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DEVELOPING NEUROPHYSIOLOGICAL METRICS FOR THE ASSESSMENT OF MENTAL WORKLOAD AND THE FUNCTIONAL STATE OF THE BRAIN

Anu Holm

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Abstract

Modern working environments are often information intensive and work performance requires acting on multiple tasks simultaneously, i.e., multitasking. Also, irregular and prolonged work schedules, shift work and night work are typical in many work sectors. This causes both acute and chronic sleep loss, which results in performance impairment, such as increased reaction times, memory difficulties, cognitive slowing, and lapses of attention. Long lasting sleep loss and sustained overloading increase the risk of human errors and may cause work related stress and even occupational burn-out.

According to the Finnish Occupational Safety and Health Act (738/2002, Työturvallisuuslaki), Section 25 *Avoiding and reducing workloads*, an employer should assess the workload the employee is exposed to. Despite the fact that this important issue is enacted in the law, the objective measures to assess the workload are lacking.

This Thesis reviews neurophysiologic methods for assessment of cognitive workload and sleep loss. Then it describes experimental studies where the feasibility of conventional event related potential (ERP) and electroencephalography (EEG) methods were tested both in assessment of internal state of participants during challenging task performance after sleep debt and in diagnostic of work-related central nervous system disorder. After that, methodological improvements both on ERPs and EEG metrics are shown: ERPs were analysed with a single-trial method, and EEG methodology was developed for estimation of both internal (caused by sleep loss) and external (caused by task demands) load. The methods were tested in healthy controls.

The most promising metric to study overall brain load, including both cognitive workload as well as sleep loss, is suggested to be theta Fz / alpha Pz -ratio. It increases both with growing cognitive workload level and time spent awake, being sensitive also to sleep loss. This metric is possible to measure both in laboratory and in the field conditions. Measurements may be carried out even during real work tasks, at least in professions where most work is done in office-like environments. As the ratio increases with cognitive brain load similar to the heartbeat with increasing physical load, the ratio was named "brainbeat".

Keywords brain, electroencephalography, EEG, event related potential, ERP, mental, workload	
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Tiivistelmä

Nykyaikaiset työskentely-ympäristöt ovat tietointensiivisiä ja työ vaatii monen tehtävän tekemistä samanaikaisesti. Lisäksi monilla aloilla on epäsäännöllisiä ja pitkiä työvuoroja sekä vuoro- ja yötyötä. Tämä aiheuttaa sekä hetkellistä että pitkittynyttä univajetta, joka johtaa suoriutumisen heikkenemiseen, kuten pidentyneeseen reaktioaikaan, muistivaikeuksiin, tiedonkäsittelyn hidastumiseen ja tarkkaavuuden herpaantumiseen. Kauan jatkunut univaje ja pitkittynyt ylikuormitus lisäävät inhimillisien virheiden mahdollisuutta ja saattavat aiheuttaa työperäistä stressiä ja jopa työuupumusta.

Työturvallisuuslain (738/.2002) 25 § mukaan työnantajan on pyydettäessä selvitettävä työntekijän terveyttä vaarantavat kuormitustekijät. Siitä huolimatta että tämä tärkeä asia on säädetty laissa, objektiivisia menetelmiä työn kuormittavuuden arviointiin on vähän.

Väitöskirjassa luodaan ensin katsaus neurofysiologisten menetelmien käyttöön mentaalisen kuormittuneisuuden ja univajeen asteen arvioinnissa. Sitten esitellään kokeellisia tutkimuksia, joissa perinteisiin aivosähkökäyrään (EEG) ja herätepotentiaaleihin (ERP) perustuvien menetelmien soveltuvuutta testataan univajeisen henkilön sisäisen tilan arviointiin kuormittavan tehtävän aikana ja työperäisen aivosairauden diagnostiikassa. Tämän jälkeen sekä EEG että ERP -menetelmiä kehitetään kahdella tavalla. Henkilön sisäisen (univaje) ja ulkoisen (tehtävän muuttuvat vaatimukset) kuormituksen arviointiin kehitetään aivosähkökäyrän taajuusanalyysiin perustuva menetelmä. Lisäksi herätepotentiaaleja analysoidaan yksittäisvastemenetelmällä. Molempia menetelmiä testataan terveillä henkilöillä.

EEG taajuusanalyysin perustuva theta Fz / alpha Pz -suhde osoittautui lupaavimmaksi menetelmäksi aivojen kokonaisvaltaisen kuormittumisen arviointiin. Suhdeluku kasvaa sekä tehtävän vaikeutta lisättäessä että unen tarpeen lisääntyessä. Suhdeluku on mahdollista mitata sekä laboratorio- että kenttäolosuhteissa. Mittaus voidaan suorittaa jopa todellisten työtehtävien aikana, etenkin toimistotyyppisissä töissä. Koska suhdeluku kasvaa mentaalisen kuormituksen lisääntyessä vastaavasti kuin sydämen syke fyysisen kuormituksen lisääntyessä, annettiin sille nimi "aivosyke".

Asiasanat aivo, aivosähkökäyrä, EEG, herätepotentiaali, ERP, mentaalinen, kuormitus	
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PREFACE

This thesis is the result of my research carried out in Brain and Work Research Centre (BWRC) of the Finnish Institute of Occupational Health (FIOH) during 2004-2010. The thesis has been a part of my work in projects funded by the Finnish Funding Agency for Technology and Innovation, TEKES.

I thank my instructor, the head of the BWRC, Prof. Kiti Müller for providing me the opportunity for this thesis work and for her support throughout all these years. She has been my manager since 1999 when I started in FIOH. I would like to thank Prof. Risto Ilmoniemi, who supervised the final steps of my thesis work, for guidance. I also thank Prof. Pekka Meriläinen, who supervised the early steps of my thesis work, for support and constructive comments.

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My warmest thanks go to my friends for support and understanding. You have offered me many moments of joy during this process.

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Even this thesis has been a part of my work duties; it has taken me away from my family during numerous evenings, nights and weekends. Thank you Micke for all patience, support, understanding and love you have shown me during this process. And princess Wilma, thank you for giving me the most valuable position I can imagine, being your mom is wonderful!

Espoo, April, 2010

Anu Holm

CONTENTS

List of original publications

This Thesis is based on the following original publications, which are referred to in the text by their Roman numerals I–V:

I Keski-Säntti, P., Holm, A., Akila, R., Tuisku, K., Kovala, T. & Sainio, M. (2007). P300 of auditory event related potentials in occupational chronic solvent encephalopathy. *Neurotoxicology*, *28*(6), 1230–1236.

II Holm, A., Ranta-aho, P.O., Sallinen, M., Karjalainen, P.A. & Müller, K. (2006). Relationship of P300 single-trial responses with reaction time and preceding stimulus sequence. *International Journal of Psychophysiology*, *61*(2), 244–252.

III Keski-Säntti, P., Kovala, T., Holm, A., Hyvärinen, H.K. & Sainio, M. (2008). Quantitative EEG in occupational chronic solvent encephalopathy. *Human & Experimental Toxicology*, *27*(4), 315–320.

IV Sallinen, M., Holm, A., Hiltunen, J., Hirvonen, K., Härmä, M., Koskelo, J., Letonsaari, M., Luukkonen, R., Virkkala, J. & Müller, K. (2008). Recovery of cognitive performance from sleep debt: do a short rest pause and a single recovery night help? *Chronobiology International*, *25*(2), 279–296.

V Holm, A., Lukander, K., Korpela, J., Sallinen, M. & Müller, K.M.I. (2009). Estimating brain load from the EEG. *ScientificWorldJournal*, *9*, 639–651.

Author's contribution

All publications of this Thesis resulted from group effort. I was responsible for the electrophysiological recordings and their time synchronisations with the Brain@Work multitask in Publications IV and V. I conceived the original idea, analysed most of the data, and was the principal and corresponding author in Publications II and V. In Publications I, III, and IV, I participated actively in the planning of the study setup, in analysing the electrophysiological and behavioural data, in discussing the results, and in writing the manuscripts.

List of abbreviations

ARI	Arithmetic task
AUD	Auditory task
B@W	Brain@Work
COM	Serial port
CSE	Chronic solvent encephalopathy
EEG	Electroencephalography
EOG	Electro-oculography
ERP	Event-related potentials
fMRI	Functional magnetic resonance imaging
Fz	Frontal midline location
HCI	Human computer interface
HRV	Heart-rate variability
LPT	Parallel port
MATB	Multiple attribute task battery
MEG	Magnetoencephalography
MEM	Memory task
NIRS	Near infrared spectroscopy
OAR	Ocular artefact reduction
PCA	Principal component analysis
PET	Positron emission tomography
Pz	Parietal midline location
REM sleep	Rapid eye movement sleep
VIS	Visual task

1 Introduction

The modern work environment is often hectic, requiring acting on multiple tasks concurrently, *i.e.*, multitasking. Shift work and irregular working hours are also common (Härmä, 1998), and may cause sleep deprivation, sleep fragmentation, and sleep restriction to a worker.

Sleep periods are an essential part of learning and memory processes: Reactivations of memory processes during rapid eye movement (REM) sleep are beneficial to memory performance (Maquet, 2000; Maquet, 2001). In addition, as one of the functions of sleep is to replenish energy resources, irregular working and sleeping conditions restrict the brain's energy resources, especially in the frontal areas (Porkka-Heiskanen *et al.*, 2003; Porkka-Heiskanen *et al.*, 1997), which are essential for multitasking. Thus, sleep loss leads to performance decreases that increase in severity with time awake and with task complexity, and even a moderate decrease in cognitive resources of the brain may cause work-related stress, which in turn can increase the risk of error and work-related diseases.

According to the Finnish Occupational Safety and Health Act (738/2002, Työturvallisuuslaki), Section 25 *Avoiding and reducing workloads,* an employer should assess the workload the employee is exposed to: "*If it is noticed that an employee while at work is exposed to workloads in a manner which endangers his or her health, the employer, after becoming aware of the matter, shall by available means take measures to analyse the workload factors and to avoid or reduce the risk."* Despite the fact that this important issue is enacted in the law, objective metrics to assess mental workload are lacking.

Physiological methods offer a direct measure of activations in the human nervous system in response to task-level changes. In this Thesis, conventional neurophysiological metrics were used and a new one was developed, aiming at the objective assessment of mental workload and for the identification of the functional state of the brain of an individual. Work simulations were used with changing task demands and in sleep deprivation to create operational situations closely resembling those of real work environment to study the performance of healthy subjects. Also, patients with exposure to solvents at work were studied with electrophysiological methods.

2 Review of the literature

2.1 Mental workload

Mental workload is defined as the portion of an individual's limited mental capacity that is actually required by task demands (Gopher & Donchin, 1986; O'Donnel & Eggemeier, 1986; Wickens, 2000). Tasks vary in difficulty and the same task can appear more difficult to some individuals than to other. Also, the functional state of the brain of an individual may deteriorate causing performance decrease which is independent of task demands. For example, sleep restriction for the duration of a work week impairs multitasking performance (Haavisto *et al.*, In Press).

The assessment of mental workload during actual work tasks (*i.e.*, identification of the effects of *external factors*, such as task demands), and recognising already a moderate decrease in the cognitive functioning state (*i.e.*, identification of the effects of *internal factors*, such as increased need to sleep), both aim at optimising the workload of a work day to a level that is in balance with available human resources.

2.2 Work simulations and multitasking

In typical workload studies, real work-task simulations are used to involve subjects in performance situations closely resembling those of actual work. The simulations have been used in research on the effects of sleep deprivation on human performance in aviation (Caldwell *et al.*, 2004) and industrial automation work (Sallinen *et al.*, 2004), and to study the complexity of multiplatform control in industrial security tasks (Murray & Caldwell, 1996). However, real work-task simulations have several limitations concerning the study of real-work demands: Experts are needed as subjects to run the simulations and the definition of the cognitive resources required to complete the simulation is complicated. The assessment of the performance is restricted to the simulation task, thus reducing the general applicability of the results. Thus, simulations are often replaced by generic multitask batteries, such as SYNWORK (Elsmore, 1994; Proctor *et al.*, 1998) and MATB (Fairclough & Venables, 2006; Fairclough *et al.*, 2005).

