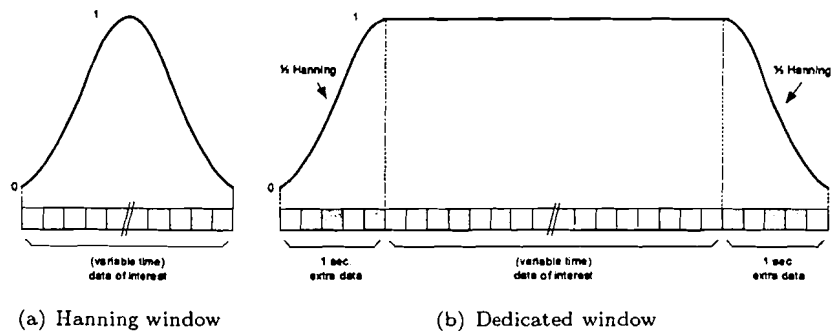


Figure 6.2: Hanning and dedicated window

The only problem of the use of windows is that when the signal is filtered and transformed back into the time domain using an IFFT, the information of the signal is changed by the multiplication with the window. For instance, in Fig. 6.1(c) the last graph is the IFFT of the Hanning windowed signal bandpass filtered between 5 and 6 Hz. The problem is that it is not possible to reconstruct the original signal before it was windowed. In case of filtering the data, the signal has to be reconstructed without the loss of data at the beginning and ending of the signal.

To accomplish this, a different window was designed for the current project. It consists of a 2 second Hanning window that is cut in half. In between the parts, an array of ones is added with a length equal to the data of interest, Fig. 6.2(b). The data of interest has to be expanded by one second of data previous to the data of interest and one second after. In Fig. 6.1(d) the signal of Fig. 6.1(a) between 1 and 6 sec. is used. Thus the signal used in Fig. 6.1(c) is expanded by 1 sec. of data at both ends, compared to Fig. 6.1(b) and 6.1(c). In the top graph of Fig. 6.1(d) the signal is multiplied with the dedicated window, and the FFT of the signal is taken and filtered between 5 to 6 Hz. If the filtered spectrum is transferred back to the time domain and we leave out one second at the beginning and at the end, the 5.5 Hz sine wave is retrieved (bottom graph). The slight interference of the filtered signal is due to the spectral leakage that, despite the use of the window, never can be remove completely.

6.2 ERD/ERS algorithms

In the next sections the implemented ERD/ERS algorithms using the Classical, Intertrial Variance and Hilbert methods are described for a set of trials containing raw EEG data that is time-locked to an internal or external event, taken from one electrode position (e.g. Pz).

6.2.1 Classical method

For the computation of the ERD/ERS using the Classical method, the following steps are performed:

1. Bandpass filtering:
 - (a) Transforming the raw data to the frequency domain using the FFT and the dedicated window;
 - (b) Setting the spectral coefficients outside the predefined frequency band to zero;
 - (c) Transforming the bandpass filtered data back to the time domain using the IFFT;
2. Squaring the samples to obtain power samples;
3. Averaging the power samples over the total number of trials;
4. Dividing the average trial into short time intervals and return the mean of the power samples within these intervals;
5. Expressing the averaged samples of each time interval as a percentage relative to a chosen reference period.

6.2.2 Intertrial Variance method

The Intertrial Variance and Classical method are almost the same, the only difference lies in step 2 and 3 of the below mentioned performed steps. The IV method can then be summarized as follows:

1. Bandpass filtering (same as in the Classical Method);
2. Computing the mean of all the bandpass filtered trials within the EEG data of the electrode position which yields to a bandpass filtered ERP;
3. Subtracting the bandpass filtered ERP from each single trial;
4. Squaring the samples of the subtracted trials to obtain power samples;
5. Averaging the power samples over the total number of trials;
6. Dividing the average trial into short time intervals and return the mean of the power samples within these intervals;
7. Expressing the averaged samples of each time interval as a percentage relative to a chosen reference period.

6.2.3 Hilbert method

The algorithm using the Hilbert transform uses the following steps for the computation of the ERD/ERS:

1. Estimating the envelope of the bandpass filtered data:
 - (a) Transforming the raw data to the frequency domain using the FFT and the dedicated window;
 - (b) Setting the spectral coefficients outside the predefined frequency band to zero;
 - (c) Performing the Hilbert transform ($= -j \cdot \text{sign}(x)$) on the bandpass filtered samples
 - (d) Transforming the Hilbert transformed data back to the time domain using the IFFT, and thus obtaining the envelopes of the bandpass filtered trials;
2. Averaging each sample of the envelope in each trial over the total number of trials;
3. Expressing the averaged samples as a percentage relative to a chosen reference period.

Chapter 7

EEG Data

7.1 Subjects

The subjects in this project consisted of 3 children with a diagnosis of ADHD and 3 control subjects (all boys). All children were right handed. The mean (M) age and standard deviation (S.D.) of the ADHD and Control group together were $M = 12.33$ and $S.D. = 1.63$, respectively. The children of the ADHD group had the age of 10.5, 12.08 and 14.25 years, were the main age and standard deviation were $M = 12.28$ and $S.D. = 1.88$, respectively. The ADHD children were clinically diagnosed according to the DSM-IV criteria [American Psychiatric Association, 1994]. Within the ADHD group no distinction was made between the three classifications inattention, hyperactivity/impulsivity and the combined ADHD. In the control group the age of the children was 10.5, 12.67 and 14 years, where the main age and standard deviation were $M = 12.39$ and $S.D. = 1.77$, respectively. All ADHD subjects did not use medication for 1 or 2 days prior to the experimentation day.

7.2 Electrophysiological recordings

The EEG activity was recorded using easy cap sintered Ag-AgCl ring electrodes from 21 scalp locations: Fp1, Fpz, Fp2, F7, F3, FZ, F4, F8, T7, C3, Cz, C4, T8, P7, P3, Pz, P4, P8, O1, Oz and O2, according the international 10-20 system by means of an electrocap. The electrode impedance was kept below 10 k Ω . The EEG data was continuously recorded using a CogniTrace EEG-ERP acquisition system interfaced with the eeMagine/ANT-software.

EEG signals were referenced to the right mastoid electrode and an average reference was used. EEG signals were amplified, low-pass filtered at 256 Hz and the DC offset was removed. The EEG data was then digitized on-line at a sampling rate of 512 Hz and stored for off-line processing and analysis.

7.3 Procedure and task

Both the data of ADHD and control subjects were recorded in a single session lasting approximately 1.5 hours. The task they had to perform was the AX continuous performance task (CPT-AX) [Bekker et al., 2004], which has been widely applied both inside and outside the context of behavioral disturbances. The uppercase letters A, B, C, D, E, F, G, H, J, L and X were presented on a screen.

The letters appeared for 200 ms and the inter-stimulus interval is approximately 2200 ms. Subjects were instructed to press a button with their righthand (because all subjects were right handed) when the letter X followed the letter A. The letters H, X and A appeared with a frequency of 20%. The remaining letters B, C, D, E, F, G, J and L appeared with a frequency of 10%. 75% of the times an A appeared, it was followed by an X. The stimuli can be categorized as follows: 'Cue' (A), 'NoCue' (B, C, D, E, F, G, H, J and L not preceded by an A), 'Go-stimulus' (X preceded by an A), 'NoGo-stimulus' (B, C, D, E, F, G, H, J and L preceded by an A) and 'X-only' (X not preceded by an A). First, the subjects received a practice block lasting about 1.5 minutes, depending on the subject it could also be shorter.

