Systematic evaluation of non-invasive brain-computer interfaces as assistive devices for persons with severe motor impairment based on a user-centred approach – in controlled settings and independent use

Inaugural-Dissertation

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„Brain Painting war meine Rettung – damit bin ich nicht mehr gefangen und werde noch lange malen können, weil es meine Gedanken immer geben wird."

Jürgen Thiele (2013)

Danksagung

Diese Dissertation wäre ohne die Hilfe und Unterstützung zahlreicher Menschen nicht möglich gewesen:

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List of Abbreviations

ACSA	Anamnestic Comparative Self-Assessment
ALS	Amyotrophic lateral sclerosis
AT	Assistive technology
ATD-PA	Assistive Technology Device Predisposition Assessment
BCI	Brain-computer interface
BUK	Beratungsstelle für Unterstützte Kommunikation
CES-D	Center for Epidemiologic Studies Depression Scale
EEG	Electroencephalography
EMG	Electromyography
ERD	Event-related desynchronization
ERP	Event-related potential
ERS	Event-related synchronization
FES	Functional electrical stimulation
fALS	Familiar amyotrophic lateral sclerosis
fMRI	Functional magnetic resonance imaging
GIP	Gesellschaft für medizinische Intensivpflege mbH
GUI	Graphical user interface
ICT	Information and communication technology
ISI	Interstimulus interval
ISO	International Standards Organization
ITR	Information transfer rate
LDA	Linear discriminant analysis
LRP	Lateralized readiness potential
MD	Muscular dystrophy
MEG	Magnetoencephalography
MI	Motor imagery
MND	Motorneuron disease
MS	Multiple Sclerosis
NASA-TLX	National Aeronautics and Space Administration Task Load Index
NIRS	Near-infrared spectrography
PEG	Percutaneous endoscopic gastrostomy
OKI	Optimized communication interface
PIADS	Psychosocial Impact of Assistive Devices Scale
QUEST	Quebec User Evaluation of Satisfaction with assistive Technology
QW	QualiWorld
SeiQol	Schedule for the Evaluation of Individual Quality of Life
sALS	Sporadic amyotrophic lateral sclerosis
SCI	Spinal cord injury
SCP	Slow cortical potentials
SMA	Spinal muscular atrophy
SMR	Sensorimotor rhythm
SSVEP	Steady state evoked potential
SWLDA	Stepwise linear discriminant analysis
UCD	User-centred design
VAS	Visual analogue scale
WHO	World Health Organization

Abstract

Brain-computer-interfaces (BCIs) are devices that translate signals from the brain into control commands for applications. Within the last twenty years, BCI applications have been developed for communication, environmental control, entertainment, and substitution of motor functions. Since BCIs provide muscle independent communication and control of the environment by circumventing motor pathways, they are considered as assistive technologies for persons with neurological and neurodegenerative diseases leading to motor paralysis, such as amyotrophic lateral sclerosis (ALS), muscular dystrophy, spinal muscular atrophy and stroke (Kübler, Kotchoubey, Kaiser, Wolpaw, & Birbaumer, 2001). Although most researcher mention persons with severe motor impairment as target group for their BCI systems, most studies include healthy participants and studies including potential BCI end-users are sparse. Thus, there is a substantial lack of studies that investigate whether results obtained in healthy participants can be transferred to patients with neurodegenerative diseases. This clearly shows that BCI research faces a translational gap between intense BCI research and bringing BCI applications to end-users outside the lab (Kübler, Mattia, Rupp, & Tangermann, 2013). Translational studies are needed that investigate whether BCIs can be successfully used by severely disabled end-users and whether those end-users would accept BCIs as assistive devices. Another obvious discrepancy exists between a plethora of short-term studies and a sparse number of long-term studies. BCI research thus also faces a reliability gap (Kübler, Mattia, et al., 2013). Most studies present only one BCI session, however the few studies that include several testing sessions indicate high inter- and intra-individual variance in the end-users' performance due to non-stationarity of signals. Long-term studies, however, are needed to demonstrate whether a BCI can be reliably used as assistive device over a longer period of time in the daily-life of a person. Therefore there is also a great need for reliability studies.

The purpose of the present thesis was to address these research gaps and to bring BCIs closer to end-users in need, especially into their daily-lives, following a user-centred design (UCD). The UCD was suggested as theoretical framework for bringing BCIs to end-users by Kübler and colleagues (Kübler et al., 2014; Zickler et al., 2011). This approach aims at the close and iterative interaction between BCI developers and end-users with the final goal to develop BCI systems that are accepted as assistive devices by end-users. The UCD focuses on usability, that is, how well a BCI technology matches the purpose and meets the needs and requirements of the targeted end-users and was standardized with the ISO 9241-210.

Within the UCD framework, usability of a device can be defined with regard to its effectiveness, efficiency and satisfaction. These aspects were operationalized by Kübler and colleagues to evaluate BCI-controlled applications. As suggested by Vaughan and colleagues, the number of BCI sessions, the total usage duration and the impact of the BCI on the life of the person can be considered as indicators of usefulness of the BCI in long-term daily-life use (Vaughan, Sellers, & Wolpaw, 2012). These definitions and metrics for usability and usefulness were applied for evaluating BCI applications as assistive devices in controlled settings and independent use. Three different BCI applications were tested and evaluated by in total N=10 end-users: In *study 1* a motor-imagery (MI) based BCI for gaming was tested by four end-users with severe motor impairment. In *study 2*, a hybrid P300 event-related (ERP) based BCI for communication was tested by four severely motor restricted end-users with severe motor impairment. *Study 1* and *2* are short-term studies conducted in a controlled-setting. In *study 3* a P300-ERP BCI for creative expression was installed for long-term independent use at the homes of two end-users in the locked-in state. Both end-users are artists who had gradually lost the ability to paint after being diagnosed with ALS.

Results reveal that BCI controlled devices are accepted as assistive devices. Main obstacles for daily-life use were the not very aesthetic design of the EEG-cap and electrodes (cap is eye-catching and looks medical), low comfort (cables disturb, immobility, electrodes press against head if lying on a head cushion), complicated and time-consuming adjustment, low efficiency and low effectiveness, and not very high reliability (many influencing factors). While effectiveness and efficiency in the MI based BCI were lower compared to applications using the P300-ERP as input channel, the MI controlled gaming application was nevertheless better accepted by the end-users and end-users would rather like to use it compared to the communication applications. Thus, malfunctioning and errors, low speed, and the EEG cap are rather tolerated in gaming applications, compared to communication devices. Since communication is essential for daily-life, it has to be fast and reliable. BCIs for communication, at the current state of the art, are not considered competitive with other assistive devices, if other devices, such as eye-gaze, are still an option. However BCIs might be an option when controlling an application for entertainment in daily-life, if communication is still available. Results demonstrate that BCI is adopted in daily-life if it matches the end-users needs and requirements. Brain Painting serves as best representative, as it matches the artists' need for creative expression. Caveats such as uncomfortable cap, dependence on others for set-up, and experienced low control are tolerated and do not prevent BCI use on a daily basis. Also end-users in real need of means for communication, such as persons in the locked-in state with unreliable eye-movement or no means for independent communication, do accept obstacles of the BCI, as it is he last or only solution to communicate or control devices. Thus, these aspects are “no real obstacles” but rather “challenges” that do not prevent end-users to use the BCI in their daily-lives. For instance, one end-user, who uses a BCI in her daily-life, stated: “*I don’t care about aesthetic design of EEG cap and electrodes nor amplifier*”. Thus, the question is not which system is superior to the other, but which system is best for an individual user with specific symptoms, needs, requirements, existing assistive solutions, support by caregivers/family etc.; it is thereby a question of indication. These factors seem to be better “predictors” for adoption of a BCI in daily-life, than common usability criterions such as effectiveness or efficiency. The face valid measures of daily-life demonstrate that BCI-controlled applications can be used in daily-life for more than 3 years, with high satisfaction for the end-users, without experts being present and despite a decrease in the amplitude of the P300 signal. Brain Painting re-enabled both artists to be creatively active in their home environment and thus improved their feelings of happiness, usefulness, self-esteem, well-being, and consequently quality of life and supports social inclusion. This thesis suggests that BCIs are valuable tools for people in the locked-in state.

Zusammenfassung

Gehirn-Computer Schnittstellen (engl. *Brain-computer interfaces*, Abk.: BCIs) sind technische Systeme, die Gehirnsignale in Kontrollbefehle für Computeranwendungen übersetzen. In den vergangenen zwanzig Jahren wurden verschiedenste BCI Anwendungen entwickelt, beispielsweise zur Kommunikation, Umweltsteuerung, Unterhaltung und Ersatz von Motorfunktionen. Da BCIs muskelunabhängige Kommunikation und Kontrolle ermöglichen, werden sie als mögliche Hilfsmittel für Personen mit neurologischen und neurodegenerativen Krankheiten, die zu motorischen Lähmungen führen, wie beispielsweise bei Amyotrophe Lateralsklerose (ALS), Muskeldystrophie, Spinale Muskelatrophie und Schlaganfall, in Betracht gezogen (Kübler, Kotchoubey, et al., 2001). Auch wenn die meisten BCI Forscher Personen mit starken motorischen Einschränkungen als Zielgruppe für ihre BCI Systeme angeben, so testen sie ihre Systeme nur in Stichproben von gesunden Probanden. BCI Studien, die Patienten einschließen, sind dagegen selten. Daher gibt es einen beträchtlichen Mangel an Studien, die untersuchen, ob die Forschungsergebnisse, die basierend auf einer gesunden Stichprobe verzeichnet wurden, auch auf Patienten mit neurodegenerativen Erkrankungen übertragen werden können. Das macht deutlich, dass es in der BCI Forschung eine erhebliche Translationslücke zwischen der intensiven BCI Grundlagenforschung und dem Transfer von BCI Anwendungen aus dem Labor zu den Patienten, den sogenannten BCI End-Nutzern, gibt (Kübler, Mattia, et al., 2013). Es werden deshalb Translationsstudien benötigt, die untersuchen, ob BCIs von stark motorisch eingeschränkten Patienten verwendet werden können und ob diese sogenannten End-Nutzer BCIs als Hilfsmittel akzeptieren. Zusätzlich ist eine deutliche Diskrepanz zwischen der Vielzahl an Kurzzeitstudien und der geringen Anzahl an Langzeitstudien zu verzeichnen. BCI Forschung ist daher auch mit einer Reliabilitätslücke konfrontiert (Kübler, Mattia, et al., 2013). Die meisten Studien basieren nur auf einer BCI Sitzung, jedoch zeigen die wenigen Studien, die auf mehreren Sitzungen beruhen, hohe inter- und intraindividuelle Varianz in der Performanz der Patienten. Langzeitzeitstudien werden daher benötigt, um aufzuzeigen, ob ein BCI reliabel als Hilfsmittel über einen längeren Zeitraum im Alltagsleben eines Patienten verwendet werden kann. Demzufolge gibt es einen starken Bedarf an Translations- und Reliabilitätsstudien.

Das Anliegen der vorliegenden Dissertation war es, diesen Forschungslücken zu begegnen und, basierend auf einem nutzerzentrierten Vorgehen, BCIs näher zu den BCI End-Nutzern zu bringen, besonders in ihr Alltagsleben. Der nutzerzentrierte Ansatz wurde von Kübler und Kollegen (Kübler et al., 2014; Zickler et al., 2011) als theoretisches Gerüst nahegelegt, um BCIs näher zu Patienten zu bringen. Dieser Ansatz beabsichtigt eine enge und iterative Interaktion zwischen BCI Entwicklern und den End-Nutzern mit dem finalen Ziel BCI Systeme zu

entwickeln, die von den End-Nutzern als Hilfsmittel akzeptiert werden. Der nutzerzentrierte Ansatz fokussiert auf die Benutzbarkeit, das heißt, wie gut eine BCI Technologie den Bedürfnissen und den Ansprüchen der Zielgruppe entspricht. Dieser Ansatz wurde standardisiert mit dem ISO 9241-210. Demnach ist die Benutzbarkeit eines Gerätes definiert hinsichtlich der Effektivität, Effizienz, und Zufriedenheit. Um BCI Systeme zu evaluieren, wurden diese Aspekte von Kübler und Kollegen operationalisiert. Nach Vaughan und Kollegen können die Anzahl der BCI Sitzungen, die Gesamtnutzungsdauer und der Einfluss eines BCIs auf die Lebensqualität einer Person als Indikatoren der Nützlichkeit eines BCI betrachtet werden (Vaughan et al., 2012). Diese Definitionen und entsprechenden Operationalisierungen wurden in dieser Dissertation verwendet, um BCI Anwendungen hinsichtlich ihrer Benutzbarkeit und Nützlichkeit als Hilfsmittel zu evaluieren. N=10 End-Nutzer testeten und evaluierten drei BCI Anwendungen: In *Studie 1* wurde ein auf Bewegungsvorstellung basiertes BCI (engl. motor imagery, Abk: MI) zur Steuerung einer Spielanwendung von vier potentiellen End-Nutzern mit unterschiedlichen neurologischen Erkrankungen getestet. In *Studie 2* wurde ein Hybrid BCI, das das P300 ereignis-korrelierte Potential (EKP) und Muskelaktivität als Inputkanäle zur Steuerung eines Kommunikationsprogramms verwendet, von vier potentiellen End-Nutzern getestet. *Studie 1* und *2* sind Kurzzeitstudien, welche in einem kontrollierten Design durchgeführt wurden. In *Studie 3* wurde ein P300-EKP basiertes BCI zum künstlerischen Ausdruck bei zwei End-Nutzern zuhause für einen experten-unabhängigen und längerfristigen Gebrauch implementiert. Beide End-Nutzer sind Künstler, die, aufgrund der Diagnose ALS und der damit verbundenen fast kompletten körperlichen Lähmung (Locked-in Zustand), nicht mehr in der Lage waren zu malen (*Studie 3*).

Die Ergebnisse zeigen, dass BCI Systeme als Hilfsmittel akzeptiert werden. Das nicht sehr ästhetische Design der EEG-Kappe und der Elektroden (Kappe zu auffällig, sieht medizinisch aus), der geringe Komfort (Kabel stören, Immobilität, Elektroden drücken gegen den Kopf), die komplizierte und zeitaufwändige Einstellung und Anpassung, die geringe Effizienz und geringe Effektivität und die nicht sehr hohe Reliabilität (viele Einflussfaktoren), wurden jedoch für einen Alltagsgebrauch als problematisch angesehen. Obwohl die Effektivität und Effizienz beim MI BCI geringer, verglichen mit beiden P300-EKP BCI Systemen, waren, wurde das MI basierte BCI-Spiel von den End-Nutzern besser akzeptiert und die End-Nutzer konnten sich eher vorstellen es im Alltag zu verwenden, als das Kommunikationsprogramm. Das zeigt, dass Störungen und Fehler, eine geringe Geschwindigkeit, und die EEG Kappe bei BCI Systemen zur Unterhaltung eher toleriert werden, als bei Systemen zur Kommunikation. Da Kommunikation im Leben essentiell ist, muss sie schnell und zuverlässig sein. BCI Systeme zur Kommunikation sind daher zum aktuellen Stand der Technik nicht konkurrenzfähig mit anderen Hilfsmitteln, wenn andere Hilfsmittel zur Kommunikation, wie Augensteuerung, verwendet werden können.

BCI Systeme sind aber eine Option im Bereich Unterhaltung, sofern Möglichkeiten zur Kommunikation (noch) bestehen. Die Ergebnisse zeigen, dass ein BCI für einen Alltagsgebrauch übernommen wird, wenn es den Bedürfnissen und Anforderungen des End-Nutzers entspricht. Brain Painting zeigt hierbei beispielhaft, wie negative Facetten, wie die wenig komfortable EEG Kappe, die Abhängigkeit von anderen aufgrund der komplexen Einstellung, und eine subjektiv empfundene geringe Kontrolle toleriert werden, da es genau den Bedürfnissen der Künstler sich kreativ auszudrücken entspricht. Ebenso Patienten, die Bedarf an Kommunikation haben, wie Patienten im Locked-in Zustand, die keine zuverlässigen Augen-Bewegungen aufweisen, oder Patienten, die keine Hilfsmittel zur unabhängigen Kommunikation haben, akzeptieren diese Umstände beim BCI Gebrauch. Das zeigt, dass diese Umstände keine richtigen „Hindernisse“, sondern vielmehr Herausforderungen sind, die eine Übernahme eines BCI im Alltag eines Patienten nicht verhindern. Es ist daher nicht die Frage, welches BCI System überlegen ist, sondern welches BCI System das Beste für ein Individuum mit spezifischen Symptomen, Bedürfnissen, Ansprüchen, vorhandenen Hilfsmitteln, Unterstützung durch Familie und Pflegern, ist; es ist deshalb eine Frage der Indikation. Eine End-Nutzerin, die ein BCI im Alltag verwendet, sagte beispielsweise: „*Mir ist das ästhetische Design der EEG-Kappe und der Elektroden, oder des EEG-Verstärkers völlig egal*“. Diese Faktoren können als die besten “Prädiktoren” für eine Übernahme eines BCI Systems im Alltag eines Patienten angesehen werden, weniger hingegen die üblichen Kriterien zur Bewertung der Benutzbarkeit, wie Effektivität und Effizienz. Die Ergebnisse hinsichtlich des Alltagsgebrauches belegen ferner, dass ein P300-EKP basiertes BCI mit hoher Zufriedenheit über einen Zeitraum von 3 Jahren, ohne die Hilfe eines BCI Experten, und trotz einer Abnahme der Amplitude des P300-Signales verwendet werden kann. Brain Painting ermöglichte beiden Künstlern sich wieder kreativ auszudrücken und beeinflusste somit positiv das Empfinden von Freude, das Gefühl von Nützlichkeit, das Selbstwertgefühl, das Wohlbefinden und folglich die Lebensqualität der Künstler und förderte ihre soziale Inklusion. Die vorliegende Dissertation zeigt, dass BCIs wertvolle Hilfsmittel für Personen im Locked-in Zustand sein können.

1. Introduction

In 1929 Hans Berger demonstrated the possibility of recording brain signals from the human scalp by using electroencephalography (EEG; Berger, 1929). Since then, people developed the idea to use EEG signals to control a machine. In 1973 Jacques J. Vidal brought up the question whether brain signals can be used to control external devices: "*Can these observable electrical brain signals be put to work as carriers of information in man-computer communication or for the purpose of controlling such external apparatus as prosthetic devices or spaceships?*" and already in those days, he answered his question with "*yes*" (Vidal, 1973; p.157). The present thesis aims at answering the question whether brain signals can be used for controlling assistive devices in people with severe motor impairment.

1.1 Brain-computer interfaces

The connection between the brain and a computer is called *brain-computer interface* (BCI). A BCI acquires input signals from the brain, which are filtered, classified, and translated into an output signal for controlling an application (see **figure 1**). This output relates to the brain response or pattern of the BCI user and represents the respective intention of the user. The user receives then feedback of the action (e.g., the movement of a cursor on a monitor), thereby implying a closed-loop between the user and the external device (e.g., computer). BCI applications have been developed for communication (Kaufmann, Schulz, Grünzinger, & Kübler, 2011; Kaufmann, Volker, Gunesch, & Kübler, 2012; Nijboer, Sellers, et al., 2008; Riccio et al., 2011; Silvoni et al., 2009; Zickler et al., 2011), entertainment (Münßinger et al., 2010; Plass-Oude Bos et al., 2010; Tangermann et al., 2009), e-inclusion (Mugler, Ruf, Halder, Bensch, & Kübler, 2010; Zickler et al., 2011) and environmental control (Aloise et al., 2011), see **figure 1**. BCIs can be invasive or non-invasive. Most often electrical activity is recorded from the brain non-invasively using EEG. Other non-invasive measures record brain activity by means of functional magnetic resonance imaging (fMRI; Nair, Purcott, Fuchs, Steinberg, & Kelso, 2003; Weiskopf et al., 2004), magnetoencephalography (MEG; Mellinger et al., 2007) or near-infrared spectrography (NIRS; Sitaram et al., 2007). BCIs can also record brain activity invasively, from the cortex using electrocorticography (ECOG) or from single neurons using single unit recording (for a review, see Zander & Kothe, 2011). Main advantages of non-invasive BCIs using EEG are that they are portable, easy to use, comparable low cost and that they have a high temporal resolution. Another advantage is that the EEG has been thoroughly investigated, since its discovery by Hans Berger (Berger, 1929). Disadvantages are low spatial resolution and sensitivity to artifacts (Kübler, Mattia, et al., 2013; Zander & Kothe, 2011). Due to its portable nature, low costs and ease of use, BCIs using EEG can be easier brought to patients' homes. Therefore the present thesis solely focuses on non-invasive BCIs that rely on EEG.

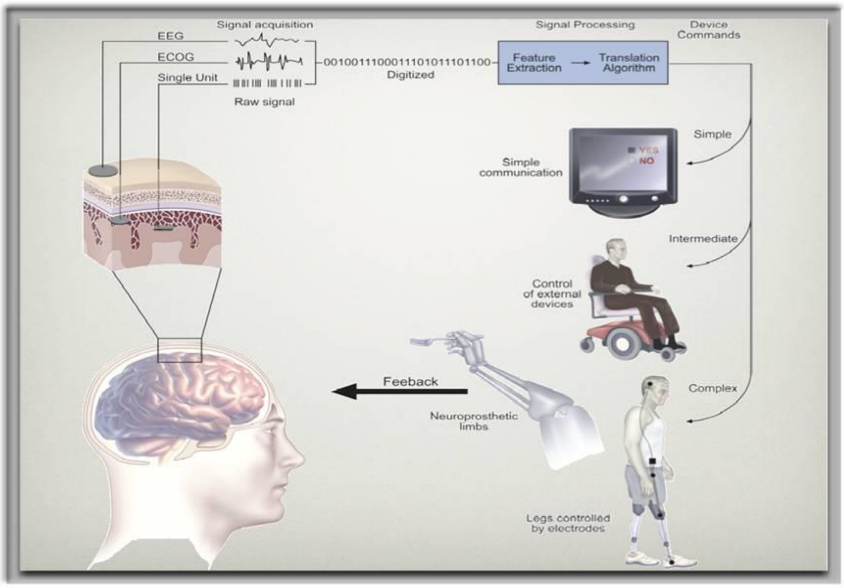


Figure 1: Brain-computer interface.

A Brain-computer interface acquires signals from the brain, extracts relevant components and classifies them into output commands for controlling an application (e.g., a computer program or wheelchair). Source: http://www.etsu.edu/cas/bcilab/pictures/Leuthardt.jpg).

1.1.1 Existing EEG based BCI systems (input)

According to Zander and Kothe (2011) non-invasive EEG based BCIs can be divided into active, passive and reactive systems (Zander & Kothe, 2011). More recently also hybrid BCI systems are of interest in BCI research, but are described separately in section **1.4.3.1.2. Hybrid approach**.

1.1.1.1 Active BCI

An active BCI is controlled by the voluntary regulation of a specific component of the electrical activity of the brain. The user of an active BCI regulates his or her brain activity actively by mental processes, for instance imagination of movements (motor imagery, MI), counting and relaxation. Most frequently used input signals for an active BCI are sensorimotor rhythm (SMR) activity and slow-cortical potentials (SCPs). Regulation of EEG activity can be achieved by neurofeedback. Based on the principle of operant conditioning the subject trains to control his/ her brain activity while receiving continuous feedback about the state of the own brain signals. After a successful trial (e.g., a cursor was moved up or down by motor imagery), the subject receives a positive feedback; after a failed trial a negative feedback is presented.

1.1.1.1.1 SMR/MI BCI

MI BCIs use SMR activity as input (see **figure 2**). Therefore they are also called "SMR BCIs". The sensorimotor rhythm is a rhythmic activity in the EEG within a frequency of 7-13 Hz (alpha-rhythm) that is usually accompanied by 18-26 Hz (beta-rhythm; Niedermeyer & Lopes da Silva, 2005; Pfurtscheller & Aranibar, 1979; Pfurtscheller & Lopes da Silva, 1999). SMR is recorded with EEG-electrodes from primary somatosensory and motor cortical areas. While a person is resting, neurons from central motor cortex fire synchronously, resulting in a pronounced SMR activity. In active state, for instance while moving or imagining a movement, SMR desynchronises (i.e., the power of this activity decreases/neurons fire desynchronized; Pfurtscheller & Lopes da Silva, 1999). This SMR modulation constitutes input signal for a MI BCI. Most MI BCIs trigger control signals for two classes, for example imagining movement of the right or the left hand. The topographic distribution of these hand areas are separated in sensorimotor cortices and thus enable two distinguishable classes. The user receives continuous feedback about his performance during the imagery tasks (i.e., a cursor moves to the left or right); see **figure 2** and chapter **1.1.3 Feedback (output)**. A big issue is however that a large number of subjects (up to 30%) are not able to achieve sufficient control in a MI BCI, a problem that was called "BCI illiteracy" (Blankertz et al., 2010; Guger et al., 2009; Guger, Edlinger, Harkam, Niedermayer, & Pfurtscheller, 2003; Kübler & Müller, 2007; Vidaurre & Blankertz, 2010). It was however suggested by Kübler and colleagues to replace this term by "BCI inefficiency" to better stress that the inability may be inherent in the system, not in the user (Kaufmann, Schulz, et al., 2013; Kübler, Blankertz, Müller, & Neuper, 2011). Performance in MI BCI thus varies strongly across persons (Blankertz et al., 2010). It could however been shown that performance varies stronger in the earlier training phase and that control increases with training (e.g., over several weeks or months; Kübler, Nijboer, et al., 2005; McFarland, McCane, & Wolpaw, 1998). Because MI does not only induce a desynchronization of SMR activity in the EEG, but also other components, some studies refer to this BCI "MI BCI", because the name "SMR BCI" is not accurate, if not only SMR activity but also high beta or gamma oscillations are considered as input signals for a MI based BCI (Höhne et al., 2014; Rohm et al., 2013), see *study 1*. Besides communication and control, MI BCIs are of current interest for motor rehabilitation (e.g., De Vico Fallani et al., 2013; Pichiorri et al., 2011).

1.1.1.1.2 SCP BCI

A BCI that relies on SCPs uses activity of the EEG within a frequency range between 0.1 to 1 Hz, see **figure 2**. A negative polarity indicates excitation or information processing, a positive polarity cortical inhibition or relaxation processes (Elbert, Rockstroh, Lutzenberger, & Birbaumer, 1980). As for SMR BCIs a subject trains to regulate his or her brain activity by mental processes using a closed-loop design. The subject learns within several training sessions to actively influence and control his or her brain activity. This paradigm can be used to move a cursor on a screen to select a letter from a matrix (Elbert et al., 1980), see **figure 2**. First BCI studies that included patients demonstrated that patients diagnosed with amyotrophic lateral sclerosis (ALS) can control a SCP BCI for communication and internet surfing (Birbaumer et al., 1999; Karim et al., 2006; Kübler et al., 1999; Neumann & Kübler, 2003), for a review see (Kübler & Birbaumer, 2008). However by now SCP BCIs are mostly used for neurofeedback for rehabilitation of cognitive and motoric functions (e.g., Real, Kübler, & Kleih, 2014) or for treatment of mental or behavioural disorders, such as attention deficit hyperactivity disorder (e.g., Strehl et al., 2006).

1.1.1.2 Reactive BCI

A reactive BCI derives its input from brain activity that is elicited in reaction to external sensory stimulation. In contrast to SMR or SCP BCIs, which depend on volitional processes, reactive BCIs are based on external stimuli. Most frequently used components of the evoked brain activity, are the event-related potential (ERP) or the steady state evoked potential (SSVEP). Stimulation can be provided in the visual, auditory or tactile modality.

1.1.1.2.1 ERP BCI

The ERP is the result of shifts in the polarisation of the EEG of a person, that correlates with stimulus perception, see **figure 2**. The P300 is a positive deflection in the EEG, 200 to 400ms (or 200 to 800ms, depending on the task) after occurrence of a rare or infrequent stimulus (Picton, 1992; Polich, 2007). A pronounced P300 can be detected using the oddball paradigm. In an oddball paradigm many stimuli, frequent and infrequent ones, are presented consecutively. The subject is instructed to focus on one item. This item, which is called the target stimulus or oddball, occurs less frequent compared to all other stimuli (non-targets). While focusing on the target stimulus, a P300 response is elicited. The first P300 BCI, the so called P300 speller, was introduced by Farewell and Donchin in 1988 (Farwell & Donchin, 1988): Subjects are presented with a P300 matrix (e.g., 6x6 matrix) comprising 36 characters (see **figure 2**) and the user attends to the desired character (the target). While flashing in rows and columns the intended letter represents the target, whereas all other letters represent non-targets. Every time the target is highlighted, a P300 response is elicited, which can be detected by the BCI. The BCI converts this brain response into an output command that is here the selection of the letter of the matrix. More recent findings indicate that the oddball paradigm does not only elicit the positive component around ~300-400ms on central brain regions, but also several other components of the ERP, such as positive peaks at ~250ms (P200) and at ~120ms (P100), and a negative peaks at parieto-occipital sites at ~150ms (N100) and ~300ms (N200) post-stimulus (Allison & Pineda, 2006; Kaufmann, Hammer, & Kübler, 2011; Treder & Blankertz, 2010); thereby the term ERP BCI is more accurate. However because the term P300 BCI or P300 speller is often used in the BCI literature, the term P300-ERP BCI is used in the following text. In a classical P300-ERP speller (row-column paradigm) 72.8% of 81 healthy participants were able to spell with 100% accuracy and only less than 3% did not gain control (Guger et al., 2009).

Aside from visual modality, BCIs that rely on nonvisual modalities, such as auditory (Furdea et al., 2009; Halder et al., 2010; Höhne, Krenzlin, Dahne, & Tangermann, 2012; Höhne, Schreuder, Blankertz, & Tangermann, 2010, 2011; Klobassa et al., 2009; Nijboer, Furdea, et al., 2008; Schreuder, Blankertz, & Tangermann, 2010; Sellers & Donchin, 2006), or vibrotactile (Brouwer & van Erp, 2010; Kaufmann, Herweg, & Kübler, 2014; Kaufmann, Holz, & Kübler, 2013; Müller-Putz, Scherer, Neuper, & Pfurtscheller, 2006; van der Waal, Severens, Geuze, & Desain, 2012), have been developed; for a review see (Riccio, Mattia, Simione, Olivetti, & Cincotti, 2012). In auditory BCI paradigms, the target stimulus could be a higher pitch tone (rare oddball stimulus) presented in a stream of lower pitched standard tones, all presented via stereo headphones. Different approaches have been developed, using two target tones differing in loudness, pitch, or direction (left or right ear) within standard frequent tones (pink noise; Halder et al., 2010); or spatial location of a stimulus as discriminating cue, for instance subjects had to attend to the sound of one spatial location (Schreuder et al., 2010); or a combination of spatial location of sounds and pitch variation leading to a nine class BCI system, embedded in a predictive text system; or numbers that indicate rows and columns of a 5x5 matrix and thus items of a visual spelling matrix (visual support matrix; Furdea et al., 2009; Kübler et al., 2009); or words in a four-choice auditory speller "yes", "no", pass", "end" (Sellers & Donchin, 2006). P300 ERP BCIs that rely on tactile vibration use vibration units (called tactors) that are placed on the participants' body, for example on fingers, hands, wrists, arms, legs or waist (Brouwer & van Erp, 2010; Kaufmann et al., 2014; Kaufmann, Holz, et al., 2013; Severens, Van der Waal, Farquhar, & Desain, 2014; Thurlings, van Erp, Brouwer, Blankertz, & Werkhoven, 2012; van der Waal et al., 2012). Similar to the visual or auditory modality paradigm, tactors stimulate in random order and subjects focus their attention on one of the tactors.

In most of the studies classification accuracy and performance was found to be lower in non-visual paradigms, as compared to the visual modality. Based on the data obtained in healthy subjects, Aloise and colleagues (2007) found the visual modality superior to the auditory and tactile modality (Aloise et al., 2007). In a study by Furdea and colleagues (2009) nine of 13 healthy participants performed above 70%, a predefined criterion level of control for communication (Kübler, Neumann, et al., 2001; Kübler, Neumann, Wilhelm, Hinterberger, & Birbaumer, 2004), however compared to a visual spelling system, subjects' performance was lower and also latencies of the auditory evoked ERPs were delayed. Same was evident in the target group: Four persons with ALS used the same auditory paradigm (Kübler et al., 2009) and performed with lower accuracies; two performed at or very close to chance level, and two patients performed above chance level, but below criterion level for meaningful communication (70%). The same patients achieved accuracies of at least 70% when using a visual ERP BCI (Nijboer, Sellers, et al., 2008). The authors argue that the auditory condition is more difficult, as the subject has to maintain the target number of the row and column of the visual support matrix in short term memory and has thus an additional effort that influences brain signals and classification. Käthner and colleagues (2013) tested a new auditory P300 ERP BCI that uses a combination of pitch and directional cues in 20 healthy participants. In addition the auditory speller was compared to a visual speller. Whereas 16 of 20 participants performed at or above a level necessary for satisfactory communication (70% spelling accuracy) with the auditory BCI, subjects' performances were significantly higher in the visual (mean: 94%) compared to auditory (mean: 66%) condition. Furthermore, healthy subjects and patients with ALS performed better in a covert visual ERP BCI system (88% and 85%) as compared to a tactile ERP BCI (56% and 53%; Severens et al., 2014). Also multimodal paradigms have been developed. Brouwer and colleagues (2010) combined visual presentation mode with a tactile mode and compared the unimodal to bimodal condition, and found that the bimodal (visuo-tactile) stimulation is superior in terms of classification accuracy (47% to 83%), as compared to unimodal stimulation mode (tactile: 47% to 70%; visual: 47% to 68%; Brouwer, van Erp, Aloise, & Cincotti, 2010). Authors conclude that bimodal stimuli could enhance classification results in BCI systems.

1.1.1.2.2 SSVEP BCI

Another type of BCI utilizes SSVEPs. In this approach, subjects attend to one or more stimuli that oscillate at different constant frequencies. When the subject focuses attention to one of those stimuli, EEG activity can be detected over occipital areas with the corresponding frequency.

Thereby SSVEP BCIs infer the user’s intent by measuring brain responses within specific frequencies (Allison et al., 2008). SSVEP BCIs have been proven to work in healthy subjects. In a study by Guger and colleagues (2012) a SSVEP BCI was tested by 53 healthy participants. Subjects had to focus on a SSVEP box, which had four LEDs oscillating at 10 Hz (top box), 11 Hz (right box), 12 Hz (bottom box) and 13 Hz (left box). Subjects tested the BCI in one up to four runs with four minutes per run. Average accuracy was 95.5%. About 96.2% of the subjects reached accuracies above 80%, and none of the subjects had accuracies below 60%. This study demonstrates that, using a SSVEP based BCI system, most of the healthy subjects are able to reach very high accuracies after only a very short training period (Guger, Allison, et al., 2012). Another study (Allison et al., 2010) reported that some people could not use a SSVEP BCI system, however this was the case in a very few persons (less than 10 out of 106 people had an accuracy less than 60%). It remains questionable however whether results can be transferred to persons with neurodegenerative diseases.

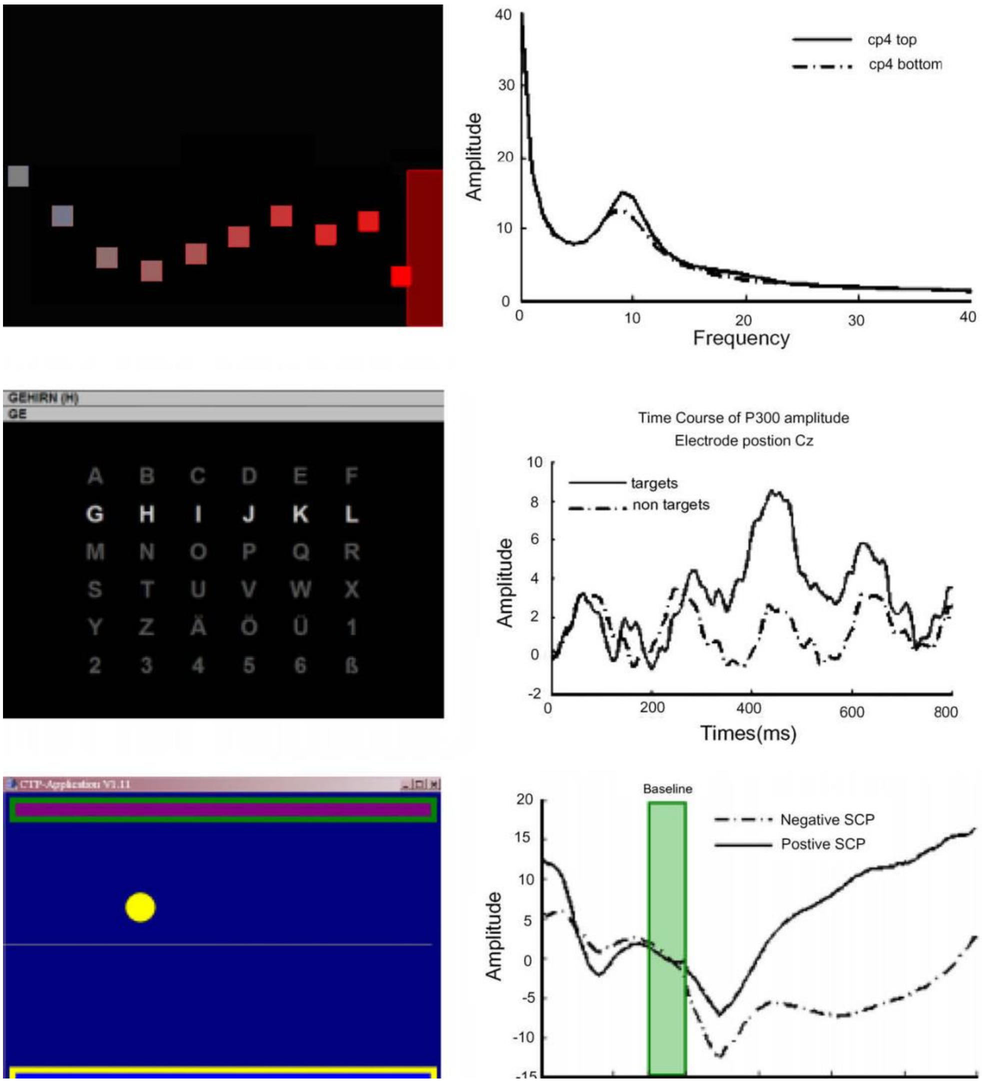


Figure 2: Most frequently used EEG components for a BCI.

Top: the SMR BCI: targets are presented at the top or bottom right margin of the screen. Users' task is to move the cursor into the target. Cursor movement is indicated by the squares; the cursor moves steadily from left to right; vertical deflections correspond to the SMR amplitude. Top right panel shows amplitude of the EEG as a function of frequency separated by task requirement (top vs. bottom target). A difference in amplitude can be clearly seen around the 10 Hz SMR peak. Middle: P300 BCI: a 6x6 letter matrix is presented. Rows and columns flash in random order, indicated by the bright row. The user has to copy-spell the word "Gehirn". Right panel depicts EEG for targets and non-targets. A clear difference in signal for targets vs. non-targets can be seen. Bottom: SCP BCI: targets are presented at the top or bottom of the screen. Patients' task is to move the cursor (yellow ball) toward the target. The cursor moves steadily from left to right and its vertical deflection corresponds to the SCP amplitude. Right panel illustrates time course of the SCP amplitude separated by task requirement. A negative SCP amplitude moves the cursor toward the top, positive SCP amplitude toward the bottom target. Positive and negative SCP amplitude shifts are clearly distinguishable; source: Kübler, A., & Birbaumer, N. (2008). Brain-computer interfaces and communication in paralysis: extinction of goal directed thinking in completely paralysed patients? *Clinical neurophysiology*, *119(11)*, 2658-2666, p. 2661.

1.1.1.3 Passive BCI

A passive BCI derives its output from arbitrary activity of the human brain that arises without the purpose of voluntary control (Zander & Kothe, 2011). Covert aspects of the user state, which can hardly be measured on the basis of behavioural data, have been investigated in different studies, for instance detection of the interpretation of other humans' movements (Gaertner, Klister, & Zander, 2008) or inattentiveness (Schubert et al., 2008), mental workload (Kohlmorgen et al., 2007) in driving situations or mental states of a user for avoiding accidents in industrial environments (Venthur, Blankertz, Gugler, & Curio, 2010), for a review see (Zander & Kothe, 2011).

1.1.2 Signal processing and feature extraction (input > output)

A BCI aims at translating signals recorded from the brain into an output command for a computer or other devices. For that, the BCI needs to understand what the user wants. In an optimal condition the BCI always identifies the correct brain state of the user (i.e., with a 100% correct accuracy). However in real scenarios the detection of the user's intent is not always clear to identify, because the brain is complex and different information processes are running at the same time. The processing and translation of the brain signals is thus an important step in the brain-computer interface cycle (van Gerven et al., 2009). A BCI aims at finding at least two discriminative features in the brain that can be coded for outputs in a respective task (e.g., cursor moves to the left or right; or selection of target or non-target). Most commonly linear methods are used to discriminate different classes of signals. The most often used classification method for ERP BCIs is the stepwise linear discriminant analysis (SWLDA). This method aims at identifying a suitable discriminant function by adding spatiotemporal features (i.e., the amplitude at a particular electrode channel and time sample) to a linear model. Mostly up to 60 spatiotemporal features including signals from different electrodes are used. The discriminant function is then used for online classification (Krusienski, McFarland, & Principe, 2012; Krusienski et al., 2006; McFarland & Krusienski, 2012). Typically a linear classifier aims at eliminating as much redundant features as possible, thereby improving performance and interpretability of results (van Gerven et al., 2009). Other linear methods are the Fisher's linear discriminant or Pearson's correlation method (Krusienski et al., 2006). **Figure 3** illustrates artificially generated data that are classified. Data was drawn from two Gaussian distributions simulated potentials recorded at two scalp electrodes FCz and CPz; both channels contribute to the discrimination of the two classes (Blankertz, Lemm, Treder, Haufe, & Müller, 2011). Before signal extraction, different preprocessing methods can be applied to improve the classification of the signals, such as artifact detection, spectral filtering and spatial filtering (van Gerven et al., 2009).

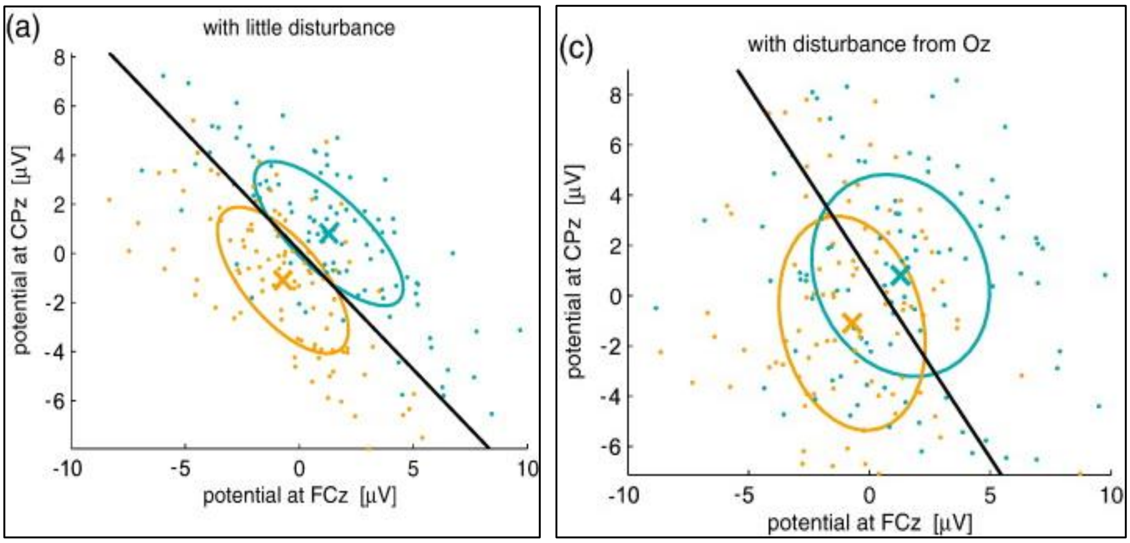


Figure 3: Classification for two conditions target vs. non-target in an ERP BCI.

A linear classifier is used to discriminate two conditions/classes in an ERP BCI. Classification of two conditions target (cyan) and non-target (orange). Left: Two dimensional Gaussian distributions generated to simulate scalp potentials at two electrodes with relative high signal to noise ratio. Right: Same data is disturbed by another signal (simulated visual alpha activity). This results in a substantially decreased separability in the original two dimensional space. Source: Blankertz, B., Lemm, S., Treder, M., Haufe, S., & Müller, K. R. (2011). Single-trial analysis and classification of ERP components--a tutorial. *Neuroimage*, *56(2)*, 814-825, p. 817.

1.1.3 Feedback (output)

A BCI translates input signals into output commands, thus closing the BCI cycle by providing the user with an observable feedback. In a MI BCI (see **figure 2**) the most commonly feedback is a cursor that has to be moved by brain activity to a target on a PC screen (e.g., up and down). The user receives real-time feedback about his/her performance by observing the cursor on the screen. In addition feedback about trial outcome (i.e., success or failure) is provided to reinforce correct behaviour and, thus, enhancing user's performance. Very similar feedback is provided in a SCP paradigm (see **figure 2**). In a visual P300-ERP BCI the user receives feedback about his/her performance at the end of a trial by the presentation of the selected item on the top of an ERP matrix (see **figure 2**). McFarland and colleagues (1998) investigated short-term effects of the presence of the feedback in a MI BCI (McFarland et al., 1998). Classical cursor paradigm (see **figure 2**) was used to train subjects to control their SMR by MI. After a training phase of ten sessions, in which subjects were given the opportunity to acquire EEG control, in the following two sessions the role of feedback on BCI control was evaluated. They tested two conditions, in the first condition movement of the cursor was removed for periods of several minutes and the subject saw only the target and the terminal event signaling a hit or miss. In the second condition neither the cursor nor the terminal event appeared on the screen. Results show that, in the short-term, removal of feedback did not appear to degrade overall performance. Thus, after a training phase subjects were able to sustain control level also without sensory input provided by cursor movement (McFarland et al., 1998). However in some subjects feedback had inhibitory as well as facilitory effects on EEG control. The authors discuss different reasons for these effects: The feedback provided by cursor movement can have facilitory effects in the way that the cursor might support motivation as well as guidance (McFarland et al., 1998; Salmoni, Schmidt, & Walter, 1984). It also might improve performance by allowing rapid reaction to cursor movements that are in the wrong direction (McFarland et al., 1998). Cursor movement in the correct direction and positive feedback (hits) might lead to reinforcement of the correct behaviour and conditioning of EEG responses. On the other hand, cursor movements may distract the person, if paying attention to the moving cursor may prevent that the person focus on internal states such as MI (McFarland et al., 1998). In addition cursor movement might influence BCI control negatively as it could produce EEG responses that interfere with the signal necessary for EEG control (i.e., SMR). Cursor movement could have negative effects in users that have no or very low control, as the cursor movement in the wrong direction can elicit frustration, and thus prevents improvement or learning. In this case removal of the feedback could then again be beneficial (McFarland et al., 1998).

Besides visual feedback, output can be presented in the auditory (Furdea et al., 2009; Nijboer, Furdea, et al., 2008) or vibrotactile mode (Chatterjee, Aggarwal, Ramos, Acharya, & Thakor, 2007; Cincotti et al., 2007; Schreuder, Thurlings, Brouwer, Van Erp, & Tangermann, 2012), or a combination of modes, for example visual and auditory (Hinterberger et al., 2004). Nijboer and colleagues (2008) tested the influence of feedback modes in a MI BCI system in three training sessions (Furdea et al., 2009; Nijboer, Furdea, et al., 2008). Feedback was presented either in the visual or auditory mode. In the visual group subjects had to move a cursor into a target at the bottom or top on the screen by regulating SMR. If the trial was successful (i.e., cursor hit the target), the target flashed in yellow. Feedback about SMR amplitude was presented by a cursor that had to be moved into the target at bottom or top. In the auditory condition harp or bongo sounds indicated the required task. If motor imagery/SMR desynchronization was required, bongo sounds were presented at the beginning of the trial, and if relaxation/SMR synchronization was required harp sounds. The more the direction of the cursor movement corresponded with the target direction (not visible to the user) the more the harp or bongo sounds increased in loudness. A voice was saying at the end of the trial whether the task was "correct" or "incorrect". Results revealed that visual feedback of SMR amplitude led to better average BCI performance than auditory feedback. This difference however vanished after the third training session. Thus, auditory feedback required more training, but lead to approximately the same level of performance at the end of training (Furdea et al., 2009; Nijboer, Furdea, et al., 2008). Similar results were made in another study by Hinterberger and colleagues (2004). Three groups (visual, auditory, visual-auditory) of feedback modes were compared in a SCP controlled BCI. Results showed that auditory as well as combined visual-auditory feedback was feasible, however, the visual feedback group showed higher accuracies as compared to the auditory feedback group. Accuracy was lowest in the combined feedback modality and subjects showed smallest learning effects (Hinterberger et al., 2004). Summarizing, the visual mode is superior to auditory mode; auditory feedback is however also feasible for BCI communication provided with sufficient time for learning; multimodal feedback may rather impede learning. Moreover Cincotti and colleagues (2007) explored the benefits of vibrotactile feedback during users' training and control of a MI BCI in three studies with 33 subjects including three with spinal cord injury (Cincotti et al., 2007). Subjects received either visual or vibrotactile feedback. Feedback was given discretely because continuous feedback was not possible due to technical set-up. No differences were found between training with either vibrotactile or visual feedback. Authors thus conclude, that vibrotactile feedback could be used as an alternative to visual feedback for learning to control a MI BCI. Moreover vibrotactile feedback seemed to positively impact performance when the subject's attention is highly loaded by a simultaneous visual task. Thus it can be assumed that the vibrotactile feedback mode can be effective in relieving the visual channel in complex visual tasks. Interestingly, most subjects reported that vibrotactile feedback felt more natural, as compared to visual feedback (Cincotti et al., 2007).

Even though continuous feedback is a common practice to provide the user of an MI BCI with direct feedback of his/her performance, it is not the case for ERP based BCIs. The only study that systematically manipulated the feedback type in an ERP BCI is a study by Schreuder and colleagues (2012). In this study is was explored whether feedback can benefit the user of an ERP BCI to improve his performance (Schreuder et al., 2012). Using auditory stimuli and vibrotactile feedback that were designed to be congruent in direction, a truly closed-loop and multimodal ERP based BCI system was realized. Users received either no feedback (NoFB), short feedback pulses after 200ms (200ms) or continuous feedback (Cont). Ten subjects were surrounded by six speakers and fitted with a belt of six tactors, one for each speaker direction. During online task subjects had control over the vibrotactile feedback. Results indicate that, concurrent stimulation and feedback does not improve, but rather degrades performance classification (online performance: NoFB: 46.1%; 200 ms: 42.2%; Cont: 40%; chance level: 16%), and behavioural scores (counting the number of target tones). Online and offline classification performance are considerably lower than reported in previous works (Schreuder et al., 2010; Schreuder, Rost, & Tangermann, 2011). Five of ten subjects reported that the feedback was annoying (physically and mentally), or only helpful when it matched the target. The majority of subjects preferred the no feedback condition, indicating that the feedback was distracting them from the task (Schreuder et al., 2012). Furthermore it has been shown that immediate feedback is superior to delayed feedback (McFarland et al., 1998; Salmoni et al., 1984), more realistic feedback (e.g., in virtual reality) is better than conventional two-dimensional feedback on a screen (Gruzelier, Inoue, Smart, Steed, & Steffert, 2010; Ortner, Irimia, Scharinger, & Guger, 2012) and kinaesthetically MI leads to increased performance as compared to solely visual MI (Neuper, Scherer, Reiner, & Pfurtscheller, 2005).

1.1.4 BCI hardware and software

1.1.4.1 Software applications

Recently different BCI programs have been developed. The best established and widely distributed BCI software is BCI-2000 developed by Schalk and colleagues (2004). It can be used with different BCI input signals, such as ERP, SMR and SCP, and can be freely downloaded from the internet platform www.bci2000.org. Research labs can use BCI-2000 in its existing form, or combine it with self-programmed modules, for instance implement new stimulation modalities or new P300 matrices (Schalk, McFarland, Hinterberger, Birbaumer, & Wolpaw, 2004). Another system was developed by researchers in Berlin around Klaus-Robert Müller, Benjamin Blankertz and Gabriel Curio. Their system, called Berlin BCI (BBCI), aims to improve the detection and decoding of brain signals acquired by EEG by focusing on new sensor technology, improved understanding of the brain and the analysis of brain signals using modern machine learning methods (http://bbci.de/). Another BCI, the so-called Graz BCI, developed around Gert Pfurtscheller, was one of the first online EEG based BCI introduced over 20 years ago. To date, it comprises various applications, including spelling devices, computer games, and navigation in virtual environments (http://bci.tugraz.at/). Another recently developed open-source software is OpenVibe (http://openvibe.inria.fr/).

1.1.4.2 Hardware features

Hardware of an EEG based BCI system consists of the EEG cap with electrodes that records EEG signals, an EEG amplifier that reinforces signals and a computer that processes them. The BCI can be set up by any EEG recording system (e.g., EEG system by BrainProducts, Munich, Germany or g.tec Medical Engineering GmbH, Austria). However for end-user testing hardware needs to be light/not heavy (easy to carry to the patient's home) and easy to set up. For that purpose the system by g.tec is most commonly used. It consists of a light and small amplifier (g.USB amp) that can be combined with a customized number of EEG electrodes. By now, most BCIs studies used passive or active wet electrodes. Passive electrodes are based on abrasive gel or paste that is filled into electrodes for preparing the scalp area by light abrasion to reduce electrode-scalp impedance and for conduction of signals. Active electrodes have some built in circuitry which amplifies the electrical current. It improves signal quality; active electrodes do thus not rely on abrasion procedure; however they are also based on a transparent conductive gel. More recently wireless EEG and dry or semi-dry electrodes (without gel) are available (Guger, Krausz, Allison, & Edlinger, 2012; Zander et al., 2011) and systematic tests regarding reliability and robustness are ongoing. Because above mentioned BCI systems are very expensive, and almost not acquirable for a single person, more recently low-costs custom-made EEG systems are developed by different BCI labs (Debener, Minow, Emkes, Gandras, & de Vos, 2012).

1.1.4.3 Commercially available BCI systems

Also "user-ready" BCI systems have been developed, that can be acquired by purchase, for example the speller intendiX, that can be used with P300 and SSVEP input signals (http://www.intendix.com/) by g.tec (Medical Engineering GmbH, Austria). As stated by the company "*intendiX is designed as a personal BCI that anyone can use without technical training or outside support*". This however has not been proven in standardized studies including end-users yet.

