Dissertation

Brain-computer interfaces based on induced and evoked changes in EEG

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Abbreviations

ALS amyotrophic lateral sclerosis

ANOVA analysis of variance

BCI brain-computer interface

CAR common average reference

CSP common spatial patterns

EEG electroencephalogram

EMG electromyogram

EOG electrooculogram

EP evoked potential

ERD event-related desynchronization

ERP event-related potential

ERS event-related synchronization

FES functional electrical stimulation

fMRI functional magnetic resonance imaging

FN false negative

FP false positive

hBCI hybrid brain-computer interface

ITR information transfer rate

LDA linear discriminant analysis

MI motor imagery

MRCP movement-related cortical potential

NIRS near infrared spectroscopy

SCI spinal cord injuri

SCP slow cortical potential

SMR sensorimotor rhythm

SNR signal-to-noise ratio

SSAEP steady-state auditory evoked potential

SSEP steady-state evoked potential

SSSEP steady-state somatosensory evoked potential

SSVEP steady-state visual evoked potential

TN true negative

TP true positive

Abstract

The research goal of this thesis is to evaluate whether and to what extent induced and evoked changes in EEG can be combined for BCI applications. There are several potential advantages to this combined approach: first, BCIs based on induced and evoked changes could be combined in different ways with a common goal; second, employing different experimental strategies would increase the likelihood that at least one of them works in the end-users; and third, novel combinations of induced and evoked changes in EEG could increase reliability of results and robustness against artifacts.

In this thesis it was shown how to successfully combine induced and evoked changes in EEG for BCI applications. Furthermore, it was demonstrated that a single auditory selective attention task can modulate both induced and evoked changes in EEG, thus paving the way for further BCIs that exploit both of these types of brain signals. Notably, the novel experimental paradigms can facilitate such endeavours and their transition from a laboratory to end-users.

In a related work, the state of the art in the BCI technology was evaluated in patients with disorders of consciousness. Furthermore, a contribution was made by comparing different types of mental tasks and attempted movements within patients, as well as by exploring new venues.

Zusammenfassung

Das Forschungsziel dieser Dissertation ist es zu evaluieren, ob und inwiefern induzierte und evozierte Veränderungen im EEG für BCI Anwendungen kombiniert werden können. Es gibt mehrere potentielle Vorteile in dieser kombinierten Herangehensweise: erstens, BCIs basierend auf induzierten und evozierten Veränderungen im EEG könnten in unterschiedlicher Art und Weise zur Erreichung eines gemeinsamen Ziels kombiniert werden; zweitens, durch Verwendung unterschiedlicher experimenteller Strategien könnte die Erfolgswahrscheinlichkeit in EndbenutzerInnen erhöht werden; und drittens, neuartige Kombinationen von induzierten und evozierten Veränderungen im EEG könnten die Verlässlichkeit und die Robustheit der Ergebnisse gegenüber den Artefakten erhöhen. In dieser Dissertation wurde gezeigt, wie man erfolgreich induzierte und evozierte Veränderungen im EEG für BCI Anwendungen kombinieren kann. Es wurde weiters demonstriert, dass eine einzelne, auf der auditorischen selektiven Aufmerksamkeit basierende, Aufgabe sowohl induzierte als auch evozierte Veränderungen im EEG modulieren kann, wodurch der Weg für künftige BCIs, die diese beiden Arten von Gehirnsignalen ausnutzen, geebnet worden ist. Insbesondere können diese neuartigen experimentellen Paradigmen solche Unterfangen, sowie deren Transition vom Labor zu den EndbenutzerInnen erleichtern. In einer themenverwandten Arbeit wurde der Stand der Technik in der BCI Technologie in PatientInnen mit Bewusstseinsstörungen evaluiert. Ferner wurde ein Beitrag geleistet, indem sowohl unterschiedliche Arten von mentalen Aufgaben und versuchten Bewegungen innerhalb der PatientInnen verglichen wurden, als auch neue Gebiete erforscht wurden.

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Chapter 1

Introduction

1.1 BCI

1.1.1 Overview and definition

When a person is unable to communicate through words, gestures, or standard assistive technology (AT), brain-computer interfaces (BCIs) could, in theory, provide alternative means of communication. Similarly, in spinal-cord injured end-users, BCIs could bypass the injury and restore the muscle control through functional electrical stimulation.

But what is a BCI? A widely accepted definition of a BCI [24, 185] is that it is a system that relies on intentional brain activity without neuromuscular pathways, and provides real-time feedback. This definition has recently been extended to also include the so called passive BCIs, that do not rely on intentional control. Figure 1.1 presents an overview of the basic components of an electroencephalogram (EEG) based BCI system.

The vast majority of BCIs are based on one of two types of brain activity: the first one is induced through willful modulation of ongoing oscillatory activity through mental imagery; the second one is evoked by external stimuli and modulated through focused attention. These induced and evoked changes each have their merits and drawbacks. The overall hypothesis behind this thesis is that combining these two types of changes could strengthen their merits and weaken their drawbacks.

1.1.2 Types of brain signals and recording

Signal acquisition can be performed non-invasively using EEG, or invasively using electrocorticogram (EcOG), single, and multi-unit activity. Signal quality is proportional with the level of invasion. EEG is the method of choice for the majority of reported BCIs, mainly due to its high temporal resolution and its widespread availability. It also has a long history, with the first EEG measurements in man conducted as early as 1924, by Hans Berger [15]. The EEG reflects the sustained spontaneous electrical activity of the human brain. Measured on scalp with 4-10 mm diameter large electrodes, commonly placed

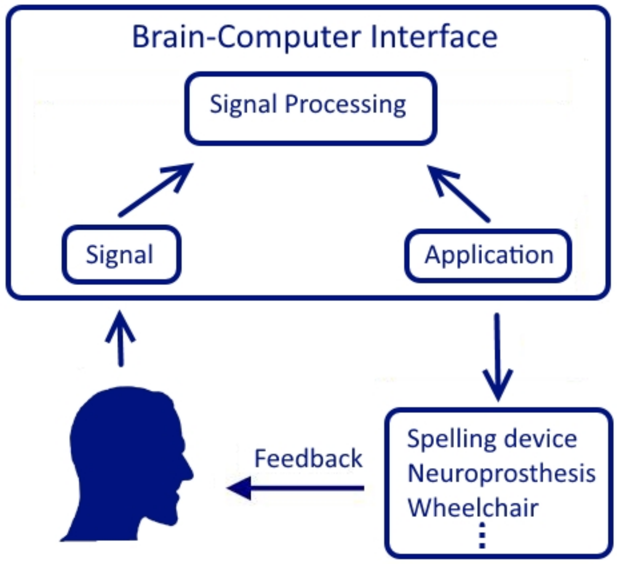

Figure 1.1: Overview of the basic components of an EEG based BCI system.

according to the International 10-20 electrode system [80], the EEG measures the spatial and temporal summation of the activity of millions of neurons, plotted as the changes in voltage over time. The EEG can be divided into several frequency band, commonly defined as alpha (α, 8-13 Hz), beta (β, 14-30 Hz), gamma (γ, 30-100 Hz), theta (θ, 4-7 Hz), and delta (δ, 0.5-3.5 Hz).

1.1.3 Experimental strategies and neuroelectrical phenomena

Common experimental strategies include operant conditioning through neurofeedback (e.g., slow cortical potentials [19]), stimulus induced responses modulated by focused attention in various sensory modalities [41, 51, 124, 125, 168], and various forms of mental imagery [26, 147, 120, 47]. Following is a short description of experimental strategies and associated neuroelectrical phenomena most relevant for this thesis.

Stimulus induced responses modulated by focused attention

Event-related potentials While evoked potentials (EPs) represent time- and phase-locked brain's physiological response to external stimuli, event-related potentials (ERPs) represent transient EEG amplitudes related to cognitive processing (e.g., attention, perception, etc.). Distinct ERPs reflecting focused attention to stimuli have been reported, foremost the P300 component, named after its characteristic large positive peak amplitude occurring around 250 to 500 ms post stimulus [157]. Other notable ERPs include: mismatch negativity (MMN), reflecting the preattentive change detection on the level of auditory sensory memory [127]; late positive component (LPC), reflecting the switch of attention onto the new information [190]; N400 [95] and P600 [60], related to semantic processing.

Oddball paradigm The P300 is usually elicited by the oddball paradigm, where an infrequent (e.g., 20%) deviant stimulus is presented among frequent (e.g., 80%) standard stimuli [102]. Central to this paradigm is attention of the participant, who is often instructed to silently count how often the deviant stimulus occurs. The properties of the oddball paradigm (e.g. the deviant to standard ratio) can be exploited for design of a P300 speller system [41].

Steady-state evoked potentials If the frequency of stimuli presentation is so high that the transient EEG amplitudes do not fade before a new stimulus occurs, a so called steady-state evoked potential (SSEP) can be found. SSEPs can be induced in in auditory (steady-state auditory evoked potential, SSAEP [153]), somatosensory (steady-state somatosensory evoked potential, SSSEP[162, 125]), and visual modality (steady-state visual evoked potential, SSVEP [162, 183]). Focusing on the stimuli enhances the SSEPs.

SSVEP SSVEP are elicited by presenting repetitive visual stimuli faster than 6 Hz, and can be recorded at occipitally mounted EEG electrodes [162]. Stimulation for an SSVEP-based BCI can be delivered via lights (e.g., light-emitting diodes, LED) or via targets presented on a monitor, flickering with different frequencies [189, 192]. These flickering stimuli typically elicit occipital oscillations at harmonics of the stimulating frequency, as well as the fundamental frequency itself [162, 62].

Rhythms of the sensorimotor cortex

Sensorimotor rhythms (SMR) are distinguishable from each other by topography, frequency, and timing. Common sensorimotor rhythms include μ rhythm, normally found in the lower and upper alpha bands (8-12 Hz), and central β (13-30 Hz) rhythms. Motor imagery (MI), without any actual performed movements, can decrease band power in the μ-frequency range and also to some extent in the β-frequency range relative to the band power in a reference interval preceeding the MI onset [145]. This decrease of power is called event-related desynchronization (ERD), and is often followed by an increase of the band power in the lower and upper β band relative to the band power in a reference interval preceeding the MI onset, also known as event-related synchronization (ERS) [145]. However, participants need to imagine the movement kinaesthetically in order to produce EEG patterns similar to actual movements [134]. Non-motor mental imagery can also modulate rhythms of the sensorimotor cortex, e.g. mental arithmetic, spatial navigation, cube rotation and other [166, 37, 161].

Postmovement beta ERS Beta EEG changes, i.e. ERS and ERD as described in the previous section, have been reported in multiple studies [5, 133, 148, 178]. After an ERD appearing briefly before and during the movement, bursts of beta oscillations (beta rebound, beta ERS) occur approx. 1-s following movement offset [145]. Beta rebound has been demonstrated following voluntary [133, 178, 150, 116], passive [116, 28] and imagined [146] movements, as well as movements due to functional electrical stimulation [116].

1.1.4 Signal processing

Signal processing is composed of preprocessing, feature selection, and classification steps. The preprocessing step applies filters to the recorded signals, and handles various artifacts. The feature selection step usually transforms the time or frequency features with goal of reducing the dimensionality. The classification step adapts to the extracted features and provides basis for the feedback.

In addition to time and spectral domain features, common feature extraction methods include logarithmic bandpower features (logBP), common spatial patterns (CSP), lock-in analyzer (LIA), and canonical correlation analysis (CCA) [21, 160, 121, 17]. These features are then classified using various linear and non-linear classification methods such as linear discriminant analysis (LDA), support vector machines (SVM), and random forests [39, 179].

1.1.5 Modes of operation

There are two basic modes of operation: (i) cue-based, also known as synchronous, in which the signal processing is done in predefined time windows; and (ii) self-paced, also known as asynchronous, in which the signal processing is done continuously. Challenge in the synchronous mode of operation is the discrimination between automatic brain responses caused by the cue stimuli, and the willful modulation caused by participants focused attention. Similarly, challenge in the asynchronous mode of operation is to detect any willful modulation of brain activity and to minimize the number of false detections.

1.1.6 Applications

In a recently published roadmap for the BCI community [24], following future use cases are outlined for the five BCI applications mentioned in the [1]:

replace Unlocking the completely locked-in [18]

restore BCI-controlled neuroprosthesis [126, 164]

enhance Enhanced user experience in computer games [171]

improve Upper limb rehabilitation after stroke [81, 152]

research tool Cognitive neurosciences [187, 24]

One important application of BCIs is in connection with assistive technology (AT). But how does this connection take place? Obviously, one cannot expect that numerous AT devices and software already in use be adapted to BCIs, so the BCIs themselves need to adapt. In order to do so, they need to conform to the human / AT interface [32] already employed in the vast majority of existing AT. The human / AT interface can be broken down in various elements, such as control interface, selection set, and selection methods. Selection methods, for example, differ on whether they are direct or indirect. Indirect selection methods are widely used in BCIs, and can be divided into:

automatic scanning where items are presented sequentially

step scanning where the user moves sequentially through the list of items by repeatedly activating a switch

inverse scanning where the items from the selection set are automatically scanned by activating and holding a switch, and selected when the switch is released.

Revisiting different BCIs in the context of selection methods, one can recognize that the classical visual P300 speller employs automatic row / column scanning, albeit with random presentation. The SMR based BCIs are well suited for automatic and step scanning, and the SSS(V)EP based BCIs support all three scanning modes, but not all are easy to use.

Various AT techniques can be applied to BCIs to improve their performance. For example, in end-users having difficulties with eye-gaze control the symbols can be presented in the center, with additional auditory cues. Various activation and deactivation techniques can be applied to reduce the number of false activations, examples of which are discussed in the "Hybrid BCIs" section. Finally, the selection rate can be enhanced by integrating a language model into BCI [177], and through techniques such as abbreviation expansion or word completion [32].

However, not all AT techniques can be equally applied to BCIs. For example, common approaches to the scanning rate enhancement include optimization of the group-item presentation (e.g. by presenting the most frequently used symbol first), and dynamic rearrangement of symbol presentation. The former has limited use in BCIs due to a relative high number of false activations, thus warranting multiple presentations of the selection set. The latter is applicable only to some BCIs, at it is at odds with the oddball experimental design widely employed in the state-of-the art BCIs for spelling applications.

Most of the BCI development in the past focused on maximizing metrics such as accuracy and information-transfer rate (ITR), which was highly successful in healthy participants, but often failed miserably as an AT device in end-users. In order to close this translational gap, recent efforts adopted the so called user-centered design (UCD) to BCI research and development [94].

The key aspects of the UCD, according to which usability of applications and devices is evaluated, are their efficiency, effectiveness, and satisfaction. In **Kübler et al. (2014)** [94], these aspects were used to evaluate BCI applications in 19 end-users with severe motor impairment. To that end, efficiency was considered to be equivalent to ITR and the amount of invested work, and effectiveness to selection accuracy. Also, questionnaires were used to assess satisfaction. The main findings were: efficiency was found to be low to high for the ITR, and low to medium for the workload; effectiveness was found to be moderate to high; and finally, satisfaction was moderate to high, depending on the type of application.

1.2 EEG based BCIs in healthy

1.2.1 P300 component of event-related potentials

The first P300 speller system was a 6-by-6 matrix, containing the letters of the English alphabet and basic punctuation signs [41]. Here, the oddball sequence was comprised of visual highlighting of either a row or a column of the matrix, two of which (i.e. the target letter row / column) elicited the P300 response. This basic paradigm design was subsequently exploited in various visual P300 based applications, enabling healthy participants to communicate letters [41], control environments [14], control computer mouse [30], and browse the internet [114, 154].

One disadvantage of visual P300 based BCIs is their dependence on eye-gaze control. A study by **Brunner et al. (2010)** [25] found that the performance of the visual P300 speller in healthy participants considerably depended on the gaze direction, thus limiting its use in end-users having difficulties with eye-gaze control. Several studies tried addressing the issue of eye-gaze dependency by means of gaze-independent BCIs [182, 101, 2]. Common to these studies was the assumption that the visual stimuli and / or the central fixation point can always be presented in the end-users foveal vision:

Treder et al. (2010) [182] compared a two level speller, made from six circles forming an invisible hexagon, to the classical row / column matrix layout of symbols in 19 healthy participants. Both overt and covert attention were investigated - in the covert attention, participants simultaneously fixated a central dot and attended to a peripheral target. Whereas both overt and covert attention could be employed in an ERP based BCI, the former yielded better results than the latter. In the covert attention condition the hexagonal two-level speller outperformed the row / column speller, mainly due to stronger modulation of early ERP components (i.e. N1 and P2).

Liu et al. (2011) [101] realized a gaze independent speller through a covert visual search task. To that end, clusters of characters were sequentially presented near the center. The participants' task was to fixate their gaze on the center, and to search and recognize the target character with covert shift of attention. They managed to select characters with accuracy of up to 96%.

Acqualagna and Blankertz (2013) [2] investigated rapid serial visual presentation (RSVP) as a paradigm for spelling applications in 12 healthy participants. To select a letter, the participants attended to target letters in the pseudo-random stream of visual symbols. The participants communicated on average 1.43 symbols per minute, with a mean accuracy of 95%.

Whereas these BCIs reduced the eye-gaze dependence to various extent, they still relied solely on visual modality, thus making them of little use in end-users who can have limited control of their eye-gaze. Reducing the eye-gaze dependence even further, several studies evaluated auditory-visual P300 based BCIs in healthy participants:

Klobassa et al. (2009) [86] evaluated the performance of an auditory BCI, in which six environmental sounds were used to denote the equal number of rows / columns of a P300 based matrix speller. Additionally, the impact of visual cues on the performance in the early stages of training was assessed using a two group-design: in the first group (A, N=5), only auditory stimuli were presented over a course of 11 experimental sessions. In the second group (AV, N=5), simultaneous auditory and visual stimuli were presented in the initial experimental sessions, after which the visual stimuli were gradually removed. Both online and offline results showed equivalent group accuracies, with four participants achieving an online accuracy higher than or equal to 75%, at an average bitrate of 2 bits / min.

Schreuder et al. (2010) [174] proposed a multi-class paradigm, employing spatially distinct auditory cues. Ten healthy participants attended to auditory cues of various length, randomly presented by up to eight speakers, with each speaker placed at an individual spatial location. In the offline part of the experiment all eight speakers were used, with speakers arranged in a circle, in midst of which the participant was seated. The same stimulus was presented from each of the eight speakers. In the online part of the experiment, based on the findings from the offline part, only the frontal five speakers were used. Here, one unique stimulus was presented from each of the five speakers. The mean online binary classification accuracy (i.e. target vs non-target) was 75% for the best condition (inter-stimulus interval of 175 ms length). The mean online target location detection accuracy increased with the number of trials averaged, reaching 94% (N=12 averaged trials) in the best conditions. The corresponding bit rate was reported for lesser accuracy (i.e. 90%, N=9 averaged trials) as 16 bits / minute.

In addition to visual and auditory modality, also tactile modality can be used to set up a P300 based BCI. The latter modality was employed in

Brouwer et al. (2010) [22], who analysed EEG responses to vibro-tactile stimuli, equally spaced around a waist. In the first experiment, the effect of the number of tactors (two, four, and six) was investigated. Here, no difference in classification performance was found. In the second set of experiments, the effect of the timing of the tactile stimuli was investigated, with stimulus onset asynchrony (SOA) ranging from 626 ms to 188 ms. Here, an optimal SOA was found to be at 376 ms, as reducing the SOA below this threshold did not further improve the performance. In both experiments, the onesample t-tests against zero on classification accuracy corrected for chance showed that classification accuracy was well above chance for all conditions (all p-values ¡ 0.01). Further details on the performance are given in tables and figures of the original manuscript [22].

Tactile modality was also employed in **Ortner et al. (2014)** [139], where two different approaches were evaluated in twelve healthy users and six LIS patients: a first approach utilizing three tactile stimulators and a second one utilizing eight tactile stimulators for the stimuli delivery. In healthy participants, the three-stimuli approach yielded higher accuracy (mean accuracy of 80%) compared to the eight-stimuli approach (mean accuracy of 69.4%). The three-stimuli approach in LIS participants yielded substantially lower accuracies compared to the healthy participants (mean accuracy of 53.3%), but five out of six LIS participant performed abow the chance level (33

1.2.2 Steady-state somatosensory potentials(SSEPs)

SSEPs based BCIs can be setup in auditory [63], somatosensory [125], and visual modality [183]. From these different modalities, only the visually evoked steady-state potentials will be employed in this thesis.

SSVEP One of the earliest SSVEP based BCI systems was reported in **McMillan et al. (1995)** [110]. In this early work, the intensity of two fluorescent lamps, mounted behind a diffusing screen, was sinusoidally modulated at 13.25 Hz in order to elicit a steady-state response in occipital EEG. Healthy participants learned to control (i.e. to increase or decrease) the amplitude of this response, which was in turn translated into control commands for the roll position of a simple flight simulator.

Self-regulation of EEG responses to flickering stimuli was again investigated in healthy participants in the first experiment reported in **Middendorf et al. (2000)** [111]. A notable finding here was that three out of eight participants reported employing subtle eye-movements in controlling the amplitude of their EEG responses, which was also confirmed by electrooculogram (EOG) analysis. More novel was the approach used in the second experiment, employing multiple evoked responses to virtual buttons flickering on a computer display. Here, the participants were not required to actively control the amplitude of their EEG responses.

This basic paradigm design, employing frequency coded visual stimuli, was subsequently exploited in several SSVEP based BCI applications with an increasing information transfer rate (ITR):

Cheng et al. (2002) [29] developed a system enabling healthy participants to input phone numbers. To that end, twelve virtual buttons, flickering on a computer display at different rates, formed a telephone keypad. To input a phone number, participants gazed at the desired symbols. Eight out of thirteen participants suceeded in dialing a phone number. Notable was the high average ITR of 27 bits / min.

Gao et al. (2003) [51] developed a system enabling healthy participants to control environment through an infrared remote-controller. This time, however, the virtual buttons flickering on a computer display were replaced by light-emitting diodes (LEDs). The system could distinguish 48 LED targets, yielding a peak ITR of 68 bits / min. The accuracy was calculated over five groups corresponding to different stimulation frequency ranges. The average accuracy across these five groups was 87.5%.

A growing number of SSVEP based BCIs led to further development and refining of EEG signal processing for such a BCI:

Müller-Putz et al. (2005) [124] investigated the impact of harmonic frequency components on performance in five healthy participants. A significant ($p < 0.01$) increase in classification accuracy was achieved through use of the first three SSVEP harmonic frequencies. In the feedback experiments, the classification accuracy ranged from 42.5% to 94.4%. These findings were confirmed in **Müller-Putz et al. (2008)** [121], where additionally the impact of channel selection on performance was investigated in 10 healthy participants. A large increase in classification accuracy, compared to an anterior / posterior bipolar derivation from the O1 and O2 channels, was achieved through use of the participant-specific optimal bipolar derivation. The mean classification accuracy achieved with the use of a lock-in analyzer system was 74%.

Lin et al. (2007) [100] applied the canonical correlation analysis (CCA) technique to SSVEP frequency analysis. The CCA technique facilitated the use of multiple EEG channels, thus increasing the robustness against noise and improving the results. In a subsequent online experiment by [17], healthy participants were cued to focus on one of six stimuli flickering at different frequencies. The achieved performance was an average accuracy of 95%, with an average ITR of 58 ± 9.6 bits / min.

The improvements in EEG signal processing for SSVEP based BCIs allowed for more advanced application in healthy participants, such as control of an electrical hand prosthesis [122], asynchronous control of an artificial upper limb [74], and even abdominal functional electrical stimulation [57].

An early work on using SSVEP to control motor function was reported in **Calhoun et al. (1995)** [27]. In this work, three healthy participants learned to regulate the magnitude of their steady-state visual evoked responses (SSVER), not unlike the SSVEP, by focusing on two fluorescent lamps flickering at 13.25 Hz. Through this BCI, the participants controlled a FES applied to their lower limb. The experimental task was right knee extension to a predefined target angle, according to a near real-time feedback. After three to five sessions, each lasting for several hours, all three participants were able to fulfill the experimental task, that is to position their knee to a target angle through FES, with high level of accuracy (>95%). While controlling knee angle through FES by a BCI was a novelty and an improvement compared to manual control at that time, there are some drawbacks to this approach: first, using focused visual attention to control a muscular output still seems as a workaround compared to, e.g., just attempting the movement; second, while technologically impressing, the demonstrated use-case scenario warrants real-world application; and third, even though the results obtained in healthy participants were impressive, no evaluation in motor impaired individuals was reported.

One disadvantage of the aforementioned SSVEP based BCIs is that they are overt, that is, they depend on reliable eye-gaze control. Addressing this disadvantage, several covert SSVEP alternatives were proposed:

Kelly et al. (2005) [85] investigated selective attention to targets in space outside the foveal vision. In this covert spatial SSVEP based BCI, left / right attention was detected by extracting the SSVEPs elicited by the corresponding stimuli. Reliable binary control was demonstrated in six out of eleven healthy participants [84].

Allison et al. (2008) [7] investigated whether overlapping stimuli can elicit SSVEP changes reliable enough for BCI control. To that end, healthy participants attended to one or the other of the two overlapping images, each oscillating with a different frequency. Half of the participants demonstrated SSVEP modulation through non-spatial selective attention reliable enough for potential BCI control.

Zhang et al. (2010) [191] investigated non-spatial selective attention to overlapping stimuli. In this work, two sets of dots, differing in color and in rotating direction, were used to induce perception of two superimposed illusory surfaces. The surfaces also oscillated with a different frequency, thus eliciting discriminable SSVEPs, whose amplitude could further be modulated through selective attention. After three days of training, 18 healthy participants achieved average online classification accuracy of 73% on their last day. Notable is an improvement of accuracy through training observed in eight participants.

1.2.3 SMR

Several studies modulated sensorimotor rhythms through both motor-related and cognitive tasks. In **Obermaier et al. (2001)** [138], in addition to four motor-imagery tasks (left hand, right hand, foot, and tongue), participants also performed mental calculation. Various subsets of tasks were evaluated, grouped according to separability of EEG patterns. The reported ITR peaked at 0.81 bits per decision, with various three task combinations yielding the best performance. In detail, for all three healthy participants the classification accuracy was highest for two-classes classifier (range 86.3% to 96.1%), and lowest for five-classes classifier (range 45.2% to 67.2%).

Millan et al. (2002) [159] investigated five mental tasks: relaxation with closed eyes, cube rotation, mental subtraction, and imagined movements of left / right hand. Here, feedback was delivered through colored buttons, each representing a mental task. Online evaluation of three mental tasks yielded recognition rates above 70% and error rates of less than 5%, with responses occurring every 0.5 s.

SMR was signal of choice in multiple asynchronous BCI spelling applications:

Obermaier et al. (2003) [137] reported on three healthy, operating a virtual keyboard by mental hand and leg motor imagery. The performance varied between 0.85 and 0.5 letters / min in error-free writing.

Millan et al. (2003) [158] reported an average spelling rate of around 3.0 letters per minute in 15 healthy participants using a three-class asynchronous BCI.

Scherer et al. (2004) [172] also employed a three-class BCI, using it to select letters by scrolling through the alphabet at an average spelling rate of 2.0 letters per minute in three healthy participants.

Mueller et al. (2006) [117] combined an asynchronous two-class BCI with the Hex-O-Spell application, achieving an average spelling rate of nearly 6.0 letters per minute in two healthy participants.

Going beyond spelling, **Wolpaw et al. (2004)** [186] reported a non-invasive BCI that can provide two-dimensional movement control of a cursor. The EEG control was evaluated in four healthy participants through spectral and topographical analysis of the ¿R^2 correlations between target location and the average values for the trial of the vertical and horizontal variables[186], respectively. The four participants reached the target in 89%, 70%, 78%, and 92% of the trials, respectively. The study showed that a non-invasive BCI can provide humans with multi-dimensional point-to-point movement control with comparable result to those reported with invasive methods in monkeys. This multi-dimensional control was accomplished through an adaptive algorithm that identified those EEG features that the person was best able to control.

1.2.4 Hybrid BCIs

There are two related, albeit somewhat different definitions of a hybrid BCI. The first one, introduced in **Pfurtscheller et al. (2010)** [143], defines a hybrid BCI as a composition of two systems, at least one of which is a BCI, that fulfils the following criteria: (i) the signals of interest are recorded from the brain; (ii) at least one of the recorded brain signals is willfully modulated by the user; (iii) the BCI processes information and delivers response within a specified time (i.e. real-time processing); and (iv) the BCI delivers feedback to the user.

A hybrid BCI can be setup on two different EEG brain signals, where these parts can either operate in a simultaneous, or in a sequential manner [143, 6, 149].

An example of a hybrid BCI operating in a simultaneous manner was reported in **Allison et al. (2010)** [6] and **Brunner et al. (2011)** [23]. In these studies, a hybrid BCI simultaneously combining ERD and SSVEP based BCIs was compared to its parts (e.g. ERD based BCI) in terms of accuracy and subjective measures. The described hybrid approach, while feasible, was not significantly better than a comparable SSVEP based BCI, and the participants found the hybrid approach slightly more difficult.

An example of a hybrid BCI operating in a sequential manner was reported in **Pfurtscheller et al. (2010)** [149]. In this study, a brain switch (i.e. an ERS-based BCI) was used to control an SSVEP-based hand orthosis. The described hybrid approach reduced by about half the number of false positives occurring while using the SSVEP based BCI alone.

Whereas the previous two hybrid BCI examples relied solely on EEG brain signals, a hybrid BCI can also be setup brain signals derived using different recording techniques. One such example was reported in **Bauernfeind et al. (2009)** [12] where hemodynamic changes, measured through near-infrared spectroscopy (NIRS), were used to activate an SSVEP-based hand orthosis. In another example, **Fazli et al. (2012)** [43] investigated whether NIRS can be used to enhance the EEG approach in a real-time SMR paradigm. Evaluation in 14 healthy participants showed a significant ($p < 0.01$) improvement of the classification accuracy of motor imagery in over 90% of participants, with an average increase in performance by 5%.

The second definition of a hybrid BCI, introduced in **Müller-Putz et al. (2011)** [118], defines a hybrid BCI not as a BCI system itself, but more as a concept of combining existing input devices with a BCI. In this hybrid BCI (hBCI) concept, common assistive devices are integrated with different types of BCI, with a major goal of bringing " ...the BCI technology to a level where it can be used in a maximum number of scenarios in a simple way." [118]. To enable this integration, four standardized interfaces are used to build and interconnect BCI systems: signal acquisition, preprocessing, feature extraction, classification, and the application. These interfaces allow for: (i) exchange of data within a programming language; (ii) exchange of data between different programming languages through shared memory; and (iii) exchange of data between different computers, thus allowing for distributed processing [119].

In addition to a brain signal, hybrid BCIs can also take non-brain signals as inputs, such as biosignals or signals originating in external devices. Example for the former was reported in **Scherer et al. (2007)** [173], where heart rate was used to self-initiate (i.e. switch on and off) an SSVEP based BCI. Example for the later was reported in **Vilimek et al. (2009)** [184], where an eye tracker was used determine the object the participant was interested in, which could then be selected by an motor imagery based BCI.

In addition to the four interfaces, the concept of the hBCI introduces two new modules: fusion, and shared control. The fusion module decides which control signal is used for application control. For example, fusing EMG and EEG activity can increase accuracy [98], thus yielding a more stable control. Another example is combining EEG and joystick activity, switching between input signals depending on the quality, thus potentially prolonging the control duration [88]. The fused control signal is forwarded to the shared control module.

The shared control module improves upon the control signal from the fusion module by harnessing the contextual and environmental information. What this means is that an intelligent device handles the low-level details, whereas the human makes the high-level decisions. For example, the shared control applied in a BCI-controlled mobile platform can handle the low-level navigation tasks, whereas the participant decides the high-level target. In this way, both the time and the number of commands needed in order to reach the destination are reduced [181].

Two studies combined an MI based BCI with an added input from a sensor:

Rohm et al. (2013) [163] combined an MI based BCI with an analog shoulder position sensor. The imagined movements of the right hand acted as a brain-switch, toggling between the elbow and the hand control. The upward / downward movements of the shoulder controlled the elbow flexion / extension or the hand opening / closing. The hybrid BCI system enabled a highly paralyzed end-user to perform various daily living actions [163, 164].

Kreilinger et al. (2013) [89] combined an MI based BCI with a sensor monitoring the elbow joint angle for neuroprosthesis control. Nine healthy users and one end-user with a high-level spinal cord injury (SCI) generated either discrete commands through short MI (approximately one second) or continuous commands with MI longer than 1.5 s. The control commands were contingent upon the current elbow joint angle, as interpreted by a shared control logic. The neuroprosthesis was comprised of a non-invasive FES system for stimulation of lower and upper arm muscles, and a lockable electronic elbow orthosis. The users were instructed to perform a series of movement sequences with the neuroprosthesis. Four healthy users and the SCI user were able to complete more than half of the sequences at an average true positive rate of 60%. Notably, the SCI user achieved the second best overall performance.

1.3 EEG based BCIs in end-users

1.3.1 Impact of BCIs in end-users

The EEG based BCI technology can benefit end-users with individual functional deficits. One important area is restoration of motor function. In end-users suffering from a spinal cord injury (SCI), the BCI together with functional electrical stimulation (FES) can help restore motor functions, and lead to a dramatic increase in quality of life. For example, the restoration of grasping function could reduce a dependency on helping person. In stroke patients, BCI could provide feedback for motor imagery therapy, thus possibly enhancing the effect of such a therapy on stroke.

Arguably the most important area is replacement of communication. In a longitudinal study with twenty seven amyotrophic lateral sclerosis (ALS) end-users [107], the end-users were asked which areas of their life they consider most relevant for their quality of life. The authors found that the only component of quality of life whose relevance increased over time, while physical competence decreased, was communication.

To give an impression of what impact the EEG based BCIs can have in these areas, this section provides notable examples of such BCIs for restoration of motor function, and replacement of communication. Finally, the application of BCI in art is discussed, as it has a particularly positive impact on end-users.

1.3.2 Restoration of motor function

Pfurtscheller et al. (2003) [144] and **Müller-Putz (2004)** [120] developed a so called BCI controlled neuroprosthesis, aimed at restoring weak or lost grasp functions in spinal-cord injured individuals. To that end, the output of an SMR based BCI was connected to an external FES system, with surface electrodes stimulating the hand / forearm muscles. Through this combined BCI / FES system, an SCI injured individual was able to grasp a cylinder with the paralyzed hand by imagining feet movements [144]. Notably, this work demonstrated for the first time restoration of hand grasp function in a tetraplegic end-user by non-invasive means (i.e. EEG and surface FES). In a second feasibility experiment, an individual with tetraplegia was able to control a FES system implanted in his left hand by imagined movements of his right hand [120]. Today's research has advanced even further, e.g., by incorporating elbow function for restoration of upper limb functions [163, 89, 164].

While the current state of the art in EEG based BCIs for direct (motor) control is impressive, it is an open research question on how it compares to invasive BCIs, e.g. in number of degrees-of-freedom one can control. There are, however, scenarios where non-invasive BCIs may be preferable, such as in teleoperation (e.g. manipulation of an external robotic arm), or navigation (e.g. wheelchair control), where high-level commands can be combined with intelligent systems [181]. Furthermore, EEG based BCIs can be integrated with other assistive technology, thus providing another potential control signal [119]. Further applications of EEG based BCIs for direct (motor) control are a subject of ongoing research.

1.3.3 Improvement of motor function

Another important research area is clinical application of EEG based BCIs in stroke recovery. A growing body of literature suggests that EEG based BCIs can improve motor control in end-users in twofold manner [104]: first, by training end-users in producing normal brain activity for motor function control; second, by connecting the control signal from a BCI to a movement assisting device, thus achieving a more natural control. Some of the notable findings include:

Kaiser et al. (2012) [81] investigated the relationship between ERD and ERS patterns and the degree of stroke impairment. To that end, EEG was recorded in 29 monolateral stroke end-users, with upper limb motor deficit of varying degree, during imagined and executed movements. ERD was found to be stronger in the unaffected hemisphere with higher impairment, and stronger in the affected hemisphere with higher spasticity. ERS was found to be stronger in the affected hemisphere with both higher impairment and higher spasticity.

Pichiorri et al. (2015) [152] evaluated whether a motor imagery (MI) based BCI can enhance standard rehabilitation care in subacute stroke end-users. To that end, 28 end-users with severe motor impairments were randomly split into two groups: in the first group (BCI, n=14), MI was performed within a BCI system; in the second group (control, n=14), MI was performed outside a BCI system. The main finding of the study was a higher probability of clinically relevant improvement in motor function restoration, as indexed by Fugl-Meyer Assessment (FMA). Furthermore, the MI training with the paralyzed hand in the BCI group led to greater involvement of the ipsilesional hemisphere, with stronger ERD in the alpha and beta bands.

Ang et al. (2015) [8] presented two strategies of using BCI for neurorehabilitation after stroke: (i) triggering feedback by MI detection; and (ii) providing physical practive with a robot concomitant with MI detection. These two strategies were evalueted in three randomized control trials employing upper limb rehabilitation, where a total of 125 chronic stroke patients was screened over a period of six years. The results of this screening were: (i) 103 (82%) of stroke patients can use an EEG based BCI; (ii) 75 (60%) of stroke patients yielded accuracies above 70%; and (iii), in 26 out of 67 stroke patients that underwent BCI neurorehabilitation employing these two strategies, a significant ($p < 0.05$) motor improvement of 4.5 measured by Fugl-Meyer Motor Assessment of the upper extremity was found.

Further review of the literature on this research area can be found elsewhere [164, 8]. Notable is that, in addition to brain plasticity, spinal cord plasticity occurs in both healthy and motor impaired participants, offering "... numerous possible avenues for inducing functional recovery beyond that possible with current therapies." [165].

1.3.4 Replacement of communication

One of the earliest works on using EEG to replace communication in end-users [19] employed slow cortical potentials (SCPs) to drive a language support program. In this work, two locked-in end-users with ALS learned to voluntary control their brain responses, enabling them to select letters of the alphabet by driving a cursor on a screen. In detail, the participants learned after extensive training to change their SCPs to meet specific criterions (i.e. positivity greater than a specific, random, amplitude during the response period). The spelling program employed a scanning paradigm, where the alphabet was split into consecutive halves until a letter was selected. This paradigm enabled the participants to communicate, which they were not able to do using muscular output.

Whereas SCPs enabled some end-users to establish a reliable enough communication, not all of the end-users were able to communicate by means of SCPs. Furthermore, writing sentences by means of SCP was very time consumin g. To address these issues, several studies investigated whether a BCI based on oscillatory components might enable additional end-users to communicate, and to do so faster than by means of SCPs.

