BCCI - A BIDIRECTIONAL CORTICAL COMMUNICATION INTERFACE

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Abstract: Therapeutic methods based on efferent signals from the patients' brain have been studied extensively in the field of brain-computer interfaces and applied to paralysed and stroke patients. Invasive stimulation is used as a therapeutic tool for patients with Parkinson disease, intractable chronic pain and other neurological diseases. We give a short review of currently used applications for cortical stimulation for stroke patients and brain-computer interfaces for paralyzed patients. We propose a refined approach for stroke rehabilitation as well as the extension of the use of invasive cortical stimulation to ALS patients with an experimental setup inspired by classical conditioning to facilitate the communication with brain-computer interfaces for LIS and CLIS patients. A closed-loop system is described with sophisticated methods for the identification of recording and stimulation sites, feature extraction and adaptation of stimulation algorithms to the patient in order to design a bidirectional cortical communication interface (BCCI).

1 INTRODUCTION

Brain-computer interfaces (BCI) are a tool for communication without the need of muscle use by modulation of brain waves and brain states by the user. These modulations can be detected online or offline by feature extraction algorithms and fed to classification or regression algorithms that try to determine the intention of the BCI user. The aim of these BCI systems is to allow communication with the surrounding world even if the normal muscular communication channels are severly impaired. Possible applications can be found in the field of neuroprosthetics, for example control of a wheelchair or a robotic limb or they can be designed to enable patients to select letters in order to spell sentences (Birbaumer et al., 1999)(Donchin et al., 2000). There exist different paradigms for BCI, for example slow cortical potentials, sensory-motor rhythms or P300. A detailed description of these paradigms is found in (Birbaumer and Cohen, 2007). The signals are measured most commonly by electroencephalography (EEG), but magnetoencephalography (MEG) and blood-oxygen-level dependent functional MRI (fMRI) BCIs are also used as non-invasive methods. The advantage of an invasive approach is a better signal quality. Penetrating multi-electrode arrays are used in experimental studies, but epicortical grids are more promising in regular clinical applications because of the good tradeoff between procedural risk and signal quality.

Patients that can benefit from the use of BCIs as a communication tool might be suffering from diseases like brain stem lesion, spinal cord injury or amyotrophic lateral sclerosis (ALS). These conditions can lead to a locked-in syndrome (LIS) which means that the patient is severly impaired in his ability to interact with the outside world. Stroke patients on the other hand can use brain signals as an addition to standard rehabilitative actions such as physiotherapy (Buch et al., 2008). We propose in this paper a new approach for communication with locked-in patients as well as a therapeutic approach in stroke rehabilitation using epicortical electrical stimulation. The stimulation parameters will be adapted to the background activity that is measured before stimulus onset. Background activity is assumed to profoundly change the properties of signal transmission of neurons and thus interfere with the activity evoked by stimulation (Destexhe et al., 2003). Animal experiments have shown, that a closed-loop system for adaptation of the parameters is feasible, at least for single-electrode measurements (Brugger et al., 2008).

The paper is structured as follows: We describe in section 2 state of the BCI systems for ALS and stroke patients. Section 3 contains an overview over the therapeutic application of cortical stimulation for stroke patients. We present in section 4 our new approach for a closed-loop system in stroke rehabilitation and as an improvement for communication with ALS patients.

2 BRAIN-COMPUTER INTERFACES FOR ALS AND STROKE

2.1 ALS

Amyotrophic lateral sclerosis is an adult-onset motor neuron disease characterized by degeneration of the first and second motor neurons (Lakerveld et al., 2008). Over the course of the disease, the patient gradually loses control of the muscles, develops weakness and spasticity and dies from respiratory failure usually within a few years, unless artificially ventilated and fed. Cognitive functions are said to be spared even in the latest stages of ALS except for patients with frontal lobe dementia (Lakerveld et al., 2008). The patient might communicate in this state by controlling devices with single muscles. Therefore, a BCI can be useful to allow the patient to carry out complex tasks, for example the control of a web browser (Bensch et al., 2007) and to provide a communication channel after muscular control has been lost. There has been extensive research on the use of BCIs for ALS patients and about 75 % of these patients was able to control a BCI (Kuebler and Kotchoubey, 2007). However, none of these results could be transferred to patients in the completely locked-in state (CLIS) and not a single CLIS patient has regained communication via a BCI (Birbaumer and Cohen, 2007). Because of this, new approaches for BCIs have to be tested to train LIS patients in their use, hoping that the training effects might carry over to the CLIS state.