During the recording and procedure, the child was sitting in a comfortable chair in front of a computer screen at a distance of 50 cm.

7.4 Data pre-processing

Trial

The recorded EEG data was first bandpass filtered from 0.3 to 30 Hz using the eeMagine/ANT-software. From this bandpass filtered EEG data trials (data-blocks) that consists of samples taken within a time span of 4 seconds before and 2 seconds after the stimulus X appearing after an A ('Go-stimulus'). This means that the data within the trials contain the moments between the appearance of a 'NoCue' followed by a 'Go-stimulus'.

Artefact detection

During an EEG recording session it is most likely that the electrical activity contains components that do not originate from the brain. These disturbances are called *artefacts*. There are three types of artefacts that frequently occur during EEG recording, namely muscle movement, electrode movement and eye movement and/or blink activity (ocular artefacts). The muscle and electrode movement can be reduced by placing the subject in a comfortable chair in a resting position. However, for most subjects it is very hard to control blinks and eye movement adequately for long recording sessions. It is known that ocular artefacts are much more frequent in children than in adults. Above all, half of the children included in the current study have a hyperactive disorder which means for them it is even harder to concentrate on not moving or blinking their eyes. Because these artefacts are mostly larger (order 100–200 μ V) than the EEG signal (order 10–60 μ V), they can mask the desired EEG signal. Therefore EEG data containing an artefact has become useless for further analysis and has to be removed from the data-set.

One problem with eye movement or blinking is that these artefact signals decrease rapidly over the skull with increasing distance from the eyes. Besides, when a subject receives a visual trigger during event-related research, a reaction to the trigger is often a blink with the eyes which results in an artefact. The problem here is that the artefact occurs at a moment within the EEG data set (shortly after the trigger/event) that is of great interest for event-related analysis. Therefore, the artefact detection of the EEG data is divided into two sets of electrode positions. The first set consists of the electrode positions Fp1, Fpz and Fp2 (FrontoPolar), the second set include the other electrode positions within the international 10-20 system. This way the eye movement/blink can be detected by

the FrontoPolar electrodes which are positioned close to the eyes and where the artefact signal is still strong enough to be measured and can be distinguish from the EEG signal. Moreover, the artefact detection at the FrontoPolar electrodes can be set more sensitive than for the other electrodes. Using this approach we make sure that also small eye movements/blinks which interfere with the actual EEG signal are detected and no trials are unnecessary excluded because of a too sensitive detection of artefacts over the whole skull.

The trials where the peak-peak value exceeds $140\mu V$ for the FrontoPolar and $300\mu V$ for the other electrode positions were considered to be not artefact-free and under those conditions the entire trial of all electrode positions were excluded for further analysis. This ensures that the total number of available trials for all electrode positions remain equal. The total number of artefact free trials that are used for the quantification of the ERD/ERS varies from 30 to 56.

7.5 Data analysis

7.5.1 Determination of the reactive frequency bands

For the determination of the reactive frequency bands the method of Klimesch et al. [1998b] was used. This method is described in Section 4.2. It uses the Individual Alpha Frequency as a reference point for adjusting the different frequency bands. The way to determine the IAF can be done using different procedures, each of which will be given here.

Eyes closed procedure

In this procedure the approach outlined by Posthuma et al. [2001] was followed. They used the EEG recording of an eyes-closed (EC) condition to determine the maximum power within the frequency of 7 to 14 Hz (alpha band). In this project, for each subject the power density spectrum was computed using a Fast Fourier Transform applied on 2 minute eyes-closed EEG recording of the electrode positions O1, Oz and O2. An artefact detection was performed on the 2 minutes of eyes-closed EEG recording, in which the peak-peak value of the eyes-closed EEG had to be below $300\mu V$. The IAF of the power spectra was determined as the highest peak within the frequency range of 7 to 14 Hz.

Single trial procedure

In the article of Klimesch et al. [1998a], Klimesch and co-workers used a method to determine the mean IAF to find the reactive frequency band. They first computed the power spectrum over an entire trial and determined the IAF for that trial. This was done for all the trials of each electrode position, in this case F3, F4, Cz, Pz, O1, and O2. The mean IAF was then computed by averaging the IAF over all trials and electrode positions. The mean IAF was the anchor point for the frequency bands of all the subjects.

Reference period procedure

The IAF is determined by comparing the power spectrum of a reference period to that of an active period, as explained in Section 4.2. In this case the reference period (R) was chosen from 0.5 s to 1.5 s of the artefact free trials determined in Section 7.4. For the active period two periods were chosen, period A1 was chosen right before an X appeared on the screen (3 to 4 s) and period A2 represents the

period right after an X appeared (4 to 5 s) of the same trials as the reference period. In Fig. 7.1 the periods are visualized.

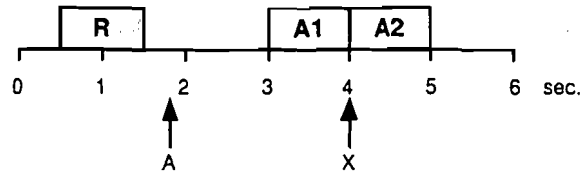


Figure 7.1: Visual representation of the periods R, A1 and A2 within a trial.

The power spectra of the 3 periods within the trials of the electrode positions F3, F4, Cz, Pz, O1 and O2 are computed. The spectra of the different trials of each electrode position were averaged and visualized. The highest peak within the frequency band 6-13 Hz of the reference period was determined as the IAF.

7.5.2 ERD quantification

For the computation of the ERD/ERS the Classical, Intertrial Variance and Hilbert method were used, as discussed in Chapter 5.

In the first steps of all three methods the artefact free trials were filtered with a fast Fourier transform (FFT) filter in the four different frequency bands: theta (IAF-6 Hz to IAF-4 Hz), lower1-alpha (IAF-4 Hz to IAF-2 Hz), lower2-alpha (IAF-2 Hz to IAF) and upper alpha (IAF to IAF+2 Hz). The FFT filter used is described in Section 6.1. The other steps of the ERD computations Classical, Intertrial Variance and Hilbert method are described in Sections 6.2.1, 6.2.2 and 6.2.3, respectively.

One step of the Classical and Intertrial Variance method requires dividing a trial into intervals and averaging the samples over time within these intervals, in order smooth the data and reduce the variability, see Section 5.1. The optimal length of these intervals is half a period of the slowest frequency component under study [Knösche and Bastiaansen, 2002]. In this project the interval length is chosen equal for each frequency band (e.g. theta band), see Table 7.1. The length of the intervals are chosen at the lowest frequency of that specific band determined by the IAF. Because the sample rate lies at 512 Hz and the data length is in the order of seconds the choice was made to only use interval length of 2^n samples, where n are real numbers, so the complete data can be averaged over the same interval length.

Table 7.1: Interval length for each frequency band.

Frequency Band	Interval Length
Theta	128 samples
Lower1-Alpha	64 samples
Lower2-Alpha	64 samples
Upper-Alpha	32 samples

The reference period needed to express the ERD/ERS as a percentage taken from 500 ms tot 1500 ms from the beginning of the trials, and lies between a 'NoCue' letter and the 'Cue' letter A. Because the time between the appearance of the letters is the same, the subject can estimate the appearance of a new letter. Therefore during this reference period the subject is in a state of resting readiness and makes it a good reference for the active period between the 'Cue' A and the X.

