An exploration of neural dynamics of motor imagery for people with amyotrophic lateral sclerosis

An Exploration of Neural Dynamics of Motor Imagery for People with Amyotrophic Lateral Sclerosis

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Abstract. *Objective.* Studies of the neuropathological effects of amyotrophic lateral sclerosis (ALS) on the underlying motor system have investigated abnormalities in the magnitude and timing of the event-related desynchronization (ERD) and synchronization (ERS) during motor execution (ME). However, the spatio-spectral-temporal dynamics of these sensorimotor oscillations during motor imagery (MI) have not been fully explored for these patients. This study explores the neural dynamics of sensorimotor oscillations for ALS patients during MI by quantifying ERD/ERS features in frequency, time, and space. *Approach.* Electroencephalogram (EEG) data were recorded from 6 patients with ALS and 11 age-matched healthy controls (HC) while performing a MI task. ERD/ERS features were extracted using wavelet-based time-frequency analysis and compared between the two groups to quantify the abnormal neural dynamics of ALS in terms of both time and frequency. Topographic correlation analysis was conducted to compare the localization of MI activity between groups and to identify subject-specific frequencies in the μ and β frequency bands. *Main Results.* Overall, reduced and delayed ERD was observed for ALS patients, particularly during right-hand MI. ERD features were also correlated with ALS clinical scores, specifically disease duration, bulbar, and cognitive functions. *Significance.* The analyses in this study quantify abnormalities in the magnitude and timing of sensorimotor oscillations for ALS patients during MI tasks. Our findings reveal notable differences between MI and existing results on ME in ALS. The observed alterations are speculated to reflect disruptions in the underlying cortical networks involved in MI functions. Quantifying the neural dynamics of MI plays an important role in the study of EEG-based cortical markers for ALS.

Keywords: Amyotrophic lateral sclerosis (ALS), electroencephalogram (EEG), event-related desynchronization (ERD) and synchronization (ERS), motor imagery (MI).

1. Introduction

Amyotrophic lateral sclerosis (ALS), one of the most common motor neuron diseases, is typically characterized by the progressive atrophy of motor neurons (Fiori et al. 2016). Establishing neural markers that are sensitive to the diagnosis and prognosis of ALS remains an open research question (Vejux et al. 2018). Synchronization variations in electroencephalographic (EEG) sensorimotor oscillations in the μ (8-12 Hz) and β (13-25 Hz) frequency bands are considered a hallmark of several motor-related components including motor planning, motor execution (ME), and motor imagery (MI) (Pfurtscheller and Lopes da Silva 1999). These oscillatory modulations are known as event-related desynchronization (ERD) and event-related synchronization (ERS) (Pfurtscheller and Neuper 1997; Pfurtscheller and Aranibar 1977). Time-locked but not necessarily phase-locked μ and β amplitude suppression (ERD) and enhancement (ERS) linked to imagination onset have been successfully translated to several areas including brain-computer interfaces (BCI) for non-muscular communication and control purposes to enhance quality of life for ALS patients (Yuan and He 2014; Jeon et al. 2011; Pfurtscheller and Lopes da Silva 1999). An important characteristic of these frequency specific variations is that their dynamics are closely related to the functional state of the underlying cortical neural networks. Spatio-spectral-temporal quantification of ERD/ERS dynamics in ALS is important in determining EEG-based cortical markers of this disease. Along with understanding the neuropathological effects of ALS and its relation to alterations in underlying motor system functions, this may support multiple applications including diagnostic and prognostic techniques as well as MI-based BCI systems.

Few studies have investigated the electrophysiological correlates of ALS using experimental tasks involving motor functions (Riva et al. 2012; Bizovičar et al. 2014; Proudfoot et al. 2017). However, tasks involving direct ME may not always be plausible for patients with ALS, who eventually lose all voluntary muscle control. MI is generally associated with ERD/ERS patterns similar to those associated with ME but with reduced magnitudes (McFarland et al. 2000; Pfurtscheller et al. 1997). To date, far fewer studies have directly quantified the neural features of MI in patients with ALS. In a study by Kasahara et al. (2012), the authors identified significantly smaller ERD patterns for ALS patients than in healthy controls (HC). Other studies relying on ME reported incongruous results. For example, Riva et al. (2012) reported no change in the ERD amplitudes for ALS patients during actual movement but a significant reduction in post-movement ERS in the β frequency band. Bizovičar et al. (2014) investigated a ME task and reported no

significant difference for μ ERD but a significant weakening in β ERD during preparation for ME in ALS. A magnetoencephalography (MEG) study (Proudfoot et al. 2017) reported increased β desynchronization for patients during motor preparation and execution, which contradicts with EEG results. Previous studies have also investigated correlations between clinical measures of ALS progression including the upper limbs and respiratory functions with ERD/ERS amplitudes. Only significant negative correlations between ERD amplitude and disease duration in addition to bulbar functions were reported (Kasahara et al. 2012). Neural oscillatory impairments during MI, however, are not yet understood for patients with ALS, who will eventually need to rely on MI rather than ME due to their progressive loss of executive motor functions. Quantification of MI-sensorimotor rhythms and their associations with clinical scores may introduce possible motor and cognitive markers in ALS which may support enhanced diagnostic and prognostic techniques.