Multitasks are composed of subtasks, which are run simultaneously and call for known cognitive resources, such as perception, information updating and short-term memory. These functions are needed in several work tasks (Alluisi, 1967; Proctor *et al.*, 1998). Generic multitasks have also limitations in the general applicability of the results, but they are more feasible than the real-work simulations, since no domain expertise is needed to perform the task and also the limits of good performance are easier to define. The multitask approach has been used to study, for instance, the effects of sleep deprivation, time on task, and aging on the performance of several concurrent tasks (Caldwell & Ramspott, 1998; Caldwell *et al.*, 2004; Elsmore, 1994; Molloy & Parasuraman, 1996; Salthouse *et al.*, 1996), and the effects of individual monetary incentives with and without feedback (Bucklin *et al.*, 2003).

The hypothetical model of the relationship between performance and mental workload, developed by O'Donnel and Eggemeier (Eggemeier & Wilson, 1991), suggests that within the range of low and moderate mental workload, a subject has the capability to fully compensate for increases in the mental workload. When the mental workload is too high to be fully compensated for, the performance begins to gradually deteriorate. In extremely high mental workload levels, an individual's performance declines to its lowest level, and thus further increases in mental workload are not any more manifested as decreases in performance.

The multiple resource model of human information processing by Wickens (Wickens, 2002; Wickens, 2008) proposes that human information processing is not one central resource, but consists of several processing resources that can be used simultaneously when needed, *e.g.* in multitasking. The model suggests that overall workload is partly determined by the extent to which the time-shared tasks place demands on the same cognitive resources: As one task becomes more loading there are fewer resources left for the others. This may cause cognitive overload and result in performance tradeoffs. The model can be used to predict when cognitive resources are overloaded during multitasking. This information can be used to avoid overcapacity conditions by work design.

However, in more realistic environments task demands are less structured. Even though one work-task can be modelled with the multiple resource model, all tasks the worker is involved with can not usually be taken into account. Cognitive resources must be divided between competing activities, sometimes under time pressure or under non-optimal conditions. Also, there are individual differences in the cognitive capacity of workers and the functional state of an individual can change due to, for example, sleep deprivation (Hancock & Szalma, 2007; van Dongen & Belenky, 2009). Thus, the assessment of the mental workload and the identification of the functional state of the brain of an individual, could help both in optimising work tasks and planning the work-rest rhythm in order to avoid hazardous errors at work, as well as in avoiding sustained overloading, which may result in work related stress and even burn-out.

2.3 Neuroergonomics

Neuroergonomics is the study of brain and behaviour at work (Parasuraman, 2003). Neuroergonomics research integrates the areas of neuroscience and ergonomics (human factors) in order to maximise the benefits of each (Sarter & Sarter, 2003). The neuroscientific study of brain structure and functioning is made in the context of human cognition and behaviour at work and at home.

Several techniques, based on the measurement of blood flow or glucose metabolism in the brain (positron emission tomography PET, near infrared spectroscopy NIRS and functional magnetic resonance imaging fMRI) or the measurement of the electromagnetic activity of the brain (electroencephalography EEG, event related potentials ERPs and magnetoencephalography MEG), can be used in neuroergonomics research (Eggemeier *et al.*, 1991; Kramer, 1991). The EEG has good temporal resolution (milliseconds), but poor spatial resolution. However, it's advantages are the ease of use, low-cost measurements, and the possibility of measuring it continuously during everyday activities (Baldwin, 2003; Gevins & Smith, 2003).

Methods for assessing mental workload during actual work performance as well as for identifying work related diseases are needed. The mental workload should be properly distributed throughout the day, and kept at a manageable level, in order to avoid both overload or under load situations (Gopher & Donchin, 1986; Hockey, 1986; Hockey, 1997). The overall well-being of workers would benefit from mental workload assessment; with sustained overload individuals become more tired, which results in memory lapses. Methods sensitive to cognitive overload may also be usable in detecting brain related diseases in an early stage, when even simple life style change interventions could help in restoring brain function thus avoiding the need for medication. The assessment methods should be easy to use, *e.g.* the measuring, analysis, and the interpretation of the results should be straightforward. This should hold true for both clinical purposes as well as for mental workload assessment and identification of functional state of an individual during real work-tasks. Measurements should be unobtrusive and they should have adequate time resolution fitting on the objective. It would also be a benefit, if both external (task load) and internal (subject's functional state) factors could be assessed with the same method.

As some EEG contents, as well as ERPs, are related to higher cognitive functions and offer a direct measure of neural activations in the brain during task execution, this Thesis evaluates their usability in the neuroergonomic framework.

2.3.1 Measuring the electrical activity of the brain

EEG is usually measured as the potential difference between two electrodes on the scalp. The electrodes are typically located according to the International 10−20 system (Klem *et al.*, 1999), and referenced to an electrode placed elsewhere on the scalp or body, typically to the mastoid, or the earlobe. In the system, the nasion−inion distance is measured and the electrodes are placed at locations 10% or 20% of this distance apart from each other. The names of the electrode locations are derived from the lobes of the brain: frontal, temporal, central, parietal and occipital. Uneven numbers are on the left and even numbers on the right hemisphere. In the healthy, awake adult brain, the peak-to-peak amplitude for EEG measured from the scalp is under 100 µV, and most of the spectral power comes from rhythmic oscillations under the frequency of 30 Hz.

Scalp-recorded EEG represents the synchronous activity over large neuronal populations. The scalp recorded EEG activity contains also contaminating potentials from eye movements and blinks, muscle activity, and also from movements and other physiological and instrumental sources of artefacts. The data with artefacts is either rejected from analyses or corrected for with some suitable method, for example blinks can be subtracted from the EEG (Gratton *et al.*, 1983; Jung *et al.*, 2000).

2.3.2 Spontaneous brain activity, EEG

EEG is an essential tool in certain clinical applications, such as epilepsy and sleep disorder diagnostics, the assessment of awareness during anaesthesia, and monitoring brain function in neuro-intensive care units (Viertiö-Oja *et al.*, 2004; Young, 2009).

The EEG spectrum is typically decomposed into four frequency bands: delta (1–4 Hz), theta (4–8 Hz), alpha (8–12) and beta (12–30 Hz). Of these frequency bands, theta and alpha activity are the most used ones in studies on changing task demands.

The background resting EEG is often obtained from subjects in eyes open/eyes closed conditions. The subjects lay quietly and relaxed in a bed but are not allowed to fall asleep. Mean absolute delta, theta, alpha, and beta powers decrease from the eyes-closed to the eyes-open condition. In addition, theta decreases locally at posterior areas whereas alpha decreases globally. The global decrease in alpha activity is connected to increased arousal levels, whereas the focal decrease in theta activity is related to cortical processing of visual input (Barry *et al.*, 2007). The overall EEG spectrum power decreases as subject age increases (Polich, 1997). This decrease is mainly caused by reduced power at delta, theta, and alpha frequencies (Smulders *et al.*, 1997).

In addition to resting conditions, EEG content has been studied during cognitive task performance. Theta activity seems to be related to memory processes, encoding, and retrieval as well as the transfer of information between short and long-term memory (Sauseng *et al.*, 2006; Ward, 2003). The amount of theta activity increases during memory retrieval (Kahana *et al.*, 1999; Klimesch *et al.*, 1997), whereas alpha activation decrease is thought to reflect long-term memory activation (Sauseng *et al.*, 2006), or changes in attention demands of a task (Ward, 2003). Task related changes in the theta band are typically strongest in the frontal areas, whereas alpha activity changes are most pronounced at posterior electrode sites (Klimesch *et al.*, 1997; Sauseng *et al.*, 2006).

2.3.3 Event-related brain activity, ERP

Event-related potentials reflect the brain's neural response to sensory, motor, or cognitive events. ERPs are very small changes in voltage (0.1-30 μV) whereas the magnitude of spontaneous EEG activity is measured between 10 to 100 μV. ERPs are usually calculated from the EEG by averaging EEG epochs time-locked to a particular event. As the signal to noise ratio of event-related potentials is quite poor, averaging dozens of responses is generally used to estimate ERPs. With averaging it is assumed that each single ERP is exactly the same for repeated stimuli produced during long lasting measurement sessions and is independent of the ongoing EEG.

Early studies in the 1970s and 1980s correlated ERP responses with reaction time and accuracy demanded from the subjects (Kutas *et al.*, 1977), with selective attention (Hillyard *et al.*, 1973), and with workload (Isreal, 1980c; Kramer *et al.*, 1985).

The naming of potentials has generally been based on the polarity and the order of the component in the ERP waveform. Thus, P1 stands for the first positive component and N1 for the first negative one. Another way of naming is to use the latency of the component, for example P300 stands for a positive potential with the latency of 300 ms from stimulus onset.

One of the most studied ERP components is the P300 peak, see Figure 1. A commonly used paradigm to produce P300 is the so called oddball paradigm, where a subject listens to two kinds of tones and presses a button when a target tone occurs. Typically 15–25% of the presented tones are targets. The inter stimulus interval is usually one to two seconds. About twenty artefact-free EEG epochs are needed for calculating the average response (Cohen & Polich, 1997).

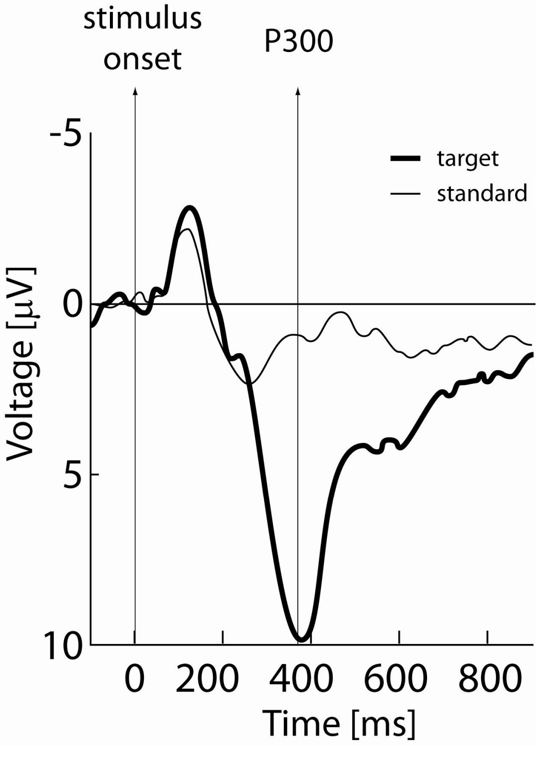


Figure 1: The ERP average response, measured during a classical oddball paradigm, at Pz location to standard tones (no response required, thin line) and to target tones (button press required, medium line).

The P300 component is thought to reflect updating of the working memory in response to task-relevant events, and to be unrelated to response selection (Donchin, 1981; Donchin & Coles, 1988). This view has been criticised, and a role for the P300 in linking perception processing with response processing has been suggested (Verleger *et al.*, 2005).

In single task conditions, the amplitude of the P300 component increases with task difficulty and stimulus relevance (Iguchi & Hashimoto, 2000). The increase of the amplitude with task difficulty correlates positively with individual differences in working memory capacity (Nittono *et al.*, 1999). The P300 amplitude decreases with age (Kok, 2000; McEvoy *et al.*, 2001; Polich, 1997), especially at parietal areas (Fjell & Walhovd, 2001). The young adults' P300 is largest in the parietal and smallest in the frontal areas of the brain, whereas there is no significant amplitude change across electrode sites in the elderly (Friedman *et al.*, 1993; McEvoy *et al.*, 2001).

