Effect of TESS on Motor Imagery of Same Limb Fine Hand Movements

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May 9, 2021

I. Introduction

Non-invasive EEG-based Brain Computer Interfaces (BCIs) are hugely valuable for patients suffering from neuromuscular impairments and allow patients to use conventional augmentative communication methods. Motor imagery (MI) based BCIs, in which subjects imagine limb movements (without muscle contraction) to control external systems, have been subject to extensive research [1, 24]. Despite the rapid development of the MI based BCI technology in the past decades, several challenges remain, limiting the practical use of such systems in real-life environments. One of such challenges is the lack of accuracy in classifying fine, same-limb, complex MI tasks. EEG has low signal to noise ratio (SNR) and low spatial resolution. Specifically, EEG signals suffer from the volume conduction effect, and as a result neural markers of distinct MIs can be smeared and distorted by cortical activities from adjacent channels, thereby reducing MI decoding accuracy [8]. This is especially the case for same-limb MIs (e.g. hand Flexion/Extension), which activate closely located cortical sources [28]. Consequently, the number of MI tasks that can be used to successfully control a BCI is limited, and the ability to classify same-limb MI will greatly increase the dimensions of an MI BCI.

Sensorimotor rhythms (SMRs), the voluntary modulation of frequency-specific EEG signal in the sensorimotor cortex, contain well-known neural markers of MI production. These markers are often termed event-related desynchronization (ERD) and even-related synchronisation (ERS) within the alpha/mu (8-13 Hz) and beta (13-30 Hz) bands.

Recent research has shown that MI performances can be improved with the help of external, assistive stimulation devices. For instance, in [7] Corbet et al. demonstrated that sensory threshold neuromuscular electrical stimulation (St-NMES) as a somatosensory feedback/guidance method during MI training fostered hand-closing MI performance and enhanced MI brain patterns. This somatosensory feedback modality did not elicit any muscular contraction, thereby minimizing interference on recorded MI EEG signal. In [25], Vidaurre also combined MI training with St-NMES guidance and found that classification of MI for hands and feet improved as a result of an increase in ERD/ERS amplitudes. Transcutaneous electrical spinal stimulation (TESS) is another novel, non-invasive stimulation technique and stimulates the spinal cord from the surface of the skin. At the spinal level, TESS modulates the excitability of sensorimotor circuits, bringing interneurons and motor neurons closer to their motor thresholds [16]. TESS has shown therapeutic potential in long-term restoration of motor (both upper and lower), bladder, and cardiovascular functions [5, 10, 11]. These literature generally used a low stimulation frequency (e.g. 5-50 Hz) with a high carrier frequency between 5-10 kHz to permit stimulation at high current intensities of 80-120 mA without causing pain or discomfort. These parameters are shown to have parallel effects on the excitability of cortical and spinal networks. In [5] Benavides et al. found that a single 20 minutes session of TESS at 30 Hz pulses with a 5 kHz carrier frequency on the C5/C6 vertebrae of subjects during Rest increased corticospinal excitability. Interestingly, TESS at these parameters also increased inhibition at the cortical level by suppressing ascending nociceptive transmission.

The relationships between MI performance and corticospinal excitability as well as cortical inhibition remain largely unknown. Some recent evidence suggests that MI performance is related and perhaps even correlated to corticospinal pathway excitability. For instance, several studies measured motor-evoked potentials (MEPs) using transcranial magnetic stimulation (TMS) and suggested that increased corticospinal excitability generally occurs during MI [21, 23, 9]. Nielson et al. suggested that corticospinal excitability is greatly increased when subjects feel compelled to pay stronger attention to the execution of movements [18]. Directing stronger attention to imagined movements may facilitate better MI performances. Regarding the relationship of MI with cortical inhibition, recent evidence in [17] found that short-interval intracortical inhibition (SICI) in the motor cortex is larger during MI than Rest. MI probably recruits cortical SICI inhibition circuits to prevent production of overt movement while the motor system is activated [12]. Indeed, neuroimaging evidence in [4] suggests that activity in the primary motor cortex is suppressed by other regions such as the supplementary motor area during MI. This may suggest that cortical inhibitory circuits are necessary for the success of MI, and increased cortical inhibition in motor cortex may facilitate improved MI production.

