Stroke lesion location influences the decoding of movement intention from EEG

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Abstract— **Recent studies have demonstrated the efficacy of brain-machine interfaces (BMI) for motor rehabilitation after stroke, especially for those patients with severe paralysis. However, a cerebro-vascular accident can affect the brain in many different manners, and lesions in diverse areas, even from significantly different volumes, can lead to similar or equal motor deficits. The location of the insult influences the way the brain activates when moving or attempting to move a paralyzed limb. Since the essence of a rehabilitative BMI is to precisely decode motor commands from the brain, it is crucial to characterize how lesion location affects the measured signals and if and how it influences BMI performance. This paper compares the performances of an electroencephalography (EEG)-based movement intention decoder in two groups of severely paralyzed chronic stroke patients: 14 with subcortical lesions and 14 with mixed (i.e., cortical and subcortical) lesions. We show that the lesion location influences the performance of the BMI when decoding the movement attempts of the paretic arm. The obtained results underline the need for further developments for a better individualization of BMI-based rehabilitative therapies for stroke patients.**

I. Introduction

Stroke is the leading cause of long-term adult disability, which in more than 85% of the cases results in motor deficits [1]. From stroke survivors showing no active arm function at hospital admission, the degree of recovery is small or null in 56% of the cases [2]. The most popular technique to try to recover stroke-related motor deficits is physical therapy [3], although more sophisticated robotic therapies have also been proposed [4]. However, these two options are not suitable for patients with very limited or no residual movement [5].

For chronic patients with complete hand paralysis, brain-machine interfaces (BMI) have been proven as the only means to induce motor recovery [6], since no residual active movement is required. A BMI consists of a system that acquires and processes the brain activity in real time, for instance by using electroencephalography (EEG), and that translates it into commands for controlling an external device. When this device is used to contingently link the neural activity related to movement intention with peripheral stimulation of the paralyzed limb, it can induce Hebbian plasticity and even functional motor improvements [6], [7].

In the same way as traditional physical therapies have to be adapted to the capabilities of each patient, BMIs have to be personalized, too [8]. This is even more evident in stroke patients, since each lesion affects the brain in a different manner, and it can corrupt their already-unique cortical patterns related to movement intention [9]. For this reason, the study of how different lesion locations affect cortical activity is relevant to understand how BMIs can be adapted to each patient. Magnetic resonance imaging (MRI) studies have described the differences in activation of different brain regions between stroke lesions involving or not the sensorimotor cortex [10]. Some of these differences can also be captured using EEG, revealing that injuries affecting the motor cortex entail smaller event-related desynchronization (ERD) during the attempts of movement [11], [12].

However, the influence of these lesion-dependent differences in brain activity on BMI performance has not been reported to date. We hypothesize that patients with lesions involving the motor cortex will have poorer decoding accuracies of their movement intention with a BMI. We recruited 28 chronic stroke patients, 14 of them with subcortical lesions and 14 with mixed lesions (i.e., with cortical and subcortical involvement). A BMI decoder is implemented to decode, in a pseudo-online manner, the movement attempts of their paralyzed hand and the movement executions of their healthy hand. With this study we aim at showing the potential differences in BMI applicability for stroke patients with subcortical only or cortico-subcortical lesions.

II. Methods

A. Patients

Twenty eight chronic stroke patients were involved in this study. All the patients suffered hand paralysis resulting in no residual finger extension in the paretic arm. Regarding the location of the stroke, 14 of the patients presented subcortical and the other 14 had mixed (i.e., cortical and subcortical) lesions. Table I summarizes the demographic data of both patient groups and their score in the modified upper-limb motor scores combined Fugl–Meyer assessment (cFMA, excluding coordination, speed and reflexes scores; max. 54 points). There were no significant differences in any of the displayed variables (i.e., number of male/females, age, time since stroke, lesion side, cFMA) between both groups (Mann–Whitney U tests, $p > 0.05$ for all the comparisons). More details about the inclusion and exclusion criteria can be seen elsewhere [6]. The experiments were conducted at the University of Tübingen, Germany. The study was approved by the ethics committee of the Faculty of Medicine of the University of Tübingen, and all the patients provided written informed consent before participation.