The variation of single trial ERPs was noticed early in ERP studies (Brazier, 1964). ERPs may for example habituate during long measurement sessions and different components can overlap with each other. This has led to the design of a wide variety of special signal processing procedures to improve the estimation of ERP waveforms. Variation of the P300 has been studied widely with selective averaging techniques, where single ERP trials are divided into different classes, for example, according to stimulus relevance (Castro & Diaz, 2001; Falkenstein *et al.*, 1991). The P300 component is also known to vary due to local changes in the stimulus sequence (*i.e.* number of preceding standard tones): with selective averaging it has been shown that the amplitude of P300 increases with the increasing number of preceding standard stimuli (Golob & Starr, 2000; Kilpeläinen *et al.*, 1999; Squires, 1976). Increases in the target-to-target interval also increase the P300 amplitude (Croft *et al.*, 2003). Procedures with correlation techniques have also been used in attempts to take the trial-to-trial variability into account (McGillem & Aunon, 1977; Woody, 1967). With correlation techniques a cross-correlation between a single-trial ERP and a template, obtained by *e.g.* averaging a set of single-trial ERPs, is performed. This approach aims at improved averaging, not to single-trial estimation. Also statistical information can be utilised in single trial estimation: In the principal component analysis (PCA), large sets of ERP waveforms are compared by producing a set of principal components, and extracting features of set of waveforms that are common to all of the responses (Donchin & Heffley, 1978). PCA gives information on the second order statistics of the set of waveforms and it can been used, for example, in decomposing the overlapping ERP components (Rushby & Barry, 2009). The assumption when using this approach is that both the latency and the waveform of each components are fixed, since variance produced by latency shifts will be a source of some of the principal components, i.e. variance in the latency is likely to yield an unfaithful picture of the component structure underlying the waveforms.

2.4 Sleep deprivation, restriction, and fractioning

The sleep deprivation can be either chronic or acute, and may be caused by, for example, some disorder, living habits, or work shifts. Sleep debt can be caused by partial or total sleep deprivation. In restricted sleep settings, as well as in extended wakefulness and in total sleep deprivation, subjects are not getting any sleep. Experimental sleep fractioning is induced by arousals, such as intrusive auditory stimuli, throughout the night. It is intended to simulate common sleep disorders, in which sleep is disrupted periodically during the night, such as pauses in breathing during sleep in sleep apnoea.

2.4.1 Lack of sleep and EEG

When subjects, who are awake, suffer from sleep deprivation and perform a simple task, low frequency EEG activity (1–7 Hz) increases in frontal areas with time awake (Cajochen *et al.*, 1999b; Cajochen *et al.*, 2001; Caldwell *et al.*, 2002). The increase of low-frequency EEG in frontal areas can also be seen during non-REM sleep after sleep deprivation (Cajochen *et al.*, 1999a; Cajochen *et al.*, 1999b). Theta increase shows only little circadian modulation, whereas the alpha activity exhibits circadian modulation with time awake (Cajochen *et al.*, 1999b). Sleep fragmentation decreases the alpha/theta ratio during alternating periods of eyes open and eyes closed, suggesting lowered alertness, specifically after a second sleep fragmentation night (Cote *et al.*, 2003).

During more challenging task performance, both theta and alpha activity increase due to sleep deprivation, especially at frontal and central areas (Smulders *et al.*, 1997). However, the theta and alpha activity do not show any consistent pattern compared to subjective or objective measures of sleepiness, when sleep debt is caused by extended wakefulness up to 21 hours (Smith *et al.*, 2002).

In summary, both theta and alpha activity increase in sleep deprivation conditions during task performance as compared to a normal sleep condition. However, these changes do not show any consistent pattern compared to subjective or objective measures of sleepiness.

2.4.2 Lack of sleep and ERPs

Restricted sleep decreases the P300 amplitude during awake. The P300 amplitudes of subjects, who have been awake for 36 hours, is significantly reduced in comparison to a normally sleeping group and recovers after the sleep deprived subjects have slept for one recovery night (Gosselin *et al.*, 2005). In an extended 21 h wakefulness study setup, the amplitude of the P300 component attenuated rapidly to an asymptotic level after the participants' normal time of going to bed (Smith *et al.*, 2002). In addition, the size of the amplitude decrease correlates with the magnitude of the performance impairment of a participant. The P300 amplitude, as well as performance in a simple task involving mathematical processing, has been reported to remain intact after two nights sleep fragmentation (Cote *et al.*, 2003).

> **In summary, in extended wakefulness, the auditory oddball P300 amplitude decreases rapidly to an asymptotic level after a subject's typical time to go to sleep. However, sleep fragmentation is not identified with a decrease in the P300 amplitude.**

2.5 Mental workload

Mental workload is the amount of subject's processing capacity that is required for performance of a task at a given time (Gopher & Donchin, 1986). Performance declines both during multitasking when processing capacity demands are very high as well as during vigilance conditions which demand sustained attention.

2.5.1 Mental workload and EEG

EEG theta activity at frontal areas has been reported to increase with increasing task demands in studies on working memory load (Gevins *et al.*, 1998; Smith *et al.*, 2002), visual search task (Yamada, 1998), multiple attribute tasks (Fournier *et al.*, 1999), and flight simulations (Smith *et al.*, 2001). In addition to frontal sites, theta activity increase has also been reported at parietal areas in response to increased task demands (Fairclough *et al.*, 2005). The frontal theta activity is also connected to increased demands on focused attention (Doppelmayr *et al.*, 2008; Yamada, 1998).

Conversely, alpha activity at the parietal sites has been reported to decrease with increases in working memory load (Fairclough & Venables, 2005; Fairclough *et al.*, 2005; Fournier *et al.*, 1999; Gevins *et al.*, 1998; Ryu & Myung, 2005; Smith *et al.*, 2001; Sterman & Mann, 1995). However, the alpha activity suppression during task performance may dissipate during sustained task execution and recover to the baseline level (Fournier *et al.*, 1999).

The amount of theta activity can differentiate a single task, or a baseline condition from a multitask situation (Fairclough & Venables, 2005; Fairclough *et al.*, 2005; Fournier *et al.*, 1999). Different difficulty levels of multitask conditions are more difficult to separate from each other, and findings are opposed to each other: In contrary to findings of Fournier *et al.* (Fournier *et al.*, 1999), Fairclough *et al.* found that the amount of theta can differentiate task demand levels in a multitask condition (Fairclough *et al.*, 2005). These studies also report different results on the behaviour of alpha activity: Fournier *et al.* found the higher alpha band (10–12 Hz) capable of differentiating both the single task from the multi task condition, as well as identifying different workload demands of multitask conditions (Fournier *et al.*, 1999), whereas Fairclough *et al.* could not repeat this result (Fairclough *et al.*, 2005).

Theta activity is insensitive to the training effect of a multitask (Fairclough *et al.*, 2005; Fournier *et al.*, 1999). Findings on alpha activity are not as clear: Contrary to a previous finding (Fournier *et al.*, 1999), practising has been manifested by suppression of parietal alpha activity during the initial 32 min performance but this effect dissipates during the second half of a 1-hour task period in a more recent study (Fairclough *et al.*, 2005). Time pressure in a visuo-motor task increases the amount of frontal and central theta, and decreases parietal alpha (Slobounov *et al.*, 2000). The power of both theta and alpha activity is larger near the end than at the beginning of the task (Boksem *et al.*, 2005; Smulders *et al.*, 1997).

Interestingly, decreases in alpha and increases in theta activity have also been connected to the accuracy of performance: A widely distributed decrease of alpha over fronto–central and parietal areas has been reported in connection with localised enhancement of frontal theta in conjunction with successful task response trials (Slobounov *et al.*, 2000). Also, in a memory task, words that are later remembered, produce a significant increase in theta activity (Klimesch *et al.*, 1997).

Theta activity increases on the frontal midline with increased task difficulty in younger adults, to a lesser degree in middle-aged, whereas no increase has been found in older subjects (McEvoy *et al.*, 2001). Alpha activity, in turn, decreases with increasing task difficulty in more widespread areas in older than in younger subjects, whose alpha activity decreases only at parietal areas. These findings are in good accordance with a previous study showing an increase in theta activity in the young and a decrease in alpha activity in the elderly during challenging task performance (Smulders *et al.*, 1997).

In summary, frontal theta activity increase and parietal alpha activity decrease have been related to increasing task demands, at least when task demand changes are large enough. The amount of alpha activity begins to recover with increasing time on task.

2.5.2 Mental workload and ERPs

The use of the P300 amplitude in mental workload assessment is based on the reciprocal behaviour of the magnitude of the P300: In a dual-task situation the increased primary task demands are associated with decreased secondary task P300 amplitudes and increased primary task P300 amplitudes (Kramer *et al.*, 1985; Singhal & Fowler, 2004; Sirevaag *et al.*, 1989). This is also true when two stimuli are presented in close temporal proximity (Nash & Fernandez, 1996).

The P300 amplitude in a dual-task condition is sensitive to changes in perceptual and cognitive task demands, but not to changes in response related demands (selection and execution of action) (Isreal, 1980a; Isreal, 1980b; Kramer *et al.*, 1985). The size of the P300 amplitude decrease is equivalent for dual tasks involving either short term or long term memory, and the decrease in amplitude can be seen both in the visual and the auditory P300 component (Singhal & Fowler, 2004). A study on simulated simple car driving shows that the P300 amplitude does not differ between dual-task (visual and auditory task) and single-task (auditory task) conditions, suggesting that tasks with different modalities can be time-shared effectively (Wester *et al.*, 2008). On the contrary, the P300 to a secondary task nearly disappears when the primary task is cognitively extremely challenging (Ullsperger *et al.*, 2001).

> **In summary, in dual task conditions, the P300 amplitude decrease is dependent of task demands. During an easy task no decrease is seen, whereas the P300 component of the secondary task response nearly vanishes with an extremely challenging primary task.**

2.5.3 Mental workload and multivariate parameters

In the assessment of mental workload, EEG measures have been made more sensitive by combining different parameters calculated from EEG frequency content, obtained from different sites to a single parameter (Gevins *et al.*, 1998; Smith *et al.*, 2001; Wilson & Fisher, 1995). EEG frequency content has also been combined with parameters calculated from other physiological measures in order to better represent the overall load in a multitask condition (Ryu & Myung, 2005; Wilson & Russell, 2003a; Wilson & Russell, 2003b).

The participant-specific multivariate function, based on neural network pattern recognition applied to EEG spectral features, has been utilised for working memory load assessment both during simple working memory task (Gevins *et al.*, 1998), and a more challenging multitasking simulation (Smith *et al.*, 2001). The method is capable of differentiating with 95% accuracy between low and high task demand conditions. However, the method needs participant specific training of the classification algorithm. In the training session, the candidate set of 18 potential features are reduced to a subset of four optimal features, uniquely selected for each participant (Gevins *et al.*, 1998).

Other parameters, such as eye blink rate, heart-rate variability, and respiration rate do not improve the classification accuracy of the index formed solely from the EEG (Wilson and Russell, 2003b; Wilson and Russell, 2003a). However, if the only parameter used from the EEG frequency content is the alpha suppression, adding blink rate and/or heart rate variability information does enhance workload evaluation (Ryu & Myung, 2005).

In human computer interface applications (HCI), EEG indices could also be used to reduce operators' mental workload and enhance performance: EEG -based adaptive automation systems detect operator disengagement or lowered attention and modify the task to increase operator involvement (Bailey *et al.*, 2006; Freeman *et al.*, 1999; Pope *et al.*, 1995; Scerbo *et al.*, 2003).

> **In summary, multivariate EEG methods can improve the accuracy of mental workload assessment. However, currently they need participant and task specific training of the classification algorithm, which is time consuming and impractical.**

2.6 Conclusions on the feasibility of ERP and EEG methods

ERP and EEG measures have been related to external task demand changes as well as to subjects' internal state, and thus show potential for neuroergonomic purposes. However, previous studies reveal restrictions in the use of these methods. For example,

- The P300 amplitude decrease is dependent on task demands. During an easy task, no decrease is seen, whereas the P300 component of the secondary task response nearly vanishes with extremely challenging primary tasks. Thus a suitable range of task demands should be defined when using the P300 amplitude in mental workload assessment.