Chapter 8

Results

8.1 Eyes closed procedure

In Table 8.1 the IAF found within the 2 min eyes closed data for each subject is given for the electrode positions O1, Oz and O2. After visually comparing the power spectra of these three positions, it was concluded that in most cases the electrode position Oz showed the clearest peak, therefore the ERD/ERS was computed using the frequency bands determined by Klimesch and co-workers with the IAF of electrode position Oz.

Table 8.1: IAF determined by finding the peak frequency within the power spectrum of 2 min eyes closed data.

Subject	Individual Alpha Frequency (IAF)			
	O1	Oz	O2	Mean of Oz (S.D.)
ADHD 1	8	8.4	7.9	9.47 (1.01)
ADHD 2	9.5	9.6	9.7	
ADHD 3	10.4	10.4	10.3	
Control 1	9.9	9.9	10	9.8 (0.46)
Control 2	10.2	10.2	9.9	
Control 3	9.3	9.3	9.3	

After computation of the theta, lower1-alpha, lower2-alpha and upper-alpha ERD/ERS the results of the ADHD subjects was compared to those of the control subjects. Especially in the lower1-alpha band, which represents visual attention, differences between the ADHD and the Control subjects were expected. However, no distinctive differences between the ADHD and the control subject were found. Moreover no similarities were found between the 3 control subjects.

Comparison between the mean of the IAF of the ADHD and the control groups of electrode position Oz reviews, that the mean IAF of the control group is slightly higher than that of the ADHD group. Besides, the IAF of O1, O2 and Oz between ADHD group lie further apart then in the control group, as can be seen in the standard deviation of Oz in Table 8.1.

8.2 Single trial procedure

Table 8.2 displays the results of the IAF found within the 6 s trials of each of the three ADHD and control children. The mean IAF of the ADHD group is lower than of the control group. Moreover, the difference between the two is even higher than the difference between the two groups of the previous procedure, of which the results are shown in Table 8.1. The standard deviation however, is almost equal in both groups.

Table 8.2: IAF determined by finding the peak frequency within the power spectrum of a single trial and averaged over the total number of trials.

Subject	Individual Alpha Frequency (IAF)						Mean (S.D.)	
	F3	F4	Cz	Pz	O1	O2	electrode positions	subjects
ADHD 1	7.2	7.4	6.9	6.9	8.1	8.1	7.43 (0.55)	7.91 (0.88)
ADHD 2	7.2	7.8	7.1	8.6	9.3	9.4	8.23 (1.02)	
ADHD 3	7.1	7.1	7.5	8.7	9.1	8.9	8.07 (0.61)	
Control 1	8.2	8.2	8.1	9.2	9	9.5	8.7 (0.61)	9.01 (0.85)
Control 2	9.4	9.7	9.7	10.1	10.3	10.2	9.9 (0.35)	
Control 3	8.1	8.1	9.6	7.6	8.4	8.8	8.43 (0.69)	

The frequency bands for computing the ERD/ERS were determined individually by averaging the IAF over the electrode positions (Table 8.2) for each subject using the method of Klimesch. However, no distinctive differences in the ERD/ERS could be found to distinguish ADHD subject from control subjects with these individual frequency bands.

From the article of Klimesch et al. [1998a], from which this procedure originates, it is not clear if the ERD/ERS was computed with individual determined frequency bands or that one averaged frequency band was used for all subjects. Therefore, the ERD/ERS was also computed with a fixed frequency band for all subjects as follows. The mean IAF over all subjects (= 8.5 Hz) was taken as a reference to determine the following frequency bands: theta 2.5 - 4.5 Hz, lower1-alpha 4.5 - 6.5 Hz, lower2-alpha 6.5 - 8.5 Hz and upper-alpha 8.5 - 10.5 Hz. The ERD/ERS of all subjects was computed for those frequency bands. Within the theta, lower2-alpha and upper-alpha no distinctive differences between the ADHD and the control subject were found. However, within the lower1-alpha there was a significant higher synchronization (ERS) for the ADHD group at electrode position Fz at the appearance of an A and at the appearance of an X on the screen, as shown in Fig. 8.1. To explain this higher ERS more research is required on more subjects.

8.2. Single trial procedure

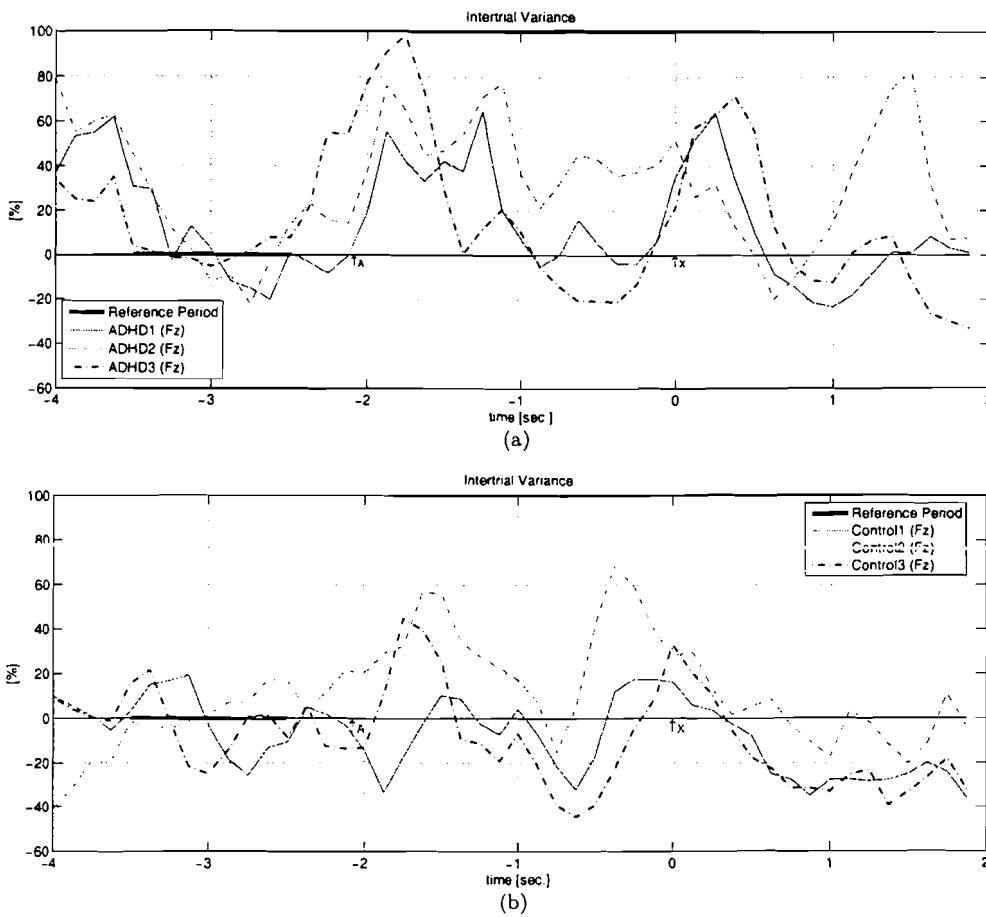


Figure 8.1: Results of the ERD/ERS computed at Fz with the lower1-alpha (4.5 - 6.5 Hz) frequency band. (a) ERD/ERS of the 3 subjects of the ADHD group showing a high synchronization at trigger A and X. (b) ERD/ERS of the 3 subjects of the control group showing a smaller synchronization at trigger A and X.