Given existing evidence in literature, we hypothesize that one stand-alone 20 min TESS session at 30 Hz pulses with a 5 kHz carrier frequency on the C5/C6 vertebrae will have a sustained inhibitory effect at the cortical level and a sustained excitatory effect at the corticospinal level. The activation of these inhibitory and excitatory circuits may causally improve same-limb Flexion and Extension MI performance in the post stimulation session, shown as an increase in discriminability

of the sensorimotor neural correlates of Extension MI, Flexion MI, and Rest. Nonetheless, it has been suggested that the usage of feedback of subjects' MI performance is important to facilitate MI learning and training, as subjects learn to modulate sensorimotor rhythms to improve performances [7, 19]. Therefore, without the element of feedback and motor learning, we expect this stand-alone TESS session to only generate slight MI improvements.

II. Material and Methods

To study the effects of TESS on the discriminability of the neural correlates of same-limb Flexion and Extension MI, this project followed several methods in [8], which also studied complex same-limb MI decoding.

A. Experimental paradigm

Two subjects took part in the experiment, which involved three separate sessions with 2 runs per session: (1) MI session of Rest, Flexion, and Extension trials (pre TESS session), (2) TESS session (stimulation session), and (3) MI session identical to the first session (post TESS session). Subject 1 performed MI on the right hand, whereas Subject 2 performed MI on the left hand. During MI sessions, EEG signal was recorded at 512 Hz from 32 channels distributed over the scalp following the 10/20 standard electrode positioning. Fig. 6 shows the structure and timing of each trial.

B. TESS modality

In the second session of the experimental protocol, subjects received TESS continuously at the cervical vertebrae C5/C6 for 20 minutes. Subjects were at resting state during stimulation, and no EEG was recorded. Consistent across the two subjects, stimulation frequency was set to 30 Hz with 5 kHz carrier frequency and an amplitude of 20 mA. The stimulation applied did not evoke any muscular contractions.

C. Preprocessing

Following the bandpass frequency band proposed in [8], raw EEG acquired from all 32 channels were bandpass filtered between 1-30 Hz using a 5th order Butterworth filter. This improves SNR of MI analysis, since neural markers of MI production are generally in the alpha/mu and beta bands within the sensorimotor cortex [6, 7, 8]. The temporal filtered EEG was then common-average referenced (CAR) to enhance spatial resolution of ERD and ERS, which can be blurred by projected scalp patterns from nearby electrodes. Trials that contained abnormally high beta ERS were considered artifactual and discarded. These are often the first and last trials of each run.

Trials extracted composed of the 2 s task cue period 4 s task window, which were kept for further analysis. The task cue period was included, as it was shown to include MI activities (e.g. ERD) in some time-frequency plots (Fig. 8, 9).

D. Computation of ERD values

To study the effects of the TESS session on sensorimotor modulations of distinct MI tasks, the ERD values were first computed for each electrode of all trials in both subjects, following the method proposed in [7]. On the trials of each session, alpha/mu and beta band power were first computed and then normalized to the average alpha/mu and beta band power of the Rest task trials (mean baseline reference) of the respective session. The extracted spectral activities of each trial were normalized by subtracting the respective mean baseline reference and then dividing by the same baseline value.

For topographical analysis, ERD values were averaged across time and also across the respective trials corresponding to the tasks, and these averaged ERD values of each electrode were used to compute a topographic map (Fig. 1).

E. Connectivity analysis

A brain network analysis at the signal level was conducted to evaluate the effects of TESS on coordination within the sensorimotor cortex. MI training and improvements in MI performances can result in enhanced functional connectivity between regions well described during MI [7, 26]. Therefore, lagged coherence, the most physiological accurate measure of functional connectivity between regions of the brain [20], was computed for each electrode channel pair and averaged over the contralateral hemisphere (Fig. 7) during task periods before and after stimulation.

