Functional electrical stimulation driven by a brain–computer interface in acute and subacute stroke patients impacts beta power and long-range temporal correlation

Johanna Krueger[1], Richard Krauth[1], Christoph Reichert[2,3], Serafeim Perdikis[4], Susanne Vogt[5],
Tessa Huchtemann[6], Stefan Dürschmid[2,3], Almut Sickert[7], Juliane Lamprecht[7], Almir Huremovic[7,8],
Michael Görtler[5], Slawomir J. Nasuto[9], Robert T. Knight[10,11], Hermann Hinrichs[2,5], Hans-Jochen Heinze[2,12], Sabine Lindquist[13],
Michael Sailer[7], Jose del R. Millán[14,15], Catherine M. Sweeney-Reed[1,3]

[1]Neurocybernetics and Rehabilitation, Dept. of Neurology, Otto von Guericke University, Magdeburg, Germany
[2]Leibniz Institute for Neurobiology, Magdeburg, Germany
[3]Center for Behavioral Brain Sciences (CBBS), Otto von Guericke University Magdeburg, Germany
[4]School of Computer Science and Electronic Engineering, University of Essex, Colchester, United Kingdom
[5]Dept. of Neurology, Otto von Guericke University Magdeburg, Germany
[6]Dept. of Neurology, University Hospital Münster, Münster, Germany
[7]Neurorehabilitation Centre, Median Hospital, Magdeburg, Germany
[8]Dept. of Neurology, Ingolstadt Hospital, Ingolstadt, Germany
[9]Biomedical Engineering, University of Reading, Reading, UK
[10]Helen Wills Neuroscience Institute, University of California – Berkeley, Berkeley, USA
[11]Dept. of Psychology, University of California, Berkeley, Berkeley, USA
[12]University Hospital Magdeburg, Otto von Guericke University Magdeburg, Magdeburg, Germany
[13]Dept. of Neurology, Pfeiffersche Stiftung, Magdeburg, Germany
[14]Dept. of Electrical and Computer Engineering, The University of Texas at Austin, Austin, USA
[15]Dept. of Neurology, The University of Texas at Austin, Austin, USA

Abstract— **Functional electrical stimulation (FES) is a standard rehabilitation approach applied by therapists to aid motor recovery in a paretic limb post-stroke. Information pertaining to the timing of a movement attempt can be obtained from changes in the power of oscillatory electrophysiological activity in motor cortical regions, derived from scalp electroencephalographic (EEG) recordings. The use of a brain–computer interface (BCI), to enable delivery of FES within a tight temporal window with a movement attempt detected in scalp EEG, is associated with greater motor recovery than conventional FES application in patients in the chronic phase post-stroke. We hypothesized that the heightened neural plasticity early post-stroke could further enhance motor recovery and that motor improvements would be accompanied by changes in the motor cortical sensorimotor rhythm after compared with before treatment. Here we assessed clinical outcome and changes in the sensorimotor rhythm in patients following subcortical stroke affecting the non-dominant hemisphere from a study comparing timing of FES delivery using a BCI, with a Sham group, receiving FES with no such temporal relationship. The BCI group showed greater clinical improvement following the treatment, particularly early post-stroke, and a greater decrease in beta oscillatory power and long-range temporal correlation over contralateral (ipsilesional) motor cortex. The electrophysiological changes are consistent with a reduction in compensatory processes and a transition towards a subcritical state when movement is triggered at the time of movement detection based on motor cortical oscillations.**