One of the earliest clinical applications of SMR based BCIs was described in **Neuper et al. (2003)** [132] and **Müller et al. (2003)** [115]. In this work, an end-user paralyzed by severe cerebral palsy was trained over the course of several months to communicate by means of SMRs. The training was administered at the end-user's clinic through a telemonitoring system, with the EEG feedback computed from band power features at specific frequency bands. The end-user learned to control a spelling application by producing two distinct EEG patterns: beta band ERD during movement imagery, and no ERD during relaxation. Further findings of this study were a significant improvement of performance over the training sessions, with correct letters selected at an average accuracy of 70% with a rate of one letter per min.

In a similar work by **Kübler et al. (2005)** [93], four ALS end-users learned to willfully modulate SMRs over the course of 20 training sessions, despite hyperreflexia in three of the end-users. The SMR rhythms were acquired over standard scalp locations over sensorimotor cortex, and analysed at mu (8 to 12 Hz) and beta (18 to 26 Hz) frequency bands. For every end-user the performance exceeded the 70% accuracy, indicating its potential use for communication.

Repetitive wrist movement execution / imagery were investigated in three ALS end-users and three primary lateral sclerosis (PLS) end-users over multiple training sessions in **Bai et al. (2010)** [9]. The imagined movements were evaluated in binary (yes / no) and four-directional control of cursor movements. In binary control experiment with imagined movements, four end-users achieved online accuracy of about 80%. In four-directional control of cursor with imagined movements, one ALS and one PLS end-user achieved online accuracy of less than 60%.

In **Höhne et al. (2014)** [66] four end-users with severe motor impairments were initially screened in imagined movements of left-hand, right-hand and feet in order to determine the most discriminative pair. In total of six experimental sessions, three out of four end-users gained BCI control. Notably, in the end-user with most severe motor impairments the BCI control outperformed other available AT, as indicated by accuracy, reaction time and ITR.

The effect of mental tasks on performance of end-users with stroke or SCI in a binary control paradigm was investigated by **Scherer et al. (2015)** [170]. To that end, within-day and between-day classification performance was evaluated for pair-wise combinations of hand / feet movements, "brain teasers" (mental subtraction, word association), and spatial navigation in nine participants. The classification performance was significantly ($p = 0.01$) higher for the individually selected pair of mental tasks.

Different BCIs were investigated by **Daly et al. (2013)** [35] in end-users with cerebral palsy (CP). To that end, mental imagery based BCI, and SSVEP based BCI were evaluated in 14 CP end-users, without previous training. Eight end-users could control at least one of the BCIs online, reaching statistically significant accuracies: six were able to control a mental imagery based BCI, and three an SSVEP based BCI. In a follow up study [36], neural correlates of movement and motor imagery were explored in CP end-users and in healthy controls. Significant differences were found in the amount of ERD and phase locking (i.e. less in the CP group), as well as in phase dynamics between the two groups. The overall findings suggested lower levels of motor cortex activation during motor imagery in CP end-users.

An alternative approach to establishing communication in some end-users is the use of ERP based BCIs, most notably based on the P300 component. Several studies have evaluated a visual P300 based system in end-users.

Sellers et al. (2006) [175] evaluated a four-choice system in an offline study in three end-users with ALS, and in an equal number of healthy participants, over the course of 10 experimental sessions. The stimuli (i.e. YES, NO, PASS, END) were presented in visual, auditory, or in both modalities. The visually elicited ERPs for the standard and deviant stimuli could be discriminated in both end-users and in healthy controls, with two end-users yielding peak offline accuracies that could support communication. The mean classification accuracy ranged from 59.4% to 79.6% in healthy, and from 49.9% to 63.6% in end-users. The auditorily elicited ERPs did not yield comparable results.

Piccione et al. (2006) [151] reported an online study in which five tetraplegic end-users (one SCI) and seven healthy participants used a visual P300 based BCI to move a screen object (ball) along a specified path, over the course of 12 experimental sessions. The movement was controlled by four visual stimuli (i.e. arrows pointing up, right, down, and left), placed on screen peripherals. Three out of five end-users achieved performance similar to that of healthy participants, with ERPs between the two groups differing in latency and amplitude of the P300. The average classification accuracy was 76.2% in healthy participants and 68.6% in end-users. Notable, the two end-users who performed significantly worse than the healthy participants were also the most impaired.

Hoffmann et al. (2008) [65] evaluated online a six-choice system in five disabled and four healthy participants. In detail, the diagnosis of the disabled participants were as follows: (i) cerebral palsy; (ii) multiple sclerosis; (iii) late-stage ALS; (iv) traumatic SCI (C4 level); and (v) post-anoxic encephalopathy. The visual stimuli were images of appliances, simulating an environmental control scenario. Whereas both groups of participants yielded similar classification accuracy, healthy participants yielded higher bitrates compared to disabled participants. The classification accuracies were reported as time plots, with four out of five disabled participants achieving 100% accuracy after 10, 15, 25, and 30 s, respectively. The remaining disabled participant yielded random results. Notable, all of disabled participants had some means of communication, ranging from speech to voluntary eye-control.

Nijboer et al. (2008) [136] evaluated effectiveness of a visual P300 based communication device in persons with advanced ALS. The visual stimuli were flashing rows or columns of a NxN matrix, with N being either 6 or 7, whereas each cell of the matrix contained one character. The study was split in two parts: in the first part six persons copy-spelled characters over the course of 12 experimental sessions; in the second part, four of these persons free-spelled messages of their own choice. In the first part, participants communicated on average 1.2 characters per minute, with a mean online accuracy of 62%. In the second part, participants communicated on average 2.1 characters, with an online accuracy of 79%. Notable, the latency and the amplitude of the P300 component stayed the same over many months.

Comparing the results of evaluation of the three previously mentioned types of BCIs - based on SCPs, oscillatory components, and the visual P300 - in end-users with ALS, **Nijboer et al. (2005)** [135] concluded that the SCP based BCI is difficult to use and very time consuming, the BCI based on oscillatory components yields the best overall performance, and while visual P300 based BCI does not require initial user training, not all end-users with ALS can use it effectively.

Another end-user evaluation of visual ERP based speller was reported in **Kaufmann et al. (2013)** [83], who improved upon the standard paradigm by using famous faces as visual stimuli. Compared to standard character highlighting, online performance was significantly higher in both healthy participants (N=16) and in end-users with neurodegenerative disease (N=9). Furthermore, two end-users unable to communicate with the standard stimuli were able to do so with the face stimuli.

In an effort to reduce the eye-gaze dependence, **Kübler et al. (2009)** [91] developed an auditory-visual P300 based BCI. To that end, a visual 5x5 matrix speller was adapted for auditory stimulation by encoding rows with auditorily presented numbers 1 to 5, and columns with numbers 6 to 10. The letters of the alphabet could then be selected by: (i) selecting the desired row; and (ii) selecting the desired column. The auditory-visual BCI was evaluated in four severely paralyzed end-users, with all of the participants performing at a better than random level. The spelling accuracies achieved with the visual BCI were significantly higher compared to those obtained with the auditory BCI. Also, end-users found it difficult to concentrate on the task in the auditory BCI, possibly due to a reduced attention span.

For end-users with vision problems, auditory BCIs may provide an alternative. A binary auditory P300 based BCI was evaluated in **Pokorny et al. (2013)** [156] in 12 end-users with disorders of consciousness and in healthy controls. The BCI was based on segregation of two tone streams, made of short beeps with infrequent random deviant tones. Command following could be detected reliably in 8 out of 10 healthy participants on a single-trial basis. Command following could also be detected in 9 out of 12 end-users, albeit after averaging all of the data segments.

Going beyond binary choice, a multi class auditory BCI was reported in **Simon et al. (2015)** [176]. Here, rows and columns of a spelling matrix were encoded through animal voices with directional cues. The spelling system was evaluated in 11 healthy participants and in an ALS end-user over the course of two experimental sessions. The healthy participants ended up spelling with an average accuracy of 90% and an ITR of 4.2 bits / min, whereas the accuracy of the ALS end-user peaked at 47%. The results improved in both healthy and in ALS between the first and the second session, indicating a strong training effect.

A case study investigating various sensory modalities in ERP based BCIs with a LIS end-user was reported in **Kaufmann et al. (2013)** [82]. To that end, visual, auditory and tactile modality were compared across classic and multi-choice oddball paradigms in a user-centered approach. The tactile modality yielded best results across different BCI systems, allowing the end-user to successfully select targets. However, in light of other AT such as partner scanning, its practical use seemed limited.

1.3.5 BCI and art

Most of the current BCIs, while enabling control of assistive technology (e.g. spelling software), are not well suited for creative expression. To enable paralyzed end-users to paint pictures, the so called "Brain Painting" application was developed. The way the "Brain Painting" works is that in a standard visual P300 speller application [38], the letters of the alphabet are replaced by symbols indicating color, various objects and their parameters, as well as zoom and cursor movements [92]. In **Münssinger et al. (2011)** [128] the "Brain Painting" application was evaluated in three end-users with ALS, with two of them reaching high accuracies (i.e. around 90%).

In a recent work, **Pinegger et al. (2015)** [155] developed an application for music composition. Similarly to the "Brain Painting" application, a visual P300 based BCI was adapted for the task at hand. To that end, the letters of the alphabet were replaced by symbols (e.g. notes, accidentals, etc.), and the output of the BCI was connected to a music composition software. The whole system was evaluated in five healthy participants, with three participants being able to compose a predetermined melody within the given time. Notable, the system was evaluated using water-based electrodes.

Other notable examples of combining BCI and art include work by **Miranda et al. (2011)** [112], and **Makeig et al. (2011)** [105]

1.4 Limitations of the state of the art

BCIs based on mental imagery, as well as ERP based BCIs, have been shown to work in healthy participants with real-world applications, and have also made good progress towards achieving similar results in end-users. This progress notwithstanding, recent work on hybrid BCIs [143, 119] demonstrated various scenarios in which combining these two types of BCIs may be advantageous. While these scenarios gave direction for future work, they also indicated room for improvement in such combinations. For example, whereas **Pfurtscheller et al. (2010)** [149] reported a sequential combination of ERD and SSVEP based BCIs, an experimental proof on whether two different BCIs can, in principle, be used in parallel with a common goal, was missing. Such an experimental evaluation is needed, as it may provide further insights into combined BCIs. Furthermore, whereas some combined BCIs were integrated into a real-world AT application, others were not, leaving open the question how such an integration could take place. Therefore, a paradigm enabling further integration of BCIs based on induced and evoked changes in EEG is needed to address these questions. Note that the more recent work, such as **Kreilinger et al. (2012)** [90] reporting on combination of MI with error-related potentials, will be discussed in the Discussion section, as it was unavailable prior to addressing the aforementioned questions through studies conducted in this thesis.

One common challenge all BCIs face is the so called BCI "illiteracy", meaning that the success and acceptance of BCIs in end-users varies from person to person, and that the best control strategy is highly unique [47]. For example, some severely motor impaired persons have difficulties performing the motor imagery [31], but might benefit from alternative mental tasks [46]. One way of addressing this challenge is evaluating different types of BCIs in order to find the most reliable one. However, BCIs based on induced and evoked changes can differ substantially in control strategies, and it is unclear how these differences can be overcome in common AT control scenarios. Thus, reducing these differences to an extent that makes different BCIs interchangeable within a common AT application could mitigate the BCI "illiteracy".

Another challenge for BCIs is the reliability of results. While ERP based BCIs yield good results in ideal conditions, they are often eye-gaze dependent and prone to artifacts, limiting their usability in end-users. The mental imagery based BCIs are more robust in presence of artifacts, but in some end-users the associated brain responses can be difficult to detect for various reasons (e.g. delayed and attenuated brain responses in persons with MCS). Combining BCIs based on induced and evoked changes in EEG could increase reliability of results and robustness against artifacts. Though, only few such combinations have been proposed, all of them utilizing two different tasks [143]. This means, that in order to achieve the desired goal in dual-task designs the users must split their attention between two different tasks. The extent to which a single task can result in both induced and evoked changes in EEG, and how these changes can be combined for BCI applications, is an open research questions.

Two further works investigated hybrid BCIs based on induced and evoked changes in EEG, using two different tasks and executed / imagined movements that are triggered by an external stimuli [167, 52].

Salvaris et al. (2010) [167] reported on ten healthy participants performing one of three tasks triggered by target stimuli in an oddball paradigm. The tasks were movement execution, movement imagery, and mental counting. The average classification accuracy for the target vs. non-target discrimination was 90% for movement execution, 85% for movement imagery, and 79% for mental counting. Notably, the classifier was setup on ERPs only, ignoring the sensorimotor rhythms.

Geuze et al. (2014) [52] investigated neural correlates of executed movements to perceived semantic relations. To that end, healthy participants performed two tasks: (i) they kept a prime word in mind and compared it to the presented prime words; and (ii) they indicated a relation between a presented probe word and the prime word by a single finger tap. A movement detector combined both the evoked (ERP) and induced (ERD) responses elicited with the two tasks, achieving an average single trial accuracy of 67%.

Last but not least, while there are plenty of studies on EEG based BCI evaluation in healthy participants, such studies in end-users are comparably few. Recent efforts focused on translating these fMRI paradigms to electroencephalography (EEG) technique, as it is widely available, cost effective, and applicable at bedside, even in persons with metal implants. For example, **Goldfine et al. (2011)** [56] instructed the participants to imagine complex motor and familiar spatial navigation tasks, and analyzed EEG power spectra over a wide range of channels and frequencies. By analysing the EEG power spectra, evidence for performance of mental imagery tasks was found in healthy controls and patients with severe brain injury. In another study, **Cruse et al. (2011)** [33] asked the participants to imagine movements of their right-hand and toes to command, and analyzed the EEG responses to specific commands. Three of 16 patients (19%) generated repeatedly and reliably suitable EEG responses to two distinct commands, even though they were behaviorally unresponsive. In a follow-up study, **Cruse et al. (2012)** [34] addressed some of the methodological challenges, and found EEG evidence for attempted movements to command in an UWS patient.

Following gaps in knowledge regarding the suitability of EEG based BCIs for end-users with disorders of consciousness exist: (i) evaluation of simple and complex motor imagery within persons with disorders of consciousness; (ii) passive feet movement as a mean of an initial classifier setup; and (iii) rapid delivery of biased feedback). Addressing these gaps could yield useful insights for further adaptation of existing BCIs to the needs and capabilities of the end-users.

1.5 Motivation and aim

The research aim of this thesis is to evaluate whether and to what extent willful modulation of induced and evoked EEG activity can be combined for BCI applications. There are several potential advantages motivating this combined approach: first, BCIs based on induced and evoked changes could be combined in different ways with a common goal. Second, employing different experimental strategies would increase the likelihood that at least one of them works in end-users. Third, novel combinations of induced and evoked changes in EEG could increase reliability of results and robustness against artifacts.

The applied aim of this research is to evaluate the state of the art in the BCI technology in end-users with disorders of consciousness and to address gaps in knowledge. Motivation for this aim is further adaptation of the existing BCIs to the needs and capabilities of the end-users.

1.6 Workplan

Central to addressing the research aim of this thesis is to increase the level of integration of BCIs based on induced and evoked changes in EEG within the same system. To this end, existing BCIs need to be combined with a common goal. Building upon this common goal, further integration can be achieved through new methodological approaches in common standard AT use cases. Finally, a common experimental strategy can modulate both induced and evoked changes in EEG.

First and foremost, it is unclear whether two different BCIs can, in principle, be used in parallel with a common goal. Therefore, the aim of the first work will be to evaluate whether and to what extent the existing BCI systems can be made to work together.

Connecting the output of a BCI to an existing AT seems outright. Nevertheless, developing a paradigm enabling further integration of induced and evoked changes in EEG, and use of BCI in various end-users and various AT applications is a formidable task, to be tackled in the second work.

The third work will further elaborate on the research aim of the thesis, on one hand by evaluating induced EEG changes triggered by an external stimuli, and on the other hand by evaluating event-related potentials associated with a cognitive task, both within a common application. To this end, strategies for using EEG responses for spelling through listener-assisted scanning will be developed.

Addressing the applied aim of this research, the fourth work will evaluate the state of the art in the BCI technology in end-users with disorders of consciousness. To achieve this goal, existing BCIs will be adapted to the needs and capabilities of the end-users.

Finally, the fifth work will evaluate the extent to which a single task can result in both induced and evoked changes in EEG, and how these changes can be combined for BCI applications. Building upon the previous work, a single auditory selective attention task will be used to modulate both induced and evoked changes in EEG in a standard AT use case.

Chapter 2

Materials and Methods

2.1 Primary Publications

This thesis is composed of five primary contributions to peer-reviewed journals [79, 123, 67, 70, 68], one additional contribution to a peer-reviewed journal resulting from the author's master thesis [74], and multiple secondary publications [78, 73, 77, 75, 76, 71, 69, 72]. Adopting the approach outlined in the introduction, **Horki et al. (2011)** [79] made two different BCIs work together, one of which was reported in **Horki et al. (2010)** [74]. Next, **Müller-Putz et al. (2013)** [123] developed a paradigm enabling further integration of different BCIs, **Horki et al. (2015)** [70] developed strategies for using EEG responses for spelling through listener-assisted scanning, and **Horki et al. (submitted)** [68] provided experimental proof that a single auditory selective attention task can modulate both induced and evoked changes in EEG. Last but not least, mental imagery and attempted movements were evaluated in end-users with MCS in **Horki (2014)** [67].

2.1.1 Parallel use of two BCIs

[79] Horki, P., T. Solis-Escalante, C. Neuper and G. R. Müller-Putz: *Combined motor imagery and based BCI control of a 2 DoF artificial upper limb*. Medical and Biological Engineering and Computing, 49:181–191, 2011

The first work evaluated whether and to what extent the existing BCI systems can be made to work together. For this purpose, two different BCIs, one based on MI and the other one on SSVEP, were used to extend the number of degrees-of-freedom in an artificial upper limb control scenario. The combination of MI and SSVEP based BCIs allowed for a more finer control compared to the previous work. It also showed that two different BCIs can, in principle, be used in parallel with a common goal.

Contribution to this work Demonstration that two different BCIs can be used in parallel with a common goal.

2.1.2 BCI in the context of assistive technology

A single-switch BCI based on passive and imagined movements: toward restoring communication in minimally conscious patients

[123] Müller-Putz, G. R., C. Pokorny, D. S. Klobassa and P. Horki: *A single-switch BCI based on passive and imagined movements: toward restoring communication in minimally conscious patients*. International Journal of Neural Systems, 23(2), 2013

In the second work a scanning paradigm was developed, allowing for the use of an ssBCI for binary communication in auditory scanning mode, but also enabling further integration of induced and evoked changes in EEG. To that end, both time-locked and non time-locked control signals are supported through a semi-synchronous design.

Future use of BCI in various end-users and various AT applications is enabled through support for different sensory modalities, different selection methods, and binary and multiclass selections.

This work also addressed the issue of initial classifier setup by exploiting similarities of the sensorimotor EEG changes of the motor cortex during passive and imagined movements. To this end, data obtained from the passive movements was used to setup an initial classifier that was used to detect imagined movements.

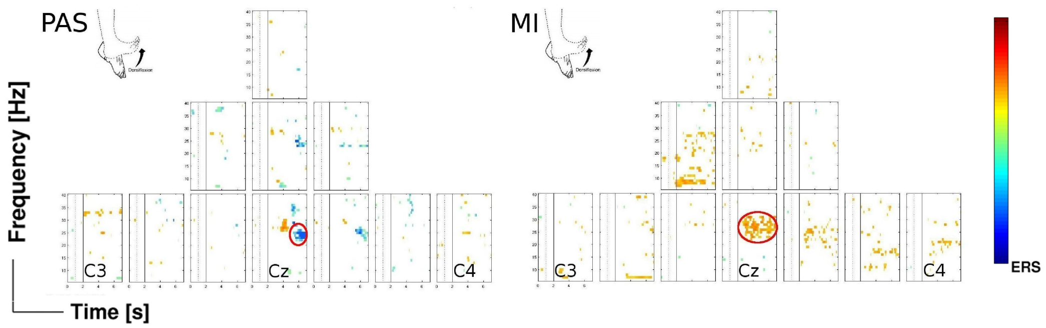

Figure 2.1: Time-frequency analysis of patterns corresponding to passive (PAS) and imagined (MI) brisk feet movements at 11 orthogonal Laplacian derivations in one participant. In the feet condition significant (p=0.01) power changes were found for both the passive and the imagined movement task.

Contribution to this work Design and development of a scanning paradigm enabling further integration of induced and evoked changes in EEG, and use of BCI in various end-users and various AT applications. Evaluation of an ssBCI for binary communication in auditory scanning mode.

2.1.3 New paradigms for induced and evoked BCIs

Evaluation of healthy EEG responses for spelling through listener-assisted scanning

[70] Horki, P., D. S. Klobassa, C. Pokorny and G. R. Müller-Putz: *Evaluation of Healthy EEG Responses for Spelling Through Listener-Assisted Scanning*. IEEE Journal of Biomedical and Health Informatics, 19 (1):29–36, 2015

The fourth work addressed a relevant issue in combining BCIs based on induced and evoked changes in EEG, namely the substantial differences in their experimental paradigms. Reducing these differences to an extent that makes different BCIs interchangeable allows for further integration of BCIs based on induced and evoked changes within a single paradigm, as well as mitigation of the so called BCI "illiteracy" through choice of different control signals.

To facilitate the transfer of the proposed solution to real-world scenarios, listener assisted scanning, an alternative communication method for persons with severe motor and visual impairments but preserved cognitive skills, was chosen for evaluation (Figure 2.2).

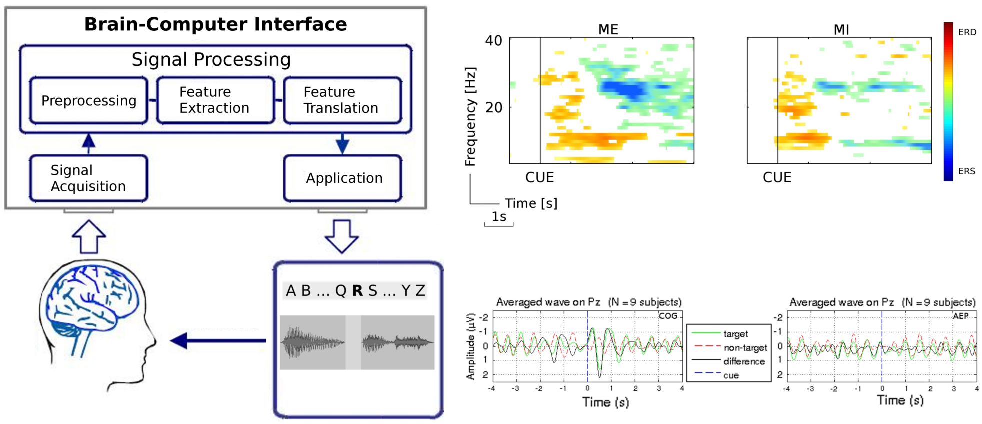

Figure 2.2: Evaluation of Healthy EEG Responses for Spelling Through Listener-Assisted Scanning (parts of the figure adapted from [59]). Here, it was investigated whether listener-assisted scanning, an alternative communication method for persons with severe motor and visual impairments but preserved cognitive skills, could be used for spelling with EEG. To that end spoken letters were presented sequentially, and the participants made selections by performing motor execution/imagery or a cognitive task. The motor task was a brisk dorsiflexion of both feet, and the cognitive task was related to working memory and perception of human voice.

Contribution to this work Different types of BCIs were made interchangeable, thus mitigating the BCI "illiteracy". A single cognitive task (COG), related to working memory and perception of human voice, was found to modulate ERP components reflecting three different stages of selective attention. The obtained results for the motor and for the COG conditions provided guidelines for the further development.

2.1.4 Application in persons with disorders of consciousness

Detection of mental imagery and attempted movements in patients with disorders of consciousness using EEG

[67] Horki, P., G. Bauernfeind, D. S. Klobassa, C. Pokorny, G. Pichler, W. Schippinger and G. R. Müller-Putz: *Detection of mental imagery and attempted movements in patients with disorders of consciousness using EEG*. Frontiers in Human Neuroscience, 8:1009, 2014

In the third work the goal was to evaluate mental imagery and attempted movements in persons with disorders of consciousness. This work addressed several gaps in knowledge by evaluating:

1. simple and complex motor imagery within persons with DoC
2. passive feet movement as a mean of an initial classifier setup
3. rapid delivery of biased feedback

Contribution to this work Comparison of different types of mental tasks, foremost complex motor imagery and attempted feet movements, in persons with DoC. The obtained results provided valuable insights for further development of an EEG based communication device.

2.2 Evaluation of induced and evoked changes in EEG during selective attention to verbal stimuli

[68] Horki, P., G. Bauernfeind, W. Schippinger, G. Pichler and G. R. Müller-Putz: *Evaluation of induced and evoked changes in EEG during selective attention to verbal stimuli.* submitted to Journal of Neuroscience Methods, 2016

The goal of this study is twofold: first goal is to develop an experimental paradigm that can facilitate the performance of brain-teasers (e.g. mental subtraction and word generation) on the one hand, and can increase the experimental control (i.e. type and the timing of the task performance) on the other hand. The underlying hypothesis is that, attending to someone else's verbal performance of brain-teaser tasks leads to similar results as in self-performing the same tasks. The second goal of this study is to exploit these similarities to setup an online BCI, and to compare it in healthy participants to the current "state-of-the-art" motor imagery (MI).

We found that (i) attending to someone else's verbal performance of brain-teaser tasks leads to similar results as in self-performing the same tasks; (ii) these similarities can be exploited to setup an online BCI and used for yes / no communication in an auditory scanning paradigm; and (iii) a single task, namely selective attention to verbal stimuli, can modulate both induced and evoked changes in EEG.

This manuscript has not been published at the time of completion of this thesis, as it is still being peer-reviewed. Accordingly, this section includes the submitted manuscript.

Contribution to this work This study concludes the thesis by showing that a single auditory selective attention task can modulate both induced and evoked changes in EEG. This proof was obtained in a standard AT use case, with participants answering a series of yes / no questions in a scanning paradigm, that can generalize to further applications.

Introduction

For persons with severe motor and visual impairments but preserved cognitive skills, a brain-computer interface (BCI) might provide alternative means of communication [185]. One group of end-users who are unable to perform any motor movement to use an assistive device but have been proven to be sometimes consciously aware (i.e. their vigilance is fluctuating [97]) are persons in a minimally conscious state (MCS) [53].

The most promising results for BCIs in persons with MCS have been achieved using mental imagery, both in functional magnetic resonance imaging (fMRI) and electroencephalogram (EEG) experiments. In fMRI experiment by Owen et al. [140] one person diagnosed as being in the vegetative state was asked to either imagine playing tennis or to navigate through her own apartment. Both mental tasks resulted in very specific brain responses, which opened the possibility of establishing communication with persons in the minimally conscious state by means of simple yes/no questions, as demonstrated in Monti et al. [113] in one person.

In EEG experiments reported in Cruse et al. (2011) [33], Goldfine et al. (2011) [56], and Horki et al. (2014) [67], similar tasks and also attempted movements were evaluated in persons with MCS at their bedside. In some of these persons, EEG evidence for performance of mental imagery tasks and attempted movements was found, even when they were behaviourally unresponsive. However, a functional and accurate communication with persons with MCS, as demonstrated with fMRI, was not achieved.

Common to most of these studies is the use of one motor and one non-motor mental imagery task [56]. The motor tasks have been known to produce good results in a variety of end-user populations [33, 35, 40]. However, severely motor impaired persons having difficulties with motor imagery, either because of the underlying neurophysiology [31] or because of subjective preference [46], might benefit from alternative mental tasks.

A thorough comparison of different mental tasks in healthy participants is provided in studies reporting on their effect on classification performance [47], on the stability of the associated event-related desynchronization (ERD) and event-related synchronization (ERS) [49], and on the long-term evaluation of a 4-class imagery-based BCI [48]. In these studies, several alternatives to motor imagery were identified, most notably spatial navigation, mental calculation and word generation. Furthermore, in a followup study with persons with stroke [170], it was found that mental tasks which best complemented a motor imagery task, for example the imagined movements evaluated in end-users with severe motor impairments by Faller et al. [40], were mental subtraction and word generation. The two last-mentioned tasks can be described as so called brain-teasers [49], since they require problem specific mental work and place a variety of cognitive demands.

Before bringing these tasks to persons with MCS, two challenges need to be addressed. The first challenge is keeping these cognitive demands as low as possible so that they could be fulfilled by persons with MCS. The second challenge lies in the control of experimental protocol, i.e., how to provide as accurate instructions as possible, since the brain patterns depend both on the type (i.e. how the task is being performed) and the timing of the task performance. For example, the mental calculation can activate different brain areas depending on whether one uses a verbal or a visual strategy [58].

The aim of this work is to address these challenges, namely keeping the cognitive demands as low as possible and increasing the control of experimental protocol. For this purpose, we developed an experimental paradigm that can facilitate the performance of the brain-teasers on the one hand, and can increase the control of experimental protocol (i.e. employed strategy and the timing of the task performance) on the other hand. The underlying hypothesis is that, mentally attending to someone else's verbal performance of brain-teaser tasks leads to similar results as in self-performing the same tasks. We tested this hypothesis in the first experiment of this study for mental subtraction and word generation tasks.

In the second experiment of this study our aim was to exploit these similarities to setup an online BCI based on our approach, and to compare it in healthy participants to the current "state-of-the-art" motor imagery (MI). We performed this comparison in a twofold manner: first, we evaluated whether and to what extent attending to someone else's verbal performance of a brain-teaser task can be discriminated online from sports imagery. Second, we evaluated whether such a brain-teaser task can be used for yes / no communication in an auditory scanning paradigm, as it was successfully demonstrated with feet MI [123].

Building upon the results of the first two experiments, in the third experiment we evaluated command following in persons with MCS. Towards this aim, we employed two tasks: complex mental imagery (i.e. sport) and focused attention to verbal performance of mental subtraction.

A novelty in our approach is that it induces oscillatory changes in EEG by exploiting selective attention to verbal stimuli, normally used in event-related potential (ERP) studies [50]. Various ERPs associated with attention to and perception of external stimuli have been reported, most notably the P300 component, characterised by its large positive peak amplitude at around 300 ms following the stimulus. Further reported ERPs include late positive component (LPC), reflecting the switch of attention onto the new information [190], N400 [95] and P600 [60], related to semantic processing. ERPs can be used to setup BCIs in different sensory modalities for healthy and motor-impaired users [154, 82, 61, 176]. Promising results have also been obtained in persons with MCS using an auditory P300-based BCI [156, 11].

An experimental strategy employing both ERPs and oscillatory changes could increase reliability of results and robustness against artifacts [42]. To that end, we hypothesised that this single task, namely selective attention to verbal stimuli, can be used to modulate both induced and evoked changes in EEG. To test this hypothesis we modified the verbal performance of brain-teaser tasks to include a semantic oddball paradigm, and analysed the task related EEG changes.

Summary of hypotheses

- Attending to someone else's verbal performance of brain-teaser tasks leads to similar results as in self-performing the same tasks.
- Single task, namely selective attention to verbal stimuli, can be used to modulate both induced and evoked changes in EEG.

Summary of experimental approaches

Most of the reported studies associate (self-) induced EEG brain responses with various mental tasks, similar to the ones used in this work (i.e. brainteasers, motor imagery). The performance of these tasks is not contingent on external cue presentation, although any practical application warrants some kind of cueing (e.g. instructions, questions, etc.). In contrast, (externally-) evoked EEG brain responses are contingent on external cue presentation. However, any practical application warrants some kind of user engagement (e.g. focused attention) and / or mental task performance (e.g. counting of the deviant stimuli).

In this work, we blurred the lines between the induced and evoked responses of the brain in the following two ways:

- In the first experiment, we employed (self-) induced EEG brain responses that are, at least partially, contingent on external cue presentation.
- In the scanning paradigm of the second experiment, in addition to the (self-) induced EEG brain responses, we employed (externally-) evoked EEG brain responses that are, at least partially, contingent on the mental task performance (i.e. mental subtraction).

In other words, in this work we focused on the similarities, and not on the differences, between induced and evoked responses of the brain.

Methods

PARTICIPANTS

All the experiments (see Figure 2.3, section EXPERIMENTAL PARADIGM) were approved by the local ethics committee (Medical University of Graz) and are in accordance with the ethical standards of the Declaration of Helsinki [188].

Healthy Eleven healthy participants (8 female; 23 to 40 year old, mean age 26) participated in this experiment. They were recruited through university public notice boards (i.e. newsgroup, forum). Participants gave informed consent prior to the beginning of the experiments and received monetary compensation afterward. Half of the participants had no prior experience with EEG experiments. During the measurements, the participants were seated in an electrically shielded room.

Ten healthy participants performed both sessions of the first experiment (the eleventh participant performed only the first measurement session). Six participants, all of which already performed the first experiment, were also available for the second experiment (the rest was not available). The second experiment was carried out on a separate day, between 1 and 2 weeks later.

Persons with MCS Two persons diagnosed with MCS took part in this study (one women, one man). The persons with MCS, not in intensive care and in an overall stable medical condition, were selected by the medical staff of the Albert Schweitzer Clinic (Graz, Austria) where all measurements were conducted. Exclusion criteria were gravidity, infections, or participation in other studies. Informed consent was obtained from the legal representatives of persons with MCS.

The persons with MCS were behaviourally assessed using the Coma Recovery Scale-Revised (CRS-r) within 24 h before or after each EEG measurement in order to keep track of their fluctuations in responsiveness. The CRS-r is composed of 23 items divided into 6 subscales dealing with auditory, visual, motor, oromotor, communication, and arousal functions [54]. The standardized scoring has been shown to produce "... reasonably stable scores over repeated assessments ..." [55] and is capable of discriminating persons in MCS from those with unresponsive wakefulness syndrom (UWS, [96]; vegetative state (VS) can also be used in addition to UWS).

The persons with MCS participated in the third experiment, where command following was evaluated with two sessions. The idea was that each person with MCS, if possible, would participate in two sessions on different days to compensate for possible fluctuations in responsiveness. For the two persons with MCS, the follow-up session was carried out between 1 and 2 weeks later.

Table 2.1 provides background and disease related data, as well as the highest estimated CRS-r subscores, of both persons with MCS.

Table 2.1: Overview about participants with MCS

	PA01	Age	Sex	PA02	Age	Sex
		78	F		31	M
Etiology	Trauma			Metabolic		
Auditory Function	Reproducible Movement to Command			Localization to Sound		
Visual Function	Fixation			Fixation		
Motor Function	Object manipulation			Localization to Noxious Stimulation		
Verbal Function	Vocalization/Oral Movement			Vocalization/Oral Movement		
Communication	Non-Functional: Intentional			None		
Arousal	Attention			Eye Opening w/o Stimulation		
Additional Diagnoses	MCS			MCS		

RECORDING

Healthy Persons The EEG was recorded with 29 active electrodes (g.tec, Guger Technologies, Graz, Austria) covering the frontal, central, and parietal scalp areas. In detail, the electrodes were placed at positions AF3, AFz, AF4, F5, F3, F1, Fz, F2, F4, F6, FC3, FC1, FCz, FC2, FC4, C5, C3, C1, Cz,

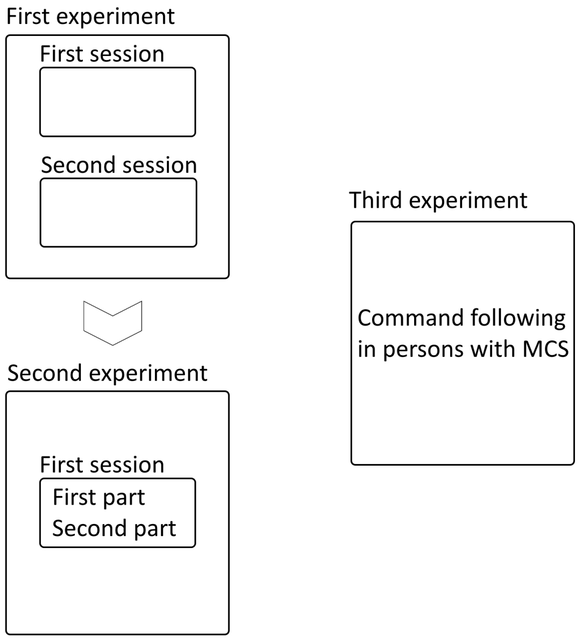

Figure 2.3: Shown here is an overview of the number and sessions of experiments.

C2, C4, C6, CP3, CP1, CPz, CP2, CP4, P5, P3, P1, Pz, P2, P4, P6, PO3, POz and PO4 according to the international 10/20 electrode system. The EEG electrodes were referenced to the left ear lobe with the ground electrode placed on the right ear lobe. The electrodes were integrated into a standard EEG cap (Easycap GmbH, Herrsching, Germany.

In addition to EEG, electrooculogram (EOG), electrocardiogram (ECG) and respiration were recorded. The EOG was recorded with three active electrodes, positioned above the nasion, and below the outer canthi of the eyes. The ECG was recorded from a single bipolar derivation. The negative lead was attached to the chest at the left (mid) clavicular line and the 2nd intercostal space, and the positive lead was attached to the chest at the left midaxilar line and the 6th intercostal space. The ground electrode was placed on the right hip. Self-adhesive Ag-AgCl electrodes were used for these recordings. The respiration was recorded with a CE-certified piezoelektric respiration sensor (PRO-TECH Respiratory Belt, Model: 1467).

The EEG amplifiers were set up with a band-pass filter between 0.5 and 100 Hz, and a notch filter at 50 Hz. The EEG and EOG were sampled with 512 Hz.

Persons with MCS Recording in persons with MCS was very similar to that in healthy, with main differences being use of a reduced channel setup, and no EOG recording. In detail, the electrodes were placed at positions AFz, F3, F1, Fz, F2, F4, FC3, FCz, FC4, C5, C3, C1, Cz, C2, C4, C6, CP3, CPz, CP4, P3, P1, Pz, P2, and P4 according to the international 10/20 electrode system.

In addition to EEG, electrocardiogram (ECG) and respiration were recorded. Again, the ECG was recorded from a single bipolar derivation, and the respiration was recorded with a CE-certified piezoelektric respiration sensor (PRO-TECH Respiratory Belt, Model: 1467).

The EEG amplifiers were set up with a band-pass filter between 0.5 and 100 Hz, and a notch filter at 50 Hz. The EEG was sampled with 512 Hz.