This study explores ERD/ERS alterations associated with ALS during MI. We quantified ERD/ERS dynamics in time, frequency, and space to explore spatio-spectral-temporal signatures of MI in the cortical areas involved in motor preparation and imagination tasks. We investigated features of μ and β ERD/ERS, testing the hypothesis that ALS patients have significantly weaker ERD/ERS responses relative to HC in MI-related tasks. Furthermore, we hypothesized that ALS patients might have delayed ERD onset as a possible pathological signature related to the inefficiency in the neural circuitry underlying motor planning. Localization of MI activity in μ and β frequency bands were also compared between HC and ALS groups to investigate potential disease-related variations in their topographical maps. Finally, correlations between the quantified ERD/ERS features and relevant ALS clinical scores were analyzed. Correlations with bulbar functions, evaluated with the bulbar subscore of the ALSFRS (ALSFRS-R-B), and disease duration were analyzed based on results from Kasahara et al. (2012). Similarly, cognitive functions were evaluated using the ALS Cognitive Behavioral Screen (ALS-CBS) test (Cedarbaum et al. 1999; Woolley et al. 2010) and analyzed for potential associations with quantified ERD/ERS features.

While prior studies have largely focused on abnormalities in sensorimotor oscillations in people with ALS during motor execution tasks, our study investigated motor imagery as a more tenable procedure for ALS patients lacking voluntary muscle control. The insights obtained throughout this study may contribute to a better characterization of the dynamics of motor oscillations in ALS, a better understanding of underlying cortical network abnormalities, and eventually improved EEG–based cortical marker research in ALS.

2. Materials and Methods

2.1 Participants

Seventeen subjects participated in our study; six patients diagnosed with ALS (5 males, average age: 57.0±15.7 years) with varying degrees of disability assessed using the ALSFRS-R (mean 12.3±8.9, range (0-23), out of 48) and eleven age-matched HC (4 males, average age: 62.0±9.7), with no reported history of neurological or psychiatric disease. Half of the patients were completely dependent on mechanical ventilation (MV), one of whom, the youngest (ALS1), was in a late-stage locked-in state (LIS). All participants were right-handed except for one ALS patient (ALS6). For the cognitive functions evaluation, due to bulbar and limb dysfunction and communication difficulties, the information and retrieval (fluency) section of the ALS-CBS test could not be used effectively, and so only the three portions of the CBS test corresponding to attention, concentration, and tracking were evaluated. Three of the ALS participants (ALS1, ALS2, and ALS4) had very poor ALSFRS-R scores (ALSFRS-R from 0 to 7) and did not have any verbal communication. In order to overcome communication difficulties in the CBS test for these patients, the one participant (ALS1) who was in the late-stage locked-in state, (ALSFRS-R=0) could not reliably use the eye tracking system, but could use a P300 speller application through the BCI2000 software (Schalk and Mellinger 2010) to answer the questions using his residual eye gaze control. The P300 speller allows ALS patients to select from a matrix of letters with randomly flashing rows and columns by focusing on the desired letter, and requires minimal eye gaze control. Two other ALS participants (ALS2 & ALS4) who retained fine eye gaze control could reliably communicate using an eye-tracking system (Tobii EyeX). A computer-based automated CBS test was developed in the NeuralPC lab at the University of Rhode Island (URI) for this purpose, and the test was used successfully by these patients in order to evaluate their cognitive functions. In addition, communication with patients was also required following the task performance to verify their level of attention and engagement. While ALS participants 2 and 4 (ALS2 & ALS4) could reliably communicate through the eye tracking system (although the communication with ALS4 required some engagement on the part of his caregiver), ALS participant 1 (ALS1) was completely dependent on his caregiver for communication. For this patient, the caregiver could identify his engagement level through his residual eye movement in response to yes/no questions. Table 1 shows the patients' demographics and related clinical information for all ALS participants. The

study protocol was approved by the Institutional Review Board (IRB) of URI and written informed consents were provided directly by each subject or patient's caregiver.

Table 1: ALS Subjects Demographic Information.

ALS Subject No	*Age*	*Gender*	*Disease Duration (years)*	*ALSFRS-R (out of 48)*	*ALSFRS-R-B (out of 12)*	*ALS-CBS score (%)*
1	29	M	4	0	0	100.0
2	55	M	11	4	0	93.8
3	70	M	8	14	5	93.3
4	67	M	2	7	5	86.6
5	69	F	11	23	11	80.0
6	52	M	3	22	12	89.1
Mean (±SD)	**57.0±15.7**	**-**	**6.5±4.0**	**12.3±8.9**	**5.5±5.2**	**90.5±6.9**

2.2 Data Acquisition and Experimental Protocol

EEG signals were recorded from thirteen Ag/AgCl electrodes referenced to the left earlobe. The electrodes covered the pre-motor (FC3, FC4), primary motor (C1, C3, Cz, C2, C4), sensorimotor (CP1, CP3, CP2, CP4), and parietal (P3, P4) areas of the brain according to the 10-20 system. An additional electrode was placed at FCz as the ground electrode. Data acquisition was handled by BCI2000 software (Schalk et al. 2004).