I. INTRODUCTION

Stroke is among the leading causes of motor disability [1]. Functional electrical stimulation (FES) is commonly provided to the affected limb to facilitate movement attempts as a part of rehabilitation programs to promote motor recovery. Recent studies have shown greater motor recovery in chronic stroke patients when FES is delivered tightly temporally bound to movement attempts using a brain–computer interface (BCI) [2], [3]. Providing visuo-proprioceptive feedback in a narrow time window with the movement attempt is thought to assist in re-establishing corticomuscular connectivity. The precise timing of movement attempts can be derived from the oscillatory power in electroencephalographic (EEG) signals recorded over the motor cortex. The sensorimotor rhythm of electrical activity in motor cortical regions oscillates in the alpha (8-12 Hz) and beta (13-30 Hz) frequency ranges. Movement is reliably associated with event-related desynchronization (ERD), or power reduction, and event-related synchronization (ERS), or power increase, of these oscillations [4]. These changes in power arise not only during movement preparation and execution, but also when a movement is attempted [5]. As a result, they are suitable for use

not only in patients with mild paresis, but also in those with complete paralysis. Using EEG data recorded during an initial training session involving movement attempts and rest, a classifier is trained to identify movement attempts for an individual patient. It is subsequently used online during the treatment sessions to detect attempted movement, providing the timing for FES delivery to support or generate actual movement. The classifier features comprise the locations of the scalp EEG electrodes and the oscillatory frequencies at which the greatest differences are observed between sensorimotor rhythm power during movement attempts compared with rest.

The amplitude of alpha and beta oscillations shows not only intermittent fluctuations (ERD/ERS) associated with movement, but also long-range temporal correlation (LRTC), which differs during different motor tasks and compared with rest [6], [7]. LRTC can be considered as a type of electrophysiological memory [7]. Physiological memory of previous activity is thought to develop and persist in neuronal networks through continuous modification of ongoing oscillations, as a result of recurrent interactions between ongoing activity and stimulus-induced changes in activity [7]. In this way, the past continues to influence future activity, with somatosensory stimuli resulting in evoked neural activity, which affects functional connectivity patterns [7]. This memory can be indexed by LRTC, or a slower than exponential decay of autocorrelation. The amplitude envelope of alpha and beta oscillations displays power-law decay of autocorrelation over hundreds of seconds, suggesting a self-organized dynamical critical state [7]. LRTC is considered to facilitate information transfer in neuronal networks [8], optimizing information storage capacity [9] and enabling rapid adaptation to cognitive processing demands [10]–[12]. Activity-dependent plasticity leads to cumulative modifications in network functional connectivity, which could provide the physiological mechanism underlying the power law correlations in ongoing oscillatory neuronal network activity, influencing future recruitment of neurons to engage in specific oscillatory networks [7]. We hypothesized that tight temporal coupling between ongoing oscillatory power and the somatosensory feedback instantiated by a BCI-driven FES delivery concomitant with movement attempts would result in alterations in LRTC following a rehabilitation program involving BCI-FES.

Here we compared electrophysiological correlates of movement or movement attempts after an approximately three-week rehabilitation program with those before treatment, contrasting a patient group receiving FES timed using a BCI (BCI group) with a Sham group, who also received FES, but with no temporal relationship to movement attempts as determined from the patients' EEG signals. The patients were a subgroup of the Magdeburg patient cohort in a multi-center international study (German Clinical Trials Register: DRKS00007832; DRKS00011522). To enable direct comparison between the BCI and Sham groups, we analyzed the data from the largest subgroup of patients with comparable stroke lesion location: a subcortical lesion affecting the non-dominant side. The clinical evaluation included all such patients. The electrophysiological analysis included only purely right-handed patients, to enable direct comparisons. We recorded high-density EEG data before and after the three-week rehabilitation program and compared the oscillatory motor cortical rhythms in the frequency ranges selected as features for classification in the BCI. We evaluated changes in oscillatory power and LRTC in the alpha and beta frequency ranges, examining potential relationships with the features used in the classification during the treatment program.

II. METHODS

A. Patients and clinical outcome measure

Patients with a first stroke, lasting >24 hours, either < 1 month (acute) or 1-6 months (subacute) after stroke onset, with reduced/absent wrist extension, were recruited on the University Hospital Magdeburg stroke ward, or at the Neurorehabilitation Centre, Median Hospital Magdeburg, Germany. Patients and clinicians were blinded to the pseudorandom, counterbalanced BCI/Sham group allocation. Handedness was evaluated using the Edinburgh Handedness Inventory (EDI). The primary outcome measure was the Fugl-Meyer Assessment upper extremity (FMA-UE) score (max. 66) [13]. A repeated measures ANOVA was applied to examine the difference between changes in the FMA score over the program between the BCI and Sham groups.