1.2 BCI as assistive technology for end-users

Because BCIs are independent of muscular activity, they are considered meaningful for patients with neurological and neurodegenerative diseases that cause motor paralysis, such as motor neuron disease, muscular dystrophy or stroke. Several studies demonstrated that severely motor impaired patients can control a visual P300-ERP BCI for communication (e.g., Kaufmann, Schulz, et al., 2013; Nijboer, Sellers, et al., 2008; Sellers & Donchin, 2006; Silvoni et al., 2009;

Zickler et al., 2011), entertainment, such as painting and photo-browsing (Schreuder et al., 2013; Zickler, Halder, Kleih, Herbert, & Kübler, 2013), environmental control (e.g., Aloise et al., 2011), emailing and internet surfing (e.g., Sellers, Vaughan, & Wolpaw, 2010; Zickler et al., 2011). Initial tests show that patients with neurological disease can control a P300-ERP BCI for simple communication based on the auditory (e.g., Halder, Käthner, & Kübler, 2014a) and tactile stimulation mode (e.g., Kaufmann, Holz, et al., 2013). Moreover it was shown that people with ALS are able to control a BCI by regulating SMR (Kübler, Nijboer, et al., 2005) and SCP (Birbaumer et al., 1999; Karim et al., 2006; Kübler, Neumann, et al., 2001; Neumann & Kübler, 2003; Neumann, Kübler, Kaiser, Hinterberger, & Birbaumer, 2003) when provided with feedback and sufficient training time; for reviews see (Kleih et al., 2011; Kübler & Birbaumer, 2008; Mak et al., 2011; Millan et al., 2010). It is important to note that not all patients are able to gain sufficient control over BCI devices. McCane and colleagues (2014) presented 25 individuals diagnosed with ALS with a 6x6 P300-ERP spelling matrix. Seventeen subjects had accuracies above 70%, thereby successful communication performance (McCane et al., 2014). The other eight subjects did not gain successful control (accuracies below 40%). Most importantly many of those subjects who were severely impaired had high BCI accuracy (11 of 17). Thereby a relationship between progress of disease and BCI performance was not found, suggesting that BCI performance remains stable with progress of disease (McCane et al., 2014; Sellers et al., 2010; Silvoni et al., 2013; Silvoni et al., 2009). Based on these encouraging results, BCIs have been considered useful devices for persons diagnosed with neurological/neuromuscular, neurodegenerative or cerebrovascular diseases that cause severe motor paralysis. In the following it is referred to these persons as BCI end-users, or simply end-users, because they are considered as potential or prospective or real end-users of a BCI device. In the present thesis the term end-user and patient is used synonymously.

1.2.1 Psychological health of patients with severe motor disabilities

Even though most people would suggest that patients diagnosed with (progressive) neurological diseases are depressed and show poor quality of life, findings cannot support this. It was found that the prevalence of depression was comparable or only slightly increased in persons with ALS compared to normal population; between 0 and 22% for major depression and between 10 and 25% for all depressed disorders including subclinical depression (Bungener et al., 2005; Ferentinos et al., 2011; Ganzini, Johnston, & Hoffman, 1999; Kurt, Nijboer, Matuz, & Kübler, 2007; Nonnenmacher, Hammer, Lule, Hautzinger, & Kübler, 2013; Rabkin et al., 2005; Rabkin, Wagner, & Del Bene, 2000). However with a prevalence of 21%, anxiety disorder was twice as high in the ALS as compared to the German general population (Nonnenmacher et al., 2013). Nonnenmacher and colleagues (2013) report that individual quality of life of ALS patients was high with a mean of 72 (of 100), that is higher as compared to depressed, but physically healthy (non-impaired) patients (Moore, Hofer, McGee, & Ring, 2005) or to cancer patients (Carlson, Bultz, & Morris, 2005; Fegg, Wasner, Neudert, & Borasio, 2005). Severely impaired patients indicated significantly more frequent communication and medical assistance as being important for their quality of life as compared to less impaired patients. This can be explained by the so called response shift, meaning that internal norms and ideals are adapted to a changed life situation. The diagnosis of ALS can thus be considered as risk factor for the development of a Major Depression, however it does not correlate to the physical impairment but rather to insufficient coping strategies and to not or insufficient performed response shift. For example, depressed ALS patients considered health more important as compared to non-depressed ALS patients, indicating insufficient or not performed response shift. Matuz and colleagues (2010) found that approximately 60% of the variance of depression and quality of life can be explained by copy strategies, social support and cognitive appraisal, whereas physical impairment did not explain any variance (Matuz, Birbaumer, Hautzinger, & Kübler, 2010). Also for persons in the locked-in state quality of life is mostly comparable high as in healthy controls and other chronically ill patients without severe motor impairment; and higher compared to what caregivers and families would expect (Kübler, Winter, Ludolph, Hautzinger, & Birbaumer, 2005; Lule, Hacker, Ludolph, Birbaumer, & Kübler, 2008; Lule et al., 2009). As described above, patients with ALS (or other progressive diseases that cause locked-in state) can choose whether they opt for life prolonging measures before entering the locked-in state. As reported by Birbaumer (2006), most of the ALS patients however decide against life-prolonging measures, because most of the patients, family members and doctors believe that quality of life in total paralysis is extremely low and continuation of life constitutes a burden for the patient and the family and that it is unethical to consider emergency measures such as artificial ventilation or feeding to continue life (Birbaumer, 2006). However if patients and their families would be informed about the above described results, together with information about therapeutic options including the possibility to terminate invasive artificially ventilation and feeding, probably more patients would opt for measures to continue life (Lule et al., 2008). Even though quality of life is high, BCI technology can substantially improve the lives of people with devastating motor disorders and might additionally positively influence the decision whether they opt for life continuing measures such as artificial ventilation when it becomes necessary.

1.2.2 Potential BCI end-users

The following section describes diseases that can cause paralysis of the motor system and that are mentioned in the present thesis: Motor neuron disease (ALS and spinal muscular atrophy), muscular dystrophy, stroke and cerebral palsy.

1.2.2.1 Motor neuron disease

Motor neuron disease (MND) is a heterogenic group of neurological disorders that is characterized by a degeneration of motor neurons (retraction of nerve fibres) in either the first motor neuron (pyramidal cells of the motor cortex and pyramidal tracts) or the second motor neuron (motor cells of the anterior horn or cranial nerve nucleus), such as in spinal muscular atrophy, or a combination of both systems, such as in ALS (Poeck & Hacke, 2006).

1.2.2.1.1 Amyotrophic lateral sclerosis

The most frequent MND is ALS. ALS, also known as Lou Gehrig's disease, is a fatal neurodegenerative disease targeting motor neurons in the brain and spinal cord (Poeck & Hacke, 2006). Degeneration of motor neurons, which innervate the voluntary contractable skeletal muscles, results in muscle cramps, spasm, progressive atrophic paresis, dysarthria, dysphagia and respiratory insufficiency until complete paralysis of the body, in which also respiratory and bulbar functions are destroyed (Borasio & Pongratz, 1997). The prevalence of ALS is 3-8/100.000 and incidence 2-2,5/100.000 (Gastl & Ludolph, 2007). The ratio for men to women is 1.5:1. About 90 to 95% of all ALS cases are sporadic (sALS) and only 5 to 10% familiar (fALS). Mean age of onset is 56-58 years for sALS and 46 years for fALS. There are two different forms of onset: spinal (first symptoms in arms or legs) and bulbar (first symptoms in speaking or swallowing). Recent findings show not only altered brain activation in the motor cortex but also in other parts, for instance the frontal lobe (Ludolph et al., 1992; Paulus et al., 2002). Hanagasi and colleagues (2002) found subclinical impairment of cognitive functions in patients with ALS. Impairment was found especially in working memory, sustained attention, response inhibition, verbal fluency and complex visuo-spatial processing (Hanagasi et al., 2002). Moreover fronto-temporal dementia is described in ALS. Incidence rates of ALS dementia vary due to differing diagnostic criteria; rates of 15-22% (Murphy et al., 2007; Ringholz et al., 2005) are recently reported. The development of ALS is fatal if patients do not opt life-prolonging treatments such as artificial respiration and feeding. If they choose life-prolonging treatments, the disease progresses into the locked-in state, where only control of eye-movements is preserved (see **1.2.1.5 Locked-in syndrome**). Patients enter the completely locked-in state, in which control of the last muscular response, which is usually eye movements or the external spincter, is also lost (Birbaumer, 2006; Kübler &

Birbaumer, 2008). Patients can use rudimentary muscle control of the eyes to operate assistive devices (e.g., eye-tracking system) before entering the completely locked-in state. Patients enter the completely locked-in state several years (very heterogeneous) after opting for artificial ventilation and feeding.

1.2.2.1.2 Spinal muscular atrophy

Spinal muscular atrophy (SMA) is a severe neuromuscular disease characterized by degeneration of motor neurons in the spinal cord, resulting in progressive proximal muscle weakness and paralysis (D'Amico, Mercuri, Tiziano, & Bertini, 2011). SMA is caused by homozygous disruption of the survival motor neuron 1 gene by deletion, conversion, or mutation (Lunn & Wang, 2008). Brother and sisters of these patients are often ill as well (Poeck & Hacke, 2006). Pearn (1973, 1978) found a prevalence of SMA of 1.20 per 100.000 and an incidence of 1 in 24.100 live births (Pearn, 1973, 1978); others report prevalences and incidences of 1 in 10.000 or 1 in 60.000 live births (Cusin, Clermont, Gerard, Chantereau, & Elion, 2003; D'Amico et al., 2011; Lunn & Wang, 2008; Nicole, Diaz, Frugier, & Melki, 2002; Poeck & Hacke, 2006; Prior et al., 2010). SMA has been divided into four clinical types on the basis of age of onset and motor function achieved: (1) infantile severe type I (Werdnig–Hoffmann disease); (2) intermediate type II (Dubowitz disease); (3) mild type III (Kugelberg–Welander disease); and (4) adult-onset type IV (D'Amico et al., 2011; Lunn & Wang, 2008). SMA type 1 is the most severe and common type (around 50% of all patients diagnosed with SMA). Classically SMA type I manifests before six months of age. Infants never acquire the ability to sit unsupported and generally do not survive beyond the first two years if no intervention is provided. Patients have severe hypotonia, weakness and paralysis, and often no head control. SMA type II is characterized by onset between 7 and 18 months. Patients achieve the ability to sit unsupported but most of them are not able to walk independently. Weak swallowing and affected ability to chew can be present. Some patients at the weak end of the spectrum may develop respiratory failure requiring mechanical ventilation. SMA type III includes clinically heterogeneous patients. They typically reach all major motor milestones, as well as independent walking. However during infancy they develop proximal muscular weakness. Some of these patients need wheelchair assistance in childhood, whereas others continue to walk and live a “normal” life with only minor muscular weakness. SMA type IV describes those patients with adult onset (> 18 years) and mild course. These patients are able to walk and have no respiratory and nutritional problems (D'Amico et al., 2011).

1.2.2.2 Muscular Dystrophy

Muscular dystrophies (MDs) are a group of genetically determined myopathic diseases. The general feature is progressive weakness of the musculoskeletal system (Pearson, 1963). MDs are caused by genetic determined disruptions in the metabolism of the muscles. A prevalence of 5 of 100.000 in general population has been reported (Poeck & Hacke, 2006). More than nine forms have been described, among the most common form Duchenne. MD from type Duchenne is caused by mutations of the X-linked gene that encodes for the protein dystrophin. Dystrophin is missing or reduced to less than 3%. It affects only boys (with extremely rare exceptions) and it becomes evident when children begin to walk. Diagnosis is usually confirmed between the age of 2 and 7 years and boys become progressively weaker. By approximately 10 years of age, boys struggle to walk or stand alone and become wheel-chair bound after 10 and 15 years of age (Poeck & Hacke, 2006; Polakoff, Morton, Koch, & Rios, 1998). Through adolescence, muscle wasting progresses, self-care skills, such as feeding, toileting, eating and bathing are affected and boys become rapidly dependent on caregivers and their families (Polakoff et al., 1998). According to Biggar (2006) electrocardiographic and echocardiographic changes are present in more than 50% and pulmonary function begins to deteriorate between 9 and 11 years of age. Moreover boys develop a spinal curvature 3 to 4 years after losing ambulation (Biggar, 2006). According to Poeck and Hacke (2006), patients with Duchenne MD rarely reach an age of 25 (Poeck & Hacke, 2006). However an improvement in life expectancy since 1967, especially due to (nocturnal) ventilation, with a mean age of death of 14.4 years in the 1960s and of 25.3 years since 1990 (with ventilation) is reported (Eagle et al., 2002).

1.2.2.3 Stroke

Stroke is the brain equivalent of a heart attack. Blood must flow through the brain. If its circuits are restricted, by a blood clot moving to the brain, or by narrowing or bursting of blood vessels, brain tissue can no longer be supplied with energy; the consequence is brain damage leading to stroke (WHO, 2014a). With 80% of all cases, ischemic strokes (lack of blood flow) are more prevalent than hemorrhagic cases (Poeck & Hacke, 2006). According to the World Health Organization (WHO, 2014b) stroke was the second most frequent cause of death in 2012. Around 15 million people suffer annually worldwide a stroke. Of those, 5 million die and another 5 million are left permanently disabled, placing a burden on family and community (WHO, 2014a). Stroke is thus economically one of the most expensive diseases. In Germany, 150-200.00 people suffer a stroke each year (Poeck & Hacke, 2006). Around 70.000 people live with the consequences of a stroke. About 15-20% of the people die within the first four weeks. One third of the survivors can rehabilitate successfully, in the way that they can live as before the stroke, without restrictions. Another third is able to perform simple things in daily-life, after rehabilitation, but are restricted by paralysis in the upper or lower limbs and are not able to return to work. Another third of the survivors is heavily impaired and is in need of permanent care. This shows that stroke patients are a very heterogeneous group with very heterogeneous levels of motoric impairment and restrictions (Poeck & Hacke, 2006). Irrespective of the degree of impairment in motor functions, many persons with stroke are additionally affected in neuropsychological functions, such as attention, orientation, memory, and language (Tatemichi et al., 1994).

1.2.2.4 Cerebral palsy

Cerebral palsy (CP) is a well-recognized neurodevelopmental condition that begins in early childhood and persists through lifespan (Rosenbaum et al., 2007). It has been originally reported as “cerebral paresis” in the 19th century. Rosenbaum and colleagues (2006) claim that definition and classification of CP has to be reconsidered, as new light has been shed on the nature of the underlying brain injury. Authors define cerebral palsy as a “*group of permanent disorders of the development of movement and posture, causing activity limitations that are attributed to non-progressive disturbances that occurred in the developing fetal or infant brain. The motor disorders of cerebral palsy are often accompanied by disturbances of sensation, perception, cognition, communication, and behaviour; by epilepsy, and by secondary musculoskeletal problems*“ (Rosenbaum et al., 2007). Motor impairment of children begins very early to manifest, usually before 18 months with delayed or abnormal motor progress. Other functional impairment can appear through childhood or later (Rosenbaum et al., 2007). Functional impairment in movement and posture mean abnormal gross and fine motor functioning and organization leading to difficulties in walking, feeding, swallowing, coordinated eye-movements, articulation of speech and secondary problem with behaviour. Disturbances of sensation mean that vision, hearing and other sensory modalities can be affected. Disturbances of perception refer to incapacity to incorporate and interpret sensory and/or cognitive information (that cause further secondary disturbances as they restrict learning and perceptual development). Oskoui and colleagues (2013) report a prevalence of 2.11 per 1000 live births (Oskoui, Coutinho, Dykeman, Jette, & Pringsheim, 2013). The three most important risk factors for CP are low birth weight, intrauterine infections and multiple gestation (Odding, Roebroeck, & Stam, 2006).

1.2.2.5 Locked-in syndrome

Even though cases where already described earlier in the 19th century, Plum and Posner were the first who defined the locked-in syndrome (LIS) 1966 as a neurological state in which the patient is "*de-efferented resulting in paralysis of all four limbs and the lower cranial nerves*" (Posner, Clifford, Schiff, & Plum, 2007; p. 7). Patients are able to control vertical eye movements and eyelid opening and are fully conscious. Most common cause is a lesion due to ischemic stroke or haemorrhage in the pons that interrupts descending cortical control of motor functions. Eye movements and eyelid opening can be used for communication by using eye blinks as a code. However, patients may sometimes not be recognised as fully conscious and misdiagnosed as comatose, if responding is not reliable. This is especially the case in patients that are comatose after the ischaemic, haemorrhage or traumatic attack, however recover after several weeks and regain control over at least one muscle, for instance eye-movements. Nursing staff and families play an important role in identifying locked-in patients as such (Posner et al., 2007). Therefore clinicians have to be very suspious and careful not misdiagnosing a person. Patients in the locked-in state retain the ability for functional communication but need to be recognized in order to mobilize emerging technologies that can translate eye movements, and thereby help locked-in patients to communicate. Also other diseases can lead to a locked-in syndrome, for instance progressive diseases such as ALS, Multiple Sclerosis, Parkinson disease or subactue motor neuropathy (e.g., Guillain-Barré syndrome; Birbaumer, 2006; Poeck & Hacke, 2006). In progressive neurological disease (e.g., ALS), the patient can decide whether he or she wants to enter the locked-in state by opting for life continuing measures, it is thus a condition that can be freely chosen by the patient; different for acute/traumatic cases, as described above. In 1979 Bauer and colleagues extended the definition of the locked-in syndrome and subdivided locked-in syndrome into three categories: The "classical" locked-in syndrome, as described by Plum and Posner (complete motor paralysis except vertical eye movements and blinking), the "incomplete" locked-in syndrome, which resembles classical locked-in state with some residual muscular control (e.g., of one finger) and the "total" locked-in syndrome, in which patients are completely paralyzed, unable to communicate, but fully conscious (Bauer, Gerstenbrand, & Rumpl, 1979).

1.3 Translational and reliability gap

Even though many authors mention persons with severe motor impairment as target group for their BCI systems, most BCI studies are conducted exclusively in the laboratory with healthy subjects, and many studies do not report online results. Such studies can provide valuable information about signal extraction and classification. There is however a substantial lack of studies that investigate whether results obtained in healthy participants can be transferred to patients with neurodegenerative diseases. BCIs that work in the laboratory need to work in real life situations (e.g., at the end-user's home). Less than 10% of BCI publications include people with severe disabilities (Kübler, Holz, Kaufmann, & Zickler, 2013; Kübler et al., 2014; Kübler, Mattia, et al., 2013; Mak et al., 2011), see **figure 4**. Moreover only few studies about long-term independent use of a BCI exist (see **1.4.2.2 Long-term independent use**). This clearly shows that BCI research faces a translational gap between intense BCI research (e.g., aiming at improving BCIs in terms of accuracy and speed) and bringing BCI applications to BCI end-users outside the lab (Kübler, Mattia, et al., 2013). Translational studies are needed that investigate whether BCIs can be successfully used by severely disabled end-users and whether those end-users accept BCIs as assistive devices. Another obvious discrepancy between the plethora of short term studies and the sparse number of long-term studies exist. BCI research thus faces also a reliability gap (Kübler, Mattia, et al., 2013). Most studies present only one BCI session, however the few studies that include several testing sessions indicate high inter- and intra-individually variance in the user's performance due to non-stationarity of BCI recordings. Especially in the target group, many influencing factors exist, such as altered brain responses due to neuronal degeneration, muscle artifacts, attentional impairment. Long-term studies are needed, to demonstrate whether a BCI can be reliably used over a long time period that is important if BCIs should become assistive devices for end-users with neurological diseases. Therefore there is a great need for translational as well as reliability studies. Research gaps need to be addressed if BCI research aims at fulfilling its primary purpose and justifying the considerable support that their development receives from governments and other funding sources (Vaughan et al., 2012).

Why is there such a low number of translational studies? Working with prospective end-users causes many issues and challenges. Working with a vulnerable target group includes dealing with expectations and desires of prospective end-users and their caregivers (Sellers, Arbel, & Donchin, 2012). Some persons may have difficulties to work with patients because they do not know how to behave or they are afraid of raising false hopes, because in most studies BCI has to be taken away at the end of the study. Recruitment of patients is more time-consuming compared to healthy participants and there are higher costs, for instance for traveling to the patients' homes or clinics or residential homes because most of them cannot come to the laboratory. Furthermore testing is more time-consuming, because more pauses are required (e.g., for medical treatments or due to lower concentration) and due to slower communication (e.g., if only „yes" and „no" communication available). Sometimes no testing is possible because physical state of locked-in patients is highly instable. Taking a new BCI system from a highly controlled laboratory environment out into a complex and unpredictable environment to the end-user's home causes problems, such as electromagnetic noise that affects EEG recordings. Testing of end-users is challenged by other artifacts that influence data, such as involuntary muscle contractions due to spasm. Another reason could be that researchers may not want to test patients any further, because of frustration or disappointment due to lacking success in previous studies, for example if patients were not able to control the BCI. Or they do not want to test patients because they just do not like to do BCI research in the target group, but in a healthy population; for instance aiming at developing BCIs for the detection of the user's cognitive state, intentions, situational interpretations and emotions in traffic or transport situations (Zander & Kothe, 2011). Why are there only few long-term and/or home use studies (reliability gap)? There are different reasons: There are high costs for the BCI system (~15.000 Euros) and continuous costs for oversight. Then there arise practical and ethical problems, in case of lack of future funding (e.g., can the BCI be taken away after several years, if the patient benefit of the BCI?); or when BCI performance degrades due to progressing disease (Sellers et al., 2012).

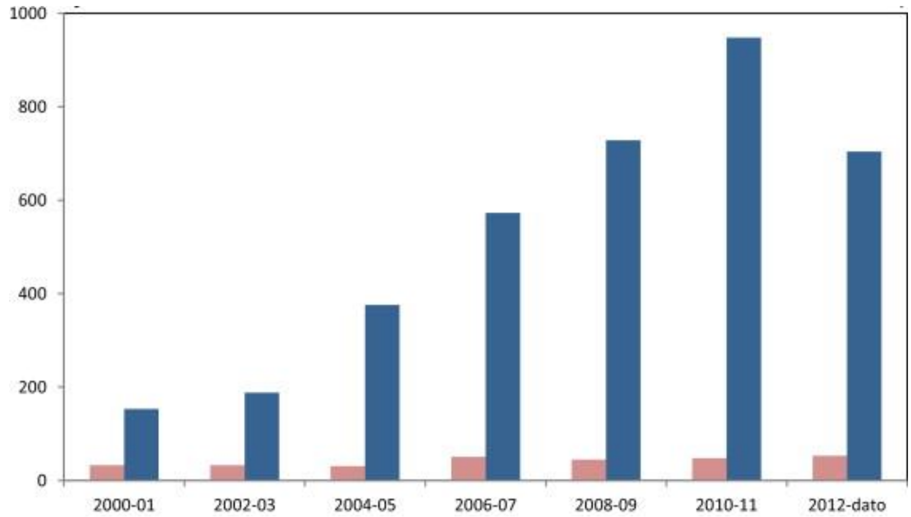


Figure 4: Results of a coarse screening for BCI papers in PubMed by Kübler et al. (2013).

Search terms were "brain AND computer AND interface" (blue bars); for patients "AND patient" was added (red bars). Number of publications are depicted per 2-year-period since 2000. Note that the last columns for 2012-dato include publications from 2012 until submission/revision of the paper in Spring/Summer 2013. According to the authors, who report an almost exponentially trend, in 2012-2013 more publications, as compared to 2010-2011 can be expected. Source: Kübler, A., Mattia, D., Rupp, R., & Tangermann, M. (2013). Facing the challenge: bringing brain-computer interfaces to end-users. *Artificial intelligence in medicine, 59(2),* 55-60. doi: 10.1016/j.artmed.2013.08.002, p. 56.

1.4 Bridging gaps

According to Kübler and colleagues (2013) the translational gap can be bridged by short term evaluation studies based on a user-centred design (UCD) that investigate problems and obstacles that emerge when BCIs are applied to end-users with severe motor impairment in their home environment (Kübler, Mattia, et al., 2013). Translational studies should include quantitative and qualitative evaluation of BCI devices. Bridge building is already in progress by considerable improvements in functionality, easiness of use and independent use (see **1.4.3 User-centred improvements of BCI applications**). The reliability gap can be bridged by long-term studies, especially on independent BCI use at the end-user's home. Reliability studies need to take into account several factors that may contribute to successful BCI control (Kübler et al., 2011; Kübler, Holz, et al., 2013; Kübler et al., 2014; Kübler, Mattia, et al., 2013).

1.4.1 UCD for evaluation of usability of BCI applications

While most BCI researchers evaluate BCIs in terms of pragmatic parameters such as efficiency (e.g., speed) and effectiveness (accuracies and online performance), single research groups have begun to take psychological variables, such as motivation and mood, learning, personality, cognitive and performance variables (Hammer et al., 2012; Hammer, Kaufmann, Kleih, Blankertz, & Kübler, 2014; Kleih et al., 2011; Kleih & Kübler, 2013; Kleih, Nijboer, Halder, & Kübler, 2010; Nijboer, Birbaumer, & Kübler, 2010; Nijboer, Furdea, et al., 2008) or user experience and usability aspects such as workload, learnability, satisfaction, enjoyment, and frustration, into account (Käthner, Wriessnegger, Müller-Putz, Kübler, & Halder, 2014; Lorenz, Pascual, Blankertz, & Vidaurre, 2014; Nijholt, Plass-Oude Bos, & Reuderink, 2009; Pasqualotto, Simonetta, Gnisci, Federici, & Belardinelli, 2011; Pasqualotto, Simonetta, Gnisci, Federici, & Belardinelli, 2009; van de Laar, Nijboer, Gürkök, Plass-Oude Bos, & Nijholt, 2011; van de Laar, Plass-Oude Bos, Reuderink, Poel, & Nijholt, 2013). These studies however include solely healthy participants. Studies including prospective BCI end-users are of utmost importance to investigate whether a BCI device can be accepted as assistive technology (AT) and whether BCIs would be adopted for use in daily-life. To bridge this translational gap, Kübler and colleagues adapted the user-centred design to BCI research and development, which focuses on a holistic user experience that is mandatory for transferring BCIs from laboratory of the developers to end-users in need (Kübler et al., 2014). The UCD thus includes an iterative process between end-users and developers on the basis of an evaluation procedure. The UCD approach focuses on usability, that is how well a specific technology suits its purpose and meets the needs and requirements of the prospective BCI end-users and was standardized with the ISO 9241-210 (ISO-9241-210, 2008). It implies six basic principles (see **table 1**): P1: understand the user, the task and environmental requirements; P2: encourage early and active involvement of users; P3: be driven and refined by user-centred evaluation; P4: iterate developmental process of design solutions; P5: incorporate the whole user experience; P6: encourage multi-disciplinary design. Accordingly four practical stages were defined (see **table 1**). The goal of this user-centred evaluation process is to develop a new BCI application into a final product, that matches the end-users' needs and requirements, is accepted well by the end-users and is adopted in their daily-lives (Holz et al., 2012; Kübler et al., 2014; Maguire, 1998; Zickler et al., 2009; Zickler et al., 2011).

Table 1: Principles of the user-centred design.

The principles (P)	**BCI controlled applications**
P1: understand the user, the task and environmental requirements	Choose appropriate metrics, apply questionnaires for first definition (Zickler et al., 2009)
P2: encourage early and active involvement of users	Interaction between users and developers to define the first version of a prototype; BP: (Kübler, Halder, Furdea, & Hösle, 2008), P300-QL: (Riccio et al., 2011)
P3: be driven and refined by user-centred evaluation	Valid evaluation metrics (Zickler et al., 2011)
P4: iterate developmental process of design solutions	Continuous interaction between developers and end-users in their home environment leading to several prototypes, BP: (Münßinger et al., 2010; Zickler et al., 2013) and *study 3* (present thesis); P300-QL: (Zickler et al., 2011), Hybrid P300-QL: (Riccio et al., 2015) and *study 2*, present thesis; Connect-Four: *study 1*, present thesis
P5: incorporate the whole user experience	Evaluation metrics that covers all aspects of "usability", i.e., effectiveness, efficiency, satisfaction (Zickler et al., 2013; Zickler et al., 2011) and *study 1-3* present thesis
P6: encourage multi-disciplinary design	BCI team of computer scientists, engineers, psychologists, medical doctors, neuroscientists, AT experts
The stages (S)	
S1: understand and specify the context of use	Identified need and potential impact, BP: (Kübler et al., 2008; Münßinger et al., 2010; Zickler et al., 2009); P300-QL: (Zickler et al., 2009)
S2: specify the user requirements	Questionnaires and interviews (Münßinger et al., 2010; Zickler et al., 2009)
S3: produce design solutions to meet user requirements	Prototypes available for testing: P300-QL (Zickler et al., 2011); Hybrid P300-QL: (Riccio et al., 2015) and *study 2*, present thesis; BP: (Zickler et al., 2013) and *study 3* present thesis
S4: evaluation the designs against requirements	Evaluation metrics (effectiveness, efficiency, satisfaction) compared across all prototypes, see general discussion, present thesis

Note: Left column: Principles and iterative stages needed for implementation and development. Right column: Examples for different BCI applications P300-ERP Qualilife (P300-QL) communication and the P300-ERP BCI Brain Painting (BP), in which this iterative appraoch has been realized. Modified from: Kübler, A., Holz, E. M., Riccio, A., Zickler, C., Kaufmann, T., Kleih, S. C., Staiger-Sälzer, P., Desideri, L., Hoogerwerf, E.-J., & Mattia, D. (2014). The user-centered design as novel perspective for evaluating the usability of BCI-controlled applications. *Plos one, 9(12)*, e112392, p. 3.

1.4.1.1 Users' needs and requirements (P1 and P2)

In a study by Zickler and colleagues (2009) 77 patients with different neurological or cerebrospinal diseases were asked how satisfied they were with their current ATs, which new AT applications they would desire and what they consider as most important aspects for new assistive devices (Zickler et al., 2009). Between 16 to 30% of the patients were dissatisfied with their current solutions for communication, manipulation, computer access and environment. The majority of the patients had independent access to different devices for communication and entertainment; however 10 to 22% had no access to e-media. About 52 % would like to improve their current AT for mobility, 46% for activities of daily-living and 33% for occupation/ employment. Participants who used communication aids wanted to improve their independence in areas of mobility (44%), activities of daily-living (40%) and expression of thought/opinions/ideas (24%). The authors thus expected that a BCI could contribute to the end-users' quality of life, in the areas of manipulation, communication, environmental control and entertainment. Most notably, besides communication, patients who are severely disabled may wish to be able to pursue other satisfying leisure activities that enhance quality of life; in line with (Kübler et al., 2008; Münßinger et al., 2010). Considering the adoption of a new AT solution such as BCI, patients indicated functionality, easiness of use and independent use as most important (Zickler et al., 2009). Within the EU-project TOBI (http://www.tobi-project.org/) different prototypes have been developed in accordance with the UCD, for communication, e-inclusion, entertainment, wheelchair control and tested and evaluated in an iterative cycle by potential BCI end-users.

1.4.1.2 Valid evaluation metrics (P3)

The ISO 9241-201 defines usability as the "*extent to which a [...] product [...] can be used by specified users to achieve specified goals with effectiveness, efficiency and satisfaction in a specified context of use*" (p.2). This definition of usability implies that BCI-controlled applications cannot be evaluated without including end-users. Effectiveness refers to how accurate users can accomplish tasks and indicates how effective a system is for a specified user. Efficiency relates the invested costs that are user's effort and time, to achieve effectiveness. User's satisfaction refers to the perceived comfort and acceptability while using the product. These metrics were adapted for evaluation of BCI controlled applications by Kübler and colleagues (Kübler et al., 2014; Zickler et al., 2013; Zickler et al., 2011) and defined as follows (see **table 2**):

1.4.1.2.1 Usability

1.4.1.2.1.1 Effectiveness

Effectiveness, a measure of how accurate and complete a user can accomplish a BCI controlled application is how often the intended selection can be achieved. Accuracy, the number of correct selections (e.g., moving a cursor to the left or right or selection of a letter or symbol out of a matrix) divided by the total number of selections, was used as indicator of effectiveness.

1.4.1.2.1.2 Efficiency

Efficiency, a measure of the related costs (i.e., effort and time) invested to achieve effectiveness was defined as information transfer rate (ITR; Wolpaw, Birbaumer, McFarland, Pfurtscheller, & Vaughan, 2002) and user's subjective workload (National Aeronautics and Space Administration Task Load Index (NASA-TLX); Hart & Staveland, 1988). ITR takes the available number of possible selections and the time needed for a selection [bits/minute] and the accuracy of intended selections into account and is an objective measure of efficiency for applications. The ITR incorporates thus speed as well as accuracy in one single value and constitutes the transmitted information rate in a specified time interval. The ITR, or bitrate (bits/trial, B), is calculated according to Wolpaw and colleagues (Wolpaw et al., 2002): B=log2(N)+P*log2(P)+(1-P)*log2((1-P/N-1)). With N being the number of possible selections and P being the accuracy of the end-user. This value (B) can then be multiplied with the number of selections per minute, resulting in the number of bits/minute. Subjective workload was assessed using the NASA-TLX (Hart & Staveland, 1988). Subjective workload is defined in the NASA-TLX as "*hypothetical construct that represents the costs incurred by a human operator to achieve a particular level of performance*" (p.140). The NASA-TLX measures the overall subjective workload experienced in a specific task, but also identifies the main sources of the workload: mental, physical and temporal demand, effort, performance and frustration. Mental demand describes how much mental and perceptual activity is required (low/high; e.g., thinking, deciding, remembering, looking, searching). Physical demand means how much physical activity is required (low/high; e.g., pushing, pulling, turning, controlling, activating) in conducting a specific task. Temporal demand describes how much time pressure a person feels due to the rate or pace at which the task or task elements occurred (low/high). Performance asks how successful the person thinks he/she accomplished the task (good or poor), and effort asks the person how hard he/she had to work (mentally and physically) to accomplish the level of performance (low/high). The frustration scale describes how insecure, discouraged, irritated, stressed and annoyed versus secure, content, relaxed a person felt during a specific task (low/high). First, end-users rate their workload on six bipolar subscales ranging from 0 to 100. Then, in 14 pair-wise comparisons users indicate which dimension contribute more to their workload. A weighting procedure identifies the total workload, ranging between 0 and 100, and the relative contribution of each dimension to the total workload. The highest possible score for the overall workload is 100, while for the weighted subscales the highest possible score is 33.3.

1.4.1.2.1.3 Satisfaction

User’s satisfaction, referring to the perceived comfort and acceptability while using a product, was assessed with the extended Quebec User Evaluation of Satisfaction with assistive Technology (extended QUEST; Demers, Weiss-Lambrou, & Ska, 2000), the Assistive Technology Device Predisposition Assessment (ATD-PA) device form (M. J. Scherer, 2007) and a visual analogue scale (VAS satisfaction). The QUEST 2.0 is the only standardized satisfaction assessment tool designed for ATs. It gives qualitative and quantitative information about how satisfied a user is with different aspects of a product and how well a user accepts a device as AT and comprises twelve items. For the extended version, four items (durability, service delivery, repairs/servicing, follow-up services) were removed and replaced by four new items which are important for evaluation of BCI devices (reliability, speed, learnability and aesthetic design; Zickler et al., 2011). Satisfaction is rated on a scale between 1 and 5, (1=“not satisfied at all”, 5=“very satisfied”). End-users are asked to give comments, if they are not very satisfied (score 1 to 4). In addition users are asked to indicate the three most important items. The ATD-PA is a set of questionnaires based on the Matching Person and Technology Model of Scherer (M. J. Scherer, 2007). The ATD-PA device form was used to assess the match between the person and AT. The ATD-PA device Form comprises 12 items asking respondents to rate their predisposition to use the AT under consideration, for example “*This device will help me to achieve my goals*” and “*This device will benefit me and improve my quality of life*”. End-users rate their predisposition on a 5-point Likert-scale from 1 (not at all - 0% of the time) to 5 (all the time - 100% of the time). End-users indicate “0” if the item is not applicable. The total score is calculated by averaging all item scores. The highest possible score is 5.0. A score between 4.0 and 5.0 indicates a good match of person and AT-device, scores below 4.0 indicate that the match could be improved and a score of 3 or less indicates a risk of device non-use (M. J. Scherer, 2007; Zickler et al., 2011). VAS satisfaction obtains general satisfaction and enables quick assessment of satisfaction after a specified BCI session or task and is rated on a scale, ranging from 0 to 10 with 10 as highest satisfaction.

1.4.1.2.1.4 Application specific metrics

As BCI applications differ considerably and thus to obtain more application specific details, any face valid measure can be added to the proposed evaluation metrics (Kübler et al., 2014). For instance, in *study 3* visual analogue scales for the assessment of enjoyment and frustration were introduced.

1.4.1.2.2 Usefulness

In controlled setting, end-users were asked whether they could imagine to use the BCI in their daily-lives. Moreover for assessing the whole user experience and the prospective potential for the end-user, meaning the usefulness of the BCI, end-users were enrolled in an open interview. For independent use, the number of BCI sessions, the total usage duration and the impact of the BCI on the life of the person can be considered as indicator of usefulness, as suggested by Vaughan and colleagues (Vaughan et al., 2012). The influence of an AT on the life of the person was measured with the Psychosocial Impact of Assistive Devices Scale (PIADS; Day & Jutai, 1996; Jutai & Day, 2002), consisting of 26 items describing perception on three dimensions competence, adaptability and self-esteem. Competence (12 items) measures feelings of competence and efficacy and is sensitive to the impact of an AT on performance and productivity. Adaptability (6 items) refers to the willingness to try out new things and to take risks and is sensitive to the enabling and liberating aspects of an AT. Self-esteem (8 items) includes feelings of emotional health and happiness and is sensitive to the impact of an AT on self-confidence and emotional well-being. The end-user indicates whether the AT has a positive or negative impact and the degree of this impact on the specified dimension (range, -3 to 3; -3 indicates maximum negative impact, 3 maximum positive impact and zero no perceived impact.

Table 2: Evaluation metrics.

Evaluation metrics				
	Aspects	**Transfer to BCI applications**	**Metrics**	**Assessment**
Usability	**Effectiveness**	Accuracy	% correct responses	each session
	Efficiency	Information transfer rate	Bits/min	each session
		Subjective workload	NASA-TLX	each session/task
	Satisfaction	General aspects of the AT	Extended QUEST	end of prototype testing
		BCI related aspects	4 added items	end of prototype testing
		Match between product and user	ATD-PA device form	end of prototype testing
		Overall satisfaction	VAS satisfaction	each session
Usefulness	**Use in daily life**	Interview	Semi-structured	end of prototype testing
		Use in daily-life	Single item	end of prototype testing
		Face valid measures of daily-life use	Number of sessions, and total usage time	each session
	Influence on life of the person	Influence of the BCI on the life of the person	PIADS	After several months of use

Note: NASA-TLX=NASA Task Load Index; extended QUEST=extended Quebec User Evaluation of Satisfaction with Assistive Technology; ATD-PA=Assistive Technology Device Predisposition Assessment; VAS=visual analogue scale; PIADS=Psychosocial Impact of Assistive Devices Scale; Modified from: Kübler, A., Holz, E.M., Riccio, A., Zickler, C., Kaufmann, T., Kleih, S. C., Staiger-Sälzer, P., Desideri, L., Hoogerwerf, E.-J., & Mattia, D. (2014). The user-centered design as novel perspective for evaluating the usability of BCI-controlled applications. *Plos one*, *9(12)*, e112392, p. 5.

1.4.1.3 Iterative developmental process of design solutions (P4)

The EU-project TOBI (http://www.tobi-project.org/) aimed at developing BCI applications in accordance with the UCD. The first two prototypes that have been developed and tested in an iterative user-centred cycle (see **table 1**) are introduced in the following section: The P300-ERP Qualilife BCI (P300-QL) for communication and the P300-ERP BCI for creative expression (Brain Painting, BP). The P300-QL BCI combines P300-ERP BCI with a standard commercially distributed AT software (see **figure 5**). The P300 stimulation was superimposed on the AT software (Qualiworld by QualiLife Inc., Paradiso-Lugano, Switzerland) enabling the end-users to enter text, send emails or surf the internet. The prototype development included: (P1, P2, S1) Assessment of end-user's needs and requirements and potential impact of a BCI for communication (Zickler et al., 2009); followed by initial tests and early involvement of users, investigating performance and workload levels in two conditions: visual stimulation overlaid on the application's graphical user interface or presented on a separate screen (Riccio et al., 2011) and modifications; then (P3) usability metrics were defined (Zickler et al., 2011); and then (P4, P5, S3) the first finalized prototype tested with end-users and systematic evaluation (Zickler et al., 2011). Brain Painting (see **figure 6**), a P300-ERP based application for creative expression, was developed including the steps: (P1, P2, S1) Identified need and potential impact of Brain Painting including tests of proof-of-principle and early involvement of users (Kübler et al., 2008; Münßinger et al., 2010; Zickler et al., 2009); (S2, P4) then initial testing by healthy subjects and end-users to assess user requirements (Münßinger et al., 2010); and redesign of the P300-ERP matrix to a black-and-white version and more self-explanatory symbols, as effectiveness and ease of use were not satisfying compared to a spelling matrix (Münßinger et al., 2010; Zickler et al., 2009); (P3) development of evaluation metrics (Zickler et al., 2011); (P4, P5, S3) in next cycle BCI prototype was tested with a larger group of end-users (N=4) and systematically evaluation incorporating the whole user experience (Zickler et al., 2013).

1.4.1.4 Incorporation of the whole user experience (P5)

1.4.1.4.1 P300 BCI for communication

Four severely motor impaired possible end-users tested and evaluated the BCI (Zickler et al., 2011) in four conditions: Copy-spelling, free-spelling, email sending, and Internet surfing task. Accuracy (effectiveness) ranged between 70% and 100% correct responses and for all end-users internet surfing was the most challenging task. Information transfer rates (efficiency) ranged between 4 and 8.6 bits/minute. Subjective workload (efficiency) was moderate in three end-users (15-49 of 100) and very low in one end-user (9-12 of 100). Main sources of workload were mental and temporal demand, while effort was rated low in all tasks. Satisfaction was high for learnability, safety and professional services, but low to moderate for dimensions, comfort, adjustment, ease of use, effectiveness, speed and aesthetic design. End-users indicated the low speed and the too low effectiveness as the main obstacles for using the BCI for communication purposes in daily-life. In addition the long adjustment time and EEG cap/wet electrodes would be problematic in daily-life. Thus none of the end-users could imagine using the BCI in daily-life unless substantially improved (Zickler et al., 2011). For daily-life use, end-users requested especially easier adjustment of EEG-cap and electrodes, improvement of aesthetic design and comfort of the EEG cap and higher functioning of the BCI in terms of accuracy and speed. End-users suggested also an interface that integrated BCI with other input channels (hybrid BCI). Ease of use, such as simple set-up procedure for the software and EEG equipment, was indicated as most important aspect of a BCI device and prerequisite for independent BCI home use.

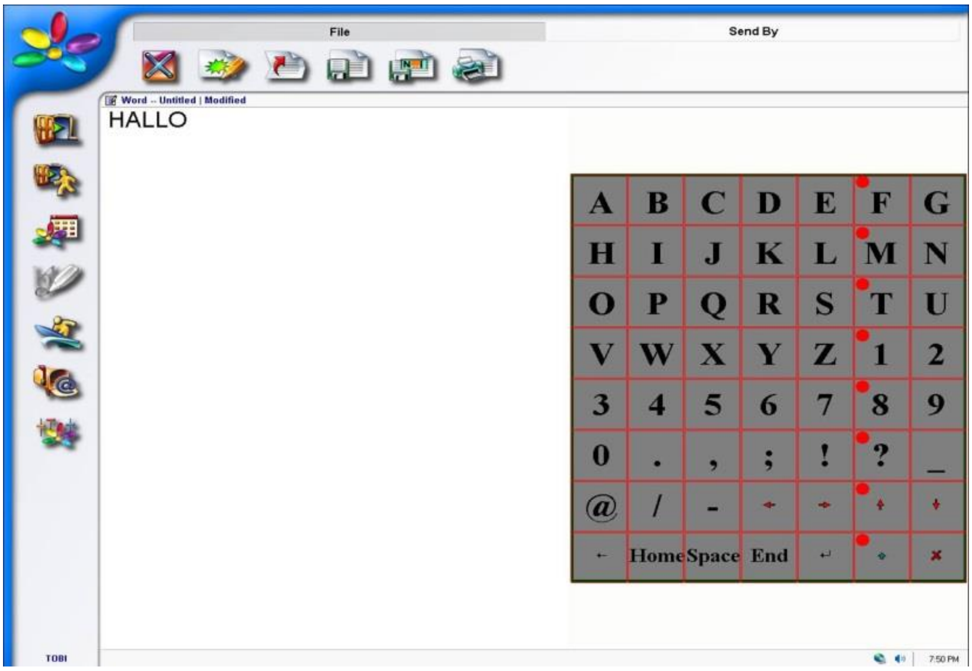


Figure 5: Spelling-matrix in P300-ERP prototype (Zickler et al., 2011).

The text matrix can be opened by selection of the communication program in the GUI (a pen). Then the matrix opens for spelling. Here, the matrix is superimposed with little red dots that appear close to the items. Source: Zickler, C., Riccio, A., Leotta, F., Hillian-Tress, S., Halder, S., Holz, E. M., Staiger-Sälzer, P., Hoogerwerf, E. J., Desideri, L., Mattia, D., & Kübler, A. (2011). A brain-computer interface as input channel for a standard assistive technology software. *Clinical EEG and neuroscience, 42(4)*, 236-244, p. 239.

1.4.1.4.2 Brain Painting

Four end-users tested and evaluated Brain Painting (Zickler et al., 2013). All end-users received high effectiveness, with accuracies above 80% in the copy-spelling, copy-painting and free-painting sessions (mean accuracy equal or higher than 80%). ITR (efficiency) ranged between 4.47 and 6.65 bits/minute in the copy-tasks. Highest ITR in the free painting sessions was 5.22 bits/minute. Subjective workload (efficiency) was low to moderate across all tasks and end-users (21-49 of 100). End-users expressed highest satisfaction for learnability, safety and professional services. They were least satisfied with dimensions, aesthetic design and comfort of the EEG cap (e.g., restricted movement due to cables, BCI hardware too complex), adjustment of the BCI (e.g., time-consuming adjustment of EEG cap) and speed (too slow). Overall satisfaction was thus moderate to high. Two end-users had a good match with the BCI (4.3 and 4.3, of 5). End-users enjoyed painting and indicated that they would like to use Brain Painting in their daily-life, once or twice per week. For daily-life use, end-users recommended less electrodes/gel, no cables, new design of the EEG cap, an easier adjustment of EEG-cap/electrodes, a simpler set-up procedure for the software and improvement in terms of speed. Ease of use was indicated as most important aspect of the BCI device and prerequisite for future use in daily-life.

Figure 6: End-user testing with Brain Painting.

End-user while testing the Brain Painting application in the study of Zickler et al., 2013. On the right PC the P300-ERP matrix including different tools for painting is presented; the left PC serves as “digital canvas”.

1.4.1.5 Refinement and iterative testing and evaluation (P4)

On the basis of these evaluation outcomes, the P300 based communication prototype was redesigned and improved (P4) and consequently tested in a next evaluation cycle by severely motor restricted end-users (*study 2*, present thesis). Brain Painting was further redesigned (P4) and prepared for independent home-use (e.g., simpler and easier to use software) and continuously evaluated in daily-life including further refinement of the BCI (*study 3*, present thesis). A third prototype, a MI controlled BCI application for gaming (Connect-Four) has been developed and tested in a first cycle with prospective end-users (*study 1*, present thesis).

1.4.2 Long-term and independent BCI studies in target population

1.4.2.1 Long-term use in controlled settings

One important research question that needs to be addressed is, whether a BCI can be reliably used over a long time period for several weeks, months or years. Initial results for the P300 based BCI are encouraging. Sellers and Donchin (2006) showed reliable use of a four-choice (Yes, No, Pass, End) P300-ERP BCI, in the visual and auditory mode by three people with ALS over a time period of six weeks (ten sessions; means: 64%, 60%, 50%; Sellers et al., 2012; Sellers & Donchin, 2006). Nijboer and colleagues (2008) tested a visual P300-ERP BCI for communication with eight persons with ALS over a time period of 40 weeks. Mean accuracies for copy-spelling ranged between 62% and 82%, indicating high variance between end-users and between sessions. Kübler and colleagues (2005) trained four severely motor restricted patients with ALS to control a cursor by regulating SMR over 20 sessions within three to seven months. All four patients reached successful control above 70% correct responses (76-81%; chance level: 50%). All end-users improved over time, thus a training effect of time was evident. In a recent study by Rohm and colleagues (2013) an end-user with sustained traumatic spinal cord injury (SCI) underwent extensive training with a hybrid BCI neuroprostheses, combining functional electrical stimulation (FES) and MI, over the time course of one year (Rohm et al., 2013). The end-user had FES training two to three times per week over six months and MI BCI training in 43 sessions over 12 months. The end-user was able to control the hybrid BCI by MI and thereby elicited reactive components in the beta frequency bands (23-26 Hz), with an average accuracy of 70.5%. There was however a high day-to-day variance in BCI performance (50-93%) and in 46% of all training days no reliable discriminative brain patterns could be obtained. Most surprising, when considering performance for the whole 43 sessions, no training effect was evident. In a study by Silvoni and colleagues (2009) 21 persons with ALS tested a four-choice P300-ERP speller, five of them in a follow-up study one year later; also three in three years follow-up (Silvoni et al., 2013). It was found that clinical status did not influence BCI performance and that performance was not deteriorated in the follow-up. In a recent case study by Halder and colleagues (2014) multi-modal (auditory, tactile, visual) P300 BCI testing were conducted with an end-user suffering from intracranial haemorrhage of the cerebellum and brainstem. Albeit gaining control clearly above chance level, performance varied strongly across the four testing days implying that fluctuations of vigilance affect BCI performance considerably (Halder, Käthner, & Kübler, 2014b). Sellers and colleagues (2014) present in a recent study long-term BCI use over a period of 13 months with an individual in the locked-in state after brainstem stroke. A total of 62 sessions were conducted on 34 different days during the 56-week duration of the study. Six different visual P300-ERP BCI paradigms were tested. Among these, the end-user performed best with a 3x6 matrix and a four-choice speller. The averaged accuracy over a 5-week period with the four-choice BCI was 94.7%. Using the 3x6 matrix, average accuracy over 11 successful sessions was 81.5%. The user was able to use the BCI in a free-spelling mode. The BCI thus enabled independent communication for the locked-in end-user, while other means of independent communication failed (e.g., eye-tracking) and other means, such as communication with a letter board, depend on other persons. In 22 of 62 sessions (33%) however the end-user did not gain sufficient control over the BCI (accuracy <70%). Thus performance was not stable, depending on the paradigm and also on the constitution of the end-user (Sellers, Ryan, & Hauser, 2014). **Table 3** gives an overview of long-term BCI studies in controlled settings.

Table 3: Long-term studies in controlled settings.

Study	BCI paradigm	Number of end-users	Time	BCI accuracy (percent correct, %)
Sellers and Donchin (2006)	four-choice P300-ERP BCI (visual & auditory)	n=3	6 weeks (ten sessions)	*M*=64%, 60%, 50%
Nijboer et al. (2008)	visual P300-ERP BCI	n=8	40 weeks	Range: 62-82%
Kübler et al. (2005)	MI BCI	n=4	3-7 months (20 sessions)	Range: 76-81%
Rohm et al. (2013)	Hybrid BCI (MI BCI & FES)	n=1	MI BCI: 12 months, 43 sessions	*M*=70.5%; range: 50% to 93%
Silvoni et al. (2009)	four-choice P300-ERP BCI (visual)	n=21; n=5 in FU	11 days (4 sessions) FU1: 1 year later (2 sessions)	*M*=77.5%; FU:*M* =81.5%
Silvoni et al. (2013; extension of study from 2009)	four-choice P300-ERP BCI (visual)	n=24; FU1: n=9; FU2: n=5; FU2: n=5; FU3: n=3	See Silvoni et al., 2009; FU1: 1 year later, FU2: 2 years later, FU3: 3 years later	*M*=79.2%; FU 1: *M*=77.7%; FU 2: *M*=77.0%; FU 3: *M*=75.9%
Halder et al. (2014)	multi-modal (auditory, tactile, visual) P300-ERP BCI	n=1	4 sessions	Varying performance level, above chance level
Sellers et al. (2014)	6 different visual ERP BCI paradigms	n=1	13 months (62 sessions)	Varying performance level: four-choice: 94.7%; 3x6 matrix: 81.5%. in 22 sessions: accuracy <70%

Note: *M*=Mean accuracy; FU=Follow-up.

1.4.2.2 Long-term independent use

Two individuals with ALS in the locked-in state used the "thought translation device" at home for communication (Birbaumer et al., 1999) and internet browsing (Karim et al., 2006) by regulating SCPs. One individual used the BCI also in expert-independent use (see note of **table 4**). The BCI spelling device was used for several hundred sessions with mean accuracies above 70%. This patient has been trained over a period of 4 years, in which he developed to an expert for his own mental strategies to self-control his SCP (Neumann et al., 2003). However it was many years later that another BCI system was successfully implemented at the home of an end-user for independent use. In this study a P300 BCI has been used independently of BCI experts, but with close oversight, by an end-user with ALS for word processing, writing email, speech generation, environmental control for specific devices, and for his science career for more than 2.5 years (Sellers et al., 2010). Most notably the P300 BCI performance (median: 83%) did not deteriorate over 2.5 years; in line with others (Silvoni et al., 2013; Silvoni et al., 2009). Also the P300 amplitude for target and non-target stimuli remained stable over time (Sellers et al., 2012; Sellers et al., 2010); in accordance with (Nijboer, Sellers, et al., 2008). This is the longest time period that a P300 BCI has been used. Taken together, there exist only few studies on long-term and independent BCI home use, however initial results are promising (see **tables 3 and 4**).

Table 4: Long-term studies in independent use.

Study	**BCI paradigm**	**Number of end-users**	**Time**	**BCI accuracy (percent correct, %)**
Birbaumer et al., 1999, Karim et al., 2006, Neumann et al., 2003	SCP BCI for spelling and internet browsing	n=1*	Up to 4 years	*M* >70%
Sellers et al., 2010	P300-ERP BCI	n=1	2.5 years	*MD*=83%

Note: *This end-user used the BCI independently from BCI experts with the support by his family and caregivers; expert-independent daily-life use is however not directly documented in these publications; information from Prof. Dr. Andrea Kübler, who was working with this end-user for many years; *M*=Mean accuracy; *MD*=Median accuracy.

1.4.3 User-centred improvements of BCI applications

As stated above, functionality, easiness of use and independent use were indicated by AT users as most important for use of a new AT, such as BCI. Much effort has been made to improve and address these aspects.

1.4.3.1 Functionality

Different approaches have been developed to improve functioning of a BCI in terms of accuracy, reliability and speed.

1.4.3.1.1 Stimulus mode and signal processing

A recent approach for improving classification accuracy in a P300-ERP BCI is to optimize the properties of the stimulus in the spelling matrix. By improving the stimulus, signal to noise ratio in the EEG can be improved and thereby spelling bitrate. It has been shown by Tangermann and colleagues (2011) that the percentage of correct selected items of an ERP speller can be increased using a mask overlay in form of a grid. Grids overlay items in the matrix, instead of highlighting (Schreuder et al., 2013; Tangermann et al., 2011). Grid overlays proved to improve accuracy in healthy subjects as they elicit stronger cortical responses (Tangermann et al., 2011). This optimized visual stimulation seems to improve accuracy also in the target group, as shown in a first case study with an end-user with brain stem stroke. By eliciting multiple discriminative components, such as P100, N200, P200 and P300 of the ERP, the end-user achieved almost perfect control with an accuracy of 100% in four of five sessions (Schreuder et al., 2013). However stimulation with grids was not compared to other visual ERP speller and only one end-user was tested, which limit generalization of results.