The signals were amplified using a g.USBamp amplifier (g.tec medical engineering), digitized at 256 Hz and zero-phase bandpass filtered (1-45 Hz). The impedance of the EEG electrodes was kept below 5KΩ. Data recording from ALS patients was performed in their own homes or care centers. An adjustable holder was used to allow patients to view the monitor in bed or in their wheelchair at their desired angle. Recording sessions from healthy controls were carried out in the NeuralPC Lab. The subjects sat comfortably in an armchair and were instructed to relax their arms and avoid movement.

The task was designed using the BCI2000 stimulus presentation module for MI (Schalk et al. 2004). Participants attended two EEG data recording sessions in separate days. Each session consisted of 3 runs separated by approximately 5 minutes of rest. During each run, the subject was instructed to respond to three types of visual cues presented on-screen and respond accordingly with three types of mental activities: (a) left-hand motor imagery (LMI) when the cue appears on the left side of the screen, (b) right-hand motor imagery (RMI) when the cue appears on the right

side of the screen, and (c) resting when the cue appears in the middle of the screen (Figure 1). The imagination cue was the image of a hand, and participants were instructed to imagine moving their own hand, for example, to imagine squeezing a stress ball. The resting cue was a green circle positioned in the middle of the screen to help them relax and not think about any movement. A total of 10 trials for each type of MI task per run randomly alternated with rest trials in between. We followed a simple alternation between rest and imagination, where the participant was intuitively pacing and preparing for the next imagination task at the end of each preceding rest block (Figure 1). None of the participants had previous BCI experience. However, the first session was used for subjects to become familiar with the MI task, while the data recorded from the second session was used for the data analysis. Two healthy subjects could not attend a second session due to their availability, and data from their first recorded session therefore was used for data analysis.

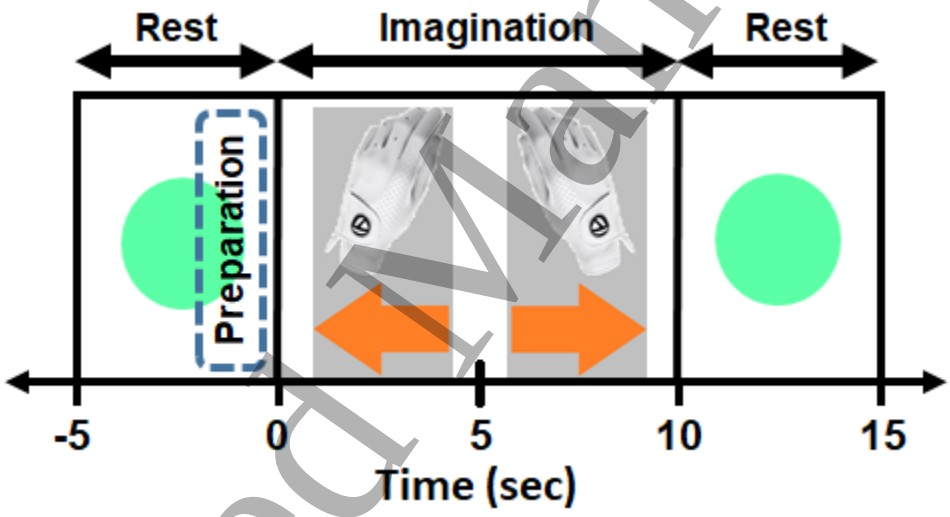

Figure 1: Overview of task blocks and timing. Note that at each imagination block, only one of the pictures of the right- and left-hand was depicted for subjects.

2.3 Data Analysis

2.3.1 Data Pre-processing

Offline preprocessing and analysis were performed in MATLAB (MathWorks Inc.). The data were spatially filtered using a common average referencing (CAR) filter (McFarland et al. 1997). CAR was chosen instead of Laplacian transformation as the latter is highly dependent on the number of channels (McFarland et al. 1997) while only 13 channels were used in this study. CAR involves re-referencing the data to the average of all the channels in order to filter out any global artifacts appearing simultaneously in all of the channels. Eye movement artifacts and noise due to

mechanical ventilation (in the case of ALS patients) were removed using the extended Infomax Independent Component Analysis (ICA) algorithm (Lee et al. 1999; Brunner et al. 2013). The artifactual components were identified by visual inspection of the independent components' spatial topographies in addition to the spectral analysis of their time courses. The artifact-free EEG signal was then reconstructed after removing the predominant artifactual components and the data was segmented into 10-sec trials synchronized with the appearance of the visual cues (Rest/LMI/RMI).

