Quantitative EEG as Biomarkers for the Monitoring of Post-Stroke Motor Recovery in BCI and tDCS Rehabilitation

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Abstract—This study investigates the neurological changes in the brain activity of chronic stroke patients undergoing different types of motor rehabilitative interventions and their relationship with the clinical recovery using the Quantitative Electroencephalography (QEEG) features. Over a period of two weeks, 19 hemiplegic chronic stroke patients underwent 10 sessions of upper extremity motor rehabilitation using a brain-computer interface paradigm (BCI group, n= 9) and transcranial direct current stimulation coupled BCI paradigm (tDCS group, n= 10). The pre- and post-treatment brain activations, as well as the intervention-induced changes in the neuronal activity, were quantified using 11 QEEG features and their relationship with clinical motor improvement was investigated. Significant treatment-induced change in the relative theta power was observed in the BCI group and the change was significantly correlated with the clinical improvements. Also, in the BCI group, the relative theta power and interactions between the theta, alpha, and beta power were identified as monitory biomarkers of motor recovery. On the contrary, the tDCS group was characterized by the significant change in brain asymmetry. Furthermore, we observed significant intergroup differences in the predictive capabilities of post-intervention QEEG features between the BCI and tDCS group. Based on the intergroup differences observed in this study and convergent results from the other neuroimaging analysis performed on the same cohort, we suggest that distinctly different mechanisms of neuronal recovery were facilitated by tDCS and BCI interventions and these treatment specific mechanisms can be encapsulated using QEEG.

I. INTRODUCTION

Stroke is one of the leading causes of acquired long-term disabilities in adults and approximately two-thirds of stroke patients require rehabilitation. Upper extremity (UE) motor impairments is a significant problem among stroke survivors and in recent years, Brain-Computer Interface (BCI) based neuro-rehabilitation paradigms have emerged as an important tool for UE motor function restorations [1]. Moreover, the use of transcranial Direct Current Stimulation (tDCS) along with the BCI treatment have also been found to be effective in post-stroke motor rehabilitation in the chronic state [2].

The post-stroke clinical recovery is facilitated by various structural and functional changes in different brain areas and the quantification and monitoring of these neuronal changes is an essential aspect of image-guided rehabilitation. Various quantitative electroencephalographic (QEEG) features have been reported to encapsulate these neuronal changes in subacute stage[3]. Also, the monitoring capabilities of QEEG features, in particular, frequency specific features and features quantifying brain asymmetry are well established in the acute phase [4] but very few studies have explored the utility of these features in the chronic state [5]–[8]. Moreover, only two previous studies have reported the usefulness of QEEG features in chronic state rehabilitation, but to the best of authors’ knowledge, no other study have explored the effectiveness of QEEG features as biomarkers of treatment evolution during BCI and tDCS motor rehabilitation.

To address this gap, the proposed study analyzes the possible utility of QEEG features as monitory biomarkers in chronic stroke patients undergoing BCI and tDCS coupled BCI rehabilitation. Moreover, this study also investigates inter-treatment differences in the evolution of neuronal activity during the BCI and tDCS coupled BCI rehabilitation.

The results suggest that various QEEG features may be informative in quantifying the neuronal changes occurring during BCI and tDCS coupled BCI intervention in the chronic state. Additionally, we observed a significant differences in the mechanism of neuronal repair in the patients undergoing these two different interventions.

II. METHODS AND MATERIALS

A. Patients and rehabilitation protocol

Nineteen hemiplegic chronic stroke patients (14 male, 13 ischemic, 18 subcortical, mean age = 54.1 years, mean time post stroke = 34.6 months) who had their first ever stroke at least nine months prior were recruited in a randomized control trial (RCT) accessing the efficacy of tDCS coupled BCI intervention in post-stroke UE motor rehabilitation [2]. The clinical trial was approved by Institutional Review Board, National University Hospital Singapore. All the participants were randomly assigned to the tDCS (n=10) or BCI (n=9) groups and underwent ten 1-hr sessions of a BCI rehabilitation carried over a 2 week period. The BCI intervention involved BCI triggered robotic movement of the paretic hand upon the detection of motor imagery (MI). In a trial-based setting, patients performed MI of the reaching task using the paretic hand, which was identified online using EEG and successful detection of MI was rewarded by immediate passive movement of the paretic hand by the MIT-MANUS robot. Each rehabilitation session involved four therapy runs with 40 such trials in each run constituting, in total, 160
repetitions. Along with this BCI therapy, the patients in tDCS group received 20 minutes of 1mA bi-hemispheric tDCS (the anode over the ipsilesional M1 and the cathode over the contralesional M1) before the start of every session. Being an RCT, the BCI group also received a similar but sham-tDCS where the current was applied only for the first 30s. In total, all patients participated in 10 rehabilitation sessions.