B. Brain–computer interface

Both groups received 16 EEG electrodes over motor cortex bilaterally at each treatment session (mean number of sessions 18.8 [SD 5.7]). While the individual number of sessions varied, clinical findings were corrected for the number of sessions. A maximum of 5 sessions were performed per week, with no more than one session per day. The patients were instructed to attempt to extend their wrist on presentation of a green up-arrow on a screen or to remain at rest in response to a red down-arrow. Feedback was provided by a bar moving up or down the screen respectively. Time 0 s corresponds with the appearance of the movement cue. EEG power spectra over 8-30 Hz in 2 Hz bands, at each electrode, were calculated in 1 s windows and classified as accompanying a movement attempt or rest.

Data from a training session, comprising 4-6 blocks lasting ~5 minutes each, were used to identify up to 10 features for initial training of the classifier, based on canonical variates analysis [14]. During the therapy, continuous EEG recordings were classified online 16 times per second to detect movement attempts. On movement attempt identification, FES was delivered over two electrodes placed 5 cm apart over the extensor digitorum communis of the affected upper limb to induce wrist extension. A single therapy session comprised 3-7 blocks, according to patients' fatigue, each containing 15 movement attempts. Including breaks, therapy sessions were 10-25 minutes. The classifier was retrained weekly using the most recent therapy EEG data. The frequency of stimulations was balanced between the groups by using the classifier output of an arbitrarily selected BCI group patient for each Sham group patient.

C. Electrophysiological features

High-density EEG data were recorded before and after the therapy program from 60 channels (Fs: 500 Hz) during twelve runs, comprising 10 movement and 5 rest trials in a pseudorandom order. Custom Matlab scripts and the FieldTrip toolbox [15] were used. The data were divided into 1.7 s epochs, from the movement cue, and time-frequency decomposed (4 to 31 Hz) through convolution with 5-cycle Morlet wavelets. Spectral power was compared between groups pre- and post-treatment using cluster-based permutation tests (CBPT) with 500 randomizations (paired t-tests threshold: $p = 0.05$).

Detrended fluctuation analysis (DFA) enables evaluation of the decay in autocorrelation between remote parts of a sequence in non-stationary data, such as EEG data. It was developed as an alternative to autocorrelation function (ACF) analyses, as ACFs may detect spurious long-range correlations when applied to non-stationary data [16]. LRTC can be quantified in EEG data in the frequency domain by estimating the slope of the $1/f$ power spectrum on a log–log scale and computing the scaling

exponent. A DFA log-log plot is calculated at different time scales from the residual fluctuations of the locally linearly detrended signal and yields a quantification of the Hurst exponent [6], [16]. Calculation of the Hurst exponent H provides a more practical and therefore the most common approach to estimating LRTC in non-stationary signals and has been shown to yield consistently related results [17]. LRTC is deemed to be present when H is between 0.5 and 1 [18].

The topography of LRTC in alpha and beta oscillations has been shown to overlap partially with the power distribution, and a weak positive correlation has been reported between the two measures (Nikulin & Brismar, 2005). We therefore calculated H in 1 Hz steps in the time and frequency range and at the electrode location where the power differences from pre- to post-treatment between the BCI and Sham groups were greatest. The data were time–frequency decomposed using the wavelet transform, and amplitudes were extracted for the relevant frequencies. As long signal segments are required for estimating H [19], we applied DFA in 2 s sliding windows to the concatenated movement trials [6], labelling each window with the time of the first data point, as follows. Time series x was integrated to yield time series y:

$$y(k) = \sum_{i=1}^{k} x(i) - \bar{x} \qquad \text{Eq. 1}$$

which was then divided into N/n non-overlapping windows of length n, where n indicates the individual timescales at which fluctuations were calculated. The trend was computed by least square linear fit at each scale n as follows:

$$F(n) = \sqrt{\frac{1}{N} \sum_{i=1}^{N} (y(i) - y_n(i))^2} \qquad \text{Eq. 2}$$

The LRTC was compared after with before the treatment program in each group using Wilcoxon tests.