2.3.2 Time-Frequency Analysis

In order to characterize the dynamics of the oscillatory activity associated with MI, time-frequency analysis of the EEG data was performed via complex Morlet wavelet convolution. A wavelet family was created ranging from 3 to 40 Hz in 38 linear frequency steps and a variable number of cycles (4 to 10) to compromise between time and frequency resolution based on the uncertainty principle (Tallon-Baudry et al. 1999). Individual 10-sec trials were convolved with the set of complex wavelets, normalized with uniform scale energy. The time-frequency power maps for each channel were obtained by squaring the magnitude of the convolution result for each individual trial. Averaging the time-frequency maps over trials for each task (Rest/LMI/RMI) gives the total time-frequency power, which includes both phase-locked and non-phase-locked activities.

A common conception is that ERD/ERS power modulations reflect band-limited, oscillatory activity non-phase-locked to an external stimulus, as opposed to phase-locked EEG activity which results from an event-related component (Pfurtscheller and Lopes da Silva 1999; David et al. 2006). In order to disambiguate the non-phase-locked oscillatory (induced) component from the phase-locked component (evoked), the procedure in Cohen et al. (2013) was adopted. Before applying the time-frequency analysis as described before, the non-phase-locked power was obtained by subtracting the time-domain trial average i.e. the event-related potential (ERP) corresponding to each task (Rest/LMI/RMI) from the time-domain EEG signal of each individual trial corresponding to the same condition (Kalcher and Pfurtscheller 1995). Then the oscillatory activity was analyzed as described for the total power in the previous paragraph. After averaging the time-frequency maps corresponding to individual trials with the evoked responses removed, the induced time-frequency power maps ($TFM(t,f)$) were obtained for each subject and used for further analysis. The mean power for each frequency from the pre-stimulus rest period -5 to -2 sec before the imagination cue onset was used for baseline normalization separately for each frequency band ($B(f)$).

In order to compute ERD/ERS time courses for further quantification, the time-frequency power spectra at the subject-specific frequency, or the most task-influenced frequency band within each of the μ (8-12 Hz) and β (13-25 Hz) bands (McFarland et al. 2000), were extracted from the time-frequency power maps of each MI task for each subject. Subject-specific frequencies were calculated using correlation analysis for each MI task being defined as the frequency associated with the highest Pearson correlation value of the corresponding MI (RMI/LMI) task vs rest. Further details are explained in the following sections.

The paradigm consisted of alternating 10 seconds rest trials and 10 seconds imagination (LMI/RMI) trials. The last 5 seconds of the pre-stimulus rest trials, the 10 seconds imagination (LMI/RMI) trials, and the first 5 seconds of the post-imagination rest trials were concatenated to form 20 second rest-imagination-rest ERD/ERS time courses.

The final ERD/ERS data for each subject represents the relative change of instantaneous power values in the averaged data in relation to the mean baseline power, calculated for a subject-specific frequency according to the following equation: $ERD/ERS\ (t)\ (\%) = (TFM(t,fs) - B(fs))/B(fs) \times 100$, where fs is the subject-specific frequency, t is the time (-5 to 15 sec), $TFM\ (t,fs)$ represents the time course of spectral power values defined at the subject-specific frequency fs extracted from the induced time-frequency power map and $B\ (fs)$ the mean of the spectral power during the baseline period (-5 to -2 sec) used for normalization. The final ERD/ERS time course was downsampled to 8 Hz for further interpretation of the results.

2.3.3 ERD/ERS Feature Quantification

In order to quantify the dynamics of the ERD/ERS patterns and identify discrepancies between the participants with ALS and HC, four ERD/ERS features were extracted from $ERD/ERS(t)(\%)$ time course corresponding to subject-specific frequencies within both μ and β bands. The ERD/ERS features were defined within three task-relevant activities: preparation (-2 to 0 sec), imagination (0 to 10 sec), and post-imagination (10 to 15 sec). The ERD/ERS features consisted of the ERD onset latency (ERD_{onset}), the mean activity (ERD_{mean}), the minimum (ERD_{min}), and the maximum (ERS_{max}) activities according to the interval of interest. For feature extraction, we considered the two seconds immediately preceding the imagination cue as the preparation interval (-2 to 0 sec) (Pfurtscheller and Lopes da Silva 1999) and the first five seconds of the imagination task (0 to 5 sec) as the imagination interval. We did not consider the full (10 sec) time course of the imagination activity as the first five seconds were hypothesized to be the interval of optimum subject engagement in the task. During each of the preparation and imagination intervals, the

ERD_{min} and ERD_{mean} were calculated, whereas for the post-imagination interval (10 to 15 sec) the ERD_{mean} and ERS_{max} values were computed. The maximum was considered instead of the minimum as the post-imagination interval is when we expect the ERS relative power to increase (Jeon et al. 2011). Similarly to Zhang et al. (2008) and Leocani et al. (2005), the ERD onset latency was calculated as the time point at which the power first decreased steadily below 15% of the baseline period (-5 to -2 sec). Starting from the preparation interval (-2 to 0 sec), the onset was measured as the latency at which the percent power started to decrease steadily below 15% of the baseline period (-5 to -2 sec).