F. Feature extraction and selection

To evaluate whether TESS affects the discriminability of same-limb MI EEG patterns, 3-class (Flexion, Extension, and Rest) classification performance was studied on the pre and post TESS sessions. Features extraction and selection again followed methods in [8]. Time-frequency features were extracted from each trial (2 s task cue + 4 s task window) and two different electrode groupings (all motor and contralateral motor) to capture the components of varying oscillatory activities. All motor includes all FC, C and CP line electrodes, whereas contralateral motor only includes the contralateral subset of these electrodes (Fig. 7) To accomplish this, time-frequency representations from complex Morlet wavelet decomposition were segmented into 0.5 s time windows and 2 Hz frequency bands covering the 5-30 Hz range, and averaged magnitude lengths of wavelet coefficients in each segment was extracted as features. This process resulted in 4992 features extracted from each trial. Note that this feature extraction method is suitable only for offline studies. In online studies, features must be extracted from short time windows instead of an entire trial to reduce latency between subjects' motor commands and machine decisions.

Two different feature extraction methods were used: Mahalanobis distance and Fisher score. Mahalanobis distance was used as a multivariate method following methods in [8], whereas Fisher score, on the other hand, is a much simpler, univariate method. In each method, the 15 most

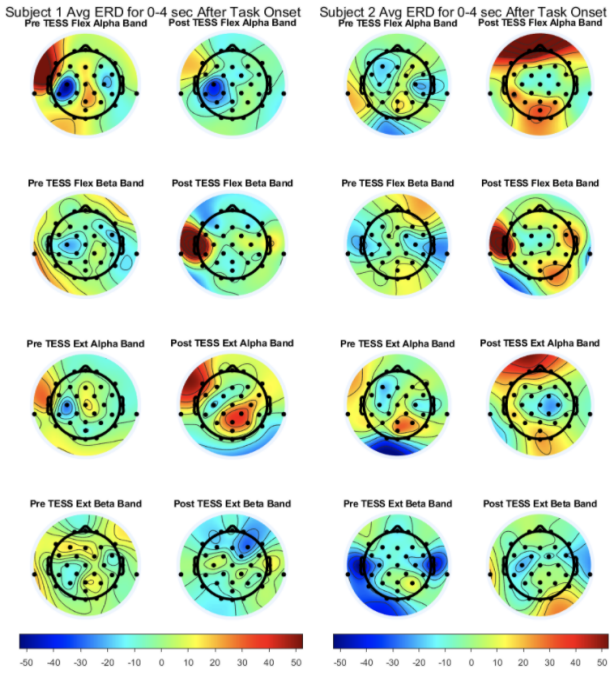

Fig. 1. Topological analysis of Subject 1 (left two columns) and 2's (right two columns) alpha and beta band ERD values during the tasks window (0-4 s after task onset) of different MI tasks (Flex: Flexion, Ext: Extension) for pre and post TESS.

discriminant features were selected. Each of these feature selection techniques was applied to features spaces consisting of 2 electrode groupings, all motor and contralateral motor, so the result was 4 different feature spaces after selection.

G. Classification

Classification of the 3 classes (Flexion, Extension and Rest) was performed using a linear discriminant (LDA) with a diagonal covariance matrix, also used in [7] to classify hand-closing MI vs. Rest. Two classifiers were built separately on the pre and post TESS sessions. To estimate accuracy of each classifier, 2-fold run-wise cross validation was performed to respect the temporality of non-stationary EEG signals. Accuracy (%) was used as an evaluation metric since the number of trials of the 3 task types were balanced, and confusion matrices were plotted as well to evaluate misclassifications between different tasks.

III. Results

A. Topological analysis: MI neural correlates

Topological plots of the baseline referenced ERD values in Fig. 1 depict the alpha and beta band neural correlates of different MI tasks across electrodes both pre and post TESS. Visual inspection shows an ERD in the contralateral sensorimotor cortex in both bands and tasks of Subject 1 in the pre TESS session. The contralateral region covers CP, FC and C line electrodes, representative of frontoparietal regions well described during MI [13]. In Subject 2's pre TESS session, this ERD is evident in both bands and tasks, but not restricted to the contralateral hemisphere. Though less visible, some task-related desynchronization was also seen in alpha band of time-frequency plots (figures 8, 9). These confirm that subjects were performing MI in a sustained matter. In both subjects and bands, this ERD correlate of MI is less visible and focal post TESS.

Preliminary visual inspection shows that contralateral ERD magnitude in Subject 1 overall decreased in both bands and tasks after TESS, suggesting that discriminability of MI neural correlates against Rest may deteriorate after TESS. In both subjects and bands, the magnitude difference of ERD values between Flexion and Extension is slightly amplified post TESS, hinting at a possible increase in discriminability of neural correlates of same-limb MI tasks.

