Movement-related brain oscillations vary with lesion location in severely paralyzed chronic stroke patients

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***Abstract*— In the past few years, innovative upper-limb rehabilitation methods have been proposed for chronic stroke patients. These methods aim at functional motor rehabilitation using Brain-machine interfaces to constitute an alternate pathway from the brain to the muscles. Even in patients with absence of residual finger movements, recovery could be achieved. The extent to which these interventions are affected by individual lesion topology is yet to be understood. In this study EEG was measured in 30 chronic stroke patients during movement attempts of the paretic arm. We show that the magnitude of the event-related desynchronization was smaller in patients presenting lesions with involvement of the motor cortex. This could have important implications on the design of new rehabilitation schemes for these patients, which might benefit from carefully tailored interventions.**

I. INTRODUCTION

Stroke is a major global health problem. Millions of stroke survivors have to live with persistent motor disabilities and depend on assistance for their daily life [1]. Those patients with severe limb weakness cannot benefit from Constraint-induced movement therapy or bilateral arm training [2]. However, Brain-Machine interface-based robot-assisted training is an option for them.

Training of arm and hand movements using an orthotic robot that is controlled by the brain activity has been shown to be an effective method to persistently decrease impairment in chronic stroke patients [3]. The brain signals are translated into control commands of a robot that moves the limb of the patients. The Brain-Machine interface (BMI) thus constitutes an alternative pathway between brain and muscles. Processes of associative learning can be induced by contingently linking neural correlates of movement intention of arm and hand and visuo-proprioceptive feedback of the movement, which in turn leads to functional improvements [3], [4], [5]. These BMIs utilize the characteristics of the sensorimotor rhythm (SMR).

As each stroke patients' demographics, the extent of the infarct and the severity of disabilities are different, it is of great interest to understand how these differences influence the characteristics of sensorimotor oscillations and if they potentially affect the efficacy of BMI-based rehabilitation schemes. Extent of the lesion to the motor cortex and to the motor pathways have been correlated with measures of motor deficit in imaging studies [6], [7]. Other studies show that differences resulting from injuries of the motor cortex can also be observed in electroencephalographic measurements (EEG). The magnitude of event-related desynchronization (ERD) is lower in patients that had a stroke as compared to healthy individuals [8], [9]. In addition to that, Park et al reported that these differences in brain oscillations can also be observed in stroke patients suffering from moderate or mild paralysis presenting different grades lesions severity [9].

However, up to now there are no works that show a similar relationship in severely impaired stroke patients. We hypothesize that in these patients, lesion location influences the magnitude of the ERD, too. More precisely, we expect that patients with lesions involving the motor cortex show less brain activation during movement attempts as compared to patients without infarction of the motor cortex. The brain activation is quantified by ERD of the alpha and beta frequency ranges. For this study, we recruited 30 chronic stroke patients, 13 of which presented lesions in the primary motor cortex (M1) and primary sensorimotor cortex (S1). They performed repeated movement attempts of their arm while EEG was recorded. The mean ERD response of each of them was extracted and compared between groups. This investigation aims at showing potential differences in the ERD caused by the two lesion types. The result could help improving the design of future BMI-based rehabilitation systems.

II. METHODS

A. Study Design

Thirty patients with chronic stroke took part in this study. They all suffered from complete paralysis of one hand and presented no active finger extension. None of them had neurological or psychiatric conditions besides stroke. Patients with cerebellar lesions were excluded. Table I summarizes the demographic data of the patients, also showing their scores of the combined Fugl-Meyer assessment (cFMA) of the upper limb. The cFMA-values were obtained by summing the scores of the affected hand and arm. More details of the inclusion and exclusion criteria can be found elsewhere [3].

Informed written consent was obtained before participation and the study was approved by the ethics committee of the Faculty of Medicine of the University of Tübingen.