Another very promising implementation for optimizing the stimulus that is used for eliciting ERPs has been made recently (Kaufmann, Schulz, et al., 2011). Kaufmann and colleagues (2011 and 2013) implemented pictures of famous faces into the classical row-column ERP speller (see **figure 7**). By flashing with faces, not only a P300 signal is elicited, but also face specific components, such as the N170 (negative component around 130 and 200ms) and the N400 (negative component between 300 and 500ms). Multiple evoke signals improve the signal to noise ratio, thereby class discrimination and spelling bitrate. In the famous face condition a significant less number of sequences was needed to reach 100% accuracy as compared to the classic flashing paradigm. Furthermore two-third of all participants achieved a performance level of 70% already after the first stimulus sequence when using a face paradigm as compared to the classical character flashing. The presentation of flashing faces transparently superimposed on characters in the spelling matrix significantly decreased the number of sequences required and thus improved the spelling bitrate impressively (Kaufmann, Schulz, et al., 2011). Most importantly this effect was also evident in the target group (Kaufmann, Schulz, et al., 2013). End-users with neurodegenerative disease performed worse in the classical spelling paradigm compared to healthy controls; this difference however vanished, when using face stimuli. With only one flashing sequence end-users had an average accuracy of 11.4% in the classical speller, however above 77% in the new face speller. Results imply that the face speller can effectively help patients with severe motor impairment to overcome BCI inefficiency. Interestingly, in end-users, face stimuli not only evoked face specific components (e.g., N170 and N400), but additionally increased the P300 amplitudes significantly, as compared to the classical paradigm. In sum, the presentation of flashing faces transparently superimposed on characters in the spelling matrix significantly decreased the number of sequences required as compared to simple highlighting of the characters. Further optimized visual stimulation modes were developed for the visual P300-ERP speller, such as the hex-o-spell (Blankertz et al., 2011; Treder & Blankertz, 2010), checkerboard (Townsend et al., 2010) and colored checkerboard and other chromatic flashing patterns (Takano, Komatsu, Hata, Nakajima, & Kansaku, 2009). Recent approaches, have been proven to improve effectiveness and efficiency in auditory BCIs, such as combining pitch and spatial information (Schreuder et al., 2010); also in combination with a predictive text entry system (Höhne et al., 2011). More recently it was shown that training positively affects BCI performance in an auditory BCI (Halder et al., 2013). And also new implementations, such as dynamic stopping, improve speed in the visual (Kindermans, Tangermann, Müller, & Schrauwen, 2014), auditory (Schreuder et al., 2011) and tactile (Kaufmann et al., 2014) BCI impressively. Improvements on signal processing and the development of novel classification techniques in ERP BCIs (Krusienski et al., 2006) and machine learning approaches in MI BCIs (Vidaurre, Sannelli, Müller, & Blankertz, 2010) improve accuracy and efficiency.

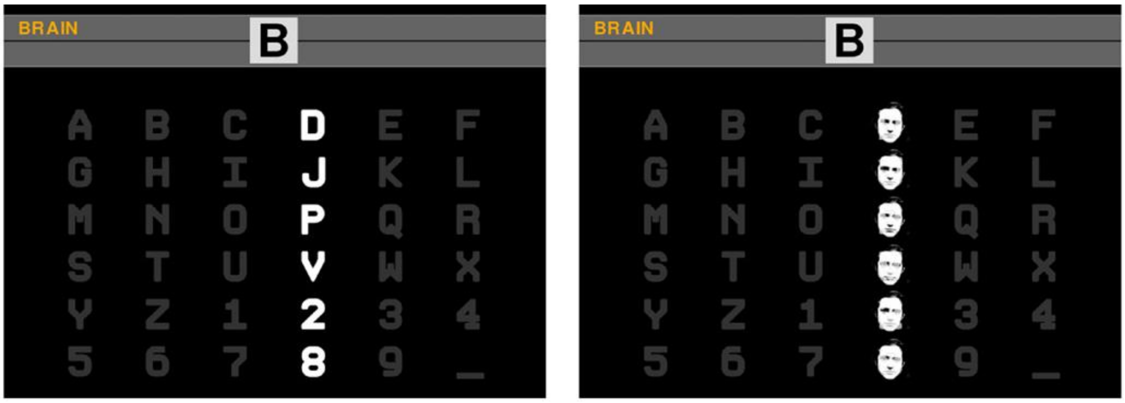


Figure 7: P300-ERP spelling matrix.

Left: Classical P300 speller (BCI-2000 based). The person is instructed to spell the word “BRAIN”. While flashing in rows and columns, the subject is instructed to focus attention to the letter „B“. Every time a row or column, containing the letter „B“, is flashing, a P300 is elicited, which can be registered by the classifier. Right: Face speller (BCI-2000 based): Items are not highlighted within a flashing sequence, but the letters are overlaid by rows and columns of face stimuli. This elicits not only a P300 signal, but also face recognition components, the N175 and N400. These components are recognized by the classifier. Source: Kaufmann, T., Schulz, S. M., Grünzinger, C., & Kübler, A. (2011). Flashing characters with famous faces improves ERP-based brain-computer interface performance. *Journal of neural engineering, 8(5)*, 056016. doi: 10.1088/1741-2560/8/5/056016, p. 4.

1.4.3.1.2 Hybrid approach

Recently a hybrid approach is of interest of the BCI community (for a review see Millan et al., 2010; Pfurtscheller et al., 2010). A hybrid BCI is a combination of different signals with at least one BCI input channel. The rationale behind such hybrid approaches is to increase effectiveness and efficiency of a BCI. A hybrid BCI can consist of (at least) two types of brain signals, for instance two EEG signals (e.g., P300 signal and SMR signal; Höhne et al., 2014) or exploit different electrophysiological and imaging techniques, such as EEG and MEG, fMRI, NIRS, for a review see (Millan et al., 2010). Also a combination of EEG and other biosignals, such as electromyographic (EMG) activity or BCI and other AT devices is possible (Millan et al., 2010). For example, combining signals from the brain (e.g., P300 and SMR activity) should improve classification and therefore effectiveness of a BCI. Hybrid BCIs are considered significant for end-users, because they enable higher flexibility by using any signal that can be reliably classified and BCI can therefore be adapted to the user’s individual brain responses (Höhne et al., 2014). Moreover, a hybrid BCI, that combines activity from the brain (e.g., EEG signals) and other AT input devices, such as a joystick, as input, could enable severely disabled end-users to switch between input signals depending on their physical state or preference and/or performance. For example a patient with muscular dystrophy may use a joystick as input for his/her PC in the morning, but could use brain activity as input in the evening when muscle activity is reduced or unreliable due to fatigue. Another advantage could be that persons with progressive diseases can be enrolled in early training by controlling their current AT with existing muscular control, but also with the BCI, before entering the completely locked-in state, in which cognitive capacity is deteriorated and learning of a new (BCI) device challenged (Millan et al., 2010). A few examples of hybrid BCIs already exist: Some combined two EEG brain signals, such as SSVEPs with SMR (Allison et al., 2012; Brunner et al., 2010); others brain signals and biosignals, such as a SSVEP controlled prosthetic combined with an on/off switch controlled by heart rate variation (R. Scherer, Müller-Putz, & Pfurtscheller, 2007); or EMG with EEG activity recorded parallel while performing movements (Leeb, Sagha, Chavarriaga, & Millan, 2011); or EMG and P300-ERP signal (Riccio et al., 2015); EEG signals and eye gaze (Danoczy, Fazli, Grozea, Müller, & Popescu, 2008), or residual muscular activity and SMR (Rohm et al., 2013).

Despite a considerable number of studies, by now, most hybrid BCIs were in tested in healthy subjects only few studies include end-users. Those including end-users exploit residual muscular activity of end-users as second input for the hybrid device (Perdikis et al., 2014; Riccio et al., 2015; Rohm et al., 2013). A non-invasive hybrid FES neuroprosthesis for restoration of hand and elbow function was developed by Rohm and colleagues (2013) and tested by one tetraplegic end-user with SCI, as described above. The hybrid BCI neuroprosthesis consisted of three components, FES, an analog shoulder joystick and MI BCI. The FES activated the passive structures of the muscles leading to hand opening or closing by stimulating the corresponding muscles; the shoulder joystick could control the degree of stimulation of the specific muscles (elbow flexion and extension); and the routing of the shoulder sensor (i.e, elbow or the hand or access to a pause state) was itself controlled by the MI BCI (a short detection of MI switched from hand to elbow control or vice versa; a longer detection lead to a pause state with muscle stimulation turned off and elbow joint of the orthosis locked). The end-user succeeded in performing different functional tasks (hand function test and tasks of daily-living), with an average performance in MI BCI of 70.5%, after extensive training over one year, for both, training of MI and FES. The end-user indicated that he experienced only moderate subjective workload and he was on overall highly satisfied with the hybrid BCI device. Riccio and colleagues (2015) tested a hybrid P300 based BCI for spelling in eight healthy and three severely motor impaired subjects in a pilot study (Riccio et al., 2015). Participants spelled words in a copy-spelling task with a P300-ERP BCI and in two conditions: users had to correct wrongly selected letters either with the BCI or with an additional EMG-channel placed on the hand (undo function). Results revealed that, the hybrid approach improved effectiveness (accuracy) and efficiency (total time and ITR) of the BCI in both, healthy participants and end-users. A hybrid BCI, combining MI and

EMG input for controlling a binary text speller, called BrainTree, was tested by six severely disabled end-users and ten healthy users in a study by Perdikis and colleagues (2014). The binary speller enabled input by using only two commands (i.e., 2-class MI), while the EMG channel allowed the user to return to the previous caret position. Both, healthy and end-users, were able to perform with high accuracy in copy-spelling tasks and accuracy and efficiency could be improved by the possibility of error deletion with the additional EMG channel. However it should be noted that subjects were pre-selected; out of 24 end-users, who underwent a MI pre training phase, only 50-70% reached the required inclusion criterion of 70% command accuracy and were considered in this study (Perdikis et al., 2014). These results are encouraging however show that more studies on hybrid BCIs are needed to investigate the usability and perceived usefulness of a hybrid BCI for the target group. Even though end-users with residual muscle activity can operate a hybrid BCI reliably, it is questionable whether these potential end-users would adopt a hybrid BCI for daily-life use.

1.4.3.1.3 User-centred BCI, -protocol and -training

BCI development demands for investigation of restrictions in end-users and for adaptation of BCIs according to the end-users specifics, for instance loss of ocular control or artifact contamination. For example a BCI can accommodate for such visual impairment, by switching to auditory or tactile modalities. Kaufmann and colleagues (2013) aimed to develop an individually tailored BCI solution for communication for a locked-in end-user with brainstem stroke, who had no means for independent communication. Based on a user-centred approach, different stimulus modalities (visual, auditory and tactile) and different settings for each modality (e.g., system timing, gaze requirement) for a P300-ERP BCI have been tested within several sessions over two weeks (Kaufmann, Holz, et al., 2013). It was found, that contrary to healthy subjects, in which visual modality is mostly superior before auditory and tactile modality, in this case the tactile modality was superior. It was probably the case because the end-user had difficulties to fixate, even though eye-movements were reliable. It clearly shows that results achieved with healthy subjects cannot necessarily transferred to locked-in patients. Authors further question the gaze-independence of current gaze-independent approaches. BCIs that yield lower results in healthy users may be the only possible but good solution for a particular end-user with motor impairment or in the locked-in state. Results emphasize the need for user-centred design in BCI development including a flexible BCI system for identification and adaptation of the best stimulus modality for a particular user when aiming at bringing BCIs to end-users; those have to be included in the developmental process for which the user-centred design provides such a framework (Kaufmann, Holz, et al., 2013). Also the results of the study by Sellers and colleagues (2014), as described above, point to the need for user-centred adaptation of a BCI according to the users' needs. Here six different visual matrices in a P300-ERP BCI were tested in a locked-in end-user. The end-user received a mean accuracy of 32.3% with a 6×6 matrix of the speller, but 94.7% with a four-choice speller, thus indicating that matrix configuration matters (Sellers et al., 2014). Halder and colleagues (2013) showed that training over five sessions leads to a substantial improvement in spelling accuracy in an auditory P300 BCI based on natural stimuli and spatial cues in a sample of healthy participants and in a target group (Halder et al., 2013). Other studies exist that aim to adapt the BCI according to the user's individual specifics including a systematic user-centred training protocol (e.g., Friedrich, Neuper, & Scherer, 2013). However by now, they are mostly applied to healthy participants.

1.4.3.2 Easiness of use

BCIs are usually complex systems that require scientific personnel for handling. Therefore to optimize ease of use, a so called optimized communication interface (OKI) which allows for auto-calibration and word completion on the basis of a user-friendly graphical interface has been developed (Kaufmann, Volker, et al., 2012). After set-up of the EEG cap and amplifier, the user can calibrate a P300-ERP speller with only one click. No training by BCI experts is required. Data are automatically analyzed in background and the result of the calibration procedure is fed back to the user. The system can then be used for spelling with again one click. OKI has been tested by 19 healthy subjects. They handled the BCI software completely on their own and reported that it was easy to use. The text completion improved spelling speed. Other features were developed, such as the dynamic stopping (Kindermans et al., 2014) or co-adaptive calibration, that require no calibration and reduce set-up time (Vidaurre, Sannelli, Müller, & Blankertz, 2011).

1.4.3.3 Independent use

To bridge the reliability gap, BCIs need to be implemented at the patient's home for independent long-term use. As stated above studies on independent BCI home use are very few (see **1.4.2.2 Long-term independent use**) and more studies are needed to shed light on what is further needed to establish a BCI in daily-life of an end-user. According to Vaughan and colleagues (2012) translational research that aims to establish a BCI at the end-user's home needs to answer four questions: (1) Can the BCI be implemented in a form suitable for long-term home use? (2) Who are the individuals who need and can they use it?; (3) Can their home environments support their use of the BCI, and do they actually use it?; (4) Does the BCI improve their lives?" (Vaughan et al., 2012, p. 325). BCI systems that are currently used for research purposes need to be adapted for independent use, with regard to hardware set-up and software handling. Sellers and colleagues (2010) stated necessities of BCI for independent home use: BCIs need to (1) be easy to use to be handled by non-technical personnel; (2) provide basic communication capacities in a convenient and accessible format; (3) be configurable for the needs of each user; and (4) enable periodic long-distance technical oversight (Sellers et al., 2010). They developed a system that (1) can be easily handled by caregivers after a one hour training; includes only 8 EEG channels; can be easily calibrated with only one click; (2) includes a wide range of basic communication functions, (e.g., email) and environmental control (e.g., TV) and is accessible using a simple matrix-based menu formant; (3) can be adapted to the user's need; for instance matrix size, shape and content can be changed; (4) needs very little onsite technical support, and is monitored remotely by BCI experts, thus if problems with software occur, it can be solved by BCI experts. If hardware fails, it can be replaced and send via mail. All these features seem to be important for moving a BCI system from the laboratory to the end-user's home.

One of the major questions is how to find suitable subjects for independent use. Who are the individuals who are in need of a BCI and can they use it? Vaughan and colleagues (2012) defined prerequisites/inclusion criteria for identifying candidates for prospective BCI home use; as follows: (1) Persons with little or no useful voluntary muscle control (e.g., people with late stage-ALS, MD, brainstem stroke, high-level SCI); (2) conventional assistive (i.e., muscle-based) communication devices (e.g., eye-gaze systems, EMG switches) are not adequate for their needs: they may be unable to use these devices; their control may be inconsistent or they may fatigue quickly; they may not like the devices; or they may desire the additional communication and control capabilities that a BCI could provide; (3) persons should be medically stable, with the intent, and reasonable expectation, of living for at least one year; (4) persons should be able to follow spoken or written directions; (5) absence of any other impairment (e.g., extremely poor vision in case of visual stimuli); (6) stable living environments; (7) reliable caregivers, capable of acquiring basic computer skills and supporting the subject's BCI usage; (8) subject and caregivers are able and willing to provide informed consent (Vaughan et al., 2012; p. 327). Kübler and colleagues (2015) suggested a decision algorithm for identifying BCI candidates for translational and longitudinal studies. It gives orientation and helps BCI researches, who have no or only few experience with end-users, to conduct translational studies (Kübler, Holz, Sellers, & Vaughan, 2015). The decision tree is based on the inclusion criteria proposed by Vaughan and colleagues (2012), as described above, and includes also BCI related questions, that may arise when offering a BCI to an end-user, for instance: Are cognitive abilities intact without restrictions? What kind of BCI (invasive/non-invasive)? Which stimulus mode (visual, auditory, tactile)? What signal type (ERP, SSVEP, SMR, etc.)? It is important to note that the stated inclusion criteria and the decision tree should enable to select the most suitable BCI for translational studies, especially for researchers that have little or no experience with end-users. They should enable orientation for conducting translational studies. It does however not mean that end-users, that do not match these criteria, should be excluded. The authors explicitly state, that the decision tree excluded end-users for technical issues (i.e., if there are conditions in the home that preclude good signals or if there is no available caregiver) and that exclusion criteria will be modified in the future with progress in research; for example, better EEG recording may become more tolerant toward electrical noise, and thus, an electrically noisy environment would no longer constitute an exclusion criterion (Kübler et al., 2015). Also, it may be that cognitive abilities advantageous for BCI operation are identified.

1.5 Aim of thesis

The described translational studies are very valuable; however they are not sufficient to bridge the gaps in BCI research and more studies are needed. Moreover there exist only few studies that demonstrate long-term independent use of a BCI; even though they show good functioning and ease of use of the BCI in daily-life, none of these studies documented face valid measures of daily-life use; neither evaluated usability in a standardized way; and neither investigated the impact of a BCI on the end-user's quality of life quantitatively. Accordingly, the aims of the present thesis were: Firstly to systematically evaluate the usability and usefulness of two BCI controlled applications in controlled settings on the basis of the UCD following the evaluation metrics, as proposed by Kübler and colleagues (*studies 1* and *2*); and secondly to prepare a BCI device for independent use and implement it at the end-users' homes for daily-life use; evaluate the usability of the BCI in independent daily-life usage; thirdly to document face valid measures of daily-life use and fourthly to quantify the influence of the BCI on the end-users' quality of life (*study 3*).

2. Studies

2.1 Study 1: Brain-computer interface controlled gaming: Evaluation of usability by severely motor restricted end-users

2.1.1 Introduction

The current study aimed at evaluating the usability of a new MI BCI controlled gaming prototype, called Connect-Four. The BCI prototype was developed within the EU-project TOBI (http://www.tobi-project.org/) by partners of TU Berlin and was designed in the way that it can be driven by different EEG features and their combinations, enabling user-centred adaptation by individual selection of brain signals. Because a combination of signals could be used, this system can be called “hybrid BCI”. Connect-Four has only been tested in a pre-study by TU Berlin with healthy participants (unpublished data), therefore this study includes first end-user testing (early phase/cycle in the UCD process of BCI development). Four possible BCI end-users with severe motor impairment due to neurological diseases (stroke and CP) were trained to elicit changes in the EEG by MI for controlling the MI BCI gaming application and to evaluate usability of the BCI. According to the UCD and defined metrics for BCI, Connect-Four was evaluated in terms of its effectiveness, efficiency and end-users’ satisfaction following a user-centred approach proposed by Kübler and colleagues (Holz et al., 2012; Kübler, Mattia, et al., 2013; Zickler et al., 2011). Connect-Four is the first MI controlled BCI application that is tested in the UCD of BCI development.

2.1.2 Methods

The BCI prototype was tested in a collaboration study with TU Berlin (Johannes Höhne and Michael Tangermann) in the Beratungsstelle für Unterstützte Kommunikation (BUK, Information Center for Supported Technology), Bad Kreuznach, Germany. Patients were recruited by Pit Staiger-Sälzer, head of the BUK. Testing took place in rooms of the BUK.

2.1.2.1 Description of end-users

Four severely motor impaired end-users (all male, age 47, 48, 45 and 45) were enrolled in this study. End-users were diagnosed with different neurological diseases causing hemi- or tetraplegia. End-users C and D were not able to speak, had no reliable eye-movement and an estimated communication transfer rate below 5 bits/min with their conventional assistive devices. According to Kübler and Birbaumer (2008) this thesis refers to these end-users as locked-in (Kübler & Birbaumer, 2008). End-users A and B were less impaired. Both were diagnosed with brain injuries and were still able to use a conventional PC keyboard for communication or a joystick to drive a wheelchair. End-user B was unable to speak and end-user A could speak with a voice amplifier (see **table 5** for detailed information about end-users). End-users C and D communicated with a letter board (see **figure 8**) or individual code (eye-movements or button press for yes/no or counting). End-user B indicated his answers with his finger (writing with his finger in the air). His mother who accompanied him to all testing helped in translating his gestures. End-users C and D gave only few comments since communication was exhausting for them.

Table 5: Demographic and disease related data of the end-users (Connect-Four).

	End-user A	**End-user B**	**End-user C**	**End-user D**
Age	47	48	45	45
Diagnosis	Tetraparesis after pontine infarct	Hemiplegia after cerebral bleeding (brain stem aneurysm)	Infantile cerebral palsy	Tetraparesis after cerebral bleeding in basal ganglia (right fronto-temporal lesion)
Artificial ventilation	No	No	No	No
Artificial nutrition (PEG)	No	No	No	Yes
Wheelchair	Yes	Yes	Yes	Yes
Residual muscular control	Eyes, speech, both arms and hands	Eyes, left arm and hand, head, Mimic	Eyes (unreliable), mimic, hand/arm	Eyes (unreliable), mimic, one finger of left hand (depending on daily constitution)
Computer input device	Keyboard PC	Keyboard PC	Switch with arm	Button by finger press (yes/no)
Use of ICT on a daily basis	Yes	Yes	Yes	Yes
Experience with AT ICT since	2006	1982	1986	1998
Estimated ITR with AT ICT	>30 bits/min	>30 bits/min	1-5 bits/min	0-2 bits/min
Previous BCI-experience	P300-ERP BCI (2010)	-	MI BCI (2000)	P300-ERP BCI (2005)

Note: PEG=percutaneous endoscopic gastrostomy, ICT= information and communication technology.

Figure 8: Letter board used for communication and evaluation purposes.

View-through letter board can be used with letters or numbers (in this picture). The end-user fixates the intended letter or number and the other person spells out the item that he or she thinks that it is the intended. If the item was incorrect, the user can give a command (e.g., looking to the right or down if the selection was not the intended one).

2.1.2.2 Study protocol

The protocol comprised 9 sessions: In session 1, information about the study was provided and participants or their legal representatives signed informed consent. In session 2, demographic and disease related information, depression and quality of life were assessed. In sessions 3 to 8, end-users underwent BCI training. The training consisted of 6 sessions. In the first BCI session (session 3) the end-user was screened to define the best discriminating motor imagery (MI) classes (screening session). The following 5 BCI sessions (sessions 4 to 8) started with MI-training (copy-task), followed by free-mode playing (in sessions 5 to 8). BCI prototype was evaluated by end-users in sessions 3 to 9 (for evaluation see **2.1.2.8 Evaluation**). End-users were paid for participation (8 Euros/hour). The study protocol was approved by the Ethical Review Board of the Medical Faculty, University of Tübingen.

2.1.2.3 Depression, quality of life and motivation

As previously shown that motivation can influence BCI performance and learning (Kleih et al., 2010; Nijboer et al., 2010; Nijboer, Furdea, et al., 2008), motivation was assessed to control for such moderating variables. Motivation was assessed with a visual analogue scale (VAS motivation; ranging from 0 to 10 with 0 indicating “not motivated at all” and 10 “very motivated”). Albeit depression was not correlated with BCI performance (Hammer et al., 2012; Hammer et al., 2014), the ability to concentrate was found to be correlated (Hammer et al., 2014). Thus because depression influence attention, concentration and memory (Hautzinger, 2005), the emotional status should be assessed prior to BCI training. The possible prevalence of depression was assessed with the German version of the Center for Epidemiological Studies Depression scale (CED-scale; Hautzinger & Bailer, 1993; Radloff, 1977). A score of 23 and above indicates prevalent depression. Quality of life was explored using the Schedule for the Evaluation of Individual Quality of Life (SeiQol; O'Boyle et al., 1993), and the Anamnestic Comparative Self-Assessment scale for measuring the subjective quality of life (ACSA; Bernheim & Buyse, 1984). The SeiQol is a measure of individual quality of life and requires the users to indicate the five most important domains determining their quality of life and the relative importance of these domains. Next, users have to indicate how satisfied they are with each domain. The weighted satisfaction for each domain provides the final SeiQol score (ranging between 0 and 100, with 100 indicating the highest possible quality of life). The ACSA scale is a general and simplified measure for individual quality of life. Users are required to imagine their best and worst time in life. On a scale from -5 to 5 (with -5 representing the worst and 5 the best time in life) users have to indicate their current quality of life.. Depression and quality of life were assessed once at the beginning of the study (session 1) and motivation before every BCI session.

2.1.2.4 MI controlled BCI game: Connect-Four

Connect-Four is a strategic game with two competitive players. Coins have to be placed in rows and columns with the goal to connect four coins before the opponent can do so; the first successful player wins the game. In this 2-class MI BCI game, the end-user could select a row by moving the cursor through brain activity from left to right or right to left (depending on the MI class, e.g., by left hand or right hand MI) and place a coin by moving the cursor downward (e.g., by feet MI). **Figure 9** depicts the 2-class MI game in copy-mode (see **2.1.2.7 Online tasks**).

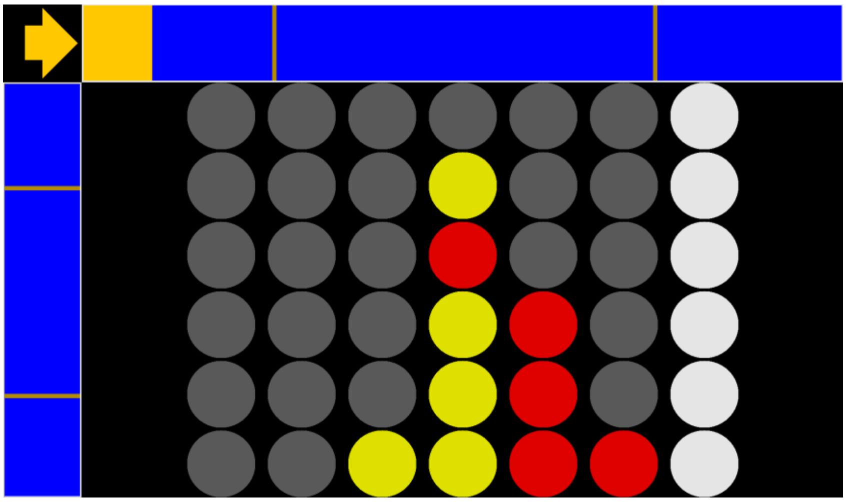


Figure 9: MI BCI Connect-Four (copy-mode).

A cue (arrow) indicates in which direction the cursor has to be moved (e.g., to the right or downward; source: Holz, E. M., Höhne, J., Staiger-Sälzer, P., Tangermann, M., & Kübler, A. (2013). Brain-computer interface controlled gaming: Evaluation of usability by severely motor restricted end-users. *Artificial intelligence in medicine, 59(2)*, 111-120., p.113).

2.1.2.5 Signal acquisition

Since this study was a collaboration study between TU Berlin and University of Würzburg, and because this study focuses on usability testing and evaluation thereof, detailed description of feature extraction, BCI input signals and operation are part of the study by Johannes Höhne (TU Berlin); this part of the study is published in (Höhne et al., 2014). For more details see also (Blankertz et al., 2011; Vidaurre et al., 2010). In the screening session (session 3), EEG was recorded with a 64-channel passive gel based EEG-cap (easyCap, BrainProducts, Munich, Germany) and amplified with a Brain Vision amplifier (2x32 channels, BrainProducts, Munich, Germany). Sampling rate was 1000 Hz. Most electrodes were placed in motor-relevant areas. EOG was recorded from right eye (electrode placed below eye), see **figure 10**. In the copy- and free-mode task EEG was recorded from 16 electrode positions with a passive EEG-cap (easyCap, BrainProducts, Munich), and amplified with a 16-channel passive g.USB-amp (g.tec Medical Engineering GmbH, Austria). Sampling rate was 1200 Hz. EEG electrodes were mostly placed in areas of the motor cortex. If possible, impedances were kept below 10kΩ.

2.1.2.6 Screening and training of individual classifier

End-users were instructed to imagine three classes of motor movement: right hand, left hand and feet. The screening determined the best discriminating classes. No BCI feedback was provided.

Figure 10: Screening session for MI BCI (Connect-Four).

EEG was recorded with a 64-channel passive EEG-cap. No BCI feedback was provided. End-users had to imagine three classes of movements: right hand, left hand and feet.

The Berlin-BCI system based on Matlab (The MathWorks, MA, USA) was used for feature extraction and classification. For feature extraction, oscillatory signals (alpha, beta, delta ERS/ERD or beta rebound) and slower potentials were extracted. EEG activity was classified with a linear discriminant analysis with shrinkage regularization (Blankertz et al., 2011; Blankertz, Tomioka, Lemm , Kawanabe , & Müller, 2008). All input signals were analyzed and brain activity (or a combination), that discriminated best between two classes, was used for training the classifier and controlling the Connect-Four application. Thus the BCI application could be controlled by oscillatory features (i.e., event-related desynchronization (ERD)/ synchronization (ERS)) in the alpha (7-13 Hz) or beta (13-30 Hz) band, beta rebound or slow movement-related potentials (i.e., lateralized readiness potential, LRP) or a combination of different features. Features were individually selected. EEG data was continuously reanalyzed after every session with the aim to find better discriminative signals after several training sessions.

Therefore selected features varied across end-users, and could also differ between sessions within one end-user ("session to session transfer"). The following individual input signals were selected for online sessions (see **table 6**): In end-user A LRP and beta rebound for left hand vs. right hand imagery was used in session 6 and all following sessions. For end-user B either beta ERD or beta ERD and LRP classifier for left hand vs. foot imagery was used. In end-user D alpha band activity in session 4 (first online session), then beta ERD for right hand and foot imagery, was selected. In end-user C no reliable feature with discriminative information could be found; nevertheless beta and LRP or only LRP were considered for training in online sessions.

Table 6: Individual input signals.

End-user	**End-user A**	**End-user B**	**End-user C**	**End-user D**
Input signals	LRP & beta rebound	Beta ERD or beta ERD & LRP classifier	Beta and LRP or only LRP (for training)	Alpha band, beta ERD
MI	Left vs. right hand	Left hand vs. foot	Right and left hand vs. right foot	Right hand vs. foot

Note: MI=motor imagery.

Results of an offline analysis of the copy-task by Höhne et al. (2014) are depicted in **figure 11**. It was investigated within offline analysis whether signal features were stable across sessions. As can be seen in the figure, discriminative features were found in all, but patient 3 (corresponds to end-user C), consistently across all sessions. Offline accuracies cannot be directly translated into online BCI accuracy reported within results section, because offline accuracy was obtained using a cross-validation procedure for each session separately. In online study, all features, trained classifier and accuracy were based on data of all sessions. Therefore the resulting online performance can be lower, if individual features changed between sessions, and could be higher if features were stable across sessions (as the online classifier was trained on the basis of more EEG data from previous sessions). These findings support the necessity of an individual and flexible BCI system, as used in this study. For details on feature extraction and individual input signals, see (Höhne et al., 2014).

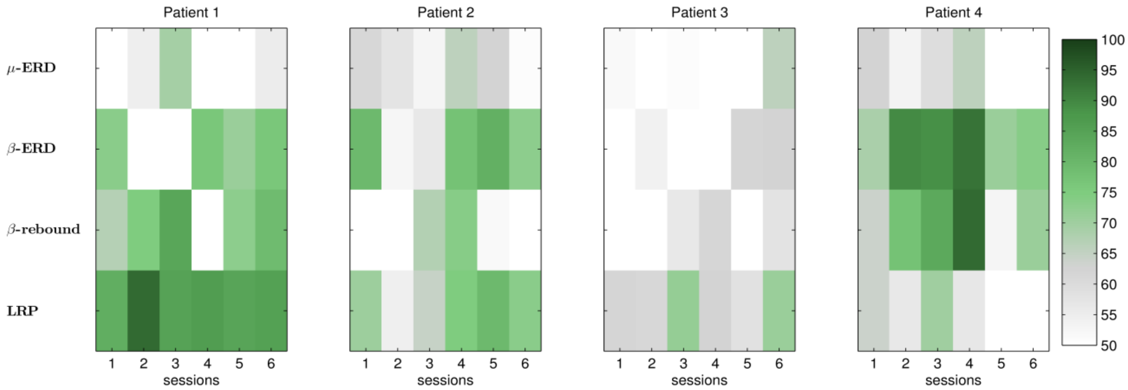


Figure 11: Discriminative power of each signal feature across sessions.

Results of analysis of brain signals. Data is obtained with offline reanalysis of the copy-task data. Note that patient 1 corresponds to end-user A in this study, patient 2 to end-user B, patient 3 to end-user C and patient 4 to end-user D, respectively. Session 1 corresponds to session 3 in this study, session 2 to session 4, and so on. White to green fields indicates accuracy as predicted by the offline analysis. Classification accuracy was then estimated with cross validation using the same parameters for each session. Source: Höhne, J., Holz, E. M., Staiger-Sälzer, P., Müller, K.-R., Kübler, K., & Tangermann, M. (2014). Motor imagery for severely motor-impaired patients: evidence for brain-computer interfacing as superior control solution. *Plos one*, *9*(6), e98322, p. 6.

2.1.2.7 Online tasks

2.1.2.7.1 Copy-task

Individual classifier and MI classes were used in the following 5 online sessions: During these sessions, end-users received online feedback (copy-task mode) of the individual features. Every session started with a copy-task consisting of 4 to 8 runs, depending on end-user's characteristics (e.g., exhaustion). The number of trials within each run varied between 20 and 40 trials (with a trial length of 4 to 7s and an inter-trial pause of 6 to 9s). Following a user-centred design including high customized and flexible BCI operation, the exact trial length and inter-trial pause was set individually according to the user needs and depending on the BCI input-signal. MI classes were individually chosen and differed between end-users.

2.1.2.7.2 Free-mode task

The copy-task was followed by the free-mode. In the free-mode, end-users decided how many times they liked to play the game "Connect-Four", which varied from 1 to 3, depending on individual factors (e.g., physical constitution or time). To reduce non-intended actions in the free-mode, an action (place coin or select column) was performed only if a predefined threshold was exceeded by the BCI signal. Therefore, in the free-mode there could be correct, incorrect and no-decision trials. The differences between copy-task and free-mode task were firstly, that the users had to decide which action they would like to execute, and to indicate to the experimenter whether it was intended. Secondly, in the free-mode no-decision trials were possible. Thirdly, there was no predefined number of runs, but times to play the game (1-3). The free-mode session started earliest in session 5. Contrary to the copy-mode, in which a cue indicated the required action, in the free-mode a question mark indicated the beginning of the trial. After appearance of the question mark, the end-user could operate the MI task for the intended action. In the free-mode, end-users could choose whether they liked to play against one of the experimenters or against the computer. **Figure 12** depicts end-user B in a Connect-Four free-mode session.

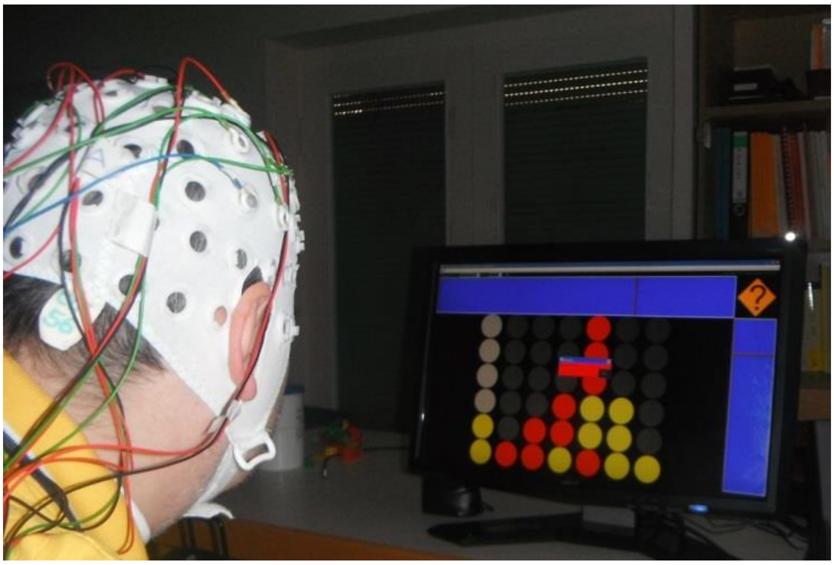


Figure 12: End-user during the free-mode.

Here, the cue (question mark) indicates the beginning of a trial. Upon occurrence of the cue the end-user (here: end-user B) has to start with the MI to move the cursor in the intended direction (place a coin or select next column). Source: Holz, E. M., Höhne, J., Staiger-Sälzer, P., Tangermann, M., & Kübler, A. (2013). Brain-computer interface controlled gaming: Evaluation of usability by severely motor restricted end-users. *Artificial intelligence in medicine, 59(2)*, 111-120, p.114.

2.1.2.8 Evaluation

Following the definition by Kübler and colleagues (Kübler et al., 2014; Zickler et al., 2011) for evaluation of BCI-controlled applications usability of MI controlled Connect-Four was evaluated in terms of its effectiveness, efficiency and satisfaction; for details see chapter **1.4.1.2 Valid evaluation metrics (P3)**.

2.1.2.8.1 Usability

2.1.2.8.1.1 Effectiveness

Accuracy was calculated by dividing the number of correct selections by the number of total selections, resulting in a percent value ranging from 0 to 100%. With binary choice, such as moving cursor downward versus right, there are only correct or incorrect trials; therefore, chance level was $p = .50$. To reduce non-intended actions in the free-mode, an action (e.g., place coin or select column) was performed only if a predefined threshold was exceeded by the BCI input signal. Therefore, trials were either correct, meaning that the intended cursor direction was achieved, or incorrect, if intended cursor direction was not achieved, but also no-decision trials, when the cursor was not moved, due to insufficient signal. Since the game is not affected by those no-decision trials, those were treated equally to pause-intervals (see ITR section below). The accuracy was calculated as the ratio of correct to correct and incorrect trials (*P*=Ncorrect/(Ncorrect+Nincorrect)).

2.1.2.8.1.2 Efficiency

Efficiency was defined as information transfer rate and user's subjective workload. Subjective workload was assessed using the NASA-TLX (Hart & Staveland, 1988). Bitrate (bits/trial, B), was calculated according to Wolpaw and colleagues (Wolpaw et al., 2002). In this binary MI BCI paradigm the number of possible selections are (*N*=2) for selection of row or column. Due to the rather slow experimental design there were approximately 4 trials per minute (selections or decisions per minute). Thus, the ITR (bits/min) in the copy-task could vary between 0 and 4 bits/min (with an accuracy of 1, the best possible bitrate was 4 bits/min). For the free-mode data, no-decision trials were treated equal to pause intervals, therefore there were, on average, less selections per minute possible and ITR lower consequently: selectionsPerMinute=60/ ((Ncorrect+Nincorrect+Nnodecision)/(Ncorrect+Nincorrect)*(trialLength+interTrialPause).

2.1.2.8.1.3 Satisfaction

Satisfaction was assessed using the extended QUEST (Demers et al., 2000; Zickler et al., 2011), the ATD-PA (M. J. Scherer, 2007) and VAS satisfaction (Zickler et al., 2011).

2.1.2.8.2 Usefulness

In a semi-structured interview, end-users were asked whether they could imagine using the BCI gaming application Connect-Four in daily-life.

2.1.2.8.3 Evaluation protocol

Before every BCI session (3 to 8) end-users were asked to indicate their motivation on a visual analogue scale (VAS motivation). After every BCI-session (3 to 8) end-users rated their subjective workload with the NASA Task Load Index as well as their overall satisfaction using a visual analogue scale (VAS satisfaction). In the last session (session 9), end-users were asked to rate their satisfaction with the BCI-device with the extended QUEST (Demers et al., 2000; Zickler et al., 2011) and with the ATD-PA device form (M. J. Scherer, 2007). Furthermore in this last session, end-users were asked for general feedback and suggestions in a semi-structured interview (usefulness).

2.1.2.9 Statistical analysis

Due to the low sample size, no inferential statistical analysis was applied to the data and individual data is reported descriptively.

2.1.3 Results

2.1.3.1 Depression, quality of life and motivation

None of the end-users was depressed (cut-off=23). Three of four end-users rated their individual quality of life high (Quality of life score: A: 80; B: 52.92; C: 81.67; D: 77.5). End-user C indicated communication as one aspect, which is important for his quality of life and that he is more or less satisfied with this aspect. End-user D indicated mobility as one important aspect influencing his quality of life with which he was very dissatisfied. End-user B stated that he is not satisfied with the areas health and more or less satisfied with his life conditions and finances. The ACSA scores for general individual well-being of the end-users were A: 1, B: 0, C: 2, D: -2, in the middle range (minimum: -5, maximum: 5). All end-users were highly motivated throughout testing sessions (see **table 7**).

Table 7: Emotional and motivational status of the end-users.

Emotional and motivational status				
	End-user A	**End-user B**	**End-user C**	**End-user D**
Depression and quality of life				
Quality of life	80	52.92	81.67	77.5
ACSA	1	0	2	-2
CES-D	3	10	7	12
VAS motivation				
S3	10.0	9.7	10.0	8.0
S4	9.0	10.0	10.0	10.0
S5	10.0	10.0	10.0	9.0
S6	9.0	8.4	10.0	10.0
S7	9.0	8.2	10.0	8.0
S8	9.0	8.5	10.0	8.0
M	**9.3**	**9.1**	**10.0**	**8.8**

Note: Motivation was rated on a visual analogue scale (VAS) ranging between 0 (“not motivated at all”) and 10 (“very motivated”); *M*=mean.

2.1.3.2 Usability

2.1.3.2.1 Effectiveness

2.1.3.2.1.1 Copy-task

Performance varied considerably between end-users and sessions: End-user A and B had moderate BCI control with accuracies between 53% and 73% for end-user A, and 46% and 64% for end-user B. End-user D had highest control with accuracies between 51% and 80%. End-user C did not gain control during training, with accuracies around chance level and no improvement over training sessions (range: 41% to 51%). **Table 8** depicts accuracy for each end-user per session 4 to 8.

Table 8: Accuracy (percent correct) and ITR [bits/min] of copy-task for the end-users.

Copy-task				
Accuracy [%correct]				
	End-user A	**End-user B**	**End-user C**	**End-user D**
S4	53	-	49	51
S5	65	46	41	79
S6	66	62	51	75
S7	73	64	50	77
S8	57	58	43	80
ITR [bits/minute]				
	End-user A	**End-user B**	**End-user C**	**End-user D**
S4	0.17	-	0.13	0.05
S5	0.56	0.07	0.32	1.41
S6	0.81	0.28	0.25	0.87
S7	1.15	0.82	0.11	1.44
S8	0.39	0.18	0.17	1.40

Note: End-user B started with copy-task in session 5 (due to technical problems screening had to be extended in session 4).

2.1.3.2.1.2 Free-mode task

It was aimed to only open free-mode task, if accuracy in copy-task was sufficient (around 70%), because it was expected that playing the game online would otherwise not be satisfying (Kübler, Neumann, et al., 2001; Kübler et al., 2004). However because end-user C asked to play the game in free-mode, he was entered, even though he had control on chance level. However, as in the copy-mode, selections in the free-mode were a matter of chance. Also for the other end-users free-mode task was sometimes started for motivational reasons and because it was desired by the end-users, even though control was lower. Free-mode data of end-user D was difficult to analyse, since end-user D could not reliably indicate whether the action was intended and actions were not always reasonable. Therefore, only free-mode data of end-users A and B were analysed. End-user A played five games in total (winning three of those games), whereas end-user B played four games in the free-mode (winning two). See **figure 13** for performances in free-mode.

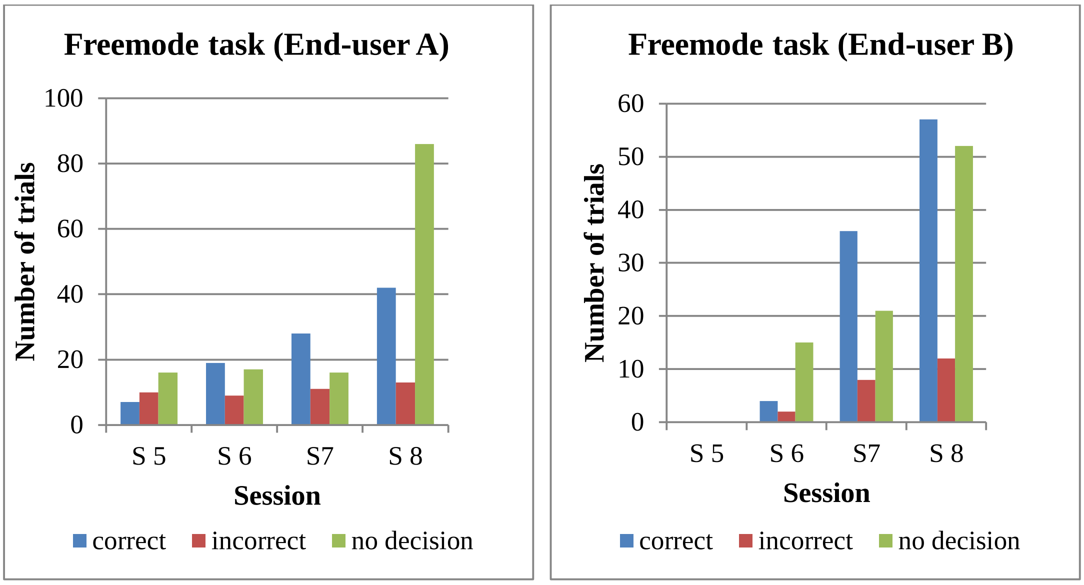


Figure 13: Online results for the free-mode for end-user A and B.

There were correct and incorrect trials, and trials in which no decision was made.

2.1.3.2.2 Efficiency

2.1.3.2.2.1 Information transfer rate (ITR)

Bitrates (bits/min) varied between 0.17 to 1.15 for end-user A, 0.06 to 0.56 for end-user B, 0.11 to 0.32 for end-user C and 0.05 to 1.44 for end-user D. See **table 8** for bitrates in the online copy-task for all end-users for the sessions 4 to 8. ITR (bits/min) in free-mode varied between 0.08 to 0.67 for end-user A and 0.13 to 1.17 for end-user B. See **table 9** for mean bitrates in free-mode for end-users A and B.

Table 9: ITR of free-mode task for end-user A and B.

	Free-mode task	
	ITR [bits/minute]	
	End-user A	**End-user B**
S 5	0.08	-
S 6	0.39	0.13
S 7	0.67	1.17
S 8	0.55	1.04

Note: For estimation of ITR only correct and incorrect trials were included (percentage of correct trials) and no-decision trials were treated equal to pause intervals.

2.1.3.2.2.2 Subjective workload (NASA-TLX)

Total subjective workload was moderate in all end-users (range: A: 17-51, B: 35-72, C: 17-53 and D: 28-56; see **table 9**). In few single sessions end-users B and D experienced high workload (52 to 70). The main sources of workload were mental (range: A: 3-19, B: 1-20, C: 0-7, D: 13-30) and temporal demand (range: A: 2-27, B: 0-13, C: 1-20, D: 1-27). In end-users A and B, frustration was a strong contributor to the total workload in single sessions (range: 0-27). End-users C and D reported no or very little frustration. Effort and subjective experienced performance were contributing least to the total workload.

Table 10: Subjective workload ratings (NASA-TLX) and VAS satisfaction (sessions 3 to 8).

Subjective Workload (NASA-TLX)								
End-user A								
Scale	**WL**	**M**	**P**	**T**	**PE**	**E**	**F**	**Sat**
3	12	3	1	2	0	7	0	7.5
4	44	7	0	27	3	4	4	9
5	36	13	2	10	0	4	7	7.1
6	51	8	0	13	1	1	27	8
7	38	19	1	13	1	4	0	9
8	17	6	0	3	1	1	7	9
M	**33**	**9**	**1**	**11**	**1**	**3**	**7**	**8.3**
End-user B								
3	12	1	4	3	0	4	0	8.2
4	12	1	1	1	8	1	0	8
5	35	10	5	4	2	14	0	4
6	72	20	1	0	10	16	25	2.2
7	52	5	0	9	8	3	27	4
8	50	11	0	13	3	6	16	4.5
M	**39**	**8**	**2**	**5**	**5**	**7**	**11**	**5.2**
End-user C								
3	21	3	3	1	8	5	0	9
4	29	7	1	10	10	1	0	10
5	17	0	4	2	10	1	0	9
6	31	7	8	6	3	8	0	9
7	53	3	16	20	3	12	0	9
8	20	3	8	2	2	6	0	6
M	**29**	**4**	**7**	**7**	**6**	**6**	**0**	**8.7**
End-user D								
3	67	27	24	10	1	5	0	9
4	57	19	8	27	1	2	0	9
5	56	21	6	27	1	1	0	9
6	-	-	-	-	-	-	-	6
7	51	30	18	1	1	1	0	10
8	28	13	1	8	4	2	0	10
M	**52**	**22**	**11**	**14**	**2**	**2**	**0**	**8.8**

Note: For end-user D data is missing in session 4. In this session he was not able to answer the questionnaire by button-presses, due to exhaustion. Data for NASA-TLX is rounded. M=mental demand, P=physical demand, T=temporal demand, PE=performance, E=effort, F=frustration, WL=total workload

2.1.3.2.3 Satisfaction

2.1.3.2.3.1 Satisfaction with the BCI device (extended QUEST)

Two of four end-users were quite to very satisfied with different aspects of the BCI device with a total QUEST score of 4.38 for end-user D and 4.25 for end-user A. The total score of the added items was 4.5 for end-user D and 4.25 for end-user A. End-user C was more or less to quite satisfied with the BCI device (QUEST score: 3.75 and added items score: 3.5). End-user B was not very to more or less satisfied with the BCI device (QUEST score: 2.75 and score for added items: 3.25). Evaluation results of the extended QUEST are depicted in **table 11**. End-users were highly satisfied with weight (*M*=4.25), safety (*M*=4.5), professional services (*M*=4.75) and learnability (*M*=4.75). Main obstacles were the EEG-cap and electrodes (dimensions), adjustment, ease of use, effectiveness, reliability and speed (*M*=2.75 to *M*=3.5). Furthermore, end-users were only moderately satisfied with comfort and aesthetic design (*M*=3.75), see **table 12** for individual comments. End-users indicate ease of use as most important (4 times), followed by reliability (2 times), see **figure 14**.

Table 11: Satisfaction with the BCI device (extended QUEST).

Satisfaction with BCI device (extended QUEST)					
	End-user A	**End-user B**	**End-user C**	**End-user D**	***M***
1: Dimensions	3	2	2	4	**2.75**
2: Weight	4	4	5	4	**4.25**
3: Adjustment	4	2	4	3	**3.25**
4: Safety	5	4	4	5	**4.50**
5: Comfort	4	2	4	5	**3.75**
6: Ease of use	5	2	3	4	**3.50**
7: Effectiveness	4	2	3	5	**3.50**
8: Prof. services	5	4	5	5	**4.75**
QUEST total score	**4.25**	**2.75**	**3.75**	**4.38**	**3.78**
9: Reliability	4	3	3	4	**3.50**
10: Speed	4	2	3	5	**3.50**
11: Learnability	5	5	4	5	**4.75**
12: Aesthetic design	4	3	4	4	**3.75**
Added items score	**4.25**	**3.25**	**3.5**	**4.5**	**3.88**

Note: *M*=mean of scores; 1=not satisfied at all, 2=not very satisfied, 3=more or less satisfied, 4=quite satisfied, 5=very satisfied.

Table 12: Individual statements indicated in the extended QUEST.

Satisfaction with BCI device (extended QUEST)	
scale	**Individual statements by end-users (N=4)**
1: Dimensions	"*Cables of EEG-cap to amplifier disturb, in daily-life too cumbersome because only little free moving space*" (A); "*Adjustment of EEG-cap and electrodes is too cumbersome*" (B); "*Due to electrode gel*" (C)
2: Weight	"*Cables are disturbing*" (A)
3: Adjustment	"*Cap did not fit immediately*", "*Because of cables - one could use infrared to date*", "*Software crashed sometimes*" (A); "*Too cumbersome/complex/time-consuming*" (B); "*Due to electrode gel and due to software/hardware*" (C) "*Could be faster*" (D)
4: Safety	"*Because of irritations on the scalp*" (C)
5: Comfort	"*I felt somewhat constricted because of the cap*", "*but if it works, use in daily-life conceivable as well*" (A); "*It is physically uncomfortable because of electrode gel and electrodes on head, and I would feel uncomfortable using this device in different environments because it looks strange wearing the EEG-cap*" (B)
6: Ease of use	"*When calibration is good*" (A); "*Because it did not work so well*" (B); "*It didn't work in my case*" (C)
7: Effectiveness	"*Because it did not work with 100%*" (B); "*It didn't work in my case*" (C)
8: Prof. services	"*More precise information would have been good in some situations*" (B)
9: Reliability	"*Due to crashes of software*" (A); "*EEG signals depend on the impedances*" (B)
10: Speed	"*Too slow, should be faster*" (B)
11: Learnability	"*Training was not exhausting*" (A); "*Would be good if one could have training every day*" (C)
12: Aesthetic design	"*EEG cap needs some re-design*" (A); "*EEG-cap looks like in hospital*" and "*Electrode cables should be eliminated*" (B); "*I would be very satisfied if everything could be smaller, e.g., compress in one device*" (C)

2.1.3.2.3.2 VAS satisfaction

End-users A, C and D were quite satisfied with the BCI application in most of the sessions (range: 6-10). The low rating of end-user D in session 6 was related to his bad physical constitution on this day, on which he asked to terminate the session before the end. End-user B was quite satisfied with sessions 3 and 4 (8-8.2), but not with the following BCI sessions (range: 2.2-4.5). Results for overall satisfaction with the BCI application are depicted in **table 10**.

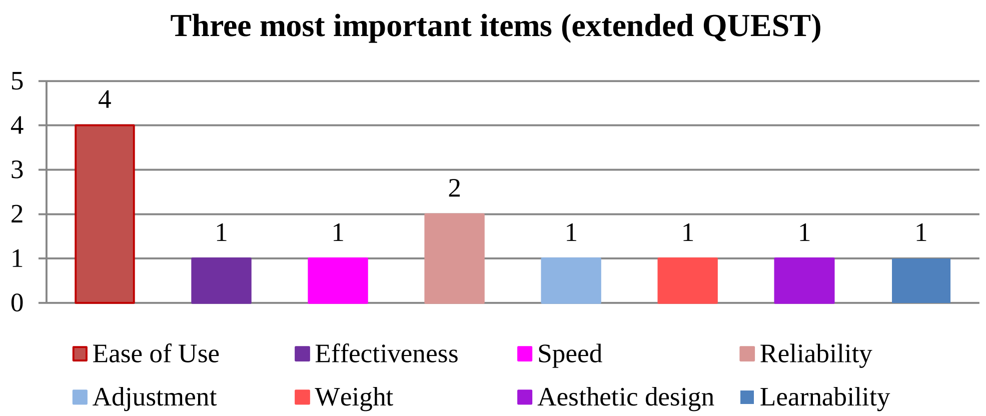


Figure 14: Three most important items (extended QUEST) in BCI game Connect-Four.

2.1.3.2.3.3 Match between person and technology (ATD-PA)

With a score of 4.25 of 5, end-user D had a good match with the BCI device (**table 13**). Two end-users showed a moderate match (A: 3.25 and C: 3.25) with room for improvement. One end-user had a non-match with the BCI (B: 2.33), indicating risk for BCI non-use. The item "*This device will benefit me and improve my quality of life*" was most important for the end-users.

Table 13: Match between person and technology (ATD-PA).

	Assistive Technology Device Predisposition Assessment (ATD-PA)				
	Item	**End-user A**	**End-user B**	**End-user C**	**End-user D**
A	This device will help me to achieve my goals.	2	2*	3*	5
B	This device will benefit me and improve my quality of life.	3	2*	3*	5*
C	I am confident I know how to use this device and its various features.	5*	5	4	5*
D	I will feel more secure (safe, sure of myself) when using this device.	1	2	4	1
E	This device will fit well with my accustomed routine.	3	1*	3	5
F	I have the capabilities and stamina to use this device without discomfort, stress and fatigue.	5*	5	3	5
G	The supports, assistance and accommodations exist for successful use of this device.	5*	5	3*	2
H	This device will physically fit in all desired environments (car, living room, etc.).	4	5	3	3
I	I will feel comfortable using this device around family.	2	1	4	5*
J	I will feel comfortable using this device around friends.	3	0	3	5
K	I will feel comfortable using this device at work.	4	0	3	5
L	I will feel comfortable using this device around the community.	2	0	3	5
	Total score (A-L)	**3.25**	**2.33**	**3.25**	**4.25**

Note: 5=All the time (100% of the time); 4=Often (around 75% of the time); 3=Half the time, neutral (about 50% of the time); 2=Sometimes (around 25% of the time); 1=Not at all (0% of the time); 0=Not applicable,"*" indicates the three most important items.