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TABLE I

SUMMARY OF THE PATIENTS

Group	Gender	Age (yr)	Time since stroke (mo)	Lesion side	cFMA Score
Subcortical	8M/6F	46.1±11.9	82.7±68.5	7R/7L	14.0±10.2
Mixed	8M/6F	49.7±14.6	47.1±44.2	8R/6L	10.1±6.6

B. Experimental protocol and data acquisition

The patients performed one experimental session, in which their electroencephalographic (EEG) activity was monitored while they opened/closed their healthy hand or attempted to open/close their paralyzed hand. Each patient performed between 4 and 6 blocks, each of which included, in a random order, 17 trials moving the healthy hand, and 17 trials attempting to move the paralyzed one. During the trials, audiovisual cues were presented to instruct the patients about the three phases: rest (5 sec), motor execution/attempt (5 secs), inter-trial interval (random duration between 3-4 sec). In the motor execution/attempt interval, the patients were asked to open and close the indicated hand at their own comfortable pace.

EEG activity was recorded with a 16-electrodes Acticap system (BrainProducts GmbH, Germany) from Fp1, Fp2, F3, Fz, F4, T7, C3, Cz, C4, T8, CP3, CP4, P3, Pz, P4, and Oz locations, with the ground in AFz and reference in FCz. Vertical and horizontal electrooculographic (EOG) derivations were also recorded to capture eye movements. Both signals were sampled at 500 Hz.

C. Movement intention decoding

A brain-machine interface (BMI) was designed to decode the movements of the healthy hand and the movement attempts of the paretic one. A pseudo-online methodology was developed in order to simulate the results that would be obtained in a real-time setup, by using causal filters, sliding windows and auto-regressive models.

We used a block-based *N*-fold cross-validation procedure, with *N* being the number of blocks recorded for each patient. The procedure was performed separately for the healthy and the paretic hands. In each fold, the data of one block was kept apart for testing, and the remaining blocks were used for training the BMI. The trials constituting the training dataset were used to extract examples of *rest* or *movement/attempt* activity. The training and test trials consisted of 7-second signals, from -3 to +4 seconds, with 0 being the presentation of the cue that instructed the patients to move.

1) Artifact removal: The training datasets were processed to remove the trials contaminated with artifacts in any of the channels used for feature extraction and for re-referencing (see *BMI training* below), following [13]. First, the influence of EOG activity was removed by using linear regressions. Subsequently, we used a variance-based method to remove trials containing low or high frequency artifacts. The power in delta ([0.1-4] Hz) and gamma ([30-48] Hz) frequency bands was first calculated on each trial, and the mean and standard deviation (std) values during the rest period were computed. We defined 3 stds above the mean as the rejection threshold, and rejected all those trials that exceeded this value either during the rest or during the movement periods. Then, we recomputed the mean and std in the rest period of the non-rejected trials, and rejected all those that exceeded the newly calculated threshold (i.e., 3 stds above the new mean) during rest or movement attempt in any of the bands.

2) BMI training: One-second windows were used to extract features from the training trials and model the *rest* and *movement* classes. The *rest* windows were extracted from the time interval [-2, 0] s, and the *movement* windows were extracted from the interval [1, 3] s (since reaction time to the cue is slow in these patients), with a sliding step of 0.25 s. Two possible combinations of EEG channels were performed to extract the features: *(i)* channels over the contralateral hemisphere to the moved/attempted hand (i.e., channels C3, CP3, and P3 for the right hand; and channels C4, CP4, and P4 for the left hand); and *(ii)* all the channels of the centro-parietal cortex (i.e., C3, CP3, P3, Cz, Pz, C4, CP4, P4). The selected electrodes were re-referenced using Laplacian derivations (for the electrodes whose 4 closest neighbors were not available, we considered the 2 or 3 available neighbors only). For each one-second window, we computed the power in alpha ([7-13] Hz) and beta ([14-30] Hz) frequency bands on each channel (i.e., 6 features if 3 channels were used, and 16 features if 8 channels were used) using an order-20 autoregressive model based on the Burg algorithm. The features were normalized to have zero mean and unit variance. A support vector machine with a radial basis function (RBF) kernel was used as classifier to discriminate between the two brain states (rest and movement/attempt).

3) Decoding evaluation: The test trials were evaluated pseudo-online, with the sliding window analyzing the interval [-3, 4] s (notice that the first output was generated at t = -2 s) and generating an output every 20 ms. The performance was quantified in terms of average accuracy (ACC), calculated as the mean between the true positive rate (TPR) and the true negative rate (TNR). The TPR was defined as the percentage of outputs of the classifier labeled as *movement* in the time interval [1.5, 4] s. The TNR was defined as the percentage of outputs of the classifier labeled as *rest* in the time interval [-2, 0] s.