EXPERIMENTAL PARADIGM: Overview

The study consisted of three experiments. The first experiment was performed twice by 10 healthy participants, on two separate days. One additional participant showed up only for the initial measurement session, and was thus discarded from the further analysis. The second experiment was performed by six of the initial 10 healthy participants. The third experiment was performed by two persons with MCS.

Stimuli Spoken letters, digits, and words of the German language, generated by a text-to-speech program (Pediaphon, Germany), were presented sequentially through headphones. For evaluation of command following in persons with MCS, the stimuli were generated with a slower pronounciation speed setting, and were presented at an reduced rate. In detail, for command following in patients the stimuli were generated with "slow" speed setting compared to "normal" speed setting used for the healthy participants. In addition, the stimuli were presented at half the rate compared to the presentation rate used for the healthy participants, effectively reducing the number of presented stimuli to one half of the number presented to the healthy participants.

EXPERIMENTAL PARADIGM: First experiment The goal of the first experiment was to evaluate whether attending to someone else's verbal performance of brain-teaser tasks leads to similar findings as in self-performing the same tasks. For this purpose, the first experiment investigated two mental tasks across different conditions, defined as follows [47]:

- word generation (WORD): generate as many words as possible that begin with the presented letter.

- Mental subtraction (SUB): perform successive elementary subtractions by a presented fixed number.

For each mental task, three different conditions were investigated: active attend, perform, and control condition. In the active attend condition, exemplified in Figure 2.4 for the WORD (upper part) and the SUB (lower part) tasks, the participants actively attended to verbal performance of the indicated mental task. In the perform condition, the participants performed the indicated mental task from the verbal cue onset (t = 2 s) to the end of the trial, but this time without listening to verbal performance of the indicated mental tasks. The cues of the control condition were identical to the active attend condition, but the participants were instructed to ignore them and to mind wander. The mental tasks were indicated in random order, and the order of the conditions was pseudorandomized.

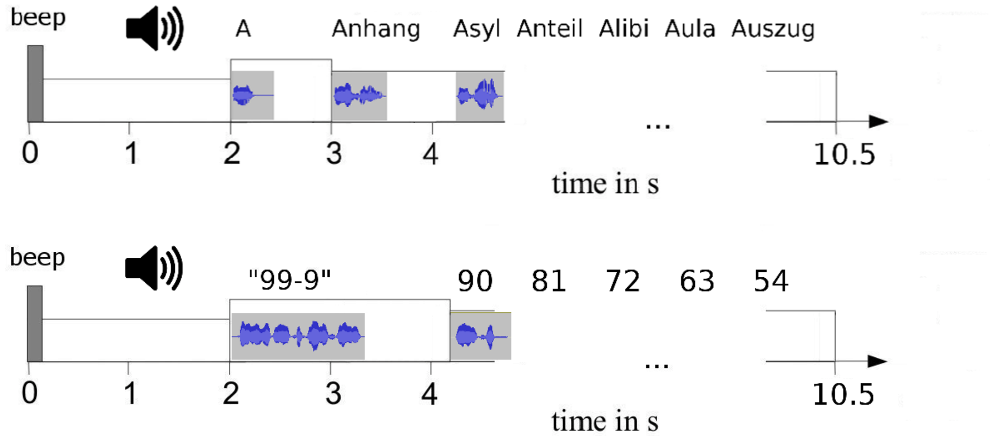

Figure 2.4: Experimental paradigm: first experiment. The two mental tasks - word generation and mental subtraction - were investigated across the following conditions: (i) active attend, listening to the verbal performance of the indicated mental task ; (ii) perform, performing the indicated mental task without verbal stimuli; and (iii) control, ignoring the verbal stimuli.

EXPERIMENTAL PARADIGM: Second experiment The second experiment consisted of two parts.

First part of the second experiment In the first part, two mental tasks were employed: (i) mental subtraction (SUB), and (ii) SPORT. The SUB task was as defined in the active attend condition of the first experiment. The SPORT task was imagined performance of one sport of participants' choice in the first person perspective (e.g. tennis, volleyball, running etc.). There was no perform condition in the second experiment. This part was split into four runs, separated by short breaks of 1-2 min length in order to avoid fatigue. The first two runs were for calibration, meaning the participants received no feedback. The second two were "online" runs, meaning the participants received feedback.

For the resting state the participants were instructed to sit relaxed and to avoid movements and excessive artifacts. They were neither instructed to fixate their eyes, nor to watch anything.

Within a run, each mental task was randomly indicated 16 times, resulting in a total of 32 calibration and 32 "online" trials for each task. The timing of a single trial was the same as in the first experiment (see Figure 2.4. The SPORT task was performed from the verbal cue onset ("Sport" @ t = 2s) to the end of the trial ("Pause" @ t = 10.5s), without any further cues.

In the "online" runs the participants received biased positive feedback at the end of a trial (i.e. "Sport / subtraction recognized" in case of correct classifier output, "Pause" otherwise).

Second part of the second experiment In the second part of the second experiment, the healthy participants communicated a yes / no answer to a series of verbal questions, performing only the SUB task. Towards this aim, a scanning protocol ([123]), see Figure 2.5, was adapted as follows:

- Following the presentation of each question, "yes" ("ja" in German) and "no" ("nein" in German) scan periods were presented three times.

- Each "yes" / "no" scan period was denoted by a spoken "yes begins"/"no begins" cue at the beginning, and "pause" at the end.

- During each scan period, verbal performance of the SUB task was presented. To communicate their intent (e.g. a yes response), the participants actively attended to the verbal performance during the desired scan period, and ignored it otherwise. For example, to communicate a no response, the participants actively attended the verbal presentation following a spoken "no begins" cue, and ignored the verbal presentation following a spoken "yes begins" cue.

Throughout the experiment, breaks of random length were inserted to prevent rhythmic cueing.

The questions, generated using a text-to-speech synthesizer, were delivered through headphones in pseudorandom order. A total of 20 different questions was split during 4 runs, each comprised of 5 questions. Each question had only one meaningful response, with a balanced number of yes/no responses, thus allowing the experimenter to know the response the participants intended to communicate. Nevertheless, before the scanning protocol was evaluated, all of the questions were presented to the participants once. Also, their responses to the questions were noted. Two exemplary questions are shown in Figure 2.5.

Feedback was based on majority vote from the classifier output for the three yes / no scan periods. Following the presentation of yes / no scanning periods, four options were possible: (i) "yes" detection; (ii) "no" detection; (iii) both "yes" and "no" detection; and (iv) no detection. The corresponding auditory feedbacks, presented following the three yes/no scan periods, were: (i) "Yes selected"; (ii) "No selected"; (iii) and (iv) "Unclear response" (in German language).

Additionally, the verbal performance of brain-teaser tasks included a semantic oddball paradigm. To that end, during the "yes" scan periods an additional "yes" word was randomly interleaved with the verbal performance of the mental subtraction, and during the "no" scan periods an additional "no" word was randomly interleaved with the verbal performance of the mental subtraction. When actively attending to the verbal stimuli, the "yes" and "no" words were perceived as the deviant cue during the corresponding scan period.

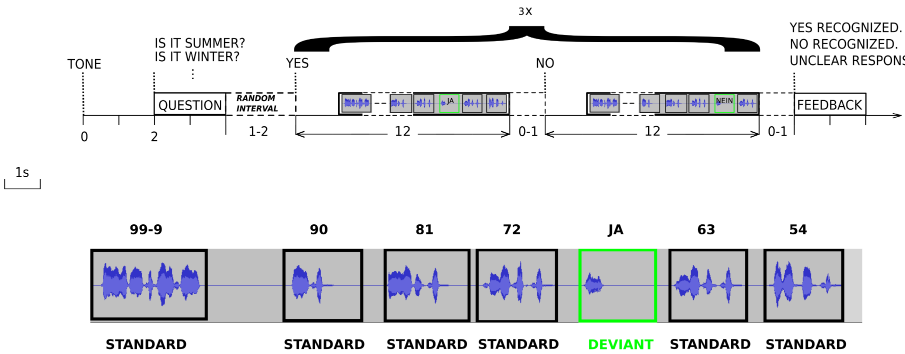

Figure 2.5: Experimental paradigm: second experiment. UPPER PANEL: the scanning protocol employed in the second part. Following the presentation of each question, "yes" and "no" scan periods were presented three times. During each scan period, verbal performance of the SUB task was presented. To communicate their intent (e.g. a yes response), the participants actively attended to the verbal performance during the desired scan period, and ignored it otherwise. LOWER PANEL: the verbal performance of brain-teaser tasks included a semantic oddball paradigm. For this purpose, during the "yes" scan periods an additional "yes" word was randomly interleaved with the verbal performance of the mental subtraction, and during the "no" scan periods an additional "no" word was randomly interleaved with the verbal performance of the mental subtraction. When actively attending to the verbal stimuli, the "yes" and "no" words were perceived as the deviant cue during the corresponding scan period.

EXPERIMENTAL PARADIGM: Third experiment - command following in persons with MCS Within one experimental session, up to two different tasks (i.e. sport and mental subtraction) were performed in a block design, meaning that in each run only one task was performed. The SUB task was performed either in the active attend or the control condition. The SPORT task was as defined in the second experiment in healthy participants. Each task was performed during three consecutive runs, with each run having 16 cue-based trials (auditory cue) of 13.5 s length, yielding 48 trials / task. At the beginning of a trial a beep tone was given. After 2 s, an auditory cue, generated by a text-to-speech synthesizer, was delivered via in-ear headphones. The cue was either a verbal instruction to perform the SPORT task (i.e. "sport") lasting for 1 s, or the onset of the active attend condition (i.e. verbal performance of the mental subtraction). Between the trials a random pause (also auditorily indicated) of 4-6 s length was given. Detailed verbal instructions were given to the participant by the experimenter before the measurement started. The purpose of these instructions, repeated before each run, was to inform the persons with MCS about the tasks he/she has to perform. The order of the runs was pseudo randomized across the measurement sessions. Each measurement session was conducted on a separate day for both participants.

USER EVALUATION

Healthy participants filled out the questionnaires for the first and the second session of the first experiment. No questionnaires were filled out for the second experiment, or for the command following in patients. After the measurements, the participants rated the tasks on a 5 point scale for the following aspects (questions adapted from [49]): the task ease (1 = "very exhausting and full concentration needed" and 5 = "very relaxing and possible to perform also during major distractions"), and the enjoyment (1 = "no fun at all and very frustrating" and 5 = "a lot of fun and not frustrating at all"). Additionally, users rated the verbal stimuli in the active attend condition (1 = "extremely irritating and not helpful" and 5 = "extremely motivating and helpful").

DATA ANALYSIS

First experiment and command following in persons with MCS EEG analysis was performed separately for the different mental tasks using MATLAB (MathWorks, USA) and EEGLAB. The data were high-pass filtered (third-order butterworth filter) with cutoff frequency at 1 Hz, and segmented into consecutive time segments of 0.5 s. Bad channels and prominent artifacts (i.e. swallowing, electrode cable movements, etc.) were identified by visual inspection and removed (0.5 s long time segments before ICA; whole trials containing the artifacts after the ICA). Following these steps, binary Infomax independent component analysis (ICA) was used to separate EEG and EOG signals into independent components. Independent components (ICs) representing eye movements, and eye blinks were identified by visual inspection using methods described in [109] and removed. The remaining components were multiplied by the mixing matrix produced by the ICA algorithm to reconstruct cleaned EEG.

The cleaned EEG was band-pass filtered (third-order Butterworth filter) between 8 and 30 Hz. Common spatial patterns (CSP, [160] method was used to compute most discriminative features for classification relative to a reference period (1s before the verbal cue onset). Discriminative feature vectors were obtained for 1 s EEG segments extracted from start to the end of the trial. Classification was performed by means of shrinkage linear discriminant analysis (sLDA, [21]) classifier. The accuracy was estimated using a 10-times

10-fold cross-validation for each 1 s window, relative to the reference period, from start to the end of a trial.

For percentage of relative power decrease (ERD) and relative power increase (ERS) analysis, a time-frequency map for frequency bands between 4 and 40 Hz (35 overlapping bands using a band width of 2 Hz) was calculated [59] for common-average-referenced (CAR) channels. Logarithmic band power features, calculated by band-pass filtering, squaring, and subsequently averaging over the trials, were used to assess changes in the frequency domain.

From the ECG, the QRS complexes were automatically detected based on an algorithm using a filter bank to decompose the ECG signal into various subbands [3]. Afterwards, the instantaneous heart rate (HR, in bpm) was calculated, linearly interpolated and resampled at 10 Hz. Missing heart beats, or triggering to another event, such as an extrasystole, may have large effects on the signal curve and the further processing steps, respectively [16]. Therefore, the detection process was visually inspected by an expert to avoid artefacts [13].

Statistical methods In the first experiment we analyzed classification performance across participants, tasks, and conditions with repeated measures analysis of variance (ANOVA). The analysis included a routine application of Mauchly's Test of Sphericity, and if needed a Greenhouse-Geisser correction. The dependent variable was classification accuracy, and the factors were task (2 levels) and condition (3 levels). Further analysis was done with Bonferroni corrected paired t-tests with the significance level contingent on $p < 0.01$.

Also, to determine the statistical significance of the ERD/S values, a t-percentile bootstrap algorithm with the significance level contingent on $p = 0.05$ was applied.

In the second experiment a Wilcoxon rank sum test was used to isolate differences between actively attending to and ignoring the deviant stimuli in the semantic oddball paradigm (see Figure 2.5), with the significance level contingent on $p < 0.01$.

Second experiment

Classifier setup Different classifiers were setup during the first and the second part of the second experiment for the six healthy participants. In the first part, the "SPORT vs. SUB" classifier was setup on the initial two runs, and evaluated online during the third and the fourth run. In the second part, the "SUB vs. rest" classifier was setup on the SUB data from the first part, and evaluated throughout the second part. In both cases classification was performed by means of sLDA classifier, setup using a 10-times 10-fold cross-validation for 1 s long windows. For each online trial in the first part, and each scan period in the second part, the classifier output was the class predicted for more than 50 % of the duration of the corresponding imagery period [35].

ERP analysis For event-related potential (ERP) analysis, performed of the six healthy participants of the second part, we defined a single epoch as 1000 ms following onset of a spoken letter, baseline corrected for all onsets to preceding 250 ms. The epochs were band-pass filtered (third-order Butterworth filter) between 1 and 12 Hz.

Artifact detection in online experiments The artifact detection was performed in six healthy participants of online runs in the second experiment (i.e. the third and the fourth run of the first part, and throughout the second part). Towards this aim, muscle and movement artifacts, as well as other transient non-stationarities in the ongoing EEG signals, were detected by inverse filtering [169]. Autoregressive (AR) parameters of the inverse filter were estimated from a 1-2 min segment of resting-state EEG, recorded at the beginning of each session. The detection threshold was defined as five times Root-Mean-Square from the resting-state EEG. Time periods in which the detection threshold was exceeded were discarded from the online feedback calculation.

Results

Experiment 1 The offline classification accuracies for the three conditions (i.e. active attend, perform, and control), the two tasks (i.e. WORD and SUB), and both sessions of the first experiment are given in Table 2.2 and in Figure 2.6. The results of the ANOVA for classification accuracy revealed a significant effect for task ($p < 0.01$, $F_{firstsession}(1,9) = 14.96$, $F_{secondsession}(1,9) = 17.82$) and condition ($p < 0.01$, $F_{firstsession}(2,18) = 38.90$, $F_{secondsession}(2,18) = 42.88$) in both of the sessions, and an interaction between task and condition ($p < 0.01$, $F_{secondsession}(2,18) = 15.01$) in the second session.

Figure 2.7 summarizes the results of statistical tests (Bonferroni corrected t-tests) performed to compare sample means (i) within sessions and between conditions, and (ii) between sessions and within conditions (Figure 2.7 upper panel). For the SUB task, the means for the perform and active attend condition of the first session were the same, as no significant differences were found between the corresponding means (Figure 2.7 upper panel; significance contingent on $p < 0.01$). For the WORD task, the means for the active attend and control condition of the first session were the same, as no significant differences were found between the corresponding means. Also, the means for the perform and active attend condition of the second session were the same, as no significant differences were found between the corresponding means. Comparison of means between sessions and within conditions revealed no significant differences for the WORD and SUB task, respectively. Finally, comparing the means between the WORD and SUB task within sessions and within conditions revealed significant differences for the perform condition in both sessions, but not for the active attend and the control conditions (Figure 2.7 lower panel).

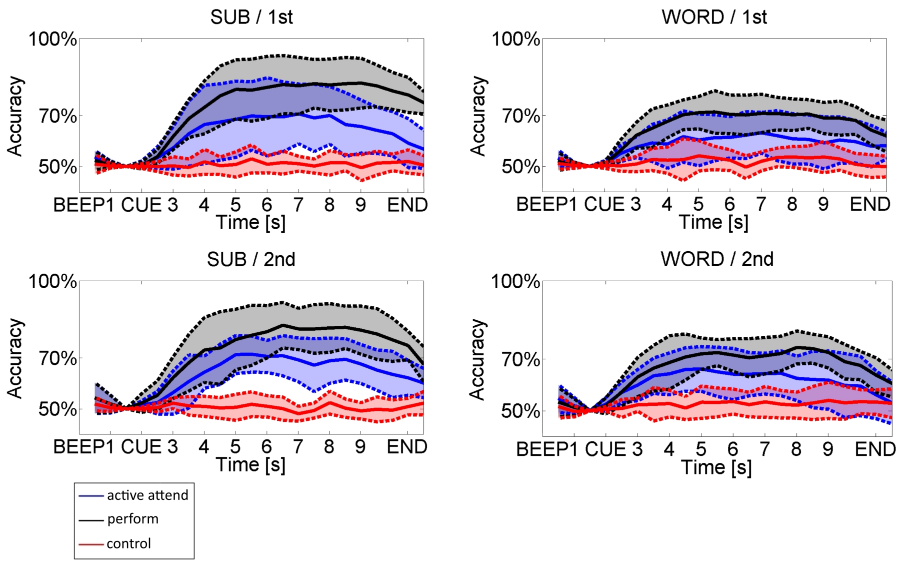

Figure 2.6: Shown here is the offline classification accuracy, estimated using a 10-times-10 cross validation, and averaged over all participants. The accuracies for the SUB task are shown in the left, and the accuracies for the WORD task in the right panel. Different conditions (i.e. active attend, perform, and control) are shown for the first (upper panel) and the second (upper panel) session.

Experiment 2 The results for the second experiment are given in Table 2.3 for the first part (SPORT vs. SUB), and Tables 2.4 and 2.5 for the second part (yes / no). The classification accuracy for the SPORT vs. SUB discrimination ranged from 48% to 70%, with mean of 58 ± 10%. The response accuracy for the SUB scanning ranged from 25% to 100% correct answers, 60% to 0% unclear answers, and 30% to 0% wrong answers. In addition, several participants demonstrated significant (p=0.01) modulation of event-related potential components related to novelty (LPC, late positive component [190]), and semantic (N400 [95]; P600 [60]) processing (Figure 2.9 middle panel), associated with the deviant (i.e. "yes" /"no") stimuli of the overlayed semantic oddball paradigm. Furthermore, actively attending to the verbal stimuli during the desired scan period resulted in significant (p=0.01) modulation of the negative (between 200ms and 250ms post cue onset) and positive (between 350ms and 450ms post cue onset) components, associated with all the verbal stimuli (i.e. standard and deviant), compared to ignoring the verbal stimuli (Figure 2.9 lower panel).

Experiment 3 The EEG results for the offline detection of different tasks for the command following paradigm in persons with MCS consist of (i) discrimination accuracy between SPORT / SUB task, and the reference (1s before the cue onset), and (ii) time-frequency analysis. Regarding (i), in participant PA01 only the SPORT task of the first session resulted in significant (p=0.05) accuracy, whereas all other cases resulted in accuracies that were not signif-

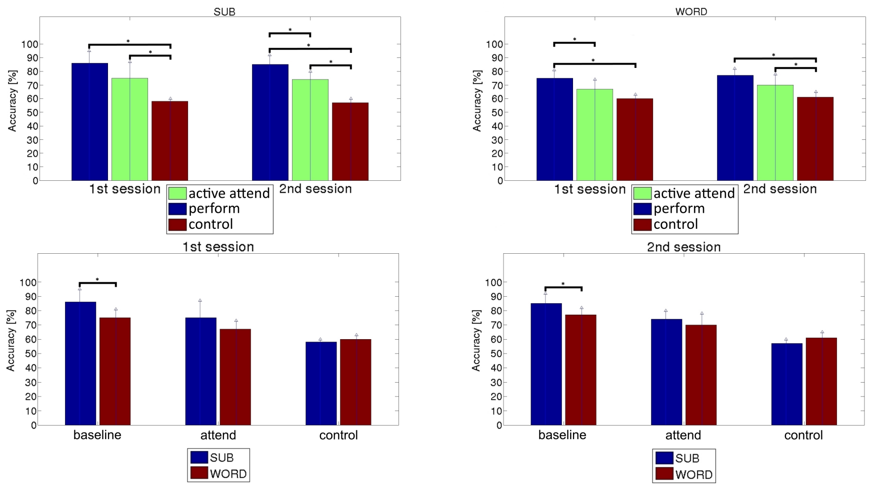

Figure 2.7: Results of statistical tests (Bonferroni corrected t-tests) performed to compare means across various conditions, sessions, and tasks. Significant ($p = 0.01$) differences are marked with an asterisk. UPPER PANEL: No significant differences were found between means for the perform and active attend condition of the first session for the SUB task, and of the second session for the WORD task. In contrast, significant differences were found between means for the active attend and the control condition in at least one of the two sessions for both the SUB and the WORD task. LOWER PANEL: Shown here is the comparison of the means between the WORD and SUB task within sessions and within conditions. Significant differences were found for the perform condition in both sessions. In contrast, no significant differences were found for the active attend and the control conditions.

Table 2.2: Classification accuracy: first experiment. Classification was performed by means of sLDA classifier. The accuracy (in %) was estimated using a 10-times 10-fold cross-validation for each 1 s window, relative to the reference period, from start to the end of a trial. The highest mean accuracy is reported. A . . . Active attend, P . . . Perform, C . . . Control, $\overline{x}$ . . . sample mean, s . . . sample standard deviation

	First session						Second session					
	SUB			WORD			SUB			WORD		
	A	P	C	A	P	C	A	P	C	A	P	C
S1	65	67	61	67	75	60	77	79	57	65	73	57
S2	82	93	57	68	72	67	77	91	60	76	78	67
S3	74	75	61	66	64	55	78	75	55	81	71	58
S4	89	89	58	86	84	61	87	85	58	86	82	59
S5	85	83	56	62	79	58	66	82	56	63	75	57
S6	56	93	60	65	72	58	72	95	52	64	80	66
S7	78	87	56	67	70	61	79	88	58	66	77	58
S8	91	94	55	63	81	61	73	78	60	69	69	64
S9	61	96	60	63	82	61	69	94	61	64	86	59
S10	69	79	56	67	75	55	67	82	57	64	76	59
$\overline{x}$	75.1	85.6	57.9	67.3	75.5	59.7	74.4	84.9	57.5	69.8	76.7	60.6
s	12	9.5	2.3	6.9	6.4	3.5	6.4	7.1	2.6	8.2	5.2	3.7

icant. In participant PA02, only the SPORT task of the first session could be evaluated. Due to a large number of strong artifacts, caused by, e.g., bad coughs and associated cramped movements, not enough EEG data was available for analysis. Time-frequency analysis of the SPORT tasks in the participant PA01 revealed task-related EEG changes over neurophysiologically plausible cortical areas (i.e. central, fronto-central, frontal; Figure 2.8). However, the classification results did not exceed upper confidence limits of a chance result ($p = 0.05$). Time-frequency analysis of the SUB task in the participant PA01 did not reveal any significant EEG changes (significance contingent on $p < 0.05$).

Discussion

In this work we tested two hypotheses: first, that attending to someone else's verbal performance of brain-teaser tasks leads to similar results as in self-performing the same tasks; and second, that selective attention to verbal stimuli can be used to modulate both induced and evoked changes in EEG.

We tested the first hypothesis in the first experiment of this work with mental subtraction and word generation tasks. Notably, the means between

Table 2.3: Online classification accuracy: first part of the second experiment. Here, the "SPORT vs. SUB" classifier was setup on the initial two runs, and evaluated online during the third and the fourth run.

Subj	S6	S4	S7	S3	S10	S1	$\overline{x} \pm s$
Acc (%)	70	69	64	51	48	48	58 ± 10

Table 2.4: Response accuracy: second part of the second experiment. Here, the "SUB vs. rest" classifier was setup on the SUB data from the first part of the second experiment, and evaluated online throughout the second part. T ... true, U ... unclear, F ... false

Subj	S3	S4	S10	S1	S7	S6
T (%)	100	75	50	40	25	25
U (%)	0	25	35	45	60	45
F (%)	0	0	15	15	15	30

the WORD and SUB task differed for the perform condition in both sessions, but not for the active attend and the control conditions. Including the session as a factor in the ANOVA revealed, in addition to aforementioned findings, a significant effect for the session. This finding is consistent with the literature, albeit this effect, while present in the initial sessions, is known to diminish as the number of sessions increases [48].

Event-related (de-) synchronization during mental subtraction, word generation, and other mental tasks was thoroughly investigated in the BCI literature [47, 49]. In Friedrich et al. [47] these two tasks showed significantly more ERD in the lower beta range (13-20 Hz) than a motor task (imagery of the right hand). Also, more ERS was found for the mental subtraction both in the lower and in the upper beta band (20-30 Hz) compared to the motor task in central regions. Significant differences were also found between the brain teasers, with mental subtraction showing more ERS than word generation in parietal regions. Otherwise, the brain teasers showed similar ERD/S patterns with a foremost left hemispheric activation, indicative of an linguistic strategy in task performance (e.g. during mental calculation). These brain teasers demonstrated some of the highest stability over sessions in both alpha bands (7-10, 10-13 Hz) and in at least one beta band (13-20, 20-30 Hz) [49].

The ERD/S analysis, exemplified in the upper panel of Figure 2.9, revealed patterns that are in concordance with the aforementioned findings by Friedrich et al. [47, 49]. The participant-specific ERD/S patterns within a task exhibited similar spatial and frequency patterns in the perform and active attend conditions, albeit the patterns for the perform condition were more pronounced compared to the patterns for the active attend condition.

Table 2.5: Event-related potential analysis: second part of the second experiment. Only significant (Wilcoxon rank sum test, p = 0.01) components are reported. LPC ... late positive component; ✓... significant difference

Subj	S3	S4	S10	S1	S7	S6
LPC		✓		✓		
N400		✓				✓
P600	✓		✓			✓

Furthermore, these patterns translated to significant (p = 0.01) classification accuracy for both the perform and the active attend condition. Importantly, for all cases the control condition neither yielded any significant (p = 0.05) ERD/S patterns, nor classification accuracy.

Healthy participants also filled out the questionnaires for the first and the second session of the first experiment. The rationale for collecting this data is to explain for possible differences between our findings, and results from similar studies. As our findings are consistent with the literature, the results of user evaluation are reported in Appendix A as an additional information for the interested reader.

In the second experiment we exploited these similarities to setup an online BCI, and compared it in healthy participants to the current "state-of-the-art" motor imagery (MI). The classification accuracies for the second experiment showed a great inter-participant variability. In the first part, the two best performing participants (S6, S4) achieved significant (p = 0.01) accuracies that could support communication. For these participants, one mental task could be used to communicate an affirmative response, whereas the other mental task could be used to communicate a negative response. For the two participants that exhibited strong bias in favour of the motor task (S7) or the SUB task (S3), a single mental task employed in a scanning paradigm may yield better results. In the two participants that achieved random accuracies only, as well as in other participants, further training sessions might lead to an improved performance.

The response accuracies for the best performing participants of the scanning paradigm are comparable to those reported in [123], indicating that selective attention to verbal performance of mental subtraction is a viable alternative to the motor imagery. Indeed, whereas participant S3 achieved random results only in the first part of the second experiment involving motor imagery (i.e. SPORT vs. SUB), the same participant was able to achieve a 100% accuracy in the second part (SUB scanning).

To test the second hypothesis we modified the verbal performance of the SUB tasks to include a semantic oddball paradigm, and analysed whether, in addition to the aforementioned ERD/S patterns, this task can also modulate ERPs. We found that several participants demonstrated modulation of event-related potential components related to processing of novelty (LPC [190]),

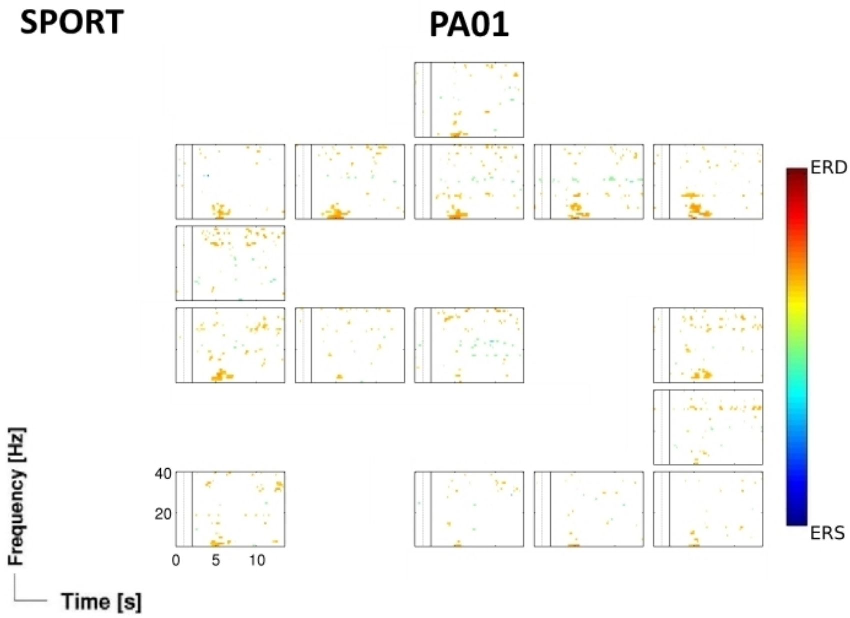

Figure 2.8: Percentage of power decrease (ERD, orange) and power increase (ERS, blue) relative to a reference interval (one second pre cue) for the SPORT task in participant PA01, averaged over two sessions. Only significant (p = 0.05, t-percentile bootstrap algorithm) power changes are displayed for common average referenced channels.

and semantic (N400 [95]; P600 [60]), as shown in the middle panel of Figure 2.9. In cases where induced changes alone do not yield significant results, the evoked changes can provide evidence of command following indicative of need for further training (e.g. S10) or a different approach (e.g. S6), meaning it has potential to improve the reliability of results.

Few studies investigated hybrid BCIs in end users, some of them relying on eye-gaze [141] and muscular control [142], and other combining a BCI with an added input from a sensor [163, 89]. These studies employed two tasks in either sequential or simultaneous manner, requiring the users to split their attention between two different tasks. In this work we demonstrated that a single auditory selective attention task can modulate both induced and evoked changes in EEG. Furthermore, the employed experimental paradigm is strongly rooted in the AT applications, and can therefore facilitate transition from a laboratory to end-users.

For the selective attention to spoken words (i.e. yes/no interspersed with digits 1 to 9), not unlike employed in this work, a robust effect on the brain responses has already been observed with fMRI in healthy individuals [130]. Furthermore, in the same work individual performance was improved compared with a motor imagery task, suggesting its suitability for BCI applications. In a follow up fMRI study performed in three persons with severe brain injury (two persons with MCS, one person diagnosed as being in UWS; convenience sample), command following according to instructions (i.e. count the

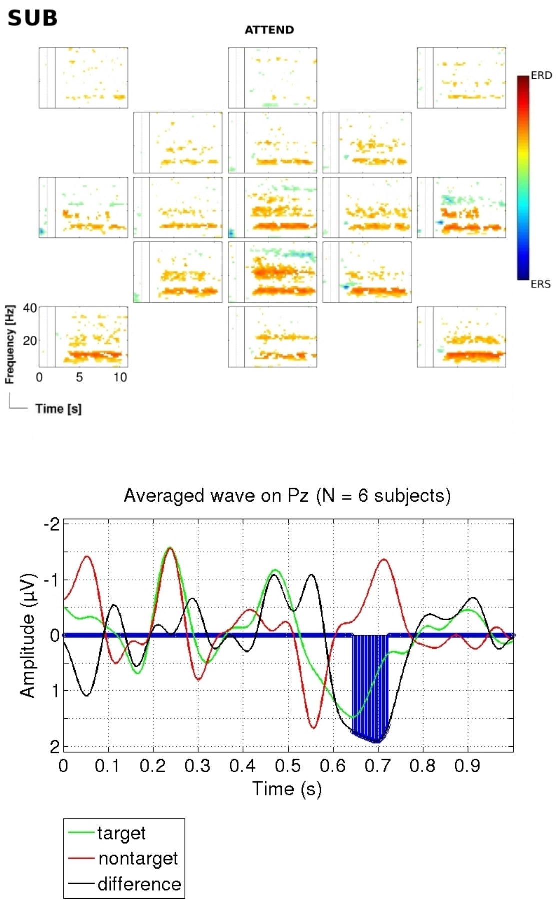

Figure 2.9: UPPER PANEL: Percentage of power decrease (ERD, orange) and power increase (ERS, blue) relative to a reference interval (one second pre cue) for active attend condition, and the SUB task in participant S4. Only significant ($p = 0.05$, t-percentile bootstrap algorithm) power changes are displayed for orthogonal Laplacian [64] derivations. MIDDLE PANEL: grand averaged ERPs at electrode Pz for six participants and for the deviant "yes" / "no" cues of the second part of the second experiment. Equal number of target and nontarget epochs was averaged. Significant ($p = 0.01$) changes are indicated with vertical bars. LOWER PANEL: grand averaged ERPs at electrode Pz for six participants and for all verbal cues of the second part of the second experiment. Equal number of target and nontarget epochs was averaged.

"yes" / "no" target word or relax) was demonstrated in all three persons [131].

Before our measurements in persons with MCS, the medical staff of the Albert Schweitzer Clinic provided valuable input that guided the modifications to the paradigms employed in healthy participants. As a result, the subtraction task was chosen over the word generation task, the stimuli were modified (i.e. slower pronunciation speed, reduced rate of presentation), and the block design was employed. As a side effect of the reduced rate of presentation, the semantic oddball paradigm was dropped in favour of a more simple paradigm with fewer stimuli.

The accuracies achieved in healthy participants are lower than many results reported in the BCI literature. Also, meaningful binary communication was achieved in only some of the participants. The inclusion of an oddball paradigm, while meaningful for the detection of command following, could not improve the online accuracy due to a slow rate of presentation. However, every aspect of our work was driven by needs and capabilities of the end-users, with little or no regard to how it would impact the results in healthy participants.

One limitation of this study is that it leaves open the question on whether and to what extent the EEG responses from attending to someone else's verbal performance of brain-teaser tasks are caused by the task-independent focused attention. To answer this question, a whole new experimental design, employing additional control conditions, would be needed. Another limitation of this study is its limited evaluation in end-users. Indeed, only one out of two evaluations in end-users with MCS resulted in usable data, with time-frequency analysis revealing no significant ($p < 0.05$) EEG changes for the brain teaser (i.e. SUB) task.

Another limitation of this study is that the temporal electrodes were not examined, mainly due to experimenters concerns regarding their contamination with artifacts. However, as there are many studies linking those regions with auditory-verbal stimuli processing, further experiments should analyze the temporal regions.

Concluding, our main findings in healthy participants are:

- attending to someone else's verbal performance of brain-teaser tasks leads to similar results as in self-performing the same tasks.
- these similarities can be exploited to setup an online BCI and used for yes / no communication in an auditory scanning paradigm.
- a single task, namely selective attention to verbal stimuli, can modulate both induced and evoked changes in EEG.

Our findings in persons with MCS are limited, as only two persons with MCS were evaluated. Significant accuracy was found for the SPORT task of the first session in one person with MCS, whereas all other cases resulted in accuracies that were not significant. While our current work did not achieve the desired results in the end-users, it outlined a novel approach to detection of command following in end-users with MCS, and its translation to binary communication.

Here, further measurements, also including other end-users (e.g. persons with locked-in-syndrome), might provide further insight in EEG changes modulated by selective attention to verbal stimuli.

Appendix A

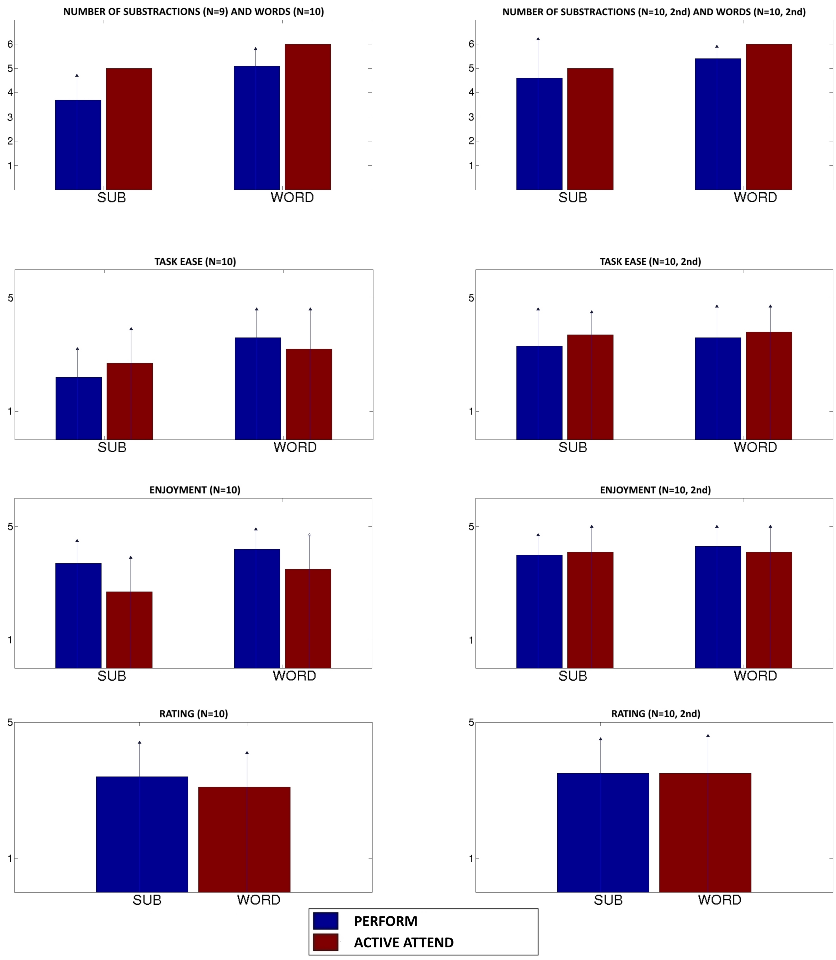

Figure 2.10: Displayed here are the results of user evaluation for the first (left panel) and the second (right panel) session. The users rated the tasks on a 5 point scale for the following aspects: the task ease, the enjoyment, and rating of the verbal stimuli in the active attend condition. Additionally, users reported the number of performed subtractions and generated words in the perform condition. Higher numbers are better.