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TABLE I. PATIENT DEMOGRAPHICS

Lesion type	Sex	Age (yr)	Time since stroke (mo)	Lesion side	cFMA score
LM	8M/5F	53.7±13.2	58.4±50.5	9R/4L	11.2±7.8
LS	10M/7F	53.7±11.2	73.1±65.6	8R/9L	12.9±9.7

The data used for the analysis presented here are part of existing data from a previous BMI-based rehabilitation intervention [3]. Electric brain activity was measured from all subjects while they performed movement attempts of the paretic arm and hand, depending on their ability. The brain oscillations (SMR) generated by the movement attempts were translated into actual movements of the arm by an orthosis attached to the patients' paralyzed arm. In the interventional study, the patients were randomly separated into two groups, the experimental group and the control group. The movements of the robot were contingently linked to the brain activity for the first group and random for those of the latter. The robot moved an equivalent amount of time for both groups. The arm orthosis was a ReoGo robot (Motorika, Cesarea, Israel). The movements were one-dimensional (forward/reach and backward again). A custom-made robot, developed in-house was used for eliciting hand movements. All the patients participated in a series of 17±1.8 sessions that were recorded on consecutive days. Only the data of the first session of the BMI training was considered for the analysis presented here, as no significant group-wise training effects on the ERD were expected on the first day of the BMI intervention. During that phase, the patients were asked to try to move their paretic arm without producing compensatory movements. Each session regularly consisted of 150 trials. Each trial was divided into three time periods: A "rest" period of 4s to 6s, during which the patients were asked to rest and avoid any movement, a short 2s "ready" phase, during which they prepared for the movement, and a "move" phase, during which the patients were asked to try to move their arm and movements of the robot were triggered. The latter phase lasted 5s.

The patients underwent a battery of tests before the BMI intervention including structural magnetic resonance imaging (MRI). Expert radiologists identified the brain regions affected by the lesion. All patients showed subcortical lesions and none had cerebellar lesions. For the purpose of the analysis presented here, the patients were separated into two groups depending on lesion location: patients with lesions involving the primary motor cortex and the primary sensorimotor cortex were assigned to group LM (n=13) and the rest to group LS (n=17).

B. Neurophysiological Recordings

The brain activity was sampled at 500 Hz using a 16 EEG channels ActiCap and BrainAmp system (Brainproducts GmbH, Munich, Germany) from the locations Fp1, Fp2, F3, Fz, F4, T7, C3, Cz, C4, T8, Cp3, Cp4, P3, Pz, P4 and Oz. The ground electrode was placed at AFz and the reference at FCz. Eye movements were recorded using vertical and horizontal electrooculographic derivations (EOG).

Trials containing cranial muscle artifacts identified by applying a threshold of the z-score of the data in the range of 110 Hz to 140 Hz at 4 standard deviations (SD), were removed from the analysis. Moreover, trials containing offset artifacts (20 standard deviations of the z-score) were removed, too[1]. Surface EMG activity was recorded from 4 different muscle groups on both arms and analyzed by computing the Waveform length (WL) following [10] using a 250ms sliding window and a 25ms overlap. All the trials containing undesired muscle activity during rest on the paretic or anytime on the healthy upper limb (presenting activity above 3 SD from the resting time EMG WL mean for at least 50ms following [11]) were removed from the analysis. Artifacts stemming from ocular movements were removed from the signal using a method based on Independent Component Analysis [12].

C. Data Analysis

EEG power was characterized by computing the event-related desynchronization (ERD) in the alpha and beta frequency bands. It is defined as a frequency-specific change of ongoing EEG activity resulting from external or internal events [13]. During planning and execution of movements, a relative decrease in power as compared to a rest period can be measured in specific bands of the EEG [13]. Motion execution disrupts oscillations of large populations of neurons in the alpha frequency band (8-13 Hz) and the beta frequency band (13 Hz – 25 Hz) [14]. In the current work, we focus on the analysis of the power changes in the alpha and the beta frequency band. The mean EEG power values in both frequency ranges of the two portions of each trial, 'rest' and 'move', were computed from the respective ranges of the frequency spectrum of only the EEG-channels over the motor cortex on the lesioned side of the brain (C3, Cp3 and P3 or C4, Cp4 and P4). The 'rest' values were averaged to form a reference power value R that was used to compute the ERD values for both frequency bands of each trial (Eq. 1).

$$ERD = \left(\frac{A-R}{R}\right) \times 100\ \% \qquad (1)$$

A represents the alpha or beta power of the 'move' phases of each trial. The ERD values were averaged for each subject for all trials of the training session and for the two frequency ranges, yielding a robust estimate of the true relative power decrease during movements of the paralyzed arm for these patients.