4) Statistical analysis: Statistical comparisons were performed to analyze the influence in decoding accuracy of the factors: patient group (subcortical and mixed) and electrode-configuration used for feature extraction (contralateral to the involved limb or all the electrodes over the centro-parietal cortex). First, we evaluated, separately for each task (movement execution and attempt), the decoding differences between the two patient groups. Secondly, for each group and task, we analyzed the effect of using only contralateral electrodes or all the motor-cortex electrodes. Non-parametric tests were used for the comparisons: the Mann–Whitney U test was used for the unrelated samples (i.e., comparison between the two patient groups), and the Wilcoxon signed-rank test was used for the related samples (i.e., comparison between the two configurations of electrodes for feature

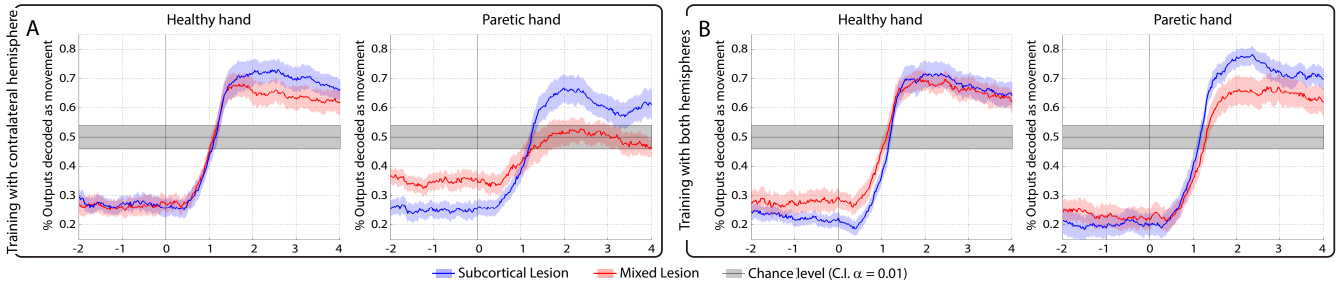

Fig. 1. BMI performances when extracting the features from the electrodes in the contralateral hemisphere to the moved limb (A) or all the electrodes in the centro-parietal cortex (B). The left part of each panel corresponds to the healthy hand, and the right part corresponds to the paretic hand. On each plot, the lines represent the average of all the patients of each group, and the shades indicate the standard error of the mean. The blue color corresponds to the patients with subcortical lesion, while the red color represents the patients with mixed lesion. The shaded gray area indicates the chance level, computed on the basis of all the test trials, according to [14].

extraction). Bonferroni correction was applied for the total number of comparisons in each analysis, and statistical significance was considered when corrected p-values were smaller than 0.05. Effect sizes are also reported, computed as $r = abs\left(\frac{Z}{\sqrt{N}}\right)$, where Z is the z-statistic of the test, and N the number of patients.

D. ERD Analysis

The degree of cortical activation during movement execution and attempt by both groups of patients was evaluated by means of time-frequency maps representing the event-related desynchronization (ERD) [15]. We computed the ERD using Morlet wavelets in the frequency range [1-50] Hz after pooling together the trials of all the patients from each group. A t-percentile bootstrap procedure was applied to verify the statistical significance of the ERD during the movement and the movement attempt [16].

III. Results

A. Movement intention decoding

Figure 1 shows the results of the pseudo-online BMI decoder for both tasks (i.e., movement execution and attempt), when performed by each group (i.e., subcortical and mixed lesions) with each channel combination (contralateral electrodes or all the motor-cortex electrodes). Table II summarizes the average accuracies for each combination.

1) Influence of lesion: For the BMI trained with the contralateral electrodes only, the patients with subcortical lesion showed significantly higher decoding accuracies than the patients with mixed lesion for the paretic arm ($p = 0.037$, $r = 0.49$). For the healthy arm, the predictions of the BMI decoder were better during the movement period for the subcortical patients also (see left panel of Fig. 1A), although the average accuracy was not significantly different ($p > 0.05$, $r = 0.10$). When all the electrodes were considered, subcortical patients also obtained slightly better performances (see Fig. 1B and Table II), but the differences were not statistically significant ($p > 0.05$ in both cases; $r = 0.13$ for healthy hand, $r = 0.17$ for paretic hand).