- EEG frequency spectrum measures do not seem to be sensitive by themselves. The same EEG spectrum findings can indicate two totally different physiological states: alpha power increases both when task demand is low and when a subject is falling asleep. It is thus not possible to differentiate whether the risk of error is low as a subject is performing a task at a low mental workload level or whether the risk of error is high because the subject is falling asleep.
- Multivariate methods can improve the sensitivity of workload assessment. However, while being capable in differentiating at least low task demands from high with 95% accuracy, currently the method needs participant specific training of the classification algorithm, which is impractical.
- So far studies have used different parameters and setups in estimating mental workload, and thus comparing the usability of the methods in the context of neuroergonomics is difficult. Also, for this reason, generalising the results is challenging.

3 Aims of this Thesis

The aim of this Thesis was to develop objective metrics for the assessment of mental workload and the identification of the functional state of the brain of an individual. The second aim was to design more generic simulations of multi-tasking for systematic study of the effects of external and internal factors on task performance.

Neurophysiological methods and experimental setups for both the assessment of cognitive workload during work performance, as well as for the identification of work-related diseases were studied and improved as follows:

- *Designing an experimental setting*: An experimental setup was developed, enabling the study of the effects of external (Publication V) and internal (Publication IV and Publication PV) load changes on task performance and brain physiology.

- *Conventional methods*: The feasibility of conventional ERP (Publication I) and EEG (Publication III and Publication IV) methods were tested in both

  a) the assessment of the internal state of the participants during challenging task performance after sleep debt (Publication IV) and

  b) the diagnosis of a work-related central nervous system disorder (Publication I and Publication III).

- *Methodological improvements:* Both ERP (Publication II) and EEG (Publication V) methods were improved and tested in healthy controls.

  a) ERPs were analysed with a single-trial method (Publication II), and

  b) EEG methodology was developed for estimating both internal and external load (Publication V).

4 Material and methods

This chapter aims to give an overview of the participating subjects, and the methods and tests used in these studies.

4.1 Subjects

The summary of the subjects, their age, and circumstances in the publications is presented in Table I.

The healthy subjects in Publication II and matched healthy controls in Publication I were laboratory/Institute personnel, volunteering for the study, and were not paid for participation. Healthy participants in Publication IV and Publication V were 19–22 yrs conscripts, who volunteered for the study and gave their informed consent. The study designs were approved by the Ethical Committee of the Hospital District of Helsinki and Uusimaa.

Patients in studies Publication I and Publication III were workers, who have been diagnosed with chronic solvent encephalopathy (CSE). CSE patients have had long-term low-level exposure to organic solvents at work. The exposure may lead to permanent central nervous system damage. The diagnostics of CSE is demanding, since there is a lack of tests that are specific to CSE and the diagnosis relies on the detection of cognitive dysfunction in the neuropsychological assessment. It is suggested that cognitive impairment in CSE is related to attention and information processing (Meyer-Baron *et al.*, 2008). ERPs and EEG have been part of the diagnostic verification protocol applied to suspected work-related nervous system disorder.

Table I: The summary of the subjects, their age, and their circumstances in the publications.

Publication	Subjects	Subject's circumstances
I	86 CSE patients, 34–61 years, 192 controls 20–65 years	Patients: occupational chronic solvent encephalopathy, matched healthy controls and laboratory controls
II	9 female, 25–39 years	Healthy
III	47 CSE patients, 32–61 years, 124 controls 25–65 years	Patients: occupational chronic solvent encephalopathy, matched healthy controls and laboratory controls
IV	16 male, 19–22 years	Healthy: sleep deprivation
V	24 male, 19–22 years	Healthy: task demand changes, sleep deprivation, time of day

4.2 Experimental setup

4.2.1 Study setups

The classical oddball paradigm was used in studying healthy subjects with selective averaging and single trial ERPs (Publication II) and in CSE patients (Publication I). The oddball paradigm was used as part of the multitask in Publication IV and Publication V. Participants responded with a button press (Publications II, IV and V), or silently counted the number of targets presented (Publication I). In the EEG study with CSE patients (Publication III), participants were sitting in a comfortable chair and relaxed with eyes open. They were not allowed to sleep. Summary of the study setups is presented in Table II.

Table II: Summary of the study setups, showing test paradigms, studied phenomena, and analyses made.

Publication	Test	Phenomena	Analyses
I	Auditory oddball, 25% targets, silent counting	Occupational chronic solvent encephalopathy	ERP P300, averaging
II	Auditory oddball, 15% targets, button press	Relationship with reaction time and preceding stimulus sequence	ERP P300, single trial
III	Eyes open	Occupational chronic solvent encephalopathy	EEG
IV	Brain@Work multitask	Sleep deprivation, recovery sleep, rest pause	EEG/EOG defined sleepiness during task execution
V	Brain@Work multitask	Task demand changes, sleep deprivation, recovery sleep	EEG, power spectrum during task execution, ERP P300

4.2.2 Brain@Work multitask

The Brain@Work multitask (B@W, Figure 2), used in Publications IV and V, was programmed at the Brain and Work Research Centre with Delphi 5 (Borland Software Corporation, California). It was further developed on the basis of an earlier multitask software SynWork (Elsmore, 1994; Proctor *et al.*, 1998), to suite the requirements of the experiments.

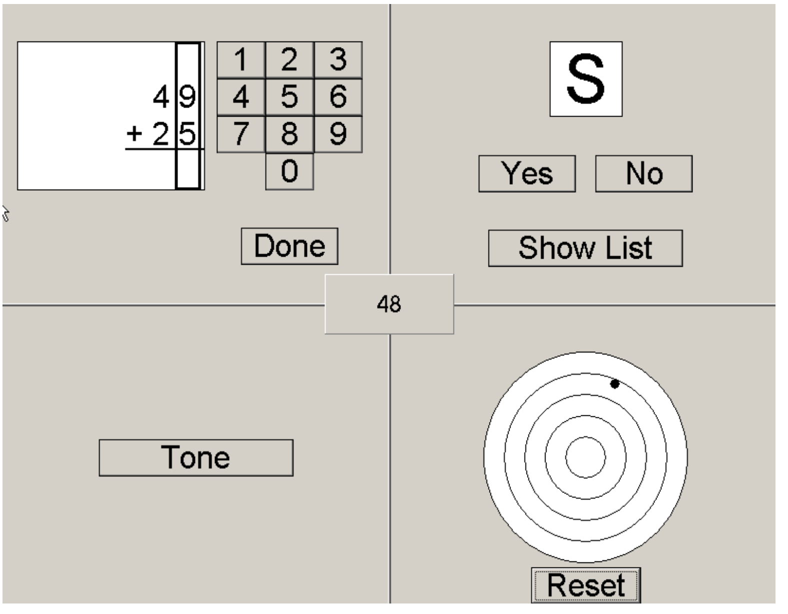


Figure 2: An example of the user interface of the computerised multitask. Top left: the arithmetic task; top right: the memory task; bottom left: the auditory attention task; bottom right: the visual vigilance task, centre of the screen: gained points.

Our B@W task, composed of four subtasks, is adjustable software. In this system, the number of subtasks to be presented simultaneously, the level of the subtask difficulty, the timing of the subtasks (stimulus display time and inter-stimulus interval) as well as the scoring of the responses can be freely defined. The software communicates with other measurement systems through a computer's parallel (LPT) and serial (COM) ports. As an output, B@W generates a log-file, which includes all information about presented stimuli and responses made by the subject during the measurement session.

The number of the concurrently active tasks could be selected and the inactive task during a test session was indicated with an empty grey square. The auditory attention task (AUD, auditory oddball task) consisted of two tones (60 dB 50 ms tones, target 1.2 kHz and non-target standard 1 kHz, 20% and 80% of tones, respectively, with an inter-stimulus-interval of 1.5 s) delivered through loudspeakers. The participant pressed a separate response pad when a target tone occurred. The ERPs were triggered to these tones.

In the arithmetic task (ARI), participants added two numbers and responded with a mouse on a number pad presented on the computer's monitor.

In the memory task (MEM), the participants classified whether the letter shown was among a list memorised before each trial. In the visual vigilance task (VIS), a dot appeared in the centre of the circle and started to move towards the outermost border of the circle. The participant had to return the dot back to the innermost circle with a button press before the dot reached the edge of the outermost circle. To motivate the subjects to keep up stable performance, they scored points with correct and lost points with wrong or missed responses.

4.2.3 Synchronisation of multitask performance and physiological measurements

The B@W multitask software provides a temporal resolution of approximately 100 ms which is too inaccurate for ERP studies. Thus, an external stimulus system was connected to the B@W task. The synchronisation of multitask performance and physiological measures is presented as a diagram in Figure 3. The STIM triggering system (Compumedics Ltd, El Paso, Texas) was used for presenting the auditory stimulus, from which the event related potentials were triggered. The STIM presented the stimulus and at the same time sent the stimulus information further to the physiological measurement system SynAmps (Compumedics Ltd, El Paso, Texas) via a serial port. The subject reacted to the target auditory stimuli with a response pad. The STIM recorded and classified the correctness of the response, and sent response codes both to the SynAmps amplifier (via the parallel port) and to the B@W -software (via the COM port). The SynAmps stored response codes in time synchrony with physiological recordings. The B@W -software registered the response codes online from the serial port (COM), added the information to the log-file, and updated the scores accordingly. Thus, the same information of the auditory stimuli was sent both to the physiological measurement system and to the B@W -software. This enables the combined analysis of the two measures of workload, i.e., synchronised analysis of both the performance in multi-task and selected physiological variables.

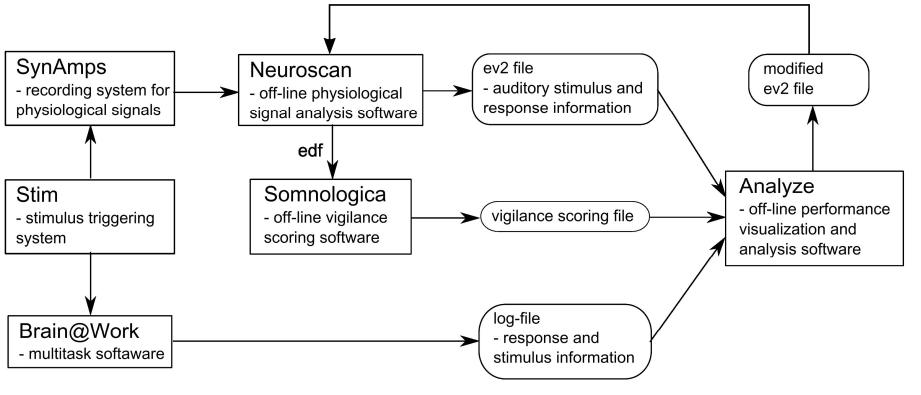


Figure 3: Synchronisation of multitask performance and physiological measurements. The same stimulus information is sent both to the physiological and performance recording systems enabling the synchronised analysis of the two.

4.2.4 Analysing multitask performance

Analysis and visualisation of performance on the B@W task was made with an analysis program Analyze, which was programmed for this purpose in our laboratory with Delphi 5. Analyze operates on Windows platform. The performance of a single subject can be examined at a time. The possibility to use batch-operations to make repetitive analyses for multiple B@W log-files is available.

The performance of a subject is measured with the scores obtained from each subtask. The performance is visualised by the performance profile, which shows cumulative performance as a function of time. An example of performance profiles during 70 min multitask performance is shown in Figure 4. Areas of interest can be freely selected from the performance profile to study performance in a certain time range. Information about quality of the performance, i.e. correctness of responses, in addition to reaction times for each subtask in the total session and in the selected areas can be saved into an ASCII-file.