2.3 Secondary Publications

[78] Horki, P., T. Solis-Escalante, C. Neuper and G. Müller-Putz: *Hybrid motor imagery and steady-state visual evoked potential based BCI for artificial arm control*. *Integrating Brain-Computer Interfaces with Conventional Assistive Technology*, 46–47, 2010

[73] Horki, P., C. Neuper and G. Müller-Putz: *Identifying "resonance" frequencies for SSVEP-BCI*. *Proceedings of the TOBI Workshop II*, 103–104, 2010

[77] Horki, P., C. Pokorny, C. Neuper and G. Müller-Putz: *Exploring the resonant properties of alpha-band in covert-spatial visual attention*. *Proceedings of the 5th International Brain-Computer Interface Workshop and Training Course 2011*, 148–151, 2011

[75] Horki, P., C. Pokorny, D. Klobassa and G. Müller-Putz: *Selection methods for communication with single-switch BCI*. *Proceedings of the 1st international DECODER workshop*, 29–32, 2012

[76] Horki, P., C. Pokorny, D. Klobassa, G. Pichler and G. Müller-Putz: *Detection of mental imagery and attempted movement in patients with disorders of consciousness using EEG*. *BBCI Workshop 2012 on Advances in Neurotechnology*, Berlin, 2012

[71] Horki, P. and G. Müller-Putz: *A novel approach to auditory EEG-based spelling*. *Proceedings of the Fifth International Brain-Computer Interface Meeting*, 316–317, 2013

[69] Horki, P., D. Klobassa, C. Pokorny and G. Müller-Putz: *Auditorily elicited neural oscillations associated with motor execution, motor imagery and non-motor mental tasks*. *Proceedings BMT(Biomedizinische Technik) 2013*, 2013

[72] Horki, P. and G. Müller-Putz: *Eye-blink related changes in EEG during an auditory working-memory task performance*. *Proceedings of the 6th Interntational BCI Conference*, 077/1 – 077/4, Graz, 2014

Chapter 3

Discussion

3.1 Overview

The research goal of this thesis was to evaluate whether and to what extent induced and evoked changes in EEG can be combined for BCI applications. A general prerequisite for combining these two types of BCIs is that each one of them serves a meaningful purpose within the same system. Therefore, central to fulfilment of the research goal was to increase the level of integration of these BCIs. As a results, new methodological approaches were developed.

The applied goal of this research was to evaluate state of the art in the BCI technology in end-users with disorders of consciousness and to address gaps in knowledge. To that end, existing BCIs were adapted to and new BCI research was driven by the needs and capabilities of the end-users.

This thesis' main contributions to the existing body of knowledge are:

1. strategies for combining induced and evoked changes in EEG for control and communication

2. enhanced auditory scanning paradigm for binary communication

3. strategies for using EEG responses for spelling through listener-assisted scanning

4. evaluation of mental imagery and attempted movements in end-users with disorders of consciousness

5. experimental proof that a single auditory selective attention task can modulate both induced and evoked changes in EEG

3.2 Brain-computer interfaces based on induced and evoked changes in EEG

3.2.1 Combined MI and SSVEP

In pursuit of combining induced and evoked changes in EEG for BCI applications, the first step was to evaluate whether and to what extent the existing BCI systems can be made to work together. To that end, [79] investigated whether two different BCIs, one based on MI and the other one on SSVEP, can be used to extend the number of degrees-of-freedom in a control scenario. In other words, this initial work investigated whether two different BCIs can, in principle, be used in parallel with a common goal.

Indeed, the combination of MI and SSVEP based BCIs in **Horki et al. (2011)** [79] allowed for a more finer control compared to previous work [74]. Nonetheless, several improvement potentials were identified: first, making the BCI more suitable for the end-users, e.g. by making the SSVEP based BCI less dependent on the eye-gaze control; second, making the whole system more cohesive, as the BCIs were used separately and for different functions.

The following work aimed at overcoming two major shortcomings of the overt SSVEP based BCI that hindered its application in end-users: first, its fixed placement of visual stimuli, which does not account for the uncontrolled head movements of the end-users; and second, its eye-gaze dependency, limiting its use in end-users having difficulties with eye-gaze control. The first shortcoming can be addressed through a wearable stimulation unit, similar to that reported in overt SSVEP experiments [103]; the second shortcoming can be addressed through a covert spatial SSVEP based BCI [85, 84, 7].

The problem with covert spatial SSVEP based BCIs is that the amplitude of the SSVEP responses diminishes as the targets move outside the foveal vision. One way of improving performance in covert spatial attention experiments is to individually select EEG channel locations [85]. An open question is whether an additional advantage, i.e. an improvement in performance, can be gained by also selecting the stimulation frequencies.

In **Horki et al. (2011)** [77] it was investigated whether individual stimulation frequencies in the alpha-band may improve performance compared to fixed stimulation frequencies outside the alpha-band. To that end, offline classification was performed for both modalities in a 2-class covert spatial attention experiment with a wearable visual stimulation unit. No significant difference could be found between classification accuracies obtained with standard and individual stimulation frequencies, with four out of six participants yielding significant (greater than 65%) accuracy in both modalities.

Why were these accuracies lower than those reported in the early covert spatial attention SSVEP based BCIs [85, 84]? One explanation for this discrepancy of results are the following methodological flaws in early works: first, use of overlapping time windows between training and test sets; second, a cross-validation procedure consisting only of training and test sets, but not of holdout sets; and third, experimental design where only consecutive runs are analysed, resulting in potential overfitting of the classifier to slow time-varying changes in EEG unrelated to the experimental task.

The pursue of a covert spatial SSVEP based BCI however was not in wane, as it provided valuable insights for further development of BCIs for the end-users. The first insight was that designing a BCI independent of eye-gaze leads to EEG responses severely diminished compared to overt BCIs. These diminished responses, while statistically significant and clearly distinguishable in grand averages, are difficult to detect on a single-trial basis and cannot be used to establish functional communication. Thus, with almost all of the advantages of visual BCIs becoming irrelevant, one can forfeit the visual stimuli altogether, and opt for an auditory based BCI. The second insight was, that in order to reliably discriminate between the willfully modulated and pure sensory EEG responses to external stimuli, these stimuli need to elicit responses reflecting cognitive processing, meaning the stimuli themselves need to be more complex. An added advantage is that more complex cues and stimuli may be more intuitive and easier to communicate to the end-users, thus facilitating the use of BCI.

3.2.2 Auditory scanning

Given the general idea of a single-switch BCI (ssBCI), namely "... to reliably detect one certain, individually trained brain pattern of the user that can be used to control all kinds of applications ..." [123], one would expect its' implementation to be trivial. However, as it is often the case when making such ideas a reality, the god is in the detail, meaning the details require careful planning and many small ideas before the general idea can be implemented.

The auditory scanning paradigm reported in **Müller-Putz et al. (2013)** [123] is an instance of a more general solution, addressing the following challenges in bringing the BCI technology to the end-users:

1. the end-users are a heterogeneous group differing in, amongst other things, their needs (e.g. visual, tactile, and / or auditory presentation) and capabilities (e.g. delayed responses).

2. there are many different kind of BCIs, differing in, amongst other things, experimental strategy (e.g. self-induced or externally evoked responses) and modes of operation (e.g. synchronous or asynchronous control).

3. the AT applications differ with respect to selection method employed, number of selection items, etc..

These challenges were addressed as follows:

1. to address differing end-users, a scanning paradigm was designed that, in principle, can be operated the same way in visual, auditory, and tactile modality.

2. to address differing BCIs, and to allow for delayed responses in some end-users, both time-locked and non time-locked control signals are supported through a semi-synchronous design. This design has been successfully evaluated with both self-induced and externally evoked EEG responses, as well as various combinations thereof [123, 70, 68].

3. the designed paradigm supports different selection methods, and is scalable with respect to the number of selection items, allowing for binary [123], and multiclass selections [70]. Furthermore, the speed can be traded off for accuracy by adjusting the number of scanning repetitions.

To summarize, this work not only allowed for the use of an ssBCI for binary communication in auditory scanning mode [123], but also enabled future use of BCI in various end-users and various AT applications.

3.2.3 Spelling through listener-assisted scanning

Setting the stage for further fusion of BCIs based on induced and evoked changes in EEG, [70] addressed the issue that these BCIs differed substantially in their experimental paradigms. These differences contributed to the difficulty of finding the most suited control signal for the task at hand. Furthermore, offering multiple choices of BCI control signals is a necessity due to the so called BCI "illiteracy", meaning that in some end-users a certain type of BCI does not work, and the only solution is to try out an alternative type of BCI.

By making different types of BCIs interchangeable, the most suited control signal can be used, and the BCI "illiteracy" can be mitigated. However, this needs to be evaluated in a standard AT application, so that it can be transferred to real-world scenarios. Arguably, the most well known AT application in end-users with severe motor and visual impairments but preserved cognitive skills was spelling through listener-assisted scanning in **Bauby (1997)** [10].

In **Horki et al. (2015)** [70], two BCIs were evaluated for spelling through listener assisted scanning: the first BCI was based on induced changes in EEG, by means of motor imagery; the second BCI was based on evoked responses in EEG, by means of a cognitive task. The MI task, a brisk dorsiflexion of both feet, resulted in pronounced patterns of ERD/S. The cognitive task, related to working memory and perception of human voice, modulated ERP components reflecting different stages of selective attention. Thus, even though these BCIs differed substantially in their experimental paradigm and the EEG responses, they were made interchangeable within a common application.

However, balancing requirements for induced (e.g., sensorimotor rhythm) and evoked (i.e., ERPs) responses in EEG, each associated with different mental tasks, led to certain compromises. For example, the maximum information transfer rate was constrained by time requirements for induced and evoked responses in EEG. Whereas increasing the rate of presentation through partially overlapping stimuli would have benefited the ERP based BCI, it would have rendered the sensorimotor rhythm based BCI useless. In contrast, the latter BCI would have probably benefited from a group-item presentation at a reduced rate. Nonetheless, the choice between different mental (i.e., motor and nonmotor) tasks is beneficial in addressing the individually specific needs in end-users.

3.2.4 Brain-computer interface based on induced and evoked changes in EEG

To the best of the authors knowledge, **Horki et al. (submitted)** [68] is the first experimental proof that a single auditory selective attention task, namely focusted attention to verbal performance of a brain-teaser task, can modulate both induced and evoked changes in EEG. In detail, attending to verbal performance of mental subtraction induced oscillatory activity similar to that of a stand-alone performance (i.e. without verbal cues). Through built in semantic deviants ("yes" / "no"), the selective auditory attention also evoked event-related potentials correlated with perceptual and semantic processing of words.

This proof was obtained in a standard AT use case, with participants answering a series of yes / no questions in a scanning paradigm, that can generalize to further applications. This online BCI was designed with end-users and their needs in mind. To that end, oscillatory activity allowed for immediate feedback, whereas in its absence the evoked potentials could still be used for post-hoc detection of command following, thus increasing the reliability of results [68]. The combination of EEG responses from both low and high frequency bands may also increase robustness to artifacts [42].

Several studies investigated hybrid BCIs based on induced and evoked changes in EEG. Common to these studies is use of two different tasks. In oneapproach, in addition to executing and / or imagining movements, the participants perform a second task, namely monitoring and evaluating the response of the BCI [20, 44, 87]. In case of an unexpected response, error-related potentials (ErrP) can be detected in the EEG, and used to improve the accuracy of the hybrid BCI system.

In a somewhat different approach [4], participants performed the following two tasks: (i) tactile selective attention to vibro-tactile stimulation of the left / right finger; and (ii) imagined left / right hand movements. Two hybrid BCIs were investigated by combining the SSSEPs from the selective attention task, and the ERD from the MI tasks, either simultaneously or sequentially. Based on data from 16 healthy participants, the sequential hybrid approach yielded best results.

In contrast to these studies utilizing a dual-task designs, where the users must split their attention between two different tasks, **Horki et al. (submitted)** [68] employed a single task, allowing the users to fully focus on the task at hand.

3.3 BCI evaluation in end-users: findings, limitations, and alternative approaches

Within this thesis, complex and / or familiar mental imagery, passive, and attempted feet movement were evaluated in end-users with DoC. To that end, six MCS end-users were verbally instructed to perform different mental imagery tasks (sport, navigation), and attempted feet movements. Statistically significant ($p < 0.05$) offline classification accuracies were estimated for all three tasks (i.e., attempted feet, sport, and navigation), and most often with motor tasks.

One limitation of this work is that the passive feet movements could be evaluated in one end-user only, as an evaluation in other end-users was not feasible due to a presence of spasticity. Indeed, [180] reported that large proportion of DOC end-users develop severe spasticity. Time-frequency analysis of passive feet movements revealed task-related EEG changes over neurophysiological plausible cortical areas. However, the estimated classification accuracy was not statistically significant ($p < 0.05$).

Another limitation of this work is its focus on experimental paradigms that do not require any vision, motivated by the findings that a patient in the completely locked-in state with ALS has lost all afferent pathways but the auditory system [129]. However, the potential BCI end-users are a very heterogeneous group, differing greatly in their needs and capabilities. End-users with no vision problems may benefit from visual ERP based BCIs, assuming there are no major differences in performance compared to healthy participants. The latter assumption was put to test in **McCane et al. (2015)** [108], who evaluated a visual ERP based speller in people with amyotrophic lateral sclerosis (ALS) and in healthy controls, and compared these two groups in terms of accuracy, speed, and ERP features (i.e. latency, amplitude, location). No significant differences in accuracy and speed of communication were found between the ALS and the healthy group. Significant differences were found for the following ERP features: amplitude of early negative component (N200); location and amplitude of the late positive component (P300); and the latency of late negative (LN) component.

In a non-spelling application, **Marchetti et al. (2013)** [106] compared two interfaces for controlling the movement of a cursor on a monitor. The two interfaces, based on either voluntary (endogenous) or cued (exogenous) orienting of covert spatial attention, were evaluated in ten ALS end-users. The ALS end-users obtained control of both of these BCIs, with endogenous interface resulting in higher accuracy and information transfer rate.

Covert attention was also investigated in **Lesenfants et al. (2014)** [99], who proposed a novel SSVEP based BCI using covert non-spatial attention to a modified checkerboard stimulation pattern (i.e. interlaced squares made of red and yellow LEDs). The BCI was evaluated online in healthy participants and six LIS end-users. Mean online accuracy for healthy participants was $74 \pm 13\%$. Command following (i.e. offline accuracy above the chance level) could be detected in two out of six LIS end-users, with one out of four LIS end-users being able to communicate online.

A hybrid visual BCI was reported in **Pan et al. (2014)** [141], who investigated whether a visual ERP and an SSVEP based BCI can be combined to detect command following in seven end-users with disorders of consciousness and one LIS end-user. To that end, the end-users were instructed to attend to one of two photos: one was their own, and the other was unfamiliar. To elicit ERPs the frames of the two photos were randomly highlighted, and to elicit SSVEP each photo flickered at a different frequency. Command following could be detected in 2 DOC end-users, the LIS end-user and in healthy controls (N=4).

In addition to BCIs relying on eye-gaze control, some end users could potentially benefit from recently reported hybrid BCIs relying on muscular control [142], or combining a BCI with an added input from a sensor [163, 89]. However, it is unclear whether and to what extent such an approach could benefit end-users with MCS.

3.3.1 Complementary approaches

Recently, various approaches were reported in bringing the mental imagery based BCIs to the end-users, that could complement the findings of this thesis. Several studies opted for individually adapted motor imagery [9, 66, 40], employed specialized paradigms [9], and advanced machine learning methods [66], and online co-adaption [40]. Whereas individually adapted motor imagery, as well as advanced machine learning methods, were already employed in this thesis, additional use of online co-adaptation could further improve the results.

Co-adaptive training paradigms were evaluated by **Faller et al. (2014)** [40] in 22 end-users with severe motor impairment. In the initial experiment, the participants performed right hand movement imagery (MI), left hand MI and relaxation. Subsequently, visual feedback was delivered for the MI task that was easier to discriminate against relaxation. In the second experiment of the study, the same participants controlled a self-paced BCI, individually adapted through auto-calibration. Statistically significant ($p = 0.01$) accuracies were estimated for 18 of 22 participants of the initial experiment, and for 11 of 20 participants of the second experiment.

However, when applying these co-adaptive training paradigms to end-users with MCS, great care must be taken to ensure that the BCI adapts to willful modulation of brain activity, and to avoid adaptation to non-task related changes.

3.4 Summary and Conclusions

Comparatively few BCI studies investigated combined BCIs, using two tasks in either sequential or simultaneous manner. One possible cause of this limited number of studies is the complexity and inherent difficulty of a two-task design: to achieve the desired goal the users must split their attention between two different tasks. Further difficulties lie in differing and conflicting requirements for experimental strategies, signal processing and mode of operation.

In this thesis, these difficulties were dealt with and it was shown how to successfully combine induced and evoked changes in EEG for BCI applications. Furthermore, it was demonstrated that a single auditory selective attention task can modulate both induced and evoked changes in EEG, thus paving the way for further BCIs that exploit both of these types of brain signals. Notably, the novel experimental paradigms can facilitate such endeavours and their transition from a laboratory to end-users.

In a related work, the state of the art in the BCI technology was evaluated in end-users with disorders of consciousness. Furthermore, it was contributed to by comparing different types of mental tasks and attempted movements within end-users, as well as by exploring new venues.

3.5 Future prospects

EEG based BCIs, eventhough they made good progress in translating the results obtained with healthy participants to end-users, are still not robust and reliable enough to be used as a sole assistive devices by the end-users. One proposed solution to this shortcoming is the hybrid BCI, also employed in this thesis, integrating common assistive devices with different types of BCI. In addition to assistive devices, BCIs could further be improved by including other types of biosignals such as ECG, EMG, and EOG.

In some end-users (e.g. in persons with MCS), due to fluctuation in responsiveness it is only occasionally possible to establish communication. Most of the current studies address this issue by repeating the measurement on a different day. Another way of addressing this issue would be to continuously record the EEG and other types of biosignals over a longer period of wakefulness. During this time period, both passive and active paradigms could be used to try and identify the periods of responsiveness.

Future BCI research in end-users with MCS could also benefit from novel experimental paradigms addressing the issues of agitation and motivation. Agitation often results in strong artifacts, rendering the EEG signals difficult to process, and motivation can be negatively impacted by monotonous experimental paradigms and lack of meaningful feedback. One future prospect of addressing these issues is through use of music. For example, **Formisano et al. (2001)** [45] reported indications that active music therapy can both reduce psychomotor agitation in persons with severe brain injuries, as well as improve their collaboration.

The approach outlined in this thesis is well suited for novel experimental paradigms that integrate engaging feedback, such as active music therapy, with various mental tasks (e.g., attempted / imagined movements). For example, year after year thousands of people spontaneously clap their hands and stamp their feet to the clapping / marching chorus of the famous Radetzky March. Another way of viewing this is that they actively attend to an auditory performance of the hand / feet motor task. And most importantly, they have fun doing it.

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Appendix A

Primary Publications

A.1 Contributions

Listed in this section is the approximate amount of work authors contributed to the five primary publications.

	Author	work	contribution
1	**P. Horki**	65%	idea, programming, measurements, analysis, writing
	T. Solis-Escalante	10%	technical advice, writing
	C. Neuper	5%	general advice, writing
	G. Müller-Putz	20%	idea, advice on paradigm, writing
2	G. Müller-Putz	30%	idea, general advice, writing
	C. Pokorny	10%	partial programming, measurements
	D. Klobassa	5%	measurements, writing
	P. Horki	55%	programming, measurements, analysis, writing
3	**P. Horki**	55%	idea, programming, measurements, analysis, writing
	G. Bauernfeind	5%	writing
	D. Klobassa	5%	measurements, writing
	C. Pokorny	5%	technical advice, measurements
	G. Pichler	5%	general advice, writing, end-users
	W. Schippinger	5%	general advice, writing, end-users
	G. Müller-Putz	20%	idea, general advice, proofreading
4	**P. Horki**	80%	idea, programming, measurements, analysis, writing
	D. Klobassa	5%	writing
	C. Pokorny	5%	writing
	G. Müller-Putz	10%	general advice, writing
5	**P. Horki**	70%	idea, programming, measurements, analysis, writing
	G. Bauernfeind	10%	technical advice, writing
	W. Schippinger	5%	general advice, end-users
	G. Pichler	5%	general advice, end-users
	G. Müller-Putz	10%	advice on paradigm, writing

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SPECIAL ISSUE - ORIGINAL ARTICLE

Combined motor imagery and SSVEP based BCI control of a 2 DoF artificial upper limb

Petar Horki · Teodoro Solis-Escalante · Christa Neuper · Gernot Müller-Putz

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Abstract A Brain–Computer Interface (BCI) is a device that transforms brain signals, which are intentionally modulated by a user, into control commands. BCIs based on motor imagery (MI) and steady-state visual evoked potentials (SSVEP) can partially restore motor control in spinal cord injured patients. To determine whether these BCIs can be combined for grasp and elbow function control independently, we investigated a control method where the beta rebound after brisk feet MI is used to control the grasp function, and a two-class SSVEP-BCI the elbow function of a 2 degrees-of-freedom artificial upper limb. Subjective preferences for the BCI control were assessed with a questionnaire. The results of the initial evaluation of the system suggests that this is feasible.

Keywords Steady-state visual evoked potential (SSVEP) · Brain–computer interface (BCI) · Neuroprostheses

1 Introduction

A Brain–Computer Interface (BCI) is a device which transforms brain signals, which are intentionally modulated by a user, into control commands for computers or machines [34]. Electroencephalogram (EEG)-BCIs based on steady-state visual evoked potentials (SSVEP) [15, 16] and based on the P300 [6] component, respectively, can be set-up with almost no training, but they require external stimuli. On the other hand, EEG-BCIs based on sensorimotor rhythms (SMR) [26] and slow cortical potentials (SCP) [3] require no external stimuli, but they require extensive user training. Self-paced control of a neuroprosthesis has been demonstrated with the event-related (de)synchronization (ERD/ERS) of SMR, induced by motor imagery (MI) [19, 27].

SSVEP are elicited by presenting repetitive visual stimuli at a frequency greater than 6 Hz, and can be recorded at occipital electroencephalogram (EEG) electrode positions [31]. For the SSVEP-BCIs, different classes can be realized by using flickering lights with different frequencies. These flickering stimuli, delivered via light emitting diodes (LED) or a computer monitor, modulate the EEG signals at the stimulating frequency and its harmonics [4, 7, 18]. The frequency components of the SSVEP can be obtained from the power spectral density analysis of the EEG, the lock-in analyzer system (LAS) and canonical correlation analysis (CCA) [2, 13, 16, 20]. Applications of SSVEP-BCIs include communication purposes [4] as well as self-paced control of electrical prosthesis [21].

In our previous work, we investigated whether an asynchronous SSVEP-BCI can control a 2 degrees-of-freedom (DoF) artificial limb [10]. In that work the SSVEP-BCI was used to toggle both the hand function (open/close) and the elbow function (flexed/extended). Eight healthy subjects and one tetraplegic patient could control the artificial limb online, with the positive predictive value varying between 69% and 83% ($76 \pm 4\%$ for all nine participants), and the false negative rate varying between 1% and 17% ($8 \pm 5\%$). One possible improvement to this previous work would be to allow for intermediate elbow positions between the full flexion and the full extension.

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Recently, hybrid BCI systems based on MI and SSVEP have been reported [1, 29]. In [29], a hybrid BCI system was created by switching a battery of flickering lights (SSVEP-BCI) on or off by using a brain switch based on the post-imagery beta ERS [22, 25, 32]. By sequentially combining the two BCIs the number of false activations in the self-paced operation of an SSVEP-based orthosis could be reduced.

Restoration of a lateral grasp was achieved in a spinal cord injured patient [27]. The patient was able to sequentially switch between grasp phases by imagining foot movements. In recent studies [22, 32], the post-movement beta rebound was shown to be strong and stable without any subject training. Also, recent work investigated, in healthy participants, the SSVEP-BCI control of a prosthesis and an orthosis [21, 23]. Based on these results, our goal is to combine MI and SSVEP BCIs for the independent control of the grasp and elbow functions. A further goal is to allow for a fast and practical BCI setup, by using a minimum number of EEG electrodes. We chose to combine the beta rebound after brisk feet MI and a two-class SSVEP-BCI. To this end, we investigate a control method where the MI-BCI controls the grasp function and the SSVEP-BCI the elbow function of an artificial upper limb with 2 DoF. We evaluated the performance of both BCIs, and assessed the participant's preferences for the BCI operation with a questionnaire.

2 Methods

2.1 Stimulation unit, subjects and EEG recording

Stimulation unit The stimuli were delivered via two red LED bars (2 cm × 5 cm) flickering at 8 and 13 Hz with a duty cycle of 50%. The LED bars were arranged in one row with a center-to-center distance of 7.5 cm

Subjects Twelve healthy subjects (7 male and 5 female, aged between 23 and 30 years) participated in the initial cue-based calibration. Two subjects showed no beta rebound following the brisk feet MI, and for one subject we could not setup an adequate classifier (meaning offline accuracy above 70% [12]); therefore they were excluded from further investigations. Two of the remaining nine subjects were not available for subsequent measurements. A total of seven subjects (4 male and 3 female) participated in an online experiment.

The experiment was undertaken in accordance with the Declaration of Helsinki, and the study was approved by the local ethics committee of the Medical University of Graz. Participants gave informed consent prior to the beginning of the experiments.

EEG recording In the initial cue-based calibration the EEG was recorded from the occipital and the central part of the head by 21 and 5 Ag/AgCl electrodes, respectively. The occipital electrodes were placed in 3 rows and 7 columns [20]. The central electrodes formed a single Laplacian [9] derivation at electrode position Cz, overlying the foot cortical representation. Figure 1 shows the electrode montage. The distance between electrodes was 2.5 cm. Reference and ground electrodes were placed at the left and right mastoid, respectively. Impedances were kept below 5 kΩ. The EEG amplifier (g.BSamp, g.tec Guger Technologies, Graz, Austria) was setup with a bandpass filter between 0.5 and 100 Hz, with a sensitivity of 100 μV. The notch filter (50 Hz) was on and the sampling rate was $f_s = 250$ Hz. Subjects were seated about 1 m in front of the stimulation unit and the monitor in an electrically shielded and slightly dimmed room.

In online BCI experiments with feedback the EEG was recorded from a subset of six occipital electrode positions (individually selected) and from Cz (Laplacian derivation) as described above. Once again, reference and ground electrodes were placed at the left and right mastoid. The EEG amplifier settings were as described above. Subjects were seated about 1 m in front of the experimental setup consisting of the stimulation unit and the artificial limb (a robotic arm mounted on a mannequin) placed in front of an artist's board.

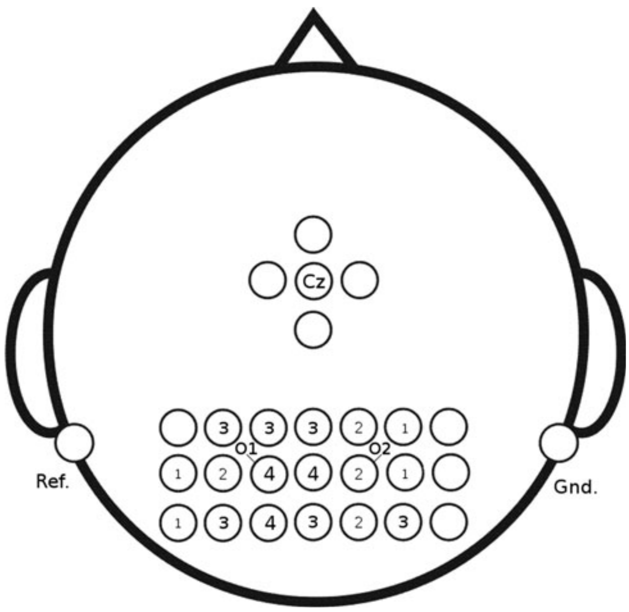


Fig. 1 EEG electrode positions used for recording in the initial cue-based calibration. Also shown is the distribution of EEG channels, individually selected from EEG data recorded in experiments without feedback. The *numbers* indicate how often each EEG channel contributed to the best accuracy. The distance between electrodes was 2.5 cm

2.2 Experimental paradigm

The experiment was divided into an offline and an online session, conducted on separate days. The offline session consisted of a short initial screening followed by 4 runs of simultaneous MI and SSVEP cue-based calibration [23]. In the online session the subjects controlled a 2 DoF artificial upper limb according to verbal instructions.

The cue-based calibration started with a short screening measurement (3 min) during which the subjects were instructed to relax and to focus their attention on a certain point on the screen. The purpose of this short measurement was to determine the alpha-band characteristics in EEG spectrum. To this end, a power spectrum analysis was performed on each of the EEG channels O1, Oz and O2. For one subject (BC4), a destructive interference of the α-band with one of the stimuli frequencies (8 Hz) was found, and for this subject the stimuli frequencies were set to 7 Hz and 13 Hz.

The screening measurement was followed by a combined MI and SSVEP calibration consisting of 4 runs containing 40 trials each, separated by short breaks of about 1–2 min to avoid fatigue. In the first run the subjects were instructed to execute a brisk feet dorsiflexion, whereas in runs two to four the subjects were instructed to only imagine the movement. The SSVEP task was to focus on one of the two flickering lights, placed below the screen. During the whole session the subjects did not receive any feedback.

Each trial lasted 8 s and the trial timing consisted of: (1) at the beginning of each trial ($t = 0$ s), a fixation cross was presented at the center of the screen, and remained visible until the end of the trial; (2) from $t = 0$ to 2 s, the participants had to look at a fixation cross, and at $t = 2$ s, a short tone catched the subject's attention; (3) from $t = 3$ to 4.25 s, a cue appeared. An arrow pointing downwards indicated the brisk feet dorsiflexion, whereas an arrow pointing left or right indicated at which flickering light the participants should focus their attention on.

Each flickering light was randomly indicated ten times within each run resulting in 40 trials for each of the two SSVEP classes. The brisk feet dorsiflexion task was randomly indicated 20 times within each of the runs two to four, resulting in 60 MI trials used for data analysis. The ME trials in the first run were not included in the data analysis.

In the online experiment we evaluated the combined MI and SSVEP based BCI in a 2 DoF artificial upper limb control scenario, repeated four times with each subject. The subjects controlled the grasp and elbow functions according to verbal instructions given by the experiment supervisor. The grasp function (gripper), controlled with the MI, could be toggled between opened and closed state by imagining brisk feet movements. The SSVEP was used to control the elbow. The elbow could be gradually moved from full extension to full flexion by using the two SSVEP classes for flexion or extension, respectively. For the elbow control, steps of variable duration in time (minimal duration 1 s, increment 1 s, full range 8 s) were employed.

The initial state of the gripper was closed and the initial position of the elbow was full extension. The middle position of the elbow, in the center between the full flexion and the full extension, was defined as an interval (approx 20% of the full range). The flexed, middle and extended elbow position intervals were marked on an artist's board, placed behind the artificial upper limb. In this way the subjects could see whether they have reached the intended position or not. Every time the desired elbow position was reached, the subjects were verbally informed. During the online experiment, the subjects were given verbal instructions to perform one of the following tasks: open the gripper (GO); close the gripper (GC); move the elbow from extended to middle position (T1); move the elbow from middle to extended position (T2); move the elbow from extended to flexed position (T3); move the elbow from flexed to middle position (T4).

The verbal instructions followed a predefined movement sequence, always defined as GO, GC, T1, T2, GO, GC, T3, T4, GO, T2, GC. After each correct execution of an MI or SSVEP task and before the subsequent verbal instruction a non-control period of random length was inserted. The subjects were instructed beforehand to relax during the non-control period and to wait for the next verbal instruction. They were also instructed to correct false activations.

To assess the subject's feeling of control, after the online experiment the subjects filled out a questionnaire with three questions. The answer to each of the questions could be rated on a scale between 1 (low) and 10 (high). The subjects were asked to answer the following questions: (1) rate your ability to control the elbow by focusing on the flickering lights; (2) rate your ability to control the gripper by motor imagery; (3) rate the ability of the system to detect non-control periods.

2.3 Data processing

2.3.1 Classification of SSVEP

EEG data recorded from occipital sites during the experiments without feedback was used to select a subject-specific set of EEG channels and to setup the SSVEP classifier for the online experiment. The SSVEP frequency recognition was based on CCA.

Canonical correlation analysis (CCA) CCA captures the interrelationship between several predictor and several response variables [11]. CCA transforms the original variables so that the resulting values correlate as much as possible with each other. The use of CCA in EEG signal analysis is based on the premise that the measured SSVEP will contain the same frequency as the stimulus signal [13]. CCA coefficients can be calculated using the EEG signals recorded from multiple channels as one set of variables, and all stimulus frequencies and associated harmonics (in our experiments second and third harmonics) as another set of variables. The frequency with the largest CCA coefficient is then the stimulus frequency of the recorded SSVEP.

Offline analysis Following the cue-based calibration procedure, single-trial EEG epochs were derived in association with each SSVEP cue, beginning 2 s prior to the cue onset and lasting for 8 s. These epochs were then split into equal-sized test and training sets. Overlapping time segments of 1 s, obtained from the EEG data from each trial, were analysed using CCA. The amount of overlap between two consecutive time segments was empirically set to 80% for the training sets and 96% for the test sets.

Classification accuracy was computed from single-trial EEG epochs. In detail, for every time segment the CCA algorithm yielded the recognized frequency (8 or 13 Hz). The number of how many times the same frequency was recognized for the time segment at a given time point across all different single trial EEG epochs was noted. For each of the different time segments this number was divided through the number of all single trial EEG epochs, yielding the classification accuracy.

Two thresholds were used in the online experiments to determine which stimulus the participant is focusing his/her attention on. The values of these thresholds were determined from the performance of CCA on the test set for the selected channels. These thresholds were calculated separately for each of the stimulation frequencies as follows: (1) previously obtained accuracies were used to calculate mean accuracies and standard deviations for two different time intervals—the reference interval between second 0 and 2 and the activation interval between second 4 and 8 (relative to the beginning of the trial); (2) the standard deviation for the reference interval was added to the mean of the reference interval yielding the reference threshold. The standard deviation for the activation interval was subtracted from the mean of the activation interval yielding the activation threshold. The threshold to be used in the online experiments was obtained by adding the reference threshold and the activation threshold and dividing the result by two.

Feature selection A modified sequential floating forward selection (SFFS) was applied to select the EEG electrode channels [30]. The criteria for selection was a combination of maximizing the accuracy in the period after the cue onset, while maintaining a chance level before the cue onset, as indicated by the classification accuracy of CCA in single EEG trials.

The following steps were applied on the 21 occipital EEG channels recorded in the initial cue-based calibration experiment:

1. In an initial step, training combinations of four channels, with two channels in each row, are analyzed, and the one with the single largest CCA accuracy is selected. If there are multiple best solutions, the mean CCA accuracy is used to discriminate between channel combinations.
2. In a step forward, the current best combination of n_F (number of channels in a forward step, $n_F = 4$ in the first step forward) channels is expanded (one neighbor at a time) with all of its neighbors, yielding several combinations of $n_F + 1$ channels. CCA accuracies of these combinations are estimated and the best combination is selected. If its accuracy is better than the accuracy of the current best channel combination, it is selected as the new current best; otherwise, the algorithm continues with the next step backward.
3. In a step backward, the current best combination of n_B (nusmber of channels in a backward step, $n_B = 5$ in the first step backward) channels is analysed. CCA accuracies of all possible combinations of $n_B - 1$ channels are estimated and the best one is selected. If its accuracy is better than the accuracy of the current best channel combination, it is selected as the new current best; otherwise, the algorithm continues with the next step forward.
4. The whole procedure is repeated until the desired number of channels (empirically set to 6) is selected.

Online classification In the online classification procedure, CCA was applied every 0.125 s on a sliding window of 1-s length. The output of the CCA classifier, i.e., the recognized SSVEP frequency—was stored in a circular buffer containing the CCA classifier outputs for the last 4 s. If the online percentage of frequency recognition, calculated separatly for each one of the stimulation frequencies from the circular buffer, exceeded the corresponding threshold, that frequency could be detected as the one the participant is focusing on (see Fig. 2). A dwell time parameter placed an additional constraint on the online classification, namely that the same stimulus frequency must be recognized during a predefined time period, in order to be eligible for a command selection. The same dwell parameter, empirically set to 1.5 s was used for all participants. For example, for a percentage threshold of 50% for the 8 Hz stimulus, at least half of the recognized frequencies in the circular buffer must had been 8 Hz. For this case a decision can could have been made in as short as 2 s.