III. RESULTS

We analyzed data from the largest patient group from the Magdeburg cohort with similar lesion location: non-dominant hemisphere (as aphasia was an exclusion criterion), subcortical stroke (BCI: n = 6; Sham: n = 6). A repeated measures ANOVA of the FMA-UE scores, with the between-subject factor *Group* (BCI, Sham), the within-subject factor *Time* (Pre, Post), and the covariates *Age*, *Sex*, *Days Post-Stroke*, and *Days of Therapy* showed an interaction only between *Time* and *Group* (F(1) = 8.03, p = 0.030) and a main effect of *Time* (F(1,6) = 8.93, p = 0.024). Post hoc tests showed a significant score increase pre- to post-treatment in the BCI (p = 0.004) but not the Sham group (p > 0.05). We examined the scores on an individual patient level in each group, and a consistent score increase over the treatment program was observed only in the BCI group (Fig. 1: showing patients for whom EEG findings are shown in Fig. 2). Including *Therapy Start* (Acute, Subacute) as a between-subject factor, the interaction *Time* x *Group* (F(1) = 6.66, p = 0.049) remained. Post hoc tests showed a significant FMA-UE score increase only in the BCI group when therapy was started in the acute phase.
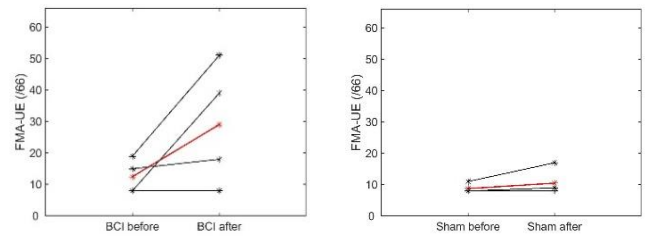

Fig. 1. Fugl-Mayr Assessment upper extremity (FMA-UE) scores in individual patients before and after the rehabilitation program. Left: BCI group. Right: Sham group. Red: mean FMA scores. The score increase was significant only in the BCI group on post hoc testing (p = 0.004). Note that these are the 8 patients whose EEG data were analyzed, as they showed pure right-handedness.

EEG data from only the purely right-handed patients, as reflected by an EDI score of 100, with a right (non-dominant) hemisphere, subcortical stroke (N = 8; BCI: n = 4, Sham: n = 4) were analyzed, to enable electrode level comparisons, as bilateral activations are more commonly observed in left-handed and in ambidextrous patients [20], [21]. The beta spectral power over the contralateral motor cortex was lower at electrode C2 after compared with before treatment, and the pre-/post-treatment reduction was greater in the BCI than the Sham group (CBPT: p = 0.044). The cluster in the time–frequency feature space extended from ~0.5 to 1.5 s after the movement cue in the upper beta (~15-25 Hz) frequency range. We examined the power on an individual level in each group in the time–frequency range in which the difference peaked, 1.2-1.4 s after the movement cue, at 15-23 Hz (Fig. 2). The power reduction was seen on an individual level in all 4 patients in the BCI group. In the Sham group, three patients showed a power reduction, with a minimal reduction in one patient, while one patient showed an increase in power. We note, however, that the initial beta power before the treatment program was more consistent across the patients in the BCI group.
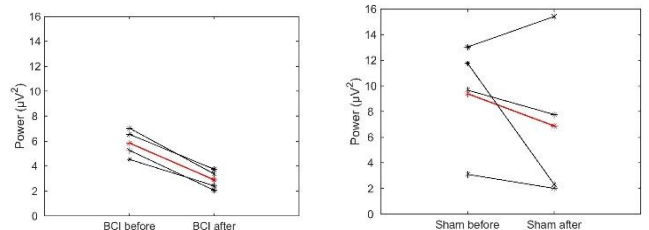

Fig. 2. Beta oscillatory power on an individual level in each group in the time–frequency range in which the difference peaked. Red: mean power.