2.1.3.3 Usefulness

End-users A and D could imagine to use the BCI in their daily-life and end-user C "*only if it works better in my case*". End-user A stated that the EEG-cap, electrodes and the set-up of the system would need to be improved ("*no cables, easier and faster set-up*") and he would like to have an "*undo-function*" for incorrect actions in the game. Also, for end-user C the EEG cap ("*no gel*") and the BCI system ("*everything more compact, simpler and easier*") would need to be re-designed. End-user B, who could not imagine using the BCI in daily-life, indicated the low speed, low effectiveness, the complex set-up, and the EEG-cap/electrodes/cables as the main obstacles: "*The BCI application is good in general, but everything takes too long, e.g., set-up of BCI and the MI-training*".

2.1.4 Discussion

Usability of a new MI BCI based gaming application was evaluated by four severely motor restricted end-users in terms of its effectiveness (accuracy), efficiency (ITR and subjective workload) and satisfaction, in accordance with the UCD for BCI development (Kübler et al., 2014; Zickler et al., 2011). Furthermore usefulness (considered daily-life use) was explored.

2.1.4.1 Depression, quality of life and motivation

None of the end-users was depressed and all end-users were highly motivated throughout the testing sessions. It can thus be excluded that motivation or general affective state influenced BCI performance in a negative way. Three of four end-users rated their individual quality of life high; and comparable to people without chronic disease (Lhussier, Watson, Reed, & Clarke, 2005; O'Boyle, McGee, & Browne, 2000), thereby replicating results of previous studies (Bromberg & Forshew, 2002; Fegg et al., 2005). Scores for general individual well-being of the end-users ranged between -2 and 2 (on a scale from -5 to 5); and are thus in the range of healthy subjects and locked-in patients (Bruno et al., 2011). One end-user indicated that he was only more or less satisfied with the aspect communication, and one end-user indicated that he was very dissatisfied with mobility. The low satisfaction scores in these domains reveal that these two locked-in end-users have needs and requirements that are not satisfactorily met by their conventional assistive technology and that there is need for improvement.

2.1.4.2 Usability

2.1.4.2.1 Effectiveness

With up to 80% correct selections, effectiveness of end-user D was high. Effectiveness of the other end-users was low to moderate (41-73%). Effectiveness was thus much lower as compared to a P300-ERP BCI (70-100%; Sellers et al., 2010; Zickler et al., 2013; Zickler et al., 2011); in line with (Kübler, Nijboer, et al., 2005; Nijboer et al., 2010). These differencing results can be explained by the nature of the paradigms; the MI BCI relies on self-regulation of brain signals and operant conditioning, the P300 BCI is based on the exogenous triggering of brain potentials. Results are consistent with findings by healthy subjects, who are more challenged in learning to control a SMR BCI. Guger and colleagues (Guger et al., 2009; Guger et al., 2003) tested 99 healthy subjects with an SMR BCI and 100 healthy subjects with a P300 BCI. In the SMR BCI 93.3% of the participants gained control above 59% accuracy, but only 6.2% of the subjects were able to control the BCI with 100% accuracy. In contrast, in the P300 BCI 72.8% of the participants were able to use a P300 BCI with 100% accuracy, already in the first session. This shows that SMR regulation has to be learned with training, whereas P300 BCI requires no learning.

Effectiveness achieved by end-users of this study was lower, as compared to effectiveness achieved by end-users with neurodegenerative diseases in an earlier SMR BCI study, in which accuracy of all four end-users was above 76% (Kübler, Nijboer, et al., 2005). And contrary to this study (Kübler, Nijboer, et al., 2005; Nijboer et al., 2010), no clear training effect was evident. It remains unclear, whether this discrepancy can be explained by differences in protocol or by individual differences. Differences in the protocol were the number of sessions, such that in the study by Kübler and colleagues end-users were trained within 20 sessions. Considering only the first 10 sessions, participants' SMR training performance was at chance level (Kübler, Nijboer, et al., 2005; Nijboer et al., 2010); in the present study end-users were trained to regulate their SMR in only 6 sessions. Additionally in the present study input signals could be different for individual sessions and it remains unclear whether the hybrid approach and the flexible adaptation are more challenging with respect to learning and that they rather impede learning effects (that is different if only one signal, e.g. SMR, is continuously trained). Nevertheless one major finding is, that effectiveness varied strongly between end-users. The phenomenon that some user gain good control over a BCI by regulating SMR activity by MI, but some users are not able to reach any sufficient control, a problem also known as "BCI inefficiency", has been found consistently across many studies (Blankertz et al., 2010; Guger et al., 2009; Guger et al., 2003; Kübler & Müller, 2007; Vidaurre & Blankertz, 2010). Even though end-user D had high performances in the copy-task, he was not able to play the game in free-mode. Higher cognitive load and more attention are required for the free-mode as compared to the copy-mode. As cognitive resources are limited, free-mode might thus been too challenging for him (Riccio et al., 2011; Schreuder et al., 2013; Sellers et al., 2014; Silvoni et al., 2009; Zickler et al., 2011). Other factors explaining intra- and inter-individual differences in performance are discussed in the general discussion (see **3.2.1.1 Inter-individual differences in performance** and **3.2.1.2 Intra-individual differences in performance**).

2.1.4.2.2 Efficiency

With a range between 0.05 and 1.44 bits/min, mean bit rate of all end-users was far below rates achieved by severely motor-restricted end-users with visual P300-ERP BCIs (4.03-8.57; Nijboer, Sellers, et al., 2008; Zickler et al., 2011). End-users indicated moderate total workload (12-72), indicating that, from a subjective perspective, controlling the BCI by MI was not too demanding for them. Nevertheless the MI BCI application was judged as higher demanding as compared to a P300 BCI application which was rated between 9 and 49 by other end-users (Zickler et al., 2011). Frustration was strongly contributing to the total workload in two end-users (A and B), that is detrimental, because frustration can influence motivation and mood, which play an important role in learning, and thus consequently BCI control and performance (Kleih et al., 2010; Nijboer et al., 2010; Nijboer, Furdea, et al., 2008). This was however not necessarily the case: in end-user B frustration increased in sessions 6 and 7, in which also motivation was decreased, however performance was not impaired, but rather increased. End-user A reported frustration in sessions 5 and 6, however motivation and performance remained unchanged. End-user C reported always highest motivation scores and no frustration, even though accuracy was at chance level. This shows that frustration does not necessarily negatively impact BCI training. This is in line with results by Nijboer and colleagues (2010), who found that motivational factors, such as challenge, incompetence fear and mastery confidence were related to BCI performance in some but not all end-users. Some end-users reported feeling frustrated about lack of improvement in MI BCI training during initial sessions, but interest in MI training remained constantly high across sessions and thus frustration did not affect motivation (Kübler, Nijboer, et al., 2005; Nijboer et al., 2010). Moreover challenge was found to be positively correlated with BCI performance in one end-user, indicating that perceiving a task as challenging can boost performance for some individuals (Nijboer, Sellers, et al., 2008).

2.1.4.2.3 Satisfaction

Three of four end-users indicated that they were satisfied with the BCI device in most of the sessions. The individual ratings of satisfaction regarding different aspects of the BCI device yielded insight into sources of dissatisfaction. All end-users were most satisfied with weight, safety, professional services and learnability. End-users indicated highest dissatisfaction with EEG-cap including electrodes and cables (dimensions), adjustment, ease of use and effectiveness. This implies that MI BCIs require improvement toward a more effective, faster and more reliable device, which can be adjusted faster (less equipment) and easier (EEG cap: no cables, no electrode gel). Somewhat surprising, speed was rated better in the MI BCI application although effectiveness and ITR were considerably lower as seen in P300 BCIs (Zickler et al., 2011). For end-user D BCI-controlled Connect-Four provided a good match between person and technology, for end-users A and C a moderate, and for end-user B a non-match implicating non-use, thereby matching satisfaction ratings and statements in the interview.

2.1.4.3 Usefulness

Two end-users could imagine using the BCI in daily-life. One end-user (end-user A) is not “in need” of a BCI, since he can move his arms and hands, however he liked the MI BCI game and indicated that he could imagine to use it in his daily-life. Nevertheless he sees problems in using the BCI in daily-life, because set-up of the system, including EEG electrodes, are time-consuming and complicated. End-user D, who is in real need of new AT devices that can offer him new possibilities to communicate and to express himself, could imagine to use a MI BCI for communication purposes (albeit not tested in this study) and for gaming. It shows that end-users with severe motor restrictions wish to be able to pursue satisfying leisure activities that enhance quality of life.

2.2 Study 2: Hybrid P300 BCI: Evaluation of usability by healthy participants and severely motor-restricted end-users

2.2.1 Introduction

The present study investigated the usability of a hybrid P300-ERP BCI system, which is the second release of the P300-Qualiworld communication prototype, tested in the study of Zickler and colleagues (Zickler et al., 2011). Based on the findings of Zickler and colleagues, showing that the EEG cap, low speed, low effectiveness and complex adjustment were the main obstacles for BCI use, the new hybrid prototype includes new features trying to face these issues. This new prototype was, same as the first, developed within the EU-project TOBI (http://www.tobi-project.org/) by partners of Foundazione Santa Lucia (FSL, Rome, Italy). The recently introduced hybrid approach, enabling the end-user to use not only EEG activity, but also EMG activity as input channel for the BCI (Millan et al., 2010), was integrated, allowing for an EMG-undo letter correction (i.e., delete wrong selected letters in the matrix). This was requested by the end-users and should improve efficiency and effectiveness of the BCI. In addition, a new P300-stimulation with bigger central dots and grid stimulation allowing for individual adaptation of stimulation mode was introduced to improve effectiveness and efficiency of the spelling device. Moreover, individual adaptation of flashing sequences was taken into account to improve efficiency (speed). To make the BCI easier to use and to reduce adjustment time, an easy to use active EEG-cap (with transparent electrode gel) was used and an option for selection of a pause mode was implemented. To test proof of principle, BCI prototype was tested by 10 healthy subjects in the BCI lab. BCI was then brought to possible BCI end-users diagnosed with different neurologic or neurodegenerative diseases for systematic evaluation of the usability of the prototype. Same as in *study 1* usability of the hybrid BCI prototype was evaluated in terms of its effectiveness, efficiency and end-users' satisfaction following a user-centred approach (Kübler et al., 2014; Zickler et al., 2011). The hybrid prototype was tested using a different protocol (with main focus on efficiency metrics) in a study by Riccio and colleagues (Riccio et al., 2015).

2.2.2 Methods

2.2.2.1 Subjects

2.2.2.1.1 Healthy Participants

Ten healthy subjects (6 female), aged 19 to 30 (*M*=24.1, *SD*=3.35) were included in this study. Another subject participated for the first session (screening), but had to be excluded from the study because classification of EEG signals was not possible (due to strong artifacts in the EEG caused by perspiration). Subjects had no neurological or psychiatric diseases. Participants were paid 8 Euros/ hour.

2.2.2.1.2 End-users

Four patients (age: A: 47, B: 41, C: 26, D: 52, 3 male) participated in this study. End-user A suffered a brainstem stroke; end-user B was diagnosed with MD (type Duchenne), end-user C with SMA, end-user D with ALS (spinal form), see **table 14**. Patients were severely motor restricted, with only residual muscular control, therefore they were considered as potential end-users for the hybrid-P300 BCI. Two patients (A and B) were tested in the Beratungsstelle für Unterstützte Kommunikation (BUK, Information Center for Supported Technology), Bad Kreuznach, Germany, one patient was visited at home (D) and one patient came to the University of Würzburg and was tested in the BCI lab. Another patient in the locked-in state diagnosed with CP, who participated already in *study 1* ("end-user C") participated in the screening session, however no classifier could be generated. It remained unsolved, whether signals could not be classified due to attention problems or problems to focus on items of the P300 matrix. End-users were paid, same as healthy participants (8 Euros/hour). End-users A, B and C were able to speak, end-user D was able to speak, however with high effort and a very weak voice, so that it was difficult to understand by novices; therefore comments were mostly translated by caregivers.

Table 14: Demographic and disease related data for the end-users (hybrid ERP BCI).

	End-user A	End-user B	End-user C	End-user D
Diagnosis	Tetraparesis after pons infarct	Muscular Dystrophy Duchenne	Spinal muscular atrophy (SMA) Typ II	Amyotrophic Lateral Sclerosis (ALS)
Age	47	41	26	52
Artificial Ventilation	No	Yes (non-invasiv)	No	No
Artificial Nutrition (PEG)	No	Yes	Yes	No
Wheelchair	Yes	Yes	Yes	Yes
Residual muscular control	Eyes, speech, both arms and hands	Eyes, mimic (minimal facial movements: lips, mouth), restricted speech (due to ventilation)	Eyes, mimic, head, speech	Eyes, mimic, head, strong restricted speech (caregiver translates)
Computer input device	Joystick and virtual keyboard	Chin-joystick and Wergen-keyboard	Normal mouse and virtual keyboard	Slowed keyboard
Use of ICT on a daily basis	Yes	Yes	Yes	Yes
Experience with AT ICT since	2006	1992	1995	2003
Previous BCI-experience	2010	2000	2011	2009

2.2.2.2 Study protocol

For the healthy participants, the protocol comprised 3 sessions: In session 1, information about the study was provided and demographic information was assessed. In session 1 calibration was carried out and in sessions 2 and 3 online tasks (see **2.2.2.7 Online tasks**) were conducted. BCI prototype was evaluated in sessions 2 and 3. Participants were paid for participation (8 Euros/hour). For end-users protocol was only slightly different: Protocol consisted of two more sessions, thus 5 sessions: In session 1 information about the study was provided and demographic and disease related information, depression and quality of life were assessed. Then the next 3 BCI sessions were the same, as for healthy participants. In the last session, (session 5) extended evaluation was assessed (see **2.2.2.8 Evaluation**). The study protocol was approved by the Ethical Review Board of the Medical Faculty, University of Tübingen.

2.2.2.3 Depression, quality of life and motivation

The assessment of the emotional and motivational status of the end-users was the same as in *study 1* (see **2.1.2.3 Depression, quality of life and motivation**).

2.2.2.4 Hybrid P300-ERP BCI application

The first prototype was based on the integration of a P300-ERP BCI and commercial AT software QualiWORLD (QW; by QualiLife Inc., Paradiso-Lugano, Switzerland). In QW users have different functions for communication (e.g., word processing with speech generation and email sending), for entertainment (e.g., music and video player, games, and photo browser) and for environmental control (e.g., access to TV). In addition, QW offers an internet browser. The QW-software can be controlled by different input channels, such as a scanning interface or a head-mouse (Zickler et al., 2011). In the second prototype, input signal was extended by an EMG channel, resulting in the fusion of P300-ERP and EMG and QW application. The hybrid BCI composed of three programs, BCI-2000 (Schalk et al., 2004), QW and a program for processing of EMG signals (developed by FSL, Rome, Italy). BCI and EMG applications were run on one notebook, QW on a second notebook, both connected by a network cable. BCI-2000 sent the P300-ERP stimulation into the QW application, for instance the text matrix or the email. In the stimulation sequence the symbols of the QW graphical user interface (GUI) were overlaid with central dots or grids in the colours green or red. Classical flashing in rows and columns within a P300-matrix was adapted to the QW GUI. For that, the BCI-2000 based matrix size was determined by the number of selectable symbols in QW. For example, if there were three possible selections in QW, then a 2x2 P300-ERP matrix (enabling 4 selections for maximum) was selected. There could be 2x2, 2x3, 3x3 and 7x8 matrices.

2.2.2.5 Signal acquisition

2.2.2.5.1 EEG

EEG was recorded from 8 active electrodes (gamma cap; g.tec Medical Engineering GmbH, Austria) from the scalp positions Fz, Cz, P3, Pz, P4, Po7, Po8, Oz (Krusienski et al., 2006) according to the 10-20 system (Jasper, 1958). EEG was amplified with a 16-channel g.USBamp (g.tec Medical Engineering GmbH, Austria), and processed by the software BCI-2000 (Schalk et al., 2004). Sampling rate was 156 Hz. Reference electrode was placed on the right ear lobe, ground on left mastoid. Impedances could not be measured with the BCI system (g.tec did not offer this tool for BCI systems comprising active gamma cap and 16-channel g.USBamp); therefore quality of signals was visually evaluated (e.g., inspection of alpha ERD with eyes open/closed).

2.2.2.5.2 EMG

EMG was recorded from two active electrodes using the same amplifier as for EEG. In healthy participants, the EMG activity was always detected from the hand muscle extensor carpi radialis longus, contracted by executing a wrist extension. In the end-users EMG electrodes were placed individually, depending on the end-user's residual movements. For end-users A, C, D set-up of the EMG was the same as for healthy participants. In end-user B EMG was recorded from the face around the muscles musculus zygomaticus major and musculus risorius, contracted by twitch of the corner of his mouth (see **figure 15**). For every subject the onset and the offset threshold of the EMG signal amplitude, necessary to elicit an UNDO with the EMG-signal was set individually. The time window for the UNDO command, meaning the time window in which the EMG onset and offset must occur in order to delete an item, was set to 4 seconds (after feedback about selection).

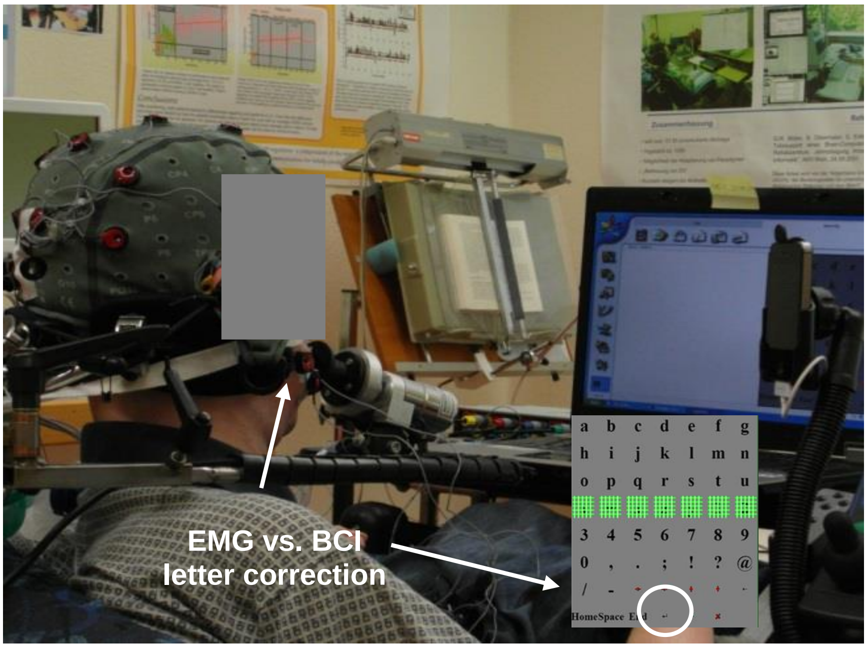


Figure 15: End-user B using the hybrid P300-ERP BCI for spelling.

In this hybrid-BCI, items could be selected from the P300-ERP matrix (in this picture with green grid stimulation). Wrong selected letters could be deleted by either selecting the delete function in the matrix (arrow to the left), or by using the EMG. Note: EMG-channel is placed on the right side of the face (corner of the mouth).

2.2.2.6 Screening, classification and classifier training

In the first BCI session a screening was performed, in which the best stimulus modality (least number of sequences needed) and number of sequences (necessary to reach 100% offline) were identified. Four different stimulation modalities were tested, composed of 2 colours (green and red) and 2 forms (central big dot and grid), resulting in four possible combinations: green dot, red dot, green grid and red grid. Participants spelled two 5 letter words (EMAIL and RADIO) per each modality with a 6x6 matrix (see **figure 16**), 8 words in total. Order of stimulus modality was randomised. Number of sequences was 10. One flashing sequence is the single flashing of every row and column of a matrix. One sequence means that the intended item flashes twice; for instance in 10 sequences 20 times. Stimulus duration and ISI were 125ms. Post-sequence duration was 1360 ms. Pre-sequence duration was 3 seconds. Using a cross-validation tool developed by the Fondazione Santa Lucia (FSL; Rome, Italy), it was determined after how many sequences an accuracy of 100% was reached. This was done for each person to obtain the individual number of sequences. The stimulus modality with the least number of sequences was taken for the consecutive tasks. Then a calibration with a 3x3 matrix was conducted (see **figure 17**), spelling twice the item order "ACEGIBDFH". This was required because there were smaller matrices (2x2 to 3x3) in the email task. For this calibration the offline-accuracy using the cross-validation tool was calculated as well. The highest number of sequences (in 3x3 and 6x6 matrix) was taken and one sequence added, taking noise/distraction into (signal to noise ratio). Thus, if a person had 100% after 3 sequences for the 6x6 matrix in offline analysis and 100% after 4 sequences in the 3x3 matrix, then 5 sequences were set for the following online tasks. In the first study by Zickler and colleagues (2011) calibration was conducted with four different matrices (3x3, 4x4, 5x5, and 6x6). Different to that, in the present study only the 6x6 and 3x3 matrix were used, because it was shown in pre-tests by FSL that calibration with these two different matrix sizes worked well such that classifier generated with this data can be used for all applications and tasks within this study (internet task not conducted). A Matlab-based (The MathWorks, MA, USA) tool, called P300-GUI (BCI-2000; Schalk et al., 2004) was used for classification of ERP-signals. Data from both calibration procedures were used for offline analysis. Feature selection and classification was performed using SWLDA. Data was segmented between 0 and 800 ms post-stimulus and up to 60 features selected using a stepwise fit approach. Selected features went into the model used for classification of signals. The classifier was then used for online tasks. Real time extraction of the linear envelope of the EMG was used to obtain the EMG pattern that was correlated with the temporal profile of contraction strength (for details see, Riccio et al., 2015). Analysis of the linear envelope revealed the individual thresholds that were set for the sessions S2 and S3 (for each user separately).

Figure 16: Screening with 6x6 matrix and stimulus red grid.

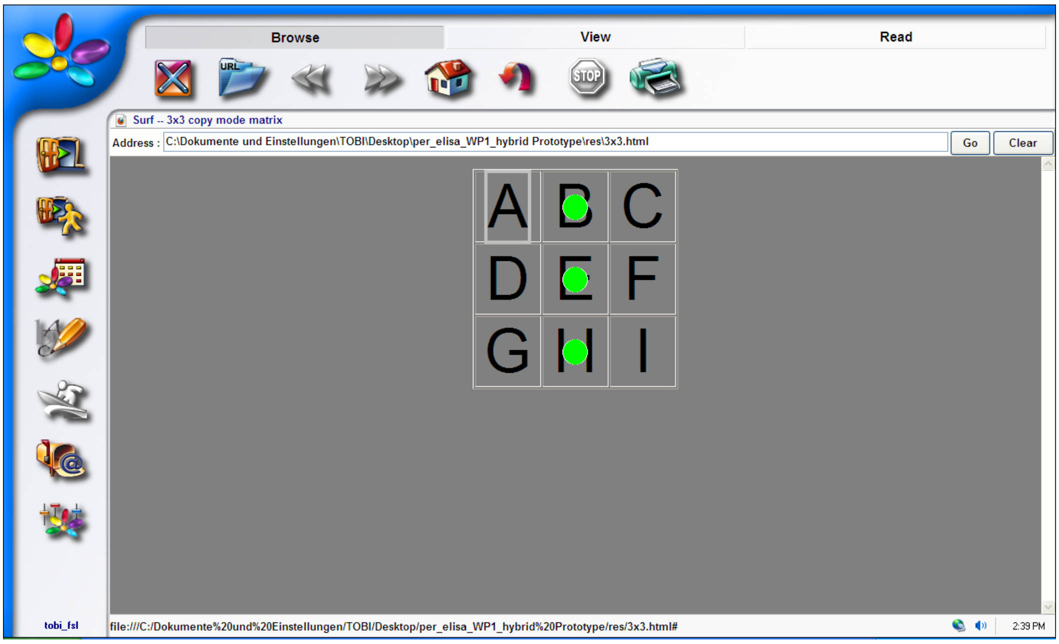


Figure 17: Screening with 3x3 matrix and stimulus green dot.

2.2.2.7 Online tasks

Online tasks were tested in 2 sessions: In the first session subjects completed a copy-task, in which the EMG was used for error correction and compared to BCI error correction. In the second session subjects had to write a sentence, choose pause mode, terminate pause mode again and sent the text by email.

2.2.2.7.1 Copy-task

Subjects had to copy-spell words using the 7x8 text-matrix. There were two conditions: BCI copy-spelling (BCI-CP) and hybrid copy-spelling (hybrid-CP). In the BCI-CP task subjects had to spell the two words “INTERNET” and “COMPUTER” and delete the last letter by selecting the delete function (arrow to the left in the last bottom row) and to re-spell the last letter again (20 selections in total). Wrong selected letters were not corrected. However if the delete function could not be selected correctly in the first trial, then subjects were instructed to select it again. In the hybrid-CP task, copy-spelling of the two words was the same as for the BCI-CP task, with the only difference that the last character had to be deleted with the EMG-UNDO function (20 selections). The text matrix was opened by the experimenter. Before spelling, a test word “BCI” was spelled in the matrix, in order to make subjects familiar with the spelling matrix and with the task. The test word was not considered in the performance of the task. **Figure 18** depicts the 7x8 spelling matrix as used in the copy-task. Grids (see **figure 16**) and central big dots (see **figure 17**) could mask items of the matrix; this was different for the first prototype, in which little dots flashed next to the selectable letters (see **figure 5, page 33**).

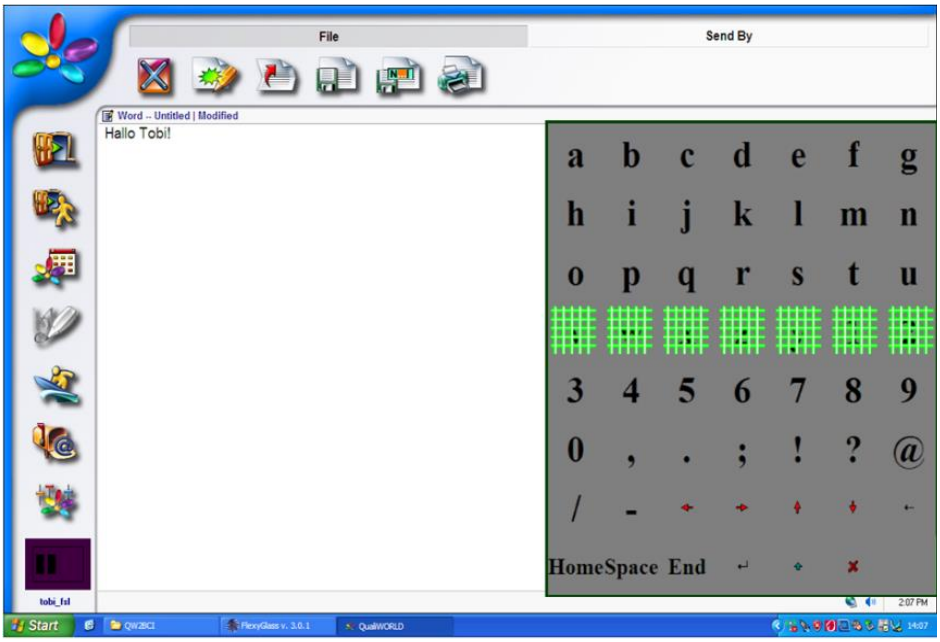


Figure 18: Copy task with spelling-matrix and green grid stimulation.

Note: Symbol of the pause is in the left bottom corner.

2.2.2.7.2 Sentence and email task

In the next session subjects had to write a sentence in the free-spelling mode with 10 characters using the EMG-correction for wrong selections and choose the pause mode (Sentence; 14 selections). Errors had to be corrected (delete with EMG and respell). The content of the sentence could be freely chosen by the subject, such as "Hello_Andi". Next, this text was sent by email to a predefined address, after terminating the pause mode (Email; 11 selections). To avoid a drop in accuracy due to confusion, subjects underwent a short standardized training to get used to the user interfaces that had to be opened for these tasks, before starting the task. **Figure 19** depicts the GUI of the email task using green grid stimulation. The P300 BCI application in the pause mode (in colour grey) is depicted in **figure 20**.

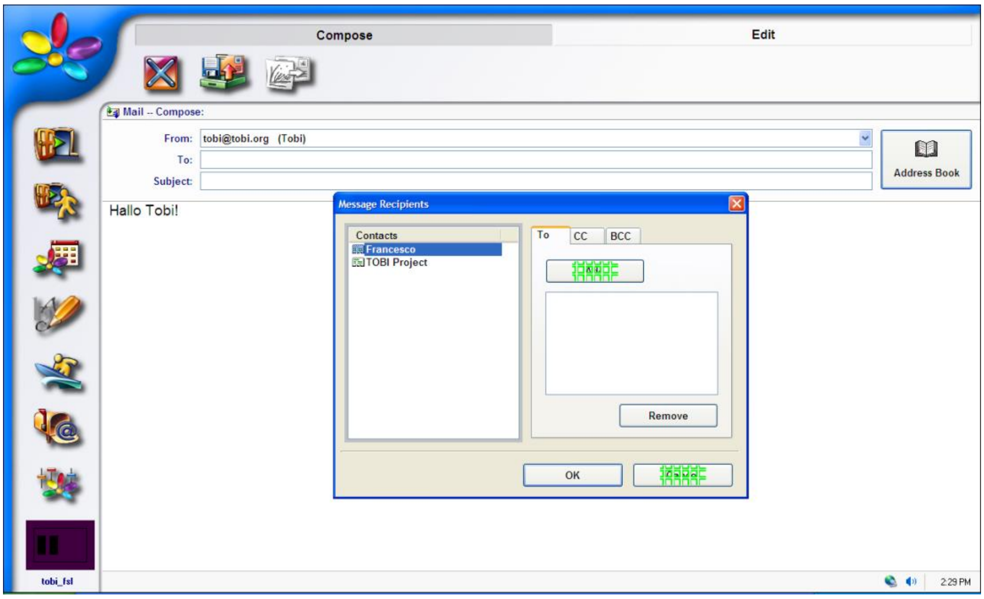


Figure 19: Email task with green grid stimulation.

Note: The icon for the pause is placed on the left bottom corner in the colour violet. The colour of the pause icon could be individually chosen by the subject, with the exception that it should not the same or similar colour as the colour of the stimulation modality.

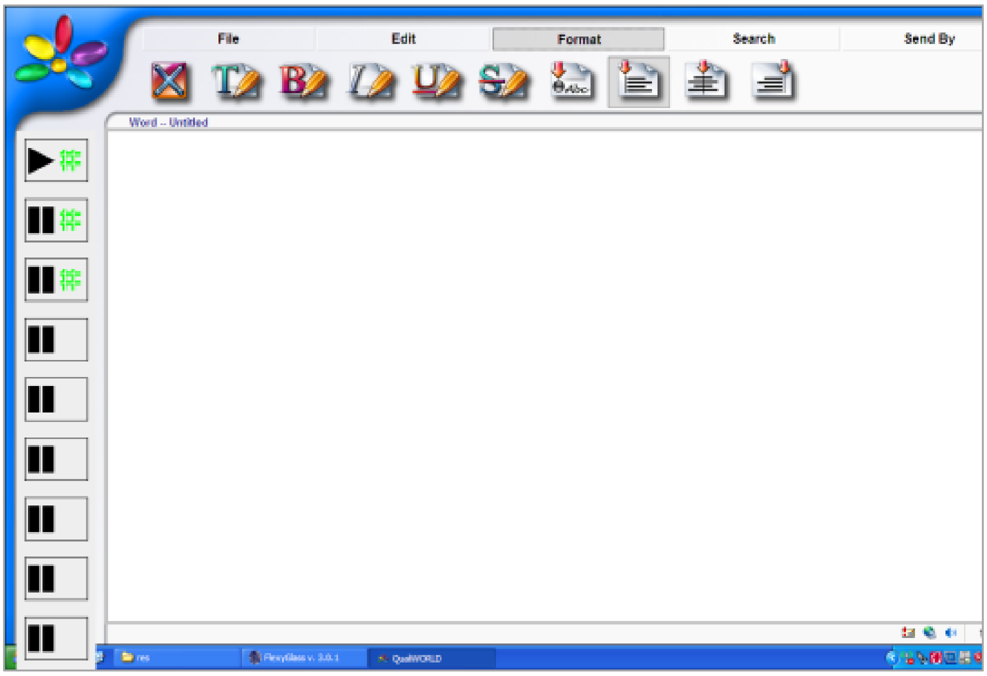


Figure 20: BCI in pause mode with green grid stimulation.

Note: The end-user had to select the item on the top (“play”) twice consecutively, to exit pause mode.

At the beginning of every online task session subjects had to spell the word "BRAIN" in order to make sure that they can spell potentially with an accuracy of 100%, based on the set number of sequences. If the test word was not spelled 100% correctly, one sequence was added and then spelled again to check whether an accuracy of 100% was reached; this adaptation procedure was needed in one end-user only. There were deviations in the protocol for three healthy participants. For the first two healthy participants, the cut-off criterium of 80% was used for the test word BRAIN. However it was realized that a criterium of 100% would be more reliable, as impedances could not be measured with this BCI system. A 100% criterium was then used for all other subjects and end-users. Subject 6 did not reach 100% accuracy in the test word BRAIN, neither after adding of one sequence, therefore a new calibration procedure was carried out.

2.2.2.8 Evaluation

Usability of the hybrid P300-ERP BCI was evaluated in terms of its effectiveness, efficiency and satisfaction, with only slight modifications for efficiency; for details see chapter **1.4.1.2 Valid evaluation metrics (P3)**.

2.2.2.8.1 Usability

2.2.2.8.1.1 Effectiveness

Accuracy was calculated by dividing the number of correct selections by the number of total selections, resulting in a percent value ranging from 0 to 100%, for example 8/16= 0.5 (=50%). Accuracy in the hybrid copy-spelling and sentence task included selections that were made with the EMG-channel (error correction).

2.2.2.8.1.2 Efficiency

Efficiency was defined as ITR and user's subjective workload (NASA-TLX; Hart & Staveland, 1988) and total time per task. Total time per task was added to compare both copy-spelling tasks (hybrid vs. BCI), because the formula for the ITR cannot include the EMG-selections, and can only be compared between copy-spelling tasks, sentence and email. Subjective workload was assessed using the NASA-TLX (Hart & Staveland, 1988). ITR, or bitrate, was calculated, based on the formula according to Wolpaw and colleagues (Wolpaw et al., 2002). The resulting value (bits/min) considers the time needed per selection, number of sequences, stimulus duration, inter-stimulus duration and pre-and post-sequence duration. Due to many different matrix sizes, the number of possible selections per trial could differ in every trial, according to the matrix size that was used for the trial (e.g., N=9 in the 3x3 matrix and N=56 in the 7x8 matrix). Thus bitrate (bits/min) was calculated for each matrix size separately. Bitrate for one task was the weighted sum of bitrates for all matrices. For example bitrate for a task with two matrices (e.g., 3x3 and 7x8) would be: bitrate (bits/min)=((Number of trials with 3x3)*(bitrate for trials on 3x3 matrix)+(Number of trials with 7x8)*(bitrate for 7x8 matrix))/number of all trials.

2.2.2.8.1.3 Satisfaction

Satisfaction was assessed using the extended QUEST (Demers et al., 2000; Zickler et al., 2011), the ATD-PA (M. J. Scherer, 2007) and VAS satisfaction (Zickler et al., 2011). End-users rated their satisfaction with the EMG vs. BCI correction with a visual analogue scale (from 0 to 10; VAS Satisfaction). For healthy participants only results of VAS satisfaction are reported.

2.2.2.8.2 Usefulness

End-users were asked in a semi-structured interview whether they could imagine using the hybrid P300 ERP BCI in their daily-lives.

2.2.2.9 EEG data analysis (ERPs)

EEG-data was analysed with Matlab (The MathWorks, MA, USA). Data was first segmented into single trials (0 to 1000ms poststimulus) and filtered between 0.1 and 30 Hz. Then target codes were enlisted manually, for every single trial (one selection) and for every subject individually. Data was then averaged for targets and non-targets. This procedure was carried out for each task separately. A negative peak for the time interval 100-250ms post-stimulus was considered as N200 component and a positive peak in the ERP in the time interval 200 to 450ms as P300 component. It is well known that the P300 is distributed over centro-parietal regions with highest amplitudes over midline scalp sites, therefore P300 amplitudes were calculated for the Cz electrode (Sutton, Braren, Zubin, & John, 1965). Since the N200 component is predominant at parieto-occipital, electrode Oz is considered for analysis (Patel & Azzam, 2005; Treder & Blankertz, 2010).

2.2.2.10 Statistical analysis

For statistical analysis IBM SPSS Statistics 22 was used. EEG data was tested for normal distribution with the Kolmogorow-Smirnow-test. To explore differences in ERP amplitudes for the four stimulus conditions (stimulus colour: red and green; stimulus modality: grid and dot) a 2x2 repeated measure ANOVA was conducted each for the ERP components P300 (from Cz) and N200 (from Oz). Dependent t-tests were run for post-hoc comparison when necessary. To compare effectiveness (accuracy) and efficiency (ITR) across tasks repeated measures ANOVAs were computed, separately for each dependent variable. Inferential statistics were computed in healthy subjects only. For end-users, data is reported descriptively due to low sample size.

2.2.3 Results

2.2.3.1 Healthy participants

2.2.3.1.1 Event-related potentials (screening)

Event-related potentials for the four screening conditions green grid, red grid, green dot and red dot are depicted in **figure 21**. For the P300 from Cz the ANOVA yielded no significant main effect (stimulus modality: F (1,9)=0.036, p=.85; stimulus colour: F(1,9)=0.585, p=.464), however a significant interaction between stimulus colour and stimulus modality (F(1,9)=5.681, p=.041, η_p^2=.39). To specify this interaction, post hoc comparisons for red vs. green grids and red vs. green dots each were computed. To avoid alpha-inflation because of multiple test, the significance level was Bonferroni corrected and set to α=.025. Post-hoc analysis revealed that red dots elicited a significantly higher P300-amplitude compared to green dots (t(9)=2.80, p=.021); see **figure 22**. For the N200 recorded from Oz, a main effect for stimulus modality (F(1,9)=38.78, p<.001; η_p^2=.81), a main effect for stimulus colour (F(1,9)=18.69, p=.002; η_p^2=.68) and a significant interaction between stimulus modality and stimulus colour (F(1,9)=11.30, p=.008; η_p^2=.56) was found. In visual inspection a hybrid interaction can be identified, therefore, only the main effect for stimulus modality can be interpreted. To specify these effect, post hoc comparisons for dots vs. grids, for red vs. green grids and for red vs. green dots were computed each (to avoid alpha-inflation because of multiple testing, significant level was Bonferroni corrected and set to α=.017). Results revealed that grids evoked a significantly higher N200 response, compared to dots (t(9)=-6.23, p<.001). In addition the red grid elicited a significant stronger N200 compared to green grid (t(9)=-4.1, p=.003); see **figure 22**. No effect was found for red vs. green dots (t(9)=0.844, p=.42). Consequently red and green grid was used in most subjects. In only one participant red dot (subject 7) was used, see **table 15**.

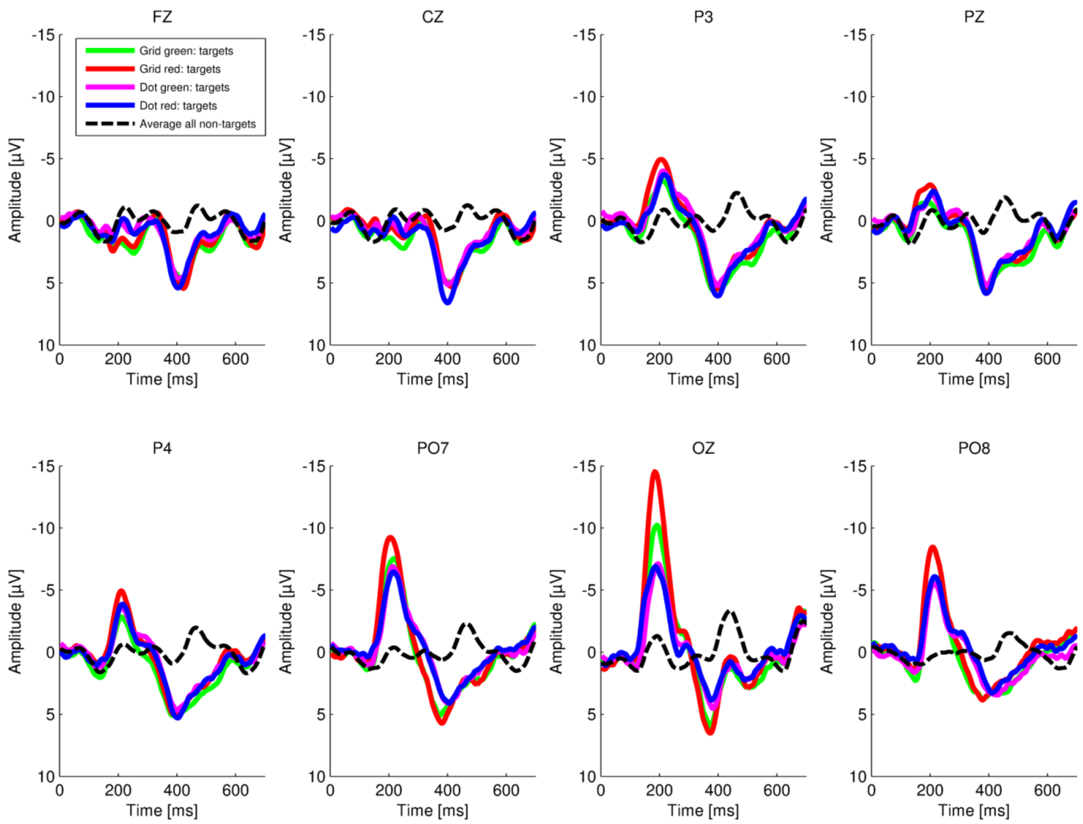


Figure 21: Event-related potentials for the screening in healthy subjects.

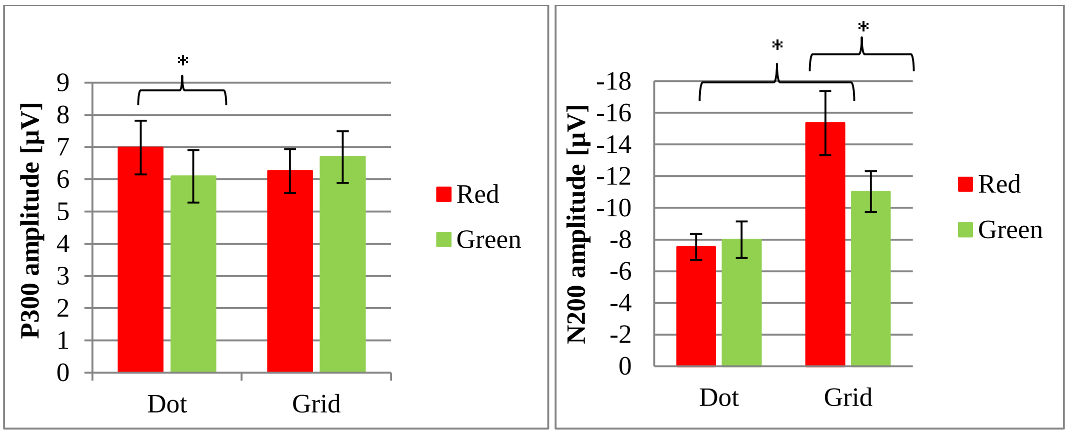


Figure 22: Amplitudes of P300 and N200 in screening condition for healthy subjects.

Left: Results for P300 from Cz; Right: Results for N200 from Oz. Note: Error bars indicate standard error of the means.

Table 15: Used stimulus condition, number of sequences in healthy participants.

Subject	Stimulus modality	Number of Sequences	EMG-threshold [mV]	
			upper threshold	lower threshold
1	green grid	2	119	75
2	green grid	6	100	62
3	red grid	3	135	80
4	red grid	3	72	39
5	red grid	4	72	45
6	green grid	3, in S3* 6	75, 65 (S3)	55, 45 (S3)
7	red dot	6	82	65
8	red grid	2	125	95
9	red grid	3	60	45
10	green grid	5	90	60

Note: *S3 = session 3. EMG-threshold: To elicit the UNDO correction, the EMG signal had to exceed the upper threshold and to fall below the lower threshold afterwards.

2.2.3.1.2 Event-related potentials (online tasks)

For comparison between online tasks both copy-spelling conditions were pooled, because no differences were expected. Repeated measures ANOVA revealed a significant main effect for the P300 component ($F(2,8)=10.31$, $p=.006$, $\eta_p^2=.72$). Post hoc comparisons for copy-spelling vs. sentence, copy-spelling vs. email and sentence vs. email were computed (due to multiple testing, significant level was Bonferroni corrected and set to $\alpha=.017$). P300 amplitudes were significantly higher in copy-spelling ($M=6.55$, $SD=3.04$) compared to sentence ($M=4.82$, $SD=2.30$, $t(9)=4.09$, $p=.003$). P300 amplitudes were again significantly higher in the sentence compared to the email ($M=2.96$, $SD=1.44$; $t(9)=3.54$, $p=.006$). Consequently P300 amplitudes were significantly higher in the copy-spelling compared to email ($t(9)=4.74$, $p=.001$), see **figure 23**. Repeated measures ANOVA for the N200 component revealed similar results ($F(2,8)=7.1$, $p=.017$, $\eta_p^2=.64$). Most pronounced N200 amplitudes were found in the copy-spelling condition, which were higher compared to the sentence, $t(9)=-3.1$, $p=.013$). N200 amplitudes in the sentence were significantly higher compared to the email task ($t(9)=-3.3$, $p=.009$), and N200 amplitudes were consequently higher in the copy-spelling compared to the email task ($t(9)=-3.98$, $p=.003$), see **figure 23**.

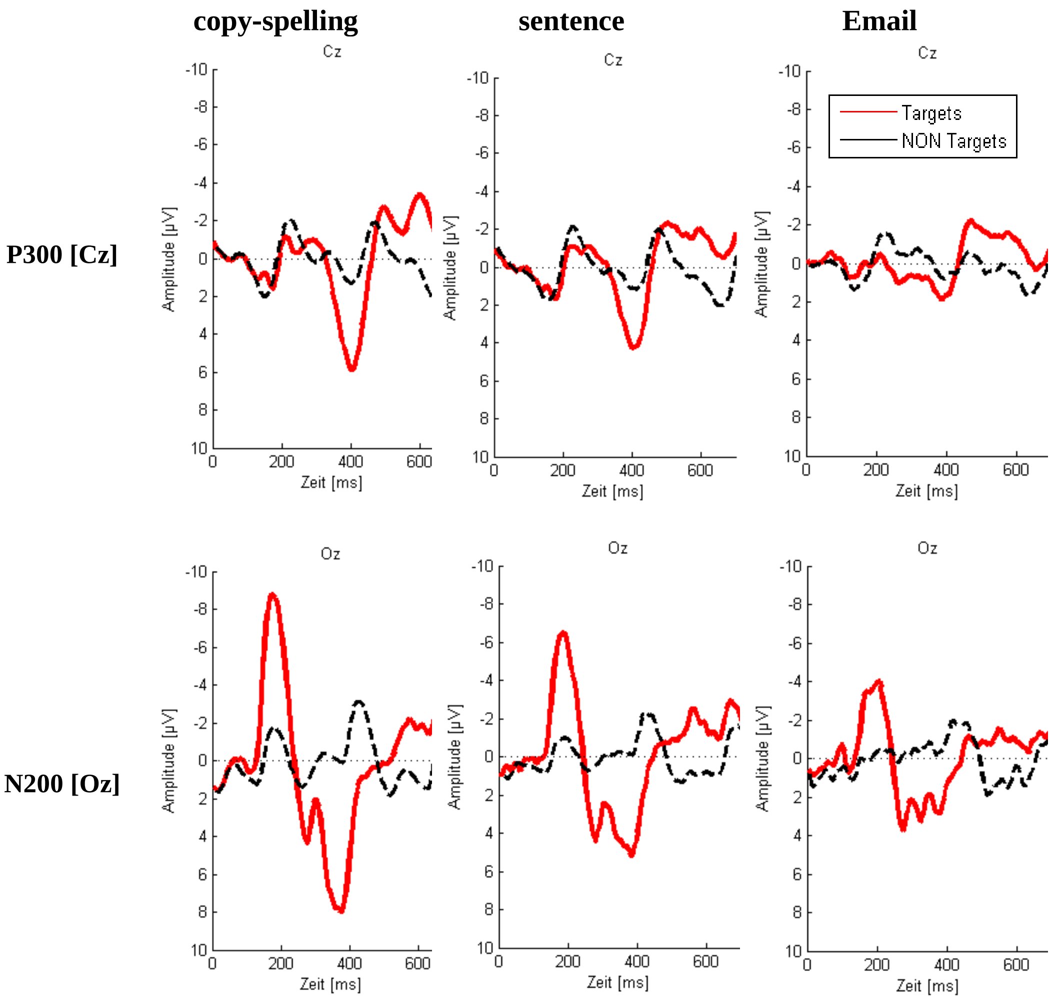


Figure 23: ERPs for healthy subjects for electrode position Cz and Oz (online tasks).

ERP plots for the copy-spelling, sentence and email task. Data from BCI-CP and Hybrid-CP was plotted together, as no differences between conditions can be expected. Note: Figure modified from Diploma thesis of Johanna Reichert.

2.2.3.1.3 Effectiveness

Participants performed best in the copy-spelling tasks with mean accuracies of *M*=94.85% (*SD*=6.5, BCI CS) and *M*=92.1% (*SD*=8.4, hybrid CS); see **table 16.** In the other two tasks, subjects' performance was higher than 80%; in the sentence *M*=84.37% (*SD*=12.03) and email *M*=83.1% (*SD*=17.7). It is noteworthy that in five participants number of sequences was less or equal than 3, one subject had 4 and one subject 5 sequences. Highest number of sequences was 6, see **table 15**. Repeated measures ANOVA comparing accuracies across all four tasks did not yield significant results ($F(2,7)=7.1$, $p=.117$). However accuracy in the both copy-spelling tasks (average of both task: *M*=93.45%) significantly differed from accuracy in the sentence/email tasks (average of both task*:* *M*=83.71%), $t(9)=-3.25$, $p=.01$.

Table 16: Accuracies, ITR and time for all online tasks for healthy participants.

Accuracy [%]					
Subject	Hybrid CS	BCI CS	Sentence %	Sentence N (Undos)	Email
1	85.0 (17/20)	95.5 (20/21)	73.1 (19/26)	4	80.0 (12/15)
2	95.0 (19/20)	73.9 (17/23)	85.0 (17/20)	3	50.0 (26/52)
3	100.0 (20/20)	91.7 (20/22)	93.8 (15/16)	1	100.0 (11/11)
4	100.0 (20/20)	95.0 (19/20)	93.3 (14/15)	0	92.3 (12/13)
5	100.0 (20/20)	100.0 (20/20)	80.0 (20/25)	3	92.9 (13/14)
6	83.5 (19/23)	90.5 (19/21)	100.0 (14/14)	0	76.5 (13/17)
7	90.0 (18/20)	82.5 (18/22)	60.0 (21/35)	5*	57.7 (30/52)
8	100.0 (20/20)	100.0 (20/20)	87.5 (14/16)	0	81.3 (13/16)
9	95.0 (19/20)	100.0 (20/20)	77.27 (17/22)	3	100.0 (13/13)
10	100.0 (20/20)	91.7 (20/22)	93.75 (15/16)	1	100.0 (11/11)
***M* (SD)**	**94.85 (6.5)**	**92.1 (8.4)**	**84.37 (12.03)**		**83.1 (17.7)**

Total time [s]				
Subject	Hybrid CS	BCI CS	Sentence	Email
1	122.4	139.0	272.2	126.1
2	257.4	310.6	442.3	731.3
3	156.2	186.9	233.3	112.9
4	156.1	169.9	229.9	133.5
5	189.9	207.4	408.9	155.0
6	181.6	178.3	348.1	249.3
7	257.4	310.6	699.2	748.9
8	122.4	132.4	188.1	133.9
9	156.1	169.9	296.9	136.6
10	223.6	269.4	330.9	142.2
***M* (*SD*)**	**182.3 (49.8)**	**207.4 (66.3)**	**345.0 (148.0)**	**267.0 (252.2)**

Information transfer tate [bits/min]				
Subject	Hybrid CS	BCI CS	Sentence	Email
1	21.2	26.7	14.1	14.7
2	11.6	7.7	9.3	2.8
3	22.3	18.9	18.9	19.9
4	22.3	20.1	18.9	16.2
5	18.0	18.0	11.2	14.9
6	15.7	18.5	20.4	6.9
7	10.4	9.2	4.1	4.2
8	29.4	29.4	22.9	14.6
9	19.9	22.3	12.3	20.1
10	15.1	12.8	13.1	15.0
***M* (*SD*)**	**18.59 (5.7)**	**18.36 (7.0)**	**14.53 (5.8)**	**12.93 (6.1)**

Note: Accuracies (percentage of correct selections) for the hybrid BCI condition and for the sentence include EMG selections. * EMG UNDO was not elicited although activated by the subject.

2.2.3.1.4 Efficiency

2.2.3.1.4.1 Information transfer rate (ITR) and total time

Participants needed significantly less time for the copy-spelling with EMG-correction (*M*=182.3s), as compared to the copy-spelling with BCI-correction (*M*=207.4s), *t*(9)=-4.04, *p*=.003). Repeated measures ANOVA revealed that ITR significantly differed across the four tasks, *F*(3,7)=8.58, *p*=.01, η_p^2=.79). To explore this effect, post hoc comparisons for all possible combinations were computed (6 pairs; to avoid α inflation due to multiple testing, significant level was Bonferroni corrected and set to α=.008). Post-hoc comparisons revealed that ITR was significantly higher in the hybrid copy-spelling (*M*=18.36) as compared to the sentence (*M*=14.53; *t*(9)=3.45, *p*=.007) and email (*M*=12,93; *t*(9)=3.93, *p*=.003) task. Other comparisons were not significant. See **table 16** for time per task and ITR.

2.2.3.1.4.2 Subjective workload (NASA-TLX)

Total workload was slightly lower in the hybrid copy-spelling task (*M*=46.33, *S*D=19.61**)** and highest in the sentence task (*M*=57.80, *SD*=18.87). However repeated measures ANOVA did not reveal significant differences in the total workload across all four tasks (*F*(3,7)=2.86, *p*=.11, η_p^2=.55). Repeated measures ANOVA with the factor dimension (mental demand, physical demand, temporal demand, performance, effort and frustration) yielded a significant main effect (*F*(5,5)=6.46, *p*=.03, η_p^2=.87). This effect was explored in post-hoc analysis (15 pairs; to avoid α inflation due to multiple testing, significant level was Bonferroni corrected and set to α=.003). Post-hoc analysis revealed that ratings for mental workload (*M*=20.83, *SD*=9.03) were higher as compared to all other dimensions (except for dimension effort (*M*=11.60, *SD*=6.52). Furthermore effort was significantly higher than frustration (*M*=2.67, *SD*=3.83; *t*(9)=4.02, *p*<.003), see **table 17**.

Table 17: Subjective Workload (NASA-TLX) for healthy participants.