B. Task related desynchronization

To better investigate the effects of TESS on task-related desynchronization of different MI tasks, the computed ERD values of both bands, tasks, and subjects were averaged over the 5 electrodes of the contralateral sensorimotor cortex (Fig. 7), averaged over the MI task window (0-4 s after task onset) and plotted in figure 2. The baseline reference (zero value) is the ERD of Rest task windows. Negative values represent a desynchronization (ERD), whereas positive values represents a synchronisation (ERS) compared to Rest. Two significance tests were conducted: **(1)** unpaired t-test to examine the change in ERD of a task and band pre and post TESS (e.g. Flexion alpha band ERD pre and post TESS) and **(2)** ANOVA analysis on the ERD differences between Flexion, Extension, and Rest MI tasks, conducted for each band on pre and post TESS separately. Amongst these tests, only Subject 1's beta band ERD in Flexion MI returned significant difference between pre and post TESS ($p < 0.05$). Note that pre and post ERD values of each subject are treated as independent groups of measurements given the lack of subjects in this study.

Despite the lack of significance results, an examination of the absolutes differences in Flexion and Extension mean ERD values suggests improvement in discriminability of neural correlates of Flexion and Extension MIs in both bands and subjects post TESS (Fig. 2). In regards to the discriminability of the neural correlates of MI tasks against Rest, ERD analysis suggest that Subject 1's Flexion vs. Rest may improve and Extension vs. Rest may deteriorate after TESS. In Subject 2, Flexion vs. Rest may deteriorate and Extension vs Rest remains inconclusive. Interestingly, these trends were not picked up by the significance tests.

C. Connectivity

The network analysis of the contralateral sensorimotor cortex revealed an increase in Subject 1's functional connectivity following TESS in the alpha band for both tasks, but a decrease in both tasks for the beta band. Subject 2's connectivity increased in the beta band for both tasks, but only the alpha band connectivity value associated with Flexion increased after stimulation. None of the aforementioned increases or decreases were deemed to be statistically significant (Fig. 10).

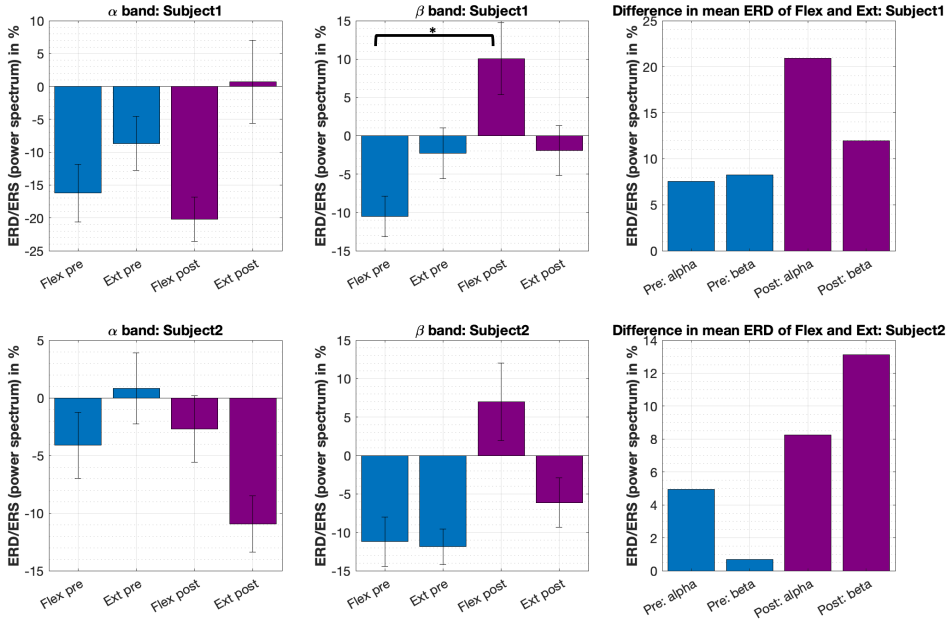

Fig. 2. ERD values averaged over the contralateral sensorimotor cortex (Fig. 7), computed for both subjects, bands, and tasks (Flex: Flexion, Ext: Extension) for both pre and post TESS. Subject 1's Flexion beta band ERD reported significant change between pre and post TESS. $*p < 0.05$