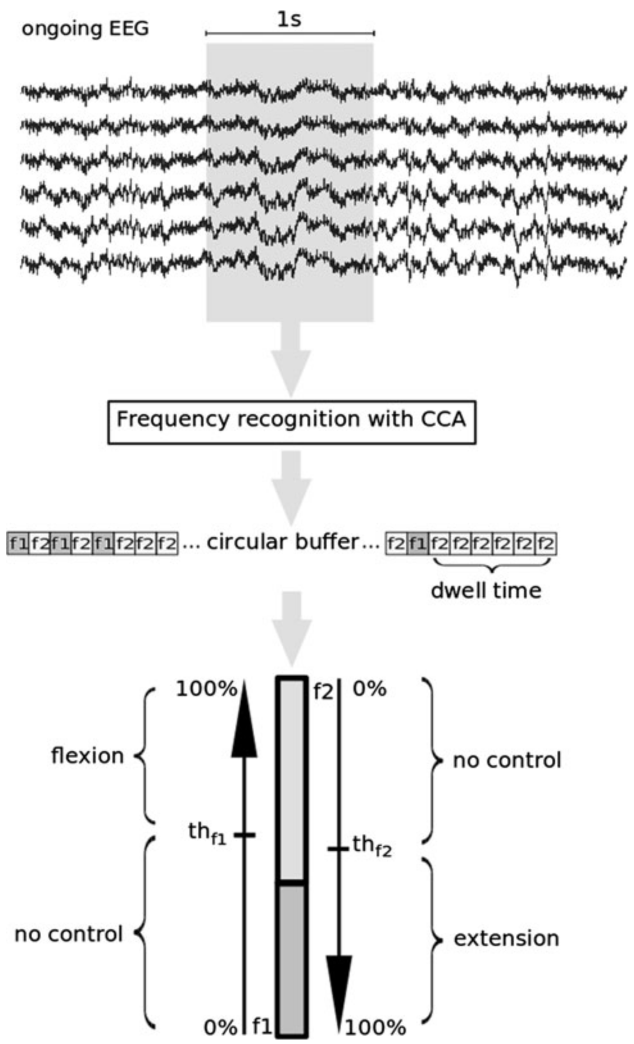


Fig. 2 Online classification procedure. The CCA was applied every 0.125 s on a sliding window of 1-s length. The output of the CCA classifier—that is the recognized SSVEP frequency—was stored in a circular buffer containing the CCA classifier outputs for the last 4 s. If the online percentage of frequency recognition, calculated separately for each stimulation frequency, from the circular buffer exceeded the corresponding threshold, than this frequency was detected as the one the participant was focusing on

2.3.2 *Classification of motor imagery*

Time–frequency maps analysis To analyze the percentage of power decrease (ERD) or power increase (ERS) relative to a reference interval [24] (0.5–1.5 s), time–frequency map for frequency bands between 6 and 40 Hz (35 overlapping bands using a band width of 2 Hz) was calculated [8]. Sinusoidal wavelets were used to assess changes in the frequency domain, the spectrum was calculated within a sliding window, squared and subsequently averaged over the trials [14]. To determine the statistical significance of the ERD/ERS values a *t*-percentile bootstrap algorithm with a significance level of $\alpha = 0.05$ was applied [5].

Classification Fisher's Linear discriminant analysis (LDA) is used as a classifier based on one logarithmic band power feature corresponding to the brisk feet MI, obtained by band-pass filtering, squaring and averaging over 1 s in a sample by sample way. A 10×10 cross-validation was applied to calculate the accuracy for each 0.5 s from $t = 0$ to 8 s. The highest accuracy classifier was used in the online experiment with an additional threshold in the foot MI class. For detection of foot MI, the threshold was defined as the the mean plus standard deviation of the simulated LDA output for the whole EEG recording. This threshold was recalibrated in a first test run to the final value [22].

2.3.3 *Online evaluation*

To assess the performance of the combined BCI we evaluated the performance of MI-BCI during the gripper control tasks and the performance of the SSVEP-BCI during the elbow control tasks. For the MI-BCI we computed a histogram of the time needed to activate the gripper relative to the verbal cue. For the SSVEP-BCI movement trajectories were obtained from linear potentiometers mounted on the artificial upper limb.

3 Results

3.1 BCI control

The offline classification accuracy (cross-validated) calculated from the MI trials obtained during the initial

Table 1 Summarized results of the cue-based calibration

Subject	acc_{MI} (%)	f_{MI} (Hz)	acc_{SSVEP}
AE9	81	23–27	99
AL9	95	17–29	87
AN7	89	19–27	93
AO3	89	26–30	94
AQ9	91	19–30	95
AV1	88	22–25	92
AV2	79	21–25	92
BC2	92	20–26	92
BC4	78	19–23	76
$\bar{x}$	87		91

Shown here are the offline accuracy for the MI (acc_{MI}) task with corresponding frequency bands (f_{MI}), and the offline accuracy for the SSVEP (acc_{SSVEP}) task

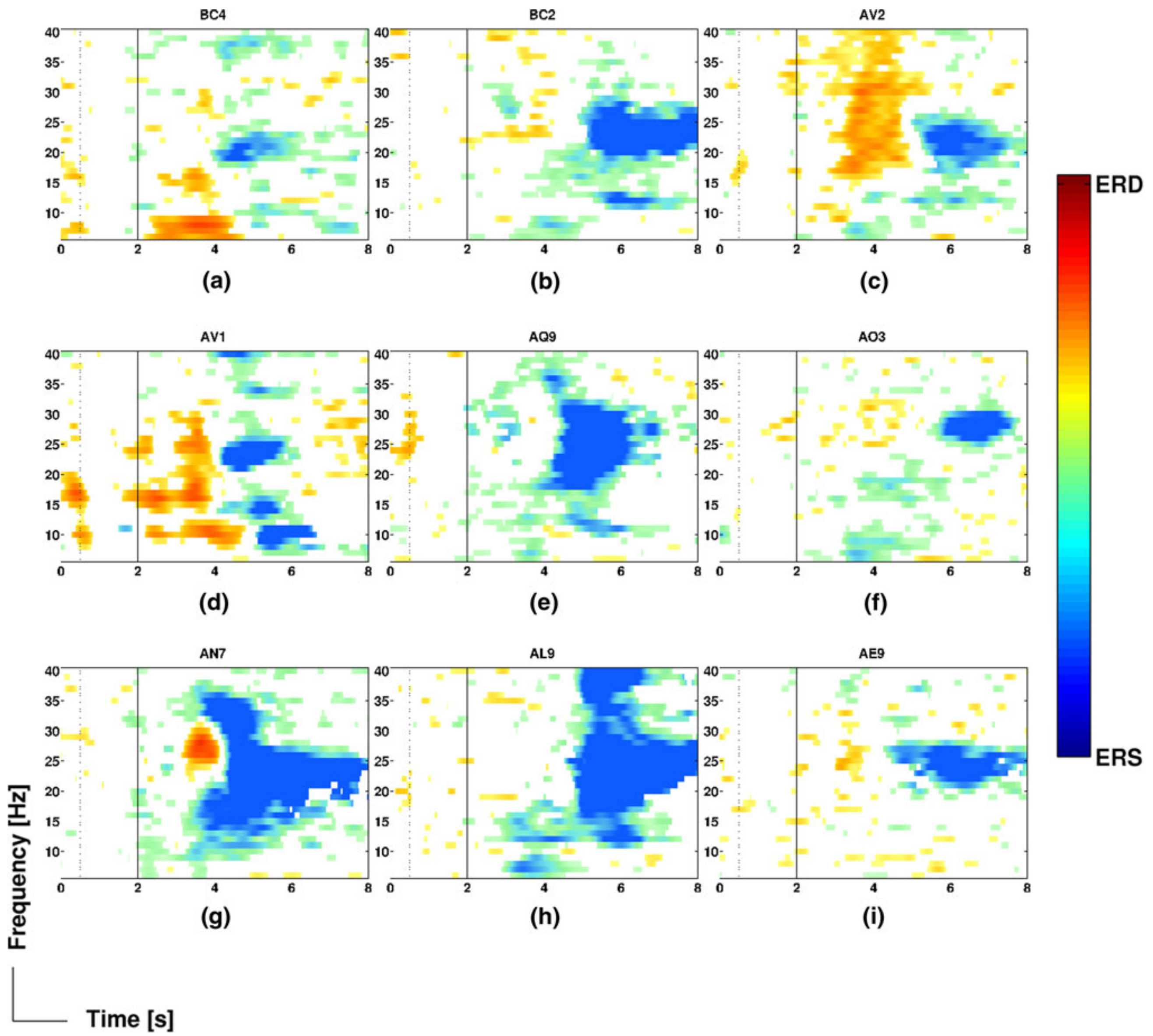


Fig. 3 ERD/ERS time–frequency maps. Reference interval was calculated from second 0.5 to 1.5; movement onset was at second 3 and the shown frequency range starts at 6–40 Hz

cue-based calibration is shown in Table 1. Additionally, the selected frequency bands are given. The corresponding ERD/ERS maps are displayed in Fig. 3. In Table 1, the offline accuracies calculated from the SSVEP trials are shown.

The online MI-BCI control is presented in Fig. 4. For comparison purposes, Fig. 4a shows the average number of commands given at a certain latency. Noteworthy, most of the activations occurred in the first 10 s, relative to the experimenter indications. Furthermore, it is reasonable to assume that the histogram could be approximated by a decaying exponential, suggesting a fast activation of the MI-BCI. Figure 4b–h shows the participant-specific activation histograms for the operation of the MI-BCI (gripper control), together with the cumulative sum of commands. One subject (BC4) needed 7 s at most to activate the gripper.

The online SSVEP-BCI control is presented in Fig. 5 and in Table 2. Elbow movement trajectories and the corresponding control tasks, during a single run for each one of the subjects, are shown in Fig. 5. Generally, the subjects had no difficulties in moving the ellbow to the desired position. However, they had difficulties in sustaining the reached position, due to false activations. Note that it takes approximately 8 s for the artificial upper limb to cross the full range between the flexed and the extended position.

Figure 1 shows the distribution of occipital EEG channels, individually selected from EEG data recorded in the

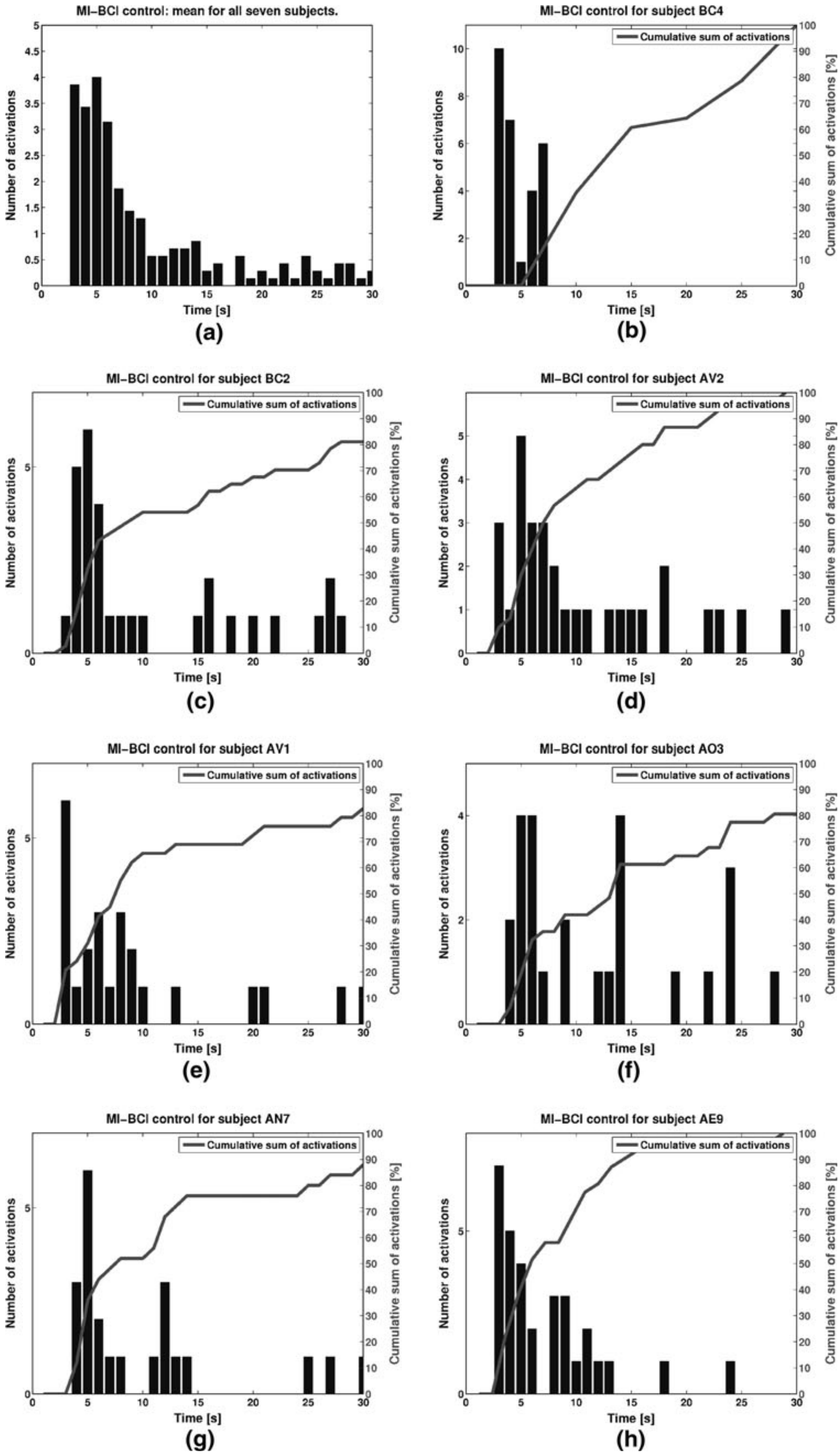


Fig. 4 Gripper performance. **a** The average number of activations across time, as subjects perform the motor imagery task, for all 7 subjects is shown. (**b**–**h**) Shows the time needed to activate the gripper and the cumulative sum of activations for each of the subjects and for all four runs (**b**–**h**)

initial cue-based calibration, and used in online experiments with feedback. The numbers indicate how often each EEG channel contributed to the best accuracy. The channels selected most often were Oz, O1 and the channel posterior to O1.

All subjects were able to perform the movement sequence consisting of 11 movements, albeit with movement corrections. On average the subjects had to correct 3 ± 2 movements while performing the sequence.

3.2 Subjective measures

The subjects rated their ability to control the elbow with 7.7 ± 1.6 (on a scale from 1, low, to 10, high). To control the gripper their rating was 6.3 ± 1.8. Finally, the performance of the system to detect non-control periods was rated with 5.8 ± 1.7.

4 Discussion

In this work, we investigated whether it was possible to combine the MI and SSVEP BCIs in a way so that they can be used for the control of both, grasp and elbow function, independently. The MI-BCI was used to control the grasp function and the SSVEP-BCI was used to control the elbow function of a 2 DoF artificial upper limb. The results of the initial evaluation of the system suggests that this is feasible, although further work is needed to improve the performance of the system during the non-control periods. One possible improvement would be identifying "resonance-like" frequencies for SSVEP-based BCI. Another aspect worth improving is the computation of the thresholds in the offline SSVEP analysis, chosen for its initial good results and for its simplicity. Indeed, there are more sophisticated methods to discriminate between two classes when their means and standard deviations are known (e.g. using the correlation coefficients as features to train a Fisher's linear classifier [35]).

The SSVEP control (elbow) generally resulted in a higher number of false activations than the MI control (gripper). However, most of the subjects perceived their ability to control the elbow to be higher than their ability to control the gripper. One explanation for this may be that subjects perceived that correcting false elbow activations was easier compared to correcting false gripper activations. Another explanation may be that the resolution of the elbow control is finer compared to the gripper control.

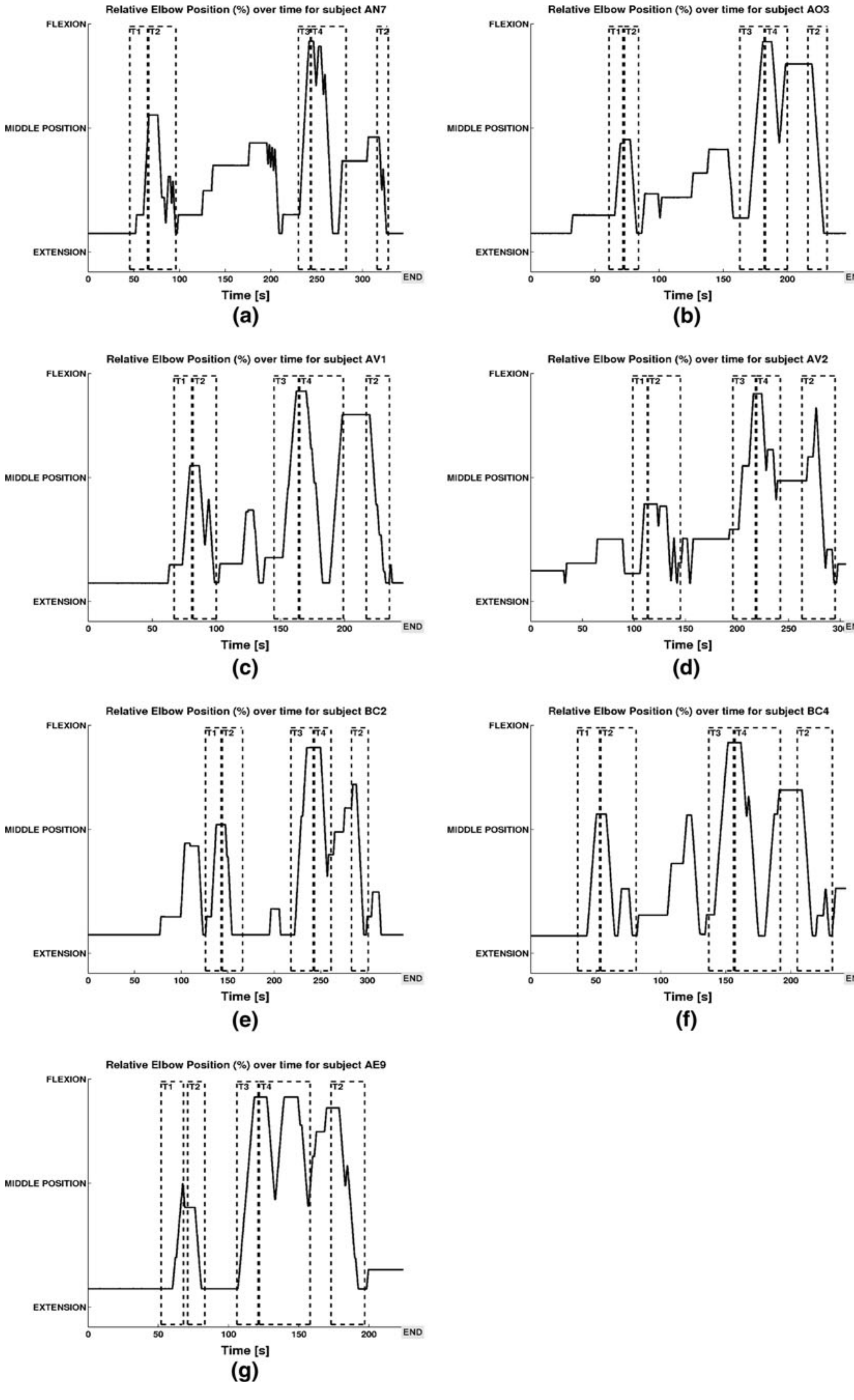
The combination of BCIs for control of an application has been presented as a "hybrid BCI" [28]. In their paper, the authors described different ways on how a hybrid BCI can be constructed. A hybrid BCI is composed essentially of two or more BCIs that are operated sequentially or simultaneously. The combination of at least one BCI and other assistive technologies also constitutes a hybrid BCI [33]. Until now, SSVEP- and MI-based BCIs were combined sequentially to reduce the false activations during non-intentional control [29]. To achieve this, the MI-based BCI enabled/disabled the SSVEP-based BCI and thus, the control of the application (i.e., SSVEP-based hand prosthesis) was not continuously available to the user. On the other hand, the simultaneous operation of these two BCIs was focused on improving the classification accuracy or on reducing the illiteracy of the BCI users [1]. That is, both BCIs worked together for providing a binary decision in a cue-paced experiment.

In our case, two BCIs are operated simultaneously for controlling a hand and elbow neuroprosthesis; providing independent control of the elbow flexion/extension with an SSVEP-based BCI and, the gripper open/close with a MI-based BCI. Such approach is novel for these two types of BCI and for the hybrid approach itself. The hybrid design presented here allows the user to operate both BCIs continuously with two different purposes that serve the common goal of controlling a 2 DoF artificial arm.

Our design investigated a possible scenario where more than one BCI is being controlled by the same user simultaneously. Evaluating the performance of the individual BCI components and the system as a whole has to be done carefully. Assessing the performance of the SSVEP-BCI during the continuous control of the elbow posed a whole new set of challenges, compared to the discrete MI-BCI control of the gripper. For example, it is difficult for subjects to assess the elbow position while they are focusing their attention on the flickering LEDs. Therefore, situations can occur when subjects continue focusing at the flickering lights, unaware that they have reached the desired position. Further, when full extension or full flexion is reached, subsequent detections provide visual feedback (elbow movement) in one direction only. One possible solution to this problem would be to include an additional auditory feedback. In an alternative approach one could attach the flickering lights directly on to the artifical limb.

Future work will focus on developing a fully self-paced BCI system. To this end, the subjects can learn the whole movement sequence in advance. Our final goal is to use the combined BCI system to control hand and elbow neuroprosthesis.

Fig. 5 Elbow performance. Elbow movement trajectories and the corresponding control tasks during a single run for each one of the subjects. The SSVEP tasks were the following: move the elbow from extended to middle position (T1); move the elbow from middle to extended position (T2); move the elbow from extended to flexed position (T3); move the elbow from extended to middle position (T4). These runs were chosen as representative of the tasks being performed ▶



Relative Elbow Position (%) over time for subject AN7
Relative Elbow Position (%) over time for subject AO3
Relative Elbow Position (%) over time for subject AV1
Relative Elbow Position (%) over time for subject AV2
Relative Elbow Position (%) over time for subject BC2
Relative Elbow Position (%) over time for subject BC4
Relative Elbow Position (%) over time for subject AE9
FLEXION
MIDDLE POSITION
EXTENSION
T1
T2
T3
T4
END
Time [s]
(a)
(b)
(c)
(d)
(e)
(f)
(g)

Table 2 The time needed (mean ± standard deviation) to complete each of the SSVEP control tasks for all subjects

subject	T1	T2	T3	T4	T2′
AE9	18.6 ± 4.7	12.5 ± 2.7	19.6 ± 6.7	13.2 ± 3.5	14.4 ± 4.9
AN7	13.0 ± 4.3	22.9 ± 6.3	21.2 ± 11.4	18.5 ± 10.2	17.3 ± 5.1
AO3	18.8 ± 7.1	7.1 ± 2.6	14.6 ± 2.2	9.9 ± 0.9	14.7 ± 4.0
AV1	10.9 ± 6.2	12.4 ± 3.8	18.2 ± 4.0	12.6 ± 0.7	17.1 ± 4.9
AV2	16.1 ± 4.3	15.7 ± 4.4	14.4 ± 6.0	16.8 ± 7.8	16.5 ± 9.7
BC2	11.0 ± 2.2	10.2 ± 2.3	19.5 ± 2.1	11.3 ± 0.4	11.5 ± 4.0
BC4	16.7 ± 4.3	10.7 ± 2.4	14.1 ± 1.5	12.0 ± 1.3	12.2 ± 2.3
$\bar{x} + \sigma$	15.0 ± 4.7	13.0 ± 3.5	17.4 ± 4.8	13.5 ± 3.5	14.8 ± 5.0

The SSVEP tasks were the following: move the elbow from extended to middle position (T1); move the elbow from middle to extended position (T2); move the elbow from extended to flexed position (T3); move the elbow from flexed to middle position (T4); move the elbow from middle to extended position for the second time (T2′)

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A SINGLE-SWITCH BCI BASED ON PASSIVE AND IMAGINED MOVEMENTS: TOWARD RESTORING COMMUNICATION IN MINIMALLY CONSCIOUS PATIENTS

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We investigate whether an electroencephalography technique could be used for yes/no communication with auditory scanning. To be usable by the target group, i.e. minimally conscious individuals, such a brain-computer interface (BCI) has to be very simple and robust. This leads to the concept of a single-switch BCI (ssBCI). With an ssBCI it is possible to reliably detect one certain, individually trained, brain pattern of the individual, and use it to control all kinds of applications using yes/no responses. A total of 10 healthy volunteers (20–27 years) participated in an initial cue-based session with a motor imagery (MI) task after brisk passive feet/hand movement. Four of them reached MI classification accuracies above 70% and, thus, fulfilled the inclusion criterion for participation in the 2nd session. In the 2nd session, MI was used to communicate yes/no answers to a series of questions in an auditory scanning mode. Two of the three participants of the 2nd session were able to reliably communicate their intent with 90% or above correct and 0% false responses. This work showed, for the 1st time, the use of a ssBCI based on passive and imagined movements for communication in auditory scanning mode.

Keywords: Brain-Computer Interface (BCI); single-switch; electroencephalography (EEG); motor imagery; auditory scanning, minimally conscious state (MCS).

1. Introduction

A Brain–Computer Interface (BCI) provides a possible means to establish communication or control, of computers or machines, for people who are unable to use traditional assistive devices. BCIs were mainly developed as a means of communication,[1–5] for control of wheelchairs[6,7] and for control of neuroprosthetic devices.[8,9] Although BCI research has now been conducted for more than 20 years, only some research labs have successfully applied the use of BCI systems to patients.[10–15] Some attempts have been made to provide patients with so-called locked in syndrome with an electroencephalography (EEG)-based communication device,[16] however, this communication channel has been observed to be very difficult and time consuming to establish.

Another group of patients who are unable to perform any motor movement to use an assistive device but have been proven to be consciously aware are people in a minimally conscious state (MCS).[17] This mainly occurs after traumatic brain injury. These patients are not able to communicate and it is not fully understood to what extent they are conscious. Functional magnetic resonance imaging (fMRI) experiments by Owen *et al.*[18] and others[19] have shown that it is possible to get in contact with a patient fulfilling the criteria for the (mis)diagnosis of vegetative state (VS). Here, patients were asked to either imagine playing tennis or to navigate through their own apartment. Both imaginations led to very specific activations which could then be used to establish a communication channel with people in the MCS by means of simple yes/no questions.[20]

Transferring such fMRI-based paradigms to EEG-based paradigms would have the advantage of making them suitable for standard clinical, or even home, use with MCS patients. Cruse *et al.*[21] assessed bedside detection of awareness with EEG in 16 patients in VS. Patients were asked to imagine movements of their right hand and toes to assess command following. In three patients, who were behaviorally completely unresponsive, appropriate EEG responses to two distinct commands could be reliably detected. Provided consciousness is detected, a need arises for an EEG-based communication device, a BCI that would empower these patients to reliably communicate yes or no responses. To be usable by the target group, i.e. the minimally conscious individuals, such a communication device has to be very simple and robust, meaning it should function even when only a single brain pattern of the patient can be reliably detected. It should employ auditory cues and feedback, since recently it was shown that a patient in the completely locked-in state with amyotrophic lateral sclerosis has lost all afferent pathways but the auditory system.[22] Our goal is to develop such a BCI and use it for communication in the auditory scanning mode.

As it seems very difficult to perform motor imagery-based (MI) BCI training as it is usually done[10,23] the so-called beta rebound phenomenon will be exploited. A number of EEG studies reported event-related desynchronization and synchronization (ERD/ERS) of sensorimotor rhythms (SMR) in the beta band, i.e. a decrease and increase of spectral amplitudes of central beta rhythms in the range from 13 to 35 Hz.[24–27] Following an ERD that occurs shortly before and during the movement, bursts of beta oscillations (beta ERS, beta rebound) appear within a 1-s interval after movement offset.[28] Such a post-movement beta ERS has been shown after voluntary hand movements,[25,27,29,30] passive movements (PASs),[30,31] movement imagery[32] and also after movements induced by functional electrical stimulation.[30]

A brain-switch based on the beta rebound was first described in Refs. 33–36. Here, the beta rebound after brisk feet dorsiflexion was used to elicit a single control signal. We hypothesize that a brain-switch can be employed in an auditory scanning mode for reliable communication of yes/no responses. As it is unclear whether the target patient group will show a pattern during brisk foot movement, hand movement should also be investigated. Our goal is to realize such a single-switch BCI (ssBCI), i.e. to reliably detect one certain, individually trained brain pattern of the user that can be used to control all kinds of applications. This means that any existing assistive technology (AT) that can be controlled by a conventional single switch can, as a final goal, also be controlled by an ssBCI.

2. Materials and Methods

2.1. *Participants*

A total of 10 healthy people (gender balanced, aged between 20 and 27 years, mean age 23.3 years) participated in the initial cue-based session. They had no previous experience with any kind of SMR-based BCI experiments. Participants gave informed consent prior to the beginning of the experiments and received monetary compensation afterwards. A handedness test[37] was performed and confirmed that all participants were right handed. Due to the results of the initial cue-based session 4 of the 10 participants (3 male, 1 female) fulfilled the inclusion criteria for participation in the 2nd session.

2.2. *Recording*

In the initial cue-based session, the EEG was recorded from 31 channels mounted around electrode positions C3, Cz and C4, overlying the sensorimotor and premotor areas. In the 2nd session, only one participant-specific orthogonal Laplacian derivation[38] was used (see Fig. 1). The EEG derivations were referenced to the left ear lobe with the ground electrode placed on the forehead. Active Electrodes (g.tec, Graz, Austria) were integrated into a standard EEG cap (Easycap GmbH, Herrsching, Germany) with an inter-electrode distance of 2.5 cm and connected to EEG amplifiers (g.tec, Graz, Austria). The EEG amplifiers were set up with a bandpass filter between 0.5 and 100 Hz, and a notch filter at 50 Hz. Participants were seated in an electrically shielded room.

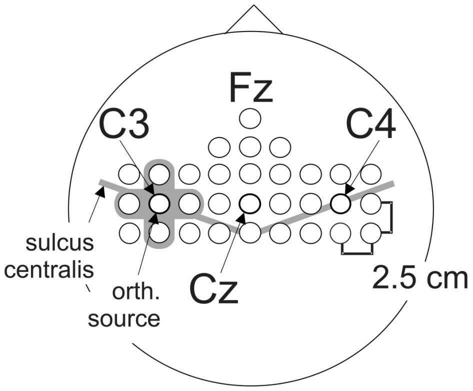

Fig. 1. EEG recording illustrated. The 31 channels recorded in the initial cue-based session, as well as an example of a manually selected orthogonal Laplacian derivation (marked orth. source) are shown.

The electromyogram (EMG) was recorded from both legs and from the right forehand. Two EMG electrodes were placed over the *musculus tibialis anterior* of each leg and over the *flexor digitorum profundus* of the right hand. The ground was placed above the pelvis on the right side. Both, EEG and EMG were sampled at 1200 Hz.

Wrist and feet angles were measured with goniometers (Biometrics Ltd, United Kingdom) placed on the wrist and ankle. For the wrist angle measurement the telescopic endblock of the goniometer was attached to the dorsal surface approximately over the third metacarpal with the center axis of the hand and endblock coincident. The fixed endblock of the goniometer was attached to the forearm so that when viewed from the dorsal plane the axes of the forearm and endblock are coincident. For the feet angle measurements the goniometers were placed in positions analogous to those on the wrist. Goniometer signals were recorded by custom-made hardware.

2.3. *Experimental paradigm*

2.3.1. *Initial cue-based calibration*

The goal of the initial cue-based session was to identify the individual EEG pattern for each participant. To this end, the experiment consisted of two tasks with two different conditions each. The tasks used in this experiment were passive brisk dorsiflexion of both feet and wrist extension of the dominant (right) hand. These two tasks were investigated for the following conditions: PAS with custom-made hardware and MI. For each task/condition combination two runs of 40 trials each were conducted, and the order in which the tasks were performed was counterbalanced.

Passive movement condition (PAS)

Feet task In order to execute passive feet movement, an inclined plane (size 44 cm × 32 cm, angle about 8°) was mounted at the bottom part of a comfortable armchair the participants were sitting in. The participants' feet were placed in parallel on this plane. Using a manual cable pull, the plane could be tilt up to an angle of about 37° (see Fig. 2).

Hand task In order to execute PAS of the participants' right hand, a small padded platform (size 12 cm × 24 cm, initial angle 0°) was mounted at the front part of the right arm rest of the armchair the participants were sitting in. The participants' right hand was comfortably placed on this platform, slightly fastened using an elastic bandage to avoid single finger movements during passive hand movement. Using a manual cable pull, the platform could be tilted up to a maximum angle of about 70° (see Fig. 3).

Paradigm In one half of the trials a PAS was executed ($t = 2$ s after trial onset) by the experimenter, standing outside the EEG recording chamber and acting according to the visual cues visible to her/him only. In the other half of the trials the participants rested and focused their gaze on an eye-level fixation point for the trial duration. The participants had no knowledge whether a PAS execution will take place or not in any given trial. Additionally, fabric was used to hide their limbs, so that they could not see their hands or legs moving.

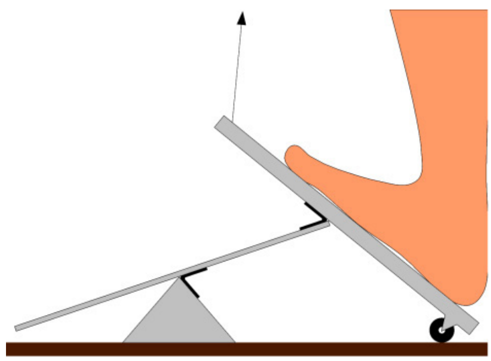

Fig. 2. Apparatus for passive feet movement.

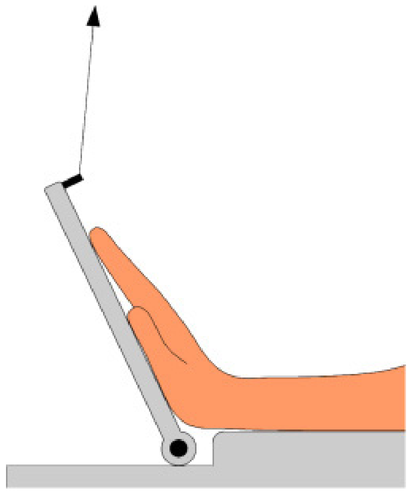

Fig. 3. Apparatus for passive right hand movement.

The beginning of each trial was marked by a short tone, and the end ($t = 7$ s after trial onset) was marked by a spoken word ("pause"). The trials were separated by short breaks of random length (3–4 s), and the order of the trials was randomized.

Motor imagery condition (MI)

Following the PAS condition of the brisk feet dorsiflexion/hand wrist extension task, the participants fulfilling the inclusion criteria performed the same task for the MI condition.

Paradigm In one half of the randomized trials, participants imagined a brisk movement, and in the other half they rested while focusing their gaze on a fixation point placed approximately 1 m in front of them. All of the participants were instructed to avoid any muscular activity during the imagination of the brisk feet/hand movements.

Similar to the PAS condition, the beginning of each trial was marked by a short tone, and a random break of 3–4 s length followed each trial. Auditory instructions were presented 2 s after the beginning of a trial ($t = 2$ s after trial onset) as either the name of the corresponding task ("feet"/"hand") or as "rest".

Feedback Discrete auditory feedback was presented at the end of the trial ($t = 7$ s) as follows (translated to English from German):

- "Feet/hand correctly recognized" was played if the feet/hand MI was recognized during an activation trial.
- "Feet/hand falsely recognized" was played if the feet/hand MI was recognized during a rest trial.
- "Pause" was played if no feet/hand MI was recognized, also indicating the end of a trial.

2.3.2. *2nd session*

In the 2nd session, the participants imagined performing brisk feet or hand movements to communicate a yes/no answer to a series of questions. To this end, a scanning protocol[39] (see Fig. 4) was employed where spoken yes/no words were used as external synchronization signals for the corresponding three scan periods. To communicate their intent, i.e. a yes/no response, the participants performed the MI task during the desired scan period. Random length breaks were employed throughout the experiment to avoid rhythmic cues.

A total of 5 runs, with 10 questions each, were conducted. In total, 25 different questions, with only one meaningful response, were delivered twice in pseudorandom order. Each question was repeated during a different run, and yes/no responses were balanced. The nature of these questions ensured that the experimenter knew the responses the participants intended to communicate. Nonetheless, at the beginning of the session the participants were presented with all questions once. Additionally, they

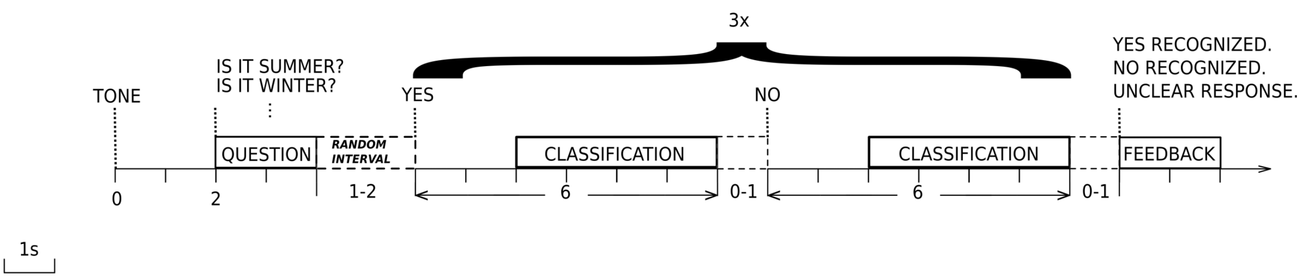

Fig. 4. Experimental paradigm of the 2nd session.

read a list containing both the questions and the responses. The questions were generated by a text-to-speech synthesizer and were delivered by loudspeakers.

Only those participants fulfilling the inclusion criteria participated in the 2nd session. The classifier used was adapted to one optimal EEG pattern derived from a single orthogonal Laplacian derivation.

Following each repetition, four cases were possible: activation after "yes", activation after "no", activation after both "yes" and "no" and no activation at all. After three yes/no scan periods, discrete auditory feedback was provided (i.e. "Yes selected", "No selected" or "Unclear response" in German language). Feedback was selected according to majority vote based on the three yes/no scan periods and the corresponding output. "Unclear response" was presented when either no activation or an equal number of yes/no activations was selected.

2.4. *Data analysis*

Various feature extraction and classification methods have been proposed for continuous analysis of different mental tasks in EEG signals.[40–48] The methods presented here were chosen for their robustness and reliability.

2.4.1. *Time–frequency analysis*

To analyze the percentage of power decrease (ERD) or power increase (ERS) relative to a reference interval (second 1–2 in the paradigm), a time–frequency map for frequency bands between 6 and 40 Hz (35 overlapping bands using a bandwidth of 2 Hz) was calculated.[49] Logarithmic band power features, calculated by bandpass filtering, squaring and subsequently averaging over the trials, were used to assess changes in the frequency domain. To determine the statistical significance of the ERD/ERS values, a t-percentile bootstrap algorithm with a significance level of $\alpha = 0.01$ was applied.

2.4.2. *Inclusion criteria*

As reported in Kübler *et al.*[50] an accuracy of at least 70% is a prerequisite for reliable BCI communication. Accordingly, we used this as the inclusion criteria, based on evaluation of one orthogonal Laplacian derivation (see Fig. 1). We conducted time–frequency maps analysis on all 11 Laplacian channels and manually selected the one with the most pronounced pattern of significant ($p \leq 0.01$) ERD/ERS values to setup the classifier.

The EEG data recorded during the PAS were used to setup the classifier for the initial MI experiment, which in turn yielded data used to setup the final classifier.