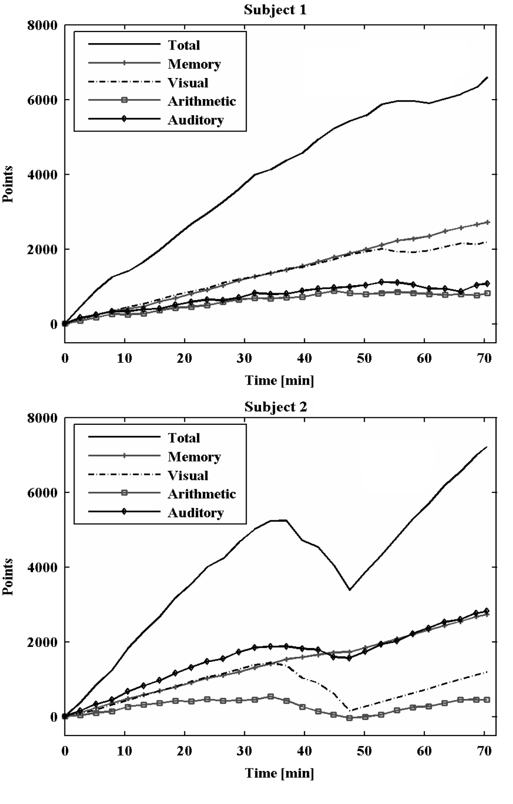


Figure 4: An example of performance profiles during 70 min multitask performance. Subjects 1 and 2 reached approximately the same end result (~ 7000 points) in the test but had different performance profiles: Subject 1 collected points steadily throughout the test session, whereas Subject 2 lost points in the middle of the test but collected points faster at the beginning and at the end of the task.

The Analyze software utilises the NeuroScan ev2 -data format for communication with physiological analysis software. Areas of interest, selected in Analyze, can be exported to the corresponding ev2 -file. This modified ev2 -file can be imported back to the corresponding physiological measurement session in NeuroScan. Since Analyze also reads the area definitions from the ev2 -file, the area selections made in other analysis systems can be imported into the performance profile.

4.3 Recordings

EEG-recordings in projects, where healthy subjects were studied (Publications II, IV, and V), were measured with a SynAmps amplifier. The subjects sat in front of a computer screen during the measurement, Figure 5. In CSE-patient studies (Publications I and III) a Cadwell Spectrum 32 system (Cadwell Laboratories, Inc, Kennewick, Washington) was used. The patients sat in a comfortable chair and listened to audio tones. The electrodes were placed according to the 10-20 System with a reference electrode located at the right mastoid (SynAmps, Publications II, IV, and V) or linked ears (Cadwell, Publications I and III).

Figure 5: A subject sitting in front of the computer screen with the EEG electrodes on.

4.3.1 Measurement setup in Publications IV and V

The subjects in the studies with the B@W -multitask (Publications IV and V) were trained to maintain a stable performance on the B@W task. During a training day, the difficulty of the task was adjusted according to one's own cognitive capacity. First, the number of remembered letters was assessed as well as the ability to add digits in the arithmetic task. These two parameters (number of remembered letters and number of digits in adding tasks) were adjusted for each participant. After that, all four tasks were presented concurrently and the presentation rate of ARI and MEM tasks was shortened until performance reached the level of 70% of the maximum points (see Publication IV for detailed description of task adjustment).

External task demands were varied in the multitask study Publication V. The different levels of task load in computerised cognitive tasks were achieved with variations in the number of simultaneous tasks. The number of tasks to be performed concurrently was varied between single (AUD), dual (AUD+ARI), and multi (all four tasks simultaneously at medium-pace) sessions.

The sleep deprivation setup (Publications IV and V) is shown in Figure 6. In short, a within-subject study design was used. The participants visited the laboratory three times. The first visit was for learning the task and for sleeping a habituation night at the laboratory. On the second and third visits they performed the actual test protocol and were allowed to sleep either for 2 or 8 hours during the first night.

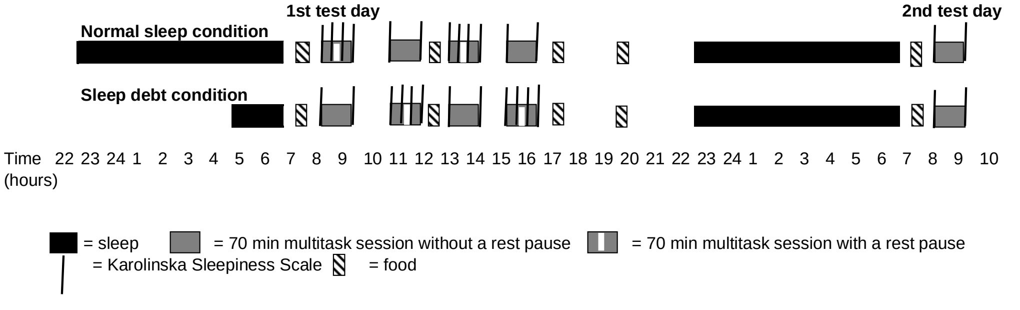


Figure 6: Study design in Publications IV and V. All participants underwent both conditions in a counterbalanced order. Every second 70 min multitask session contained a 10 min rest pause during the 1st test day.

Multiple physiological signals were measured simultaneously in all sessions using SynAmps and Embla (Medcare, Reykjavik, Iceland) systems. Both systems were used to ensure recordings; in case of failure of either system, the other one could be used as backup. In addition, the use of both systems enabled more versatile analysis of data, e.g. ERPs (with SynAmps and Neuroscan) software and vigilance/alertness scoring (with Embla and Somnologica). The electrodes were connected to the preamplifier of the SynAmps, and four channels (electro-oculography, respiratory movements, galvanic skin response, and continuous blood pressure) further connected to the Embla system. Two EEG signals (Fp1, Fp2) were only recorded with Embla.

Instead of using the auditory vigilance subtask in the software, an external equipment STIM was used to generate and control the auditory stimuli, as described in the previous section. Subjects gave responses to the auditory vigilance task with a separate response pad (STIM) using their left hand, and used a mouse with their right (dominant in all subjects) hand to respond to the other three subtasks of the B@W software presented on the computer monitor.

EEG was measured continuously with silver electrodes, referenced to the right and grounded to the left mastoid (impedance <5 kΩ), pass-band filtered (0.5–50 Hz), and digitised at 500 Hz using a SynAmps amplifier.

4.4 Data analysis

With Scan Edit 4.3.3 utility, we transformed the data measured to 4-sec epochs, corrected for eye movement artefacts with the ocular artefact reduction (OAR) utility, excluded epochs containing other artefacts (±70 μV), and computed spectrograms for the 10–20 system derivations Fz, Cz, and Pz using a Fast Fourier transformation. The sweeps were smoothed using a 2048-sample Hanning window, and absolute spectral power values for theta (4–8 Hz) and alpha (8–12 Hz) were calculated.

For P300 analysis in Publication IV, EEG was transformed to epochs of –100 to 900 msec relative to the onset of the target tones in the auditory attention task. Eye movements were corrected for and artefacts removed as in the EEG analysis. The response for auditory target tones was computed for the 10–20 system derivations Fz, Cz, and Pz. The average waveforms were low-pass filtered at 20 Hz, and the P300 component detected as a maximum positive peak within 250–550 msec. The amplitude of P300 was measured relative to the 100-msec pre-stimulus baseline.

The EEG and ERP data measured during the multi-task performance (Publications IV and V) and single trial ERPs (Publication II) were analysed with Scan 4.1 and partly with Matlab. The data from CSE-patients (Publications I and III) was analysed with the Cadwell Spectrum 32 system. The visual scoring of sleepiness during multitask sessions (Publication IV) was performed by laboratory technicians with Somnologica software.

In Publication II, the continuous EEG data were transformed off-line to epochs of – 100 to 500 ms relative to the onset of each stimulus. Epochs containing eye movement artefacts were excluded from further analysis, using both automatic (trial exceeding ± 70 μV) and visual inspection of the data. Based on previous literature described in the Introduction, both amplitude and latency of the P300 are expected to vary in relation to reaction time and preceding stimulus sequence. Thus, selective averaging and the Subspace regularization-based method, described in (Karjalainen *et al.*, 1999), were used to study the relationship of P300 amplitude and latency with reaction time and with the preceding stimulus train. The method allows trial-to-trial variation both in the latency and in the amplitude of the P300 component while still suppressing most of the noise and was thus suitable for this purpose. The method is a modification of the ordinary least squares solution, which minimises the squared norm of the difference between the single-trial measurements and a model. In Publication II, the Gaussian based vectors were used to model the evoked potentials and the statistical information, extracted from the measured event-related potentials, to represent information about the measurement set. With a regularisation parameter, the balance between these two can be adjusted. The exact formulation of the method is described in Publication II (Appendix A).

The single trial analysis was performed with Matlab. Statistical testing was made with SPSS in Publications I, II and V and with SAS in Publication II and IV.

5 Summary of results

5.1 Experimental setup

The study setup with the synchronisation of multitask performance and physiological state of the subject was used in Publications IV and V. In off-line analysis we noted that sometimes the synchronisation between physiological measurements and multitask performance failed: the B@W-software did not recognise all the information sent by STIM. As we saved the same data with different systems (STIM, SynAmps and B@W software), we were able to manually synchronise also that failed data.

The Publications IV and V consisted of a variety of measurements of 26 subjects. In Publication IV, each subject underwent ten multitask sessions lasting 70 minutes and in Publication V, six recordings lasting ten minutes. This resulted to 160 recordings lasting 70 -minute and to 120 recordings lasting ten minutes. The time synchronisation between the measurement devices and the stimulus program succeeded automatically in 88% of measurements, in 11% of 70-minute measurements the data was synchronised offline, and in 1% of the measurement the data was lost.

5.2 Conventional methods in a neuroergonomic framework

5.2.1 ERPs in the identification of mild cognitive impairment

The P300 latency measured from the CSE patients (Publication I) was longer than that measured from the laboratory controls, but there was no difference between patients and matched healthy controls, Figure 7. The P300 amplitude measured from CSE patients differed from both laboratory and matched healthy controls at group level, but the classical oddball paradigm does not seem to be sensitive at an individual level in the occupational clinical diagnostics, Figure 7. However, as the amplitude of P300 correlated with Digit Symbol test results, which were impaired in CSE patients, it is suggested that measuring neurophysiological indices during neuropsychological test performance may improve the clinical usefulness of the ERPs in the early diagnosis of CSE.

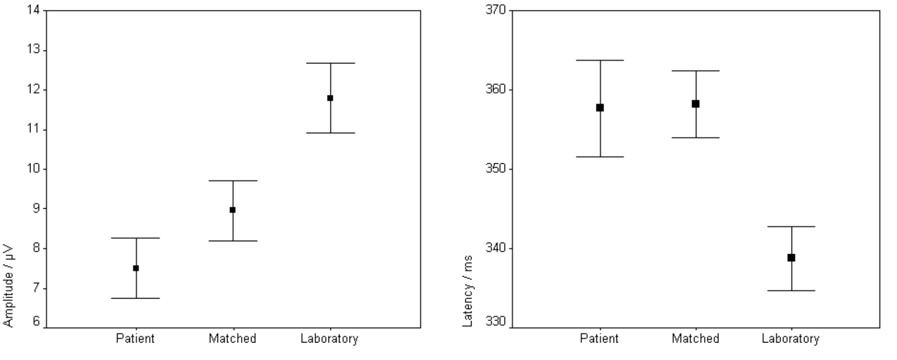


Figure 7: The mean and confidence intervals for the P300 amplitudes (left) and latencies (right), measured form patients, matched controls, and laboratory controls. (Data is from Publication I).

5.2.2 EEG in the identification of mild cognitive impairment

The conventional resting EEG spectrum analysis in CSE patients (Publication III) showed increased theta activity at frontal areas compared to the laboratory controls. However, when compared to the age-matched controls, this difference vanished. Also, the level of occupational solvent exposure did not associate with the amount of increased activity. Thus, the clinical usefulness of the conventional EEG spectrum analysis remains inadequate in CSE patient identification.