D. Features analysis

Mahalanobis Distance Feature Selection Analysis (All Motor)

Feature Type	Sub 1 Pre	Sub 1 Post	Sub 2 Pre	Sub 2 Post
Contralateral Ch.	42.9%	93.3%	40.0%	46.7%
Ipsilateral Ch.	57.1%	6.7%	60.0%	53.3%
Alpha Band	50.0%	33.3%	60.0%	40.0%
Beta Band	42.9%	53.3%	26.7%	40.0%
Cue Period	35.7%	26.7%	46.7%	20.0%
Task Period	64.3%	73.3%	53.3%	80.0%

TABLE I
PERCENTAGES OF FEATURE TYPES SELECTED USING MAHALANOBIS DISTANCE FEATURE SELECTION ON ALL MOTOR ELECTRODES

Fisher Score Feature Selection Analysis (All Motor)

Feature Type	Sub 1 Pre	Sub 1 Post	Sub 2 Pre	Sub 2 Post
Contralateral Ch.	100.0%	86.7%	26.7%	53.3%
Ipsilateral Ch.	0.0%	13.3%	73.3%	46.7%
Alpha Band	26.7%	20.0%	46.7%	46.7%
Beta Band	73.3%	73.3%	33.3%	40.0%
Cue Period	73.3%	86.7%	53.3%	26.7%
Task Period	26.7%	13.3%	46.7%	73.3%

TABLE II
PERCENTAGE OF FEATURE TYPES SELECTED USING FISHER SCORE FEATURE SELECTION ON ALL MOTOR ELECTRODES

To evaluate what types of features were being selected by the two feature selection algorithms as well as how TESS affected the features selected, we calculated the percentage of certain feature types that were selected, including contralateral vs. ipsilateral electrodes, alpha vs. beta band, and cue period vs. task period, shown in tables I and II. For Mahalanobis selection on all motor electrodes, there was an increase in contralateral electrodes selected for both subjects post TESS, while Fisher selection on all motor electrodes showed this same increase in Subject 2. In summary, channels selected from feature selection generally become more physiologically relevant to MI post TESS. Both feature selection methods revealed an increase in task period times selected for Subject 2 post TESS. In all cases, there was an increase in beta band features selected and decrease in alpha band features selected post TESS. Additionally, it should be noted that feature analysis agrees with previous topological analysis for Subject 2, as MI activities appear to not be restricted to the contralateral region since many ipsilateral electrodes are being selected in both pre and post TESS.

E. Cross validation results

To evaluate classification performance for each session, accuracy and confusion matrices were computed across cross-validation runs for each session and the 4 selected feature spaces. Looking at the trends in accuracy values plotted in Fig. 3, Subject 2 showed a decrease in performance post TESS for both Mahalanobis feature spaces. Upon further analysis, it was observed that this decrease was more significant for the contralateral only feature space, which in turn makes sense since Subject 2 showed notable activity in the ipsilateral hemisphere during MI execution. Subject 1's performance is more variable dependent on the feature selection method and features space, showing an increase in Mahalanobis all motor and Fisher contralateral feature spaces. In all cases Subject 2 did not show improvements in post TESS CV results. In summary, from figure 3 it is difficult to reach conclusive observations due to the inter-subject variability.

Fig. 4 and 5 show the confusion matrices for Mahalanobis selection and Fisher selection, both on only contralateral electrodes, respectively. We analyzed misclassifications between

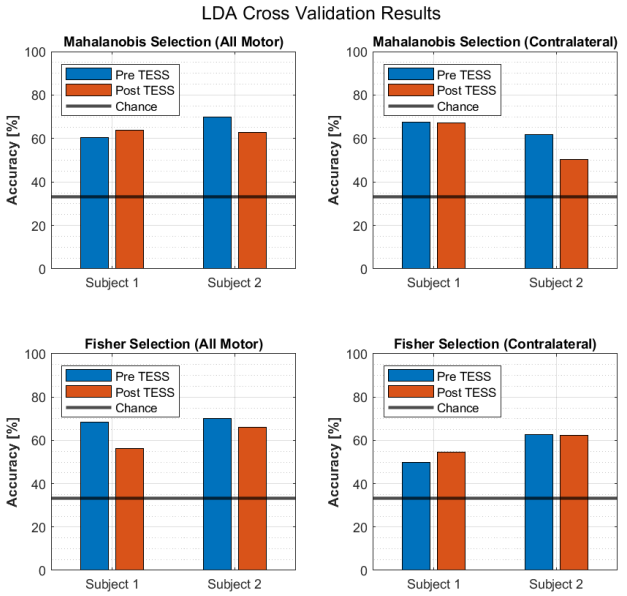

Fig. 3. LDA cross validation accuracy (%) results, averaged across runs, for all feature selection techniques compared against chance level predictions