2) Influence of electrodes for feature extraction: When decoding the attempts of movement of the paretic hand, the use of all the electrodes–with respect to using only the contralateral ones–led to a significant improvement in accuracy both for patients with subcortical lesion ($p = 0.005$, $r = 0.61$) and for patients with mixed lesion ($p = 0.007$, $r = 0.59$). For the movements of the healthy arm, however, the accuracies were not significantly different when using the subset of electrodes contralateral to the movement or all of them ($p > 0.05$ in both cases; $r = 0.20$ for the subcortical group, $r = 0.11$ for the mixed group).

TABLE II

Average accuracies for each combination of patient group, task, and electrode set for feature extraction

		Healthy arm	Paretic arm
Contralateral electrodes	**Subcortical**	$71.6 \pm 11.1\%$	$68.4 \pm 11.0\%$
	Mixed	$69.0 \pm 11.5\%$	$57.5 \pm 10.0\%$
All centro-parietal electrodes	**Subcortical**	$72.8 \pm 10.8\%$	$76.5 \pm 9.5\%$
	Mixed	$69.4 \pm 12.1\%$	$70.7 \pm 14.3\%$

B. ERD Analysis

Figure 2 depicts the degree of cortical activation for both groups of patients when moving the healthy hand or attempting to move the paretic one. Notice that, for a clearer representation, we swapped the left and right-sided lateralized electrodes of the patients with right hemispheric lesion. Therefore, we averaged all the patients considering that the movement executions (i.e., healthy side) are done with the left hand, and the movement attempts (i.e., paretic side) are done with the right hand. Patients with subcortical lesions showed strong alpha and beta ERD on the contralesional hemisphere during the movement executions and attempts. On the other hand, patients with mixed lesion showed weaker contralesional activations during the motor executions, and almost negligible activity during the movement attempts.

IV. Discussion and Conclusions

This paper reported for the first time the existence of differences in BMI performance dependent on lesion location in severely affected chronic stroke patients. A continuous decoder, mimicking real-time BMI operation allowed us to simulate an ecological protocol with a clinically relevant

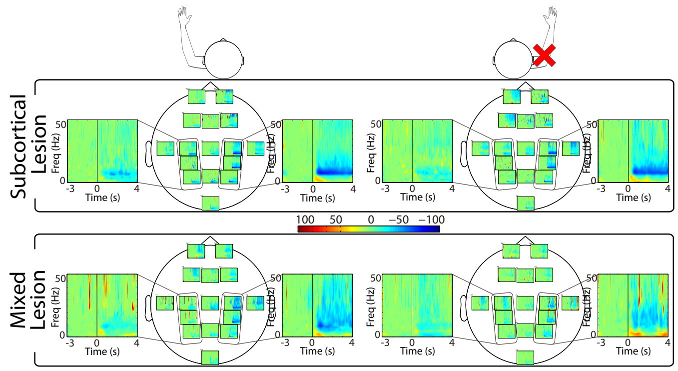

Fig. 2. ERD activations of patients with subcortical lesion (upper panel) and patients with mixed lesion (bottom panel). The left part of each panel corresponds to the movement of the healthy hand (reorganized to correspond to the left hand for all of them), while the right part corresponds to the movement attempt of the paretic hand (representing the right hand of all the patients).

population of stroke patients with complete hand paralysis. This result underlines the need of further developments for the individualization of BMI-based rehabilitative therapies.

We confirmed our initial hypothesis, showing that stroke patients with no cortical damage get higher decoding accuracies, despite both patient groups had, on average, the same degree of motor impairment. A more detailed categorization of patients, and a higher number of subjects, would help to better understand the influence that the damage on each specific brain region can have in BMI usage.

Interestingly, we observed that patients with mixed lesions (i.e., with cortical damage) showed very low performances–close to chance–when their attempt to open and close the paretic hand was decoded with the electrodes placed over the ipsilesional hemisphere only. This performance could be significantly improved by including also the electrodes placed over the contralesional hemisphere. However, superior associative learning has been hypothesized when the contingent connection between the neural correlates of intention to move and the feedback of the movement is established using the ipsilesional hemisphere [6]. Therefore, further research should address the improvement of the BMI performance for these patients, for instance, by combining the features used for movement decoding (i.e., the ERD) with some other features of cortical origin, such as the movement-related cortical potentials [17], or even with residual electromyographic activity of the paralyzed limbs [18].

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