For the statistical evaluations non-parametric tests were used. As the samples were independent a Wilcoxon rank-sum test was used for the comparison between the two groups to assess the mean difference in ERD values between them using a significance level of 0.05. The effect size was computed using the rank-biserial correlation [15].

[1] This procedure follows the description for removing artifacts from the EEG signal in the Field Trip toolbox [24]

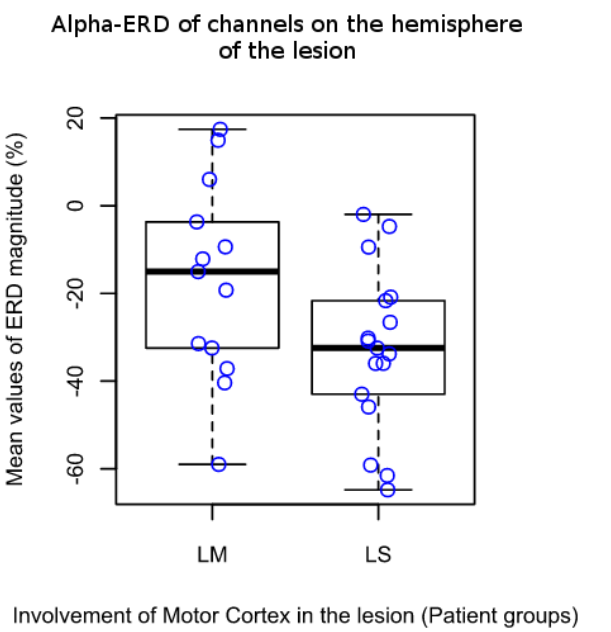

Fig. 1: Boxplot showing how the values of the alpha-ERD magnitude differ between the two groups of lesion locations. Those patients suffering from an involvement of the motor cortex show less negative alpha-ERD magnitude on average than those patients whose motor cortex is not touched by the lesion. The mean values of the alpha-ERD magnitude of each patient are overlayed as blue circles. They are randomly jittered around the vertical center of the boxes to increase clarity. The difference is not statistically significant, when employing a Wilcoxon rank-sum test.

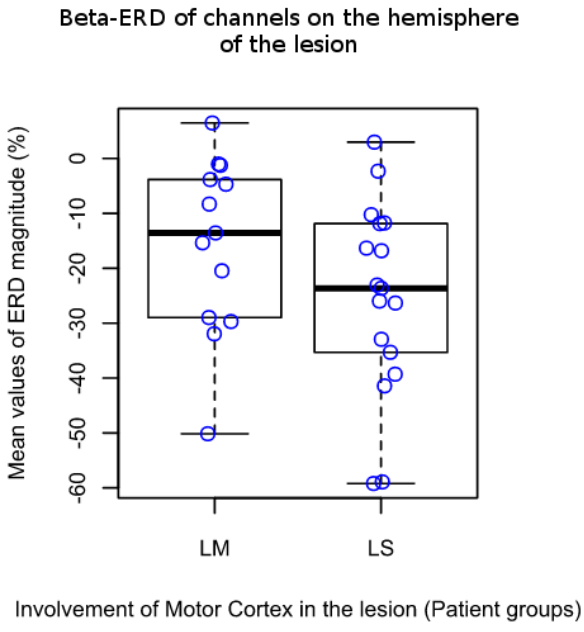

Fig. 2: Boxplot showing how the values of the beta-ERD magnitude differ between the two groups of lesion locations. Those patients suffering from an involvement of the motor cortex show slightly less negative beta-ERD magnitude on average than those patients whose motor cortex is not touched by the lesion. The mean values of the beta-ERD magnitude of each patient are overlayed as blue circles. They are randomly jittered around the vertical center of the boxes to increase clarity. The difference is not statistically significant, when employing a Wilcoxon rank-sum test.