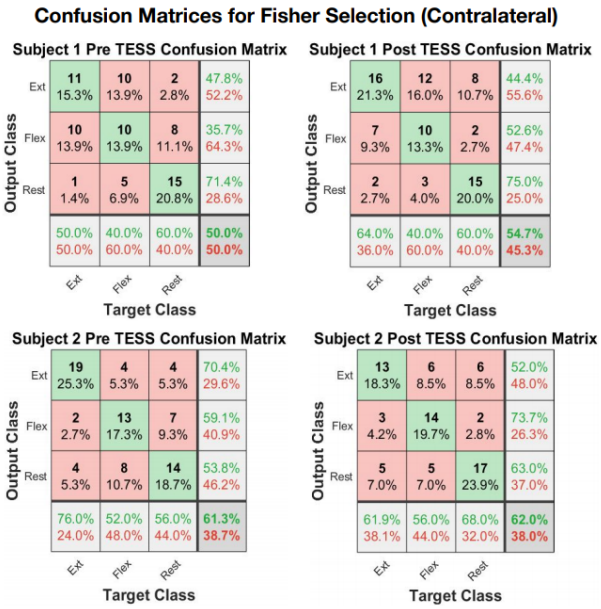

Fig. 5. Confusion matrices for Fisher score feature selection on contralateral motor electrodes

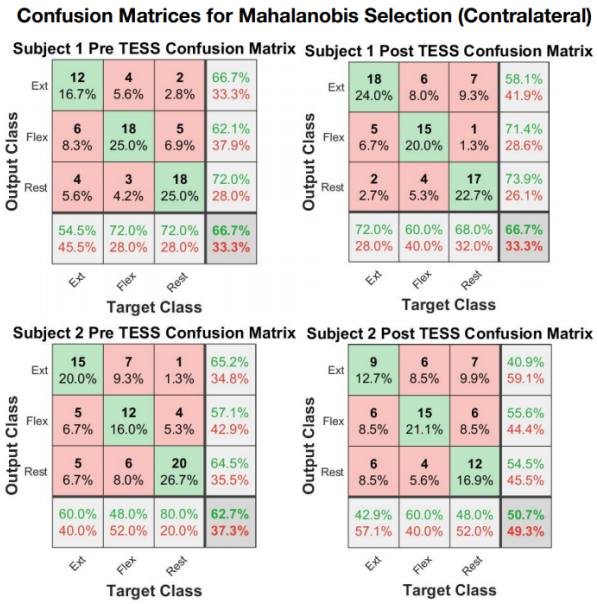

Fig. 4. Confusion matrices for Mahalanobis distance feature selection on contralateral motor electrodes

classes to draw conclusions on which tasks became more or less discriminate from others. For Fisher selection specifically, in agreements with some aspects of our ERD analysis, we noticed increased Flexion vs. Rest performance and decreased Extension vs. Rest performance for both subjects post TESS. Surprisingly, in opposition to general trends observed in ERD analysis, Flexion vs. Extension showed slightly decreased performance post TESS for Subject 2, and this was relatively unchanged for Subject 1.

IV. Discussion

A. *Same-limb MI performance after TESS*

In general, the decoding of same-limb motor imagery (Flexion vs Extension) did not improve in the session following TESS based on the mixed results explained in section III-E, thereby violating our hypothesis. However, ERD/ERS analysis results in section III-B do indicate that TESS may improve the discriminability of neural correlates associated with same-limb MI, although these trends were not reported statistically significant nor reflected in classification results.