	Subjective Workload (NASA-TLX)						
task	**M**	**P**	**T**	**PE**	**E**	**F**	**WL**
Hybrid CS	18.53 (10.50)	4.20 (6.20)	6.17 (5.19)	4.13 (2.94)	10.93 (8.48)	2.37 (3.6)	**46.33 (19.61)**
BCI CS	20.50 (9.39)	4.87 (6.96)	7.97 (7.77)	4.77 (3.67)	10.93 6.49)	1.50 (2.62)	**50.53 (17.42)**
Sentence	22.87 (7.80)	5.93 (6.09)	7.17 (6.46)	5.53 (5.15)	12.97 (6.55)	3.33 (3.89)	**57.80 (18.87)**
Email	21.43 (9.22)	5.77 (6.03)	5.30 (6.04)	4.20 (2.94)	11.57 (5.92)	3.50 (5.54)	**51.77 (19.67)**
Total	**20.83 (9.03)**	**5.19 (6.11)**	**6.65 (5.57)**	**4.66 (3.00)**	**11.60(6.52)**	**2.67 (3.83)**	

Note: M=mental demand, P=physical demand, T=temporal demand, PE=performance, E=effort, F=frustration, WL=total workload.

2.2.3.1.5 VAS satisfaction

Repeated measures ANOVA revealed no significant effects for VAS satisfaction across the four tasks, ($F(3,7)=3.21$, $p=.09$, $\eta_p^2=.58$), see **table 18**. Subjects indicated higher satisfaction for the EMG correction ($M=7.6$, $SD=2.8$) than for the BCI correction ($M=5.6$, $SD=2.4$), however this difference was not significant ($t(9)=1.63$, $p=.14$).

Table 18: VAS Satisfaction for healthy participants.

	VAS satisfaction					
Subject	**CS EMG**	**CS BCI**	**Sentence**	**Email**	**EMG corr**	**BCI corr**
1	8.3	10	6.5	7.9	10	8.6
2	7.4	5.5	6.3	4.8	7.1	3.0
3	8.3	8.6	3.5	8.8	7.7	4.8
4	6.7	8.8	7.1	7.1	7.7	9.2
5	8.5	8.5	6.7	7.4	9.5	5.4
6	5.1	5.7	3.4	3.1	2.2	4.1
7	7.8	8.0	5.5	4.9	10	6.7
8	6.7	7.8	7.1	7	9.1	3.2
9	8.5	8.5	7.7	8.8	2.9	8.2
10	8.1	6.4	6.8	9.8	9.4	3.2
***M* (SD)**	**7.5 (1.1)**	**7.8 (1.5)**	**6.1 (1.5)**	**7.0 (2.1)**	**7.6 (2.8)**	**5.6 (2.4)**

Note: EMG/BCI corr=EMG/BCI correction.

2.2.3.2 End-users

2.2.3.2.1 Event-related potentials (screening)

In end-users A and C red grid pronounced largest P300 amplitudes and was consequently used for the online tasks. For end-users B and D highest amplitudes were found for red grid, however contrary as expected from ERP deflections (P300 and N200), red dot (end-user B) and green dot (end-user D) was selected as best class-differentiating condition by the cross-validation tool and therefore taken for online tasks (see **figures 24** and **25**). This can be explained by the fact that the cross-validation procedure does not only take the largest N200 and P300 amplitudes into account, but any difference in the signal that differentiates consistently between targets and non-targets. It is thus possible, that for end-user D large P300 and N200 amplitudes were pronounced in the red grid condition, but unreliably (only for few trials), but in the green dot condition stable components were reliably detected, however with lower amplitude. Note that the architecture of the ERPs differs compared to healthy participants. Whereas a P300 component is found for all end-users, a N200 component is not or it is difficult to identify as such. Only in end-user D a pronounced N200 for the target stimuli compared to the non-targets can be found. In three of four end-users number of sequences was lower than 10. For end-user B one sequence had to be added in the second online task session (to reach 100% in the test word). Number of sequences, individual stimulus modalities and EMG thresholds are depicted in **table 19**.

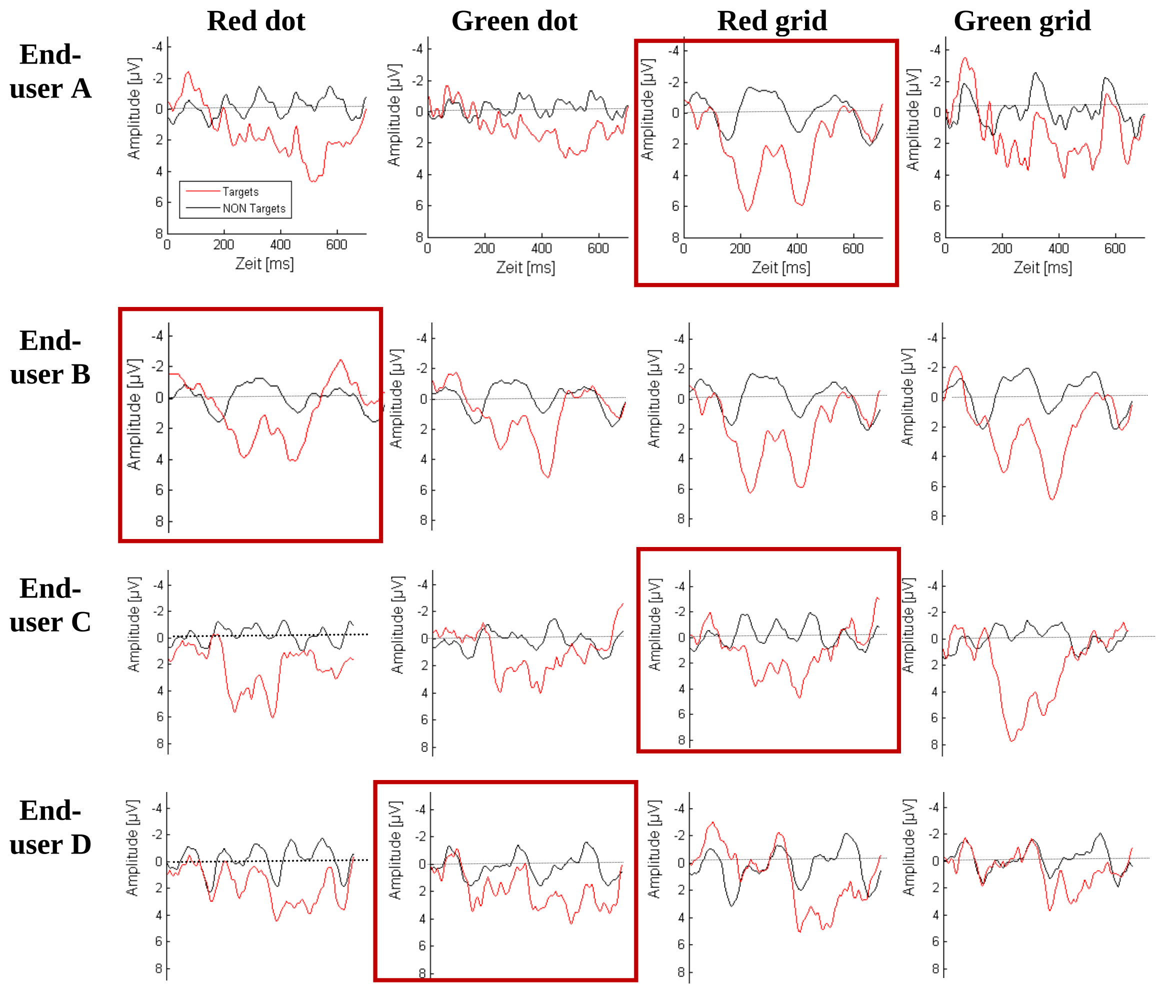


Figure 24: ERPs from electrode Cz for the end-users in the screening.

ERPs for each of the four stimulation modalities: red dot, green dot, red grid, green grid. Red rectangles indicate selected stimulus modality for each user. Note: Figure modified from Diploma thesis of Johanna Reichert.

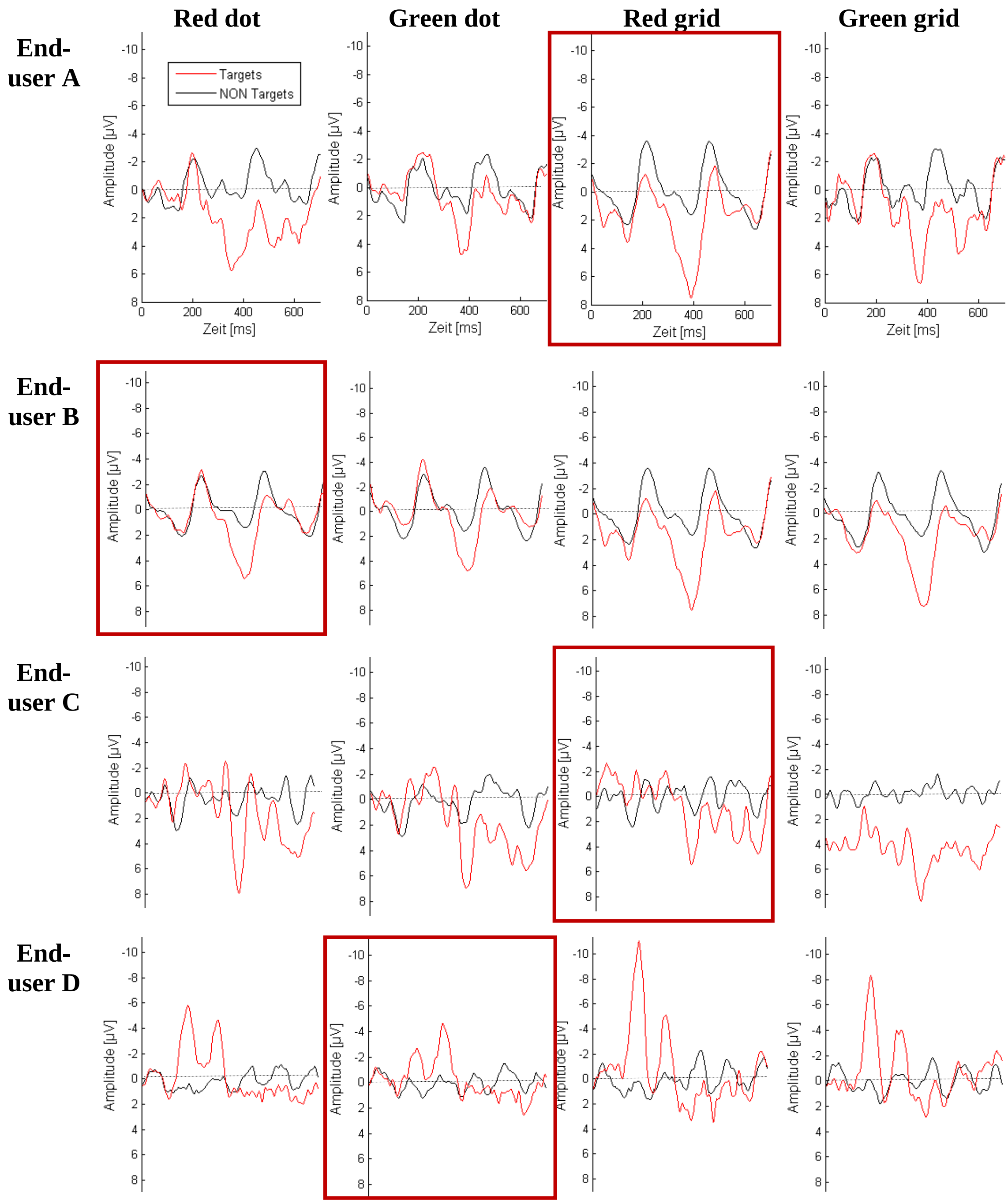


Figure 25: ERPs from electrode Oz for the end-users in the screening.

ERPs for each of the four stimulation modalities: red dot, green dot, red grid, green grid. Red rectangles indicate selected stimulus modality for each user. Note: Figure modified from Diploma thesis of Johanna Reichert.

Table 19: Stimulus modality, number of sequences and EMG thresholds.

	Stimulus modality	Number of sequences	EMG-threshold [mV]	
			upper threshold	lower threshold
End-user A	red grid	5	135	80
End-user B	red dot	6; 7 (S3)	11	7
End-user C	red grid	9	37	20
End-user D	green dot	10	44	26

2.2.3.2.2 Depression, quality of life and motivation

Assessment of depression revealed no prevalent depression for end-users A, B and C, however a slight depression for end-user D (cut-off=23), see **table 20**. All end-users rated their quality of life high (range: 64.17-76.34). ACSA scores for general individual well-being of the end-users were A: 3, B: 3, C: 2, D: -2, and thus in the middle range (minimum: -5, maximum: 5). All end-users were highly motivated throughout testing sessions (range: 6.5-10), see **table 20**.

Table 20: Emotional and motivational status of the end-users.

Emotional and motivational status				
	End-user A	**End-user B**	**End-user C**	**End-user D**
Depression and quality of life				
Quality of life	64.17	70	68.8	76.34
ACSA	3	3	2	-2
CES-D	3	9	12	25
VAS motivation				
S1	9	7.5	7.5	10
S2	9	8	6.5	10
S3	9	8	7	10
M	**9**	**7.8**	**7**	**10**

Note: *M*=Mean.

2.2.3.2.3 Effectiveness

All end-users achieved accuracies above 80% in the copy-spelling tasks and above 78% in the sentence task (see **table 21**). Email was most challenging for the end-users, same as for healthy participants, as can be seen in the lower accuracies (end-user B: 86%; end-user C: 68% and end-user D: 48%). End-user A had the highest accuracy (100%) in all four tasks. End-user D had lowest accuracies, between 48% and 95%. Her performance depended strongly on her physical state; email session had to be terminated due to high exhaustion.

Table 21: Accuracy, time per task and ITR for all four tasks for the end-users.

task	End-user A	End-user B	End-user C	End-user D
		Accuracy [%]		
Hybrid CS	100 (20/20)	90.0 (18/20)	100 (20/20)	80 (16/20)
BCI CS	100 (20/20)	100 (20/20)	100 (20/20)	95 (19/20)
Sentence (Number of EMGs)	100 (14/14) (0)	82 (18/22) (4*)	78 (18/23) (2)	80.0 (20/25) (0)
Email	100 (11/11)	86 (12/14)	68 (21/31)	48** (34/71)
		Total time per task [ms]		
Hybrid CS	223.63	257.39	358.64	392.40
BCI CS	244.90	282.38	394.92	432.38
Sentence	302.95	533.92	687.91	831.58
Email	142.25	230.86	739.19	1781.55**
		Information transfer rate [bits/min]		
Hybrid CS	15.1	10.6	9.1	5.6
BCI CS	15.1	13.0	9.1	7.5
Sentence	15.0	11.6	5.5	5.9
Email	15.1	8.2	4.6	2.6**

Note: * = 3 of 4 EMG-UNDOs were unintentionally elicited. ** = task had to be terminated before end due to exhaustion of the end-user. ITR in the hybrid condition solely includes BCI data, because EMG-selection cannot be considered.

2.2.3.2.4 Efficiency

2.2.3.2.4.1 Total time and information transfer rate (ITR)

As depicted in **table 21**, all end-users needed less time to complete the copy-spelling tasks with the EMG-correction, as compared to BCI-correction. This difference was especially higher for end-users, who had a high number of sequences. It is important to note that end-user B selected the EMG-UNDO function three times unintentionally. Highest ITRs were reached in the copy-spelling tasks (up to 15.1 bits/min). As accuracy was lower, three end-users had lower ITRs in the email tasks, compared to all other tasks (2.6 to 8.2 bits/min).

2.2.3.2.4.2 Subjective workload (NASA-TLX)

Overall subjective workload was low to moderate (*M*=13-50). End-users B, C and D experienced highest workload in the email task (B:60, C:56, D:60) and lowest workload in the copy-spelling task with EMG correction (B:22, C:41, D:33). End-user A indicated very low experienced workload across all tasks. In end-user B and D mental demand contributed most to their subjective workload, in end-user A temporal demand and in end-user C effort, respectively (see **table 22**).

Table 22: Subjective workload (NASA-TLX) for the end-users.

Subjective Workload (NASA-TLX)							
	M	**P**	**T**	**PE**	**E**	**F**	**WL**
End-user A							
Hybrid CS	2	1	13	1	2	0	**19**
BCI CS	3	1	3	1	2	0	**10**
Sentence	1	1	7	2	1	1	**13**
Email	0	1	4	1	1	3	**10**
M	**2**	**1**	**7**	**1**	**2**	**1**	**13**
End-user B							
Hybrid CS	10	2	4	3	3	1	**22**
BCI CS	10	0	8	1	6	0	**26**
Sentence	11	3	13	2	3	0	**32**
Email	23	3	6	16	12	0	**60**
M	**14**	**2**	**8**	**6**	**6**	**0**	**35**
End-user C							
Hybrid CS	3	0	8	5	22	3	**41**
BCI CS	3	0	5	8	25	5	**46**
Sentence	2	0	6	8	25	13	**55**
Email	3	0	5	10	25	13	**56**
M	**3**	**0**	**6**	**8**	**24**	**9**	**50**
End-user D							
Hybrid CS	13	8	3	4	5	0	**33**
BCI CS	13	11	1	1	8	0	**35**
Sentence	27	8	5	10	8	0	**58**
Email	23	3	6	16	12	0	**60**
M	**19**	**8**	**4**	**8**	**8**	**0**	**47**

Note: M=mental demand, P=physical demand, T=temporal demand, PE=performance, E=effort, F=frustration, WL=total workload; Total workload ranges from 0 to 100 with 100 for highest workload; *M*=Mean.

2.2.3.2.5 Satisfaction

2.2.3.2.5.1 Satisfaction with the BCI device (extended QUEST)

Overall, end-users A and D were highly satisfied with the BCI (4.13 and 4; added items: 4.25 and 4.5), end-users B and C were moderately satisfied (3.63 and 3.75; added items 3.75 and 3.0), see **table 23**. End-users were least satisfied with the adjustment (*M*=3.25 of 5), effectiveness (*M*=3.25 of 5), aesthetic design (*M*=3 of 5), speed (*M*=3.5 of 5), comfort (*M*=3.5 of 5) and dimensions (*M*=3.5 of 5), see **table 24** for individual comments. Highest satisfaction was provided for weight (*M*=4 of 5), safety (*M*=5 of 5), professional services (*M*=4.5 of 5), and learnability (*M*=4.75 of 5). Ease of use was rated higher as in the first prototype (*M*=4 vs. *M*=3.58). End-user B, who tested also the first prototype, indicated that the new EEG cap (with active electrodes, transparent gel) is better than the one used in the first study by Zickler and colleagues (2011; passive EEG electrodes, abrasive gel), but for him the improvements in terms of speed are not overwhelming and need to be improved further. End-user C indicated as well that the active electrode cap is much more usable due to the easier to set-up, better comfort and "nicer" design. Effectiveness was indicated as most important item (4 times), followed by reliability (3 times), ease of use (2 times) and speed (2 times), see **figure 26**.

Table 23: Satisfaction with the BCI device (extended QUEST).

Satisfaction with BCI device (extended QUEST)					
	End-user A	**End-user B**	**End-user C**	**End-user D**	***M***
1: Dimensions	3	4	4	3	**3.5**
2: Weight	4	4	4	4	**4**
3: Adjustment	4	2	3	4	**3.25**
4: Safety	5	5	5	5	**5**
5: Comfort	4	3	3	4	**3.5**
6: Ease of use	5	4	4	3	**4**
7: Effectiveness	4	3	2	4	**3.25**
8: Prof. services	4	4	5	5	**4.5**
QUEST total score	**4.13**	**3.63**	**3.75**	**4**	**3.88**
9: Reliability	5	5	3	4	**4.25**
10: Speed	4	3	2	5	**3.5**
11: Learnability	4	5	5	5	**4.75**
12: Aesthetic design	4	2	2	4	**3.00**
Added items score	**4.25**	**3.75**	**3**	**4.5**	**3.88**

Note: *M*=mean of scores; 1=not satisfied at all, 2=not very satisfied, 3=more or less satisfied, 4=quite satisfied, 5=very satisfied.

Table 24: Individual statements indicated in the extended QUEST.

Satisfaction with BCI device (extended QUEST)	
scale	**Individual statements by end-users (N=4)**
1: Dimensions	"*Should be smaller, without cables*" (B); "*Without cables; for EMG: one clip like for blood pressure would be good*"(A)
3: Adjustment	"*Better than electrodes before (passive), gel doesn't bother me, but cables disturb, installation of software is complex*" (A); "*Adjustment of cap takes very long, you have to be very precise (find good position). Hardware should be in one device. Adjustment of EMG takes too long, you have to be very precise to find the muscle*" (B); "*Adjustment of cap is complex and takes too long, difficult for a novice*" (D); "*Adjustment takes time and can be erroneous (e.g., positioning of the electrodes). Suggestion: A helmet with integrated electrodes and adjusted for the individual form of the head. But electrodes are better than the old electrodes (passive), because every electrode had to be checked (impedance check); Adjustment of EMG was ok*" (C)
5: Comfort	"*Comfort ok*" (B); "*It didn't hurt. Only cables were disturbing*." (A); "*Washing of the hair afterwards is annoying, cables disturb and mobility is restricted*" (D); "*Would be more comfortable with less cables. It doesn't hurt, but you sweat very fast. Use in the public would be strange, because people would stare at the user.*" (C)
6: Ease of use	"*In my case it very depends on my physical condition/concentration, which varies per day, but this is also the case for other AT (keyboard)*" (D); "*You don't need high intellectual capacities, but you need to be very concentrated, this is not always easy*" (C); "*It was easy to use*" (A); "*For me it was easy. You only need to count and concentrate*" (B)
7: Effectiveness	"*Would be more effective, when dots would be more separated in space/not to be so close to each other*" (D); "*The BCI works, but it is extremely exhausting and time-consuming to reach the intended goal*" (C); "*Should be faster, less sequences would be okay*" (A); "*Too slow, if less sequences, then more effective for me, because communication would be faster. In text-matrix too slow; for email lower speed okay*" (B)
9: Reliability	"*Everything ok*" (B); "*I would need more practical experience with the BCI to evaluate this*" (C)
10: Speed	"*Too slow, 1-3 Sequences would be okay for text-entry, for the email it can be slower*" (B); "*Takes too long for real communication or for writing longer sentences/text*" (C); "*Need to be faster, 4 or 5 flashes ok (2-3 sequences)*" (A); "*It was alright*" (D)
11: Learnability	"*It was easy*" (D); "*Not challenging, easy*" (B)
12: Aesthetic design	"*Doesn't look aesthetic. Most people probably wouldn't like to have many cables and electronic devices at one's body. Looks like a cyborg, who finds cyborgs handsome*?" (C); "*Cap looks unaesthetic/ medical/like in hospital. Symbols of QL program look infantile and sometimes not intuitive*" (B); "*Cap could be nicer, looks like bathing cap*" (D); "*For home-use or work I don't care about the aesthetic design, however in town it would be less acceptable*" (A)

Note: No comments for weight, safety and prof. services.

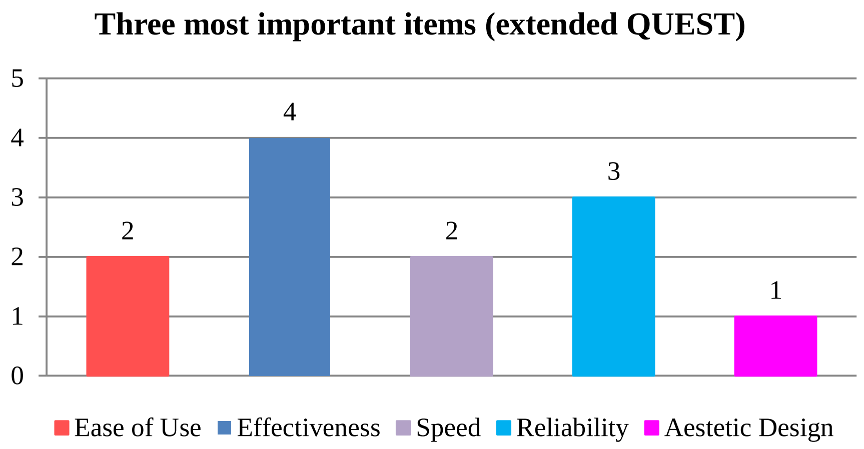


Figure 26: Three most important items (extended QUEST) in hybrid ERP BCI.

2.2.3.2.5.2 VAS satisfaction

Overall satisfaction with the BCI was high in three end-users (*M*=7.25-8.88) and moderate in one end-user (*M*=5.5), see **table 25**. End-user D was least satisfied with the email (*M*=5.0), compared to the other tasks (*M*=7.0-9.0). End-users were highly satisfied with both letter correction methods (BCI: *M*=8.25, EMG: *M*=8.50). End-user B stated "*EMG-electrodes are not comfortable in the face, but it worked fine*" and "*Same satisfaction rating for BCI as for EMG, however I would rather use BCI correction, because EMG is not logically to me, although it is faster. If I can still move any muscle, I wouldn't use a BCI. But if I could not any longer, then I would use a BCI.*"

Table 25: Results of VAS satisfaction for the end-users.

	VAS satisfaction				
	End-user A	**End-user B**	**End-user C**	**End-user D**	***M***
CS EMG	9.0	7.0	6.0	7.0	7.25
CS BCI	9.0	7.0	6.0	9.0	7.75
Sentence	9.0	7.0	5.0	8.0	7.25
Email	8.5	8.0	5.0	5.0	6.63
Total	**8.88**	**7.25**	**5.5**	**7.25**	**7.22**
EMG correction	9.5	8.0	7.5	9.0	8.50
BCI correction	9.0	8.0	6.0	10.0	8.25

Note: *M*=mean over N=4 end-users, and total=mean over all four tasks per end-user.

2.2.3.2.5.3 Match between person and technology (ATD-PA)

None of the end-users had a good match with the BCI. With scores between 3.42 and 3.64 three end-users (A, B, D) had a moderate match with indications for improvements. One end-user (C) indicated a non-match with the BCI (B: 2.33), indicating risk for BCI non-use, see **table 26**. The item "*The supports, assistance and accommodations exist for successful use of this device*" was indicated as most important.

Table 26: Match between person and technology (ATD-PA).

Assistive Technology Device Predisposition Assessment (ATD-PA)					
		End-user A	**End-user B**	**End-user C**	**End-user D**
A	This device will help me to achieve my goals.	4*	2	1	3*
B	This device will benefit me and improve my quality of life.	2*	2	1	2
C	I am confident I know how to use this device and its various features.	5	5*	4*	5
D	I will feel more secure (safe, sure of myself) when using this device.	1	0	2	0
E	This device will fit well with my accustomed routine.	2	3	1	4*
F	I have the capabilities and stamina to use this device without discomfort, stress and fatigue.	5*	5*	3	4
G	The supports, assistance and accommodations exist for successful use of this device.	5	4*	4*	2*
H	This device will physically fit in all desired environments (car, living room, etc.).	4	3	5*	4
I	I will feel comfortable (and *not* self-conscious) using this device around family	4	5	3	4
J	I will feel comfortable (and *not* self-conscious) using this device around friends	4	4	2	4
K	I will feel comfortable (and *not* self-conscious) using this device at school or work.	4	3	1	4
L	I will feel comfortable (and *not* self-conscious) using this device around the community.	1	2	1	4
	Total Score (A-L)	**3.42**	**3.45**	**2.33**	**3.64**

Note: 5=All the time (100% of the time); 4=Often (around 75% of the time); 3=Half the time, neutral (about 50% of the time); 2=Sometimes (around 25% of the time); 1=Not at all (0% of the time); 0=Not applicable,"*" indicates the three most important items.

2.2.3.2.6 Usefulness

Most of the end-users could not imagine to use the BCI in their daily-life. Only end-user D could imagine to use the BCI three times per week, however she was not sure, whether she would have the support by the caregivers. She indicated that the software is very complex and that it will be very difficult and time-consuming for the caregivers if they had to set it up regularly. End-user B stated "*No, only if I am in need. With my recent system (Wergen system) I can do 70 to 80 selections per minute! It is not an alternative to my recent AT, which is faster and more effective, BCI is not competitive. BCI would need to be improved, especially in terms of speed*". End-user C stated: "*If I were not able to use a mouse or joystick, I would first try the eye-gaze/eye-tracking system. The model that I tried once was definitely superior (compared to BCI). If I couldn't use any eye-tracking system and nor any other control systems, I would definitely use a BCI. In short: I would only use a BCI, if I could no longer operate any other assistive device*".

2.2.4 Discussion

The present study investigated the usability of a new hybrid P300-ERP BCI for communication that is the second version of the prototype tested by end-users in a previous study (Zickler et al., 2011). Usability was evaluated according to the UCD and on the basis of the BCI adapted metrics (Kübler et al., 2014; Zickler et al., 2011). Furthermore usefulness (considered daily-life use) was explored.

2.2.4.1 Depression, quality of life and motivation

No prevalent depression for three end-users, however a slight depression for one end-user (end-user D) was assessed. All end-users were highly motivated throughout the testing sessions. Thus it cannot be expected that motivation influenced BCI performances in a negative way in all end-users, neither general affective state in three end-users. However for end-user D, it cannot be excluded that depression related concentration or attention impairment influenced BCI learning and performance. All four end-users rated their quality of life high; and comparable to people without chronic disease (Lhussier et al., 2005; O'Boyle et al., 2000); in line with (Bromberg & Forshew, 2002; Fegg et al., 2005). Scores for general individual well-being of the end-users were in the range of healthy subjects and locked-in patients (Bruno et al., 2011).

2.2.4.2 Usability

2.2.4.2.1 Effectiveness

All end-users obtained accuracies above 78% in the copy-spelling and free-spelling tasks (sentence), in line with findings of other studies (Sellers & Donchin, 2006; Sellers et al., 2014;

Zickler et al., 2011), and sufficient for satisfactory communication (Kübler, Neumann, et al., 2001; Kübler et al., 2004). Effectiveness in the copy-spelling tasks was comparable to effectiveness in healthy participants, who had mean accuracies of 94.85% and 92% in both copy spelling tasks and mean accuracy of 84.37% in the free-spelling task, indicating that the user-centred adaptation of optimized stimulation mode can enhance performance in the target group; as shown also for famous face-stimulation (Kaufmann, Schulz, et al., 2011; Kaufmann, Schulz, et al., 2013). However results can only be compared with caution, because healthy participants had less number of sequences than end-users. The study with healthy participants revealed that stimulation modality matters. The effect of grids stimulation on the N200 component was remarkably and it improved signal to noise ratio, and consequently effectiveness impressively. In end-users grids also elicited a large N200 response, however grids were not the best stimulus modality for all end-users. In two of four end-users dot stimulation was identified as the best condition. These findings show that optimized stimulation modality can improve effectiveness, that findings of healthy participants cannot simply transferred to end-users and that especially for end-users individual adaptation of stimulus modality according to the user's needs and individual specifics is essential (Friedrich et al., 2013; Kaufmann, Holz, et al., 2013; Schreuder et al., 2013).

Accuracies varied strongly between subjects and tasks, in healthy as well as in end-users, but stronger in end-users. For instance one end-user had an accuracy of 100% in all tasks, however the other three end-users had much lower accuracies. For both, healthy and end-users, accuracy was lower in the more complex tasks (sentence and email), as compared to the copy-spelling tasks. This indicates that it was more challenging to select items from the standard GUI of the QW application, than from the text matrix. Users reported that they had problems selecting items in the sentence and email task, because the symbols (dot/grid) were too close to each other. For instance end-user D selected several times the line for the address of the email in the email task unintentionally. End-user C and D opened the text entry unintentionally and high effort was needed to close the text matrix again and to go back to the other functions (pause or email sending). Healthy subjects had the same problems, for example selected the pause function without purpose. High effort and more time is needed to close the pause function again (select pause symbol twice) and go back to the previous step.

Amplitude of the P300 signal was significantly reduced in the free-mode and email tasks. Lower performance in high demanding/distracting, as compared to low demanding/distracting tasks, and dimished P300 amplitude in a high workload condition, as compared to a medium workload condition has been shown by others (e.g., Käthner et al., 2014; Zickler et al., 2011). However, the drop in performance in the more complex tasks was stronger in the target group, as compared to healthy group: Two less impaired end-users received comparable results to healthy subjects, the other two end-users, who were more impaired, had lower accuracy and furthermore one of these two was unable to finish the email task, due to exhaustion. This result may be explained by the fact that end-users have impaired or only limited attentional and cognitive resources, as discussed further in general discussion (see **3.2.1.2 Intra-individual differences in performance**). Another reason that could explain lower accuracy in the sentence and email task, besides cognitive strain and workload, could be that in the email task mostly smaller matrices (e.g., 3x3) were used. This increases the target to non-target ratio and thus lower P300 amplitudes (Sellers, Krusienski, McFarland, Vaughan, & Wolpaw, 2006). In addition the contrast between background and the grids/dots was different in the email task, as compared to the copy-task and sentence task. Furthermore grids and dots were smaller in sentence and email task, for instance in the pause function or within the mask for email sending task (e.g., email address line).

2.2.4.2.2 Efficiency

Most importantly effectiveness of end-users was comparable and even slightly higher as compared to the results of Zickler et al. (2011), even though they had lower sequences. In three of four end-users number of sequences could be reduced to 5, 6 (7) and 9 instead of 10 sequences (as used as fix number in the study of Zickler et al., 2011), thus improving spelling speed. With a maximum ITR of 15.1 bits/min, ITR was thus higher as compared to the first prototype (maximum: 8.57 bits/min) or to other studies using a conventional flashing speller (Nijboer, Sellers, et al., 2008). With mean ITRs ranging between 12.93 and 18.59 bits/min, ITR of healthy participants was also higher compared to other studies with "conventional" row/column flashing speller (Münßinger et al., 2010). Spelling bitrate can thus be improved by individual adaptation of the number of sequences and optimized stimuli in the target group, which has been shown also by Kaufmann and colleagues (2013) with famous face stimulation. In the study of Kaufmann and colleagues, number of sequences could be stronger reduced and also effectiveness was higher as compared to the results in the present study. This can account for many reasons, maybe face stimulation is superior to grid/big dot stimulation. This however has not been tested yet. Another reason could be that even with optimized stimuli, in more complex tasks, further confounding factors influence performance, for instance attentional resources (see section **3.2.1.2 Intra-individual differences in performance**). More complex tasks (e.g., free-spelling or email sending), were not tested in the study by Kaufmann et al., therefore it remains unclear how end-users would have performed with face stimuli flashing in more complex tasks.

Efficiency, in terms of speed, could not only be increased by reduction of the number of sequences, but also by the hybrid approach. Results show that less time is needed in the hybrid copy-spelling condition, in which errors could be deleted with an additional EMG channel, compared to copy-spelling with the BCI only. This effect was especially evident in end-users with a high number of sequences. The EMG-channel could be used by all healthy participants and end-users, however one patient (end-user B) had some problems, as the EMG correction was three times unintentionally selected due to mimic (he was happy/smiling about a correct selection). In his case EMG had to be placed in the face, since the end-user had no sufficient residual muscular activity in his hands for eliciting an undo response. This shows that the placement of an EMG channel in the face is probably less feasible compared to placement on the hand. However healthy participants had also some problems with the EMG correction (EMG was three times unintentionally selected). But errors with the BCI correction were higher, for instance six of ten healthy participants failed to select the symbol for the BCI correction and thus the EMG correction can improve accuracy and efficiency of the BCI system; in line with (Riccio et al., 2015).

2.2.4.2.3 Satisfaction

In this second version of the P300-ERP BCI prototype, effectiveness could be improved by new improved stimuli and efficiency could be improved by adaptation of sequences and a hybrid approach. Furthermore an easy to use EEG cap with transparent gel was used and a practical pause mode was implemented. However these improvements did not or only slightly improve the acceptance of the end-users, as compared to the first study (Zickler et al., 2011). From the end-users perspective, main reasons for dissatisfaction remain, such as complicated and time-consuming adjustment, low speed and effectiveness, low comfort and the aesthetic design of the EEG cap. Concerning safety, weight, professional services and learnability, end-users were highly satisfied. Although healthy subjects tend to prefer the EMG letter correction, most of the end-users did not agree with the rationale of the hybrid approach, even though it improved efficiency: "*Same satisfaction rating for BCI as for EMG, however I would rather use BCI correction, because EMG is not logically to me, although it is faster. If I can still move any muscle, I wouldn't use a BCI. But if I couldn't not any longer, then I would use a BCI*." (end-user B). For extended discussion regarding acceptance of a hybrid BCI, see general discussion, **chapter 3.2.2.1.3.2 BCIs for communication**.

2.2.4.3 Usefulness

Most end-users indicated the speed, effectiveness and reliability as the main reasons why they would not use the BCI in their daily-life for communication purposes, because their current ATs are better and BCI is not competitive, especially in terms of speed, effectiveness and reliability. However they would use the BCI, if they were in need, as stated by end-user C: "*I would only use* *a BCI, if I could no longer operate any other assistive device*". End-user A wouldn't use the BCI because he can use a normal notebook keyboard, "*But if I were in need of a BCI, I would for sure use is, although if it were that complicated. However easier to use would be nice*". Only end-user D could imagine using the hybrid BCI, however, she doubted that she would have the support by her caregivers. She also indicated that speed "*was alright*" and that for daily-life use she would not desire any improvements *"no improvements, only a bit easier to use*". This end-user is severely disabled, almost complete paralyzed, and does not have any other competitive AT, only a slowed keyboard, that she does not use often and use is exhausting for her.

2.3 Study 3: Long-term independent home use of a P300 based brain-computer interface for creative expression improves quality of life of two paralysed artists diagnosed with amyotrophic lateral sclerosis

2.3.1 Introduction:

In the present study, a P300-ERP controlled BCI application for creative expression, called Brain Painting, was implemented at the homes of two end-users in the locked-in state. Both are artists who had gradually lost the ability to paint after being diagnosed with ALS. Brain Painting was developed and improved in an iterative UCD process (Holz et al., 2012; Kübler et al., 2008; Kübler, Holz, et al., 2013; Münßinger et al., 2010; Zickler et al., 2013; Zickler et al., 2011); see **1.4.1 UCD for evaluation of usability of BCI applications**. These studies showed that severely motor impaired end-users expressed high degree of satisfaction with the BCI device and that they would like to use it in their daily-lives. However, for daily-life use, end-users requested easier adjustment of the EEG cap and electrodes (e.g., less number of electrodes), improvements on the EEG cap (e.g., electrode gel) and higher functioning of the BCI in terms of accuracy and speed. Ease of use was indicated as most important for a BCI device and prerequisite for independent BCI home use (Zickler et al., 2013; Zickler et al., 2011). The aims of the present study were: (1) prepare the BCI for independent home use; (2) prove the concept of independent use; (3) evaluate the usability of a BCI device in independent/daily-life use (e.g., are BCIs accepted as assistive devices? How consistent and reliable and for how long can a BCI be used in daily-life?); and (4) quantify the influence of BCI on the end-users' quality of life (usefulness). To prepare Brain Painting for independent use (1) the BCI application (software) was simplified; (2) family members and caregivers were trained to set up the system; (3) an easy to set-up EEG cap with transparent electrode gel and with a few number of electrodes (8; in the previous study by Zickler et al. (2013): 16) was introduced; (4) continuous remote-supervision was provided; and (5) every session was evaluated. The herein presented BCI application accommodates for the necessities for independent BCI home use as proposed by Sellers and colleagues (Sellers et al., 2010; Vaughan et al., 2012); see **1.4.3.3 Independent use**.

2.3.2 Methods

2.3.2.1 End-users

Two end-users diagnosed with ALS were enrolled in this study (see **table 27**). Both match all inclusion criteria for independent use of a visual P300 BCI, as proposed by Vaughan and colleagues (Vaughan et al., 2012), see **1.4.3.3 Independent use**.

End-user HP is female, aged 75, and has been diagnosed with ALS (spinal form) since 2007 (see **figure 27**). She is in the locked-in state, artificially ventilated and fed, with only residual eye movement. She is able to communicate with eye-movements in the partner-scanning mode or with an eye-tracker. She lives with her family and full time caregiver. Painting was her favorite hobby. Since she had no application for creative expression, Brain Painting awoke her interest and her family contacted the Brain Painting team of the University of Würzburg. She started participating in this study in January 2012.

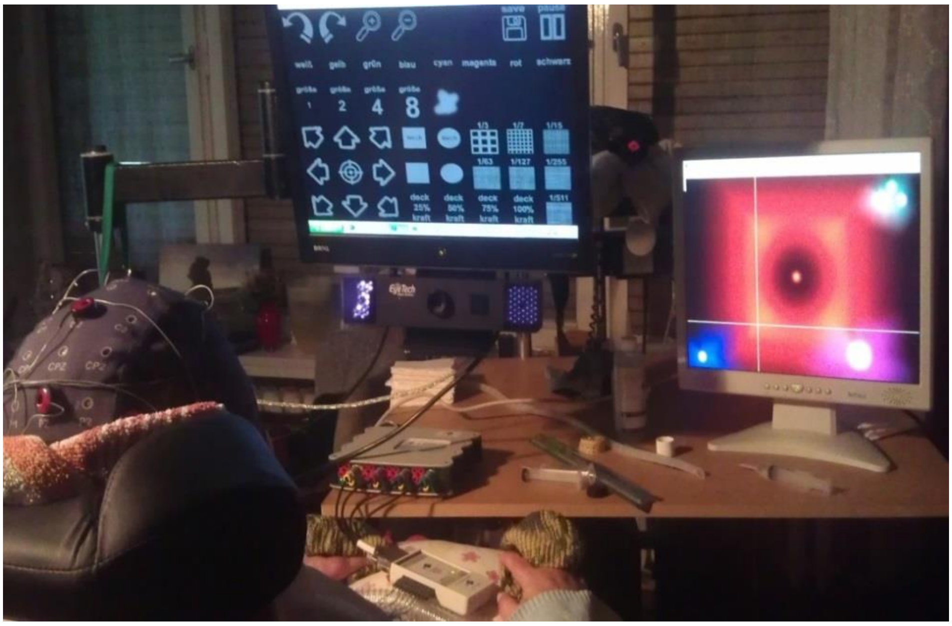


Figure 27: End-user HP during Brain Painting at her home.

While painting the Brain Painting matrix is displayed on her assistive device PC. The monitor on the right serves as digital canvas. For painting with the BCI an EEG cap with 8 active electrodes (gamma cap, and g.USBamp, both from g.tec Medical Engineering GmbH, Austria) are used. Source: Holz, E. M., Botrel, L., Kaufmann, T., & Kübler, A. (2015). Long-term independent brain-computer interface home use improves quality of life of a patient in the locked-in state: A case study. *Archives of physical medicine and rehabilitation, 96, S16-S26*, S.18.

End-user JT is male, aged 75, and has been diagnosed with ALS (spinal form) since 2006 (see **figure 28**). He is tetraplegic and has residual motor control of his head and face. At the beginning of the study (September 2013) he was still able to speak and to move his head, however after an operation in May 2014 he is only able to speak with a special cannula for his artificial ventilation. With this cannula he is able to speak only for several minutes, because ventilation is insufficient during speaking. However he is still able to move his lips, and with help of his caregivers and personal assistant words can be read from his lips or mouth movements. JT is not in use of any other assistive technology prior to BCI. He used to work as an architect, designer and artist, however with progress of disease related paralysis he was no longer able to draw or paint. His team of caregivers from GIP (Gesellschaft für medizinische Intensivpflege mbH) heard about Brain Painting in the press and contacted the Brain Painting team of the University of Würzburg. He started participating in this study in September 2013.

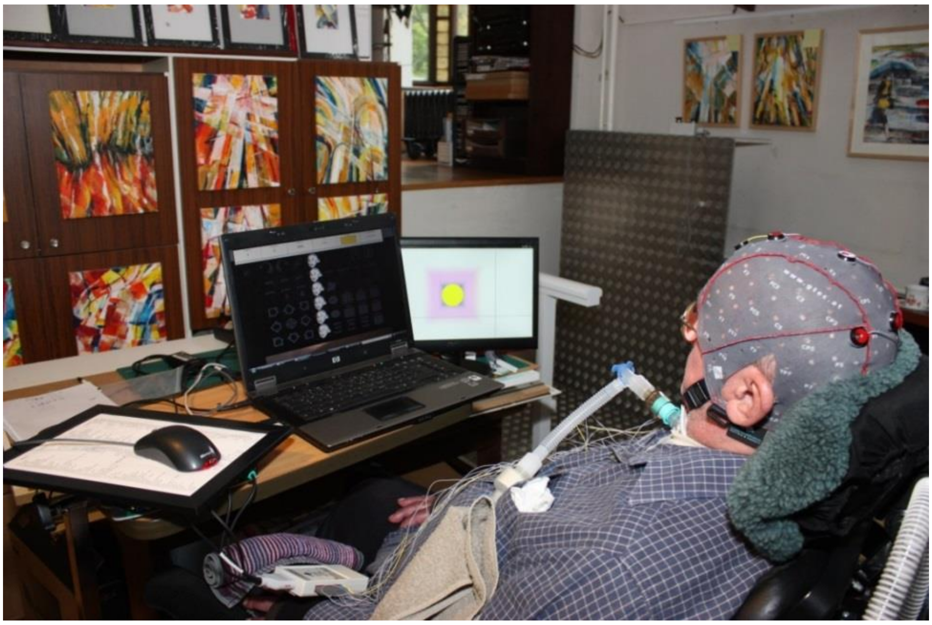


Figure 28: End-user JT while painting with the BCI in his art studio.

Source: Holz, E. M., Botrel, L., & Kübler, A. (2015). Independent home use of Brain Painting improves quality of life of two artists in the locked-in state diagnosed with amyotrophic lateral sclerosis. *Brain-Computer Interfaces, 2(2-3)*, 117-134, p. 118.

Table 27: Demographic and disease related information.

	End-user HP	End-user JT
Age	74	74
Date of diagnosis (ALS)	2007	2006
Residual muscular control	Eyes, mimic	Eyes, face, head, (speech)
Assistive devices	Electric wheelchair; eye-tracker (grid) for spelling and email/internet surfing	Electric wheelchair
Previous BCI experience	Yes (2011, P300-ERP BCI)	No
Profession	Teacher	Architect, designer, artist
Hobby	Diverse creative activities, painting	-

2.3.2.2 Easy to use Brain Painting application

In the easy to use BCI application controlled by P300 ERP the end-user is presented with a 6x8 matrix comprising 48 tools for painting and the end-user attends to the desired tool or item. The matrix flashes in rows and columns. While flashing, rows and columns are highlighted, and the item that is intended to be selected constitutes the target; it is less often highlighted as compared to all other items (non-targets). Every time the target is highlighted, a P300 response is elicited, which can be detected by the BCI. From the Brain Painting ERP matrix (see **figure 29**) the end-user can select position of cursor, shape (rectangle, circle, cloud), colour (white, yellow, green, blue, cyan, magenta, red, black), location, brush size, grid size and opacity (25%, 50%, 75%, 100%) The user can zoom in and out for working on details. A toolbox at the top of the P300 matrix displays the latest selections. The selected object is displayed on a second monitor, the digital painting canvas. Choosing the colour transfers the object to the canvas (see **figure 27** and **28**). In the present study classic flash stimulation (compare **Figure 7: P300-ERP spelling matrix**, **p. 41**) was replaced with face overlay stimulation (Einstein Brain Painting, see **figure 29**) since face stimuli increase the signal to noise ratio of the recorded event-related potentials (ERPs), thereby enhancing functioning and spelling bit rate (Kaufmann, Schulz, et al., 2011; Kaufmann, Schulz, et al., 2013). For independent use the "scientific product" Brain Painting was simplified, to enable easy handling by non-technical personnel (e.g., caregivers and family members). For that the BCI-2000 supported Brain Painting program was embedded into an interface program (Python 2.7; python.org) that enabled the user to simply open Brain Painting and automatically load individual parameters. The BCI application could be easily handled with a few clicks (e.g., open, select painting, start, end, evaluate, close). With every use, the end-user could choose a new painting or continue an existing one. Six evaluation questions and comment query were automatically presented to the end-user. There was automatically initiated transmission and storage of BCI data to a remote server for each session.

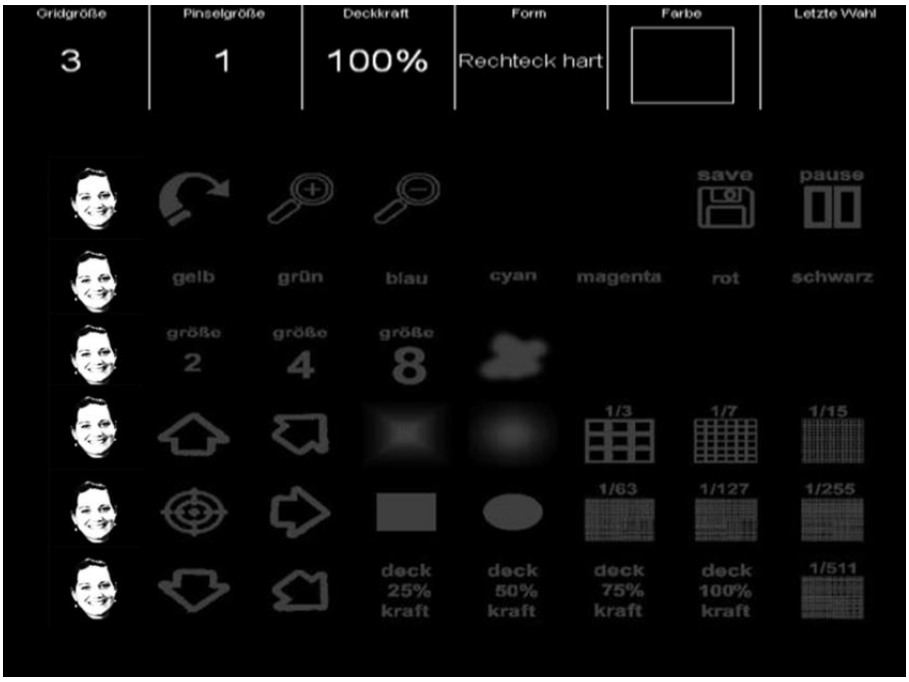


Figure 29: Brain Painting P300 matrix with face overlay stimulation.

Note: In the study the well-known face of Albert Einstein, which is not printed due to copyright issues, was used. Source: Holz, E. M., Botrel, L., Kaufmann, T., & Kübler, A. (2015). Long-term independent brain-computer interface home use improves quality of life of a patient in the locked-in state: A case study. *Archives of physical medicine and rehabilitation, 96, S16-S26*, S.18.

2.3.2.3 Onsite support at the end-users' homes

In a first meeting the Brain Painting application was installed at the end-user's home, an initial calibration was performed (calibration 1) and the family/caregivers/personal assistants were trained to set up the BCI. Throughout the study, end-users and their families or team of caregivers/assistants were using the BCI fully independently, while the BCI team was in close contact with the end-user and the family/assistants via phone and internet. BCI experts monitored BCI use on the basis of user evaluation data transmitted to a remote server. A "remote desktop" application was used enabling modifications and re-installation (e.g., after end-user received a new PC) of the program, or special requests, such as parameter modification. Number of visits (e.g., for calibration) was kept to a minimum. The BCI system was updated after 6 weeks, including extended evaluation. This was conducted using remote control. After 2 months there was a second visit to improve stability of the program. Additionally a second calibration was conducted (calibration 2). After 9 months classic flash stimulation was replaced with face overlay stimulation (Einstein Brain Painting). At the same time the system was recalibrated (calibration 3). Because the patient reported zero control after exchange of the EEG cap by the family, the BCI team visited HP for technical check-up and recalibration of the system (calibration 4; after 26 months). Calibration 1 and 2 were run using a 6x8 spelling matrix (due to software specifics (BCI-2000 version 1) calibration could not be conducted with the Brain Painting matrix). Duration of flashes was 55.5ms and inter-stimulus interval (ISI) 111.0ms; pre-run duration was 2.8s and post-run duration 1.7s. For each calibration 15 flashing sequences were set. A sequence is the flashing of every column and row of the matrix (8 columns and 6 rows), therefore the target flashes twice per sequence (30 times in 15 sequences). The first calibration included spelling of three words (BRAIN, PAINTING and POWER) using a 6x8 spelling matrix, after which a copy-spelling was performed, in which HP spelled the word BRAIN again with online feedback. After successful copy-spelling, the Brain Painting matrix was explained. Copy-painting followed and 20 indicated symbols had to be selected. Copy-spelling and copy-painting were conducted to assess online accuracy. HP had 100% accuracy after 8 flashing sequences. Taking noise/distraction into account, number of sequences was set to 10 (minimum number of flashing sequences plus 2). In the second meeting, calibration was repeated (spelling of two words, BRAIN and PAINT. Because no online test was possible in the second calibration due to exhaustion of the end-user, number of sequences was not changed. Calibration 3 and 4 were conducted using the 6x8 Brain Painting matrix. Duration of flashes was 62.5ms and ISI 125.0ms, pre-run duration was 5s and post-run duration 0s. Calibrations were conducted with 15 flashing sequences. Calibration 3 consisted of 3 runs, in which 5 items had to be selected each. One run is defined as non-interrupted painting time (from start until session pause). For example, during calibration, copy-spelling of one 5-letter word is 1 run. For calibration 3 HP reached 100% correct selections after 3 sequences (also in online test afterwards). Thus number of sequences was set to 5. In online test (two runs) the end-user performed with 100% accuracy. Calibration 4 consisted of 3 runs with 5 items each. The end-user had 100% after 2 sequences; therefore 5 sequences were set for online test, in which the end-user performed with 100% accuracy (two runs, 5 items each).

Since JT started later in this study, he received the updated and stable BCI system with implemented Einstein-face overlay stimulation. For JT the BCI system was calibrated 3 times in total. All parameters were the same as for HP. In the first calibration two runs were conducted with each 5 items that had to be selected from the Brain painting matrix. JT reached 100% offline performance after 5 sequences. Thus 7 sequences were set for online painting. He achieved online (1 run, 5 items) an accuracy of 100%. JT had no or very low BCI control around session 100, showing a very noisy EEG. After several remote supervised technical check-ups, and exchange of the BCI system, the problem persisted and JT was visited at home by the BCI experts. In this two day visit it became clear that the spikes and noise in the EEG were caused by fasciculations in the face/neck. Thus, the BCI was recalibrated (after session 111; 1 run, 5 items; calibration 2, month 11). Because these artefacts could not be filtered out online, number of flashing sequences was temporary set to 10 to improve signal to noise ratio. In the following online session (1 run, 5 items) JT had 100% accuracy. In the following free painting session (duration: 30 minutes) JT reported very good BCI control and that he was very happy to be able to paint again, albeit with lower speed. Fasciculations disappeared after several months, thus, the BCI was recalibrated (calibration 3; months 15). Two runs were conducted (5 items each) and number of sequences could be reduced again to 4 sequences. Online accuracy in the following test session was again 100%.

2.3.2.4 Signal acquisition

EEG was recorded with 8 active electrodes (gamma cap, g.tec Medical Engineering GmbH, Austria) at the scalp positions Fz, Cz, Pz, P3, P4, Po7, Po8 and Oz (Krusienski et al., 2006), according to the 10-20 system (Jasper, 1958). Recorded signals were amplified using a 16-channel g.USBamp (g.tec Medical Engineering GmbH, Austria) and processed by BCI-2000 (Schalk et al., 2004). Sampling rate was 256 Hz. A high pass filter of 0.1Hz and a low pass filter of 60Hz were used. Because g.tec did not offer a tool for impedance check-up for BCI systems comprising active gamma cap and 16-channel g.USBamp, impedances could not be measured; therefore quality of signals was visually evaluated (e.g., inspection of alpha ERD with eyes open/closed).