III. Results

The mean±SD of the alpha-ERD values of the patients suffering from a lesion that extends to the primary motor cortex (LM) was -17.0±22.6. For the other patients (LS), the values were lower on average with mean±SD of -32.9±18.4. When performing the Wilcoxon rank-sum test, which resulted in $U = 155$ and $p = 0.065$, we did not find enough evidence to conclude that the observed difference of the ERD values in the alpha range is statistically significant. The effect size, of $r = 0.40$, however, is moderate. Those patients suffering from a lesion that extends to the primary motor cortex (LM) tendentially show a lower activation on average (i.e. less negative ERD magnitude) than the patients that do not have their primary motor cortex affected (LS) (Fig. 1).

The mean±SD of the beta-ERD values was -15.6±16.0 for group LM and -25.4±17.6 for the patients whose primary motor cortex was not affected (LS). The same type of statistical test was applied to the ERD values of the beta band of the two groups. It did not show a statistically significant difference with $U = 148$ and $p = 0.1227$. The effect size, however, was moderate with $r = 0.34$. We thus conclude that at least a similar tendency of lower average activation (i.e. less negative ERD magnitude) in the beta band can be observed for patients with inclusion of the motor cortex (Fig. 2).

IV. Discussion and Conclusions

In this work, we investigated the EEG response of severely paralyzed stroke patients in the chronic stage undergoing a BMI-based training. We hypothesized that lesions that extend into the primary motor cortex would affect the power output of the EEG. Although the results did not yield statistically significant differences of the ERD magnitude of the two groups of patients, we conclude that ERD as a measure of relative EEG power is tendentially less pronounced if the motor cortex is affected by the lesion. However, this does not hamper ERD production significantly.

It has long been known that ERD is an electrophysiological correlate of ongoing cortical processing of sensory information and generation of motor behavior [14]. Patients with motor deficit due to stroke exhibit less pronounced ERD as compared to healthy controls [8], [9]. Motor output and control of movements of these patients are reduced. Their limb strength and their ability to control and direct movements of the paralyzed limb are lower than in a healthy population [16]. Lesion volume and location, on the other hand, have shown to be correlated with behavioral outcome in imaging studies [6], [7]. Our findings point in the direction of closing the argumentational loop: inclusion of the primary motor cortex in the lesion might also be correlated with less pronounced ERD. As ERD of the alpha-band potentially represents a biomarker of the excitability of cortical and spinal levels [17], [18], less ERD due to involvement of the primary motor cortex in the lesion could imply impeded progress in a rehabilitation scenario.

Brain-Machine interface approaches were reported as the only efficient method to induce improvement of the movement ability in severely paralyzed chronic stroke patients [3]. BMI-based interventions for motor rehabilitation after stroke have utilized ERD as a means of detecting movement intention [19], [20], [21] [3]. The findings of our

work might explain the differences in BMI performance of movement intention decoding reported between stroke patients with and without cortical damage [22], and could be of great importance for future studies in this field. They could help in designing intervention schemes that are better tuned to the individual neurophysiological condition of the patient and could increase efficiency of the rehabilitation intervention. SMR-based classifiers driving a rehabilitation robot could be adjusted to the less pronounced ERD signals of patients showing lesions that extend to the motor cortex, e.g. by increasing the sensitivity and thus allowing more subtle changes in the signal to produce larger effects in the control of the robot.

Therefore, further investigation of the relationship between lesion location, EEG power and motor impairments is needed. One option could be the inclusion of more patients in the study. But also extension of the analysis to all the training data and the training effect, especially of the patients of the experimental group, might reveal a significant trend. Moreover, it could be of great interest to investigate and understand the relationship of the results of the present work and other neurophysiological correlates of movement, for example motor-related cortical potentials and muscle activity.

The heterogeneity of the cortical lesions and their influence on different parts of the motor neural network, might not only affect the ERD magnitude but also the (re-) learning of the sensorimotor rhythm control. Since we observed a tendential difference in ERD and no significant difference in motor impairment between groups, it remains an open question if the ERD of the patients is directly correlated to their degree of impairment if the statistical power could be increased with a larger number of participating patients.

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