B. Clinical evaluation

The clinical assessment of motor functions of the paretic hand was performed using the motor part of the UE Fugl-Mayer Assessment (FMA) (range 0-66) at three-time points: 1. Pre-treatment (FMA_0), 2. Post-treatment: immediately after the treatment (FMA_1) and, 3: Follow-up: at a two weeks follow-up after the treatment (FMA_2). The treatment gain (∆FMA) was calculated as the difference between pre-treatment and post-treatment FMA (FMA_2 - FMA_0).

C. EEG Data acquisition, preprocessing and feature extraction

In all the rehabilitation sessions, the brain activity was continuously captured using the Neuroscan Nuamps EEG amplifier with 27 unipolar channels positioned according to the international 10/20 system at a sampling frequency of 250Hz. All the channels were referenced to the ear electrode and the electrode impedances were kept well below 5kΩ. In an offline analysis, the continuous EEG data was bandpass filtered between 0.5-45Hz using zero-phase FIR filter (with hamming window function) and was cleaned for the line noise. The single trial data was extracted from this filtered data and an expert user discarded noisy trials and channels (along with their homologous channels) with the help of PREP and FASTER toolbox. The remaining data was referenced to the common average reference and Independent component analysis (ICA) was used to remove eye blink and muscle-related artifacts. Expert user removed artefactual components with the help of SASICA toolbox. Finally, from this clean data, a 2s pre-cue resting state EEG was extracted from each trial for the analysis.

The single trial Power Spectral Density (PSD) was computed for each channel using Welch’s periodogram. The trial averaged absolute PSD was calculated and was summed across 1.0-4.0Hz, 4.0-7.5Hz, 7.5-12.5Hz, and 12.5-30.0Hz bands to obtain absolute band power in the δ, θ, α, and β power bands respectively. Moreover, the relative band power was calculated by dividing the absolute band power in each band with the total power in 1-30Hz and this relative power at each channel was averaged over the scalp to obtain global relative power features: rδ, rθ, rα, and rβ. The absolute band power at all the channels was averaged over the scalp in order to obtain a global absolute band power in δ, θ, α and, β power bands and it was used to calculate the five global ratio based features:

\[
PRI = \frac{\delta + \theta}{\alpha + \beta} = \text{Power Ratio Index} \tag{1}
\]
\[
DAR = \frac{\delta}{\alpha} = \text{Delta-Alpha Ratio} \tag{2}
\]
\[
TBR = \frac{\theta}{\beta} = \text{Theta-Beta Ratio} \tag{3}
\]
\[
TAR = \frac{\theta}{\alpha} = \text{Theta-Alpha Ratio} \tag{4}
\]
\[
TBR = \frac{\theta}{\alpha + \beta} = \text{Theta-Beta-Alpha Ratio} \tag{5}
\]

Moreover, the trial averaged PSD was used to compute pairwise-derived Brain Symmetry Index (rBSI) [9] and revised Brain Symmetry Index (rBSI)[10] which respectively quantified the brain asymmetry between the homologous channels pairs (left v/s right) in both the hemispheres and an overall global interhemispheric asymmetry. As done in the previous studies [5], the rBSI and pdBSI between 1-25Hz were calculated as:

\[
rBSI = \frac{1}{N} \sum_{i=1}^{N} \left| \frac{R_i - L_i}{R_i + L_i} \right| , \quad R_i = \frac{1}{M} \sum_{j=1}^{M} R_{ij} \tag{6}
\]
\[
pdBSI = \frac{1}{MN} \sum_{j=1}^{M} \sum_{i=1}^{N} \left| \frac{r_{ij} - l_{ij}}{r_{ij} + l_{ij}} \right| \tag{7}
\]

Here, r_{ij} and l_{ij} are the trial averaged PSD from right and left homologous channel pairs (at channel pairs j=1,2,...,M) at frequency i=1,2,...,N. R_i and L_i (similarly calculated) represent the average power over all the channels on the right and left hemispheres at frequency i. Considering these two brain symmetry features and nine band power features, in total 11 EEG features were extracted for each subject from the first (pre-treatment: EEG_0) and the last (post-treatment: EEG_2) rehabilitation session.