8.3 Reference period procedure

In Table 8.3 the results are shown of the IAF determined from the power spectrum of the 1 s reference periods for each subject.

Table 8.3: IAF determined from the power spectra of the 1 s reference period and compared to the peak of the two active periods for 6 electrode positions and all subjects.

Subject	Individual Alpha Frequency (IAF)						Mean (S.D.)	
	F3	F4	Cz	Pz	O1	O2	electrode positions	subjects
ADHD 1	6.3	6.4*	6.4	6.1	7.9*	8*	6.85 (0.86)	7.89 (1.68)
ADHD 2	6.5	6!	9.1!*	9.1	9.3	9.2		
ADHD 3	5.1	6.9!*	10.2	10.1	9.7*	9.8*		
Control 1	9.2*	9.6*	9.1*	9.6	9.5*	9.2*	9.32 (0.22)	9.76 (0.37)
Control 2	10*	10*	10.2	10.1	10.4	10.1*		
Control 3	9.7*	9.8*	9.9	9.9	9.6*	9.6*		

!, more than 1 peak was found, highest is taken

*, no equal peak in Active period 2

Just as the other procedures the mean of IAF of the ADHD group is again lower and the standard deviation is higher than of the control group. Moreover, this procedure shows that especially in the frontal region (F3 and F4) the IAF of the ADHD group is significantly lower than that of the control group. This is illustrated in the bar graph given in Fig. 8.2.

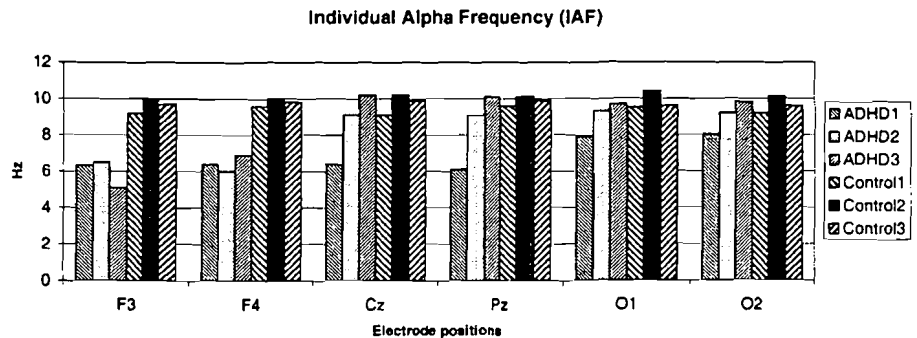


Figure 8.2: Bar graph of the Individual Alpha Frequency (IAF) found with the reference period procedure.

The ERD/ERS in this procedure was computed using the frequency bands determined by the mean IAF of the electrode positions for each subject. Similar to the results described in Section 8.2 no significant differences were found between the ADHD and the control subjects.

The power spectrum of a reference period was visually compared with that of 2 active periods with a length of 1 second, in which one active period is taken preceding the target X and the second following this target. The results were that the active period 1 showed nearly the same peak as the reference period in every

investigated electrode position and subject. However, the power spectrum of the active period 2 did not always follow the power spectrum of the reference period, as Fig. 8.3(a) illustrates for electrode position F4 from control subject 3.

In Table 8.3 the IAFs of the reference periods that were not followed by the active period 2 are indicated by (*). One can see that within the ADHD group this is found less often than in the control group, especially in the frontal region.

It is also possible that more than one peak is found in the reference period as illustrated for electrode position F4 from ADHD subject 2 Fig. 8.3(b), in this case the highest and clearest peak is given as the IAF together with the symbol (!). This was only seen in ADHD subjects 1 and 2. Further research in comparing the reference period with the 2 active periods is necessary to explain the results of this comparison.

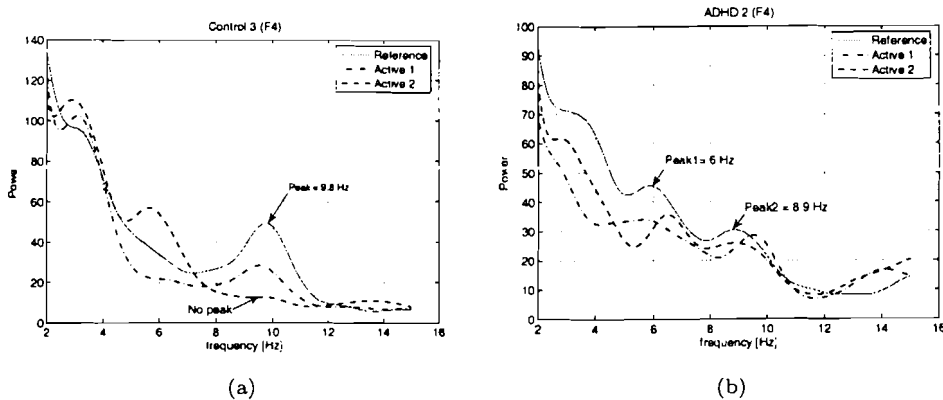


Figure 8.3: Examples of the comparison of a reference period with 2 active periods. (b) Example from subject control 3 with a clear peak at 9.8 HZ but no reaction of active period 2; (c) Example of the occurrence of 2 peaks from subject ADHD 2.

8.4 Intertrial Variance compared to Classical method

To compare the results of computing ERD/ERS using the Intertrial Variance method rather than the Classical method for lower frequency bands, both methods are used to compute the ERD/ERS for a low and a high frequency band. This should illustrate the interference of an evoked-activity (ERP). The results are displayed in Fig. 8.4. The interference is clearly visible in low frequency ERD/ERS of Fig. 8.4(a) and Fig. 8.4(b). However, for higher frequency bands the Intertrial Variance and the Classical method Fig. 8.4(c) and Fig. 8.4(d) show almost the same reaction.

For the Hilbert method the same reaction is expected as for the Classical method because like the Classical method the Hilbert method does not take into account the evoked activity. But because the values of the ERD/ERS of a Hilbert method differ from those of the Intertrial Variance and Classical method no comparison can be made.

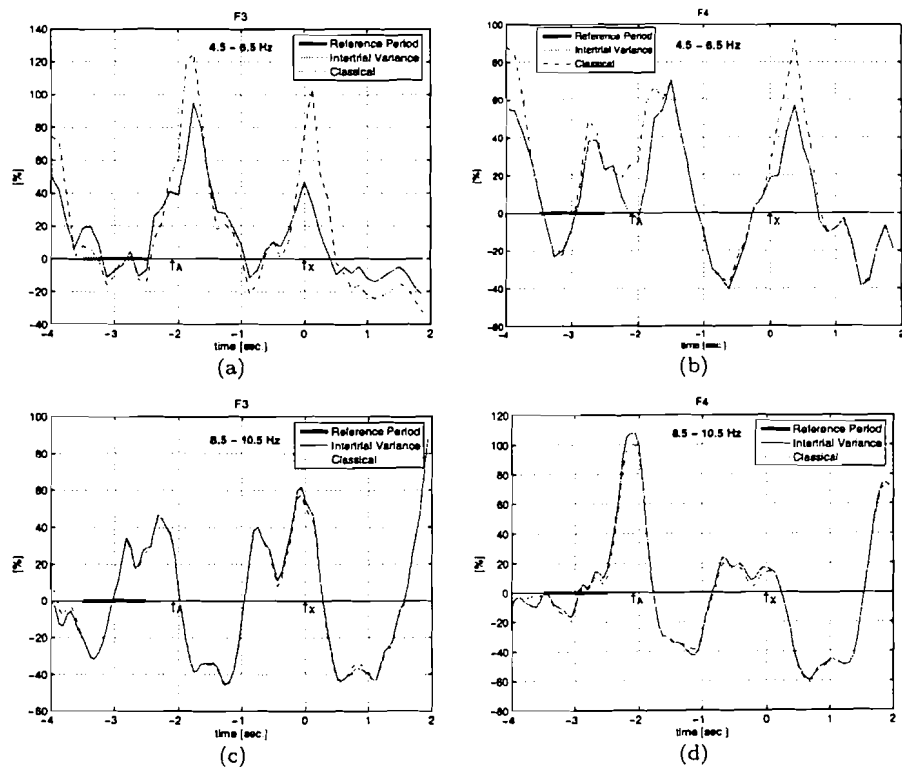


Figure 8.4: Difference between Intertrial variance and Classical Method.