2.3.2.5 Classification of ERP signals

Feature selection and classification was performed using SWLDA. Calibration data was segmented between 0 and 800ms post-stimulus, decimated to 20 Hz and up to 60 features selected using a stepwise fit approach. Selected features went into the model used for classification in all online runs. A Matlab-based (The MathWorks, MA, USA) implementation of this procedure (P300-GUI, BCI2000; Schalk et al., 2004) was used.

2.3.2.6 BCI parameters for independent home use

Flashing duration and ISI were the same as for the respective calibration. Pre- and post-sequence duration - the time after one selection, in which the end-user needs to think what she/he wants to select next - varied, but was mostly (and maximally) 11s (pre-sequence: 1s and post-sequence: 10s).

2.3.2.7 Evaluation

2.3.2.7.1 Usability

Usability of the BCI in daily-life use was evaluated with the same categories as defined by Kübler and colleagues (Kübler et al., 2014; Zickler et al., 2011) and used in *studies 1* and *2,* with few modifications for independent home use. In addition usefulness of the BCI in long-term daily-life use was assessed (Vaughan et al., 2012); for details see chapter **1.4.1.2 Valid evaluation metrics (P3)**.

2.3.2.7.1.1 Effectiveness

Effectiveness in terms of the objective assessment of accuracy and completeness of this BCI-controlled application is difficult to assess in a free-painting mode, because the user decides what he or she wants to select and not all selections result in “visible” changes on the digital canvas (i.e., only if colour is selected). In the Brain Painting study by Zickler and colleagues (2013), end-users indicated in the free-painting mode, whether the selected item was correct, thus the experimenter could document correct selections and calculate (objective) accuracy for the free-spelling mode. This was however not possible in this study on independent use. Therefore accuracy was indicated by the end-users. End-users were asked to indicate their subjective level of BCI control after every BCI session, within four categories: (1) zero (0-50%), (2) low (50-70%), (3) medium (70-90%) and (4) high (90-100%) control. Furthermore end-users rated after every BCI session whether control over BCI changed during the Brain Painting session (loss of control). Rating options were (1) worse, (2) unchanged (equal) or (3) better, compared to beginning of the session.

2.3.2.7.1.2 Efficiency

Efficiency relating the costs to effectiveness (i.e., effort and time), was defined as ITR, subjective workload and level of exhaustion. A “real” ITR could not be obtained, because no objective measurement of accuracy was possible (compare *study 1* and *2*). However for reasons of comparison, ITR was estimated for accuracies between 70-100% (range of accuracy required for basic communication (Kübler, Neumann, et al., 2001). Thus results on ITR can only be interpreted with caution. Exhaustion was rated using the categories: (1) low, (2) medium or (3) high. Subjective workload was assessed with the NASA-TLX (Hart & Staveland, 1988).

2.3.2.7.1.3 Satisfaction

Satisfaction, indicating the acceptability of the BCI device, was assessed with visual analogue scales (VAS satisfaction, VAS enjoyment and VAS frustration), the extended QUEST (Demers et al., 2000; Zickler et al., 2011) and the ATD-PA (M. J. Scherer, 2007). End-user rated their satisfaction with the BCI session and their experienced frustration and enjoyment after every BCI session (0-10, 0=not at all satisfied/frustrated/no enjoyment; 10=very satisfied/frustrated/absolute enjoyment).

2.3.2.7.2 Usefulness

As suggested by Vaughan and colleagues, the number of BCI sessions, the total usage duration (painting duration) and the impact of the BCI on the life of the person were considered as indicators of usefulness of the BCI in daily-life (Vaughan et al., 2012). A BCI session was considered valid, if the end-user painted for at least several seconds. Painting duration was the time integrated across all runs per session excluding breaks. The influence of the BCI on the life of the person was measured with the PIADS (Day & Jutai, 1996; Jutai & Day, 2002).

2.3.2.8 Collection of evaluation data

The major part of the evaluation was implemented in the BCI software, such that end-users could evaluate and comment on every BCI session. Note that in the initial test phase for HP only VAS satisfaction was applied (first 8 sessions). After this proof-of-principle phase the extended evaluation was assessed (reported for sessions 9 to 352). Other questionnaires were filled out in paper & pencil version (see **table 28**). Questionnaires were answered by the end-users with the help of the family/caregivers/assistants and sent via mail to the lab. The questionnaires NASA-TLX and extended QUEST were rated after session (number of weeks in parenthesis): HP: t1=8 (4), t2=21 (8), t3=28 (11), t4=32 (13), t5=53 (22), t6=66 (26), t7=75 (31), t8=90 (38), t9=120 (47), t10=152 (54), t11=170 (58), t12=194 (64), t13=208 (67), t14=232 (78), t15=262 (100), t16=285 (115), t17=330 (146); JT: t1=13 (3), t2=44 (11), t3=73 (19), t4=90 (28), t5=96 (41), t6=118 (50). HP answered the PIADS and ATD-PA after 9 months, JT after 11 months. HP rated the PIADS for a second time at month 34.

Table 28: Evaluation metrics used for evaluation of the BCI in long-term independent use.

Metrics	How assessed	When/how often assessed
Satisfaction, frustration, enjoyment (visual analogue scales), level of exhaustion, subjective level of BCI control and loss of control	Implemented in program	Presented automatically after every session
Workload (NASA-TLX) and satisfaction (extended QUEST)	Implemented in the program, then paper & pencil version (from t3 on in HP as preferred by the end-user and her family; in JT from t1 on)	After approximately 5 to 10 *Brain Painting* sessions in the first months and after approximately 15 to 30 sessions in later months
Assistive Technology Device Predisposition Assessment (ATD-PA) and influence of the BCI on the life of the person (PIADS)	Paper & pencil	After 9 and 34 months (HP) and 11 months (JT)

2.3.2.9 Feedback by family

Family members of HP answered seven open questions such as "how long does it take to set-up the BCI?" in a self-prepared questionnaire. Note that this questionnaire was answered 10 months after implementation of the BCI at the end-users home and set-up time can be different after consolidated use (e.g., two years after implementation).

2.3.2.10 Statistical analysis

Due to low sample size, evaluation data is mostly reported descriptively. Non-parametric statistics were used, because most data was not normally distributed. To describe the development of variables over time, for each VAS scale, subjective level of BCI control and for painting duration linear and quadratic regressions were calculated and best fitting models considered for interpretation of results. To explore the relationship between VAS scales and subjective level of BCI control, Spearman correlations were calculated. To compare subjective level of BCI control for Brain Painting and Einstein Brain Painting (in HP) the first 88 sessions with Brain Painting were compared to the first 88 sessions with Einstein Brain Painting using Wilcoxon-test. Brain Painting was used within the first 96 sessions, however subjective level of BCI control was assessed only from session 9 to 96 resulting in 88 sessions. For Einstein Brain Painting session 97 to session 184 was considered for comparison.

2.3.3 Results

2.3.3.1 Reliability of ERP signals

For HP P300 response was more pronounced in calibration 2, and again increased in calibration 3 with initiation of Einstein-face stimuli, as compared to calibration 1; see **figure 30**. ERP amplitudes were decreased in calibration 4, as compared to calibration 3. For JT amplitude of P300 was also slightly decreased from calibration 1 to calibration 3; ERP at calibration 2 was noisy due to fasciculations. ERPs from end-user HP and JT are depicted in **figure 30**.

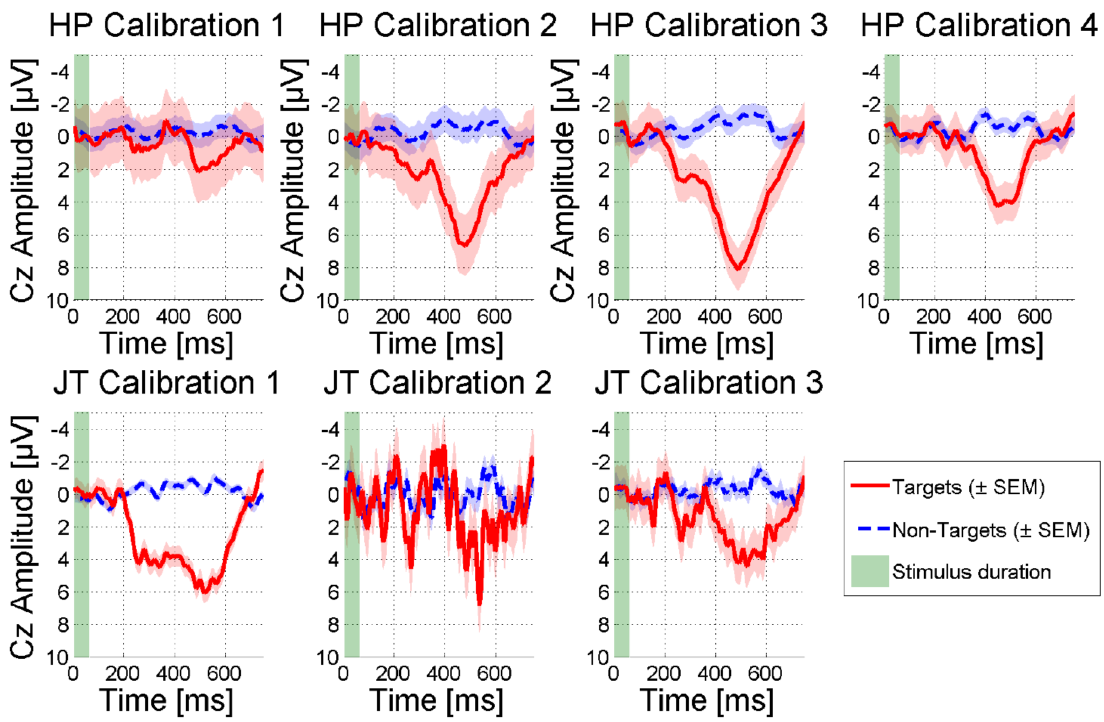


Figure 30: ERPs for Cz for calibration 1, 2, 3 and 4 (HP) and for calibration 1, 2 and 3 (JT).

HP: ERPs from electrode position Cz at calibrations 1 (at start), 2 (after 2 months), 3 (after 9 months) and 4 (after 26 months). Calibrations 1 and 2 shared the same parameters and were conducted based on a spelling 6x8 P300 matrix. Calibrations 3 and 4 were conducted with the Einstein face stimulation overlaid on the Brain Painting matrix. JT: Calibration 1 (at start), calibration 2 (11 months) and calibration 3 (15 months). All calibrations were conducted using Einstein face stimulation overlaid on the Brain Painting matrix. Red lines indicate target stimuli and blue dashed lines non-target stimuli.

2.3.3.2 Face valid measures of BCI use in daily-life

In 36 months end-user HP painted in about 352 sessions with a total painting duration of 528.10 hours and with a mean painting duration of M=90.86 minutes (SD=52.36, 0.34-230.41); see **table 29**. Painting duration of HP shows a quadratic trend over time (F(2,349)=50.21, p<.001, r^2=.22, r=.47), indicating an increasing trend within the first 200 sessions and a decreasing trend afterwards; see **figure 31**. End-user JT painted within 15 months in about 158 sessions with a total painting duration of 167.75 hours and with a mean painting duration of 63.70 minutes (SD=36.78; 2.04-148.31). Painting duration of JT slightly decreased; this linear trend is however not significant (F(1,156)=2.253, p=.14, r^2=.01, r=-.119); see **figure 32**. Mostly end-users opened one session per day (see **figure 33**).

Table 29: Study related data, number of sessions and painting duration.

	HP	**JT**
Begin of study	January 2012	September 2013
Number of visits (onsite support)	4	3
Number of calibrations	4	3
Number of sessions	352	158
Months since start (time of analysis)	36	15
Mean painting duration (minutes)	90.86	63.70
Total painting duration (hours)	528.10	167.75

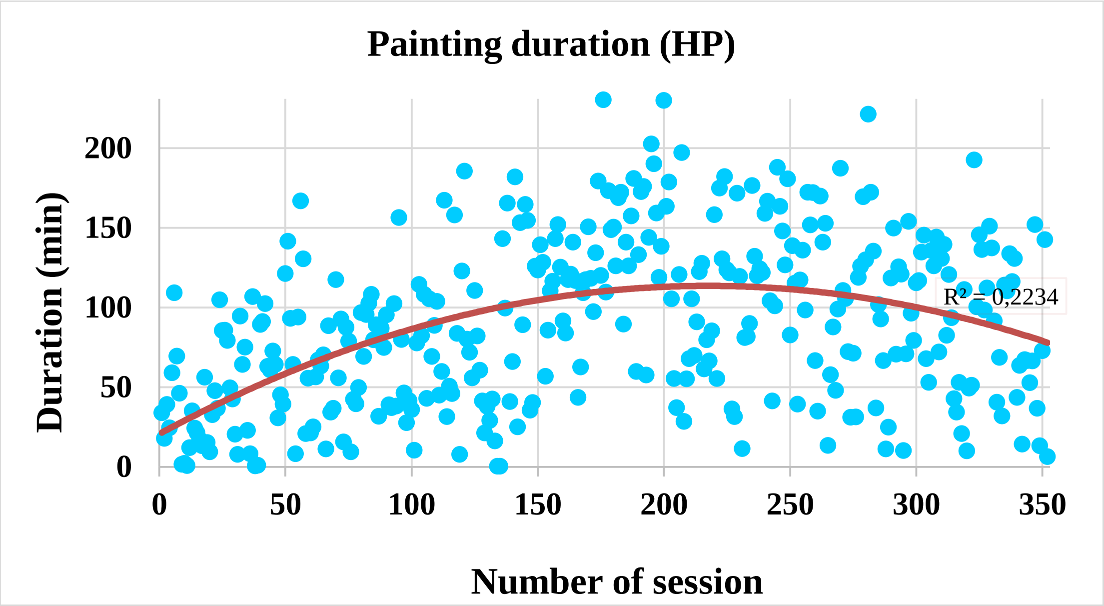


Figure 31: Total painting duration per session for HP.

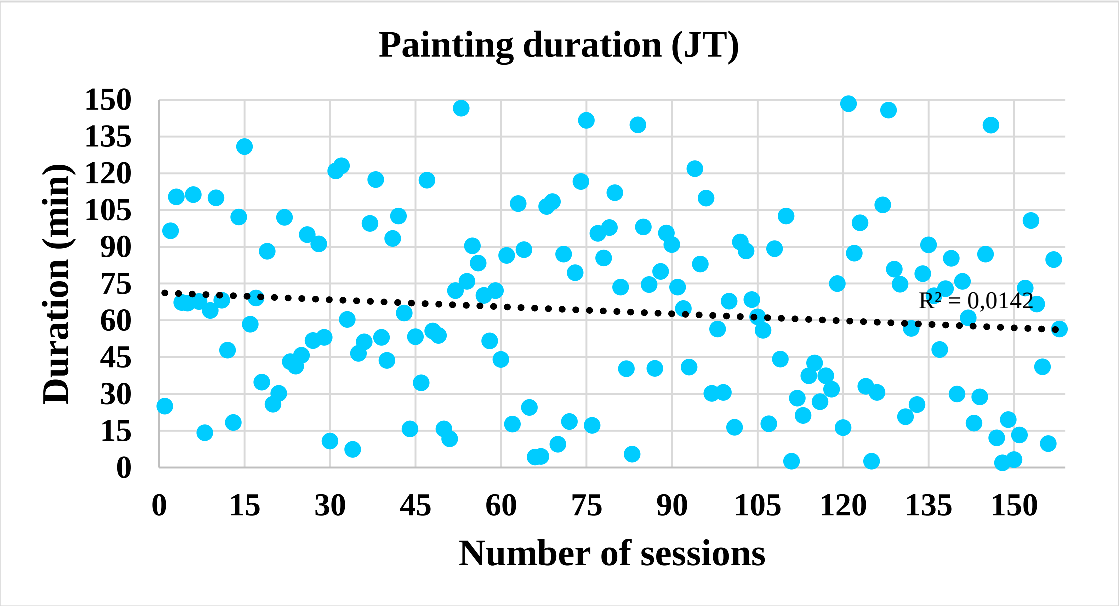


Figure 32: Total painting duration per session for JT.

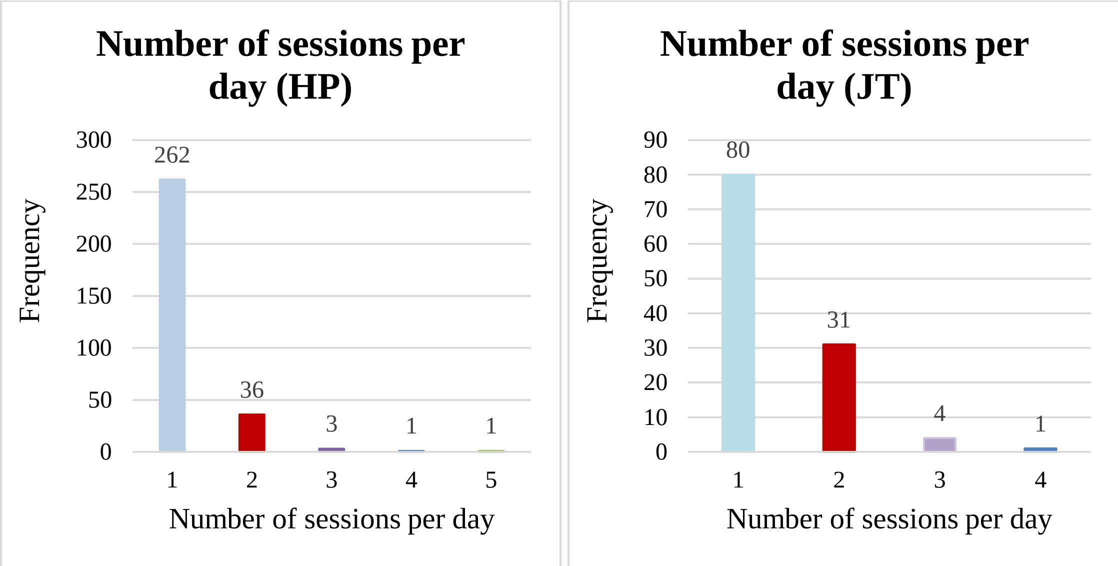


Figure 33: Number of sessions per day (HP and JT).

2.3.3.3 Usability

2.3.3.3.1 Effectiveness

In most sessions subjective level of BCI control was rated medium; in 116 sessions for HP and 69 sessions for JT (see **figure 34**). For HP level of BCI control with Einstein Brain Painting was significantly higher, as compared to Brain Painting (W=1511,00, p<.01). As depicted in **figure 35**, in HP subjective level of BCI control increased within the first 200 sessions, and decreased thereafter; thus a quadratic trend can be observed ($F(2,341)$=13.67, p<.001, r^2=.75, r=.27). In JT subjective level of BCI control was significatnly increased with time ($F(1,156)$=4.92, p<.05, r^2=.03, r=.18; see **figure 36**). In HP subjective level of BCI control decreased mostly within one session (N=151) or remained stable (N=161). In JT BCI control remained stable in most of the sessions (N=128), see **figure 37**.

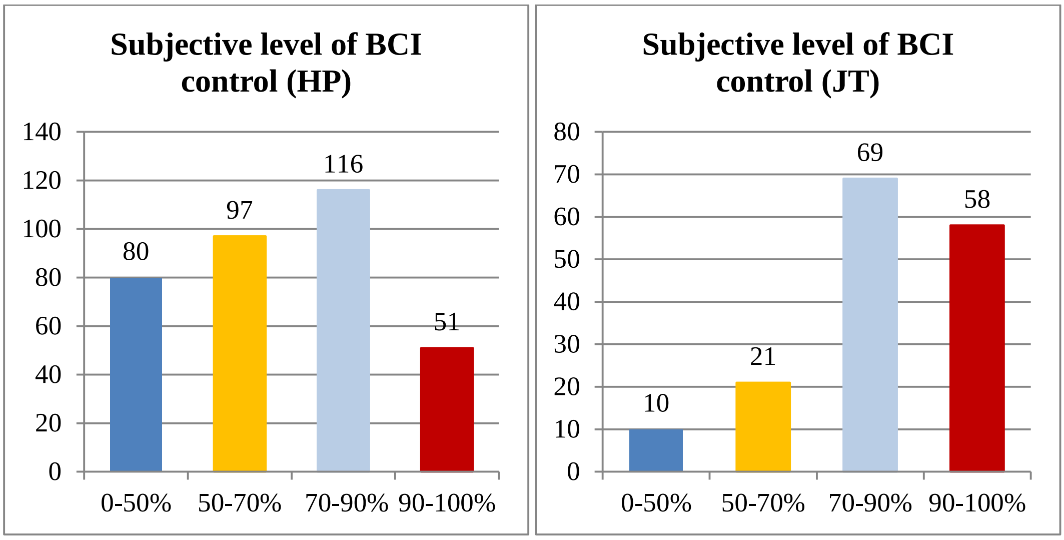


Figure 34: Subjective level of BCI control for HP and JT

Subjective control level was indicated within four classes: 0=zero (0-50%), 1=low (50-70%), 2=medium (70-90%) and 3=high (90-100%) control. Note that in HP subjective control level was not indicated within the first 8 sessions, therefore only 344 data points were included into the correlation procedure.

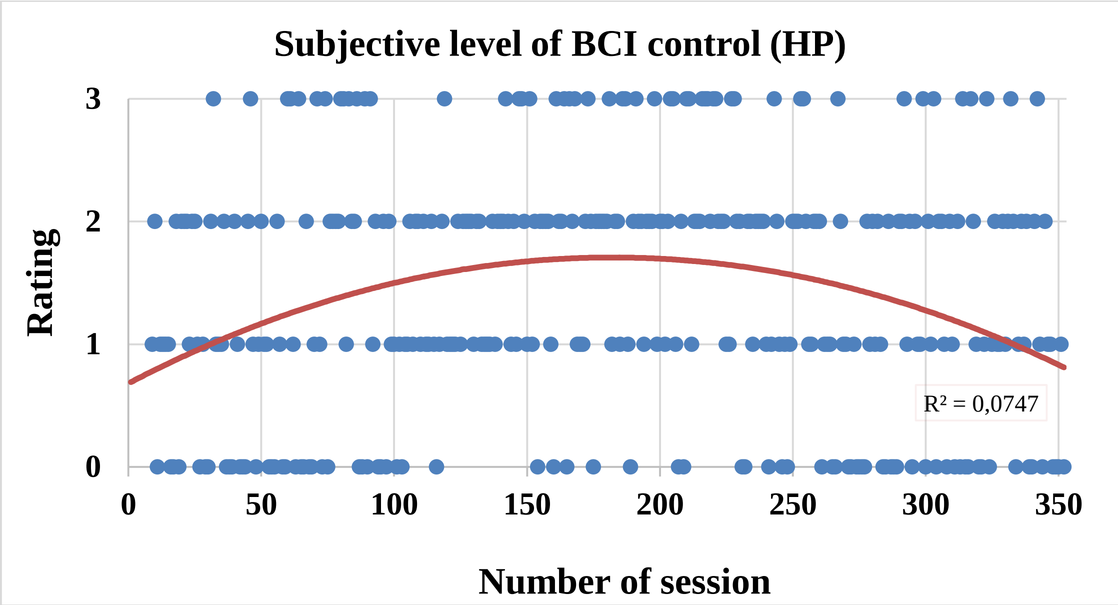


Figure 35: Trend of subjective level of BCI control over 352 sessions (HP).

Subjective control level was indicated within four classes: 0=zero (0-50%), 1=low (50-70%), 2=medium (70-90%) and 3=high control (90-100%). Note that in HP subjective control level was not indicated within the first 8 sessions, therefore only 344 data points were included into the correlation procedure.

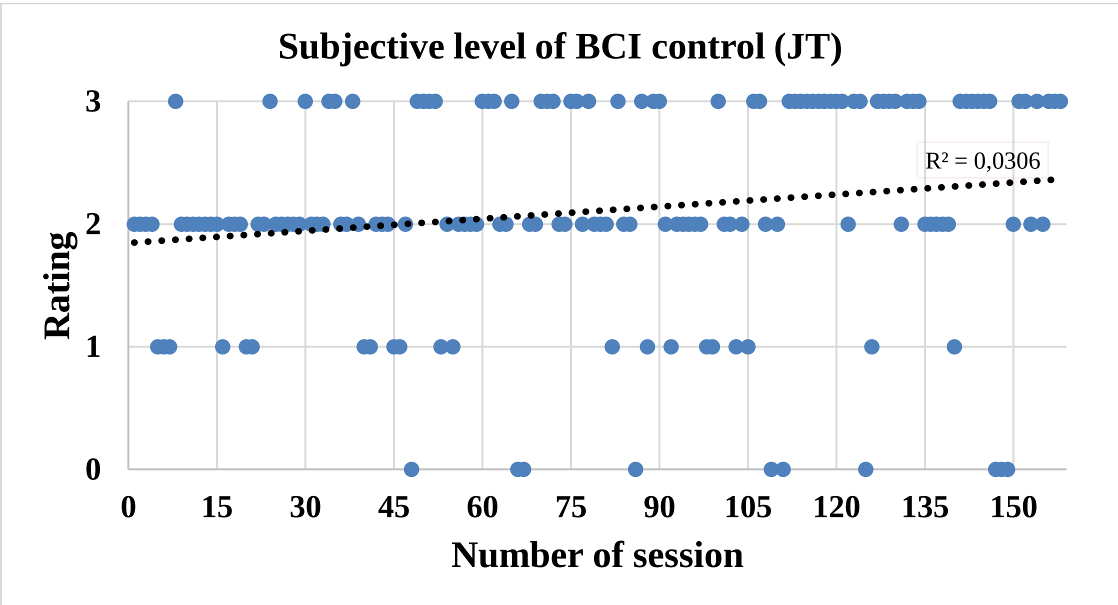


Figure 36: Trend of subjective level of BCI control over 158 sessions (JT).

Subjective control level was indicated within four classes: 0=zero (0-50%), 1=low (50-70%), 2=medium (70-90%) and 3=high control (90-100%).

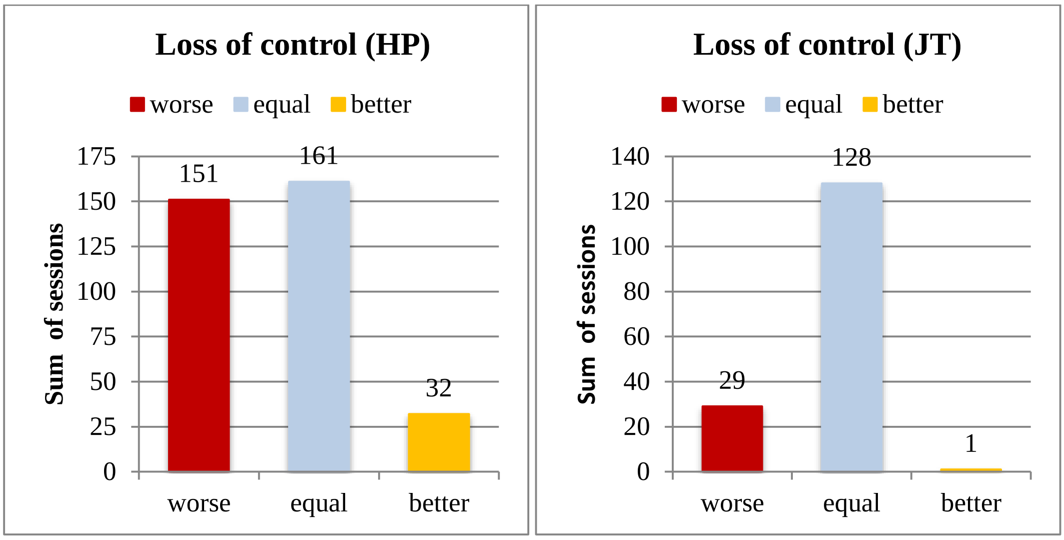


Figure 37: Loss of BCI control for HP and JT.

The end-user rated the BCI control at the end of the sessions as being (i) worse (worse), (ii) unchanged (equal) or (iii) improved (better), compared to the beginning of the session. Note that in HP loss of BCI control was not indicated within the first 8 sessions, therefore only 344 data points were included into the correlation procedure.

2.3.3.3.2 Efficiency

2.3.3.3.2.1 Estimated information transfer rate (ITR)

"Real" ITR could not be calculated, since no "objective" measure of performance (accuracy) was possible in this study. However ITR [bits/minute] was estimated by suggesting different accuracies (70-100%; **table 30**). ITR was estimated considering a large inter-trial interval (i.e., the time after one sequence, in which the user had time to think about what she or he wants to select next) of 11s (pre-sequence: 1s, post-sequence: 10s). This was the largest interval that was used by the end-users. Results indicate, that (estimated) ITR could be remarkably improved by face stimuli with a highest possible ITR of 16.97 [bits/minute] as compared to 11.76 (in end-user HP). ITR for JT is slightly lower, since he had 2 sequences more than HP (7 vs. 5 sequences).

Table 30: Estimated ITR for free-painting mode.

Estimated ITR [bits/minute] for free-painting mode			
	Old Brain Painting	**Einstein-Brain Painting (face stimuli)**	
	HP	**HP**	**JT**
70%	6.39	9.23	7.84
80%	7.90	11.40	9.68
90%	9.60	13.85	11.77
100%	11.76	16.97	14.41

Note: ITR [bits/minute] was estimated for data with old Brain Painting BCI and Einstein-BCI for an accuracy of 70-100%. A time interval, the time in which the end-user thinks about what she or he wants to select next in this free-painting mode, of 11s (pre- and post-sequence) was chosen for calculation. This is the interval that both end-users had in most of the time, constituting also the maximum time interval.

2.3.3.3.2.2 Exhaustion

In most of the BCI sessions end-users experienced low exhaustion (N=252 and N=115; **figure 38**). Importantly, HP communicated that use of the BCI was less straining than use of her eye-tracker ("*I only need to concentrate and not to blink to select*").

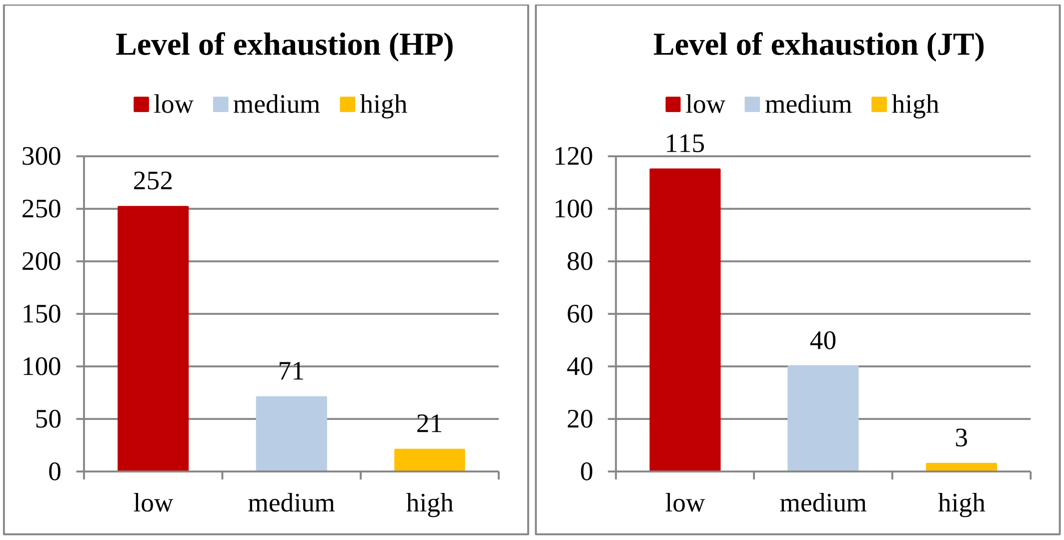


Figure 38: Level of exhaustion for HP and JT.

The end-user was asked to rate her/his experienced level of exhaustion during the Brain Painting session (low/medium/high). Note that in HP level of exhaustion was not indicated within the first 8 sessions, therefore only 344 data points were included into the correlation procedure.

2.3.3.3.2.3 Subjective workload (NASA-TLX)

On average, end-user's subjective workload was moderate (HP: *M*=44 and JT: *M*=63). In HP mental demand (*M*=10) and performance (*M*=10) were main sources of her subjective workload (see **table 31**). In JT mental (*M*=25), physical (*M*=12) and temporal demand (*M*=11) contributed most to his subjective workload (see **table 32**).

Table 31: Subjective workload (NASA-TLX) for HP for t1 to t17.

Subjective Workload (NASA-TLX)																		
Time (t)																		
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**M**
M	8	9	3	2	22	16	15	7	2	0	5	3	14	25	13	19	15	**10**
P	0	1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	**0**
T	7	0	0	7	0	0	0	2	12	8	11	20	13	19	23	7	3	**8**
PE	20	12	7	16	7	11	5	8	10	11	12	8	2	8	5	15	9	**10**
E	3	8	2	9	13	16	4	5	7	5	8	7	13	5	2	4	7	**7**
F	11	23	2	15	7	19	4	5	4	13	6	6	6	2	5	15	2	**8**
WL	**49**	**54**	**13**	**50**	**48**	**62**	**28**	**26**	**35**	**39**	**41**	**43**	**48**	**60**	**47**	**60**	**36**	**43**

Note: M=mental demand, P=physical demand, T=temporal demand, PE=performance, E=effort, F=frustration, WL=total workload. The NASA-TLX was rated after session (number of weeks in parenthesis) t1=8 (4), t2=21 (8), t3=28 (11), t4=32 (13), t5=53 (22), t6=66 (26), t7=75 (31), t8=90 (38), t9=120 (47), t10=152 (54), t11=170 (58), t12=194 (64), t13=208 (67), t14=232 (78), t15=262 (100), t16=285 (115), t17=330 (146).

Table 32: Subjective workload (NASA-TLX) for JT for t1 to t6.

Subjective Workload (NASA-TLX)							
Time (t)							
	1	**2**	**3**	**4**	**5**	**6**	**M**
M	23	25	25	25	25	25	25
P	17	17	17	7	7	7	12
T	11	11	11	11	11	11	11
PE	7	5	2	5	28	2	8
E	5	6	6	6	6	6	6
F	0	0	0	0	0	0	0
WL	**63**	**64**	**60**	**54**	**78**	**51**	**62**

Note: M=mental demand, P=physical demand, T=temporal demand, PE=performance, E=effort, F=frustration, WL=total workload. The NASA-TLX was rated after session (number of weeks in parenthesis) t1=13 (3), t2=44 (11), t3=73 (19), t4=90 (28), t5=96 (41), t6=118 (50).

2.3.3.3.3 Satisfaction

2.3.3.3.3.1 Visual analogue scales

Overall, end-users were highly satisfied with the BCI (HP: *M*=7.09, *SD*=3.48, range: 0-10; JT: *M*=7.89, *SD*=2.70, range: 0-10). Satisfaction scores of HP show a quadratic trend ($F(2,347)$=20.47, *p*<.001, r^2=.11, *r*=.36), see **figure 39**. In JT satisfaction remained stable over time ($F(1,156)$=0.41, *p*<.53, r^2=.00, *r*=-.05), see **figure 40**. Reasons for dissatisfaction (see **table 33**) were: (1) technical problems with software, mostly at the beginning of the study (in HP) or with hardware (e.g., malfunctioning of amplifier or EEG electrodes); (2) no/low control/loss of control (due to e.g., faulty set-up or malfunctioning of electrodes); or (3) subject, disease or environmental related factors, (e.g., low concentration, distraction, fatigue, tiredness, cough) that also influence BCI control; see **2.3.3.3.4 Factors influencing BCI control (effectiveness)**. VAS enjoyment ratings indicated that end-users strongly enjoyed painting with an average of *M*=7.23 (*SD*=3.40, range: 0-10; HP) and *M*=7.99 (*SD*=2.61; range: 0-10; JT). For HP enjoyment ratings show a quadratic trend of time ($F(2,341)$=15.75, *p*<.001, r^2=.09, *r*=.29), see **figure 41**. In JT, enjoyment ratings were stable over time ($F(1,156)$=2.38, *p*=.13, r^2=.02, *r*=-.12), see **figure 42**. Overall frustration was low in both end-users (HP: *M*=3.2, *SD*=3.58, range: 0-10; JT: *M*=1.93, *SD*=2.57, range: 0-10). In HP frustration decreased within the first 200 sessions, and increased thereafter, thus showing a quadratic trend ($F(2,341)$=13.16, *p*<.001, r^2=.07, *r*=.27); **figure 43**. In JT frustration significantly decreased over time ($F(1,156)$=10.76, *p*<.01, r^2=.07, *r*=-.25); **figure 44**. Satisfaction, enjoyment and frustration scores were highly correlated with subjective level of BCI control in both end-users (HP: satisfaction: *r(342)*=.78, *p*<.001, enjoyment: *r(342)*=.74, *p*<.001, frustration: *r(342)*=.74, *p*<.001; JT: satisfaction: *r(156)*=.75, *p*<.001; enjoyment: *r(156)*=.71, *p*<.001; frustration: *r(156)*=-.72, *p*<.001). Relationship between satisfaction and subjective level of BCI control is depicted in **figures 45** and **46**).

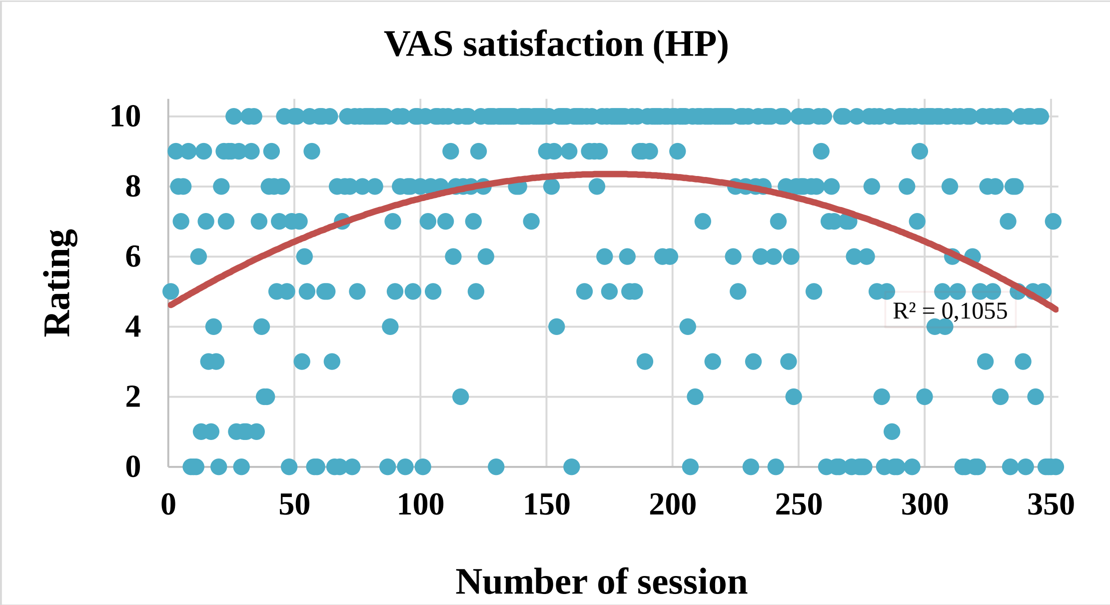


Figure 39: VAS satisfaction (HP).

Satisfaction was rated on a visual analogue scale between 0 (not at all satisfied) and 10 (very satisfied). Note: Ratings of sessions 2 and 7 are missing.

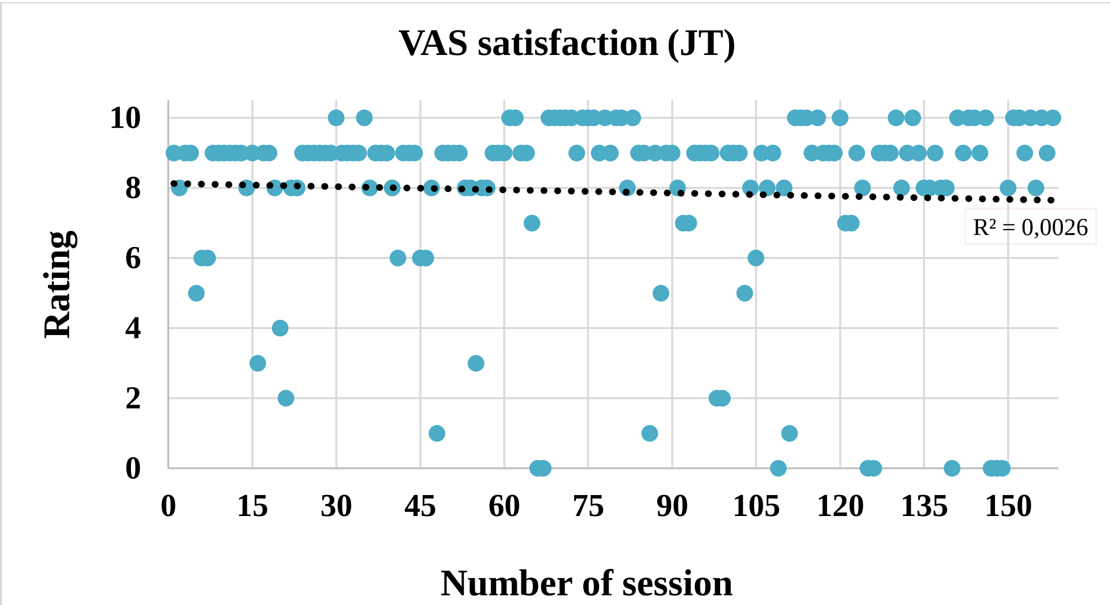


Figure 40: VAS satisfaction (JT).

Satisfaction was rated on a visual analogue scale between 0 (not at all satisfied) and 10 (very satisfied).

Table 33: Reasons for dissatisfaction with BCI session.

Technical problems (hardware/ software)	Session 11, 38, 60, 66, 68: "*Brain Painting crashed*" (HP) Session 15: "*USB amp error*" (HP) Session 96: "*Interruption due to internet advertisement*" (HP) Session 101: "*Toolbox not visible, disappears after adjustment*" (HP) Session 295: "*Electrode 7 did not work, now new try*" (HP) Session 352: "*PC didn't react to user, EEG signals looked strange from the beginning…We used enough gel, but then cancelation*" (HP) Session 6: "*The program stopped abruptly after 1.5 hours*" (JT) Session 16: "*Today we had problems with the EEG cap and connection of the second electrode to the amplifier, at the end*" (JT) Session 52: "*Program crashed twice today…*" (JT) Session 86: "*Problems with battery of the gammabox*" (JT) Session 110: "*First try after exchange of the amplifier - better, but not as good as compared to the beginning*" (JT) Session 126: "*Restart, because EEG-signals disappeared in the middle of the session*" (JT)
No/low control/loss of control	Session 35-36: "*Throughout bad control.*" (HP) Session 86: "*Bad from the beginning due to insufficient gel*" (HP) Session 160: "*Gel was missing*" (HP) Session 105: "*Not enough gel, therefore last hour worse*" (HP) Session 207: "*At the end no control…*" (HP) Session 287: "*Cap was not placed in the midline*" (HP) Session 289: "*Third time nothing worked, no control, no fun…*" (HP) Session 348: "*No control*" (HP) Session 103: "*Many wrong selections, although I am very concentrated…Two paintings already "destroyed". What is wrong?*" (JT) Session 105: "*Selections in the matrix do not represent my thoughts*" (JT)
Subject related/ disease related/ environmental factors	Session 90: "*Not enough concentrated, probably too tired…*" (HP) Session 92: "*Too tired after finishing of previous painting, I should have stopped*" (HP) Session 171: "*Dry eyes*" (HP) Session 279: "*I feel distracted by interruptions if too often as today…*" (HP) Session 284: "*HP could not work with this size and we did not realize after 5 minutes, thus she painted half hour for nothing*" (HP) Session 297: "*Same as yesterday, I should have slept before*" (HP) Session 310: "*Too tired*" (HP) Session 319: "*At the beginning worse, because of retching. Therefore painting worse*" (HP) Session 335: "*I had five sessions of twenty minutes du two times retching attacks, and therefore no control at this time*" (HP) Session 6: "*Terminated due to cough.*" (JT) Session 20: "*At the beginning we forgot to connect the amplifier with the gammabox*" (JT) Session 58: "*Due to disease recurring problems (cough, headache, respiratory problems)*" (JT) Session 66: "*We forgot to turn on the amplifier*" (JT) Session 77: "*Problems due to recurrent cough - was fun nonetheless*" (JT)

Note: Exemplary comments (due to space not all comments shown).

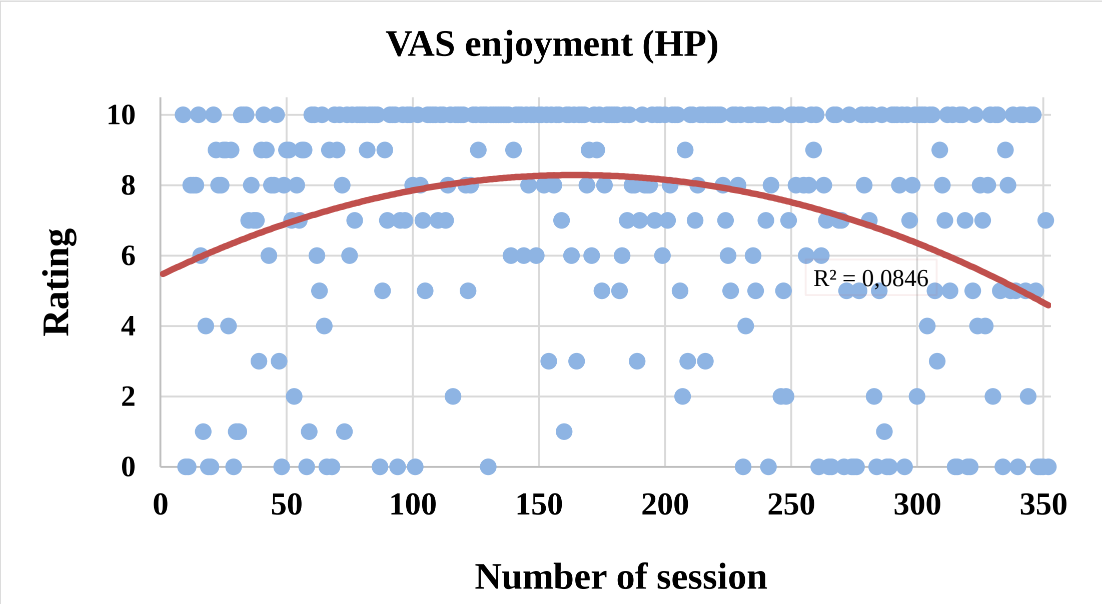


Figure 41: VAS enjoyment (HP).

Enjoyment was rated on a visual analogue scale between 0 (not at all enjoyed) and 10 (very enjoyed).

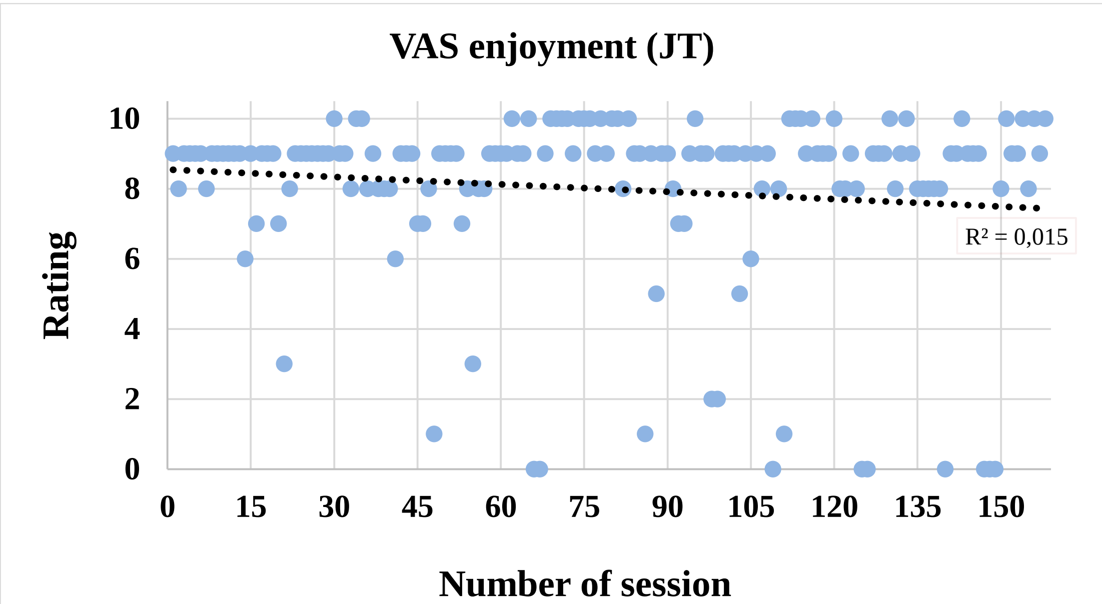


Figure 42: VAS enjoyment (JT).

Enjoyment was rated on a visual analogue scale between 0 (not at all enjoyed) and 10 (very enjoyed).

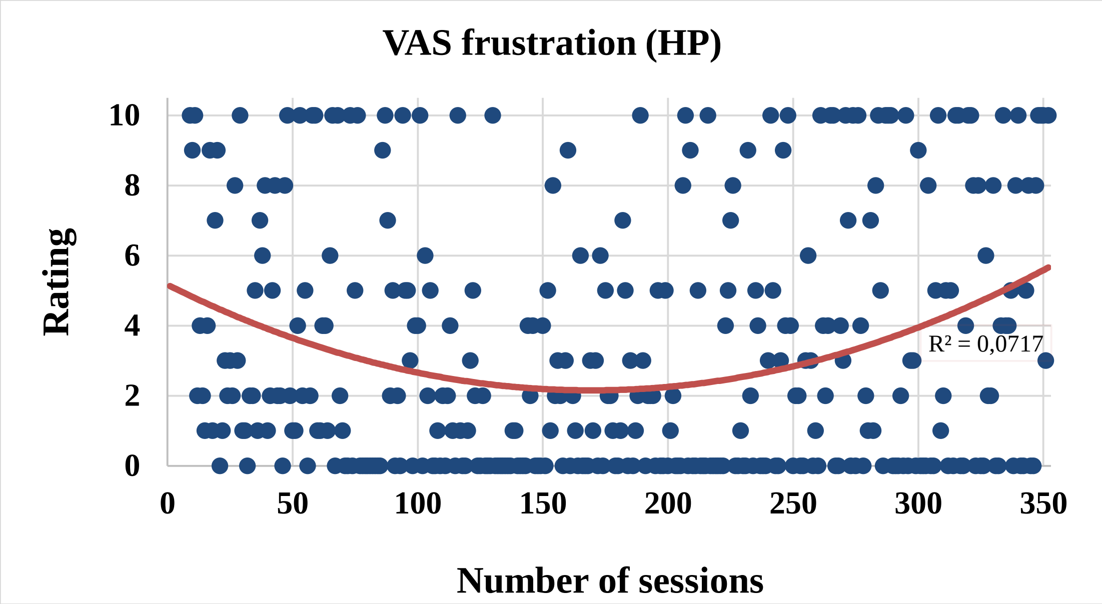


Figure 43: VAS frustration (HP).

Frustration was rated on a visual analogue scale between 0 (not at all frustrated) and 10 (very frustrated).

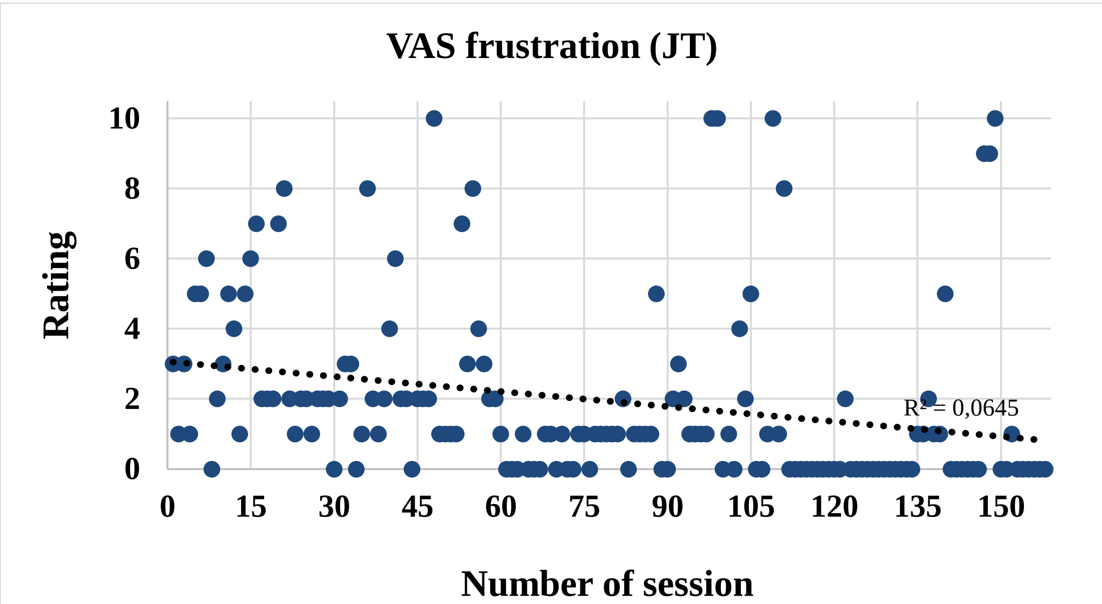


Figure 44: VAS frustration (JT).

Frustration was rated on a visual analogue scale between 0 (not at all frustrated) and 10 (very frustrated).

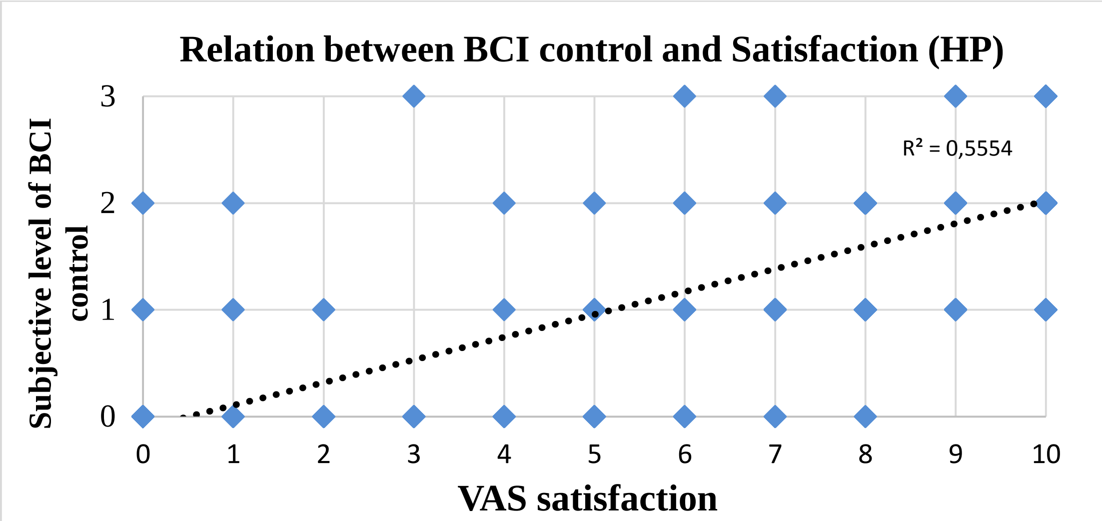


Figure 45: Relation between BCI control and VAS satisfaction (HP).