2.4.3. *Classification*

Fisher's LDA was used as a classifier based either on ERD occurring during, or beta ERS occurring after, task execution.[51] Logarithmic band power features were calculated for multiple frequency bands between 6 and 40 Hz using a bandwidth of 2 Hz. A logarithmic band power feature was obtained by bandpass filtering, squaring and averaging over 1s in a sample by sample way and finally by taking the logarithm.

A 10×10 cross-validation was applied to calculate the accuracy for each 0.5 s window from $t = 0$ s to the end of a trial ($t = 7$ s). One final logarithmic band power feature was obtained by extending the frequency range of the band with highest accuracy to include neighboring bands with accuracies greater than 70%. The corresponding classifier was used in the online experiments with an additional threshold. For the detection of the MI, the threshold was defined as the mean plus standard deviation of the simulated LDA output for the whole EEG recording.

Additionally, the 10×10 cross-validation was nested within a 10×5 outer cross-validation, thus splitting the data into an outer training set and a validation set. Classifiers at points in time with highest accuracy, selected via an inner cross-validation, were thus applied on unseen data.

A dwell time parameter placed an additional constraint on the online classification, namely that the threshold must be exceeded for a predefined time period. The same dwell time parameter, empirically set to 0.5 s, was used for all participants.

2.4.4. *Evaluation*

For the passive task of the 1st session, cross-validated percentage accuracies for the most discriminating time segment, and the corresponding frequency band, are reported. For the imagined task of the 1st session, our main interest was to what extent a classifier setup on the EEG data recorded during the PASs can be used to deliver feedback for imagined movements. To this end, we compared the results of the "passive" classifier and the classifier setup directly on the imagined movements, and also estimated the effect of adjusting the LDA threshold for the "passive" classifier on imagined movements. Additionally, time–frequency maps for the passive and imagined condition of the 1st session are compared in the context of the selected frequency bands.

For the 2nd session, true (T), false (F) and unclear (U) responses were obtained from the participants' communication of yes/no responses to a series of questions. Additional offline analysis estimated the effects of an increase in speed of communication or reliability of responses on the performance.

3. Results

The offline classification accuracy (cross-validated), calculated from the trials obtained during the 1st session for the hand/feet task and for the passive/imagined condition, is summarized in Tables 1 and 2. In Fig. 5, we estimated to what extent a classifier setup on the EEG data recorded during the PASs can be used to deliver feedback for imagined movements.

In Fig. 6 time–frequency maps, calculated from the EEG data obtained during the passive (1st row)

Table 1. Offline accuracy (acc) for the passive hand and feet movement during the 1st session with corresponding frequency band (f), selected channel and time segment.

	Feet				Hand			
Subj.	acc (%)	f (Hz)	t (s)	Ch	acc (%)	f (Hz)	t (s)	ch
BO4	90	15–26	6	FCz	87	15–22	6	C3
BX9	77	24–30	5.5	Cz	58	16–18	5	C1
BY2	60	26–28	6.5	FCz	72	16–22	5	FC2
BY6	89	22–34	6.5	∼FCz	61	24–26	5	C3
BY8	88	30–40	4.5	C1	78	18–22	5.5	∼C1
BZ2	79	22–26	6.5	Cz	93	16–28	6	∼C1
BZ4	96	16–20	5.5	Cz	91	18–24	6	∼C1
BZ5	81	15–22	5.5	Cz	79	16–22	5.5	C3
BZ6	92	22–28	6	FCz	79	10–12	5	∼C1
BZ8	54	20–22	4.5	FCz	60	18–20	4.5	∼FCz
$\mu \pm \sigma$	81 ± 14				76 ± 13			

Table 2. Offline accuracy (acc) for the imagined hand and feet movement during the 1st session with corresponding frequency band (f), selected channel and time segment. Empty table entries indicate absence of measurement due to the participant not satisfying the inclusion criteria.

	Feet				Hand			
Subj.	acc (%)	f (Hz)	t (s)	ch	acc (%)	f (Hz)	t (s)	ch
BO4	82	26–30	4.5	FCz	54	18–20	7	C3
BX9	50	20–22	5.5	Cz				C1
BY2					51	22–24	7	FC2
BY6	56	30–32	6	∼FCz				C3
BY8	60	28–30	4.5	C1	68	10–12	5.5	∼C1
BZ2	83	24–32	3.5	Cz	60	28–30	7	∼C1
BZ4	76	16–20	5	Cz	67	22–24	4.5	∼C1
BZ5	79	17–21	5	Cz	69	16–22	5	C3
BZ6	69	10–12	6.5	FCz	49	22–24	5	∼C1
$\mu \pm \sigma$	69 ± 13				60 ± 8			

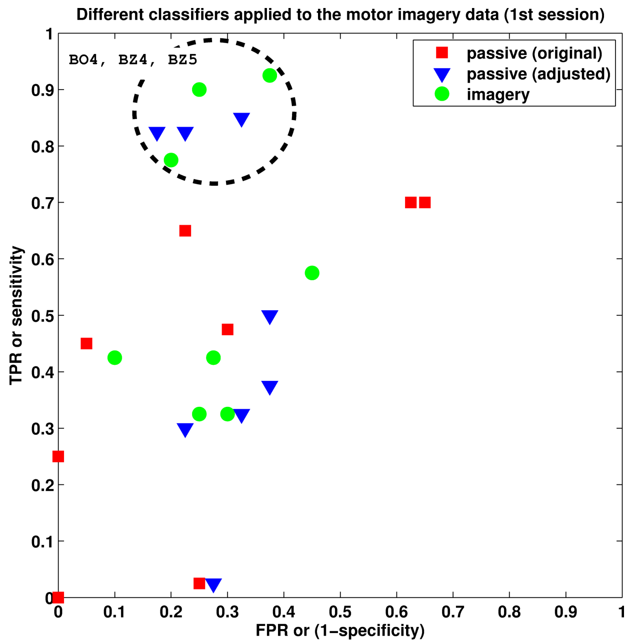

Fig. 5. Shown here are results of applying different classifiers on the imagined feet movements recorded during the 1st session, in an "offline" simulation of the online performance. To estimate the impact of the LDA threshold when applying the passive classifier on imagined movements, we considered two extreme cases: in the 1st case the threshold is estimated on the PASs only (i.e. without any adaptation on the imagined movements); in the 2nd case the threshold is estimated on the imagined movements. The imagery classifier is also evaluated online in the 2nd session. Encircled results are for the passive (adjusted) and imagery classifiers for three participants of the 2nd session.

Table 3. Shown here are the true positive rates (TPRs) and false positive rates (FPRs) depicted in Fig. 5 (see caption of Fig. 5 for details).

	Passive (original)		Passive (adjusted)		Imagery	
Subj.	TPR	FPR	TPR	FPR	TPR	FPR
BO4	25.0	0.0	82.5	17.5	92.5	37.5
BX9	70.0	65.0	37.5	37.5	32.5	25.0
BY6	0.0	0.0	30.0	22.5	57.5	45.0
BY8	70.0	62.5	32.5	32.5	42.5	27.5
BZ2	2.5	25.0	2.5	27.5	42.5	10.0
BZ4	45.0	5.0	85.0	32.5	77.5	20.0
BZ5	65.0	22.5	82.5	22.5	90.0	25.0
BZ6	47.5	30.0	50.0	37.5	32.5	30.0

and imagined (2nd row) conditions of the 1st session are shown.

The SMR-BCI performance of three (one participant BZ2 was excluded from further evaluation due to slight movements during imagination) participants in the 2nd session is summarized in Table 4 and Fig. 7. One participant (BO4) achieved a perfect score, communicating correct yes/no response to all of the questions. Another participant (BZ4) achieved good performance, communicating 90% correct responses and zero false responses. One participant performed at chance level only. Table 4 also summarizes the offline analysis of single yes/no

Table 4. Shown here are the results of the 2nd session. The online feedback section shows the percentage of true (T), false (F) and unclear (U) responses. The offline analysis section shows a stricter interpretation of true (T_{strict}) and false (F_{strict}) responses, namely that they must form the majority of yes/no scans (i.e. two out of three per question). Finally, the majority voting is broken down, and true (t), false (f) and unclear (u) responses are obtained from single yes/no scans as independent responses. All three participants performed feet imagery.

		BO4	BZ4	BZ5
Online feedback	T [%]	100	90	34
	F [%]	0	0	34
	U [%]	0	10	32
Offline analysis	T_{strict} [%]	82	64	14
	F_{strict} [%]	0	0	14
	U_{strict} [%]	18	36	72
	t [%]	77	61	25
	f [%]	0	1	24
	u[%]	23	38	51

scanning periods of the 2nd session, assuming their mutual independence.

4. Discussion and Conclusion

This work showed, for the first time, the use of a ssBCI for communication in auditory scanning mode.

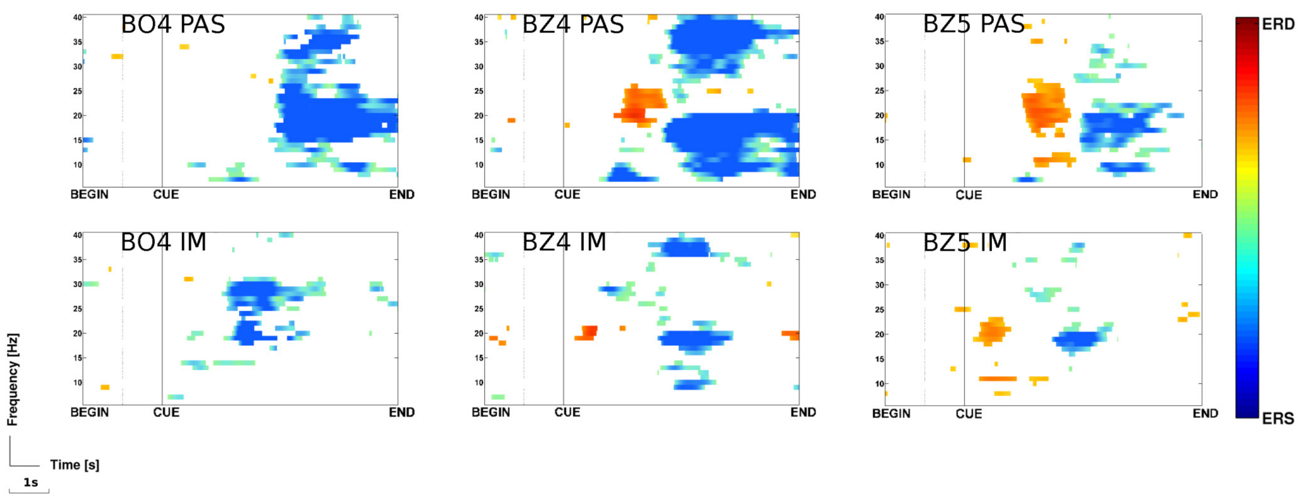

Fig. 6. (Color online) Percentage of power decrease (ERD, orange) and power increase (ERS, blue) for the passive (PAS, upper panel) and imagined (IM, lower panel) brisk feet movements in the 1st session. For each participant, the same EEG Laplacian derivation (i.e. FCz for BO4, Cz for BZ4 and BZ5) was employed for both passive and for imagined feet movements. Only significant ($p = 0.01$) power changes are shown.

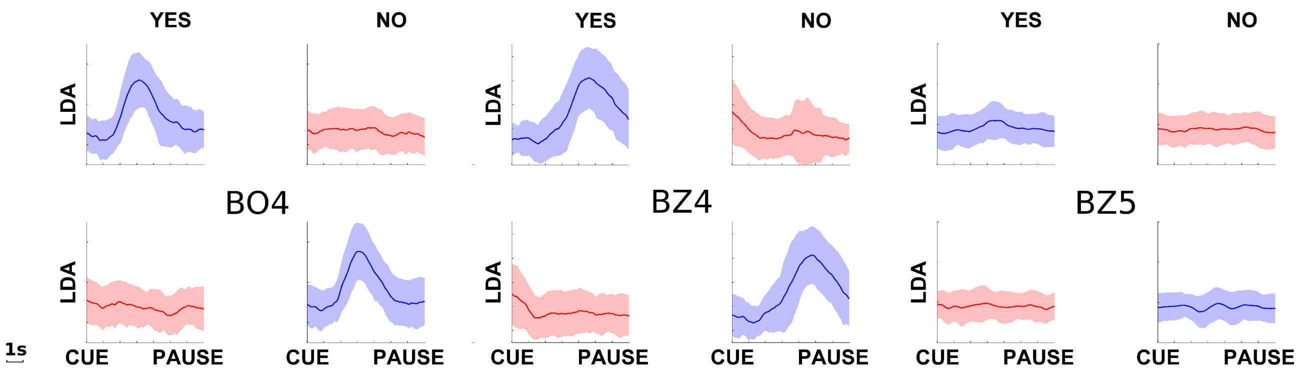

Fig. 7. (Color online) Mean and standard deviation of the LDA output for activation (blue) and rest (red) periods recorded during the 2nd session for different participants.

Such a BCI is of high importance for patients with reduced possibilities to accurately produce several brain patterns and as well as are unable to follow visual instructions on a computer screen. Patients with disorders of consciousness are such a group. As already shown in fMRI experiments,[18,20] single brain patterns can be used to communicate yes and no responses. Here, we used a brain pattern occurring automatically after brisk movement, and more importantly after mental imagery of a movement, to establish EEG-based communication. We demonstrated the idea of using this mental imagery-based ssBCI to communicate a yes or no response to a question.

Two out of three participants evaluated were able to reliably communicate their intent giving 90% or above correct and 0% false responses. The performance of one participant was only at chance level; one cause for this sudden drop in performance might be a possible change in mental imagery compared to the 1st session. This hypothesis is supported by offline analysis of the 2nd session which revealed significant ($p \leq 0.01$) ERD/ERS patterns in the two "good" performing participants and absence of the same in the random performing participant (see Fig. 8).

The robust signal detection and classification come at the price of relatively low speed of communication. However, this can be improved by reducing the number of yes/no scan repetitions, resulting in lower sensitivity (see Table 4). The reliability of communication can further be improved by also considering the "unclear" yes/no scans. The rate of false responses remained constantly low, ensuring that only intended communication took place.

In a related work Qian et al.[52] reported a MI-based brain controlled switch with a minimal false positive rate. Similar to our design, only one Laplacian channel was employed to detect brain pattern synchronized to an external signal. However, our BCI

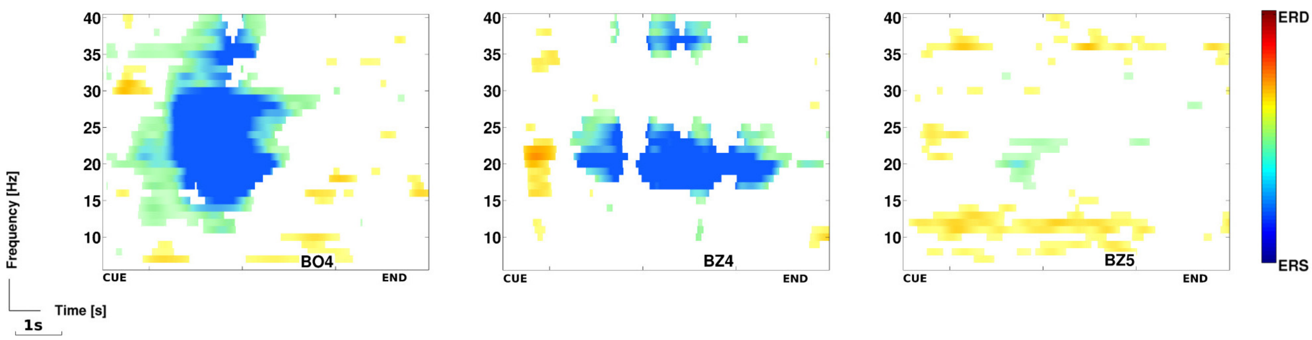

Fig. 8. (Color online) Percentage of power decrease (ERD, orange) and power increase (ERS, blue) for the activation, i.e. brisk feet imagery, scan periods in the 2nd session. The EEG Laplacian derivation are FCz (BO4) and Cz (BZ4, BZ5). Only significant ($p = 0.01$) power changes are shown.

focused on beta ERS, and employed majority voting of the consecutive activations instead of averaging the corresponding features. While we also used external synchronization signals due to inserted random breaks, these were not rhythmic and were context-dependent (i.e. yes or no response). Another novelty in our work is that we adapted the classifier to the individual EEG pattern by exploring two tasks (feet/hand) instead of one, and by selecting the optimal Laplacian derivation.

One important issue partially addressed in our study is how to setup the initial classifier. Bashashati *et al.*,[53] pointed out that generating training data for the initial system setup is problematic because no external knowledge of intention is available for individuals with severe motor disabilities. One possible solution, presented therein, is to rely on the external knowledge of the "approximate" time of the intended control. Another solution is to exploit similarities of the sensorimotor EEG changes of the motor cortex during active and PAS and MI[30,36,54] (see Fig. 6). Here, we opted for the latter solution and used EEG data obtained from PASs to setup an initial classifier for the detection of MI. As shown in Fig. 5, some participants could benefit from this solution assuming correct setting of the classifier threshold, e.g. by online adaptation.[55]

One shortcoming of this study is the limited number of participants evaluated in the final session, partly due to strict inclusion criteria. Indeed, by lowering the offline accuracy threshold to the upper confidence limit of a chance result (65% for $\alpha = 5\%$[56]) six out of 10 participants would have been included in the evaluation. Furthermore, by allowing for a longer training period, it is likely that further participants would have satisfied the inclusion criteria. However, our goal was not to estimate how many healthy participants are able to willfully modulate their brain activity, but instead to evaluate, with those participants who managed to do so, whether they can communicate a yes/no response in an auditory scanning paradigm. Initial results indicate that they can communicate their intent, and in future work we will seek to confirm these results in further applications (e.g. spelling software). The next step now is to apply the paradigm presented here to MCS patients. Our final goal is to enable MCS individuals to use existing AT.

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Detection of mental imagery and attempted movements in patients with disorders of consciousness using EEG

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Further development of an EEG based communication device for patients with disorders of consciousness (DoC) could benefit from addressing the following gaps in knowledge—first, an evaluation of different types of motor imagery; second, an evaluation of passive feet movement as a mean of an initial classifier setup; and third, rapid delivery of biased feedback. To that end we investigated whether complex and/or familiar mental imagery, passive, and attempted feet movement can be reliably detected in patients with DoC using EEG recordings, aiming to provide them with a means of communication. Six patients in a minimally conscious state (MCS) took part in this study. The patients were verbally instructed to perform different mental imagery tasks (sport, navigation), as well as attempted feet movements, to induce distinctive event-related (de)synchronization (ERD/S) patterns in the EEG. Offline classification accuracies above chance level were reached in all three tasks (i.e., attempted feet, sport, and navigation), with motor tasks yielding significant ($p < 0.05$) results more often than navigation (sport: 10 out of 18 sessions; attempted feet: 7 out of 14 sessions; navigation: 4 out of 12 sessions). The passive feet movements, evaluated in one patient, yielded mixed results: whereas time-frequency analysis revealed task-related EEG changes over neurophysiological plausible cortical areas, the classification results were not significant enough ($p < 0.05$) to setup an initial classifier for the detection of attempted movements. Concluding, the results presented in this study are consistent with the current state of the art in similar studies, to which we contributed by comparing different types of mental tasks, notably complex motor imagery and attempted feet movements, within patients. Furthermore, we explored new venues, such as an evaluation of passive feet movement as a mean of an initial classifier setup, and rapid delivery of biased feedback.

Keywords: EEG, mental imagery, attempted movements, passive movements, disorders of consciousness

INTRODUCTION

Functional magnetic resonance imaging (fMRI) studies by Owen et al. (2006) and others Boly et al. (2007), Monti et al. (2010), demonstrating detection of awareness in the unresponsive wakefulness syndrome (UWS, Laureys et al., 2010), paved the way for the development of brain–computer interfaces (BCI) as a means of communication in this patient group. In these studies, patients were asked to imagine playing tennis, or to navigate through their own apartment. Such imaginations led to very specific activations which could then be used to establish a communication channel with people in the minimally conscious state (MCS, Giacino et al., 2002) by means of simple yes/no questions (Monti et al., 2010).

Recent efforts focused on translating these fMRI paradigms to electroencephalography (EEG) technique, as it is widely available, cost effective, and applicable at bedside, even in persons with metal implants. For example, Goldfine et al. (2011) instructed the participants to imagine complex motor and familiar spatial navigation tasks, and analyzed EEG power spectra over a wide range of channels and frequencies. By analysing the EEG power spectra, evidence for performance of mental imagery tasks was found in healthy controls and patients with severe brain injury. In another study, Cruse et al. (2011) asked the participants to imagine movements of their right-hand and toes to command, and analyzed the EEG responses to specific commands. Three of 16 patients (19%) generated repeatedly and reliably suitable EEG responses to two distinct commands, even though they were behaviorally unresponsive. In a follow-up study, addressing some of the methodological challenges, EEG evidence for attempted movements to command was found in an UWS patient (Cruse et al., 2012).

Notable in these efforts are the different approaches to motor tasks—attempted hand/feet movements in Cruse et al. (2012), and complex motor imagery in Goldfine et al. (2011). It is unclear which approach is more suitable, as both have their merits. On one hand, attempted movements lead to well investigated frequency band-specific oscillatory changes over appropriate areas of the sensorimotor cortex (see Pfurtscheller and Da Silva, 1999). On the other hand, imagery of complex movements has been shown to elicit stronger activation than imagery of simple ones with fMRI (Kuhtz-Buschbeck et al., 2003; Boly et al., 2007), encouraging its study with EEG. Furthermore, a recent EEG study performed by Gibson et al. (2014) found that complex and familiar mental tasks can enhance single-trial detectability of imagined movements.

One common challenge facing these EEG efforts is the initial classifier setup for detection of the brain responses. While the delay and variability in brain responses can be addressed with different methods, there is no way of telling whether and when the MCS individuals performed the tasks. However, one could address this challenge by exploiting similarities of the brain responses during passive and attempted movements. In a recent work our group exploited similarities of the sensorimotor EEG changes of the motor cortex during active, passive and imagined movements to setup an initial classifier for the detection of motor imagery in healthy participants (Müller-Putz et al., 2010, 2013a). However, it is an open research question whether this approach is feasible for detection of attempted movements in MCS individuals.

While the current efforts could in theory establish a two-way communication with some of the patients, a real-time feedback on classification of mental imagery with EEG is yet to be evaluated in MCS patients. Such an evaluation is important, as feedback might benefit patient's performance. For example, it is unclear whether rapid delivery of biased (i.e., positive) feedback would benefit patients performing close to chance level, as it has benefited healthy participants (Barbero and Grosse-Wentrup, 2010). Addressing the above mentioned gaps in knowledge—first, an evaluation of both simple and complex motor imagery within patients; second, an evaluation of passive feet movement as a mean of an initial classifier setup; and third, rapid delivery of biased feedback—could provide valuable insights for further development of an EEG based communication device. To that end, the goal of the current work was to investigate whether complex mental imagery, passive, and attempted feet movement can be reliably detected in patients with disorders of consciousness (DoC).

MATERIALS AND METHODS

PATIENTS

Six patients diagnosed with MCS took part in this study (one women, five men; age range 21–66 years, mean and standard deviation 41.7 ± 17.8 years). The patients, not in intensive care and in an overall stable medical condition, were selected by the medical staff of the Albert Schweitzer Clinic (Graz, Austria) where all measurements were conducted. Exclusion criteria were gravidity, infections, or participation in other studies. The patients participated in two parts (command following part and online feedback part) with a different number of sessions. The idea was that each patient, if possible, would participate in two session on different days to compensate for possible fluctuations in responsiveness. For patients who participated in more than one session, the follow-up sessions were carried out between 1 and 2 weeks later when possible.

The patients were behaviorally assessed using the Coma Recovery Scale-Revised (CRS-r) within 24 h before or after each EEG measurement in order to keep track of their fluctuations in responsiveness. The CRS-r is composed of 23 items divided into 6 subscales dealing with auditory, visual, motor, oromotor, communication, and arousal functions (Giacino et al., 2004). The standardized scoring has been shown to produce "... reasonably stable scores over repeated assessments..." (Giacino et al., 2009) and is capable of discriminating patients in MCS from those with UWS.

Table 1 provides background and disease related data, as well as the highest estimated CRS-r subscores, of all patients.

Informed consent was obtained from the patient's legal representatives. The study was approved by the local ethics committee (Medical University of Graz) and is in accordance with the ethical standards of the Declaration of Helsinki.

EXPERIMENTAL PARADIGMS

The study consisted of two parts. The first part (performed by 4 patients; age range 21–66, mean (μ) and standard deviation (σ) 39.8 ± 20.3 years, all men) comprised a command following paradigm. The second part was an online paradigm which was performed by 4 patients (one women and 3 men; age range 27–66 years, μ and σ 46.0 ± 18.9 years), of which two already participated in the first part.

Command following paradigm

Within an experimental session, up to four different tasks (i.e., sport, navigation, attempted/passive feet movement) were performed in a block design. Each task was performed during three consecutive runs, with each run having 15 cue-based trials (auditory cue) of 12 s length, yielding 45 trials/task (see **Figure 1**). At the beginning of a trial a beep tone was given. After 2 s, an auditory cue, generated by a text-to-speech synthesizer, was delivered via in-ear headphones. The cue was a verbal instruction to perform the current task (i.e., either "sport," "navigation," or "feet") lasting for 1 s. For the "passive feet" task, no cue was given to the patients, as it was only audible to the caregiver performing the passive feet movement. Between the trials a random pause (also auditorily indicated) of 4–6 s length was given. Detailed verbal instructions were given to the participant by the experimenter before the measurement started. The purpose of these instructions, repeated before each run, was to inform the patient about the tasks he/she has to perform. The order of the tasks was pseudo randomized across the measurement sessions. Each measurement session was conducted on a separate day.

In more detail, for the "sport" task the participants were instructed to imagine performing one sport of their choice in the first person perspective. For measurements with non-responsive patients there is no way of knowing for sure which sport they chose. However, they were instructed to keep their choice while performing this task. For the "navigation" task the participants were instructed to imagine navigating through their house, looking around each room, without focusing on the movement. For the "feet" task the participants were instructed to repeatedly

Table 1 | Overview about participants for both the command following and the online feedback paradigm.

Participant	Age	Sex	Onset
P1	**45**	**M**	**April 2010**
Etiology	Traumatic brain injury with craniotomy and evacuation of a traumatic right sighted subdural hematoma, plus a left-sided temporo-parietal subarachnoid hemorrhage, bilateral temporopolar and right-sided temporo-occipital contusion hemorrhages		
Auditory function	Reproducible movement to command		
Visual function	Object recognition		
Motor function	Automatic motor response		
Verbal function	Vocalization/Oral movement		
Communication	Non-functional: intentional		
Arousal	Eye opening w/o stimulation		
Additional diagnoses	Epilepsy, spastic tetraparesis (left more than right), anarthria		
P2	**66**	**M**	**March 2011**
Etiology	Traumatic brain injury with left sighted subdural hematoma and left sighted epidural hematoma		
Auditory function	Consistent movement to command		
Visual function	Object localization: reaching		
Motor function	Object manipulation		
Verbal function	Vocalization/Oral movement		
Communication	Non-functional: intentional		
Arousal	Attention		
Additional diagnoses	Epilepsy, tetraparesis (right more than left), dysphagia, anarthria		
P3	**21**	**M**	**December 2008**
Etiology	Hypoxic brain injury after resuscitation after mixed drug intoxication		
Auditory function	Reproducible movement to command		
Visual function	Object localization: reaching		
Motor function	Localization to noxious stimulation		
Verbal function	Oral reflexive movement		
Communication	Non-functional: intentional		
Arousal	Eye opening w/o stimulation		
Additional diagnoses	Anarthria, severe spastic tetraparesis		
P4	**27**	**M**	**December 2007**
Etiology	Traumatic brain injury with left sighted subdural hematoma and right sighted epidural hematoma, hydrocephalus with ventriculo-peritoneal shunt, st. p. craniectomy left with reimplantation of an artificial bone		
Auditory function	Localization to sound		
Visual function	Visual pursuit		
Motor function	Flexion withdrawal		
Verbal function	Oral reflexive movement		
Communication	None		
Arousal	Attention		
Additional diagnoses	Epilepsy, severe spastic tetraparesis, anarthria		
P5	**58**	**F**	**March 2002**
Etiology	Hypoxic brain injury		
Auditory function	Localization to sound		
Visual function	Visual pursuit		
Motor function	Localization to noxious stimulation		
Verbal function	Oral reflexive movement		

(Continued)

Table 1 | Continued

Participant	Age	Sex	Onset
P5	**58**	**F**	**March 2002**
Communication	None		
Arousal	Eye opening w/o stimulation		
Additional diagnoses	Spastic tetraparesis, osteoporosis		
P6	**33**	**M**	**January 2002**
Etiology	Traumatic brain injury after car accident		
Auditory function	Localization to sound		
Visual function	Visual pursuit		
Motor function	Flexion withdrawal		
Verbal function	Oral reflexive movement		
Communication	Non-functional: intentional		
Arousal	Eye opening w/o stimulation		
Additional diagnoses			

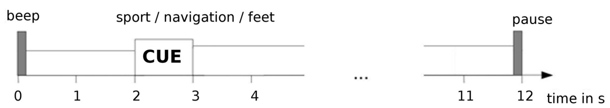

FIGURE 1 | Experimental paradigm for measurements in patients. Timeline of a single trial is shown here.

attempt feet dorsiflexion (i.e., several consecutive attempts during a single trial). In the "passive feet" task, a caregiver performed a brisk (i.e., ~1 s long) dorsiflexion of both feet. The cue was the same as for the "feet" task, but it was only audible to the caregiver.

Online feedback paradigm

The online feedback paradigm built upon the command following paradigm by introducing feedback. In general the transition from offline to online paradigm within a measurement session was possible but contingent upon results (i.e., accuracy, confusion matrix), statistical significance (i.e., number of trials, leave-one-out or blockwise crossvalidation), plausibility of results (i.e., neurophysiological plausible EEG channels), and patient's condition (i.e., fatigue, indicated by an obviously reduced vigilance). To that end, it started with recording of a few minutes resting state EEG, followed by a run of command following paradigm without feedback, and afterwards an initial classifier setup. The next step was contingent upon the estimated accuracy and patient's condition. In case of promising results, the next run was for the online feedback paradigm, again followed by a classifier setup in order to obtain a more reliable estimate of the accuracy. This step (i.e., a run of online feedback paradigm, followed by a classifier setup) was repeated depending on the estimated accuracy and patient's condition. Furthermore, the following changes were made compared to the initial command following paradigm: (i) only motor tasks (i.e., sport, attempted feet) were employed, based on offline analysis of shared common patient data recorded in the command

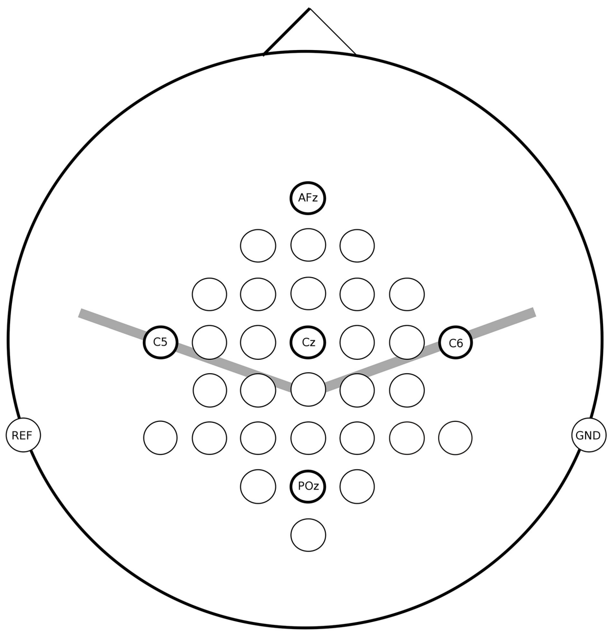

FIGURE 2 | EEG channel locations used for measurements in patients.

following paradigm (Müller-Putz et al., 2013b); (ii) a varying number of trials, separated in blocks of 15 trials by short breaks, were recorded for each task; (iii) in case the initial command following led to online feedback, the second task was discarded.

RECORDING

For all measurements the EEG was recorded from 32 active electrodes (g.tec, Guger Technologies, Austria) located over frontal, central and parietal areas (for details see **Figure 2**). The signals were acquired with a g.UBSamp amplifier (Guger Technologies, Austria) with 512 Hz sampling rate, 0.5 Hz high-pass, and 100 Hz low-pass filter, and an additional 50 Hz notch filter.

DATA ANALYSIS

Preprocessing

For the offline analysis, artifacts were removed from EEG with an elaborate projection method which automatically detects neuronal and artifactual source components derived from independent component analysis (ICA). We used the binary Infomax independent component analysis by Enghoff (1999), based on the Matlab version of Scott Makeig and collaborators, to separate EEG and EOG signals into independent components (Makeig et al., 1996). We identified independent components (ICs) representing eye movements, eye blinks, and muscle activity by visual inspection using methods described in McMenamin et al. (2010), and removed them. We multiplied the remaining components by the mixing matrix produced by the ICA algorithm to reconstruct cleaned EEG.

For the online feedback delivery, due to time and resources constraints (i.e., short breaks between consecutive runs and a single laptop certified for clinical measurements, respectively) artifacts were rejected. To that end, muscle and movement artifacts, as well as other transient non-stationarities in the ongoing EEG signals, were detected by inverse filtering of orthogonal Laplacian derivation (Scherer, 2008). Autoregressive (AR) parameters of the inverse filter were estimated from a 1 to 2 min segment of resting state EEG, recorded at the beginning of each session. The detection threshold was defined as five times Root-Mean-Square from the resting-state EEG. Trials in which the detection threshold was exceeded were discarded from the analysis.

Time-frequency analysis (ERD/ERS calculation)

Event-related desynchronization (ERD) and event-related synchronization (ERS) are defined as the percentage of power decrease (ERD) or power increase (ERS) in a defined frequency band in relation to a reference interval (Pfurtscheller and Da Silva, 1999). To analyze the percentage of power decrease (ERD) or power increase (ERS) relative to a reference interval (second 1–2 in the paradigm), time-frequency map for frequency bands between 6 and 40 Hz (35 overlapping bands using a band width of 2 Hz with a step size of 1 Hz) was calculated (Graimann, 2002). Logarithmic band power features, calculated by band-pass filtering, squaring and subsequently averaging over the trials, were used to assess changes in the frequency domain. To determine the statistical significance of the ERD/ERS values a t-percentile bootstrap algorithm with a significance level of $\alpha = 0.05$ was applied (Davison and Hinkley, 1997). In the ERD/ERS maps statistically significant ERD values were plotted as red dots and significant ERS values as blue dots.

Feature extraction and classification

Feature extraction. Logarithmic band power features were calculated for multiple frequency bands (θ: 4–7 Hz; α: 7–13 Hz; β_L: 13–19 Hz; β_M: 19–25 Hz; β_H: 25–30 Hz) by band-pass filtering, squaring and averaging over 1 s in a sample by sample way.

For further analysis, a trial was divided into consecutive, non-overlapping time periods of 1 s duration. One time period, from $t = 1$ s to $t = 2$ s (i.e., 1 s before the cue onset), was designated as the reference. Finally, a single value was sampled at the middle of each time period, and was used in the subsequent classification.

Classification. We sought to identify one Laplacian channel/frequency band yielding the best results for the current task. Thus, we estimated the accuracy over different time periods relative to the reference, for each of the frequency bands (i.e., θ, α, β_L, β_M, β_H), and at each of the Laplacian channels. To that end we used a linear discriminant analysis (LDA) classifier.

To avoid overfitting cross-validation was applied to estimate the accuracy. For the offline analysis, a nested block-wise cross-validation (10 × 10 inner fold; leave-one-out-block outer fold) was applied. For the online paradigm, both leave-one-trial-out (initial runs), as well as nested blockwise (10 × 10 inner fold; leave-one-out-block outer fold; micro-averaging of confusion matrices) cross-validation were applied. Also, the classifier was recalculated following each run, based on the EEG recording from up to three previous runs.

To ensure comparable results, we performed a separate cross-validation for each channel using comparable data (i.e., randomized trial indices in inner/outer folds were held constant). Furthermore, in each cross-validation, classification was performed separately for each frequency band and time segment.

Online feedback

Feedback was only given for correct classified trials. The feedback was either "Sport/feet correctly recognized" in the case of correct classifier prediction for more than 50% of the duration of the imagery period in the trial (Daly et al., 2013a), or "Pause" otherwise (also for the trials in which EEG artifacts were detected).

RESULTS

Tables 2, **3** show *post-hoc* analysis results of the command following paradigm and online paradigm, respectively. The Laplacian channel derivation and the frequency band yielding the highest accuracy, as estimated with the blockwise nested crossvalidation, is reported. The reported results were obtained with respect to a baseline reference period, and no differentiation between the tasks was made.

In both the command following and the online feedback paradigm, offline classification accuracies above chance were reached in all three tasks (i.e., attempted feet, sport, and navigation), with motor tasks yielding significant results more often than navigation (sport: 10 out of 18 sessions; attempted feet: 7 out of 14 sessions; navigation: 4 out of 12 sessions). In the online feedback paradigm, *post-hoc* classification accuracies above chance ($p = 5\%$) were reached by three out of four patients in either the attempted feet (F) or sport (S) task. Online accuracies, as used for the feedback delivery, were below the level of significance (i.e., random) and are not reported.

The passive feet movements, evaluated once in the third session of patients P2, did not yield significant accuracies. However, time-frequency analysis revealed task-related EEG changes over neurophysiological plausible cortical areas (**Figure 3**).

Table 2 | Summary of results for the offline detection of different tasks for the command following paradigm.

Participant/Session no.	CRS-r score	Sport	Navigation	Attempted feet
P1/1	18	71% (CP1, ϑ, 0.01)	n.s.	73% (C2, α, 0.01)
2	18	n.s.	n.s.	n.s.
3	17	n.p.	n.s.	n.p.
4	19	65% (CPz, ϑ, 0.05)	n.s.	n.s.
P2/1	14	76% (Fz, ϑ, 0.01)	n.s.	69% (FC1, α, 0.01)
2	15	n.s.	72% (P3, ϑ, 0.01)	n.s.
3	14	65% (C2, ϑ, 0.05)	n.p.	80% (FC1, ϑ, 0.01)
P3/1	14	n.s.	n.s.	n.s.
2	13	66% (CP1, ϑ, 0.05)	n.s.	65% (CP1, β_M, 0.05)
3	13	n.s.	72% (POz, β_M, 0.01)	68% (Cz, ϑ, 0.05)
P4/1	9	66% (Fz, α, 0.05)	n.s.	n.p.
2	11	n.s.	72% (C4, β_M, 0.01)	n.s.
3	11	n.s.	72% (C2, β_M, 0.01)	64% (Fz, β_M, 0.05)

Discrimination between mental imagery task/attempted feet/passive feet movement, and the reference (1 s before the cue onset). Only significant ($p = 0.01$ and/or $p = 0.05$, considering the number of trials, Müller-Putz et al., 2008) accuracy is reported. CRS-r, Coma Recovery Scale-Revised; acc (ch, band, p), accuracy (Laplacian channel, band, significance level); n.s., not significant; n.p., not performed.