5.2.3 EEG defined sleepiness and the ERP P300 component in sleep deprived subjects performing a challenging multitask

Sleepiness, defined as increased slow eye movements and theta activity at central and occipital areas and scored manually, increased with sleep deprivation, Figure 8, (Publication IV). Performance in the Brain@Work -multitask deteriorated with sleep debt, Figure 9.

In Publication IV, performance clearly improved, but did not reach the level of the normal sleep condition, after the 8-h recovery night. Also the EEG/EOG defined sleepiness of subjects remained at a higher level than during the normal sleep condition. The participants, whose performance in B@W test deteriorated the most in the sleep deprivation condition tended to be the same ones whose multitask performance did not fully recover. However, EEG/EOG defined sleepiness did not show the same relationship.

Additional analysis made with that data, showed that the P300 amplitude, measured concurrently with B@W task performance, did not show any statistically significant changes due to time awake or due to the sleep deprivation, $p>0.05$ in all comparisons.

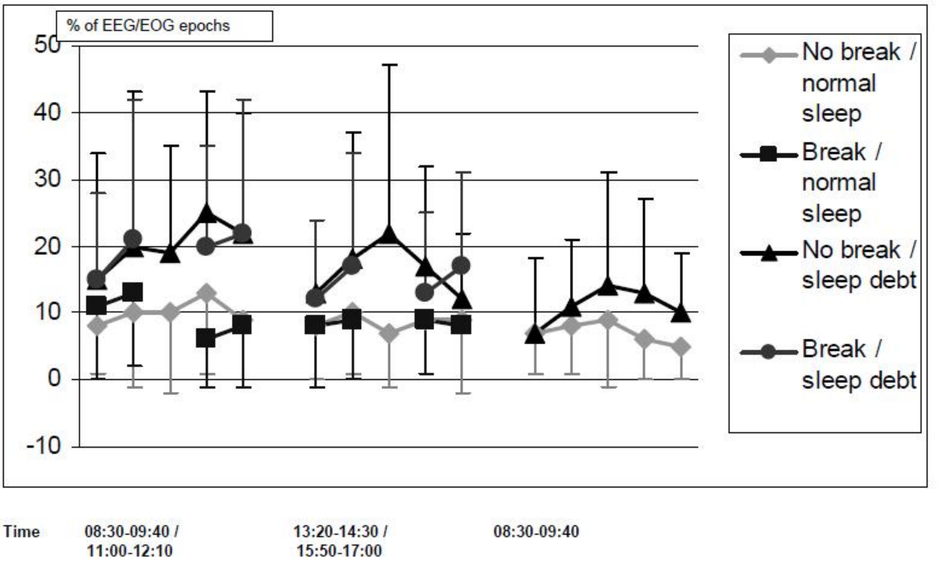


Figure 8: EEG/EOG-defined sleepiness expressed as percentage of the 20 s epochs containing signs of sleepiness during the 70 min multitask sessions (see Methods).The multitask sessions have been grouped in the forenoon sessions (08:30–09:40 / 11:00–12:10) and the afternoon sessions (13:20–14:30 / 15:50–17:00) with and without the 10 min rest pause. Each data point represents the mean proportion of "sleepy" epochs during a 15 min period, except the point in the middle that represents the mean value for a 10 min period. The vertical lines indicate standard deviations. (Original figure is in Publication IV).

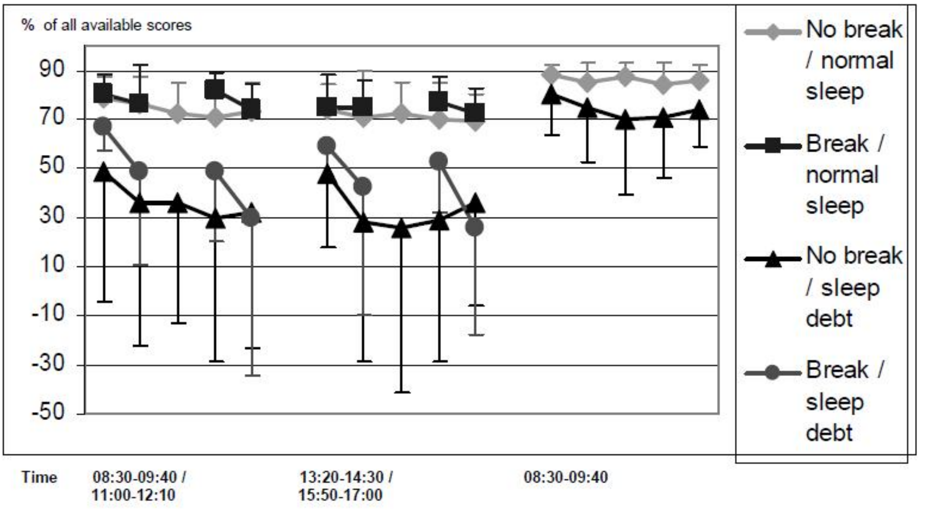


Figure 9: Multitask performance expressed as percentage of all the scores available. The 70 min multitask sessions have been grouped in the forenoon sessions (08:30–09:40 / 11:00–12:10) and the afternoon sessions (13:20–14:30 / 15:50–17:00) with and without the 10 min rest pause. Each data point represents the mean performance during a 15 min period, except the points in the middle that represent the mean performance during a 10 min period. The vertical lines indicate standard deviations. (Original figure is in Publication IV).

5.3 Methodological improvements

5.3.1 ERP single-trial analysis

The P300 latency was significantly shorter for target tones that were preceded by a large number of standard tones compared to the target tones that were preceded by a small number of standard tones, Figure 10, Publication II. This holds true regardless of the method used to analyse the responses. Thereafter, the amplitude increased with a larger number of preceding standard tones, but only when analysed with conventional averaging, Figure 10. In-depth analysis showed that single-trial amplitudes correlated positively with the number of preceding standards. It was also found that the standard deviations of single-trial latencies was larger with a small numbers of preceding standards compared to a large numbers of preceding standard tones. Thus, the amplitude decrease, seen in average waveforms with a smaller number of preceding standard tones, may partly be explained with larger latency variability, which may cause an overestimation of the effect seen in the averaged amplitudes.

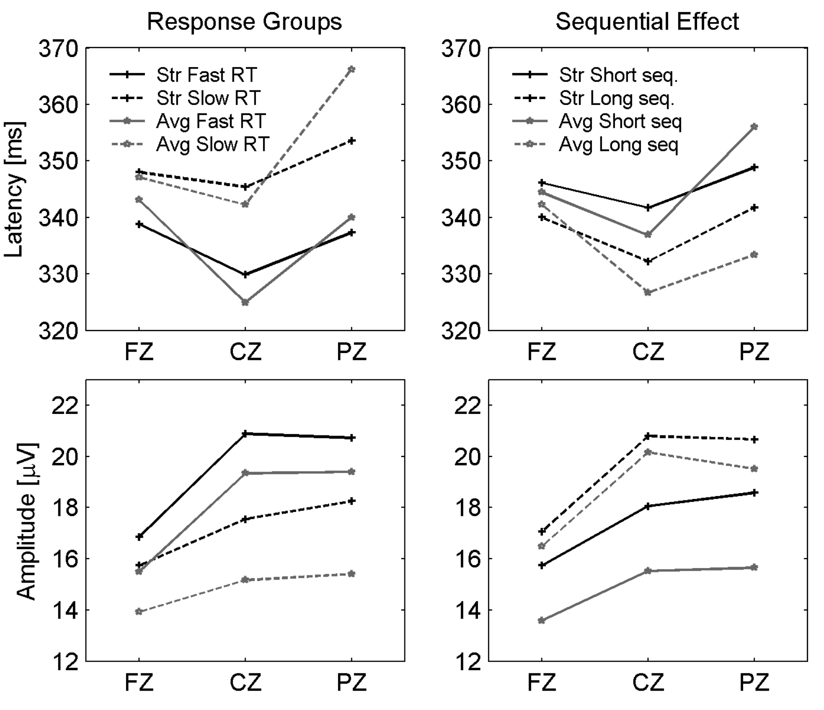


Figure 10: The relationship of reaction time (left column) and the number of preceding standard tones (right column) with the P300 latency (upper row) and amplitude (lower row) with both methods (Str = Single trial, Avg = averaging). (Original figure is in Publication II).

The single-trial responses make it possible to study the relationship between the P300 component and reaction time and preceding standards more accurately. Regression analysis showed that the latency correlated negatively with the number of preceding standard tones and positively with the reaction time. The P300 amplitude behaves in an opposite way: the amplitude correlated positively with the number of preceding standard tones and negatively with reaction times.

The single-trial analyses of ERPs give information about the dynamics of the P300 component that is lost with conventional averaging. However, the single trial method needs a sample of responses to calculate single trial estimates. Since the method weights features common to the whole measurement set, it underestimates less frequent waveforms. Thus, the method is not usable in recordings where, for example, a rare stimulus feature or a sudden change in a functional state of an individual affects the waveform radically. This also restricts its usability for neuroergonomic purposes, such as monitoring on-line changes in the functional state of an individual during actual work tasks: if some new components or features appear to the waveforms, that are not included in the model, they will be underestimated or even removed in waveform estimation. Thus, the statistical information about measured event-related potentials that is composed from alert subject may not be usable as prior information when monitoring increased need to sleep.

Thus, even though the single-trial analysis showed its potential in studying the dynamics of ERPs, it still needs simplification and some more development in order to be used out of the laboratory, at work places or occupational clinical practise.

5.3.2 EEG, task demands, and sleep deprivation

A new index, which could be used for both mental workload and fatigue estimation, is presented in Publication V. The index, calculated as the ratio of frontal theta to parietal alpha (theta Fz / alpha Pz), increases with the number of tasks to be performed concurrently and with increased time awake, both after normal sleep and sleep debt, Figure 11. Moreover, the increase of the ratio is more pronounced in the afternoon after sleep deprivation. The ratio increases with mental workload, similar to the heartbeat with increasing physical load. Thus it was named "brainbeat" by the authors.

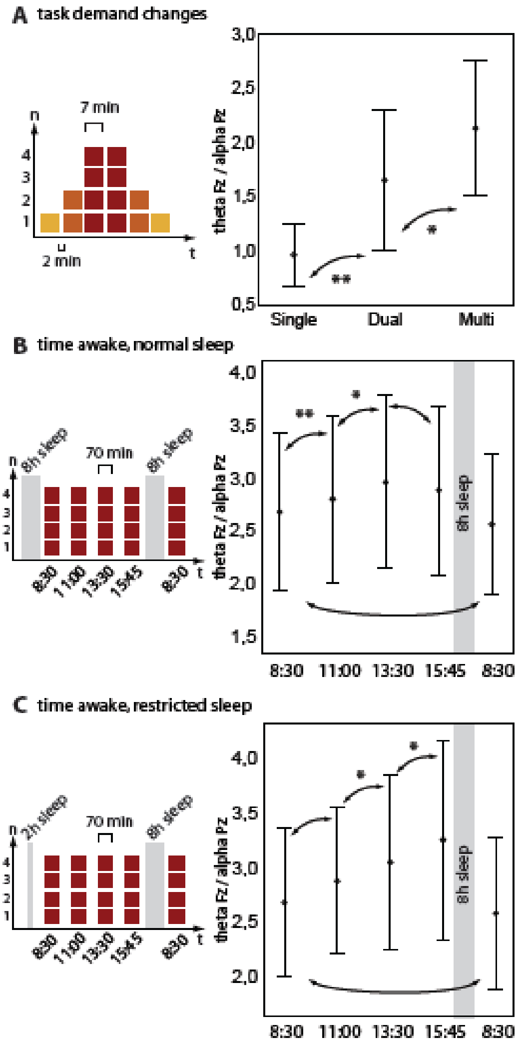


Figure 11: Theta Fz / alpha Pz -ratio correlates with external and internal factors. **a** The theta Fz / alpha Pz –ratio increased systematically with increasing task demands. **b** Normal sleep protocol. The theta Fz/ alpha Pz –ratio increased with time awake. After a well slept night the ratio returned to the baseline value, even though the performance was improved. **c** Sleep restriction protocol. The theta Fz / alpha Pz

–ratio increased with time awake. After a well slept night the ratio returned to the baseline value. a, b, c Error bars indicate S.E.M., * p<0.05, ** p<0.01. (Original figure is in Publication V).