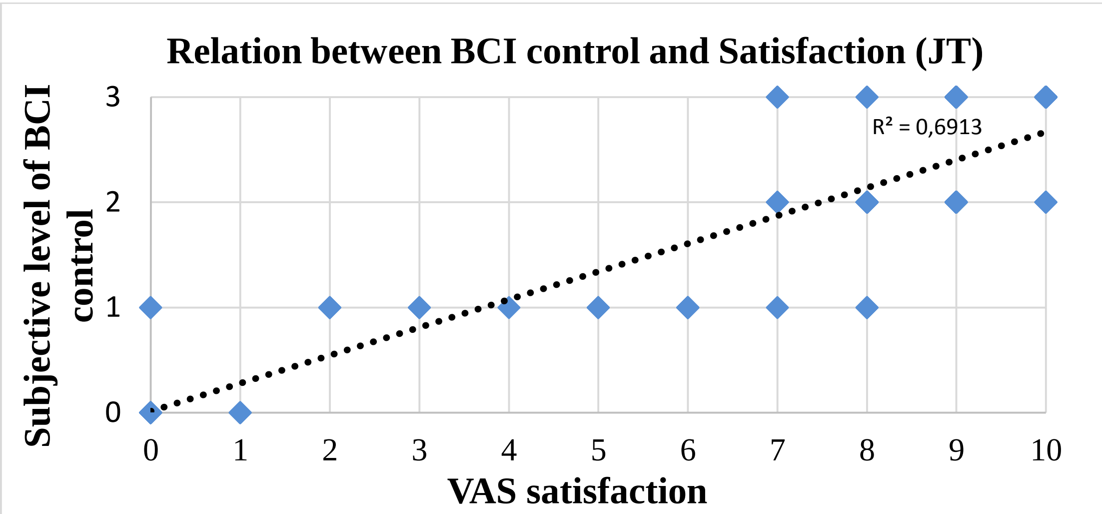


Figure 46: Relation between BCI control and VAS satisfaction (JT).

2.3.3.3.3.2 Satisfaction with the BCI device (extended QUEST)

On overall end-users expressed very high satisfaction with the BCI (range: *M*=4.47 to 5), indicating that the BCI was accepted well as assistive device by the end-users, see **table 34**. Although being very satisfied, end-users indicated lowest satisfaction for ease of use (*M*=4.47 and *M*=4.5), "*If bad concentration, then bad accomplishment*" (HP), "*High concentration needed*" (JT), effectiveness (*M*=4.65 and *M*=4.5), "*Temporary quote of errors very high*" (JT), "*Depends on adjustment and constitution*" (HP) and comfort (*M*=4.65 and *M*=4), "*Electrodes hurt after 1* *hour and electrode gel sticks hair together*" (HP), "*Immobility of head*" (JT). HP also indicated obstacles regarding dimensions (*M*=4.59), "C*ap gets slightly out of place/cap seems to bulge at some electrodes*" (HP) and reliability (*M*=4.71), "*Buckling of the EEG cap*" (HP), "*Twice error with USB amplifier*" (HP), see **table 35**. End-users indicated ease of use, effectiveness and reliability as most important items. HP also indicated speed and JT also professional services, see **figure 47**.

Table 34: Satisfaction with the BCI device (extended QUEST).

Satisfaction with BCI device (extended QUEST)			
	HP	**JT**	***M***
1. Dimensions	4.59	5	4.80
2. Weight	5.00	5	5.00
3. Adjustment	4.82	5	4.91
4. Safety	4.82	5	4.91
5. Comfort	4.65	4	4.33
6. Ease of use	4.47	4.5	4.49
7. Effectiveness	4.65	4.5	4.58
8. Prof. services	5.00	5	5.00
Total QUEST score	**4.75**	**4.75**	**4.75**
9. Reliability	4.71	5	4.86
10. Speed	4.82	5	4.91
11. Learnability	5.00	5	5.00
12. Aesthetic design	4.94	5	4.97
Added items score	**4.87**	**5**	**4.94**

Note: *M*=mean of scores; 1=not satisfied at all, 2=not very satisfied, 3=more or less satisfied, 4=quite satisfied, 5=very satisfied.

Table 35: Individual statements indicated in the extended QUEST.

Satisfaction with BCI device (extended QUEST)	
scale	**Individual statements by end-users**
1. Dimensions	t5: "*Cap shifts once in a while/gets slightly out of space*" (HP) t6: "*Cap seems to bulge sometimes at some electrodes*" (HP) t8, t10, t11: "*Electrodes hurt after a while*" (HP)
3. Adjustment	t1: "*Longer connection cables would be beneficial*" (HP) t1: "*Quite fragile for misuse (software)*" (JT) t5: "*Some electrodes are no longer contacting the scalp*" (HP) t6: "*Cap bulges and single electrodes do no longer sit well*" (HP) t8: "*Adjustment of software not always fast, depended of handling, for the patient too long, has an influence on concentration*" (HP) t11: "*Sometimes problems with gel*" (HP)
4. Safety	t9: "*Cables a bit too short between electrode box and amplifier*" (HP) t16: "*In the last weeks gel caused itching on the scalp"* (HP)
5. Comfort	t1: "*Immobility of head*" (JT) t2: "*Electrodes press against head cushion*" (HP)) t9: "*Ok for the first 1 to 2 hours; then electrodes hurt*" (HP) t13, t14: "*Electrodes hurt after 1 hour and electrode gel sticks hair together*" (HP)
6. Ease of use	t1: "*High concentration needed (also for correcting/undo)*" (JT) t2: "*If program works its fine, but if not then less satisfied*" (HP) t3: "*If bad concentration, then bad accomplishment*" (HP) t5: "*Everything is fine, as long as program is working fine*" (HP) t5: "*Quote of errors higher compared to previous months*" (JT) t13: "*Sometimes too exhausting/demanding if tired*" (HP)
7. Effectiveness	t2: "*More training is needed to implement ideal painting, frustration when everything goes wrong*" (HP) t3: "*I (still) cannot implement, what I want*" (HP) t5: "*Temporary quote of errors very high*" (JT) t8: "*Effective, if matrix matches the visual field, in the way that every symbol is exact in front of the eyes*" (HP) t10: "*Depends on adjustment and constitution*" (HP) t12: "*Most of the times ok, depends on exhaustion and concentration*" (HP)
8. Prof. services	t2: "*Excellent support and contact*" (HP)
9. Reliability	t1: "*Last three sessions did not work, amplifier interrupted two times and software did not react to user*" (HP) t5: "*Once error with USB amplifier*" (HP) t6: "*Buckling of the EEG cap*", "*Twice error with USB amplifier*" (HP); t10: "*Program freezes sometimes*" (HP)
10. Speed	t2: "*Too slow*" (HP); t3: "*Could be faster*" (HP)
12. Aesthetic design	t1: "*Lines, triangles and casual forms would be great*" (JT) t2: "*I don't care about aesthetic design of EEG cap and electrodes nor amplifier, but more choices in the matrix would be nice*" (HP) t9: "*More forms…*" (HP); t13: "*More tools…*" (HP)

Note: Exemplary statements given by HP and JT (due to space not all comments shown). For HP for t1 to t17, for JT for t1 to t6. Weight (item 2) and learnability (item 11) are not depicted in this table, because there were no comments given.

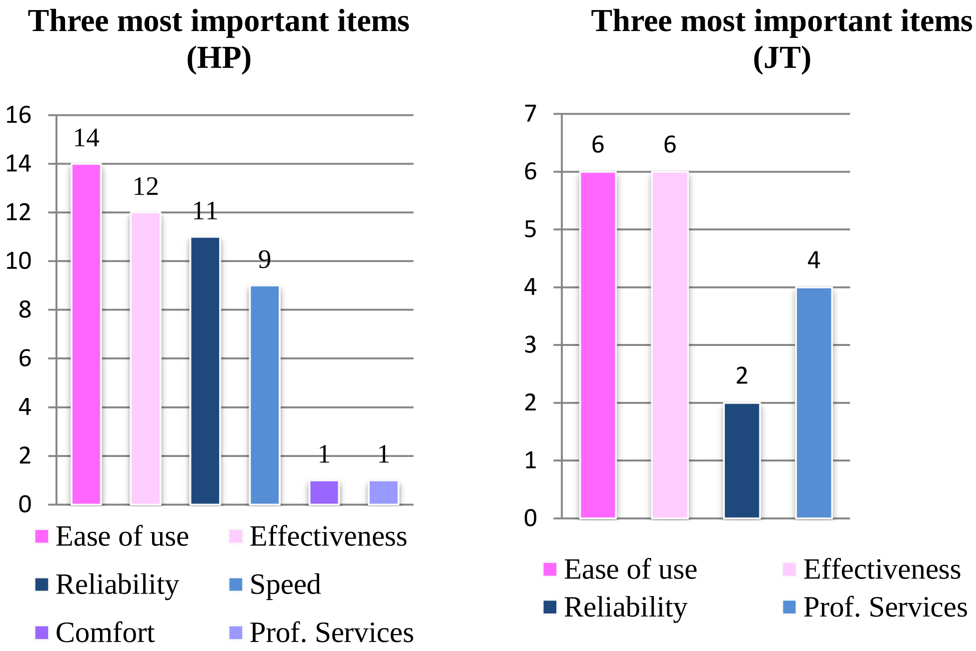


Figure 47: Three most important items (extended QUEST) in Brain Painting.

HP indicated the three most important items 16 times for t1 to t16 (missing data for t17; 48 items in total; left); JT 6 times for t1 to t6 (18 items in total; right).

2.3.3.3.3.3 Match between person and technology (ATD-PA)

With a total score of 4.8 of 5, HP and BCI technology matched perfectly indicating high probability for use in daily-life. For JT a total score could not be calculated due to many "not applicable" items. Importantly for the items "*This device will benefit me and improve my quality of life.*" and "*I have the capabilities and stamina to use this device without discomfort, stress and fatigue.*" both end-users indicated a "5" meaning highest confirmation (100% of the time), see **table 36**.

Table 36: Match between person and technology (ATD-PA).

Assistive Technology Device Predisposition Assessment			
		HP	**JT**
A	This device helps me to achieve my goals.	5*	3
B	This device benefits me and improves my quality of life.	5*	5*
C	I am confident I know how to use this device and its various features.	5	0
D	I will feel more secure (safe, sure of myself) when using this device.	5	0
E	This device fits well with my accustomed routine.	3	4
F	I have the capabilities and stamina to use this device without discomfort, stress and fatigue.	5*	5*
G	The supports, assistance and accommodations exist for successful use of this device.	5	5*
H	This device physically fits in all desired environments (car, living room, etc.).	5	0
I	I feel comfortable (and *not* self-conscious) using this device around family	5	0
J	I feel comfortable (and *not* self-conscious) using this device around friends	5	0
K	I feel comfortable (and *not* self-conscious) using this device at school or work.	0	0
L	I feel comfortable (and *not* self-conscious) using this device around the community.	0	0
	Total Score (A-L)	**4.8**	**-**

Note: 5=All the time (100% of the time); 4=Often (around 75% of the time); 3=Half the time, neutral (about 50% of the time); 2=Sometimes (around 25% of the time); 1=Not at all (0% of the time); 0=Not applicable,"*" indicates the three most important items. Items were modified to present tense.

2.3.3.3.4 Factors influencing BCI control (effectiveness)

BCI control was influenced by: (1) inaccurate set-up (EEG cap, electrodes, gel), (2) hardware related issues (shifting of cap and/or drying of gel, alteration of shape of the EEG cap, problems with amplifier), (3) subject-specific and disease related issues (e.g., concentration, fatigue, cough, retching, fasciculations, personality factors), and (4) environmental factors (e.g., interruptions, medical treatments, distraction). Both end-users reported that they need to be highly concentrated and that it has to be very silent for painting and that they cannot paint if they are too tired (e.g., after physiotherapy) or when distracted. HP stated: "*I am only distracted by interruptions. I have problems to get into it again…I get angry about myself and this is not beneficial for my concentration. At the beginning control always 100%. Later too many changes, because of interruptions/pauses for inhalation, change of position of legs, medicine, or feeding. This is* *disturbing*“ (session 259) and “*I could have skipped the last two runs, because my eyes were overstrained. Thus high frustration, because it didn't work well at the end*” (session 281). JT reported that his control over the BCI was influenced by his cough in some sessions, however he indicated that he was nevertheless satisfied with the BCI: “*I do not want to focus my attention on my cough. I have enough time and I refine until I am satisfied with it [painting]. This is the way I did it in the past as a hand painting artist […]*”. The shape of the EEG cap altered after approximately 100-200 hours of total painting duration and influenced signal quality and BCI control consequently; thus BCI cap was exchanged several times by the BCI team or by the BCI assistants.

2.3.3.4 Influence on the life of the person

2.3.3.4.1 Psychosocial Impact of Assistive Devices Scale (PIADS)

PIADS results revealed a positive impact of Brain Painting on all three subscales: Competence (HP: 1.50 and 1.33; JT: 2.33), adaptability (HP: 2.17 and 1.50; JT: 1.83) and self-esteem (HP: 1.50 and 1.63; JT: 2.38); **table 37**. For HP, the BCI device had a strong impact on adaptability (enabling and liberating aspects; e.g., willingness to take chances, ability to participate, eagerness to try new things, ability to adapt to the activities of daily-living) in the first nine months; rather than on self-esteem (self-confidence and emotional well-being), and competence (performance and productivity). In follow-up (after 34 months) a stronger impact of the BCI on self-esteem rather than on adaptability was found. In JT, the BCI had the strongest impact on competence and self-esteem. Single items reveal that Brain Painting had a strong positive impact on feeling of happiness and usefulness, self-esteem, quality of life, self-confidence, productivity and ability to participate. For both end-users a negative impact on frustration was found, indicating that end-users experience less frustration (less experienced frustration about lack of progress in achieving desires), compared to the time before using Brain Painting. A negative impact was found for independence for both end-users, indicating that Brain Painting induced a stronger feeling of being dependent on someone. In follow-up (after 34 months), HP indicated that the BCI was no longer negatively influencing, but positively impacting her feeling of independence (feeling more independent with the BCI). JT indicated a negative impact of the BCI on confusion (being less confused), indicating that he acts more decisively since using the Brain Painting.

Table 37: Psychosocial Impact of Assistive Devices Scale (PIADS).

Psychosocial Impact of Assistive Devices Scale			
R	**HP (9 months)**	**HP (34 months)**	**JT (11 months)**
3	Happiness[3], self-esteem[3], productivity[1], usefulness[1], self-confidence[3], expertise[1], capability[1], quality of life[1], performance[1], willingness to take chances[2], ability to participate[2], eagerness to try new things[2], ability to adapt to the activities of daily living[2]	Happiness[3], self-esteem[3], productivity[1], usefulness[1], self-confidence[3], expertise[1], well-being[2], performance[1], willingness to take chances[2], ability to participate[2]	Happiness[3], efficiency[1], self-esteem[3], productivity[1], security[3], usefulness[1], self-confidence[3], expertise[1], skillfulness[1], well-being[2], quality of life[1]
2	-	capability[1], sense of power[3],	Competence[1], adequacy[1], capability[1], performance[1], sense of power[3], sense of control[3], ability to participate[2], eagerness to try new things[2], ability to adapt to the activities of daily living[2], ability to take advantage of opportunities[2]
1	Adequacy[1], sense of control[3], ability to take advantage of opportunities[2]	quality of life[1], Independence[1]	-
0	Competence[1], confusion[1], efficiency[1], security[3], skillfullness[1], well-being[2], sense of power[3], embarrassment[3]	Adequacy[1], sense of control[3], Competence[1], confusion[1], efficiency[1], security[3], skillfullness[1], embarrassment[3], eagerness to try new things[2], ability to adapt to the activities of daily living[2], ability to take advantage of opportunities[2]	Embarrassment[3], willingness to take chances[2]
-1	Independence[1]		Independence[1]
-2	Frustration[3]	Frustration[3]	-
-3	-	-	Confusion[1], frustration[3]
	Competence: 1.50 Adaptability: 2.17 Self-esteem: 1.50	Competence: 1.33 Adaptability: 1.50 Self-esteem: 1.63	Competence: 2.33 Adaptability: 1.83 Self-esteem: 2.38

Note: The end-user has to indicate whether the AT has a positive or negative impact and the degree of this impact on the specified dimension. Scores can range between -3 and 3 with -3 to 0 indicating a negative (decrease) and 0 to 3 a positive (increase) impact on quality of life. Zero indicates no perceived impact. R=rating; [1]Competence, [2]adaptability, [3]self-esteem. A negative impact on frustration and confusion means less experienced frustration (being less upset about lack of progress in achieving desires) and confusion (being less unable to think clearly/act more decisively). Answered after 9 and 34 months (HP) and 11 months (JT).

2.3.3.4.2 Personal statements

HP stated: "[…] *I paint about two or three times a week and enjoy this immensely as my former art is given back to me, even if it is a new form of painting. A completely new art form, far more challenging, but also pure fun and absolutely rewarding if you can put your picture in mind on canvas and finally see it with your own eyes. That is a great moment for me as somebody who has been paralysed for six years* […]" (July 2013). She further summarized[1] "*2012 I got the opportunity to (brain) paint that enriched my life. It requires discipline, concentration and is limited to determined forms, opacities and components, but it also gives me the opportunity to express myself creatively again. Conclusion: Brain Painting makes me everytime happy and satisfied again, if it works - if not, then frustration and disappointment. Fortunately this happens in only few cases. BP completely changed my life. I can paint again and be creative again using colours. It is time-consuming– time in which I am only sitting in front of my (PC) screen, I can neither answer nor read emails, nor go outside enjoying fresh air. One has to decide whether this is a sacrifice. For me it is not. It is certainly a big win. Even though my life would certainly be rich without BP, too, I would never have known BP. I am very thankful for this enrichment* […]*".* JT reported in personal contact that Brain Painting significantly contributes to his quality of life that he is glad that he is able to use Brain Painting in his home environment. He stated[2]: "*I always said, if I cannot paint any longer, I am dead, and then came Brain Painting"* and *"Brain Painting was my relief – I am no longer captured and I will still be able to paint for a very long time, because my thoughts will always exist".* In January 2014 he wrote in an email to the BCI lab: "*BP encourages me for my future, because it makes so much fun and because it works so fine. I have so many ideas with shapes and colours.* […]. *By the way, now I call myself a picture maker*" […].

2.3.3.4.3 Social inclusion: Exhibitions and paintings

Paintings of end-user HP were exhibited for the first time at the Annual Meeting of the German Biological Psychology Society in Würzburg, Germany, and thereafter at the International BCI Meeting 2013 in Asilomar, USA. Her first private exhibition was in the Town Hall of Easdale Scotland, in July 2013. In her recent exhibition she exposes 45 of her paintings in the Forum of the Volksbank in Würzburg (from July to December 2014; see **figures 48** and **49**): "*Brain Painting is like sunday breakfast for the soul…Something, to what I am looking forward everytime again. It activates, satisfies and relaxes me. If it works - if not then frustration, being such an emotional person as I am. After three and a half years of speech- and motionlessnesss, Brain*

[1] In an interview with Bayerischer Rundfunk (BR; November 2013)

[2] In an interview with GIP in autumn 2013: http://www.gip-intensivpflege.de/brainpainting/

Painting gave me a new form to express myself, and I am very grateful to every involved person for that… Now I can again indulge in colours and show, that an apparently total helpless person can enjoy the nature and community. I always enjoyed being around other people or being in the nature. I hope that this can be recognized in my brain paintings. Despite all adversities, you always encourage yourself to proceed, and of course painting now helps as well for that case!" (June 2014). She has already sold several paintings. Example paintings of HP are depicted in **figure 50**. JT exposed some of his Brain Paintings together with his water color paintings, which he created by "hand" before complete motor paralysis of the body, in May 2014 in his exhibition "Aqua-Rell" (see **figures 51** and **52**).

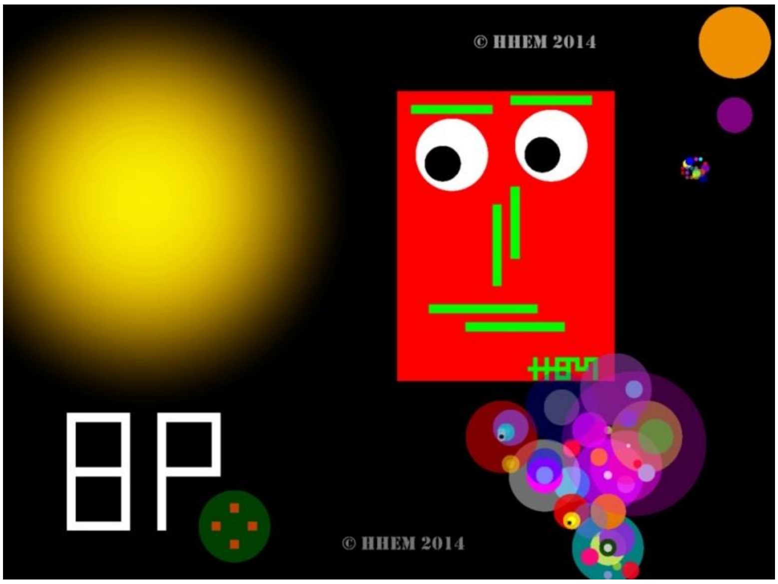
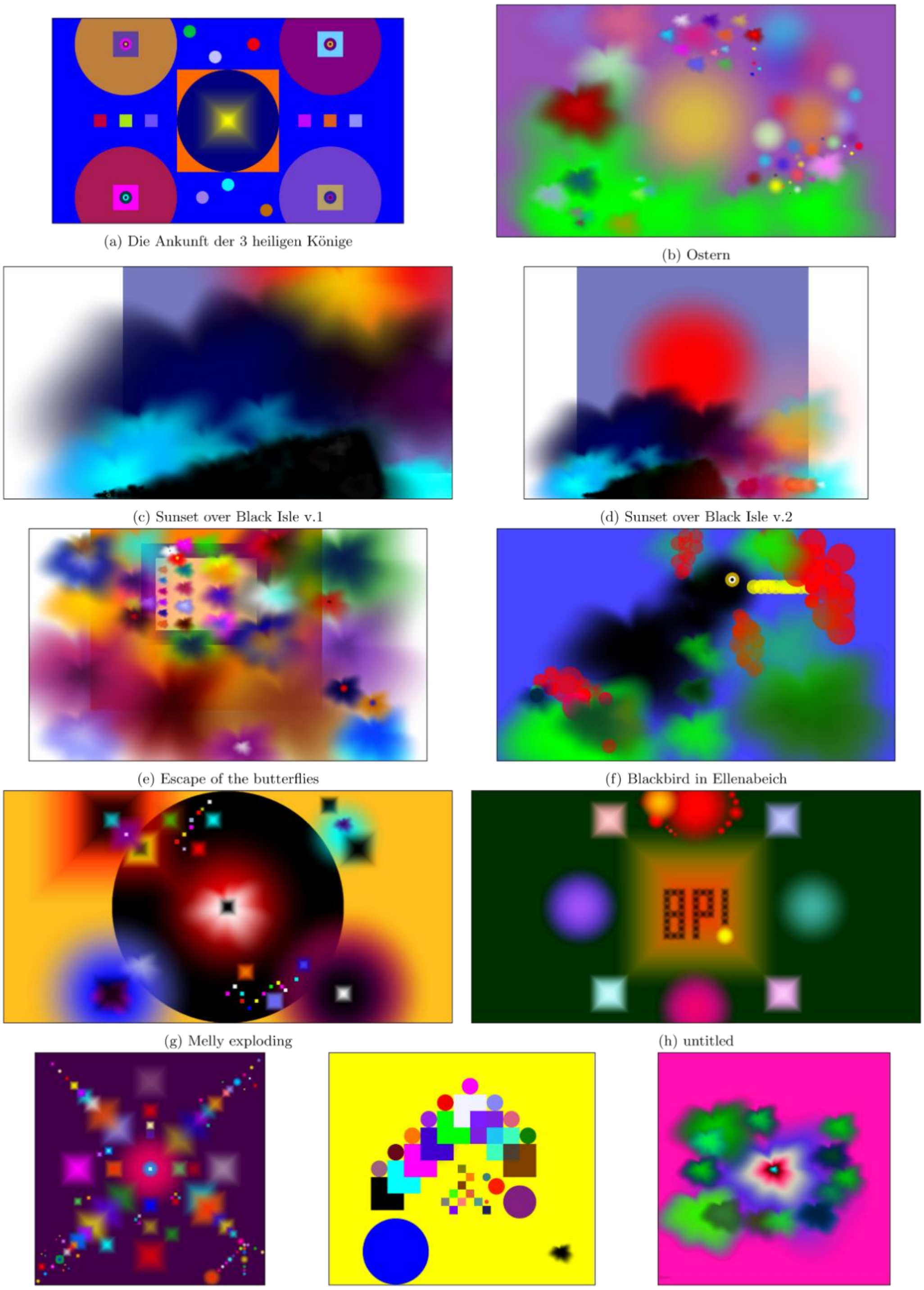


Figure 48: Cover picture of the exhibition in Forum of the Volksbank in Würzburg.

Picture has the title *Sonntagsfrühstück (sunday breakfast)*. HHEM is the artist's pseudonym. Source: Holz, E. M., Botrel, L., & Kübler, A. (2015). Independent home use of Brain Painting improves quality of life of two artists in the locked-in state diagnosed with amyotrophic lateral sclerosis. *Brain-Computer Interfaces*, *2(2-3)*, 117-134, p. 128.

Figure 49: Brain Painting exhibition in Forum of the Volksbank in Würzburg.

In this exhibition 45 Brain Paintings by HHEM were exposed from July until December 2014. Source: Holz, E. M., Botrel, L., & Kübler, A. (2015). Independent home use of Brain Painting improves quality of life of two artists in the locked-in state diagnosed with amyotrophic lateral sclerosis. *Brain-Computer Interfaces, 2(2-3)*, 117-134, p. 128.



(a) Die Ankunft der 3 heiligen Könige
(b) Ostern
(c) Sunset over Black Isle v.1
(d) Sunset over Black Isle v.2
(e) Escape of the butterflies
(f) Blackbird in Ellenabeich
(g) Melly exploding
(h) untitled
(i) Waiting for June
(j) Hurra Hurra, die Post ist da
(k) Lichtblick

Figure 50: Example Brain Paintings of HP.

Paintings by HP. With her paintings she is able to express emotions: Painting (h) was painted after recurring hardware related problems were solved and she wanted to show to everyone that BP works again with the statement “BP!”; she painted “Waiting for June (i) for a journalist who was pregnant when she came for an interview to her home; june was the month of expected delivery. Other paintings are related to events that were emotionally relevant for her: She painted

“Melly exploding” (g) after her caregiver Melly was “exploding” when she was confronted with a technical problem while starting Brain Painting; the paintings “Die Ankunft der heiligen 3 Könige” (arrival of the 3 holy saints; a) and “Ostern” (Easter; b) refer to public holidays; (c) Sunset over black isle version 1 and 2 (c and d) and “Blackbird in Ellenabeich” (f) are related to the Island Easdale in Scotland, where her daughter lives and where they spent many holidays together. Source: Holz, E. M., Botrel, L., & Kübler, A. (2015). Independent home use of Brain Painting improves quality of life of two artists in the locked-in state diagnosed with amyotrophic lateral sclerosis. *Brain-Computer Interfaces*, *2(2-3)*, 117-134, p. 127.

Figure 51: Exhibition "Aqua-Rell" with Brain Paintings.

The brain painting which is depicted in this figure has the title „Perlenverlegung“ (see **figure 52**). Source: Holz, E. M., Botrel, L., & Kübler, A. (2015). Independent home use of Brain Painting improves quality of life of two artists in the locked-in state diagnosed with amyotrophic lateral sclerosis. *Brain-Computer Interfaces*, *2(2-3)*, 117-134, p. 130.

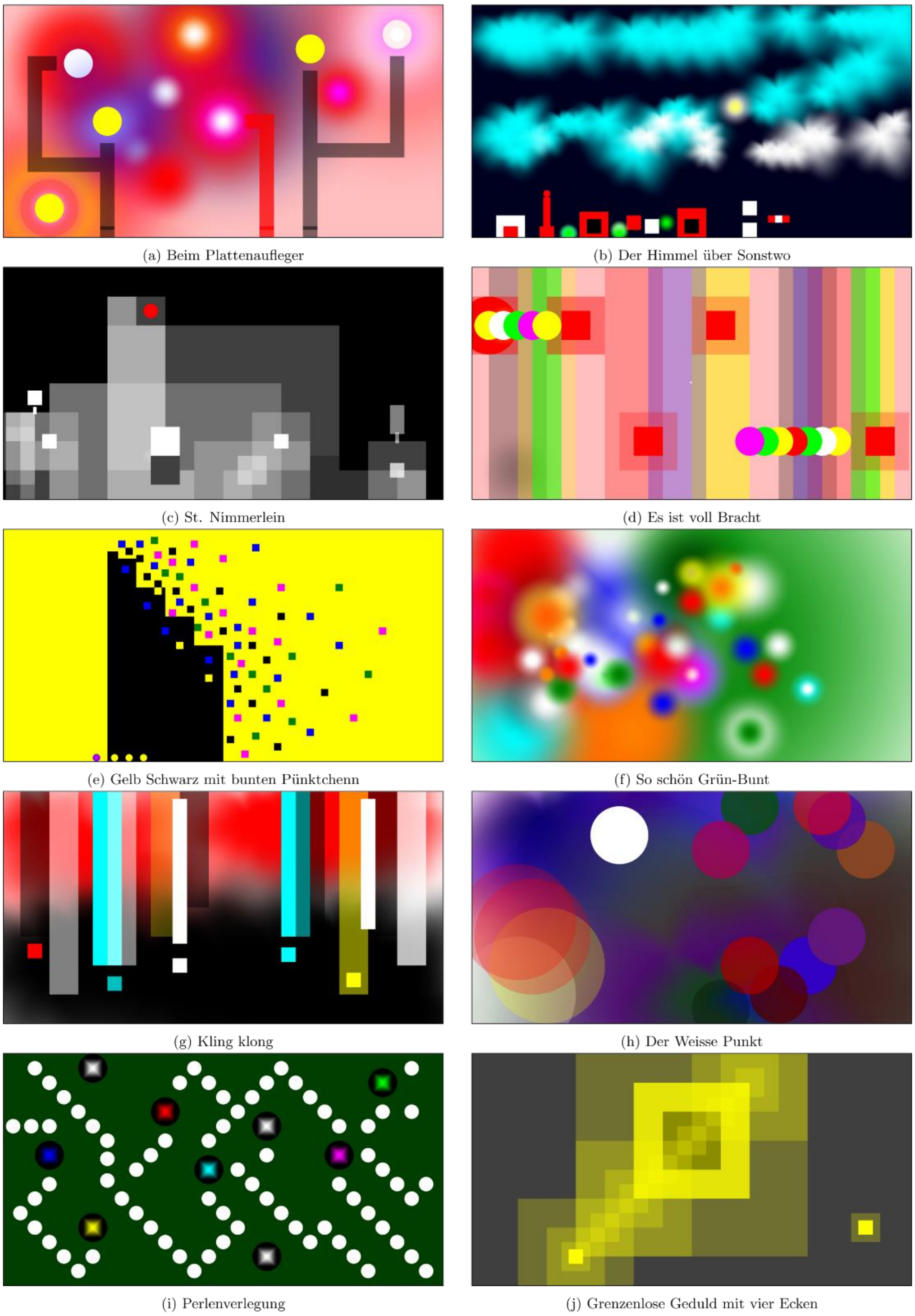


Figure 52: Example Brain Paintings of JT.

Paintings by JT. When he was still able to paint with his hands, lines, stripes and paths were fundamental in his paintings. With Brain Painting he used a sequence of squares to create lines and paths, as can be seen in (a), (d), (g). Source: Holz, E. M., Botrel, L., & Kübler, A. (2015). Independent home use of Brain Painting improves quality of life of two artists in the locked-in state diagnosed with amyotrophic lateral sclerosis. *Brain-Computer Interfaces, 2(2-3)*, 117-134, p. 129.

2.3.3.4.3 Comments provided by the family (HP)

Regarding critical aspects of the BCI the family reported that "*electrode gel sticks on the scalp and hair, but it can be removed easily*". Time investment is moderate "*when everything is well adjusted and works well*". For improvements they indicated "*more forms and colours*" and also an "*emergency call option*". They reported further that with Einstein the BCI is more effective, and "*dry electrodes would be brilliant*". With respect to the time effort the family indicated that "*it is justifiable for the benefit*", "*because all caregivers and family members help, it is no problem*". For set-up time, they reported that they need 20 to 40 minutes to set-up the BCI session. Time is depending on different factors, such as how much time is needed to find the right position for the end-user to paint, good position to communicate with the eye-tracker and also on the person that is setting up the system. Another 10 to 20 minutes is needed for the set-up of software "*if everything works good*", meaning that they find the correct file for painting that the end-user wants to continue working on. The family stated: "*Great invention; very good possibility to express his-/herself for a paralyzed creative person, enabling finally to be creative again*"

2.3.4 Discussion

In this study a P300-ERP BCI for creative expression, Brain Painting, was implemented at the homes of two artists in the locked-in state due to ALS. End-user HP has been using the BCI 1 to 3 times per week for 3 years (36 months) and end-user JT also several times per week for 15 months (by now). The usability of the BCI as assistive device was evaluated in terms of effectiveness, efficiency and satisfaction. Furthermore the usefulness of the BCI, in terms of face valid measures of BCI use in daily-life and the influence of the BCI on the end-users' lives, was assessed.

2.3.4.1 Face valid measures of BCI use in daily-life

End-users opened the BCI application for painting in a remarkable number of sessions (HP: 352 sessions and JT: 158 sessions). They painted with the BCI for more than 528 hours (HP) and 168 hours (JT). It is important to note that total painting duration does not represent the total session duration, which is much higher due to breaks (e.g., caregivers make a pause after approximately every 30 minutes). It can be derived that the cap stays on the head for much longer time and that reliability of the EEG electrodes (including gel that dries out) stays stable for several hours up to estimated 4-5 hours. Independent BCI use of a patient in locked-in state has been demonstrated earlier by the BCI team around Sellers (Sellers et al., 2010). Authors report that the BCI is used by the patient 6-8 hours/per day over 2.5 years. However face valid measures of every-day life, such as number of sessions and total usage time/session duration, are not reported in this study. Therefore the present study documents for the first time in BCI research quantitative data on independent BCI use.

2.3.4.2 Usability

2.3.4.2.1 Effectiveness

End-users rated their level of control in 44% (HP) and 80% (JT) of all BCI sessions as being equal or higher than 70% and therefore above the cut-off proposed by Kübler and colleagues necessary for satisfactory communication (Kübler, Neumann, et al., 2001; Kübler et al., 2004). Level of BCI control, albeit subjective, was comparable to "objective" accuracy assessed in long-term home use of a BCI communication program in one ALS end-user, who had a consistent mean accuracy of 83% over 2.5 years (Sellers et al., 2010). It can be argued that this subjective rating of level of BCI control does not represent an objective accuracy, however Brain Paintings by the artists do not appear randomly generated, but rather deliberately and precisely designed, thus perceived level of BCI control may represent objective BCI performance. HP stated however that she rated BCI control usually lower as it actually was, because she was biased by decreasing BCI control at the end of the session. The experience of low control may also arise when selected forms or colour do not match what was imagined even if it is correctly selected.

Results indicate that subjective level of BCI control varied strongly between sessions. Additionally, end-users indicated a decreasing BCI control in 44% and 18% of all BCI sessions. BCI control was influenced by several factors, such as deficient set-up of the EEG-cap. As reported by the family of HP they tried to avoid using a large amount of electrode gel, because it was difficult and time-consuming to remove the gel from hair and it also caused itching on the scalp if it was not fully removed. Furthermore level of BCI control was influenced by hardware related issues, such as shifting of the EEG cap and/or drying of gel after 2-3 hours of painting or altered shape of the EEG cap after several (100-200) BCI sessions. Also personal factors influenced level of BCI control (e.g., concentration, tiredness, distraction, personality). HP stated in personal contact that she needs to be highly concentrated for painting and that she learned that she cannot paint if she is too tired (e.g., after physiotherapy). Personality traits also impacted BCI performance. HP stated: "[…] *Brain Painting not only gives me back indulging in colors, but it is also a challenge. Being very emotional and spontaneous, it is really hard work for me to concentrate and be systematic*". HP stated further that thinking "*too long about what I want to* *paint next*" influences her subjective level of BCI control. Moreover disease related issues influenced BCI control. JT reported that his control over the BCI was influenced by his cough in some sessions, however he indicated that he was nevertheless satisfied with the BCI: "*I do not want to focus of my attention on my cough. I have enough time and I refine until I am satisfied with it* [painting]. *This is the way I did it in the past as a hand painting artist* […]". Also, environmental factors, such as medical treatment (e.g., cough assist or feeding with percutaneous endoscopic gastrostomy), during the BCI session influence her/his concentration. These personal and environmental factors appear difficult to be fully removed. However implementation of an auto-calibration function (Kaufmann, Volker, et al., 2012; Sellers et al., 2010) may improve BCI control. More extended discussion in **3.2.1.1 Inter-individual differences in performance** and **3.2.1.2 Intra-individual differences in performance**.

In HP perceived effectiveness increased within the first 200 sessions and was significantly higher with Einstein Brain Painting despite lower number of sequences. Face-overlay stimulation enlarged P300 amplitude in HP, as previously reported for other patients with neurodegenerative disease (Kaufmann, Schulz, et al., 2013). Even though both effects may also be influenced by other factors such as consolidated use (more training, better adjustment of EEG cap or adapted BCI parameters), it can be assumed that Einstein face stimulation improved effectiveness, as was expected from studies of Kaufmann and colleagues (Kaufmann, Schulz, et al., 2011; Kaufmann, Schulz, et al., 2013). Same as for HP (for the first 200 sessions), perceived effectiveness in JT increased with time (for all 158 sessions). Because JT started later in this study with the already improved Brain Painting with Einstein face stimulation, increased effectiveness in JT may result from consolidated use of the BCI system. Within the sessions 200 to 352 HP's perceived effectiveness decreased again. This result is somewhat alarming as it may indicate a gradual loss of control. However further recalibrations and evaluation will show whether this trend remains preserved or whether perceived level of control again increases. The finding that BCI performance decreases is contrary to results by Sellers and colleagues (2010), who found no deterioration in BCI performance over 2.5 years in one person with ALS (Sellers et al., 2010).

2.3.4.2.2 Reliability of ERP signals

HP's P300 amplitude was decreased in calibration 4 (26 months), as compared to calibration 3 (9 months), same for JT from calibration 1 (start) to calibration 3 (15 months). These results are in contrast to results by others, who found no deterioration of P300 amplitude when using a ERP BCI over several weeks (Nijboer, Sellers, et al., 2008; Sellers & Donchin, 2006) and years (Sellers et al., 2010). Amplitude of the P300 signal could be degraded by different factors: Habituation or decreased amplitude with repeated stimulus presentation have been found within different ERP paradigms (Kinoshita, Inoue, Maeda, Nakamura, & Morita, 1996; Ravden & Polich, 1998, 1999) and have been discussed as an issue for long-term BCI use (Kübler, Kotchoubey, et al., 2001); age related differences in ERP responses have been reported, such as longer latencies and reduced amplitudes in older as compared to young adults (Donchin, Miller, & Farwell, 1986); McCane found significantly lower P300 amplitudes in individuals with ALS who had visual impairments as compared to individuals with ALS who had not (McCane et al., 2014). However and most importantly the amplitude of the P300 signal does not necessarily hamper BCI control, such as offline classification results were better in calibration 4 (100% offline accuracy after 2 sequences) as compared to calibration 3 (100% offline accuracy after 3 flashing sequences) in HP, same for JT (calibration 1 compared to 3); in line with (Silvoni et al., 2013; Silvoni et al., 2009). Taken together, although rating of level of BCI control was subjective, it can be concluded, that the P300 signal can be used as input channel for a BCI device over more than several months and years despite decreased amplitude of the P300.

2.3.4.2.3 Efficiency

Subjective workload was moderate for both end-users and did not increase nor decrease over time and in most of the sessions (HP: 73% and JT: 73%) exhaustion was low. This is an important finding, indicating that the BCI can be used by people with ALS over a long time period of months and years without high workload or effort. More importantly, HP stated that the BCI would be less exhausting than her eye-tracker and that she would not prefer to control the painting application with her eye-tracking system. Assuming an accuracy of 80% (70-90% was mostly indicated), end-users would have an (estimated) ITR of 11.4 and 9.68 (bits/minute). This is remarkably higher as compared to the previous Brain Painting study by Zickler and colleagues (2013), in which the highest ITR in free-painting was 5.22. These findings indicate that face-stimulation improved efficiency, as previously shown by (Kaufmann, Schulz, et al., 2011), also in people with neurodegenerative diseases (Kaufmann, Schulz, et al., 2013). Interestingly HP asked after several intervals to increase the post-sequence interval (from 5 to 7s and from 7 to 10s). She indicated that she needed more time to think what she would like to select next. This shows that speed was not so important. Thus a large time interval of 10 seconds was also set when implementing the Brain Painting at the home of JT and he was very satisfied with the timing of the device (i.e., never asked to reduce the interval, when asked). More extended discussion in general discussion (**3.2.2 Translational gap**).

2.3.4.2.4 Satisfaction

Overall satisfaction and enjoyment was high for both end-users, and frustration low (VAS). Albeit in JT frustration decreased over time, in HP satisfaction and enjoyment decreased and frustration increased, related to her decreased subjective level of control. For both end-users satisfaction, enjoyment and frustration ratings were highly predicted by subjective level of BCI control, indicating that a minimum level of performance above 70% needs so be achieved for satisfactory use of the BCI (Kübler, Neumann, et al., 2001; Kübler et al., 2004). Albeit there was only low BCI control in some sessions, end-users' acceptability of the BCI as assistive device was high, as derived from high satisfaction rating in extended QUEST. This is in line with results by others, who found that low speed and low effectiveness are rather tolerated for entertainment, however, for communication, which is essential for interaction and quality of life, errors are less tolerated (Kübler et al., 2014; Zickler et al., 2013). Both end-users requested more forms, such as lines, triangles and more colours. The option to draw lines and to adapt the painting matrix to individual preferences and choices, has currently been developed (Botrel, Reuter, Holz, & Kübler, 2014).

2.3.2.3 Quality of life

Brain Painting had a positive impact on happiness, self-esteem, productivity, performance, quality of life, usefulness, self-confidence. HP stated that painting with the BCI satisfies her, because she has a result "*in front of her eyes*" – it makes her "*happy and free*". In both end-users the BCI had a negative impact on independence. End-users have to wait for their caregivers/assistants to be available for setting up the BCI. HP stated: "*I am using the Brain Painting 1 to 3 times per week, but if I could, I would use it every day*." In HP, a positive impact on independence was found in follow-up, indicating that she did no longer experience that the BCI increases a feeling of dependence on others, but rather increases her independence. Furthermore a negative impact on frustration was found; meaning that less frustration is experienced. With an improved self-esteem, HP feels stronger and encouraged (e.g., willingness to take chances, eagerness to try new things, ability to adapt to the activities of daily living), "*Brain Painting is like sunday breakfast for the soul…Something, to what I am looking forward everytime again. It activates, satisfies and relaxes me"*. Brain Painting supported social inclusion in both end-users, as they can exhibit their paintings in public exhibitions and sell their paintings (ability to participate). Thus Brain painting positively impact the quality of life of the end-users because it exactly matches the artists' need for creative expression: "[…] *Brain Painting makes me happy and satisfied everytime again, if it works - if not, then frustration and disappointment. Fortunately this happens in only few cases. BP completely changed my life. I can paint again and be creative again using colours* […]" (statement of HP, November 2013). Sellers and colleagues (2010) stated that the BCI impacted the life of the locked-in end-user, as derived from reports by the user, caregivers and family members (Sellers et al., 2010). However no empiric data is reported in their study, thus it can be assumed that the present study is the first that assessed quantitatively and qualitatively the impact of the BCI on the lives of two locked-in persons.

3. General Discussion

3.1 Summary of results

The aim of the thesis was to contribute to a reduction of the translational and reliability gap in BCI research (Kübler, Mattia, et al., 2013). Three different BCI applications for entertainment and communication were tested in controlled settings and in independent use. In all three studies potential end-users with severe motor restrictions, in total N=10, were included. Three were in the locked-in state and two in the incomplete locked-in state. In *study 1* a MI controlled BCI gaming prototype was tested by four severely disabled end-users (two in the locked-in state). In *study 2* ten healthy subjects and four severely disabled end-users tested a hybrid BCI for communication, combining EMG and EEG (P300-ERP) input signals. In *study 3* a P300-ERP controlled BCI for creative expression, was implemented at the homes of two artists diagnosed with ALS for independent home use. In accordance with the user-centred design, usability of the BCI was evaluated in terms of its effectiveness, efficiency and satisfaction, following the definitions by Kübler and colleagues, with slight modifications/extensions (Kübler et al., 2014; Zickler et al., 2011). Effectiveness was defined as accuracy, subjective level of BCI control and loss of control. ITR and subjective workload as well as total time per task and level of exhaustion were considered as efficiency metrics. Measurements of satisfaction were VAS satisfaction/VAS enjoyment/VAS frustration, satisfaction with BCI as assistive device (extended QUEST) and assessment of the match between person and BCI technology (ATD-PA). Furthermore usefulness of the BCI was assessed: in *study 1* and *2* end-users were asked whether they could imagine using the BCI in their daily-life, in *study 3* face valid measures of daily-life use and the influence of the BCI on the life of the person (PIADS) were assessed. Summarizing results the following findings were obtained:

3.1.1 Usability

3.1.1.1 Effectiveness

Highest effectiveness was achieved with the P300-ERP BCI. Here all end-users received accuracies above 80% in the copy-spelling tasks. With the MI BCI only one of four end-users reached an accuracy of 80%. Accuracy in the P300-ERP BCI was lower for the free-spelling and email task. In independent use subjective level of BCI control was rated as being equal or higher than 70% in most of the sessions. Therefore for the P300-ERP BCIs, irrespective of setting (controlled or independent use), effectiveness was mostly above the cut-off for satisfactory communication proposed by Kübler and colleagues (Kübler, Neumann, et al., 2001; Kübler et al., 2004), whereas in the MI BCI it was not. In *study 2* effectiveness was lower compared to healthy subjects for some but not all end-users. Effectiveness was improved by optimized stimulation mode (grids and famous faces; in *study 2* and *3*). In one end-user perceived effectiveness decreased over the time course of 36 months (*study 3*).

3.1.1.2 Efficiency

Accordingly, ITR was lower in the MI BCI as compared to the P300-ERP BCI. As a consequence of lower effectiveness, in the P300-ERP BCI, ITR was lower in end-users (range: 2.6-15.1 bits/minute) as compared to healthy subjects (range: 12.93-18.59 bits/minute). Spelling bitrate was improved by grid/face stimulation and by implementation of a hybrid approach. Subjective workload was moderate across all BCI applications and tasks indicating that the BCI was not too challenging or demanding for the end-users. Highest workload was indicated in some sessions in the MI BCI; and the more complex tasks (email and free-spelling) engaged higher workload as compared to the less complex tasks (e.g., copy-spelling) in the P300-ERP BCI. Workload did not increase over time (36 and 15 months) in independent use. Exhaustion in daily-life use was low for most of the BCI sessions and one end-user reported that the BCI is less exhausting than her eye-tracker. Contrary to that, most of the end-users expressed in personal statements that spelling with the hybrid-P300 BCI was challenging/exhausting because high concentration is needed. Also one end-user indicated high workload ratings for several time intervals for the P300-ERP BCI in independent use.

3.1.1.3 Satisfaction

Even though effectiveness and efficiency of the MI BCI were lower as compared to the hybrid P300-ERP application, the MI BCI application was better accepted by the end-users. Highest satisfaction was expressed for the easy to use Brain Painting, which was used in daily-life. For both BCI prototypes that were tested in controlled settings, main obstacles for daily BCI use were the EEG cap and electrodes, time-consuming and complicated adjustment, low effectiveness and reliability and low speed. End-users were highest satisfied with safety and learnability.

3.1.2 Usefulness

3.1.2.1 Daily-life use/face valid measures

Two of four end-users could imagine using the MI BCI gaming application in daily-life and one of four end-users could imagine to use the hybrid BCI for communication. Results of *study 3* show that a P300-ERP BCI can be used in daily-life for more than 3 years, in more than 352 sessions and for more than 528 hours in one end-user. These positive findings could be replicated in another end-user, who used the BCI for more than 15 months, in 158 sessions and with a total painting time of 168 hours, by now.

3.1.2.2 Impact on the life of the person

BCI improved feelings of happiness, usefulness, self-confidence, self-esteem, productivity, well-being, ability to participate and consequently quality of life of the end-users in the locked-in state. A negative influence was found on frustration, confusion and independence, indicating that these dimensions were less present when using the BCI in daily-life.

3.2 Bridging gaps

3.2.1 Reliability gap

Many BCI studies exist that introduce improvements in accuracy or bit rate, the main measurement of performance in BCI research. Most BCI studies include only healthy subjects, and rely on single sessions. However only few deal with targeted end-users, where multiple sources of artefacts exist such as altered brain responses and changes in health status. Thus BCI research is confronted with a reliability gap, because little is known about intra- and inter-individual variance in performance of those end-users. One important research question that needs to be addressed is, whether a BCI can be reliably used over a long time period for several weeks, months or years. The reliability gap can thus only be bridged by including end-users in the field, in short-term, but especially long-term studies, and by investigating the aspects that influence successful BCI performance.

3.2.1.1 Inter-individual differences in performance

Results revealed differences in performance between healthy participants and end-users and also high variances in performance within the target group, indicating inter-individual differences. High differences in performance has also been found in other BCI studies with potential end-users, due to heterogeneity in paradigms and type/progression of disease (Kübler, Nijboer, et al., 2005; Nijboer, Sellers, et al., 2008; Silvoni et al., 2009; Zickler et al., 2011), for reviews see (Kübler & Birbaumer, 2008; Mak et al., 2011). Even though a relationship between the progress of disease and BCI performance was not confirmed (Kübler & Birbaumer, 2008; Nijboer, Sellers, et al., 2008; Prior et al., 2010; Silvoni et al., 2013; Silvoni et al., 2009), disease related factors seem to influence BCI performance in some end-users: End-users present neuronal loss/altered brain structure due to stroke, accident or neuronal degeneration. For example in end-user D (*study 1*), part of the skullcap was missing since an operation after cerebral bleeding several years ago. Altered ERP patterns were found in some end-users: For instance the P300 signal was not reliable found in all end-users in *study 2*. Changed ERP patterns due to neuronal degeneration, such as dimished P300 amplitude and prolonged latency, have been found in several studies (Hanagasi et al., 2002; Paulus et al., 2002; Silvoni et al., 2009). Another factor that influences BCI control is noise: EEG signals are noisier in the target group due to muscle artifacts caused by involuntary muscle contractions (e.g., spasm, fasciculations). Spasm influenced the quality of brain signal recording in two end-users in *study 1* (end-user C and D; diagnosed with infantile cerebral paresis and stroke). In one end-user in *study 3* (end-user JT) fasciculations influenced signal quality and BCI control level consequently. Small involuntary muscle contractions (fasciculation) are frequently present in persons with MND (Mateen, Sorenson, & Daube, 2008). Another confounding factor may be medication. For example intake of antidepressants have been found to influence brain signals, such as a reduction of P300 amplitude (d'Ardhuy et al., 1999). Moreover attentional and cognitive problems after stroke are a well-known problem that can influence BCI performance (Tatemichi et al., 1994). Schreuder and colleagues (2013) found that an end-user with brain-stem stroke was unable to gain control in a spatial hearing multi-class auditory P300-ERP paradigm, whereas healthy subjects were able to (Schreuder et al., 2013). This end-user was, however, successful in a less complex visual P300-ERP spelling task. The authors assessed neurophysiological data and found deficits in attention, memory and executive capacities in this end-user. According to the authors, higher cognitive capacities (e.g., for maintaining items or target number in short term memory) are demanded in the auditory ERP BCI, as compared to a visual ERP BCI, and since resources are limited, end-users are more challenged in more complex tasks; in line with (Nijboer, Furdea, et al., 2008). Similar results were made by Silvoni and colleagues (2009). Comparing the ERPs of a group of patients with ALS and a control group, authors found no difference in the P300 signal in a simple two class oddball paradigm, however in a more complex four-class BCI task (Silvoni et al., 2009). Neurophysiological assessment revealed mild cognitive impairment (e.g., attentive and executive functions) in some end-users. Authors argue that the more complex tasks strain more attentional resources, which are limited in the target group; they are thus more challenging for the end-users, as compared to healthy controls. According to the authors, smaller P300 amplitudes are a correlate of these affected attentional resources. Unfortunately in the present thesis neuropsychological data was not assessed because, due to the already extensive evaluation protocol, time schedule was limited. Other factors, such as compromised vision can influence performance in a P300-ERP BCI. For example McCane and colleagues (2014) found in individuals of a rather homogenous target group (all diagnosed with ALS), that those, who were unable to control a P300-ERP BCI, had visual impairment, such as ptosis, diplopia, nystagmus (McCane et al., 2014).

A major aim of this thesis was to include end-users with a broad spectrum of diagnoses. For persons diagnosed with CP establishment of ICT is challenged due to a wider spectrum of impairment. Communication solutions are available, however these depend on motor activity and the assistance of others; therefore BCI devices could offer new opportunities for this target group (R. Scherer et al., 2014). Implementation of a BCI was however challenged in this patient group. End-user C (*study 1*) was unable to gain control in the MI BCI. He neither gained control in an earlier study with a SCP BCI (Kübler & Birbaumer, 2008); and was included in the calibration procedure in the hybrid P300-ERP BCI (*study 2*), however, no differentiable signals could be found, neither with the 6x6, nor the 3x3 matrix; discriminative signals were neither elicited with the face speller by Kaufmann and colleagues (unpublished data). In other attempts to establish communication with the face speller (Kaufmann, Schulz, et al., 2011) in persons with CP also failed (unpublished data). Main challenges were muscular artifacts due to spasm and (presumably) cognitive impairment (e.g., sometimes due to problems with oxygen supply). Current BCI teams aim at establishing communication with BCI in this target end-users by, for example, implementing superior artefact detection algorithms (R. Scherer et al., 2014). A user-centred development and adaptation of features according to the users' needs and requirements is therefore of utmost importance for bringing BCI to end-users.

3.2.1.2 Intra-individual differences in performance

The present thesis revealed intra-individual differences in BCI performance. For instance performance varied across tasks (e.g., copy- vs. free-mode task or copy-spelling vs. email task). Similar results were found in the Brain Painting study by Zickler and colleagues (2013), in which end-users showed higher cognitive load in the free-painting task, as compared to the copy-painting tasks, resulting in a higher variation in BCI performance (Zickler et al., 2013). Limited cognitive/attentional resources in the target group, as described above, can also explain such intra-individual differences. Especially higher ISI can help to enable end-users enough time (e.g., for moving attention to the digital canvas on the second screen and to think about what to select next and focusing again on the matrix). Independent of the complexity of the BCI task, intra-individual differences in BCI performance were also found within the tasks (e.g., always painting in the free-mode in *study 3* or always copy-task in MI BCI in *study 1*). BCI performance was influenced by disease related factors (e.g., fasciculation, cough, "*dry eyes*"). Furthermore BCI control level was influenced by personal and environmental factors (e.g., tiredness, concentration, distraction, medicine intake, etc.), "*If bad concentration, then bad accomplishment*", "*In my case it very depends on my physical condition/concentration, which varies per day, but this is also the case for other AT* (keyboard)". In *study 3* end-users reported that they need to be highly concentrated for painting and that they cannot paint if they are tired/exhausted (e.g., after exhausting physiotherapy) or distracted (e.g., by medical treatments or cough). HP stated regarding effectiveness of the BCI: "*Most of the times ok, depends on exhaustion and concentration*". Furthermore end-users' personality had an influence on BCI performance, such as thinking *"Too long about what I want to paint next*" and *"Being very emotional and spontaneous, it is really hard work for me to concentrate and be systematic".* BCI control was also influenced by faulty BCI set-up (e.g., position of the cap and electrodes, filling of the electrode gel), and/or hardware reliability (e.g., cap bulges after several sessions and does not fit to the head any longer; electrodes show malfunctioning after several sessions, especially for end-users, because they lie on a head pillow resulting in a high pressure on the electrodes).