Table 3 | Summary of results for the *post-hoc* offline detection of different tasks for the online feedback paradigm.

Participant/ Session no.	CRS-r score	Sport	Attempted feet
P2/1	18	n.s.	n.p.
2	17	68% (CP2, α, 0.01)	n.p.
P4/1	11	64% (Fz, ϑ, 0.05)	n.p.
2	11	65% (FC2, β_M, 0.05)	n.p.
P5/1	11	n.p.	n.s.
2	11	n.p.	n.s.
P6/1	11	n.s.	64% (CP2, β_M, 0.05)
2	12	71% (C3, β_M, 0.01)	n.p.

Discrimination between motor imagery task/attempted feet movement, and the reference (1 s before the cue onset). Only significant ($p = 0.01$ and/or $p = 0.05$, considering the number of trials, Müller-Putz et al., 2008) accuracy is reported. CRS-r, Coma Recovery Scale-Revised; acc (ch, band, p), accuracy (Laplacian channel, band, significance level); n.s., not significant; n.p., not performed.

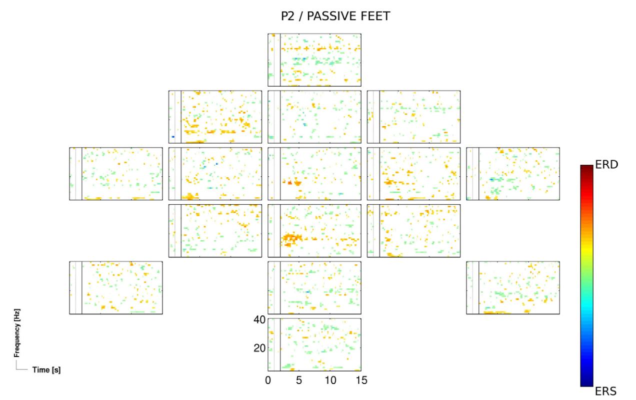

FIGURE 3 | ERD/S map for the participant P2 and for the passive feet condition of the 3rd session, calculated for Laplacian channel derivations.

DISCUSSION

In the current work involving patients with DoC our aim was threefold: (i) to evaluate different types of motor imagery; (ii) to evaluate passive feet movements as a mean of an initial classifier setup; and (iii) to evaluate rapid delivery of biased feedback. To that end, we investigated whether complex mental imagery, attempted, and passive feet movements can be reliably detected in patients with disorders of consciousness (DoC).

The two motor tasks, the sport imagery and attempted feet movement, accounted for almost two thirds (i.e., 62%) of sessions yielding significant ($p < 0.05$) accuracies, with similar outcomes within sessions. This is in line with previous findings indicating that, among other tasks, motor imagery rather than spatial navigation most frequently results in better classification performance (Friedrich et al., 2012). The sport imagery resulted in activations in theta (centro-parietal, central, and frontal), alpha (centro-parietal, frontal), and middle beta band (fronto-central, central). The attempted feet resulted in activations in theta (fronto-central, central), alpha (central), and middle beta band (centro-parietal, frontal). In **Figure 4**, ERDS patterns for the sport and attempted feet tasks are exemplified for the participant P1 and the first session.

The passive feet movements were evaluated in only one out of four patients (P2), as an evaluation in other patients was not feasible due to their medical conditions (i.e., spasticity). The evaluation in P2 yielded mixed results: on one hand, time-frequency analysis revealed task-related EEG changes over neurophysiological plausible cortical areas (**Figure 3**); on the other hand, classification results were not significant enough ($p < 0.05$) to setup an initial classifier for the detection of attempted movements. However, the attempted feet movements performed after the passive feet movements yielded highly significant ($p < 0.01$) accuracies, prompting the question whether this was more than a mere coincidence.

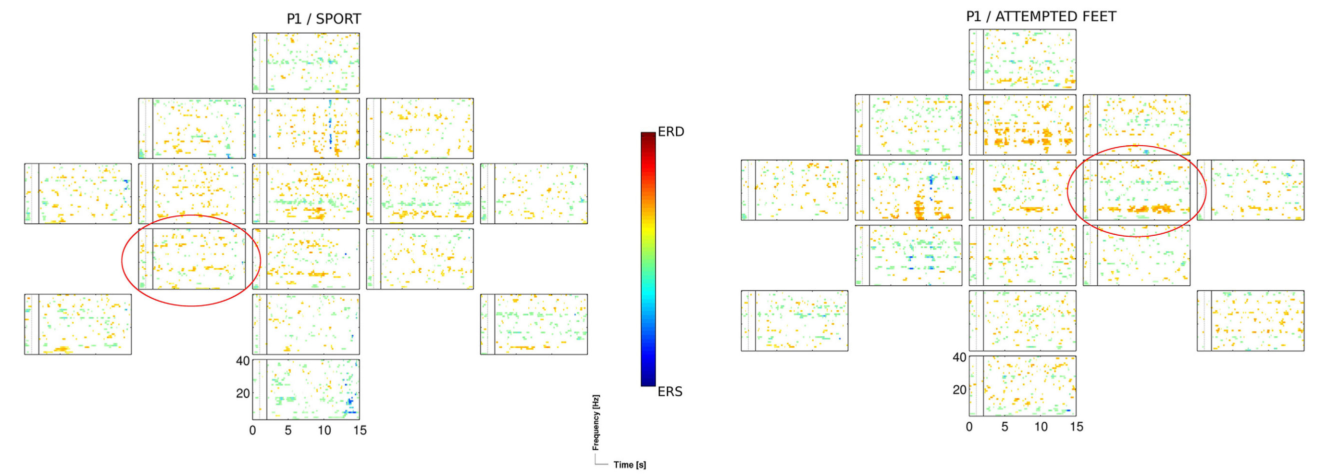

FIGURE 4 | ERD/S map for the participant P1 and for the sport, and the attempted feet task of the 1st session, calculated for Laplacian channel derivations. Marked with the red circle is the Laplacian channel derivation yielding the highest accuracy, as estimated with the blockwise nested crossvalidation.

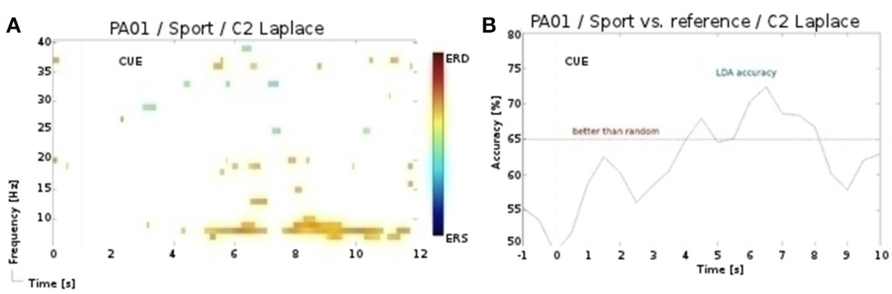

FIGURE 5 | (A) ERD/S map for the participant P1 and for the sport task of the 2nd session. **(B)** LDA accuracy over trial duration for this participant, sport task, and α band during the 2nd session.

The online feedback paradigm led to ERDS patterns in MCS patients that, when analyzed *post-hoc*, could be detected at around 70% accuracy with blockwise crossvalidation. However, online detection of these ERDS patterns was at the random level only. One possible explanation for this discrepancy is that, while a longer mental imagery period may be beneficial for inducing the desired ERDS patterns, a shorter detection period may be needed in order to reliably detect these patterns. In the latter case, a continuous auditory feedback may be more suitable than a discrete auditory feedback. Further investigation is needed to assess whether and to what extent the MCS patients could benefit from an auditory feedback.

In Cruse et al. (2011) consistent and robust responses to command for attempted movements were observed in the EEG of 5 out of 23 of the MCS patients. Similarly, we estimated highly significant (i.e., $p = 0.01$) accuracy for attempted feet movements in two out of six of the MCS patients. Worth pointing out is that we employed longer trials to accommodate for more complex mental imagery tasks. In Goldfine et al. (2011) two out of three patients (one patient in MCS and one in LIS) showed evidence of motor imagery task performance, which is similar to our findings with 62% ($N = 21$) of sessions yielding significant ($p < 0.05$) accuracies for either sport or attempted feet task.

In our initial analysis (Müller-Putz et al., 2013b), we employed manual artifact rejection instead of the ICA, and obtained partially different results. Notably, for the participant P1 and for the sport task of the second session we found activation over central sensorimotor area (see **Figure 5**), yielding significant ($p < 0.01$) accuracies. However, following the ICA artifact rejection, the significance of these patterns diminished. In only one additional, case namely for the participant P6 and for the sport task of the first session, did we observe a similar discrepancy in results. One explanation for these discrepancies is, that the rejected electromyography (EMG) components also entailed the signal of interest, i.e., discriminative periods of neural activity (McMenamin et al., 2010). In contrast, for the navigation task significant accuracies were obtained only after the ICA preprocessing, as this task was especially prone to artifacts. Whereas in healthy participants these issues can be addressed by rejecting the artifactual EEG, doing so in the patients is rarely an option, as it is often ridden with artifacts. Therefore, we are aiming to address these issues with an automated and online artifact removal method, combining wavelet decomposition, independent component analysis, and thresholding (Daly et al., 2012, 2013b, 2014).

The above mentioned tasks were chosen due to previous investigations: for example the passive and attempted movement conditions were already investigated by our group in studies with healthy subjects (Müller-Putz et al., 2007, 2013a; Solis Escalante et al., 2012). In Müller-Putz et al. (2013a) 10 healthy subjects performed brisk passive feet/hand movements and reached mean offline classification accuracies of 81% (±14) and 76% (±13) for passive hand and feet task, respectively. In Müller-Putz et al. (2007) EEG-changes during passive and attempted foot movements were investigated in 10 healthy subjects and seven patients suffering from a complete sensor and motor paralysis. In this study healthy subjects showed distinctive ERD/ERS patterns similar to earlier studies focusing on active movements (Neuper and Pfurtscheller, 1996, 2001; Stancak et al., 2000; Müller et al., 2003) and passive movements (Cassim et al., 2001; Müller et al., 2003). Furthermore, in in five out of seven patients during attempted movement diffuse ERD/ERS patterns were found. Finally, attempted movements were already used by Cruse et al. (2012) to detect awareness in a patient who had been diagnosed to be in UWS.

In the command following paradigm we opted for a block-design instead of a pseudo randomized design mainly for the following two reasons: first, we wanted to reduce the cognitive demand by performing only one condition at a time, instead of pseudo randomizing up to four different conditions (i.e., sport, attempted feet, navigation, and passive feet); second, in case a measurement session had to be ended prematurely (e.g., due to patients obvious reduced vigilance) block design would increase the probability that at least for some of the conditions (i.e., the initial ones) enough data has been gathered. We reduced the risk of the task-irrelevant intrablock correlations in the EEG significantly accounting for the classification results through: (i) rigorous removal of artifacts with ICA; (ii) use of a simple and robust classifier with few features; (iii) control for physiological plausibility of results by means of time-frequency analysis.

It is important to note, that even though the results presented in this study are consistent with the current state of the art in similar studies (Cruse et al., 2011; Goldfine et al., 2011), a functional and accurate communication with MCS patients, as demonstrated with fMRI, is yet to be achieved with EEG and will be the primary goal of our further investigations.

Concluding, we contributed to the state of the art by comparing different types of mental tasks, notably complex motor imagery and attempted feet movements, within patients. Furthermore, we explored new venues, such as an evaluation of passive feet movement as a mean of an initial classifier setup, and rapid delivery of biased feedback. Further application of online feedback, as well as of an auditory scanning method, as described recently in Müller-Putz et al. (2013a), has to be investigated.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: http://www.frontiersin.org/journal/10.3389/fnhum.2014.01009/abstract

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Evaluation of Healthy EEG Responses for Spelling Through Listener-Assisted Scanning

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***Abstract*—We investigated whether listener-assisted scanning, an alternative communication method for persons with severe motor and visual impairments but preserved cognitive skills, could be used for spelling with EEG. To that end spoken letters were presented sequentially, and the participants made selections by performing motor execution/imagery or a cognitive task. The motor task was a brisk dorsiflexion of both feet, and the cognitive task was related to working memory and perception of human voice. The motor imagery task yielded the most promising results with respect to letter selection accuracy, albeit with a large variation in individual performance. The cognitive task yielded significant ($p = 0.05$) albeit moderate results. Closer inspection of grand average ERPs for the cognitive task revealed task-related modulation of a late negative component, which is novel in the auditory BCI literature. Guidelines for further development are presented.**

***Index Terms*—Assistive technology, brain–computer interfaces, electroencephalography.**

I. Introduction

When Jean–Dominique Bauby woke up following a massive brain stem stroke, he found himself physically paralyzed with only residual head and eye movements. Despite his condition, the so-called locked-in syndrome, he wrote "The Diving Bell and the Butterfly" [1]. How did he manage to communicate a whole book? He used the listener-assisted scanning method, where messages or letter choices are presented to a person in a sequential fashion until a selection is made. To select a letter of the alphabet, repeatedly recited by a caregiver, he blinked with his eyelid.

Persons transitioning from locked-in to complete locked-in state often find themselves unable to communicate due to loss of voluntary muscle control. For such persons with severe motor and visual impairments but preserved cognitive skills, a brain–computer interface (BCI) might provide alternative means of communication [2], thus increasing their quality of life [3]. The majority of reported BCIs are based on electroencephalography (EEG), mainly due to following three reasons: first, it has a high temporal resolution [4]; second, it is widely available; and third, it is applicable in persons with metal implants. Whereas different BCIs for spelling applications based on changes of oscillatory components have been proposed [5]–[10], we will focus on auditory based ones, as it was shown that a patient in the completely locked-in state has lost all afferent pathways but the auditory system [11].

An auditory BCI for spelling applications can be realized by utilizing the spatial features of auditory cues [12], [13]. However, it is an open research question to what extent behaviorally nonresponsive patients can process these spatial features. In a recent study using oddball design [14], preattentive processing of different features of auditory cues (i.e., location, pitch, intensity, duration, and complexity [15]) was investigated in nonresponsive patients. The main result was that pitch and intensity deviants could be discriminated by almost all patients, whereas other deviants could be discriminated only in some patients. Whereas these results, given the small number of participants involved, should be interpreted with caution, it is reasonable to assume that some patients might benefit from an auditory BCI for spelling applications independent of spatial features of auditory cues—a listener-assisted BCI for spelling applications [16].

Does it make sense to pursue a listener-assisted BCI for spelling applications? At first glance, the answer might be no since the oddball experimental design, as employed in state-of-the-art auditory BCIs for spelling applications, is contingent upon random presentation of items. However, random presentation of letters of the alphabet is difficult to process, which causes the evoked responses in EEG to diminish [17]. In spite of this problem, several lines of evidence suggest that a listener-assisted BCI for spelling applications might be feasible: first [18], demonstrated that a periodic protocol can outperform the standard oddball protocol within the context of an visual BCI; second [19], demonstrated gaze-independent spelling based on rapid serial visual presentation; and third [20], enhanced the performance of an auditory attention-based brain–computer interfaces by employing an active mental task.

Another approach would be to employ a linear scanning protocol based on sensorimotor rhythm-based selection. Such an approach was already demonstrated in a multichoice visual [21] and a binary auditory [22] paradigm, but it is unclear whether it is feasible for multichoice auditory paradigm.

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Our aim is to investigate whether listener-assisted scanning could be used for spelling with EEG. Our hypothesis is that when spoken letters are presented sequentially, the participants can communicate the intended letter by performing a mental task. To test this hypothesis, we evaluate whether the intended letter can be detected through induced and evoked EEG responses associated with different mental tasks. The results of this evaluation will form the basis of a listener-assisted BCI for spelling applications and guide its further development.

II. Methods

A. Subjects

Eleven healthy subjects (5 male, 6 female; 22 to 29 year old, mean age 26) participated in this experiment. They were recruited through university public notice boards (i.e., newsgroup, forum). Participants gave informed consent prior to the beginning of the experiments and received monetary compensation afterward. Half of the participants had no previous exposure to EEG experiments. The experiment was undertaken in accordance with the Declaration of Helsinki.

B. Recording

The EEG was recorded with 29 active electrodes (g.tec, Guger Technologies, Graz, Austria) overlying the frontal, central, and parietal scalp areas. In detail, the electrodes were placed at positions AFz, F3, F1, Fz, F2, F4, FC2, FC1, FCz, FC4, C5, C3, C1, Cz, C2, C4, C6, CP3, CP1, CPz, CP2, CP4, P3, P1, Pz, P2, P4, and POz according to the international 10/20 electrode system. The EEG electrodes were referenced to the left ear lobe with the ground electrode placed on the right ear lobe. The electrodes were integrated into a standard EEG cap (Easycap GmbH, Herrsching, Germany) with an interelectrode distance of 2.5 cm and connected to EEG amplifiers (g.tec, Graz, Austria).

The electrooculogram (EOG) was recorded with three active electrodes (g.tec, Guger Technologies, Graz, Austria), positioned above the nasion, and below the outer canthi of the eyes. The electromyogram (EMG) was recorded with four electrodes from both legs (musculus tibialis anterior). The EEG amplifiers were set up with a band-pass filter between 0.5 and 100 Hz, and a notch filter at 50 Hz. The EEG and EOG were sampled with 512 Hz, the EMG with 2000 Hz. Participants were seated in an electrically shielded room.

C. Stimuli

Spoken letters of the English alphabet, generated by a text-to-speech program (AT&T Natural Voices, AT&T, USA), were presented sequentially in alphabetical order through a right head phone for one of several predefined words. Presenting acoustic cues through one ear only, keeps the other ear free for incoming communication from surroundings. The task irrelevant acoustic cues (i.e., cues specifying the target letter, pause, report) were presented in either male or female voice, balanced across all the subjects.

Stimulus onset asynchrony was set to 550 ms, including a 50 ms pause. Thus, it took 14.3 s for a single presentation of the whole alphabet. For each target letter, indicated through a verbal cue, the alphabet was repeated one to three times, for a total of two to four alphabet presentations, followed by a short break of random length (i.e., 4 to 6 s).

D. Experimental Paradigm

The experimental paradigm is depicted in Fig. 1. For the investigation the predefined words "brain," "power," "husky," and "magic"—had to be spelled in copy spelling mode. They were chosen because their letters are distributed across the whole alphabet range. Each word was spelled letter by letter within a single run. Runs were separated by short break of 1–2 min to avoid fatigue.

The participants were instructed verbally to perform one of the following tasks whenever a target letter was presented: 1) brisk feet motor execution (ME), 2) brisk feet imagery (MI), 3) discrimination of the target voice's gender and comparison to the following repetition (i.e., whether the target voice's gender has changed or it remained the same, reporting through single/double button press with index finger of the right hand in a dedicated time window) as a cognitive task (COG), and 4) mental repetition of the target letter as a control condition (auditory evoked potentials, AEP). The participants were also verbally instructed to avoid any movements.

We balanced the order of motor (ME, MI) and nonmotor conditions (COG, AEP). ME condition always preceded the MI condition. The COG and AEP conditions were pseudorandomized. We randomized the order of words, and balanced the voice of presentation (male/female). Participants received no feedback.

E. Data Analysis

EEG analysis was performed separately for motor and nonmotor mental tasks using MATLAB 2009a (MathWorks, USA) and EEGLAB version 11 [23]. The analysis consisted of preprocessing, feature extraction, and classification.

1) Preprocessing: The data were high-pass filtered (third-order butterworth filter) with cutoff frequency at 1 Hz, and segmented into consecutive epochs of 0.5 s. Bad channels and prominent artifacts (i.e., swallowing, electrode cable movements, etc.) were identified by visual inspection and removed. Following these steps, binary Infomax independent component analysis (ICA) by Sigurd Enghoff [24], based on the MATLAB version of Scott Makeig and collaborators, was used to separate EEG and EOG signals into independent components [25]. Independent components (ICs) representing eye movements, eye blinks, and muscle activity were identified by visual inspection using methods described in [26] and removed. The remaining components were multiplied by the mixing matrix produced by the ICA algorithm to reconstruct cleaned EEG.

a) Feature extraction–motor tasks: For motor tasks analysis, we defined a single epoch as 1 s following onset of a spoken letter. The epochs were band-pass filtered (third-order Butterworth filter) between 8 and 30 Hz. Common spatial patterns (CSP, [27]–[29]) method was used to compute most discriminative features for classification.

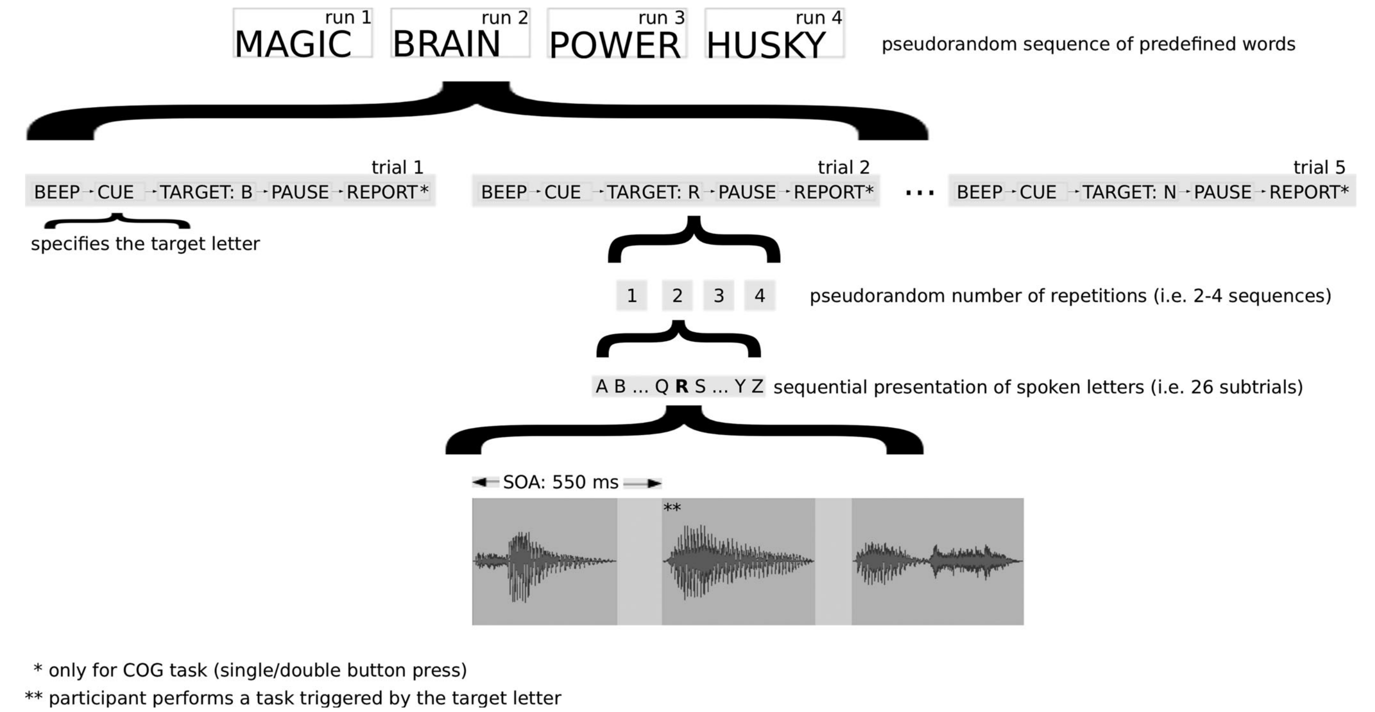

Fig. 1. Experimental paradigm: the four predefined words (i.e., "brain," "power," "husky," and "magic") had to be spelled in copy spelling mode. To that end, spoken letters of the English alphabet, generated by a text-to-speech program, were presented sequentially in alphabetical order through a right head phone. The participants were instructed to perform one of the following tasks whenever a spoken target letter was presented: i) brisk feet motor execution (ME), ii) brisk feet motor imagery (MI), iii) discrimination of the target voice's gender and comparison to the following repetition (COG), and iv) mental repetition of the target letter (AEP). Participants received no feedback. The task irrelevant acoustic cues (i.e., cues specifying the target letter, pause, report) were presented in either male or female voice, balanced across all the subjects.

Discriminative feature vectors were obtained for a fixed time segment (one second post letter onset) extracted from a balanced number of target and randomly chosen nontarget epochs of the initial run. Four feature vectors (first two and last two) were preselected, and downsampled to 32 equally spaced samples. The size of the feature vector used for subsequent classification was 128 (i.e., four CSP feature vectors by 32 time points).

For percentage of power decrease (ERD) and power increase (ERS) analysis, we defined a single epoch as 1 s preceding and 5 s following onset of a spoken letter. To that end, a time-frequency map for frequency bands between 4 and 40 Hz (35 overlapping bands using a band width of 2 Hz) was calculated ([30]) for one orthogonal Laplacian derivation overlying Cz. Logarithmic band power features, calculated by band-pass filtering, squaring, and subsequently averaging over the trials, were used to assess changes in the frequency domain. To determine the statistical significance of the ERD/ERS values, a t-percentile bootstrap algorithm with a significance level of $p = 0.05$ was applied.

b) Feature extraction–nonmotor tasks: For nonmotor task analysis, we defined a single epoch as 1000 ms following onset of a spoken letter, baseline corrected to preceding 250 ms. The epochs were band-pass filtered (third-order Butterworth filter) between 1 and 7 Hz, downsampled to 32 equally spaced samples, and the features were extracted from nine preselected electrodes (F3, Fz, F1, C3, Cz, C1, P3, Pz, P1). The size of the feature vector used for subsequent classification was 288 (i.e., 9 channels by 32 time points).

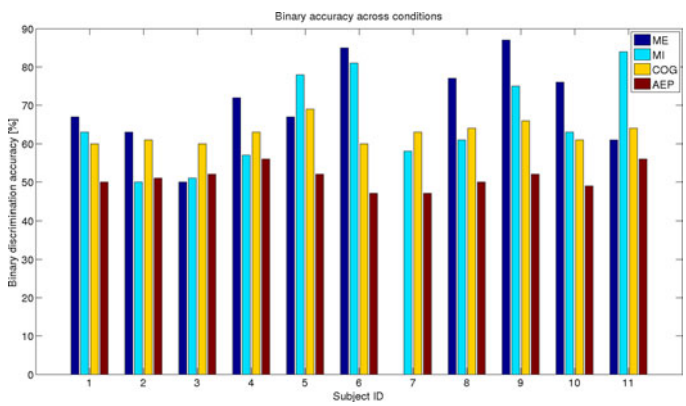

Fig. 2. Shown here is the binary discrimination accuracy for all subjects and for different conditions, calculated as the percentage of correctly classified target/nontarget epochs in outer folds of the nested cross validation. Balanced number of target and nontarget epochs was used. In subject 7, ME condition was discarded due to movement artifacts, that could not be removed with the artifact rejection. ME/MI ... brisk feet motor execution/imagery; COG ... discrimination of the target voice's gender and comparison to the following repetition; AEP ... mental repetition of the letter.

3) Classification: To avoid over fitting, we used Bayesian linear discriminant analysis (BLDA, [31]) as a classifier, and nested cross validation.

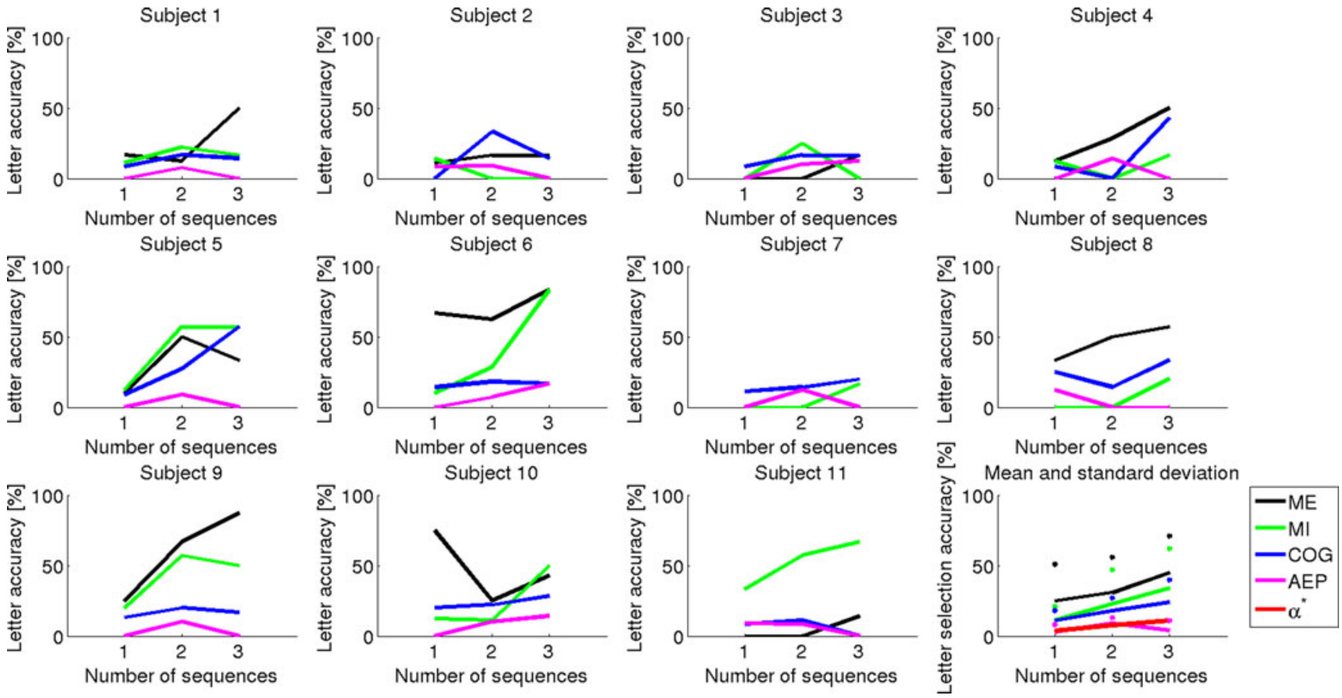

Fig. 3. Shown here is letter selection accuracy, calculated as the percentage of correctly "guessed" letters (i.e., letters with highest classifier probability within a sequence). The x-axis indicates whether single sequences (i.e., for $x = 1$), sequence pairs (i.e., for $x = 2$) or sequence triplets (i.e., $x = 3$) were used to accumulate the classifier probability. Mean values and upper limits of one standard deviation (marked by an asterisk) are displayed in lower right corner for all subjects, together with the type-I error. ME / MI ... brisk feet motor execution/imagery; COG ... discrimination of the target voice's gender and comparison to the following repetition; AEP ... mental repetition of the letter; α^* ... type-I error.

Each inner cross validation (five-fold with ten repetitions) was repeated five times with randomly selected nontarget epochs (i.e., to balance the number of target and nontarget epochs), followed by an evaluation on the outer fold.

Three outer folds were employed, constructed to allow for the evaluation of both binary (i.e., target versus nontarget) as well as letter selection accuracy. The three outer folds were obtained by pseudorandomly splitting the data into roughly three equal parts as follows:

1) First outer fold was created by randomly choosing within trial sequence-triples. Given there was a total of 20 trials (i.e., letters to spell) within a condition, this resulted in approximately six sequence-triplets constructed from a total of 18 sequences.
2) Second outer fold was created by randomly choosing within trial sequence-pairs, resulting in approximately six sequence-pairs constructed from a total of 12 sequences.
3) Third outer fold was created from the remaining sequences (varying number due to artifact rejection).

For the motor tasks, we discarded the initial run used for CSP filters calculation.

4) Evaluation: Outer cross-validation folds were used to estimate both the binary discrimination accuracy (i.e., on a balanced number of target versus nontarget epochs) as well as to estimate the letter selection accuracies (i.e., on sequence-triplets, -pairs, and single sequences). The reported values are means over the three outer folds, with each outer fold evaluated five times with repeated inner cross validation.

The binary discrimination accuracy (acc_{bin}) is the percentage of correctly classified target (TP) and correctly classified nontarget epochs (TN) in each outer fold as in (1), averaged over all outer fold evaluations. The target/nontarget epoch pairs were selected from same sequences

$$\mathrm{acc\_bin} = \frac{TP + TN}{\#\mathrm{epochs}}. \tag{1}$$

We analyzed classification performance across subjects and conditions with repeated measures analysis of variance (ANOVA). The independent variable was binary discrimination accuracy, and the factor was condition (4 levels). Further analysis was done with a Bonferroni corrected paired t-tests.

The letter selection accuracy is the percentage of correctly "guessed" letters (i.e., letters with highest classifier probability within a sequence). Note that for sequence-pairs and triplets, the classifier probability was accumulated over two and three sequences, respectively.

III. Results

The results of binary discrimination accuracy for all subjects across different conditions are shown in Fig. 2. In subject 7, ME condition was discarded due to movement artifacts, that could not be removed with the artifact rejection, resulting in an overestimate of the classification accuracy. The mean and standard deviation are 71% ± 11% for ME, 66% ± 12% for MI, 63% ± 3% for COG, and 51% ± 3% for AEP condition (the

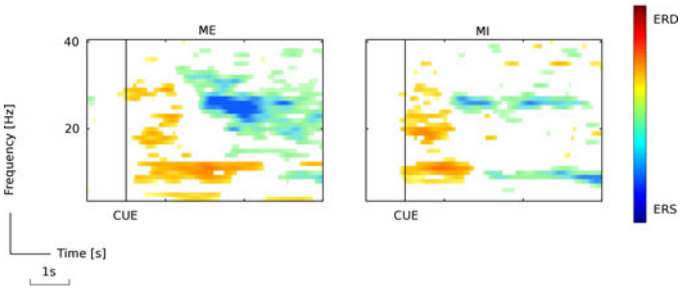

Fig. 4. Percentage of power decrease (ERD, orange) and power increase (ERS, blue) relative to a reference interval (one second pre cue) for motor execution (ME, left) and motor imagery (MI, right) condition in one subject. One orthogonal Laplacian derivation overlying Cz was used for both conditions. Only significant ($p = 0.05$, t-percentile bootstrap algorithm) power changes are shown. The CUE corresponds to the onset of target letter voice presentation.

TABLE I
ANOVA RESULT FOR CLASSIFICATION PERFORMANCE

Effect	DFn	DFd	P
Cond	3	27	0.00018

The factor condition is abbreviated as Cond. F is the value of the f-statistic, with degrees of freedom DFn and DFd.

upper 95% confidence limit of a chance result was estimated to be 60% [32]).

Table I shows the results of the ANOVA for classification performance, showing a significant effect for Condition ($p < 0.01$). The classification performance for the ME, MI, and COG condition was significantly higher than for the AEP condition (paired t-test, Bonferroni adjusted alpha levels: $\alpha < 0.01$ for ME, MI; $\alpha < 0.05$ for COG). No significant ($p < 0.05$) difference was found when comparing the ME, MI, and COG classification performance between each other.

The results of letter selection accuracy for all subjects across different conditions, and varying number of sequences used to accumulate the classifier probability, are shown in Fig. 3. Notable is a large variation in individual performance, with best performing participants achieving 88% for ME, 83% for MI, and 57% for COG. The upper limit of the letter selection accuracy chance level was estimated to be 11% (see evaluation). The nonmonotonic trend visible for the lower performing participants, as well as the mean for the AEP condition, could be explained by a lack of an underlying signal benefiting from an increased signal-to-noise ratio. The AEP condition yielded, same as in binary discrimination, random results only and thus will not be analyzed any further. Also shown in Fig. 3 are the corresponding mean and standard deviation. The type I error (i.e., α) when repeatedly testing with accumulating probabilities was estimated as $\alpha^* = 1 - (1 - \alpha)^k$, with $\alpha = 1/26$ (i.e., number of letter choices in a trial) and $k = 1, 2, 3$.

In Fig. 5, selection accuracy is reevaluated with increased time windows for ME, MI, and COG conditions, respectively. To that end, letter selections immediately before and after the target letter (i.e., 1.5 s time window being equivalent to the target letter plus one letter before and one letter after; 2.5 s time window being equivalent to the target letter plus two letters before and two letters after) are counted as correct. Pooled accuracy is obtained as percentage of all correct selections (i.e., a single percentage accuracy estimated from all of the sequence-triplets, sequence-pairs, and single sequences). Notable is a large increase in pooled accuracy for the ME and MI conditions in the

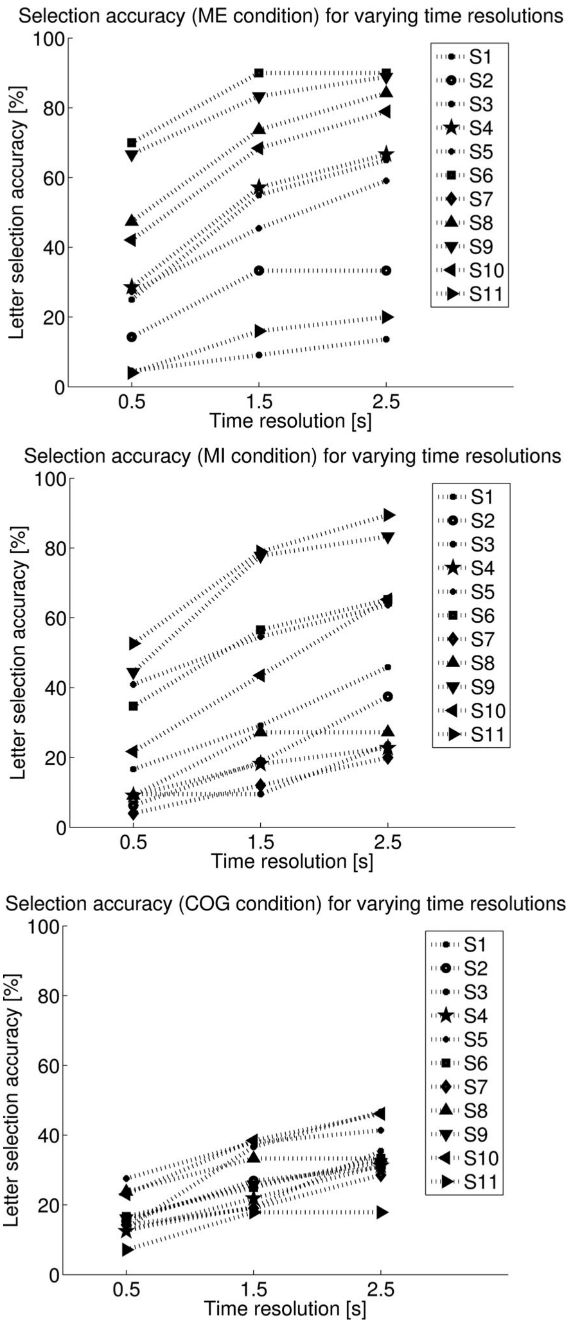

Fig. 5. From top to bottom: selection accuracy for ME, MI, and COG condition and for varying time resolutions (i.e., 1.5 s time window equals the target letter plus one letter before and one letter after, etc.). The increasing time windows simulate a decreased rate of presentation. Pooled accuracy is obtained as percentage of all correct selections (i.e., from all of the sequence-triplets, sequence pairs, and single sequences).