D. Statistical analysis

A non-parametric statistical analysis was performed owing to the non-normal distribution of the underlying data. The relationship between EEG features and the clinical outcome was assessed using Spearman’s rank correlation. The predictive capabilities of any features were compared by statistical comparison of their correlation coefficients (CC) using Fisher Z-transformation. The statistical difference between the pre- and post-treatment EEG features was tested using Wilcoxon signed-rank test and, the intergroup difference in the features was assessed using Wilcoxon rank sum test. Assuming Spearman’s rank correlation coefficient of 0.6, the sample size of the study was just enough (n≥9) to achieve a statistical power of 80% with significance level of α = 0.05. Moreover, owing to the small sample size in each group and the exploratory nature of the study, the family-wise error rate correction was not performed.

III. Results

A. Correlation between pre-treatment EEG features and pre-treatment FMA

The separate group analysis of the correlation between pre-treatment EEG features (EEG_0) and FMA_0 showed a significant negative correlation between TBR_0 and FMA_0 (p = 0.025) for the BCI group. Although no significant relationship was observed for the tDSC group, the intergroup comparison of correlation coefficients revealed that there
was no intergroup difference in the predictive capabilities of any EEG features. Hence, the combined group analysis (All subjects) was performed and significant negative relationship was observed between $FMA_{T0}$ and $r_{T0}$ ($p = 0.005$, Fig.1(a)), $TBR_{T0}$ ($p = 0.038$, Fig.1(b)), $TBAR_{T0}$ ($p = 0.029$, Fig.1(c)) and, $r_{BSI_{T0}}$ ($p = 0.045$, Fig.1(d)). All the correlation coefficient values are presented in Table I.

### B. Post-treatment change in the EEG features and their correlation with the functional improvement

The statistical analysis of pre and post treatment EEG feature values revealed that there was a significant treatment induced change in the relative theta band power ($p=0.039$) in the BCI group. Also, although not significant, BCI group displayed a marginal change in TAR ($p = 0.054$) and TBR ($p = 0.074$). In the tDCS group, a significant change was displayed a marginal change in TAR ($p = 0.054$) and TBR ($p = 0.029$, Fig.1(c)) and, $r_{BSI_{T0}}$ ($p = 0.045$, Fig.1(d)). The tDCS and BCI group were mutually exclusive, no statistically significant between-group difference in pre-treatment EEG as well as in change in EEG features was observed.

Post-identification of the EEG variables which changed significantly, we investigated if this change correlated with clinical improvements. The correlation analysis between $\Delta EEG$ and $\Delta FMA$ revealed that there was a significant negative correlation between $\Delta FMA$ and $\Delta \theta$ ($p = 0.022$, Fig.2(a)), $\Delta TAR$ ($p = 0.045$, Fig.2(b)) and, $\Delta TBR$ ($p = 0.045$, Fig.2(c)) in the BCI group. Despite the significant change, pdBSI did not show any significant correlation with $\Delta FMA$ in the tDCS group. Furthermore, right-tailed Fisher z-test revealed that the correlation between $\Delta FMA$ and $\Delta \theta$ showed marginal change in the BCI group than the tDCS group ($p = 0.064, 0.076, 0.079$). Table II(A) reports the correlation between all the $\Delta EEG$ features and $\Delta FMA$.

### C. Correlation between post-treatment EEG features and post-treatment FMA

After the analysis of the correlation between $\Delta EEG$ and $\Delta FMA$, the relation between post-treatment clinical score ($FMA_{T2}$) and post-treatment EEG features ($EEG_{T2}$) was investigated. The analysis revealed that, in the BCI group, $FMA_{T2}$ exhibited significant negative correlation with $TBR_{T2}$ ($p = 0.021$, Fig.3(b)) and, $TAR_{T2}$ ($p = 0.037$, Fig.3(c)) and a marginal negative trend with $r_{T2}$ ($p = 0.087$).