8.5 High frequency dependency

To investigate the sensitivity of the reactive frequency bands, the ERD/ERS is computed from 2 different frequency bands with the same length only slightly shifted from each other.

In Fig. 8.5 the ERD/ERS of C4 is computed from the control subject 2 using the Hilbert method. First the upper-alpha frequency band using the IAF from the single trial procedure (IAF = 9.9 Hz from Table 8.2) is used to compute the ERD/ERS. Secondly, the frequency band using the IAF of the reference period procedure (IAF = 10.1 Hz from Table 8.3) is used. The result of both computations are displayed in Fig. 8.5(a) and Fig. 8.5(b), respectively. Despite the fact that the frequency bands are shifted for only 0.2 Hz of each other, Fig. 8.5(b) shows a much larger and longer synchronization (ERS) than Fig. 8.5(a).

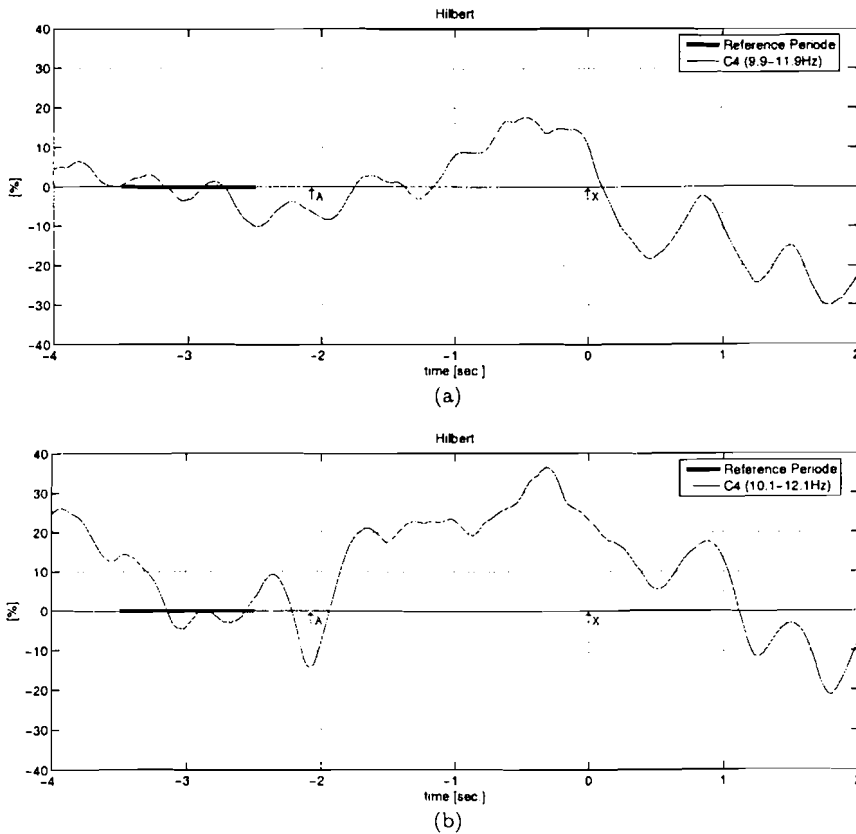


Figure 8.5: Difference between small frequency variations.

Chapter 9

Conclusions and Recommendations

9.1 Conclusions

If the Mean IAFs, found using the 3 different procedures, of the ADHD group are compared to those of the control group, we can conclude that the IAF of the ADHD group is significant (on average about 1 Hz) lower than that of the control group. Especially in the frontal region where the difference is very clear. This corresponds to Biederman's statement: "... studies of ADHD across the life cycle support the hypothesis that deficits in frontal lobe functions and the connections between the frontal lobe and key subcortical regions underlie this disorder" [Biederman, 2005]. Because the mean age and the standard deviation of both groups are almost the same, little age related differences in the IAF are present. Therefore, this is an important finding and should be taken into account in future research of ADHD.

The most important part of ERD/ERS analysis is the choice of the frequency band. As shown in Fig. 8.5 small variations within a frequency band can cause significant different ERD/ERS results. This means the frequency bands have to be chosen very accurate before computing an ERD/ERS.

As far as the ERD/ERS quantification method is concerned the Intertrial Variance method and the Classical method show clear differences in the lower-alpha bands, because of the interference of evoked activity. Within the higher frequency bands they show the same results due to the fact that in this region there is no or little interference of evoked activity (ERP). Therefore, the Intertrial Variance method is recommend for use in the lower frequency bands, below the upper-alpha.

The evoked activity also interferes with the ERD/ERS computed with the Hilbert method however, if ERD/ERS of upper-alpha frequency bands and above are investigated, the Hilbert method is recommend because of its ability of automatically adapting the time resolution to any frequency under investigation. Therefore, it is easier to use than the IV method.

The use of the Classical method is not recommended, after all if there is interference of evoked activity then the IV method is used and if no evoked activity is present the IV method shows the same results as the Classical method.

Within the ERD/ERS of ADHD children and children with no attention disorders investigated during this study no significant differences were found. Only using a fixed frequency band for the lower 1-alpha band determined using the mean Individual Alpha Frequency (IAF) of all subjects, a higher synchronization in the electrode position Fz was found for the ADHD group.

The method of Klimesch and co-workers used to determine the reactive frequency bands is always applied on adults and not on children. It is plausible that there are differences between the determination of the frequency bands because the peak alpha frequency in children is much lower than in adults. It is very likely that this is one of the reasons why recognizing children with ADHD from the ERD/ERS failed in this study.

9.2 Recommendations

Some suggestions for future work within the ADHD project are:

- More research has to be done on finding the correct frequency bands for children. For instance by:
 - determining the difference of the TF and the IAF within healthy children and children with an attention disorder;
 - determining the IAF not only from the eyes-closed data but also validating at which frequency alpha power decreases the most when opening the eyes [Posthuma et al., 2001];
 - checking the article of Doppelmayr et al. [1998] who suggest to define the width of the frequency bands by using the IAF multiplied with a certain percentage;
- Investigating the ERD/ERS of the beta bands, which was beyond the scope of the current project but should be investigated in future projects;
- Using more data from more ADHD and control children to allow a better statistical comparison between the two;
- Determining beyond which frequency the Hilbert method can be used instead of the IV method, in which there are no interferences of evoked activity present anymore in the data;
- Discriminating between the 3 different categories within ADHD and the presence of comorbidity.