2.2 Stroke

Stroke is a leading cause of paralysis and disability worldwide with several hundred thousand incidents per year. The outcome of such an incident depends heavily on the location and the size of the stroke area, but is fatal in about a third of all cases during the first year after the stroke and leaves most of the surivors with persisting neurological deficits. A possible deficit is a movement impairement on the contralateral side, if the stroke affects motor areas like the primary motor cortex M1 or the supplementary motor area (SMA). Rehabilitative procedures for movement impaired stroke patients consist mostly of physiotherapy, which can lead by itself to improvements especially in lower limb functions like standing or walking. Therapy of upper limb function on the other hand still needs to be improved (French et al., 2007).

Brain computer interfaces are a promising tool to aid in the rehabilitation process of stroke patients. This idea is based on the standard BCI paradigm of motor-imagery experiments. Intuitively, the best way to improve rehabilitation is to couple the physiotherapy and the movement intention of the patient in order to get a causal relationship between the planning of the movement, which should still be possible, and the sensory feedback of the movement. One paradigm in BCI research is ‘motor-imagery’ tasks. The patient imagines movements of different limbs, for example foot, hand or tongue. This leads to a detectable event-related desynchronization of the μ-rhythm originating in sensorimotor areas (Pfurtscheller et al., 2005). In the MEG BCI study of Buch (Buch et al., 2008), patients were asked to imagine movements of the paralyzed hand which were detected by the BCI system and effected the timed openings and closings of the orthosis. The patients were able to learn to reliably control the orthosis. This ability did not lead to functional rehabilitation of the affected hand.

3 CORTICAL STIMULATION FOR STROKE REHABILITATION

Since the 1990s, non-invasive stimulation has been used on stroke patients for prognostic and diagnostic measure as well as a tool for pathophysiological research. Transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS) are the best known representatives of this group of methods.

TDCS is applied directly on the scalp with large sponge electrodes soaked in saline. A direct current of a few milliampere is applied to the electrodes. Even if most of the current travels directly through the scalp because of the low conductivity of the skull, this

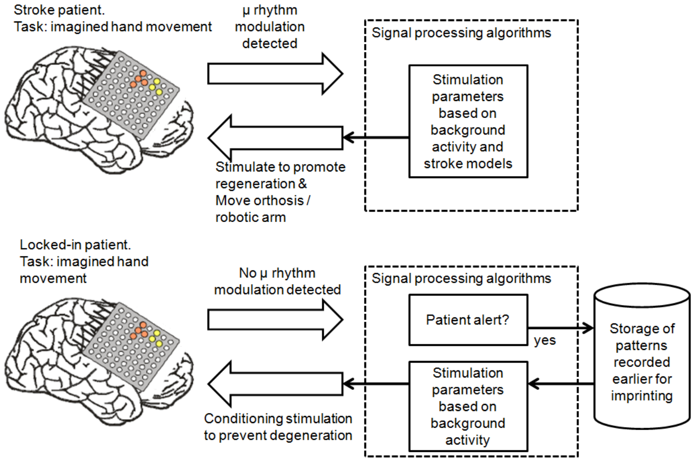

Figure 1: Overview of a stimulation paradigm for stroke patients (top) and locked-in patients (bottom).

method still influences brain tissue.

TMS on the other hand utilizes strong magnetic fields typically with a coil placed directly above the area of interest. Magnetic fields are less influenced by the low conductivity of the skull than electrical currents which leads to induction of currents in the underlying brain tissue. Measureable aftereffects of this method can last for several minutes to more than an hour, depending on the stimulation protocol used (Fitzgerald et al., 2006). It is possible to enhance or decrease cortical excitability depending on the stimulation frequency of repetitive TMS and the stimulus polarity in case of tDCS. A review on noninvasive brain stimulation can be found in (Wagner et al., 2007).

In recent years, these non-invasive techniques were applied to stroke patients to improve the success rate of standard physiotherapy (Hummel et al., 2008). A disadvantage of the application of tDCS is the loss of effect focality as the affected area is stretched out between two large electrodes. TMS is not affected by this issue, but the aftereffects of TMS are not long-lasting.