### Table I

<table>
<thead>
<tr>
<th>EEG Features</th>
<th>Correlation coefficient between $FMA_{T0}$ and $EEG_{T0}$ features ($p$)</th>
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<tr>
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<tr>
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<tr>
<td>$r_{BSI_{T0}}$</td>
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*Bold numbers denote statistical significance ($p < 0.05$). No significant between-group difference in the predictive capabilities of any $EEG_{T0}$ features was observed.

### Table II

<table>
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<tr>
<th>EEG Features</th>
<th>Correlation coefficient between $FMA_{T2}$ and $EEG_{T2}$ features ($p$)</th>
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<tr>
<td>$\Delta BSI$</td>
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</table>

*Bold numbers denote statistical significance ($p < 0.05$). pdBSI is significant in tDCS group.
and, $T \text{BAR}_{T2}$ ($p = 0.058$). Also, a strong positive correlation was observed between $r_B T2$ and $FMA_T2 (p = 0.009, \text{Fig.3}(a))$ in the BCI group. No $EEG_{T2}$ feature correlated with the $FMA_{T2}$ for the tDSC group. The correlation results are presented in Table II(B).

IV. DISCUSSION

The QEEG features have been reported to be informative for stroke monitoring in (sub-)acute states [3], and in this study we assessed their utility for continuous monitoring of chronic state BCI and tDSC rehabilitation. We observed that there was a significant treatment induced change in the interhemispheric asymmetry in the tDSC group captured using pdBSI. Although this difference did not correlate with the functional improvements, the result is consistent with the neuroimaging analysis of the same study cohort where increased interhemispheric cerebral blood flow asymmetry was observed in the tDSC group alone [11].

In the BCI group, relative theta power, TAR and, T BAR displayed a substantial change during the treatment and the change was correlated with the change in FMA. Moreover, pre-treatment $r_B$, TBR, and T BAR displayed a correlation with pre-treatment FMA and post-treatment $r_B$, TBR, TAR, and T BAR displayed a correlation with post-treatment FMA in BCI group. These results collectively indicate that relative theta and beta power and the interactions between theta, beta, and alpha oscillations can be highly suitable monitory biomarkers of BCI based rehabilitation.

Moreover, all the features in the BCI group indicated a positive association between improved motor functions and brain oscillations in the higher frequency bands which is in line with the reported literature [3], [5]. Although, the involvement of theta activity is not very common in motor rehabilitation studies, it is reported to be associated with the ischemic penumbra[12] in acute state. Considering this relation, we suspect that the motor recovery in the BCI group might be indicative of the training-induced activation of dysfunctional neuronal population.

Despite the absence of any pre-treatment inter-group differences and similar clinical outcomes, the comparative analysis in BCI and tDSC cohort revealed that the QEEG features displaying significant change during the intervention were distinctly different between the two groups. The tDSC intervention was characterized by a substantial change in brain asymmetry whereas the change in the relative theta power was observed to be a signature feature of the BCI interventions. Also, a marginal inter-treatment difference was observed in the predictive capabilities of post-treatment QEEG features. Moreover, a combined analysis of Diffusion and perfusion MRI and transcranial magnetic stimulation(TMS) in the same trial also reported significant differences in mechanisms of recovery between these two groups [11].

Considering the coherent results from the EEG as well as MRI and TMS analysis, we suggest that an altogether different neuronal mechanism was facilitated by tDSC coupled BCI intervention as opposed to the BCI intervention alone and these mechanisms are specific to the intervention. Along the similar lines, we speculate that the clinical recovery during different rehabilitation paradigms might be facilitated by intervention specific neuronal changes and identifying these distinct neuronal repair mechanisms will be helpful to better understand the brain dynamics during clinical recovery.

V. CONCLUSION

The results of this study indicate that QEEG features can be informative in the chronic stroke motor rehabilitation. Moreover, the results from the clinical trial and neuro-physiological analysis suggest that different rehabilitation paradigms may have distinct mechanisms of neuronal recovery. Notwithstanding the fact that the sample size used in this study is small and needs to be supported with larger cohort, the results from this study provide novel insights in the neuronal change during different rehabilitative interventions in the chronic state and further investigation in this direction is necessary.

REFERENCES