Additional correlation analysis with the data in Publication V showed that the subjects, whose recovery from sleep debt was the worst (as indicated by increased theta Fz / alpha Pz -ratio after recovery night), tended to be the same persons, who also exhibited most elevated theta Fz / alpha Pz -ratios during the afternoon after sleep debt (Spearman correlation coefficient = 0.829, $p<0.001$), Figure 12. As described in section 5.2.3, the EEG/EOG defined sleepiness could not reveal the same relationship.

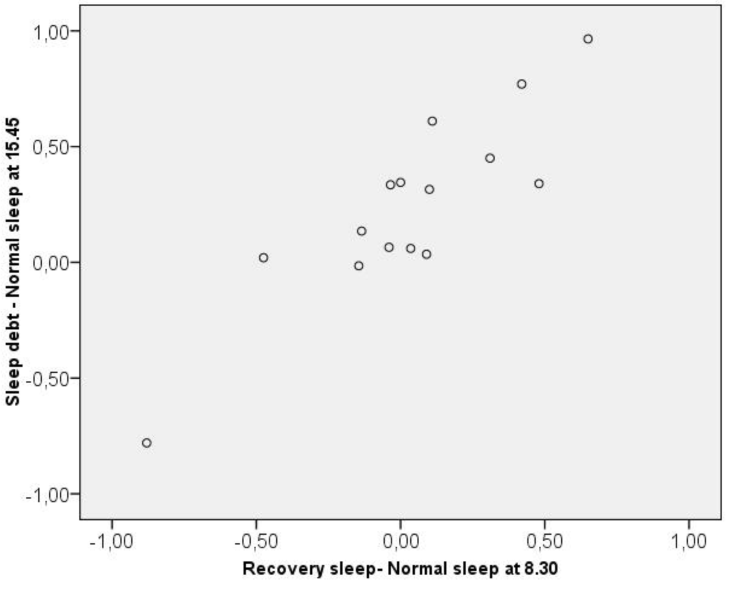
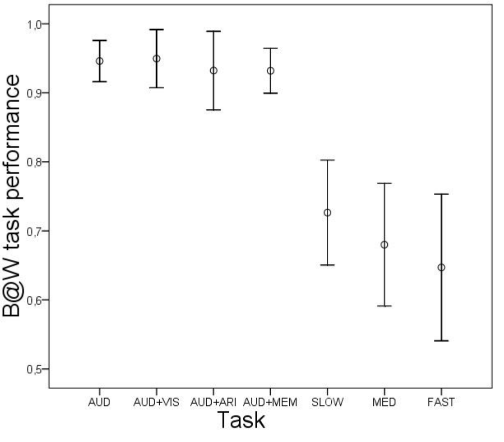
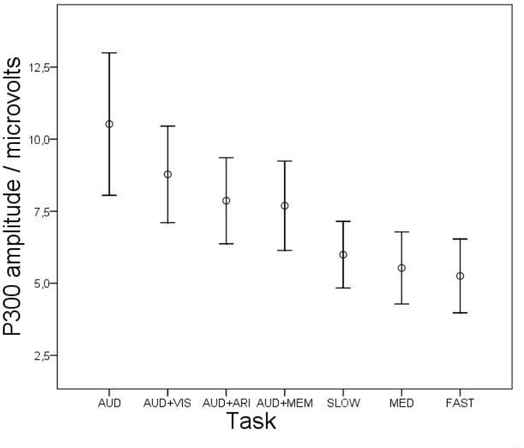


Figure 12: Individual differences in the response to sleep deprivation and recovery: The difference in the theta Fz / alpha Pz -ratio between restricted sleep and normal sleep nights as a function of the difference in the ratio between recovery sleep and normal sleep nights. (Data is from Publications IV and V).

It was also shown in Publication V that the sensitivity of the index in differentiating the single task condition from the multitask condition was at the same level with the sensitivity of the ERPs. The P300 amplitude decreases approximately 20% from the baseline condition when an auditory oddball task is combined with visual, arithmetic, or memory subtasks, Figure 13. During this amplitude decrease, the performance accuracy remains stable. The theta Fz / alpha Pz ratio increases approximately 50% from the baseline condition when additional tasks are presented. In the multitask condition (four concurrent tasks) the P300 amplitude decreases approximately 50%, the ratio increases approximately 100%, and the performance accuracy also decreases approximately 30% compared to the baseline condition. The P300 amplitude as well as theta Fz / alpha Pz ratio, remained stable when the task presentation rate was manipulated by increasing (slow-paced task), or decreasing (fast-paced task) the inter-stimulus interval by 25% from each individual's previously determined level (medium-paced task).


B@W task performance
1,0
0,9
0,8
0,7
0,6
0,5
AUD
AUD+VIS
AUD+ARI
AUD+MEM
SLOW
MED
FAST
Task


P300 amplitude / microvolts
12,5
10,0
7,5
5,0
2,5
AUD
AUD+VIS
AUD+ARI
AUD+MEM
SLOW
MED
FAST
Task

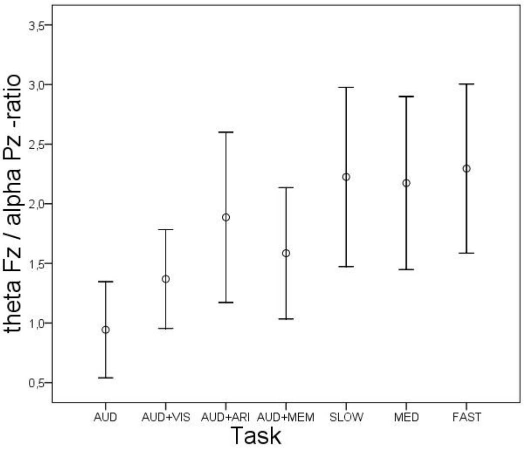

theta Fz / alpha Pz -ratio
3,5
3,0
2,5
2,0
1,5
1,0
0,5
AUD
AUD+VIS
AUD+ARI
AUD+MEM
SLOW
MED
FAST
Task

Figure 13: The task performance (top), the P300 amplitude (middle), and the theta Fz / alpha Pz -ratio (bottom) for different task conditions. The P300 amplitude decreases and the theta Fz / alpha Pz ratio increases already while the performance remains at a stable level during dual-task situations. The performance accuracy level begins to deteriorate when four tasks have to be performed simultaneously. Order of the tasks from left to right: Auditory oddball (AUD), auditory oddball concurrently with visual subtask (AUD+VIS), auditory oddball concurrently with arithmetic subtask (AUD+ARI), auditory oddball concurrently with memory subtask (AUD+MEM), slow-paced multitask situation (SLOW), medium-paced multitask situation (MED), and fast-paced multitask situation (FAST). (Data is from Publications IV and V).

As has been shown in Publication V, the preliminary results from three subjects suggested that the index could be applicable even at an individual level differentiating at least single task demands from more challenging multitask conditions, Figure 14.

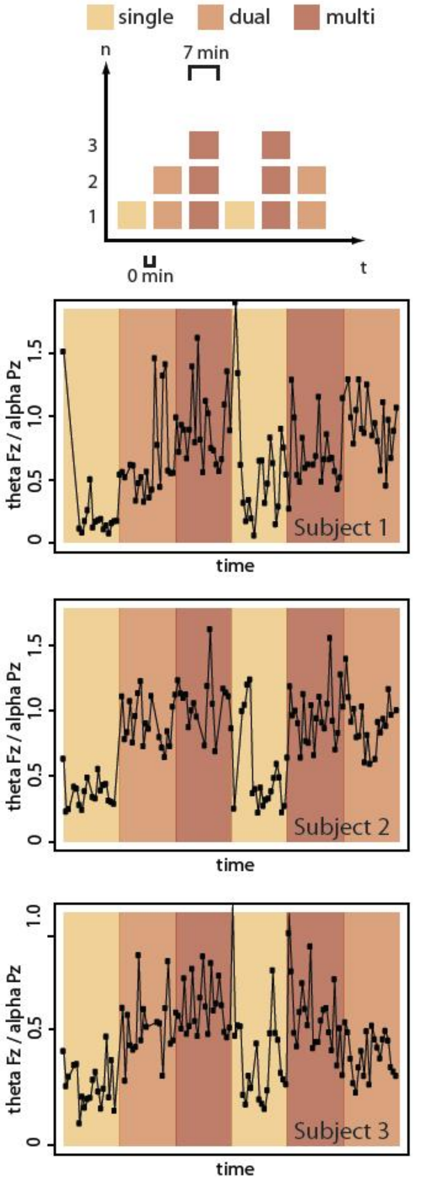

single
dual
multi
n
7 min
3
2
1
0 min
t
theta Fz / alpha Pz
0
0.5
1.0
1.5
Subject 1
time
theta Fz / alpha Pz
0
0.5
1.0
1.5
Subject 2
time
theta Fz / alpha Pz
0
0.5
1.0
Subject 3
time

Figure 14: Examples of reactivity of the theta Fz / alpha Pz -ratio to continuous changes in task demands. Task-setting: The subjects performed continuously the single, dual and multi conditions, 7 minutes per condition for a total time of 42 minutes. The value is averaged over 20 s. The difference between single compared to dual and multi was clear but between dual and multi at individual level somewhat more varied (clear in subjects 2 and 3 but not in 1). The effort put on task performance by the individual may affect the values. (Original figure is in Publication V).

6 Discussion

The aim of this Thesis was to develop neurophysiological metrics for the assessment of mental workload, caused by either or both external and internal factors, and for recognising even moderate decreases in cognitive functioning of the workers. The conventional neurophysiological methods were tested in a neuroergonomic (brain at work) framework, and a novel method for signal analysis was developed. Also, the experimental setup for studying these effects was designed.

6.1 Experimental setup

As a part of this Thesis an experimental setup, where the effects of both internal and external factors on multitasking performance can be systematically studied, was designed. The present approach is based on the time-synchronised measurements of performance and physiological signals in a multi-task environment. The performance is visualised as a continuous performance profile and the analyses of physiological variables can be channelled by this information. The approach provides unique possibilities to study changes in mental workload with interactions between performance and physiological variables, as well as with changing functional state of an individual.

Different physiological variables are sensitive to different aspects of workload. Thus no single measurement technique will be adequate in all study designs and a problem-based tailoring of the measurement setup is required (Gopher & Donchin, 1986; Hancock & Szalma, 2007; Hockey, 1997). The results of this study setup have been used extensively in the Brain and Work Research Centre, including composing thesis works, examining clinical patients and designing new study setups.

Time-synchronized physiological measurements allow the examination of several different individual-, task-, and environmental-related factors that may contribute to good performance.

6.2 Conventional methods in the identification of mild cognitive dysfunction and sleep debt

The EEG and ERP studies (Publications I and III) showed that conventional methods can reveal differences between patients (CSE) with cognitive dysfunction and normal controls at group level: the P300 amplitude was smaller in patients than in age and education matched group, or laboratory controls. Also, theta activity is increased at frontal areas in CSE patients. However, these conventional methods fail in identifying cognitive dysfunction at the level of individuals.

In manually scored EEG, sleepiness (Publication IV) increased in sleep deprivation (2 h sleep vs. 8 h sleep). However, when the performance metrics showed that the subjects whose performance recovered only partly after recovery sleep tended to be the same persons whose performance was most decreased due to sleep deprivation, the EEG scored sleepiness did not show the same pattern. Previous studies have shown that the amount of theta activity increases both due to increased need to sleep caused by sleep deprivation (Cajochen *et al.*, 1999a; Cajochen *et al.*, 1999b; Cajochen *et al.*, 2001; Caldwell *et al.*, 2002; Smulders *et al.*, 1997), as well as due to focused attention (Doppelmayr *et al.*, 2008; Yamada, 1998). EEG defined sleepiness, which relies on the amount of slow eye movements and theta activity (Publication IV), may thus be interfered by focused attention that the participant has to maintain during B@W task performance. This may explain the inconsistency between the performance and EEG defined sleepiness results.