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Appendix A

ERDTool Manual

The ERDtool is a signal processing tool designed in MatLab (version 7.0.4). The GUI (Graphic User Interface) is shown in Fig. A.1. The file formats supported by the ERDtool are .cnt, .trg and the Matlab file format .mat. The .cnt and .trg files originate from the software package EEProbe for EEG data acquisition and analysis. EEProbe was originally developed at the Max Planck Institute in Leipzig, Germany (there known as EEP), and was further developed as a commercial product by ANT Software in Enschede, in the Netherlands. The file format .cnt contains the (compressed) digitized raw EEG data of all the recorded electrode positions, including time points, sampling rate and labels of the channels (electrode positions). The trigger file .trg contains the event information such as triggers related to the EEG data in the .cnt file. In the ERDtool the .cnt and .trg files should both have the same filename and can be opened with the menubar function "OpenFile". The .mat file is used to save the computed ERD/ERS data and the settings of the computation. With the menubar "Save" and "Load" the data and settings are loaded from or saved into the .mat file.

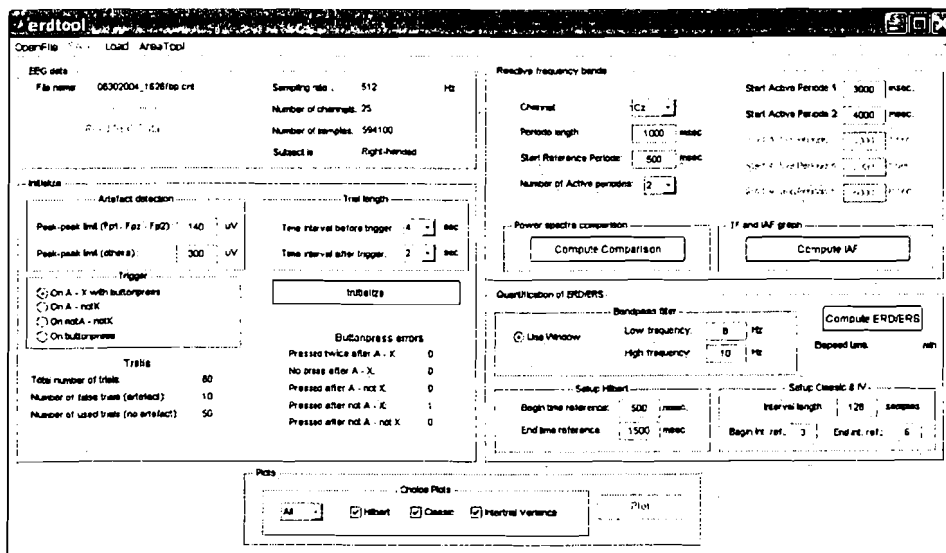


Figure A.1: GUI of the ERDtool program.

A.1 EEG data

The user first has to select a .cnt file using the menubar function "OpenFile". To read the data information from the .cnt and the .trg file the MatLab functions READ_EEP_CNT.m and READ_EEP_TRG.m are used. These functions returns the structure .eeg and .trg as given in Appendix B with all the data and event information. These functions will be executed by pressing the "Read EEG Data" button.

A.2 Initialize

The next step is the initialization of the data. Here the EEG data is divided into trials that are triggered to a certain event and moreover, these trials are examined for the occurrence of artefacts and saved for further computation. After initialization the user is able to see how many times the subject pushed the button at the wrong trigger, displayed under `Buttonpress errors`. The user is also able to see under `Trials` how many trials are found and the number of trials that contain artefacts and are artefact free, in the case of the ERD/ERS this number should at least be higher than 30 trials (Section 5).

Trigger

The EEG data extracted from the .cnt file contains continuously raw EEG data recorded during the whole session of which only the sections in which an event occurs are relevant for the ERD/ERS computation. These events are triggered by codes that are stored in the .trg file. By using these trigger codes and the accompanying time of occurrence, it is easy to find the occurrence of events within EEG data saved during the recording session. The user can select from three different triggers, namely:

- *On A-X with buttonpress*, here the trigger is the moment that the letter X appears on the screen about 2 seconds after an A appeared. The trigger is only taken into account when the subject presses a button right after the X appeared;
- *On A-notX*, the trigger is the moment that an other letter than X after an A appears on the screen.
- *On notA-notX*, all the moments where the appearing letter on the screen and the previous letter was not an X or an A.
- *On buttonpress*, here the trigger are the moments the subject pressed a button.

For this project only the "A-X trigger with buttonpress" is used. The others are implemented for use in further research within the ADHD projects. The meaning of the different triggers are further explained in Section 7.3 of the report.

Trial length

As said in Chapter 5 of the report, the ERD/ERS needs time to develop and a reference period has to be chosen some seconds before and event occurs. For the initialization the trial length can be selected by determining the time-span before the trigger, which contains the reference period and the planning phase, and the time-span after the trigger, which contains the recovery phase of the event. The

default value of the time before the trigger is 4 seconds and after the trigger is 2 seconds, which means that the total trial time in this case is 6 seconds. The trial length can only be chosen in the length of seconds and not smaller, the reason for this is that this way it is numerical easier to compute.

Artefact detection

The purpose and method of artefact detection applied in the ERD tool is explained in Section 7.4. To detect artefacts within the EEG data used in the ERDtool, the peak-peak value of the data within a trial is compared to a predefined value that can be changed by the user. If the peak-peak value of a trial is higher than the predefined value this trial is marked as containing an artefact and the whole trial is excluded for further analysis. Besides, if within a trial of one or more electrode position an artefact is detected all the trials of the other electrode positions taken in the same time span also are marked and excluded for further analysis.

The default values of the peak-peak artefact detection are $140\mu V$ for the Front-Polar and $300\mu V$ for the rest of the electrode positions.

A.3 Reactive frequency bands

A.3.1 Power spectra comparison

In this panel the comparison of the power spectrum of a reference period and an active period can be made by plotting the difference between the two spectra together with the 95% confidence interval as explained in Section 4.3.

The user has to define a channel (electrode position) from which the data is computed. The period length and the start time for the reference and active periods can be entered in *ms* and up to 5 different active periods can be computed simultaneously. If the pushbutton "Compute Frequency Bands" is pressed the computation will be performed using the technique explained in Section 4.3.

In Fig. A.2(a) an example of five different active periods is given of the plots using the Reactive Frequency Bands function compared with the reference period. If more than one active periods are computed the function automatically plots the average over all different active periods. An example of this is given in Fig. A.2(b).

A.3.2 TF and IAF graph

The panel **TF and IAF graph** computes the power spectrum of the reference period and the chosen active periods (max 5) for the Trigger A-X, see Section 4.2. The user has to select a channel (electrode position) from which the periods are computed and the beginning and length of the reference period and the active periods. The function returns the Individual Alpha Frequency (IAF), defined as the frequency within the 6-13 Hz range that shows the largest power for the reference period. Also the gravity IAF is computed, defined as the frequency of the weighted mean of the spectral power within the range of 6-13 Hz of the reference period. Both IAF are displayed in the plot of the power spectra. An example of a such a plot is shown in Fig. A.3.

The panel is only active if the user has chosen the Trigger A-X within the `initialize` panel.