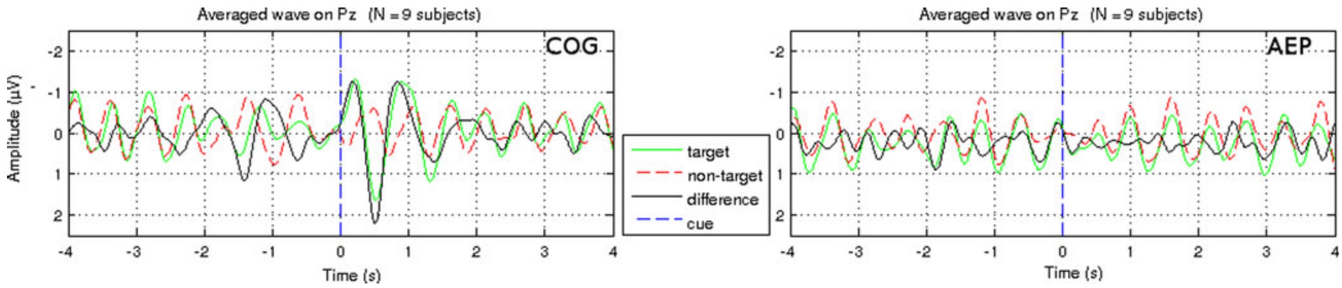

Fig. 6. Grand averaged event-related potentials (ERPs) at electrode Pz for multiple subjects, and for the COG and AEP condition. Equal number of target and nontarget epochs was averaged.

top performing subjects, and a modest increase for the COG condition.

The ERD and ERS relative to a reference interval (one second preceding the onset of a spoken target letter) for ME and MI conditions are exemplified in Fig. 4 for one subject. Visible is alpha and beta ERD during and beta ERS following the brisk feet motor execution/imagery. In both motor condition the ERD/S patterns are similar, albeit weaker in the MI condition.

In Fig. 6, grand average ERPs for equal number target and nontarget responses for the COG condition, averaged over multiple subjects at the Pz electrode position, are shown. Task-dependent modulation of early negative (around 200 ms), late positive (around 500 ms), and subsequent late negative (up to 1000 ms) component is visible.

IV. Discussion

The goal of this paper was to investigate whether induced and evoked EEG responses could enable spelling independent of muscular output through listener-assisted scanning. To that end, the results for the motor and for the COG conditions are analyzed to derive guidelines for the further development.

The motor conditions yielded the most promising results with respect to letter selection accuracy (see Figs. 3 and 5), albeit with a large variation in individual performance. Closer inspection of error distribution revealed peaks immediately before and after the target letter, indicating that the current rate of presentation (i.e., one letter pronounced every 0.5 s) might be too fast for sensorimotor rhythm-based selection. Indeed, reevaluation of selection accuracy with increased time windows (see Fig. 5, middle), simulating a decreased rate of presentation, led to a notable increase in performance, with pooled selection accuracy (i.e., estimated from all of the sequence triplets, sequence pairs, and single sequences) almost doubling for the MI condition in the top performing subjects.

Thus, the foremost guideline for further development of sensorimotor rhythm-based selection is to reduce the rate of presentation, e.g., by employing group presentation of letters and hierarchical selection.

Close inspection of grand average ERPs (see Fig. 6) for target and nontarget responses in the COG and AEP conditions, revealed modulation of several components in the COG condition: first, mismatch negativity (MMN), reflecting the preattentive change detection on the level of auditory sensory memory [33]; second, late positive component (LPC) [20], reflecting the switch of attention onto the new information; and third, late negative component, possibly reflecting reorientation back to the task-relevant information (reorienting negativity, RON) [33]. The absence of the aforementioned components in the AEP condition indicates that these modulations are task dependent for the COG condition. Whereas task dependent modulation of MMN and LPC is consistent with the BCI literature [20], modulation of RON is a novelty.

The COG condition yielded significant ($p = 0.05$), albeit moderate results with respect to binary discrimination (mean and standard deviation 63% $\pm$ 3%) and letter selection accuracy (57% for the top performing participant). While the classification accuracies for the COG condition may not seem very encouraging on the first sight, they are, in contrast to the AEP condition, accompanied by a strong physiological response (see Fig. 6). Furthermore, a monotonically increasing trend with an increase in signal-to-noise ratio can be observed on average (see Fig. 6). Given the evidence of task-dependent modulation of ERP components evident in Fig. 6, moderate results for the COG condition are likely caused by an insufficient number of sequences used to accumulate the classifier probability. Contrary to motor imagery task, reevaluation of selection accuracy with increased time windows has not led to a notable increase in performance, indicating that the current rate of presentation is not too fast. In fact, the rate of presentation could further be increased, allowing for additional sequences within a trial that could be used to accumulate the classifier probability. Thus, the foremost guideline for further development of ERP-based selection is to increase the number of sequences used to accumulate the classifier probability, e.g., by increasing the rate of presentation through partially overlapping stimuli. Notably, this issue could possibly be handled without necessarily increasing the presentation rate—the definitive method is to be determined experimentally.

The current paradigm tried to strike a balance between time requirements for induced (i.e., sensorimotor rhythm) and evoked (i.e., ERPs) responses in EEG associated with different mental tasks. As such, the primary goal was not to achieve a high, task-specific maximum information transfer rate, but to allow for an unbiased comparison between the different mental tasks. The use of different mental (i.e., motor and nonmotor) tasks was motivated by highly individually specific requirements in disabled or able-bodied persons [34]–[36]. We assumed intact cognitive abilities allowing one to understand the task requirements through verbal instructions, to attend auditory stimuli (i.e., human voice) while retaining information in working memory, and to perform the mental tasks. Whereas it is an open research question to what extent behaviorally nonresponsive patients possess these abilities, there are several case studies ([37], [38]) proving their presence at least in some individuals.

One of the weaknesses of this study is that all the 11 subjects studied were healthy volunteers and none suffered from the lock-in-syndrome. Extrapolation of research results obtained on healthy individuals to those with lock-in-syndrome and ALS is obviously fraught with risk.

V. Conclusion

We investigated whether induced and evoked EEG responses associated with motor and nonmotor mental tasks could enable spelling independent of muscular output through listener-assisted scanning, and found the most promising results with motor related tasks. We also found that a single cognitive task, related to working memory and perception of human voice, can modulate ERP components (i.e., MMN, LPC, and RON) reflecting three different stages of selective attention. These findings, as well as the recent reports that the selective attention to spoken words in auditory scanning is perceived as intuitive and easy to use in untrained participants [39], form a solid basis for further development of an EEG-based listener-assisted BCI for spelling applications.

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Appendix B

Publication resulting from master thesis

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Asynchronous steady-state visual evoked potential based BCI control of a 2-DoF artificial upper limb

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Abstract

A brain-computer interface (BCI) provides a direct connection between the human brain and a computer. One type of BCI can be realized using steady-state visual evoked potentials (SSVEPs), resulting from repetitive stimulation. The aim of this study was the realization of an asynchronous SSVEP-BCI, based on canonical correlation analysis, suitable for the control of a 2-degrees of freedom (DoF) hand and elbow neuroprosthesis. To determine whether this BCI is suitable for the control of 2-DoF neuroprosthetic devices, online experiments with a virtual and a robotic limb feedback were conducted with eight healthy subjects and one tetraplegic patient. All participants were able to control the artificial limbs with the BCI. In the online experiments, the positive predictive value (PPV) varied between 69% and 83% and the false negative rate (FNR) varied between 1% and 17%. The spinal cord injured patient achieved PPV and FNR values within one standard deviation of the mean for all healthy subjects.

Keywords: brain-computer interface (BCI); canonical correlation analysis (CCA); electroencephalogram (EEG); hand and elbow neuroprosthesis; neuroprosthesis; steady-state visual evoked potential (SSVEP).

Introduction

A brain-computer interface (BCI) provides a direct connection between the human brain and a computer [30, 32]. BCIs based on sensorimotor rhythms (SMRs), slow cortical potentials, steady-state visual evoked potentials (SSVEPs), and P300s have been used for communication, and SMR BCIs have been most promising for motor control [2, 4, 24]. By using motor imagery induced event-related (de)synchronization (ERD/ERS) of SMR, two tetraplegic patients with only residual muscle activity in parts of their upper limbs learned to open and close their paralyzed hands with the aid of functional electrical stimulation [18, 19, 25].

One disadvantage of most of the SMR BCIs is that they require training. However, this depends on subjects' previous BCI experience, electrode montage, filters, and classification procedures. In contrast to SMR BCIs, an SSVEP-based BCI requires little or no training.

SSVEPs are elicited by presenting repetitive visual stimuli faster than 6 Hz and can be recorded at occipitally mounted electroencephalogram (EEG) electrodes [29]. One of the first SSVEP BCI systems was developed in 1995 and was used to control the roll position of a flight simulator by using two flickering light sources [14]. Results of a similar experiment and also an experimental design where the task was to select virtual buttons on a computer screen was reported previously [15]. In one study [3] an SSVEP BCI that helped users to input phone numbers was designed and implemented, and in another study [5] an SSVEP BCI-based environmental controller for people with motor disorders was presented. In other reported experiments [16], an asynchronous (i.e., independent of external cues) four-class BCI based on SSVEPs was used to control a two-axis electrical hand prosthesis.

The frequency components of SSVEP in EEG are usually obtained by analyzing the power spectral density of the EEG, e.g., by means of the discrete Fourier transformation (DFT). Stimulation for an SSVEP-based BCI can be delivered via light emitting diodes (LEDs) or via targets presented on a monitor that flicker at different frequencies. These flickering stimuli typically elicit occipital oscillations at harmonics of the stimulating frequency, as well as the fundamental frequency itself [6, 29]. By using the first three SSVEP harmonics, a significant increase in classification accuracy can be achieved [17]. Furthermore, a lock-in analyzer system can increase classification accuracy in a four-class SSVEP-based BCI relative to the DFT [16].

The canonical correlation analysis (CCA) technique, first described in 1936 [8], captures the interrelationship between several predictor and several response variables. CCA transforms the original variables so that the resulting values correlate as much as possible with each other. Lin et al. [11] applied CCA to analyze the frequency components of SSVEP in EEG. Reported accuracies of the approach were higher than those using power spectral density based analysis. Furthermore, it was mentioned that the use of multiple channels might have contributed to these improved results by creating greater robustness against noise. One notable exception was stated – if the area that generated the SSVEP

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is very small, the use of broadly spaced EEG channels in the CCA approach can increase noise and thus reduce the recognition accuracy. Also, a possible improvement from using higher harmonics was suggested. Recently, online experiments with a cue-based multichannel SSVEP-based BCI system using the CCA method were conducted [1], in which subjects were instructed to focus on one of six stimuli. The reported BCI system achieved an average accuracy of 95.3% and an information transfer rate of 58 ± 9.6 bit/min.

Problems in the synchronous mode of operation lie in the impact of the cue stimuli on EEG. In one study [26], inspection of central mu and beta rhythms revealed short-lived brain state after cued motor imagery in naive subjects. Others [12] stated the necessity of asynchronous BCI for applications requiring constant user attention and irregular user-initiated control, e.g., monitoring a process and adjusting a control level when required. These types of applications are usually not communication applications but control applications. Such asynchronous control applications are widely being acknowledged as the most natural mode of interaction for neuroprosthesis control [13]. To our knowledge, no previous study has evaluated an online SSVEP BCI (with real-time feedback) based on frequency recognition using CCA in asynchronous mode of operation.

The aim of this work was the realization of an asynchronous SSVEP BCI, based on the CCA method, suitable for the control of a 2-degrees of freedom (DoF) hand and elbow neuroprosthesis. To this end, a virtual and a robotic 2-DoF limb are used as a feedback. By first training with a virtual and subsequently with a robotic feedback, the performance of the participants increases compared to training with a robotic feedback only [7]. We hypothesized that by selecting EEG channels for each subject, which discriminate best between intentional control (IC) and non-intentional control (NC) states, self-paced control of a 2-DoF hand and elbow neuroprosthesis can be obtained. A further goal was to evaluate the system in a spinal cord injured (SCI) patient. Here, we expect no difference in performance between healthy individuals and the SCI patient.

Methods

Stimulation unit (SU)

Visual stimulation was delivered via a custom-made stimulation unit, consisting of two red LED bars ($2\ \text{cm} \times 5\ \text{cm}$), arranged in one row, with a center to center distance of 7.5 cm. During all experiments the LED bars of the SU were programmed to flicker at 8 and 13 Hz, respectively. The duty to period ratio was 1/2.

Subjects

Two studies were carried out with eight healthy subjects (26.5 ± 3 years, 5 males and 3 females) and one tetraplegic patient. The tetraplegic patient was a 34-year-old man who had a spinal cord injury in April 1998. He was affected by a complete motor and sensory lesion below C5 and an incomplete lesion below C4 [25]. The study was approved by the local ethics committee of the Medical University of Graz.

EEG recording

In experiments without feedback, EEG was recorded via 21 Ag/AgCl electrodes placed in three rows and seven columns over the occipital part of the head, with O1, Oz, and O2 being the middle posterior electrode positions. The distance between electrodes was 2.5 cm. Reference and ground electrodes were placed at the left and right mastoids, respectively. Impedances were kept below 5 kOhm. The EEG amplifier (g.BSamp, g.tec Guger Technologies, Graz, Austria) used a bandpass filter of 0.5–100 Hz with a sensitivity of 100 μV. The notch filter (50 Hz) was on and the sampling rate was fs = 250 Hz. Subjects were seated approximately 1 m in front of the stimulation unit and the monitor, which was located in an electrically shielded and slightly dimmed room.

In online BCI experiments with feedback, EEG was recorded by a set of individually selected electrodes (six for healthy subjects). The time available for the measurement with the patient was limited and there was not enough time to allow the search for optimal electrode positions to complete. Therefore, the search was halted as soon as the best combination of five channels was found, which were then used in the online experiment. Reference and ground electrodes were placed at the left and right mastoid, respectively. The EEG amplifier settings were set as described above. Subjects were seated approximately 1 m in front of the experimental setup consisting of the stimulation unit, robotic limb feedback, and the slightly elevated monitor.

Experimental paradigms

Experiments without feedback The cue-based calibration experiment without feedback consisted of eight runs containing 40 trials each and were separated by breaks to avoid fatigue. Each trial lasted 6 s. Subjects were instructed to focus on one of the flickering lights, placed below the screen, according to the cue-based training paradigm [23]:

- At the beginning of each trial ($t = 0$ s), a fixation cross was presented at the center of the monitor and remained visible on the screen until the end of the trial.
- From $t = 0$ to 2 s, the participants had to look at the fixation cross.
- From $t = 2$ to 6 s, an arrow appeared indicating at which flickering light the participants should focus on.
- At $t = 6$ s, a short tone indicated the end of the trial.

Each flickering light was randomly indicated 20 times within each run resulting in 160 trials for each of the two classes.

Artificial limb feedback To provide feedback in the online experiment, a 2-DoF robotic and a virtual limb (Figure 1) were used. For the robotic limb, the 8-Hz flickering light toggled the gripper state between open and closed, and the 13-Hz flickering light toggled the elbow state between flex-

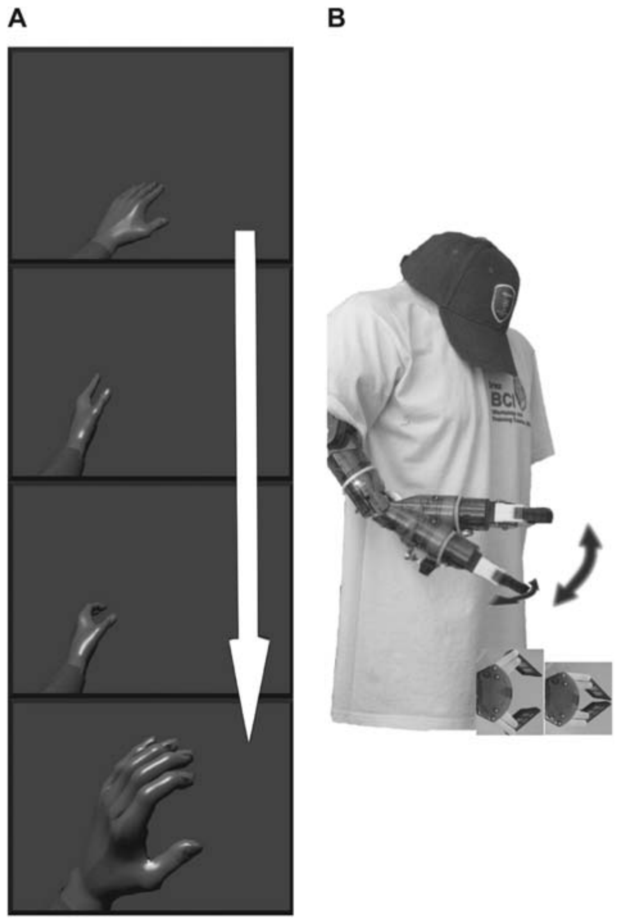

Figure 1 Virtual (A) and robotic (B) limb feedback. Both feedback approaches simulated the movement sequence usually executed when reaching for and drinking out of a glass.

ion and extension. For the virtual limb, the 8-Hz flickering light toggled the hand movement animation, and the 13-Hz flickering light toggled the elbow movement animation. In addition, the virtual limb simulated the so-called palmar grasp. The virtual limb feedback was created using the 3-D content creation software Blender (Blender Foundation, Amsterdam, Netherlands) and was visualized and animated using the Qt4 application and user interface (UI) framework (Trolltech, Oslo, Norway).

Online BCI experiments with feedback The online BCI experiments with feedback were conducted after the cue-based calibration experiment on separate days, excluding the patient, who participated in both of the experiments on the same day.

The online experiment consisted of eight runs, separated by breaks to avoid fatigue. During the first four runs, the subjects controlled an animated virtual limb by looking at the flickering lights. During the last four runs, subjects controlled the robotic limb. The subjects were verbally instructed to perform a predefined movement sequence: hand open, hand close, elbow flexion, elbow extension, hand open, and hand close.

The performance of the SSVEP BCI in the online experiment was evaluated during the IC and NC periods (Figure 2). At the beginning and before the end of every run, a 1-min NC period occurred. Between these two NC periods, subjects had to perform the above mentioned movement sequence twice (IC). They were verbally instructed to perform it each time the IC period started. These two movement sequences were separated by a 30-s NC period. There was no time limit on the duration of the IC period. After this procedure, subjects were asked whether they preferred the virtual limb feedback or the robotic limb feedback to monitor their preference.

Data processing

Canonical correlation analysis (CCA)

The use of CCA in EEG signal analysis is based on the premise that the measured SSVEP will contain the same frequency as the stimulus signal [11]. CCA coefficients can be calculated using the EEG signals recorded from multiple channels as one set of variables (***X***), and all stimulus frequencies and associated harmonics (***Y***, in our experiments first, second and third harmonics) as another set of variables [see Eq. (1), Figure 3].

$$\boldsymbol{Y}(t)=\begin{pmatrix}\sin(2\pi ft)\\ \cos(2\pi ft)\\ \sin(4\pi ft)\\ \cos(4\pi ft)\\ \sin(6\pi ft)\\ \cos(6\pi ft)\end{pmatrix} \tag{1}$$

The goal of CCA is to find such weight vectors $\boldsymbol{v}$ and $\boldsymbol{w}$ so that the resulting $\hat{\boldsymbol{x}}$ and $\hat{\boldsymbol{y}}$ values correlate with each other as much as possible [see Eq. (2)].

$$\begin{aligned}\hat{\boldsymbol{x}}&=\boldsymbol{Xv}\\ \hat{\boldsymbol{y}}&=\boldsymbol{Yw}\end{aligned} \tag{2}$$

The canonical correlation (***CR***) is then the product-moment correlation between the $\hat{\boldsymbol{x}}$ and $\hat{\boldsymbol{y}}$ values [see Eq. (3)].

$$\boldsymbol{CR}=\boldsymbol{\rho}_{\hat{x}\hat{y}} \tag{3}$$

In the EEG signal analysis, the frequency with the largest ***CR*** is the stimulus frequency of the recorded SSVEP.

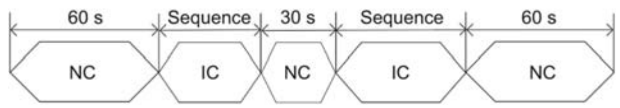

Figure 2 Evaluation procedure. An online experiment was carried out to evaluate the performance of the CCA classifier, whereby a run was divided into self-paced intentional control (IC) and timed non-intentional control (NC) periods. Each sequence consisted of six movements.

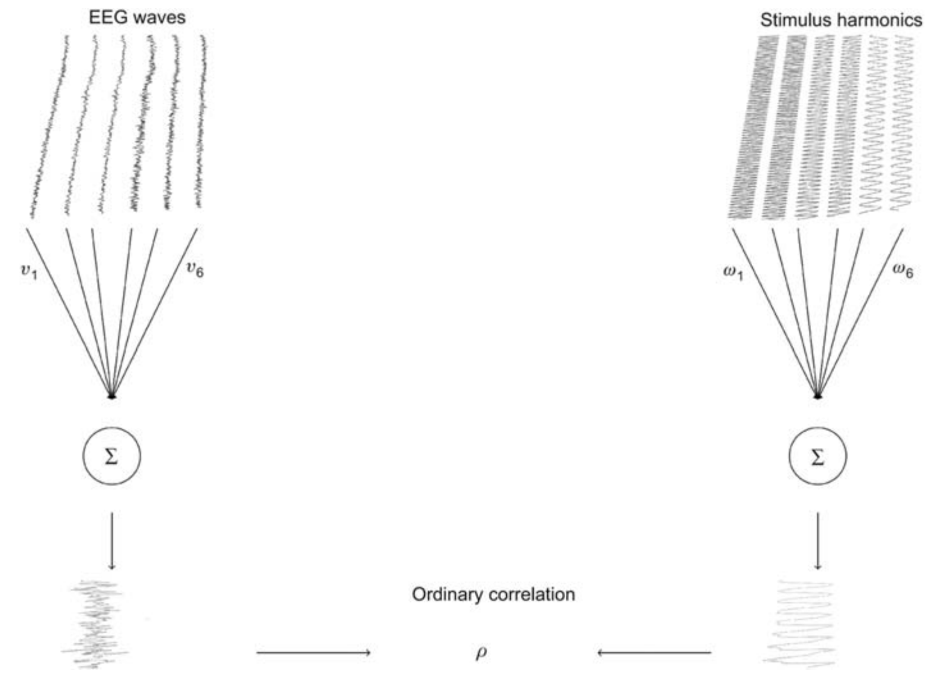

Figure 3 CCA in EEG signal analysis illustrated – modified from [11]. Using EEG signals, recorded from multiple channels, as one set of variables and stimulus frequency and associated harmonics as another set of variables, CCA coefficient can be calculated.

Offline analysis

Test and training set Following the cue-based calibration procedure, a single-trial EEG epoch was derived in association with each cue, beginning 2 s prior to the cue onset and lasting for 6 s. These epochs were then split into equal sized test and training sets. Overlapping time segments (80% overlap, between two consecutive time segments, for the training sets and 96% for the test sets) of 1 s, obtained from the EEG data from each trial, were analyzed using CCA.

Percentage accuracies For every time segment CCA yielded the recognized frequency, which in this case was either the 8- or 13-Hz. The number of how many times the same frequency was recognized for the time segment at a given time point across all different single trial EEG epochs was noted. For each of the different time segments this number was divided through the number of all single trial EEG epochs yielding percentage accuracies.

CCA thresholds CCA thresholds were used in the online experiments to determine whether and at which stimulus the participant is focusing his/her attention on. These percentage thresholds, one for each of the stimulation frequencies, were calculated as follows:

- Previously obtained percentage accuracies were averaged in time for two different time intervals: the reference interval contains accuracies for time segments with center points between and including second 0.5 and 1.5; the activation interval contains accuracies for time segments with center points between and including second 4.5 and 5.5.
- For each of the stimulation frequencies the corresponding reference and activation interval were added and divided by two, yielding the percentage threshold to be used in the online experiments. The values of these thresholds were determined from the performance of CCA on the test set for the selected channels.

Feature selection A feature selection was applied to select the EEG electrode channels. The criteria for selection was a combination of maximizing the accuracy in the period after the cue onset, while maintaining a chance level before the cue onset, as indicated by the classification accuracy of CCA in single EEG trials.

The applied approach was based on the wrapper approach to feature selection [28]. This approach to feature selection uses the classifier as the evaluation function to select a subset of the complete feature set that yields a high accuracy. In this case, CCA was used as the classifier and the complete feature set consisted of the 21 EEG channels recorded in experiments without feedback.

The simplest methods based on the wrapper approach to feature selection are the sequential forward selection (SFS) and the sequential backward selection (SBS). The SFS starts with the empty set and adds features one at a time. In contrast to the SFS, the SBS starts with the complete feature set and removes features one at a time. Both of these methods endure the so-called nesting effect: once a bad choice has been made, there is no way to undo it in the following steps. The sequential floating forward selection (SFFS) solves the nesting problem that appears in SFS and SBS by removing previously added features and by adding previously removed features [28].

A modified SFFS was used as a channel selection algorithm. This algorithm, applied on a rectangular channel arrangement with three rows and seven columns, works as follows:

1. In an initial step, training combinations of four channels, with two channels in each row, are analyzed, and the one with the single largest CCA value is selected. If there are multiple best solutions, other parameters, such as mean CCA accuracy value, are used to discriminate between channel combinations.
2. In a step forward, the current best combination of n_F (number of channels in a forward step, $n_F=4$ in the first step forward) channels is expanded (one neighbor at a time) with all of its neighbors, yielding several combinations of n_F+1 channels. The precise number of these combinations depends on the value of n_F and on the position of the previously selected channels. CCA values of these combinations are analyzed using the aforementioned criteria, and the best combination is selected. If its value is better than the value of the current best channel combination, then it is selected as the new current best; otherwise, the algorithm continues with the next step backward.
3. In a step backward, the current best combination of n_B (number of channels in a backward step, $n_B=5$ in the first step backward) channels is analyzed. CCA values of all possible combinations of n_B-1 channels are analyzed using the aforementioned criteria, and the best one is selected. If its value is better than the value of the current best channel combination, then it is selected as the new current best; otherwise, the algorithm continues with the next step forward.
4. The whole procedure is repeated until the desired number of channels (empirically set to 6) is selected or until no further improvement is possible.

Online analysis

Classification In the online classification procedure, CCA was applied every 0.25 s on a sliding window of 1-s length. The output of the CCA classifier, that is the recognized SSVEP frequency, was stored in a circular buffer containing the CCA classifier outputs for the last 8 s. If the ''online'' percentage accuracy, calculated separately for each one of the stimulation frequencies from the circular buffer, exceeded the corresponding percentage threshold, then this frequency could be detected as the one the participant is focusing on. For example, for a percentage accuracy threshold of 50% for the 8-Hz stimulus, at least half of the recognized frequencies in the circular buffer had to be 8 Hz. For this case, a decision could have been made in as short as 4 s. The dwell (do well) time parameter placed an additional constraint on the online classification, namely that the same stimulus frequency must be recognized during a predefined time period to be eligible for a command selection. The same dwell parameter of 1.5 s, or 6 recognitions, was used for all participants.

Evaluation True positive (TP) and false negative (FN) decisions were detected from the movement sequence during the IC periods, and false positive (FP) decisions were detected during the NC periods. From these numbers, the positive predictive value [PPV, see Eq. (4)] and the false negative rate [FNR, see Eq. (5)] were calculated. A PPV = 100% means that all the commands were intended by the subject, whereas a FNR = 0% means that all intended commands were detected. The evaluation was performed in the error ignoring mode [10], meaning that the artificial limb only accepted commands in the correct order, and incorrect commands were ignored.

$$\mathrm{PPV} = \mathrm{TP}/(\mathrm{TP}+\mathrm{FP}) \tag{4}$$

$$\mathrm{FNR} = \mathrm{FN}/(\mathrm{TP}+\mathrm{FN}) \tag{5}$$

Results

Eight healthy subjects and one tetraplegic patient could control the 2-DoF artificial limbs with the asynchronous SSVEP-based BCI. To further evaluate the 2-DoF artificial limb control, TP and FN decisions were obtained from the IC state, and FP decisions were obtained from the NC state (Table 1). From these numbers, the PPV and the FNR were calculated (Figure 4). The PPV varied between 69% and 83% (76 ± 4% for all nine participants), and FNR varied between 1% and 17% (8 ± 5%).

Offline accuracies were obtained from the cue-based calibration experiment (Table 2). The detailed results obtained from the EEG data recorded in experiments without feedback indicate different levels of accuracy, before and after the cue onset, when comparing the two stimulus frequencies. Therefore, different CCA thresholds were used for the 8-Hz

Table 1 True positives (TPs), false negatives (FNs), and false positives (FPs) for all subjects and all runs.

Participant	TP	FN	FP	Runs
S1	96	8	20	4 (4)
S2	96	1	22	4 (4)
S3	96	2	25	4 (4)
S4	96	8	29	4 (4)
S5	96	20	31	4 (4)
S6	96	10	33	4 (4)
S7	96	15	39	4 (4)
S8	96	8	43	4 (4)
S	96	9	30.25	Total
	12	1.13	3.78	Per run
P1	48	5	15	3 (1)
P	12	1.25	3.75	Per run

TP and FN movement selections were obtained from the control state, and FP movement selections were obtained from the non-intentional control state. The ''Runs'' column displays the number of runs conducted with the robotic (virtual) limb feedback. S is the mean of S1–S8.

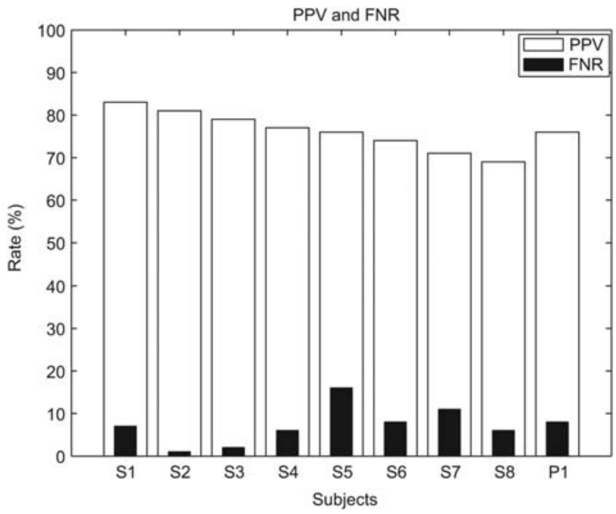

Figure 4 Positive predictive value (PPV) and false negative rate (FNR) for online experiments using the CCA method.

(83±6% in nine participant-specific thresholds) and 13-Hz (50±10%) stimulus frequencies (Table 2). Figure 5 shows the distribution of EEG channels, individually selected from EEG data recorded in experiments without feedback and used in online experiments with feedback. The channel selected most often was O1.

The average number of FPs per minute of NC period varied between 1.0 and 2.1 (1.5±0.3 average FPs per minute of NC period for all nine participants), and the average number of FNs per movement sequence varied between 0.06 and 1.25 (0.57±0.37 average FNs per movement sequence for all nine participants).

Six out of nine participants did not prefer either feedback type, and all of them stated that both feedback approaches served the purpose of simulating the desired movement sequence. One participant who preferred the robotic limb feedback described this type of feedback as being more realistic. The only participant who preferred the virtual limb feedback said it was faster and simpler than the robotic limb feedback.

Table 2 Offline accuracies calculated using first three ($ACC_{H1\text{-}3}$) and first harmonic only (ACC_{H1}), and participant-specific CCA thresholds used for the 8-Hz and 13-Hz stimulus frequencies.

Participant	ACC_{H1}	$ACC_{H1\text{-}3}$	th_8 (%)	th_{13} (%)
S1	61.7	67.9	95	30
S2	85.4	98.5	80	60
S3	81.9	92.4	85	50
S4	87.1	91.7	85	60
S5	82.8	82.9	75	60
S6	69.5	71.6	85	40
S7	88.8	92.7	85	55
S8	60.8	66.4	75	45
S	77.8	83	83	50
P1	82.1	84.8	80	50

Discussion

Our online study showed that an asynchronous SSVEP-based BCI based on frequency recognition using CCA can be used to control a 2-DoF artificial limb. In one study [21], the upper confidence limits of chance results in two-class paradigms given as 55.6% with 160 trials/class and 60% with 40 trials/class. The FNR in online experiments varied between 1% and 17% (8±5%), meaning that more than 80% of the activations were correct and thus the results are significant. The SCI patient achieved PPV and FNR rates within one standard deviation of the mean for all healthy subjects. The average bit rate, calculated from the offline accuracies using the formula from Refs. [31, 32], was 0.42 bits/trial (4.2 bits/min). The maximal bit rate achieved was 0.9 bits/trial (9 bits/min).

We assessed whether the usage of harmonic frequency components increased the accuracy after the cue onset. To this end, we employed a t-test on the percentage accuracies obtained from the cue-based calibration procedure. The average of the CCA accuracies is 83.2±11.9 for the first three harmonics and 77.8±10.9 for the first harmonic only. The CCA accuracies for the first and for the first three harmonics are significantly different ($p<0.005$). A more detailed assessment on the impact of harmonic frequency components can be found elsewhere [20]. In another study [23], a similar evaluation procedure was applied. In the aforementioned study, four subjects were trained to induce one distinctive brain pattern by motor imagery (MI) over two different durations. The results showed that participants could control grasp and elbow function with only one Laplacian EEG channel and one MI pattern. The average number of FPs per minute of NC period for the MI-based BCI varied between 0.20 and 3.10, and the average number of FNs per movement sequence varied between 1.38 and 6.50. Hence, the SSVEP and MI BCI approaches exhibited a comparable number of average FPs per minute of NC period, which varied between 1.00 and 2.11 in our SSVEP BCI. However, the SSVEP BCI averages considerably fewer FNs per movement sequence, which varied between 0.06 and 1.25.

An online, multichannel, SSVEP-based BCI system using a CCA method was recently proposed [1]. This system used nine channel locations in the occipital and parietal lobes and

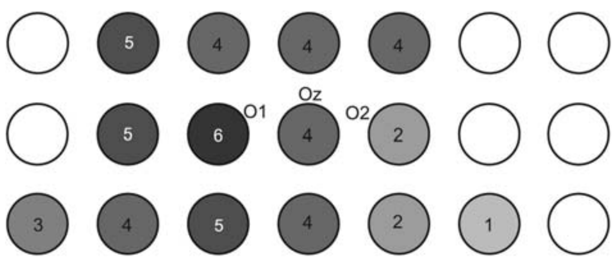

Figure 5 The distribution of EEG channels, individually selected from EEG data recorded in experiments without feedback. The frequency of selection is encoded as a color (from bright to dark, bright equals zero, and dark the highest possible value). The numbers indicate how often each EEG channel contributed to the best accuracy.

a window length of 2 s based on the first harmonic of the stimulating frequency. Furthermore, it was suggested that subject-specific channel selection and parameter optimization are not needed. Our online SSVEP-based BCI system used six channel locations in the occipital lobes, with a window length of 1 s and first three harmonic components. The classification accuracy of CCA in single EEG trials indicated that, consistent with the comments in [1], subject-specific channel selection and parameter optimization did not drastically improve the already high accuracy in the period after the cue onset. However, for most of our subjects subject-specific EEG channel selection, parameter optimization, and usage of harmonic frequency components increased the difference between the accuracy level before and after the cue onset, as reported previously [17, 20].

In one study [20], a search for optimal electrode positions in SSVEP-based BCI was conducted and an overview of the distribution of the most relevant electrodes was given. In that study, the channel Oz was very important for most subjects. In our study, the most relevant monopolar channel, that is the channel that contributed most often to the best accuracy, was O1. A possible explanation for this distribution difference could be that in the former study bipolar combinations were used and in most cases the electrode being the sink was Oz. However, in our study monopolar combinations were used with O1 being the source.

To be useful outside of the lab, a BCI must allow for fast setup. Hence, the calibration time and the number of EEG channels must be minimized. Therefore, we have applied a practical approach in which the calibration for an asynchronous BCI requires less than an hour, using as few as five EEG channels. Based on this approach, an SCI patient obtained control of 2-DoF artificial upper limbs using our asynchronous SSVEP BCI, immediately after only one short (approximately 1 h) calibration session.

A potential problem arises when a SSVEP stimulus frequency overlaps with the subject's peak alpha frequency. To ameliorate this problem, we used subject-specific CCA thresholds for each frequency. Another approach would be to choose stimulus frequencies that do not overlap the subject's peak alpha frequency [9].

This study incorporates the methods and confirms the results obtained from previous studies [1, 11, 23]; furthermore, this study includes several new results, e.g., PPV and FNR. These results provide a more complete evaluation of frequency recognition based on CCA for SSVEP-based BCIs by evaluating its performance not only during the IC time but also during the NC time. These results also support our earlier suggestion that the SSVEP-based BCI, operating in asynchronous mode, is feasible for the control of a neuroprosthetic device [16].

To further improve the asynchronous control, the number of FPs can be reduced by using two BCIs, with one of the BCIs being used as the brain switch [12]. In this way, a hybrid BCI system can be created by switching, e.g., a battery of flickering lights (SSVEP BCI) on or off by using a brain switch based on sensorimotor rhythms [22, 27]. Repeatedly switching between MI and SSVEP tasks results in fewer false positives compared to the use of a flickering light as the on/off button.

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