One reason why a stand-alone TESS session may not have improved same-limb MI performances may be that MI training should be coupled with feedback and guidance to exploit learning mechanisms such that subjects learn to modulate sensorimotor rhythms through progressive practice. In experiments described in [7, 25] MI training was combined with stimulation-based somatosensory feedback to foster MI performances. Furthermore, literature has explored other forms of somatosensory feedback to enhance MI brain patterns: passive movement of a joint using a robotic orthosis, electrical stimulation inducing muscular contraction, and vibrotactile stimulation of the targeted limb [2, 3, 15, 22, 27]. Thus, although the stand-alone 20 minute administration of TESS may have caused an inhibitory effect at the cortical level and excitatory effect at the corticospinal level that may alter MI brain patterns, it did not exploit any learning mechanisms. Literature on MI performance enhancement suggests that the timing of the stimulation may be just as important as the kind of stimulation, and that stimulation (feedback) should be contingent to motor commands. One potential method for designing somatosensory feedback conditions of different MI would be to combine some of the aforementioned modalities (e.g. St-NMES and vibrotactile) to improve richness of affer-

ent feedback.

B. Functional Connectivity after TESS

The results of the network analysis also do not indicate TESS had a significant effect on the connectivity in the contralateral sensorimotor cortex. This further corroborates that TESS did not foster MI performance improvements, as an increase in functional connectivity of this network is expected according to the results of [7, 25]. However, it should be noted that the computation of functional connectivity in the signal domain is known to be less reliable than the same computation at the voxel level due to an increase in spatial resolution and a reduction of the blurring effects caused by spatial conduction [20]. Unfortunately due to time constraints, the transformation of EEG signals from the signal domain to the source domain was not feasible. With more time the author's would follow the procedure established by [14].

V. Future work

Several methods of future work are required to further test the hypothesis more rigorously and reach a more definite conclusion. Firstly, a sham group is required in which subjects receive sham TESS intervention to ensure that MI changes are indeed a result of direct neural effects of TESS and not indirect sensory and psychological (placebo) side effects. In addition, intersubject variability witnessed in section III-E prevents experimenters from reaching a solid conclusion, therefore more subjects and trials are required to further test the hypothesis. Lastly, our hypothesis suggests that MI performance changes are resulted from alterations in TESS led physiological factors such as corticospinal excitability and cortical inhibition. Therefore, parameters such as MEPs and SICI could also be measured to relate MI performance changes to these physiological factors.

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VI. Supplementary Material

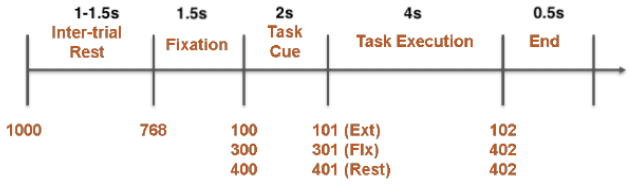

Fig. 6. Trial organization for MI sessions pre and post TESS. The 2 s task cue period and 4 s task execution period were extracted during trial extraction.

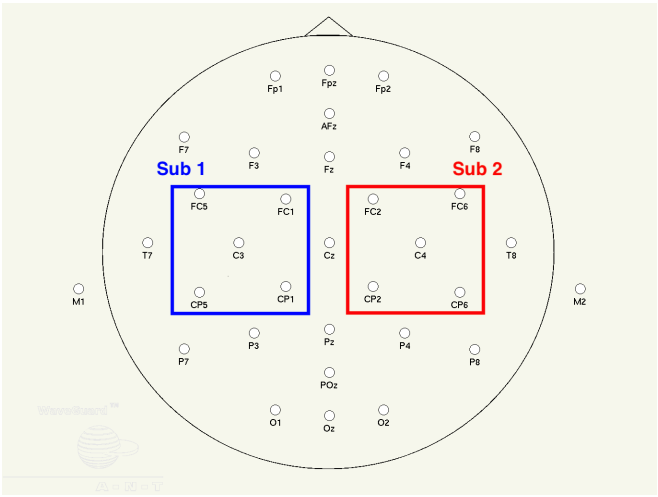

Fig. 7. Contralateral sensorimotor channels used for Subject 1 (blue) and Subject 2 (red).