Previous studies, with extended wakefulness (Gosselin *et al.*, 2005; Smith *et al.*, 2002), have reported decreased P300 amplitude, especially after the normal bed time of the subjects. On the contrary, P300 amplitude has been reported to remain intact after two nights sleep fragmentation (Cote *et al.*, 2003), suggesting that this level of sleepiness may be compensated by increased effort. We could not find a decrease in the P300 amplitude with sleep deprivation. Our participants were allowed to sleep for two hours before the measurements, which may resemble more closely sleep fragmentation than total sleep deprivation.

Methods, based on conventional EEG power spectrum and P300 measures, reveal differences at group level in mild cognitive dysfunction. EEG based manually scored sleepiness estimation is useful, but time consuming and not possible to carry out on-line. The P300 amplitude may be used in sleepiness estimation only with extended wakefulness. The inter-individual variability in these methods is high and thus they are not sensitive enough for occupational clinical diagnostic purposes.

6.3 Methodological improvement of ERPs

A study of single-trial ERPs (Publication II) confirmed that point-to-point changes in brain responses during the traditional oddball paradigm can be detected with the new analysis methodology. The single-trial analysis allows more direct comparison between brain responses and reaction times. The method was applied for the first time to real measurements. It succeeds in revealing physiologically relevant information on dynamic changes of brain state. However, as the method weights features common to the whole measurement set, it may underestimate or even remove less frequent waveforms that are likely to appear when a functional state of an individual or an external environment changes. For example, unexpected novel sounds produce an orientation reaction, which may change brain responses. Therefore, the method is most usable in situations where a functional state of an individual and component waveform is not expected to change. Also, the need for an expert to run analyses and interpret the results makes the usefulness of the single trial analyses limited. Thus, even though the single trial analysis shows potential in studying the dynamics of ERPs, it still needs some more development in order to be used out of the laboratory, at work places, or in occupational clinical practise.

The P300 amplitude can be used to indicate the increasing mental workload caused by increased task demands already while the task performance accuracy is not impaired: The decrease in the P300 amplitude varied between 20% in the dual-task to 50% in the multitask condition, compared to the single task condition. The auditory P300 amplitude decreased more when concurrent tasks require working memory processing (*i.e.*, the arithmetic or memory task) in comparison to the task condition that demands only visual vigilance. Increasing the presentation rate of the already challenging multitask does not have an additional effect on the P300 amplitude. These results suggest that the protection of performance results in physiological costs as suggested by Hockey (Hockey, 1997). Only when the mental workload is too high to be compensated with increased effort, the performance begins to deteriorate. A previous study has shown that when a concurrent task is too challenging in a dual-task condition, it is impossible to detect the P300 component (Ullsperger *et al.*, 2001). On the other hand, if the concurrent task is too easy, no changes can be detected in the P300 amplitude (Wester *et al.*, 2008).

By using dual-task ERPs in mental workload assessment other factors than those related solely to task-demand have to be taken into account. Aging increases P300 latency and decreases the amplitude (Friedman *et al.*, 1993), the stimulus sequence of the auditory oddball task affects responses (Croft *et al.*, 2003; Golob & Starr, 2000; Squires, 1976), and the cognitive capacity of the subjects may also have an effect (Nittono *et al.*, 1999). Thus, at least reference values matched for age and education are needed when using ERPs in clinical settings.

ERP methodology has been improved both by applying new signal analysis methods and/or study paradigms. Measuring neurophysiological indices during cognitive task performance may improve the clinical usefulness of ERPs.

6.4 Methodological improvement of EEG

In this thesis, the most promising method for neuroergonomics purposes, including the identification of the effects of both external (task demand changes) as well as internal (increased need to sleep) factors, was found to be the theta Fz / alpha Pz -ratio, named brainbeat and reported in Publication V.

The increase of frontal theta and decrease of parietal alpha as a result of increased task demands is a well-known phenomenon in neurophysiological studies (Gevins *et al.*, 1998; Smith *et al.*, 2002). Also words that are later remembered, produce a significant increase in theta activity (Klimesch *et al.*, 1997). The multivariate EEG method has also found the amount of frontal theta and parietal alpha to be the most important parameters in the multivariate model of Gevins *et al.* (Gevins *et al.*, 1998). However, to the best of our knowledge, the simple theta Fz / alpha Pz -ratio has not been used in the assessment of mental workload. A single congress proceeding paper mentions the possible usability of this ratio in differentiating external workload levels (Postma *et al.*, 2005). However, contrary to their conclusions, we found that also the internal state of the subject has a strong effect on the ratio: We found that time awake significantly increased the ratio. In addition, this increase was enhanced with sleep deprivation (Publication V).

As suggested in article (Publication V), changes both in internal and external factors on the subject is reflected in the brainbeat: Demanding work tasks cause a temporary loading effect that is comparable to what would be achieved as a result of time spent awake. This places restrictions to the use of the ratio in some brain computer interactions. If exactly the same parameter values of the load measure should be obtained in response to equal load levels, the state of an individual should not affect the parameter. However, in many other applications, for example in traffic safety, detecting overload situations regardless of their origin is essential in order to avoid detrimental errors.

The theta Fz / alpha Pz -ratio seems potential for neuroergonomics purposes. However, more validation work should be done even when there is extensive literature showing that frontal theta increases and parietal alpha decreases in situations where mental workload is likely to increase, supporting the usability of the ratio in assessing of mental workload. First of all, the data set where the ratio is tested has been relatively limited and should therefore be extended to allow proper cross-validation of the results. Also, the effect of other factors, such as age and disease, or the type of cognitive resources needed to accomplish task, on the behaviour of theta and alpha activity is still unclear. In addition, the effects of the combination of these factors remain open.

A similar ratio, theta / alpha calculated only from the Pz location, has also been used in neurofeedback studies with resting subjects aiming to produce a hypnagocic state, similar to the meditative or hypnotic state of relaxation (Sokhadze *et al.*, 2008). As reported in PV, that ratio is not as sensitive as the ratio calculated from frontal and parietal areas, highlighting the importance of the fronto-parietal EEG content information in overall brain load assessment.

While previous EEG indices have been reported of being capable of differentiating at least between low and high task demands with 95% accuracy (Gevins *et al.*, 1998), they currently need (participant specific) training of classification algorithms, which is time-consuming and impractical. Also, the system trained for classification of task load is not a generic solution, but needs to be trained again in order to recognise, for example, fatigue.

The theta Fz / alpha Pz -ratio, presented in this Thesis, is a promising approach for the assessment of mental workload and in the identification of increased need

to sleep. These are both factors known to have an impact on human error (Biggs *et al.*, 2007). Due to the compactness of the modern technology, EEG could be monitored outside specialised laboratory environments. The current development of dry sensors with telemetry would make it plausible to measure the index even during everyday activities. Thus, the ratio seems to have potential also out of laboratory, in real workplace applications.

7 Future research

The amount of theta activity has been related to the level of task performance (Klimesch *et al.*, 1997; Slobounov *et al.*, 2000) as well as to the consolidation of memory traces and learning (Maquet, 2001). Elevated theta activity is also seen during nonREM sleep when the need of sleep is increased (Cajochen *et al.*, 1999a). Both increased task demands and increased need to sleep have been shown to affect the energy metabolism of the brain (Hockey, 1997; Porkka-Heiskanen *et al.*, 2003; Porkka-Heiskanen *et al.*, 1997). Sleep is considered essential for brain plasticity and restoration of energy resources (Hairston & Knight, 2004). The theta Fz/alpha Pz -ratio increases both due to increased task demands and increased sleep pressure. The ratio also returns to the baseline level of an individual after a well slept night (Publication V). It is thus suggested that the consumption and the restoration of energy resources are reflected in the ratio. The relation of the external and internal factors, affecting the brainbeat, are visualised in the hypothetical model in Figure 15.

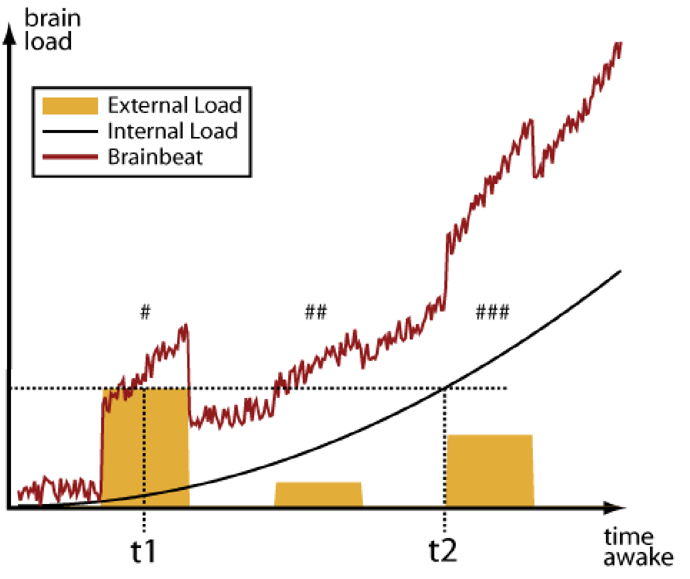


Figure 15: Suggested hypothetical behaviour of the theta Fz / alpha Pz -ratio, which is named brainbeat. The dotted line shows an equal load level. A high external load, such as demanding work (t1), causes a temporary loading effect that is comparable to what would be achieved by the gradual increase of the internal load as a result of time spent awake (t2). However, in the theta Fz / alpha Pz -ratio, these two are mixed (red line).

Typically, the effects of internal and external factors on neurophysiology are studied separately. EEG is measured and analysed from standard locations, *i.e.* from parietal areas in vigilance/sleepiness studies. Future research should be directed to validation of the hypothetical model, where the effects of external and internal factors on neurophysiology are combined. The studies include experimental setups, where external load is varied in combination with various internal state changes, such as different level of task demands with different level of sleep deprivation. Also, the relationship between recovery from sleep deprivation and cognitive overload and the ratio should be studied. In addition, the ratio should be tested among individuals, whose functional state is impaired, such as workers with burnout syndrome.

The EEG measurements may be carried out even during real work tasks, at least in professions where most work is done with a computer in an office-like environment. In these naturalistic settings movement based artefacts can be overcome making good-quality EEG recordings possible. There are also safety critical professions, such as controlling traffic or industrial processes or working in hospital intensive care units, in which early identification of an individual worker's cognitive overload is important. This information can be used to promote good neuroergonomics: the optimising work demand levels so that the risks for human errors are low. To achieve this aim, the usability of the ratio should be tested in combination with other measures of mental workload and sleepiness during real workdays.

8 Summary and conclusions

This Thesis investigated the usability of the neurophysiological metrics in the assessment of mental workload and in the identification of mild cognitive dysfunction. The aim is to promote neuroergonomics: a properly distributed and manageable workload, both at work and everyday life, supports well being. The main findings of this study can be summarised as follows:

- The experimental setup and the EEG methods, described in this Thesis, are promising tools for the assessment of mental workload as well as for recognising work related stress and mild cognitive impairment.
- The relative change in the P300 amplitude in response to changing task demand levels may be a more sensitive measure than the P300 amplitude measured during a simple oddball task. Thus, for this use, a setup with suitable tasks should be created, and reference values should be measured. The difficulty of the tasks should be at a level where performance is not yet affected.
- The EEG index, named brainbeat, was the best metric for assessing mental workload during a challenging multitask performance. The index reacts to both external task load changes as well as to changes in the internal state of the subject. It may thus be usable in measuring cognitive overload on-line as well as in cumulative workload estimation similar to radiation dosimeters.

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