2.3.4 Topographic Correlation Analysis

In order to compare MI-related topographic activities between ALS and HC, we conducted correlation analysis following the study by McFarland et al. (2000). Using the squared Pearson correlation coefficient (r^2) at frequencies within both the μ (8-12 Hz) and β (13-25 Hz) bands for all electrodes, the associations between two paired conditions of LMI vs. Rest and RMI vs. Rest (30 trials for each pair) were calculated. For further analysis, subject-specific frequencies were selected as those corresponding to the highest correlation values for both MI task conditions within each of the μ and β bands. The r^2 value was used as a measure for the proportion of variance of the EEG power accounted for by the MI task versus rest, which reflects activity localization. Averaged scalp topographies of r^2 values were compared between the two groups to investigate potential localization differences in the topographic maps of MI activity in both μ and β bands.

2.3.5 Statistical Analysis

Nonparametric permutation testing was used to test the statistical significance ($p < 0.05$) of power changes relative to the baseline (-5 to -2 sec) in each of the aforementioned time intervals of interest (i.e. preparation, imagination, and rest) on the time-frequency maps within each group (i.e. ALS, HC). To do so, relative power changes were computed at each time-frequency point through 1000 iterations, where the time points were temporally shifted by a random offset in each iteration and at each frequency bin to form a resampled distribution of differences relative to the baseline. Then, subthreshold (i.e. $p \geq 0.05$) points were set to zero to obtain clusters of significant changes formed by the remaining points. In order to account for multiple comparisons, all the clusters were then corrected with map-level thresholding at $p < 0.05$.

The between-group analysis was performed for each quantified ERD/ERS feature (ERD_{min}/ERS_{max}, ERD_{mean}/ERS_{mean}, and ERD_{onset}) value within each of the aforementioned time

intervals of interest and the two main frequency bands (μ and β) for all the channels. Statistically significant differences were analyzed using the nonparametric Mann-Whitney *U*-test. Correlations between ERD/ERS features and ALS clinical scores (i.e. disease duration, ALSFRS-R-B and ALS-CBS) were tested using the Spearman correlation coefficient (rho). The upper limb (ALSFRSul) subscore was not considered for correlation as all patients had ALSFRSul scores of zero. A statistical significance threshold of $p < 0.05$ was used in all analyses. In order to account for multiple comparison corrections, the false discovery rate (FDR) adjusted *p*-values ($p < 0.05$) were computed and reported (Benjamini and Hochberg 1995) .

3. Results

3.1 Time-Frequency Analysis Results

Figure 2 illustrates the averaged time-frequency maps across all HC (left) and all participants with ALS (right) for representative EEG channels for the hand area (Wang et al. 2009) over the primary motor cortex (i.e. C3 (top) and C4 (bottom)), during both left- and right-hand MI respectively. The black solid line indicates the borders of cluster areas formed by time-frequency points with significant power changes (i.e. $p < 0.05$) relative to the baseline. For HC, we observed that during RMI (0 to 10 sec), 100% of time-frequency points at the contralateral channel (C3) were significantly (i.e. $p < 0.05$) decreased relative to the baseline (averaging: -2.79±1.11 dB) in the μ band, while 67% of total time-frequency points were significantly decreased (averaging: -2.14±1.58 dB) in β band. However, during the post-imagination interval (10 to 15 sec), the reduction rate observed was not as profound as the reduction observed during imagination in either μ or β bands for HC. 29% of total time-frequency points were significantly decreased relative to baseline (averaging: -1.37±0.91 dB) in the μ band while only 10% of total time-frequency points were significantly decreased (averaging: -1.22±1.07 dB) in the β band during the same interval (see Figure 2 top, left). No statistically significant power changes were observed at this same contralateral channel (C3) in ALS participants (see Figure 2, top, right).

On the other hand, during LMI (0 to 10 sec) for HC, the contralateral channel (C4) showed significantly ($p < 0.05$) decreased μ band power changes relative to the baseline at 97% of time-frequency points (averaging: -2.31±1.48 dB), while 71% of total time-frequency points showed significantly reduced β band power relative to baseline (averaging: -2.13±1.27 dB). However, no substantial difference of power was observed during the post-imagination interval (10 to 15 sec) for HC. 6% of the total time-frequency points were significantly decreased relative to baseline

(averaging: -1.17±0.81 dB) in μ band while only 3% of total time-frequency points were significantly decreased (averaging: -1.08±0.76 dB) in β band during the same interval (see Figure 2 bottom, left). No statistically significant power changes were observed at this same channel (C4) in ALS participants (see Figure 2, bottom, right).

3.2 ERD/ERS Feature Quantification Results

ERD/ERS time courses corresponding to each subject-specific frequency within the μ (8-12 Hz) and β (13-25 Hz) bands during the time interval (-5 to 15 sec), relative to the imagination cue onset, were averaged within each group and compared. Figure 3 shows the averaged ERD/ERS time courses for two representative channels C3 and C4 during both left- and right-hand MI. While ERD/ERS patterns were clearly observed for all the subjects (ALS and HC) in both frequency bands and all the channels, the reduction of the relative power changes were more pronounced for the HC in comparison with the patients across all the channel locations. We observed a significant ($p < 0.05$) delayed ERD for RMI in only two channel-frequency combinations; in the μ band, $ERD_{onset\text{-}CP1}$ (HC: -0.5±0.8 sec; ALS: 0.9±1 sec; p=0.02) and in the β band, $ERD_{onset\text{-}FC4}$ (HC: 0.3±1 sec; ALS: 1±1.5 sec; p=0.01). However, these delays were not significant after FDR correction.