A possibly powerful alternative is invasive cortical stimulation by epicortical electrode strips. A craniotomy is necessary for the implantation, bearing the risk of infections or other complications, but first studies with implanted electrodes show promising results without serious complications (Levy et al., 2008)(Brown et al., 2006). Implantable devices which act autonomously or may be switched on and off by a handheld wand offer the possibility of cortical stimulation during physiotherapy. In 2007, Northstar Neuroscience conducted a multicenter Phase III clinical trial that tested a prototype of an implanted stimulator for stroke recovery with 146 patients (Levy et al., 2008). The results were promising, but the effect sizes were not as high as expected. The fraction of patients improving on the Upper Extremity Fugl-Meyer Scale or the Arm Motor Ability Test did not differ significantly between the physiotherapy group and the group that additionally received cortical stimulation. Our goal is to improve this result with a closed-loop stimulus control that utilizes the capacity of implanted electrodes to be used for stimulation and recording simultaneously. This opens a new field that is still unexplored to the best of our knowledge: Invasive stimulation of stroke patients for rehabilitation based on simultaneous recorded background activity. A possible stimulation paradigm is summarised in figure 1.

4 A CLOSED-LOOP SYSTEM FOR STROKE AND ALS

There are at least three issues that need to be addressed in order to provide optimized stimulation for the patient (Plow et al., 2009): (1) Identification of the target site and electrode placement, (2) models for the effect of the stimulation and (3) finding the optimal stimulation pattern depending on the disease and the patient.

4.1 Electrode placement

The target area will be determined preoperatively by fMRI guided TMS. EMG measurements will be used to track the arm movements initiated by the patient as well as those evoked by TMS. During surgery, the neurosurgeon will perform functional mapping of the area of interest on the motor cortex to decide upon the exact electrode placement. This is an improvement to earlier studies that used only fMRI to place the electrodes (Plow et al., 2009).

4.2 Modeling the current flow

The specific anatomy, the pathologic alterations and the influx of cortico-spinal fluid change the conductivity with respect to healthy tissue due to the creation of new shunting routes for the currents, which can distort the electric field produced by the stimulation (Wagner et al., 2006). Thus, we need to ensure that the desired brain regions are targeted by the stimulation (Plow et al., 2009). We will conduct modeling studies of the stimulation that show volume conduction effects by a finite element model (FEM). Standard models range in complexity from simple spherical head models to complex realistic head models based on MRI measurements. The different tissue classes are modeled with conductivities based on values measured during experiments. Models of the electrodes will be placed in the vicinity of the lesion to investigate the effect of stimulation on the tissue. The integration of areas affected by stroke based on MR measurements of the patients into the model will lead to further improvements of the accuracy of predictions on the current spread by volume conduction.

4.3 Patient-specific stimulation

4.3.1 ALS

Hypotheses, why ALS patients are not able to communicate with BCIs in the completely locked-in state include: (1) difficulty in performing the task because of cognitive deficits or lack of alertness (2) inability to modulate the cortical rhythms due to degeneration or missing feedback (3) unwillingness to cooperate (Hill et al., 2005). Especially because of (1), we need to ensure that the ALS patients are in a suitable cognitive state.

Cognitive deficits, for example frontotemporal dementia have been reported in ALS, so we will use cognitive tests to make sure that the patient is able to understand the instructions and operate the BCI. The alertness of the patient should be as high as possible during the experiments. Late-stage ALS patients can not report on their current level of alertness and thus, the researcher has to ensure that the patient is not drowsy or sleeping during the experiment. There are some peripheral measures that can be used as an indicator for alertness, for example the heart rate. A spectral analysis of the EEG or ECoG can also be helpful, as lack of alertness can be correlated to changes in the alpha and beta frequencies (Jung et al., 1997).

We include a third option: the analysis of connectivity patterns in the ECoG during BCI experiments based on phase synchronization and causality measures. It can be assumed, that the BCI performance of patients (which can be measured by the classification error of the BCI system) is to a certain degree related to their state of alertness. As an extreme example: One can expect, that the performance of a very drowsy or even sleeping person will be found to be somewhere around chance level.

With this in mind, an alertness classification to identify the relevant cortical activity and/or spectral patterns should be possible if we link the signals recorded before each trial to the BCI performance of the trial. We will use the activity or spectral patterns associated with particularly good and bad BCI performance to assess the alertness of the patient before an experimental session takes place. This evaluation will help to decide whether an experiment should be conducted, or if additional methods should be used to stimulate the alertness of the patient.

Degeneration of nervous tissue and cortical connections in ALS may stem from two processes: On the one hand direct pathological degeneration that prevents the patients from controlled use of their muscles and on the other hand the missing feedback due to the underused muscles. Our theory here is: if the patient is not able to affect his environment, the missing feedback leads to functional deterioration. As a result, the patient is unable to reactivate these connections which has a negative effect not only on muscle control, but might also impair his ability to imagine muscle movement for a BCI based on μ rhythm modulation (Pfurtscheller et al., 2005).