The optimal features with which to train the classifier, i.e., the frequencies and electrode locations where the separation between movement and rest trials was greatest, varied somewhat between patients. However, generally, the features selected either early or during the course of the program were bilateral motor cortical signals, with an increasing tendency to right-sided (ipsilesional, but contralateral to the movement) feature selection as the treatment program progressed. Early in the treatment program, features were predominantly in the beta frequency range, whereas by the end of the treatment period, alpha power provided better separation between movement and rest conditions.
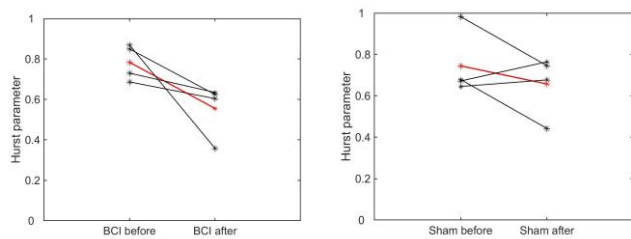
Fig. 3. Long-range temporal correlation (LRTC) at 1.2-1.4 s from 15-23 Hz after the movement cue. Left: BCI group. Right: Sham group. Red: mean LRTC, LRTC decreased in each individual patient in the BCI group, whereas in the Sham group, two patients showed an increase, and two patients showed a reduction in LRTC. H = Hurst parameter.

LRTC in the time–frequency window and at the electrode location where the change in power was greatest decreased from before to after the rehabilitation program in the BCI-FES group (Wilcoxon test: p = 0.02) but not in the Sham group (Wilcoxon test: p = 0.20).

IV. DISCUSSION

Greater motor recovery, as indexed by the FMA-UE scores, followed BCI-FES treatment than when FES was delivered temporally independently of EEG-based detection of movement attempts (Sham group), with a trend towards greater recovery if BCI-FES therapy started in the acute phase post-stroke. Beta spectral power following the cue to move decreased more in the BCI than the Sham group post-therapy. Potentially compensatory changes have been reported in the somatosensory rhythm in the contralesional hemisphere in chronic stroke patients [22]. We tentatively suggest that the reduction observed here in ipsilesional beta power could reflect reduced compensatory activity. While beta power distinguished better between movement and rest at the beginning of the rehabilitation program, by the end, alpha power provided more reliable classification. It is plausible that the reinforcement of the alpha changes with movement attempts, through the visual and proprioceptive feedback that accompanied movement that was induced through FES applied in a tight temporal window with the movement attempts, resulted in synaptic changes strengthening or maintaining the neuronal networks involved in movement generation oscillating in the alpha frequency range. The lack of reinforcement of the changes in beta power could by turn have led to a reduction in the integrity of these networks.

LRTC in the beta frequency band decreased in the BCI group but not in the Sham group. This finding suggests that a subcritical state may better facilitate motor recovery. Consistent with the proposal that LRTC reflects neuronal systems close to a critical state, which enables rapid reorganization in response to changing demands, lower LRTC in beta oscillations during an attentional task than at rest has been associated with better task performance, leading to the postulation that a sub-critical state is preferred for tasks requiring sustained attention [23].

We note that the analyses are focused on patients with a non-dominant hemisphere stroke, as these patients formed the largest subgroup with similar lesion location, enabling statistical analyses. It is plausible that this group in particular benefits from BCI-FES, due to less spontaneous recovery as a result of less use of the non-dominant hand. Further studies are required to investigate this possibility.

Limited patient numbers are well-recognized in BCI studies involving patients early post-stroke [3], [24]. Recruitment is challenging in the acute phase, as patients require an extensive range of early investigations and treatments, and completion of the rehabilitation program is frequently impeded through co-existing medical conditions, including those underlying the

occurrence of the stroke. Future work is required, likely combining the findings of multiple studies, to identify potential differences in response to BCI-FES in patients with different stroke lesion locations.

Our findings, however, support the notion that FES delivery temporally coupled with movement attempts using a BCI could improve motor recovery, particularly if started early post-stroke.

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