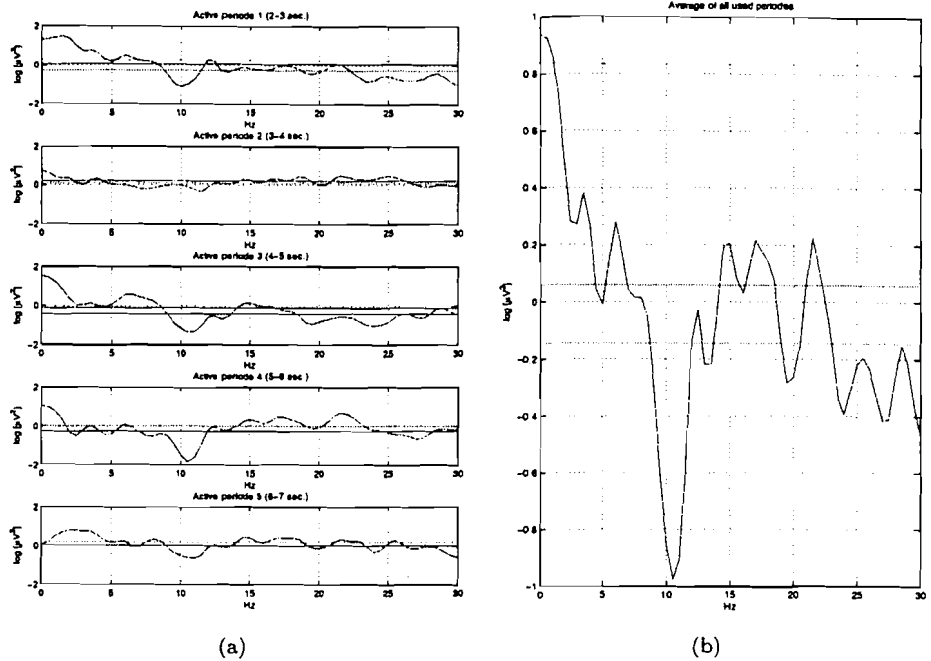


Figure A.2: In fig. (a) the difference between the 1 s during reference period and 5 different 1 s during active periods are plotted. The reference period was taken from 0.5-1.5 s of the trials of channel C3. fig. (b) shows the plot of the average of the 5 differences. In the 5 graphs of (a) and the average of (b) there is a clear ERD within the frequency band 9-12Hz.

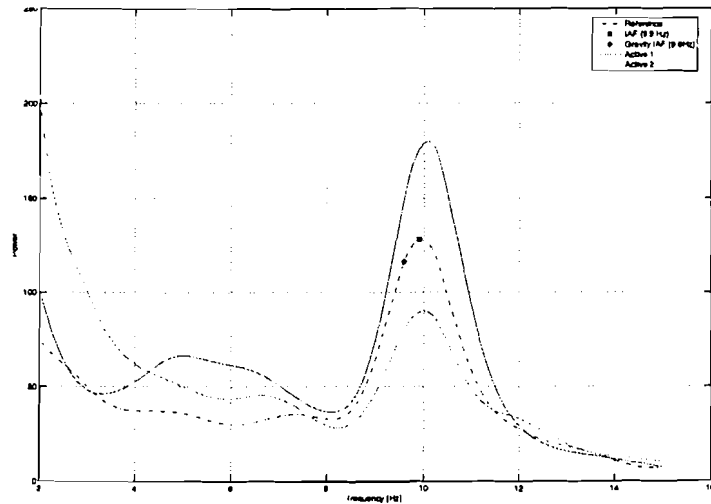


Figure A.3: Plot of the power of a reference and two active periods of electrode position Cz with use of the ERDtool.

A.4 Quantification of ERD/ERS

The methods used for the quantification of the ERD/ERS that have been implemented in the ERDtool are the Hilbert, Classical and Intertrial Variance methods.

The choice for these methods is explained in Section 5.4. The quantification steps of the methods are explained in Section 6.2.

For the Hilbert method the settings users have to enter are the beginning and ending time of the reference period. However for the Classical and Intertrial Variance methods the user also has to define the interval length on with the ERD/ERS signal is averaged to smooth the data. Because of this averaging over time intervals, the number of samples of the ERD/ERS signal are reduced. Therefore, the beginning and ending of the reference period have to be entered with the interval number. The user can manually enter the low and high frequency of the by the user defined frequency band.

A.5 Plots

After the ERD/ERS are computed the results can be plotted via the panel Plots. The user can choose which of the methods should be plotted. The results can be plotted in 2 different setups namely a plot in with the ERD/ERS of all the electrode positions are visualized according the international 10-20 system (Fig. A.4) or a plot which contains only a selected electrode position (Fig. A.5).

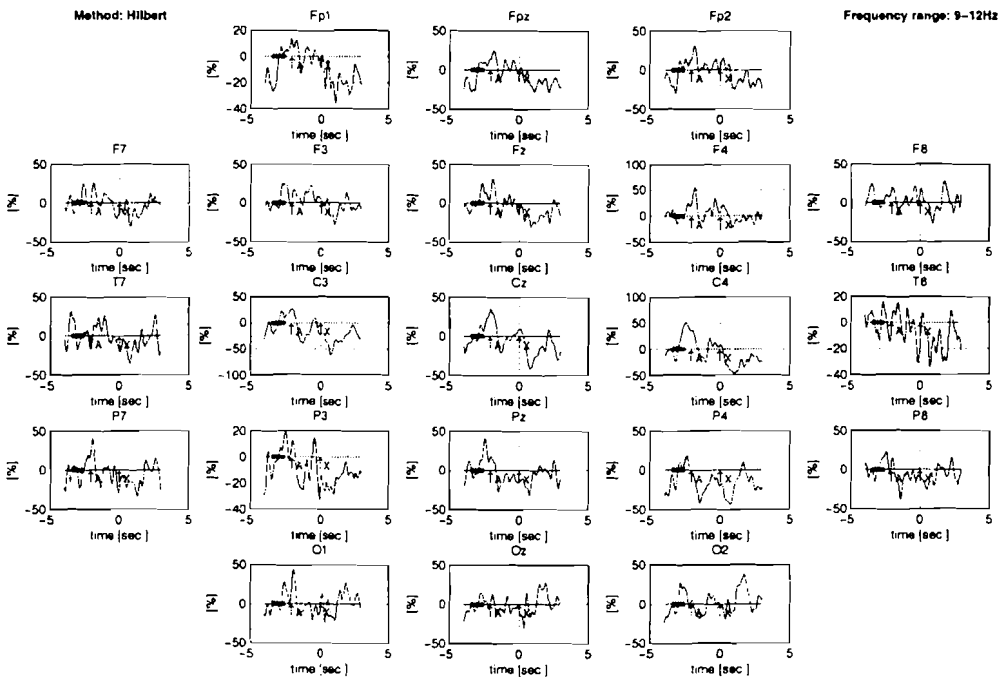


Figure A.4: Example of a plot of ERD/ERS for all electrode positions within the 10-20 system.

The settings that have been used in Figures A.4 and A.5 are the settings visible in Fig. A.1, the choice for the band of 9-12Hz is taken from Fig. A.2(a) where the is a ERD is detected within the 9-12Hz band of 4 of the 5 active periods. The computation of C3 of which the results are plotted in Fig. A.5 shows that this detection was correct.

It is also possible with the menubar function "Load" to plot the results of previous computed ERD/ERS signals that are saved with the menubar function "Save".