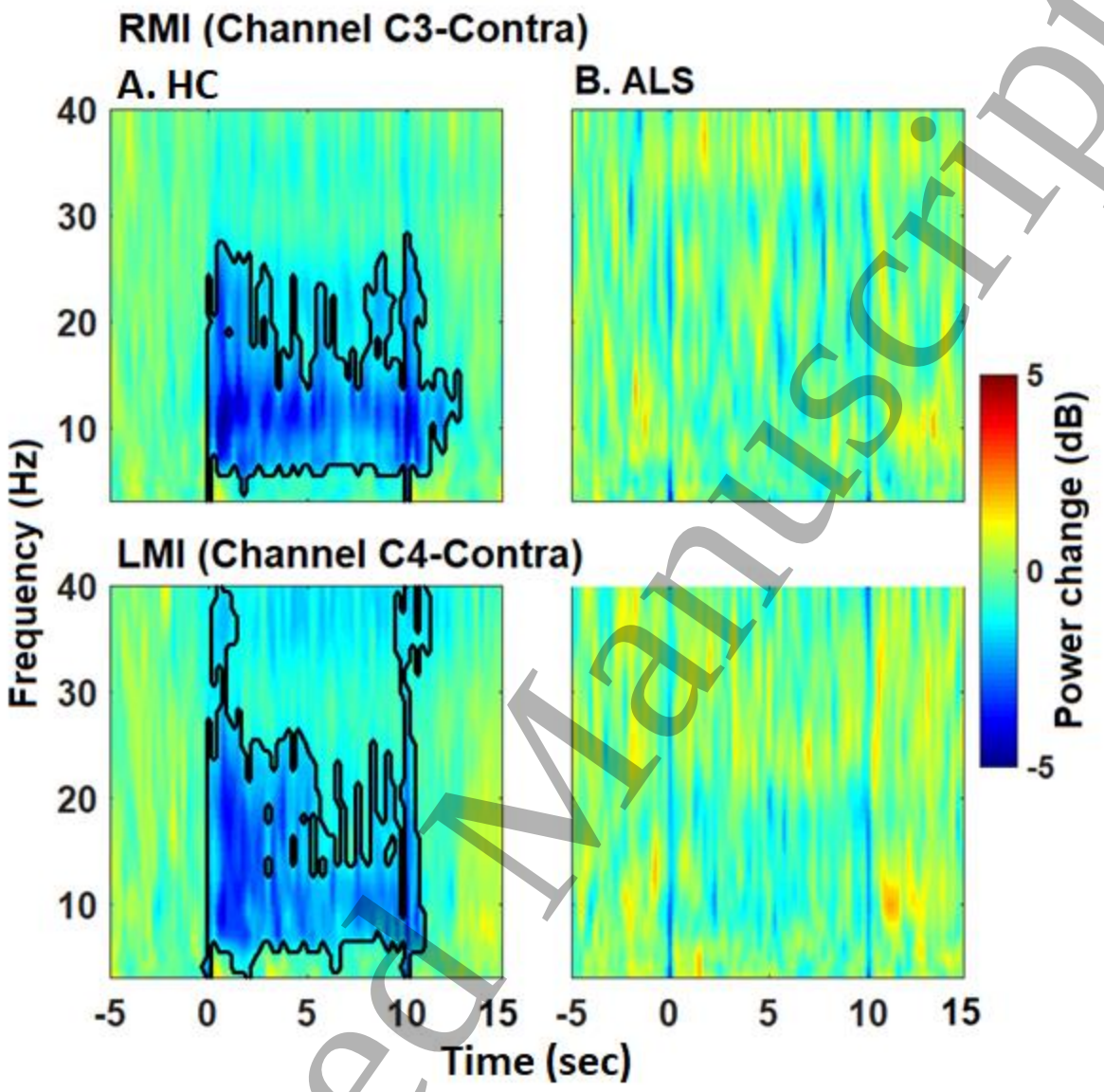

Figure 2: Averaged time-frequency maps (decibel change relative to baseline) for controls and patient participants. Data shown are for C3 and C4 channels contralateral to right- and left-hand MI respectively (RMI & LMI) during the time interval (-5 to 15 sec) relative to the imagination cue onset. The clusters of time-frequency points with significant power changes relative to the baseline are determined by black solid border lines. Dashed lines illustrate the task intervals (i.e. preparation, imagination, and post-imagination).