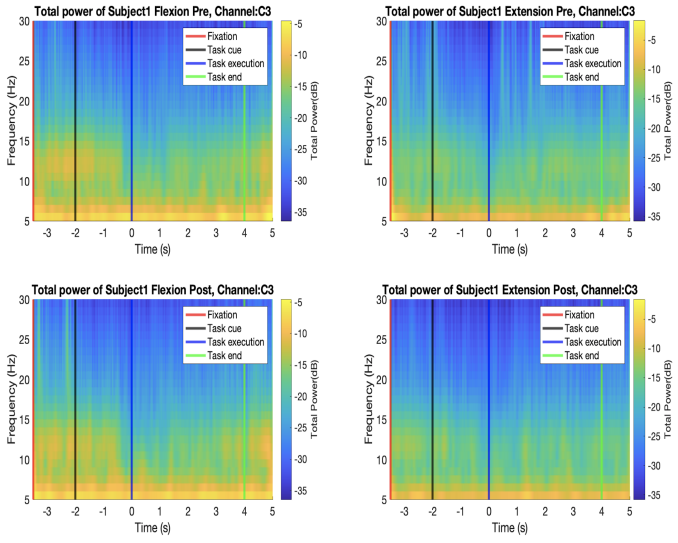

Fig. 8. Time-frequency plot over electrode C3 for Subject 1 Flexion and Extension MI pre and post TESS. In some cases, desynchronization in the alpha band can be seen during task execution.

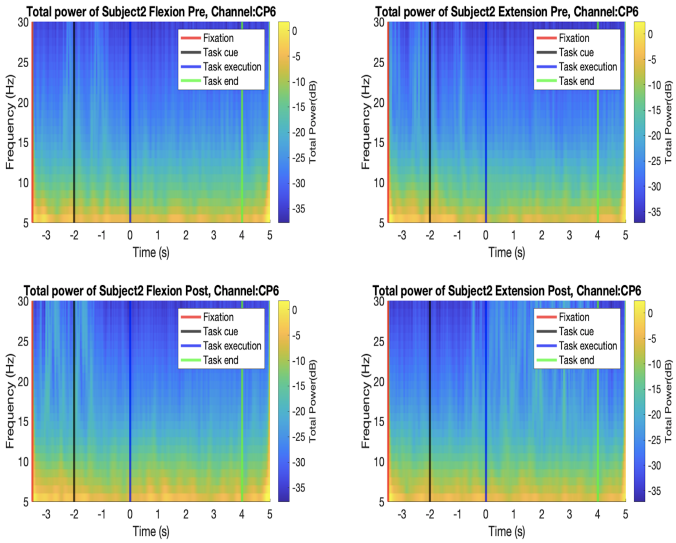

Fig. 9. Time-frequency plot over electrode CP6 for Subject 2 Flexion and Extension MI pre and post TESS. In some cases, desynchronization in the alpha band can be seen during task execution.

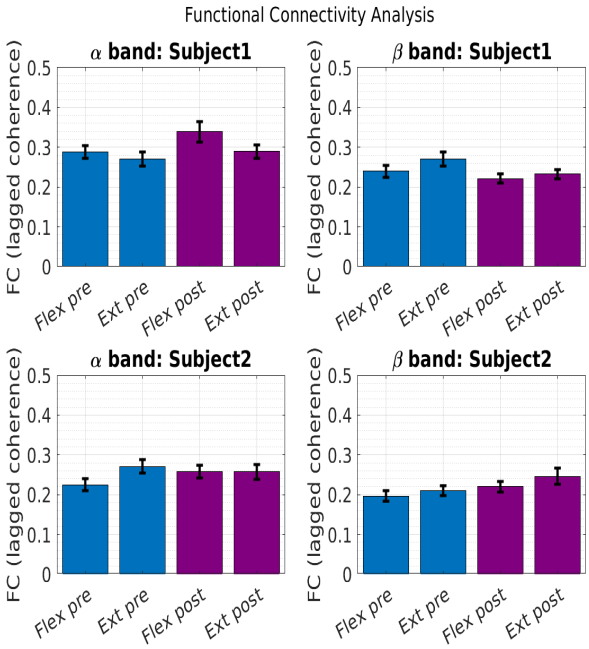

Fig. 10. Lagged coherence for electrode clusters averaged over the contralateral sensorimotor cortex (Fig. 7) in the alpha and beta band for Flexion and Extension both pre and post TESS. The error bars show the standard error of the mean.