Amplitude of the P300 signal decreased over the time course of several months and years in both end-users and effectiveness decreased in one end-user in *study 3*. These findings are in contrast with results of Sellers and colleagues (Sellers et al., 2010), who found stable ERP signals and BCI performance over 2.5 years; also in accordance with (Birbaumer et al., 1999; Neumann & Kübler, 2003; Nijboer, Sellers, et al., 2008). Dimished P300 amplitude due to neuronal degeneration have been found in several studies (Hanagasi et al., 2002; Paulus et al., 2002; Silvoni et al., 2009). P300 amplitude can also be degraded by other factors. For instance studies report on a decreased P300 amplitude due to habituation after repeated stimulus presentation (Kinoshita et al., 1996; Ravden & Polich, 1998, 1999), old age (Donchin et al., 1986) or visual impairments (McCane et al., 2014). It cannot be excluded that the P300 signal and BCI control was impacted by these factors. Nevertheless it is a critical result, as it may indicate a gradual loss of BCI control. However and most importantly the amplitude of the P300 signal does not necessarily hamper BCI control; both end-users had no deterioration in offline performance (calibration). A results that is in line with Silvoni and colleagues, who found lower amplitude in the P300 signal in a group of patients with ALS, as compared to a control group, but no significant differences in BCI performance between both group (Silvoni et al., 2013; Silvoni et al., 2009). It can be concluded, that the P300 signal can be used as input channel for a BCI device over more than 3 years despite decreased amplitude of the P300 and decreased BCI control. Further recalibrations and evaluation will show whether this trend of BCI control remains preserved or whether BCI control again increases.

3.2.1.3 Summary and derived implications

Taken these results together it can be summarized that BCI performance is influenced by many internal and external factors; as previously integrated into a "model of BCI control" by Kübler and colleagues (Kübler et al., 2011). Most factors, such as disease related, personal and environmental, appear difficult to be fully removed, however multiple toeholds for improvements exist:

(1) Evaluation: It is important to assess after each run or session if the patient was able to concentrate or if anything was disturbing (e.g., noise or pain) or unclear (e.g., instructions).
(2) Tiredness, exhaustion and distraction: It should be guaranteed that the end-user is in a silent surrounding while spelling/painting. This has to be considered especially for daily-life use. Frequent pauses and not too long session duration can prevent exhaustion and tiredness. If the end-user is getting tired or lacks of concentration within a BCI session, workload or exhaustion could be detected by a passive BCI, that stops the BCI session (Käthner et al., 2014; Zander & Kothe, 2011). New approaches, such as dynamic stopping, could help in adapting features of the BCI if a user is distracted (Kindermans et al., 2014).
(3) Cognitive/attentional issues: Cognitive impairment (e.g., attentive and executive functions) should be examined in neuropsychological assessment, if possible (Kübler et al., 2014; Sellers et al., 2014; Silvoni et al., 2009; Tatemichi et al., 1994); adaptation of timing (ISI, number of sequences, pauses) according to the user's needs seem crucial and can reduce attentional issues. Training of heart rate variability could improve capability to focus attention and to inhibit interference by distracting irrelevant stimuli (Kaufmann, Vögele, Sütterlin, Lukito, & Kübler, 2012); albeit not tested yet.
(4) Hardware related issues: Problems related to the EEG cap, such as shifting or bulging (e.g., after medical treatment and/or movement of the head), was one of the major problems in daily-life use. The consequence is that some electrodes do no longer contact

the scalp and that the EEG cannot be reliably recorded and/or noisy EEG data. Thus, electrode drifts or shifts should be automatically detected by the BCI. Such approaches have already been developed, for example a system that identified how often the backspace key is used and if it is used too often the BCI is recalibrated. This would be very useful for Brain Painting, for example if the user selects too often the "undo" option, the system should pause or automatically recalibrate (Dauce & Proix, 2013). In general more stable material for the EEG cap and more stable EEG electrodes could prevent such issues. A signal check (impedances) can proof signal quality before starting a session.

(5) Visual impairment: For patients with visual impairment, BCI in auditory or tactile mode could be a solution. Adaption of size of a P300-ERP matrix and individual adaptation of stimulus mode could further help to overcome visual problems (Kaufmann, Holz, et al., 2013).

(6) Spams or other muscular artifacts: Future work should investigate algorithms for identification of artifacts in the EEG. An optimal BCI would pause if the EEG data is too noisy. First online artifact removal procedures are available (Daly, Nicolaou, Nasuto, & Warwick, 2013; Daly, Scherer, Billinger, & Müller-Putz, 2014; Halder et al., 2007).

(7) Psychological factors: A routinely assessment of psychological variables, such as well-being and motivation (Hammer et al., 2012; Kleih et al., 2010; Nijboer et al., 2010; Nijboer, Sellers, et al., 2008) and also physical (e.g., pain) or medical state of the end-users, can enable the decision, whether a BCI session should be started or better postponed to another day (if possible), on which the user is in a better condition (less distracted, higher motivated, less frustrated, less pain, etc.).

3.2.2 Translational gap

As most of the BCI applications are tested in a healthy population, BCI research faces further a translational gap when bringing BCI to end-users. To bridge this gap the UCD was adapted to BCI research and development, which implements an iterative process between end-users and developers based on a valid evaluation procedure with the final goal to create BCI solutions that are accepted by end-users as assistive devices for daily-life use. The theoretical framework can guide the design of translational studies on how to transfer BCI-controlled applications from the laboratory of developers to the homes of end-users (Kübler et al., 2014). Five different BCI prototypes have been tested in translational studies following the UCD and on the basis of the same evaluation metrics: Four in controlled settings; two in the present thesis, Connect-Four (*study 1*) and hybrid P300-ERP BCI for communication (hybrid spelling; *study 2*); and two, P300-

ERP BCI for communication (spelling) and Brain Painting, in studies by Zickler and colleagues (Zickler et al., 2013; Zickler et al., 2011); and one, the easy to use Brain Painting, in independent daily-life use in the present thesis (*study 3*), see **table 38**. In accordance with the ISO (ISO-9241-210, 2008), usability of BCI prototypes were evaluated in terms of its effectiveness, efficiency and satisfaction; in addition usefulness of the BCIs was assessed (Kübler et al., 2014; Vaughan et al., 2012). It is important to note that there exist also other evaluation studies following a user-centred approach: In the study by Riccio and colleagues (2015) the same hybrid P300-ERP prototype, as in *study 2*, has been tested (Riccio et al., 2015), however with a different protocol; evaluation results are reviewed in (Kübler et al., 2014). Because only a rough overview of results is provided in this review, these results are not included in the following comparison/review of results. Also other studies investigated user experience based on a holistic approach in context of BCIs and several usability aspects of BCIs such as accuracy, workload and learnability (Lorenz et al., 2014; Pasqualotto et al., 2009; van de Laar et al., 2011), albeit in healthy subjects, and are thus not included in the following review.

3.2.2.1 Usability

3.2.2.1.1 Effectiveness

Highest effectiveness was obtained in the copy-spelling and copy-painting tasks in both communication prototypes and in the Brain Painting prototype (spelling: 86-100%; hybrid spelling: 80-100%; Brain Painting: 80-100%). Effectiveness in the free-mode tasks was lower as compared to the copy-mode and more variable between end-users in all BCI applications (spelling: 71-100%; hybrid spelling: 48-100%; Brain Painting: 55-100%; easy to use Brain Painting: mostly 70-90%). Effectiveness was lowest in the MI BCI (43-80%) and only two end-users had sufficient control to enter the free-mode. Results are in line with findings by Nijboer and colleagues (2010), who found higher accuracies in the P300-ERP as compared to the MI BCI in the target group (Nijboer et al., 2010); also in line with findings in healthy participants, who had lower performances in a MI/SMR BCI as compared to a P300-ERP BCI (Guger et al., 2009; Guger et al., 2003; Lorenz et al., 2014).

3.2.2.1.2 Efficiency

ITR was lowest in the MI BCI (maximum: 1.44 bits/min). Efficiency, in terms of speed and ITR, could be improved by optimized stimulation mode, adaptation of sequences and a hybrid approach; ITR was, thus, twice as high in the hybrid as compared to the classic spelling (maximum: 15 bits/min; compared to spelling: maximum: 8 bits/min). A result that is in line with results by Riccio and colleagues (Riccio et al., 2015). Even if ITR can only be estimated in independent use of Brain Painting, ITR seems to be improved with face stimuli as compared to the conventional flashing mode; maximum ITR with an estimated accuracy of 90-100% is 12-17 bits/minute (even though time between trials was very high). Total subjective workload was lowest in the P300 BCI controlled painting application (5-49 out of 100). Highest workload was indicated by the end-user that used the easy to use Brain Painting in daily-life (54-70, out of 100). These results indicate that objective and subjective measures of efficiency may considerable dissociate and that ITR alone cannot be considered as indicator of the potential usability of the targeted application (Kübler et al., 2014).

Table 38: Comparison of evaluation results for five BCI prototypes.

Note: Evaluation was based on same or very similar protocol. 11[a] end-users tested prototypes in controlled settings and 2 end-users in daily-life.

	Evaluation metrics			
		Usability		**Usefulness**
	Effectiveness[b]	**Efficiency**[c]	**Satisfaction**[d]	**Daily-life use**[e]**; Face valid measures**
Study 1: MI BCI (gaming) **N=4**	**Copy-task:** A: 52-73% B: 46-64% C: 43-50% D: 51-80% **Free-mode**: 2 end-users	**ITR (copy-task)**: maximum values: A: 1.15 B: 0.82 C: 0.32 D: 1.44 **WL**: 29-52	**QUEST score:** *M*=3.78; **added items**: *M*=3.88 **ATD-PA**:A: 3.25; B: 2.33; C: 3.25; D: 4.25	**Daily-life use:** Yes: 2 No: 2 (would use it in free-time)
Study 2: Hybrid P300-ERP BCI (hybrid spelling) **N=4**	**Copy-task (range):** A: 100%; B: 90-100%, C: 100%; D: 80-95% **Sentence+Email (range):** A: 100%; B: 82-86%; C: 68-78%; D: 48-80%	**ITR:** **Copy-task**: A: 15; B: 11-13; C: 9; D: 6-8 **Sentence+Email:** A: 15; B: 8-12; C: 5-6; D: 3-6 **WL**: 13-50	**QUEST score**: *M*=3.88; **added items**: *M*=3.88 **ATD-PA**: A: 3.42; B: 3.45; C: 2.33; D: 3.64	**Daily-life use:** Yes: 1 No: 3 (current AT for communicati on are superior)
Zickler et al. 2011: P300-ERP BCI (spelling) **N=4**	**Copy-task:** A: 100%; B: 86%, C: 100%; D: 100% **Free-spelling+Email+ Internet (range):** A: 94-100%; B: 77-90%; C: 71-90%; D: 73-89%	**ITR:** **Copy-task:** A: 8; B: 6; C: 8; D: 8 **Free-spelling+Email+Internet (range):** A: 7-9; B: 5-7; C: 4-7; D: 5-7 **WL**: 9-49	**QUEST score**: *M*= 3.81**, added items**: *M*=3.71 **ATD-PA**: not applied	**Daily-life use**: Yes: 0 No: 4 (current AT for communicati on are superior)
Zickler et al. 2013: P300-ERP BCI (Brain Painting) **N=4**	**CS/CP/FP(FP range)**[h] A: 90/95/80% (55-94) B: 95/100/89% (86-94) C: 80/80/91% (84-100) D: 95/80/80% (67-92)	**ITR: CS/CP/FP last** A: 6/6/5 B: 6/7/5 C: 5/5/5 D: 6/5/5 **WL**: 5-49 (range across users and different tasks)	**QUEST score**: *M*=4.2, **added items score**: *M*=4.4 **ATD-PA**: A: 4.3; B: 3.4; C: 4.2; D: 3.8	**Daily-life use**: Yes: 3 No: 1 (would use it 1 to 2 times per week)
Study 3: P300-ERP BCI (Easy to use Brain Painting) **N=2**	**Free-mode:** **0-50%:** HP: N=80; JT: N=10 **50-70%:** HP: N=97; JT: N=21 **70-90%:** HP: N=116; JT: N=69 **90-100%:** HP: N=51; JT: N=58	**Estimated ITR**[g]**:** **60%:** HP: 7; JT: 6 **70%:** HP: 9; JT: 8 **80%:** HP: 11; JT: 10 **90%:** HP: 14; JT: 12 **100%:** HP: 17; JT: 14 **WL**: HP: 13-62; JT: 54-70	**QUEST score**: *M*= 4.75, **Added items**: *M*=4.94 **ATD-PA**: HP: 4.8; JT: -	**Daily-life use:** N=2; HP: 352 sessions, 528 hours; JT: 158 sessions, 168 hours

[a]: N=11 end-users in controlled settings: N=4 (Connect-Four), N=4 (Hybrid P300 communication) and N=4 (Qualilife P300 communication), and N=4 (Brain Painting). Note that one end-user tested two (spelling and Brain Painting) and two end-users tested three (spelling, Brain Painting and hybrid spelling; Brain Painting, Connect-Four, hybrid spelling) prototypes, therefore total number of participants (N=16) is not the same as total number of end-users (N=11).
[b]: accuracy [%] or subjective level of BCI control [%]; Values are rounded to the nearest whole number (zero digits after the decimal point).
[c]: ITR [bits/min] or level of exhaustion and total subjective workload (range). Note: With exception for *Study 1* (MI BCI), values are rounded to the nearest whole number (zero digits after the decimal point).
[d]: satisfaction with BCI as AT (extended QUEST) and match between person and BCI (ATD-PA). For extended QUEST ratings range between 1=not satisfied at all and 5=very satisfied. For ATD-PA highest possible score is 5.0, a score between 4.0 and 5.0 indicates a good match of person and the BCI, scores below 4.0 indicate that the match could be improved and a score of 3 or less indicates a risk of device non-use.
[e]: yes/no, reasons.
[f]: number of sessions, total usage time.
[g]: free-painting mode.
[h]: accuracy for three conditions: CS=copy-spelling; CP=copy-painting; FP=free-painting.

3.2.2.1.3 Satisfaction

3.2.2.1.3.1 Main obstacles for daily-life use

Among BCIs that were tested in controlled settings, highest satisfaction was indicated for Brain Painting (*M*=4.2 and added items: *M*=4.4, highest possible score: 5). In independent use, satisfaction ratings for the easy to use Brain Painting were even higher as compared to Brain Painting that was tested in controlled setting *(M*=4.75 and *M*=4.94; highest possible core: 5). All end-users were highly satisfied with learnability, safety, professional services and weight, with only few remarks: Learnability: "*Training every day would be good*"; safety: "*Cables too short between electrode box and amplifier*", "*Gel caused itching on the scalp*", "*Because of irritations on the scalp*". The following aspects were identified as main obstacles regarding regular use in daily-life (for exemplary statements see **table 39**).

1) Aesthetic design: Cables are disturbing and restrict mobility; cap looks like device used in hospital/medical/like a cyborg.
2) Comfort: Gel sticks hair together and has to be removed afterwards by washing of the hair; electrodes hurt after several hours.
3) Adjustment/set up (software/hardware): It is judged as time-consuming and complicated (e.g., starting of different programs on the PC, placement of the EEG-cap and electrodes, cables need to be connected to the amplifier); adjustment can be erroneous, if applying not enough gel or not finding the correct position of the EEG cap (in accordance with the 10-20 system); gel is mandatory for wet electrodes, which requires hair washing

afterwards; hair washing means burden for the patient and caregiver; cables and high number of electrodes were reported to be a problem.

4) Effectiveness and reliability: It is judged as too low (many errors); selections with the BCI are experienced as exhausting and time-consuming; performance depends on physical constitution and concentration, as well as on adjustment; cap bulges after several (~100) sessions influencing signal recording and reliability/effectiveness consequently.
5) Ease of use: High concentration is needed; bad control/accomplishment when distracted or tired.
6) Speed: Is it evaluated as too slow, in comparison to other assistive devices; should be twice as fast; it is exhausting and time-consuming to reach a goal (a sequence of selections, e.g., selections that are necessary to send a text per mail).

These results are in accordance with other evaluation studies by other BCI groups which also identified these aspects as the main obstacles for BCI use in daily-life (Blain-Moraes, Schaff, Gruis, Huggins, & Wren, 2012; Huggins, Wren, & Gruis, 2011; Kübler et al., 2014), thus implying the need to address these issues in future translational studies. The results are also in line with findings by Zickler and colleagues, who reported that functionality, ease of use and independent use were indicated by AT users as most important aspects for adoption of a new AT/BCI device in daily-life (Zickler et al., 2009).

Table 39: Main obstacles for daily-life use (personal statements by N=13 end-users).

BCI aspects	Exemplary statements by the end-users (N=13)
Aesthetic design	"*Foreign body*" (spelling), "*Looks medical*" (spelling), "*Eye-catching*" (spelling), "*Should work without cables*" (Brain Painting), "*Cap and cables are not aesthetic*" (Brain Painting),"*Doesn't look aesthetic. Most people probably wouldn't like to have many cables and electronic devices at one's body. Looks like a cyborg, who finds cyborgs handsome*?" (hybrid spelling)
Comfort	*"Cap shifts and electrodes press against head cushion after 1 hour*" (easy to use Brain Painting),"*Immobility of head*" (easy to use Brain Painting), "*Gel sticks hair together*" (easy to use Brain Painting), *"Due to electrode gel*" (gaming), "*Mobility is restricted*" (spelling), "*Washing of the hair afterwards is annoying, cables disturb and mobility is restricted*" (hybrid spelling)
Adjustment/set up	„*Cap did not fit immediately*" (gaming), "*Adjustment takes time and can be erroneous*" (hybrid spelling), "*Cap bulges at some electrodes* (easy to use Brain Painting)", "*Very technical*" (spelling), "*Adjustment of software is sometimes time-consuming, depends of handling*" (easy to use Brain Painting), *"Cap did not fit immediately*" (gaming), "*Because of cables - one could use infrared to date*" (gaming), "*Adjustment of cap is complex and takes too long, difficult for a novice*" (hybrid spelling), "*Adjustment takes time and can be erroneous (e.g., positioning of the electrodes)*" (hybrid spelling)
Effectiveness/ reliability	"*Depends on adjustment and constitution*" (easy to use Brain Painting), "*Temporary quote of errors very high*" (easy to use Brain Painting), "*It did not work in my case*" (gaming), "*The BCI works, but it is extremely exhausting and time-consuming to reach the intended goal*" (hybrid spelling), "*Because it did not work with 100%*" (gaming)
Ease of use	"*High concentration needed (also for correcting/undo)*" (easy to use Brain Painting), "*If bad concentration, then bad accomplishment*" (easy to use Brain Painting), "*Sometimes too exhausting/demanding if tired*" (easy to use Brain Painting), "*In my case it very depends on my physical condition/concentration, which varies per day, but this is also the case for other AT (keyboard)*" (hybrid spelling), "*You don't need high intellectual capacities, but you need to be very concentrated, this is not always easy*" (hybrid spelling)
Speed	"*Too slow, if less sequences, then more effective for me, because communication would be faster. In text-matrix too slow; for email lower speed okay*" (hybrid spelling), "*Too slow, should be faster*" (gaming), should be "*Twice as fast*" (spelling), "*Very slow*" (Brain Painting), "*Eye-tracking systems allow faster selections*" (Brain Painting), "*Need to be faster, 4 or 5 flashes ok* (*2-3 sequences*)" (hybrid spelling), "*Twice as fast*" and "*3-4 times faster*" (spelling)

3.2.2.1.3.2 Suggested improvements

The present thesis addressed improvements on effectiveness, reliability and speed by implementing a hybrid approach (*study 1* and *2*), individual adaptation of number of sequences (*study 2* and *3*) and new optimized stimuli (grid and faces; *study 2* and *3*). Comfort, aesthetic design and montage of the EEG-cap and electrodes were improved by considering only a few number of active electrodes which rely on transparent electrode gel (*study* 2 and *3*). Furthermore ease of use and set-up of software were addressed by simplifying a BCI application enabling easy and quick handling by non-BCI experts (*study 3*). The results of the present thesis indicate that these implementations were successful. Further improvements and implementations are conceivable:

1) Aesthetic design (of EEG cap and electrodes): Wireless electrodes and also dry electrodes are currently available (Guger, Krausz, et al., 2012; Zander et al., 2011). However for some new features, such as dry electrodes, advantages and disadvantages have to be weighted. On the one hand they do not rely on electrode gel, but on the other hand (at the current state of the art), comfort seems to be lower (e.g., Sahara electrodes from g.tec, Medical Engineering GmbH, Austria), and also reliability is worse as they are highly sensitive to noise and artifacts. No testing with end-users was yet made. Interestingly very concrete suggestions were given by one end-user: "*A helmet with integrated electrodes and adjusted for the individual form of the head*."
2) Comfort: Wireless electrodes would not or less restrict mobility; less number of electrodes would require less time for hair washing; modified electrode set-up, with no electrodes at the back of the head (occipital regions), could prevent pain when lying on the head pillow of the wheelchair. Less number of electrodes or set-up without electrodes on occipital regions could however impact classification of signals, and thus effectiveness of the BCI; therefore advantages and disadvantages have to be weighted.
3) Adjustment/set-up (software/hardware): Dynamic stopping (Kindermans et al., 2014) or co-adaptive calibration approaches (Vidaurre et al., 2010) could reduce set-up time as no calibration would be needed at all. Other approaches can reduce number of electrodes to a minimum (Colwell, Ryan, Throckmorton, Sellers, & Collins, 2014), and thus saving set-up time.
4) Effectiveness and reliability: New features, such as an artifact removal algorithms (Halder et al., 2007) and auto-calibration function (Kaufmann, Volker, et al., 2012), could improve effectiveness and reliability. More extended training (more sessions) could improve effectiveness, as shown earlier for SMR BCI (Kübler, Nijboer, et al., 2005) and auditory ERP BCI (Halder et al., 2014a).

5) Ease of use: End-users desired: "A *plug-in-play mechanism, for all computer programs*".
6) Speed: New implementations are conceivable, such as predictive spelling (Ryan et al., 2011; Sellers et al., 2010) or reduction of stimulus duration or ISI. However changes on ISI can deteriorate accuracy, as classification of signals is more difficult (McFarland, Sarnacki, Townsend, Vaughan, & Wolpaw, 2011).
7) Other features: The daughter of one end-user desired an "*Emergency call option*".

Further improvements and refinement of BCI applications according to the end-users' needs and requirements are desired and essential for prospective use in daily-life. New features and implementations need however to be further tested in the target group. The present findings show, that new implementations are not always accepted by end-users (e.g., implementation of a hybrid approach including EMG input channel in *study 2*); thus new features need to be continuously evaluated. Based on the evaluation outcomes of the evaluation studies in controlled settings, especially the study by Zickler and colleagues (2013), it was possible to implement the BCI for creative expression in the daily-lives of two end-users. Based on the continuous evaluation (*study 3)* a new version of Brain Painting was developed, including more forms, the possibility to draw lines and colours and an auto-calibration (Botrel et al., 2014; Kaufmann, Volker, et al., 2012). This new version has currently been implemented at the end-users' homes (Botrel, Holz, & Kübler, 2015). The use of semi-dry or dry electrodes is planned.

3.2.2.1.3.2 BCIs for communication

Effectiveness, reliability and speed were indicated as more important for the end-users in BCI devices for spelling, as compared to entertainment BCIs (see **table 40**). For entertainment ease of use and comfort were more important than effectiveness and reliability. Most interestingly end-users indicated high satisfaction for the gaming prototype, even though effectiveness and efficiency was lower as compared to the spelling prototypes. These results indicate that when BCIs are considered for communication, end-users are in general less tolerant against "malfunctioning" as compared to entertainment. For example two end-users, who tested the hybrid BCI for spelling, stated with respect to speed: „*Need to be faster, 4 or 5 flashes ok* (*2-3 sequences*)" and "*No, only if I am in need. With my recent system (Wergen system) I can do 70 to 80 selections per minute! It is not an alternative to my recent AT, which is faster and more effective, BCI is not competitive. BCI would need to be improved, especially in terms of speed*". Same for end-users, who tested the first prototype, indicated that the BCI should be "*Twice as fast*" and "*3-4 times faster*" (Zickler et al., 2011). Thus, BCIs for communication, at the current state of the art, are not competitive if other AT-solutions are available, which are faster, more effective and reliable and easier to use.

Although healthy subjects tended to prefer the EMG letter correction, most of the end-users did not agree with the rationale of the hybrid approach, even though it improved efficiency: "*Same satisfaction rating for BCI as for EMG, however I would rather use BCI correction, because EMG is not logically to me, although it is faster. If I can still move any muscle, I wouldn't use a BCI. But if I couldn't not any longer, then I would use a BCI*." (end-user B, *study 2*). This finding is contrary to what was desired by end-users in the first study, who suggested "*An interface that integrates BCI with other input channels*" (Zickler et al., 2011; p.243). The finding that end-users do not see the hybrid approach superior to the non-hybrid, is also contrary to the findings by Riccio and colleagues (2015). In their study end-users rated their satisfaction higher for the hybrid as compared to non-hybrid condition, even though one end-user had problems with the EMG (missed three deletions) and hybrid control was found to be associated with higher level of physical demand and a trend for higher frustration in two end-users (Riccio et al., 2015). In the study by Riccio and colleagues (2015), end-users were however not asked whether they could imagine to use the BCI in their daily-lives. Therefore the present thesis presents the first study that investigated usefulness (considered adoption in daily-life) in a target group. Results indicate that a hybrid approach, combining EEG and EMG input channels, is probably not accepted by all end-users and depends on the end-users' needs and requirements. More studies are needed to find out whether a hybrid BCI is of interest for severely disabled end-users and if so, for which kind of end-users.

3.2.2.1.3.3 BCIs for entertainment

The results indicate further that - besides communication - patients who are severely disabled may wish to be able to pursue other satisfying leisure activities that enhance quality of life; in line with (Kübler et al., 2008; Münßinger et al., 2010). Most importantly, for entertainment purposes (creative expression and games) BCI obstacles (e.g., lower speed, errors, EEG-cap) do less matter. For example in *study 3* end-users indicated that they need enough time to think what to select next, thus speed is less important. These results are in line with results obtained in a healthy population. Albeit brain-computer interaction is slower and less accurate than most other modalities and even though BCI require mostly a lot of training, healthy individuals are interested to play games using a BCI. According to Nijholt and colleagues (2009) gamers are always looking for challenges and limitations that they can overcome by practice (Nijholt et al., 2009). Van de Laar (2013) showed that, in a gaming situation, the relation between fun and control is not linear; although fun increased with improved level of control, the level of fun dropped before perfect control was reached (with an optimum around 96%). Authors interpret these findings in the way that players get bored if control is (too) perfect (100%); they are however challenged if control is not perfect (van de Laar et al., 2013). Thus in BCI fun games, unreliable input can be used to create a (positively experienced) challenge for the user. However BCI performance has to be higher than chance level, otherwise gamers would be too frustrated, that would consequently hamper acceptance of the BCI gaming (Plass-Oude Bos et al., 2010; van de Laar et al., 2013).

Table 40: Most important aspects of a BCI device (extended QUEST; five BCIs).

Three most important items				
Study 1: MI BCI gaming	**Study 2: Hybrid P300-ERP BCI communication**	**Zickler et al. 2011: P300-ERP-communication**	**Zickler et al. 2013: Brain Painting**	**Study 3: Easy to use Brain Painting**
1. Ease of use 2. Reliability 3. -	1. Effectiveness 2. Reliability 3. Speed/ ease of use	1. Effectiveness 2. Reliability 3. Speed/ Comfort	1. Comfort 2. Effectiveness 3. Speed	1. Ease of use 2. Effectiveness 3. Reliability/ Prof. services

Note: Three most important items were indicated by each user in the extended QUEST, resulting in 12 indicated items (by four end-users) with exception for P300-ERP communication and easy to use Brain Painting, in which the questionnaire was applied several times. However for all prototypes, the first three ranked items were considered.

3.2.2.1.3.4 Needs and requirements

Two end-users showed a good match with the Brain Painting device, one end-user with the gaming BCI, and none of the end-users with BCI prototypes for spelling. In independent use, one end-user had an almost perfect match (ATD-PA score: 4.8; maximum: 5) with the easy to use Brain Painting; see **table 38**. Results indicate that the acceptance of the BCI and the adoption of a BCI in daily-life strongly depends on the end-users' needs and requirements. The appearance of an EEG cap might be not so important for an end-user who aims at using the BCI at home: "*I don't care about aesthetic design of EEG cap and electrodes nor amplifier, but more choices in the matrix would be nice*". However for an end-user who wants to use a BCI for communication in public places, it matters: "*Use in the public would be strange, because people would stare at the user*" and "*Doesn't look aesthetic. Most people probably wouldn't like to have many cables and electronic devices at one's body. Looks like a cyborg, who finds cyborgs handsome*" (*study 2*). Another end-user stated: "*For home-use or work I don't care about the aesthetic design, however in town it would be less acceptable*" (*study 2*).

As mentioned above, BCIs for communication, at the current state of the art, are not competitive if other AT-solutions are available, which are faster, more effective and reliable and easier to use. This holds true only for “less impaired” end-users, who have well-functioning AT for communication. Contrary for “stronger impaired” end-users with fast progressive disease (e.g., ALS), who have no or no suitable AT for communication. As stated by one end-user (*study 2*): “*If I can still move any muscle, I wouldn’t use a BCI. But if I couldn’t not any longer, then I would use a BCI*” (*study 2*). The almost completely paralyzed end-user of *study 2* could imagine to use the hybrid BCI for spelling three times per week and reported: „*It was alright*“; although she had many flashing sequences, and thus a slow spelling rate, and the lowest accuracy as compared to the other three end-users. However she was not sure, whether she would have the support by her caregivers. She indicated that the set-up of the BCI would probably be too complex and time-consuming for the caregivers if they had to set it up regularly. Also the end-user in the locked-in state in *study 1* could imagine using the slow MI BCI for communication (albeit tested with a gaming application). For these two end-users the BCI could offer them a better or even the only solution to communicate. This is in line with studies by Sellers and colleagues (2010, 2014), who demonstrated that a visual ERP BCI can be a good solution for end-users, who could no longer use conventional assistive devices (e.g., eye-tracker) for communication. The BCI enabled independent communication for one locked-in end-user, while other means of independent communication failed (e.g., eye-tracker) and other means, such as communication with a letter board, depend on other persons. These results indicate further that it cannot necessarily concluded that a P300-ERP BCI is superior as compared to a MI BCI and that P300 ERP BCIs should be the best option for the target group, because effectiveness and efficiency are higher.

The most interesting result of the present thesis is that, if the BCI exactly matches the user’s needs and requirements, BCI related obstacles do less matter – at least for entertainment – for instance the electrode gel: “*Electrode gel sticks on the scalp and hair, but it can be removed easily*” (statement by the family of one end-user, *study 3*). Also speed and aesthetic design of the EEG cap were less important for both end-users that used the BCI in independent use, as described above. Thus these aspects are “no real obstacles” but rather “challenges” that do not prevent end-users to use the BCI in their daily-lives. Albeit ease of use, effectiveness, reliability and prof. services were indicated as most important for independent use. Thus despite BCI obstacles/challenges, for some individuals BCI has still potential to be used in daily-life, especially for individuals that are in real need. For instance one end-user (*study 3*) uses the BCI as additive device. This end-user stated that the BCI would be less exhausting than her eye-tracker and that she would not prefer to control the painting application with her eye-tracking system. This is an intriguing finding, because it shows that end-users in the locked-in state can benefit of a visual P300 BCI, even if reliable eye movement is still available. This demonstrates that the choice of the optimal BCI is individual (Kübler, Kotchoubey, et al., 2001). In fact the use of a BCI for communication in daily-life strongly depends on the life-situation of the person, meaning the persons' existing solutions for communication. These results demonstrate that potential end-users in the locked-in state may have a real benefit from the BCI and that they would use it in their daily-life even if it worked with moderate accuracy or reliability, albeit control above chance is mandatory. It further underlines that effectiveness and efficiency expressed as ITR are not necessarily the most important criteria for selecting or enjoying a BCI application. Obviously, personal preferences and circumstances play an important role.

3.2.2.2 Usefulness

3.2.2.2.1 Use in daily-life

Three of four end-users could imagine using Brain Painting in their daily-lives, once or twice per week; two end-users the second entertainment prototype, Connect-Four, and one end-user the hybrid BCI for spelling. None of the end-users could imagine to use the first spelling prototype. The easy to use Brain Painting has been used in daily-life for more than 3 years (by now). As indicated by the comment of one end-user "*I would need more practical experience with the BCI to evaluate this*" (*study 2*); thus to evaluate usefulness of an AT device it has to be brought to the patients' homes for daily-life use, as realized in *study 3*. The face valid measures (*study 3*) confirmed that independent BCI use is possible.

3.2.2.2.2 Potential significance and influence on quality of life

The BCI positively influenced or retained (if presented before entering the locked-in state) quality of life of the patients in locked-in state. The BCI positively influenced feelings of happiness and usefulness, self-esteem, self-confidence, productivity, as nicely described in the statements by the end-user: "*After three and a half years of speech- and motionlessnesss, Brain Painting gave me a new form to express myself, and I am very grateful to every involved person for that… Now I can again indulge in colours and show, that an apparently total helpless person can have much joy over the nature and community* […]" and "*I paint about two or three times a week and enjoy this immensely as my former art is given back to me, even if it is a new form of painting. A completely new art form, far more challenging, but also pure fun and absolutely rewarding if you can put your picture in mind on canvas and finally see it with your own eyes. That is a great moment for me as somebody who has been paralysed for six years".* The daughter of the end-user summarized: "*Great invention; very good possibility to express his-/herself for a* *paralyzed creative person, enabling finally to be creative again*". In these two cases BCI furthermore retained or improved the ability to participate, thus social inclusion, as both end-users were able to show their Brain Paintings in public exhibitions and sell their paintings. Without the BCI this would not be possible. Thus, Brain Painting clearly impacted three of five domains that were considered relevant to quality of life (Felce & Perry, 1995): development and activity (i.e., job, leisure/hobbies, competence/independence, productivity/contribution), social well-being (i.e., community/involvement, activities and events, acceptance, interpersonal relationships), emotional well-being (satisfaction, positive affect, self-esteem, fulfilment, status/respect). Blain-Moraes and colleagues (2012) reported about attitudes of potential BCI users towards BCI technology (Blain-Moraes et al., 2012). These prospective BCI users, diagnosed with ALS, expressed high interest in using the ERP BCI for communication. They stated that the BCI may give them freedom and autonomy, may enable them to communicate and to stay connected to their family and friends, and to remain independent as their condition progressed, thereby continuing to retain their personhood. The results of the present thesis confirm these attitudes toward technology. Even though quality of life is high, BCI can still have a considerable impact on the end-user's life, as stated by the end-users: "*It is certainly a big win. Even though my life would certainly be rich without BP, too, I would never have known BP. I am very thankful for this enrichment.*" and "*I always said, if I cannot paint any longer, I am dead, and then Brain Painting came*" and "*BP encourages me for my future, because it makes so much fun and because it works so fine. I have so many ideas with shapes and colours*." BCI had a negative impact on one aspect of life that is "independence". Albeit being "independent" of the help of BCI experts, it indicates, that BCI use strongly depends on the support by caregivers and families, in setting up the BCI (e.g., EEG cap), as stated by the family of one end-user: "*Because all caregivers and family members help, it is no problem*" and (regarding time and effort) "*it is justifiable for the benefit*". Nevertheless this result is somewhat alarming, because it shows that apparatus acquisition of the BCI (e.g., set-up and operation of software and hardware, hair washing, etc.) leads to high involvement of the caregivers that is problematic because they already suffer a large burden of care and psychological distress (Neumann & Kübler, 2003; Rabkin, Albert, Rowland, & Mitsumoto, 2009). BCI research should thus focus on the development of easy to use and quickly adjustable BCI systems. It is also recommended to make a person, who is less involved in daily care, responsible for the BCI training (Neumann & Kübler, 2003).

3.2.2.2.3 Prerequisites for independent BCI use

Besides improvements requested by end-users, the present thesis demonstrates that a BCI, at the current state of the art, can be satisfactory used in daily-life. Ease of use is mandatory for independent use, as indicated by the end-users. Other prerequisites for conducting independent home use studies seem to be crucial:

Inclusion criteria defined by Vaughan and colleagues and also the decision algorithm proposed by Kübler and colleagues (see chapter **1.4.3.3 Independent use**) can help to decide whether a potential end-user of BCI controlled assistive technology is a suitable candidate for translational and long-term BCI studies (Kübler et al., 2015; Vaughan et al., 2012). For instance, suitable BCI end-users would be persons, who (1) have little or no useful voluntary muscle control; (2) have no conventional assistive devices adequate for their needs; (3) are medically stable, and with the intent, and reasonable expectation, of living for at least one year; (4) are able to follow spoken or written directions; (5) have no other particular impairment; (6) have stable living environments; (7) have reliable caregivers; (8) are able and willing to provide informed consent. In *study 3* it was evident that support of caregivers/ families or assistants is of utmost importance. There were more end-users interested in participating in this study, however there was a lack of support by the environment. Of course, a BCI can only be used as assistive device, if reliable brain signals can be identified. Unfortunately in one person with late-stage ALS who aimed at participating in the Brain Painting project no sufficient ERP signals could be obtained.

As proposed by Sellers and colleagues (see chapter **1.4.3.3 Independent use**) an easy to operate software that is adaptable to the user's needs and a long-distance remote oversight can be considered as mandatory for independent BCI use (Sellers et al., 2010). The BCI system used in *study 3* clearly matches all these criteria.

Based on the experience on 3 years independent use (*study 3*), the following techniques and services have been identified as being important and should thus be discussed more deeply: Continuous evaluation, continued support, continuous adaptation of parameters and tools:

1) Continuous evaluation: Evaluation data is a useful tool to monitor BCI daily-life use presenting information about the functioning of the BCI in long-term use. For instance VAS satisfaction in combination with a comment line, indicate technical problems, such as malfunctioning of EEG channels. This enables BCI experts to assist non-BCI personal to find out why signal quality is bad. Furthermore evaluation gives information about the usability of the BCI in daily-life by documenting problems and challenges of long-term home use (e.g., dissatisfaction and low BCI control due to drying electrode gel or shifting cap). VAS satisfaction should be implemented into the software and automatically presented to the user after every session. Furthermore automatic data transfer to a remote server is necessary.

2) Continued support: Support was needed in case of technical problems with the BCI software (e.g., bugs), malfunctioning of hardware (e.g., EEG cap, electrodes and amplifier) or other technical challenges (e.g., reinstallation of BCI software after the end-user received a new PC, exchange of EEG cap and/or recalibration). Furthermore the EEG amplifier (g.USB amp) has to be send to the company for update/check-up every two years (in accordance with g.tec Medical Engineering GmbH, Austria). Here help and support is required, as it is a high effort for the family/assistants to get in contact with the company and it also cause costs (sending it by post with insurance). Hardware issues, such as erroneous cap placement, could be prevented with longer training of the caregivers; however time schedule of caregivers is limited, therefore most of the problems arise in daily-life use and need to be solved when they occur. Additionally new caregivers have to be introduced with the BCI, this was done by the family or other caregivers, however it happened that some information was not transferred, for example that the reference (ear clip) should be placed on the right and not the left ear. In a best scenario, only one (and always the same) person operates the BCI system. This was the case in the end-user JT; issues on BCI set-up/adjustment and varying BCI control were indeed less frequent.
3) Continuous adaptation of parameters and tools: One end-user requested to change parameters, for instance extent inter-stimulus duration, because she needed more time to think what to select next, therefore requiring continuous adaptation of BCI parameters according to the user's needs. After two years she asked to reduce inter-stimulus duration again. Onsite support could be reduced if parameters could be changed by the assistants alone, however then other problems arise (e.g., errors). For other requests, such as the request of the user to implement new tools (e.g., more forms, colours, etc.) in the program, a programmer is required. Also with progress of disease needs and requirements may change, therefore update or changes in the software may be required. In accordance with Sellers and colleagues (2010) BCIs should be adapted according to the users' needs and requirements following a user-centred approach.

This long-term study (*study 3*) revealed important necessities for long-term usage of a BCI device. These criteria are the same that are found to be important for other AT devices, and thus not unique for BCIs. Battavia and Hammer (1990) investigated which factors are important for adoption of an AT device and which factors lead to abandonment of a device. Besides the utmost necessity that a device matches the needs and requirements of a person and that the user is satisfied with different aspects of the device in the first place, long-term adoption of a BCI requires also further "practical" aspects. The authors found 17 factors, that influence long-term usage or abandonment and that need to be considered in developing a device. The four most important factors for all technologies were: Effectiveness (the extent to which the functioning of the device improves the consumer's living situation, as perceived by the consumer, including whether it enhances functional capability and/or independence), affordability (the extent to which the purchase, maintenance, and/or repair of the device causes financial difficulty or hardship to the consumer), operability (the extent to which the device is easy to operate and responds adequately), and dependability (the extent to which the device operates with repeatable/predictable levels of accuracy under all conditions of reasonable use). Other important, but lower ranked factors were: Supplier repair (the extent to which a local supplier or repair shop can repair the device within a reasonable period of time, including whether replacement parts are readily available and whether the manufacturer must conduct repairs), consumer repair (the extent to which the average consumer (or his or her personal assistant) can repair the device if broken, including whether special repair equipment is needed) and ease of maintenance (the extent to which the consumer (or his or her personal assistant) can easily maintain the device to keep it operable and safe, including whether it is easy to conduct all required maintenance, cleaning, and infection control procedures) (Batavia & Hammer, 1990). In the present thesis (*study 3*) family and assistants of the end-users were supported in case of technical problems (maintenance, repair, check-up, etc.) and all effort was made to solve problems quickly and to send new BCI equipment (e.g., electrodes or caps) to the end-user’s home. In the next step in BCI research, when BCI goes out of the lab into the lives of the end-users and when BCIs are acquired by purchase on the market (and not part of a study), it should be taken into account that “special services” are needed, such as for repairing, maintenance and adaptation/modification of features. It remains questionable whether a company, such as g.tec (Medical Engineering GmbH, Austria), who state that their BCI system can be used without technical training or outside support, is able to afford such services. Future long-term independent evaluation studies should nevertheless include consumer repairability, affordability, supplier repairability in the questionnaire for assessment of end-users’ satisfaction (as in the original version of the QUEST; Demers et al., 2000).

3.3 Ethical remarks

BCI research raises a variety of ethical questions (Neumann & Kübler, 2003; Nijboer, 2015; Nijboer, Clausen, Allison, & Haselager, 2013; Schneider, Fins, & Wolpaw, 2012; Vlek et al., 2012). Some are standard issues that arise in biomedical research in general, others are unique to BCI research or to the field of neurotechnology (Schneider et al., 2012). Schneider and colleagues (2012) discuss different ethical issues that arise when working with end-users, such as physical risks, psychological risks, risk of inappropriate outputs, risk of invasion of privacy, the problem of time-limited studies and informed consent:

1) Physical risks: Physical risks of a non-invasive BCI are usually low. There can be irritation of skin due to electrode gel. The risk of irritation of the skin can be increased when the BCI is frequently used, as it is the case in home-use.
2) Psychological risks: BCI studies including end-users run the risk of disappointment and frustration if the BCI does not work as expected or if the end-user is unable to gain control over the BCI. One patient of *study 1* (diagnosed with CP) stated that he was not frustrated, although he could not control the BCI, demonstrating that end-users in the locked-in state are highly motivated such that they would train more often to achieve better BCI control even under exhausting training conditions and disappointment. Rupp and colleagues trained several patients to control a MI BCI (Rohm et al., 2013; Rupp, 2014). One individual underwent extensive training of more than six months (414 MI runs) and was provided with a BCI controlled upper extremity neuroprosthesis. The end-user's performance did not show a trend toward improvement, but remained at about 70% with day to day variances (Rohm et al., 2013; Rupp, 2014). Authors postulate that this moderate performance may be explained by the significant differences in movement-related ß-band modulations found in subjects with SCI as compared to non-injured individuals (Rupp, 2014). But also healthy subjects are challenged by learning to control a BCI by motor imagery induced modulation of sensorimotor rhythms (Blankertz et al., 2010; Guger et al., 2009; Guger et al., 2003; Kaufmann, Schulz, et al., 2013; Kübler et al., 2011; Kübler & Müller, 2007; Vidaurre & Blankertz, 2010); see chapter **1.1.1.1.1 SMR/MI BCI**. Based on their experience, authors state that it has to be clearly communicated to patients in the informed consent (before the study) that it is entirely possible that only low to moderate performance will be achieved. If not clearly communicated, persons with severe motor impairment may get the impression that in addition to their body even their brains do not work properly. This could cause additional stress or sadness and depression (Rupp, 2014). Additionally, the importance of BCI training with experts for personal well-being (e.g., receiving attention and reinforcement by BCI experts) must not be underestimated by those experts. Psychological risks may be particularly high for end-users, for whom BCI could offer a better solution to communicate or even the last option because other assistive devices have failed (e.g., eye-tracker). This was the case for two end-users in the locked-in state in *study 1* (end-users C and D). For them, BCI could offer a better option to communicate. However end-user C failed to control the BCI and even though he already participated in earlier BCI studies,

in which no reliable brain signals could be detected neither (see chapter **3.2.1.1 Inter-individual differences in performance**), he was still motivated to participate in further BCI studies in hope that BCIs improve and that he might be able to use a BCI someday: "*I don't think that you can say after a few sessions, whether a BCI works in someone's case or not. I think you have to give the possibility to the person and the brain to get used to it and to train*". It necessitates that the end-user has to be well informed that the study is limited to a defined time period and that the BCI device is not yet a final product but a prototype that will be removed at the end of the study in order to prevent unrealistic expectations and to deal with hopes. In most extreme situations subjects with progressive diseases such as ALS, and family members may want to consider the possibility to communicate using a BCI in making life decisions, such as whether accept invasive artificial ventilation or not. This potential risks should be taken into account by the research group. According to Schneider and colleagues (2012) this potential risk can be reduced by electing only those end-user who have already made the decision to accept artificial ventilation, or to include people with stable diseases who have other options for communication and control.

3) Risk of inappropriate outputs: Studies conducted in daily-life, such as independent use studies, may raise risks of inappropriate outputs. If for example a BCI for environmental control does not work with 100% accuracy, it may have tremendous consequences, such as the room temperature is incorrectly or might fail to notify a caregiver of an acute problem, such as respirator malfunction.
4) Risk of invasion of privacy: Especially long-term studies of independent BCI use may be faced with a risk of invasion of privacy, because all data collected is accessible to the research team, for instance via automatic data transfer to a remote server. It should thus be avoided to collect personal messages.
5) The problem of time-limited studies: This issue arises from the nature of most research studies. They are funded for a certain time period. For long-term/independent use studies, the period may be long, such as several months or years, but not indefinite. This constitutes a problem for subjects, for whom the BCI technology is useful, as it is the case for both end-users included in *study 3*. Thus end-users have to be well informed that the study is financed by a project that is temporary limited. However if the BCI positively impacts the quality of life of the patient, it is unethical to remove the BCI again from the end-user's home.
6) Informed consent: For subjects without reliable communication, informed consent may be obtained from persons that are legally authorized representatives. Such a person can

articulate the patient's preferences with regard to BCI study participation. In case of progressive disease, such as ALS, the patient is able to name an individual, who should make such decisions when the patient loses the ability to communicate. Nevertheless discomfort or pain are a particular concern in non-invasive BCI research for a patient with no reliable means of communication.

3.4 Limitation of studies

Low sample size limits generalization of results. Moreover generalization is difficult because persons with neurological disease are a very heterogeneous group with very individual specifics, needs and requirements. Another limitation is that online performance was only subjectively rated and it cannot be excluded that "real" performance differs (*study 3*). Also subjective rating regarding the influence of the BCI on the end-users' quality of life (PIADS) can be biased, since it was given to the end-users (*study 3*) only after introduction of the BCI. It would have been more accurate to assess quality of life before as well as after implementing the BCI in their daily-lives. Despite these few limitations the results of the present thesis are a very important contribution to BCI research and for bringing BCIs to end-users in real need. The results of the present thesis can be considered as valid, as they are in line with findings of other studies.

3.5 Outlook

Further translational studies are needed to further evaluate the usability and usefulness of BCI controlled devices and to consolidate findings of the present thesis. The suggested evaluation procedure following a user-centred approach can guide development and further refinement of BCIs. Future studies should include assessment of neuropsychological data to control for disease related influencing factors such as attentional problems. As it has been shown that mood and the emotional status influence BCI performance (Kleih et al., 2010; Nijboer, Sellers, et al., 2008), future studies on independent home use should include assessment of motivation and mood (before and after every session), if possible, to control for influencing factors and to investigate the effect of the BCI on the emotional state. Such studies should further include assessment of quality of life before the study and to compare quality of life before versus after implementation of the BCI to control for biased subjective rating. Future evaluation studies along the UCD will eventually help the BCI community to provide indication criteria for individual users and the type of the BCI, as initially suggested by Kübler and colleagues (Kübler et al., 2015). A new Brain

Painting that integrates requests from end-users (e.g., more forms, such as lines, triangles, and more colours) has currently been developed (Botrel et al., 2014) and was recently installed at the end-users' homes (HP and JT) for continued evaluation (Botrel et al., 2015).

4. Conclusion

The UCD provides a framework for translational studies in BCI research and is of utmost importance for bringing BCI driven applications in the daily-lives of end-users. Valid evaluation can only be provided by the targeted end-users and those were included in the current thesis. Results indicate that BCI controlled devices are accepted as assistive devices. BCI obstacles, such as the EEG cap and electrodes, low comfort, complex and time-consuming adjustment, the low efficiency and low effectiveness (high variance) and not very high reliability (many influencing factors) are rather tolerated for entertainment. However for communication, which is essential for life, obstacles are less tolerated. BCIs for communication at the current state of the art are not considered competitive with other AT, if other AT for communication, such as eye-gaze, are (still) an option. Thus BCIs might be an option in the field of entertainment/leisure activities, if communication is still available. However, if the BCI exactly matches the user's needs and requirements, BCI related obstacles do less matter. These aspects are no longer seen as "real obstacles" but rather "challenges" that do not prevent end-users to use the BCI in their daily-lives. Brain Painting serves as best example, as it matches the artists' need for creative expression, caveats such as uncomfortable cap, dependence on others for set-up, and experienced low control are tolerated. Same for end-users in real need of means for communication, such as patients in the locked-in state with unreliable eye-movement or no means for independent communication, do accept obstacles/challenges of the BCI, as it is the last or only solution to communicate or control devices. Thus the question is not which system is superior to the other, but which system is best for an individual user with specific symptoms, needs, requirements, existing assistive solutions, support by caregivers/family etc.; it is thereby a question of indication. These factors seem to be better "predictors" for adoption of a BCI in daily-life than common usability criterions such as effectiveness or efficiency. Nevertheless improvements regarding the EEG-cap, speed, reliability and effectiveness are desired and make it possible that BCIs will be brought to a wider spectrum of prospective BCI end-users. The face valid measures of daily-life demonstrate that BCI controlled applications can be used in daily-life without experts being present. As important, a BCI controlled application can be reliably used in the long-term although a decrease in P300 amplitude in both end-users was observed and a slight deterioration in effectiveness in one end-user. As both end-users were diagnosed with ALS, that is a neurodegenerative disease, this result is most important as it shows that BCIs can be used despite progression of disease. Specifically, one end-user has been in the locked-in state since 6 years indicating considerable neuronal loss. Still, BCI was frequently used. BCIs contribute to quality of life of locked-in end-users and support social inclusion, provided that there is a perfect match between the user and technology and sufficient support by significant others. This result is most encouraging for the BCI community as it demonstrates that BCIs can indeed fullfil its purpose of replacing lost motor function (Wolpaw & Winter Wolpaw, 2012). The results of the present thesis hopefully encourage other BCI labs to face the gaps in BCI research and to make significant and meaningful contributions for bringing BCIs in the daily-lives of people with neuromuscular disorders.

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6. Substantial contribution and publication of works

Study 1 is a collaborative work of TU Berlin and University of Würzburg (UW) within the EU-project TOBI (tools for brain computer interaction; http://www.tobi-project.org/). Johannes Höhne (JH) and Michael Tangermann (MT) were the technical experts, who programmed the BCI and carried out signal analysis and classifier training. My substantial contribution was planning of the evaluation protocol, conducting the whole study in the Beratungsstelle für Unterstützte Kommunikation (BUK, Bad Kreuznach) together with JH, with the main focus on the evaluation, and analysis of the evaluation data. Analysis of BCI signals and other outcome measures (e.g., accuracy and ITR) was conducted by JH. This collaborative work is published separately. The part on signal analysis is published by JH in the journal PLOS One (1). The evaluation part is published in the journal Artificial Intelligence in Medicine (2).

Study 2 is a collaborative work with TU Graz (TUG), Foundazione Santa Lucia (FSL; Rome, Italy) and Associazione Italiana Assistenza Spastici (AIAS; Bologna, Italy) within the EU-project TOBI. The prototype was developed by FSL and TUG and testing protocol has been developed together by all involved partners (UW, FSL, AIAS, TUG). My substantial contribution was conduction of the study protocol in Würzburg, from planning the study, data acquisition and analysis. In context of her diploma thesis the student Johanna Reichert acquired data in healthy participants, helped also in data acquisition in end-users and did parts of the data analysis, such as analysis of the ERP data, all under my close supervision. Data is compiled in her diploma thesis (3). The prototype was tested in Rome by FSL with a slightly different protocol by Angela Riccio. This work is published in the journal Archives of Physical Medicine and Rehabilitation (4).

Study 3 is a collaborative work together with my colleague Loic Botrel. Besides programming of the easy to use BCI application and technical support by Loic Botrel the whole study is based on my work (acquiring patients, monitoring of daily-life use, data analysis, etc.). Tobias Kaufmann helped with programming the new version of the Brain Painting prototype and in implementing the face-stimuli into the P300 speller. Part of this study (data of the first end-user HP) is published in the journal Archives of Physical Medicine and Rehabilitation (5). Another part of the data set, including both end-users (JT and HP), is published in the Proceedings of the 6th International Brain-Computer Interface Conference (6) and in the journal Brain-Computer Interfaces (7).

Data of all three studies is published in reviews (8) and (9).

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(2) **Holz, E.M.**, Höhne, J., Staiger-Sälzer, P., Tangermann, M., & Kübler, A. (2013). Brain-computer interface controlled gaming: Evaluation of usability by severely motor restricted end-users. *Artificial intelligence in medicine, 59(2),* 111-120.

(3) Reichert, J. (2013) Evaluation eines P300-basierten Hybrid-Brain-Computer Interface, unpublished work (diploma thesis), University of Würzburg. (Supervisor: **E.M. Holz**).

(4) Riccio, A., **Holz, E.M.**, Aricò, P., Leotta, F., Aloise, F., Desideri, L., Rimondini, M., Kübler, A., Mattia, D., & Cincotti, F. (2015). Hybrid P300-based brain-computer interface to improve usability for people with severe motor disability: Electromyographic signals for error correction during a spelling task. *Archives of physical medicine and rehabilitation*, *96*, S54-S61.

(5) **Holz, E.M.**, Botrel, L., Kaufmann, T., & Kübler, A. (2015). Long-term independent brain-computer interface home use improves quality of life of a patient in the locked-in state: A case study. *Archives of physical medicine and rehabilitation*, *96,* S16-S26.

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(8) Kübler, A., **Holz, E.M**., Kaufmann, T., & Zickler, C. (2013). A user centred approach for bringing BCI controlled applications to end-users. In R. Fazel-Rezai (Ed.), *Brain-Computer Interface Systems - Recent Progress and Future Prospects* (Vol. 1-19). Rijeka, Croatia: InTech.

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