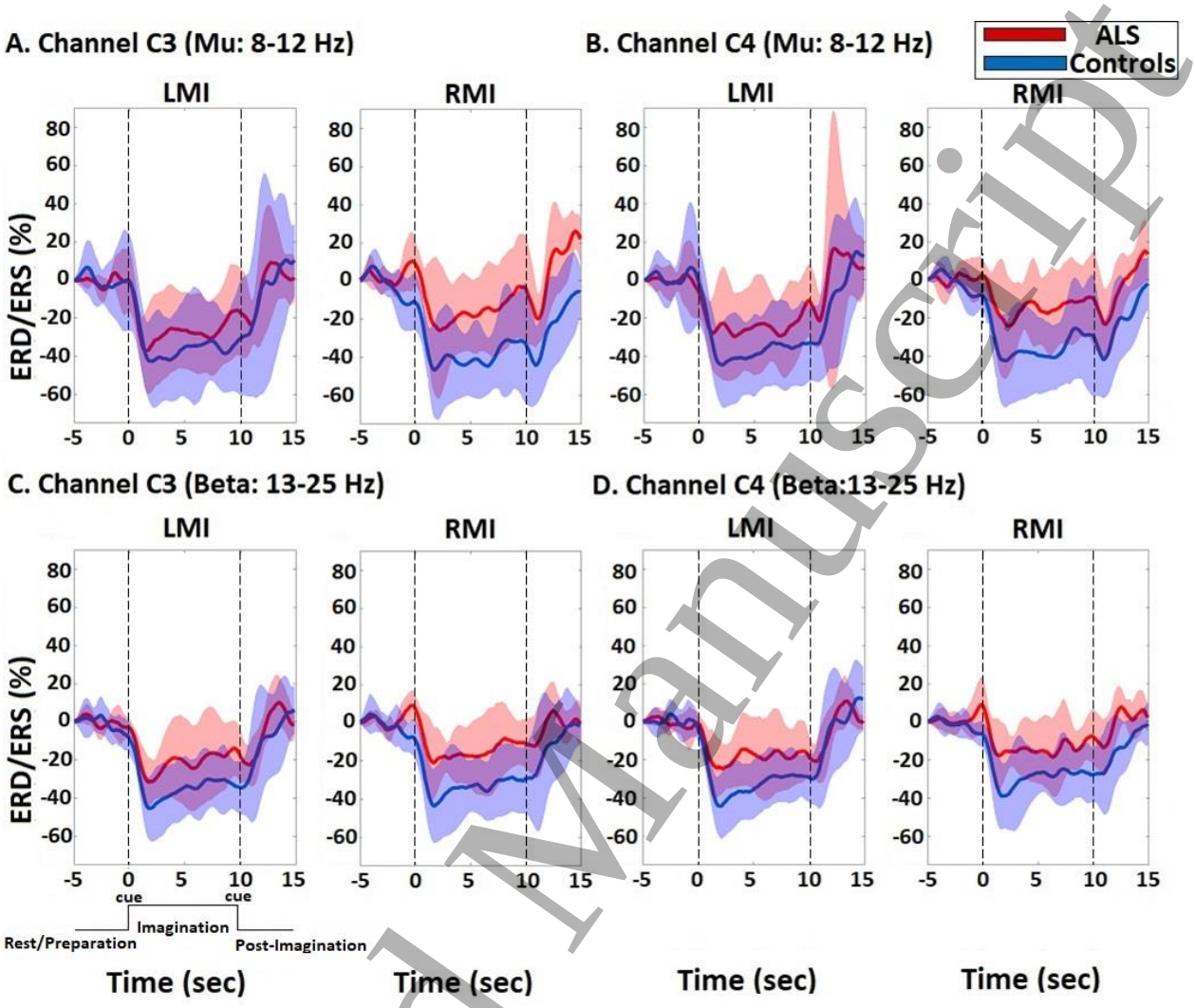

Figure 3: Grand average time courses of event-related desynchronization (ERD) and synchronization (ERS) for each subject-specific μ band (8-12 Hz, top) and β band (13-25 Hz, bottom) for HC and patients with ALS during Left/Right hand MI (Rest-LMI/RMI-Rest) from -5 to 15s The shaded bands represent the standard deviation within each group of healthy and patients.

Figure 4 shows the scalp topographies of the adjusted *p*-values for the mean ERD/ERS activity difference between HC and participants with ALS calculated during the pre-specified intervals: preparation (-2 to 0 sec), imagination (0 to 5 sec) and post-imagination (10 to 15 sec) in both the μ and β bands specifically for the RMI task. Overall, for the RMI task, patients had a significantly reduced mean ERD relative to HC during the preparation and MI intervals. For the μ band, the mean ERD during the preparation interval was significantly ($p < 0.05$) reduced in patients compared to HC in only the left hemisphere contralateral channels as shown in Figure 4. For the β band, the mean ERD during the preparation interval was significantly ($p < 0.05$) reduced in

patients compared to HC but the reduction was more bilateral in both hemispheres as shown in Figure 4. Table 2 shows the Mean ERD % during the preparation interval for the RMI task for both HC and ALS and the corresponding adjusted *p*-values.