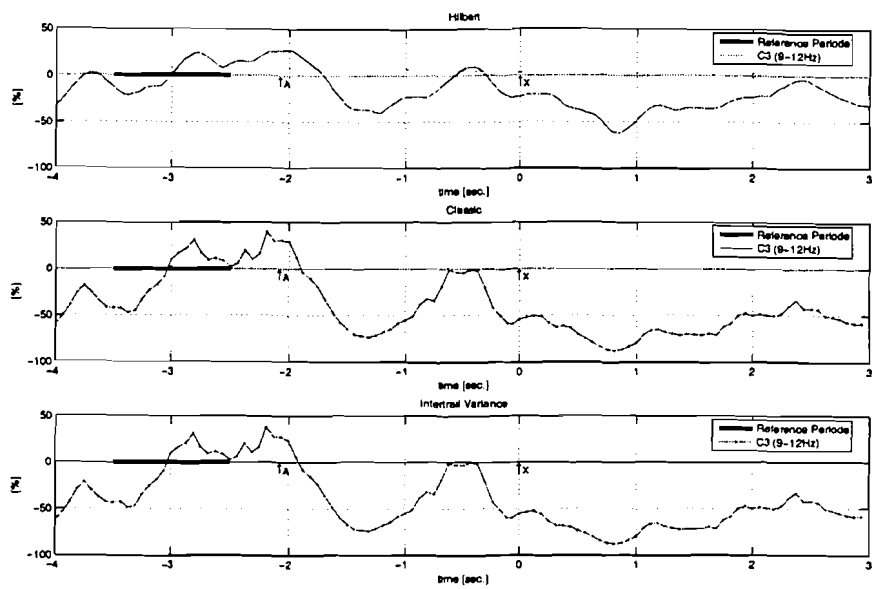


Figure A.5: Example of a plot of ERD/ERS for a selected electrode positions within the 10-20 system.

A.6 AreaTool

With the menubar function AreaTool the user can start a tool, shown in Fig. A.6 with computes the Area under an ERD and an ERS. The ERD/ERS has to be computed and saved with the ERDTool and the user can than load the saved data with the AreaTool and compute the areas of the different electrode positions and for the different methods. It is also possible to compute the area of all the electrode positions, these will be plot in a bar graph. an example of such a bar graph is given in Fig. A.7.

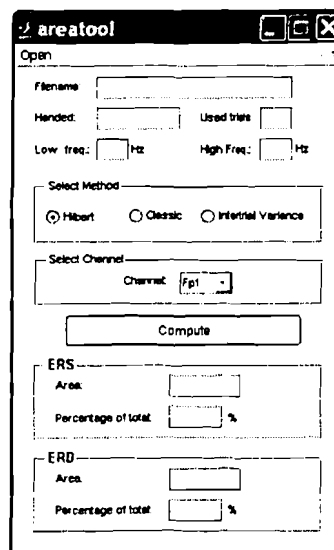


Figure A.6: GUI of the AreaTool.

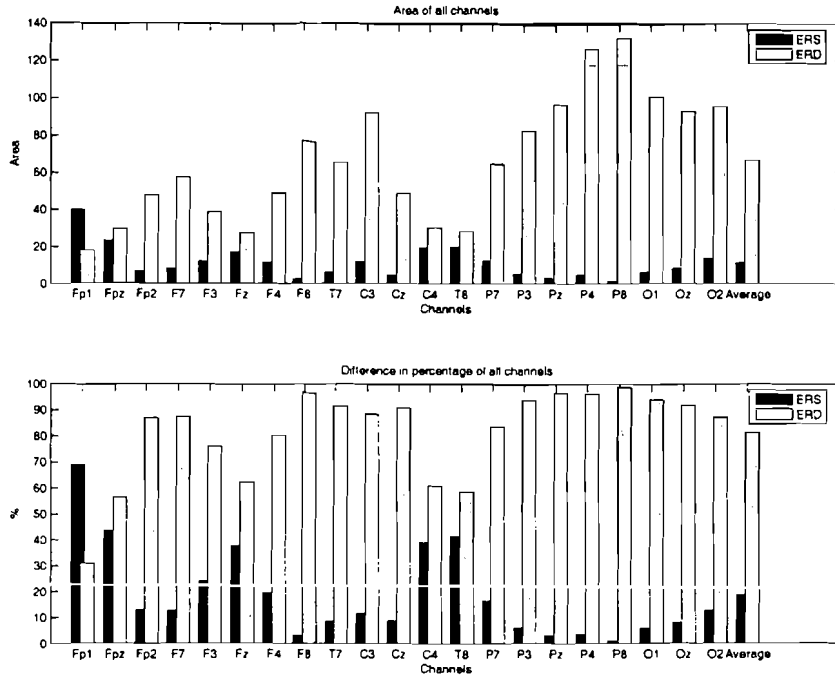


Figure A.7: Example of the bar graph plotted when the area of all electrode positions is computed.

Appendix B

Handles

To store and share data or variables between the different functions within a GUI, MatLab uses a mechanism called handles structure. In the ERDtool GUI the following handles structure are used to save data and variables to compute the ERD/ERS: eeg, trg, settings, trial and eegtrial. Below the contents of the structures are described.

eeg

.label	... labels of EEG channels
.rate	... sampling rate
.npnt	... number of samples in data
.nchan	... number of channels
.nsample	... total number of samples saved in .cnt file
.time	... array [1 x npnt]
.data	... [nchan x npnt]

trg

.time	... trigger latency in ms
.offset	... byte offset
.code	... trigger code (string)
.type	... numeric value of trg.code

settings

.filename	... 'filename'.cnt (string)
.ppart_fp	... peak-peak threshold artefact detection Fp [μ V]
.ppart_other	... peak-peak threshold artefact detection others [μ V]
.pretime	... time before trigger [sec.]
.posttime	... time after trigger [sec.]
.trigger	... trigger code
.begin_timeref	... begin (time) reference Hilbert [msec.]
.end_timeref	... end (time) reference Hilbert [msec.]
.begin_intref	... begin (interval) reference Classic and IV
.end_intref	... end (interval) reference Classic and IV
.interval	... length of interval [msec.]
.lowfreq	... low frequency of bandpass filter [Hz]
.highfreq	... high frequency of bandpass filter [Hz]
.window	... '0' don't use window, '1' use window

trial	
.handed	... '7' subject is LEFT-handed, '8' RIGHT-handed
.nchan	... '21' only positions of 10-20 system
.ntrial	... number of trials
.n	... number of trials without artefacts
.npnt	... number of samples in trial
.ipnt	... number of samples in trial after averaging over interval (Classic and IV method)
.artefact	... [1 x ntrial] '0' no artefact, '1' artefact
.begin	... [1 x ntrial] begin sample of ntrial
.end	... [1 x ntrial] end sample of ntrial
.time_hb	... [1 x npnt] Hilbert timescale
.time_civ	... [1 x ipnt] Classic and IV timescale
.errortwo	... number of two button presses after A-X
.errornopress	... number of no button pressed after A-X
.error12	... number of button pressed after notA-notX
.error13	... number of button pressed after notA-X
.error15	... number of button pressed after A-notX
.Atime	... time of appearance of A on screen [sec.]
.rate	... sampling rate
eegtrial(nchan)	
.rawdata	... [ntrial x npnt] raw eeg data of all trials
.filtered	... [ntrial x npnt] filtered eeg data of all trials
.envelope	... [ntrial x npnt] envelope of filtered eeg data of all trials