P300 BCIs and slow cortical potential BCIs rely on visual stimulus presentation and visual feedback respectively. The inability of ALS patients in CLIS to operate these types of BCI may stem from the fact that eye focussing is also affected by the disease (Birbaumer and Cohen, 2007). Thus, the visual system is not a good communication channel for ALS patients. There exist auditory P300 systems, but their efficiency for CLIS patients has not been tested yet. Our hypothesis here is, that feedback applied by cortical stimulation to the patient's brain can also be used to counter the effects of neural degeneration.

Depending on the scope of control the stimulation has over the evoked activity in terms of amplitudes and duration, we may be able to imprint cortical activity that was measured in earlier sessions of the same patient. This is a potentially interesting approach for the improvement of communication with ALS patients: When they have learned to operate a BCI in the locked-in state, we will store the relevant activity patterns for later use. If the BCI performance drops during the transition from LIS to CLIS, imprinting of the patterns recorded earlier can be considered as a form of classical conditioning and may slow down the functional deterioration.

If we are not able to perform the imprinting with sufficient precision, a simpler approach also inspired by classical conditioning is still feasible. We will generate two stimulation patterns for each patient, one representing 'No', the other one 'Yes'. True and false statements can then be used in conjunction with the respective stimulation pattern to condition the patient to involuntarily modulate brain states in the absence of stimulation. This provides the patient with a binary communication device.

While the neurosurgical procedure, the presence of the grid in the skull and the electrical stimulation imposes a risk on the patient, the inability of current BCIs to establish a communication channel with CLIS patients enforces the test of alternative approaches.

4.3.2 Stroke

The experimental setup for stroke patients will include the hand orthosis used in (Buch et al., 2008) and a robotic arm to move the arm of the patient. The patient will imagine movements of the paralyzed hand that are identified by a BCI system. If a hand movement imagination is detected, the orthosis opens or closes the hand of the patient, while elbow or shoulder movement imaginations trigger movements of the robotic arm. Additionally, electrical cortical stimulation is applied to the ipsilesional cortex. We will use it to enhance cortical excitability near the lesion in the first patients to promote regeneration. As a refinement to existing stroke studies like (Levy et al., 2008), the stimulation electrodes and parameters will depend on results of functional mapping, volume conduction modeling and the measured background activity.

If most of the brain tissue associated with upper limb function is destroyed by the stroke, cortical stimulation can be used to condition unaffected ipsilesional motor cortex areas to upper limb movements. The feasibility of this was shown by (Jackson et al., 2006) with intracortical microstimulation in macaque monkeys.

4.3.3 Stimulation parameters

Stimulation for cortical mapping or motor cortex stimulation for patients with intractable chronic pain consists of trains of short pulses, applied with frequencies around 50-100 Hz (Brown, 2001)(Franzini et al., 2003), which was found in animal studies to be a frequency range that enhances local cortical excitability (Teskey et al., 2003). Frequencies of 50 or 100 Hz were also used in the Northstar Neuroscience multicenter stroke study.

As the space of all possible stimulation patterns is very high, especially if one takes into account stimulating on multiple electrodes at the same time with a possibly free form stimulus, systematically testing all patterns on patients is out of the question. Thus, we will start with standard stimulation paradigms and record the effects of the stimulation simultaneously with the ECoG electrodes in order to analyse them and improve the stimulation in later experiments.

We use these first experiments to investigate the parameters that establish a functional relationship between the recorded data before the stimulation, the delivered stimulus and the stimulus evoked potentials. This connection between stimulation parameters and the cortical evoked potentials will then be used to construct a closed-loop system (Brugger et al., 2008). It will enable us to adapt the stimulation parameters to the ongoing activity and will allow prespecified target activities to be evoked by adaptive stimulation.

5 CONCLUSION

We propose here an extension to classical brain-computer interfaces that enhances the afferent pathway to the patient's brain using electrical stimulation by epidural electrodes controlled by a closed-loop system for recording, feature extraction and stimulation. It is summarised in figure 1. We believe, that our sophisticated approach for the placement of the epidural electrodes, the stimulation patterns used and, in case of stroke patients, the physiotherapy will lead to therapeutic improvements for stroke patients compared to standard physiotherapy and first studies on applications of cortical stimulation for patients. Current noninvasive BCI methods were not able to establish a communication channel with CLIS patients up to this date. Because of this are ALS patients a second target group of our bidirectional cortical communication interface. They might benefit by an improved ability to control brain-computer interfaces even in the completely locked-in state due to the direct interface for feedback to the patient's brain which does not rely on possibly impaired sensory systems.

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