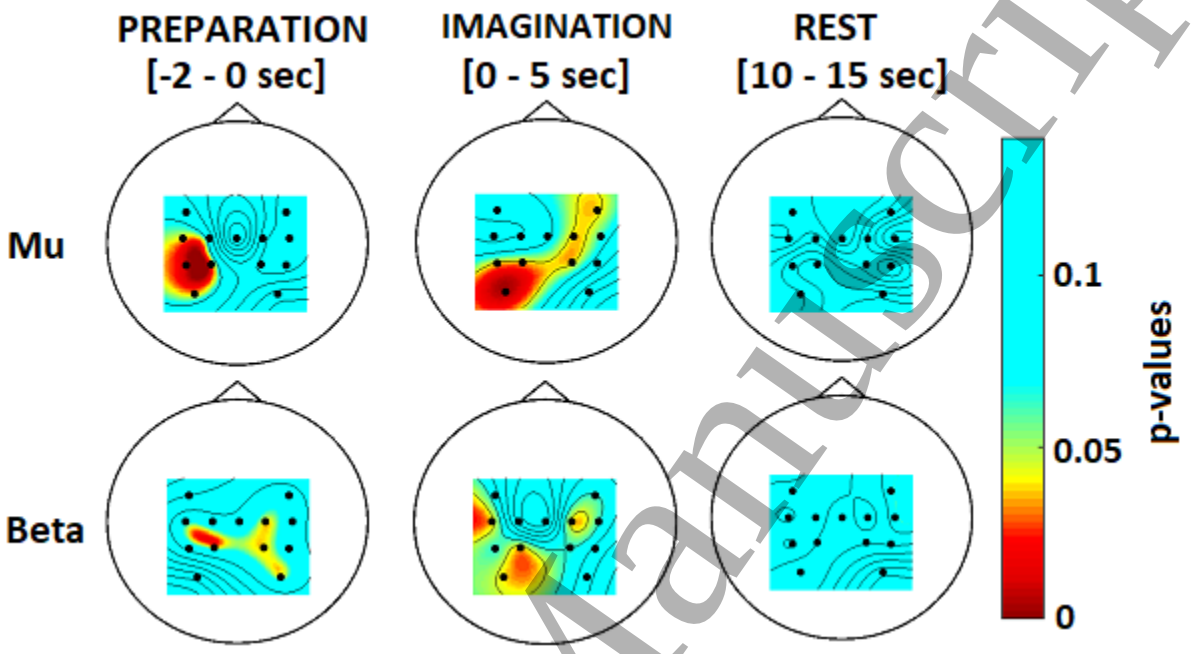

Figure 4: Adjusted p-value maps derived from the statistical comparison (ALS vs. HC) of the mean activity (ERD_{mean}) during preparation, imagination and rest for right-hand MI task (RMI) in both μ and β bands. Note: for LMI, only Cz showed the significant difference during MI which is not illustrated here.

Similarly, during the imagination interval for the RMI task, the mean ERD was significantly ($p < 0.05$) reduced for patients in the μ and β bands as shown in Figure 4. The reduction was localized in the premotor, sensorimotor and parietal areas in both frequency bands. The mean ERD% and the adjusted *p*-values corresponding to the imagination interval for both frequency bands are reported in Table 3. As for the post-imagination interval, the mean ERS activity did not vary significantly between patients and HC for either RMI or LMI in both μ and β bands.

The minimum value of ERD was also compared between the two groups. It was significant ($p < 0.05$) only for the RMI task in both μ and β bands in both the preparation and imagination intervals. The minimum ERD percentage and the adjusted *p*-values corresponding to the motor preparation and imagination intervals for both frequency bands can be found in Tables 1 and 2 in the Supplementary document. As for the maximum value during the post-imagination interval (ERS_{max}), no significant difference between HC and patients was observed.

Table 2: Comparison of Mean ERD percentage between HC and ALS during the preparation interval of the RMI task (-2 to 0 sec).

Frequency Band	*Channel*	*HC (ERD%)*	*ALS (ERD%)*	*p-value*
μ-Band	FC3	-7.2±18.3	1.9±6.4	0.11
	FC4	-7.1±9.7	4.5±7.9	0.11
	C1	-5.7±16.5	3.1±7.5	0.11
	Cz	-2.4±12.3	1.2±8.0	0.61
	C2	-6.3±10.9	4.0±14.3	0.21
	C3	-9.7±10.5	4.4±9.3	0.03*
	C4	-6.5±8.0	1.2±8.8	0.15
	CP1	-10.0±8.6	7.6±10.6	0.02*
	CP2	-5.1±16.8	4.4±10.4	0.15
	CP3	-7.6±5.8	7.6±5.0	0.008**
	CP4	-7.1±15.7	0.4±5.1	0.11
	P3	-4.8±9.4	5.3±6.7	0.03*
	P4	-3.3±21.1	-3.3±6.1	0.37
β-Band	FC3	-5.0±10.1	-1.8±3.6	0.34
	FC4	-5.1±4.5	0.5±5.15	0.11
	C1	-3.9±8.0	5.0±10.1	0.11
	Cz	-5.3±6.1	2.9±10.4	0.13
	C2	-5.8±4.6	0.8±4.4	0.03*
	C3	-5.3±7.5	4.0 ±5.0	0.07
	C4	-3.6±4.2	2.9±7.8	0.11
	CP1	-4.9±5.2	2.7±4.9	0.03*
	CP2	-3.8±8.3	2.4±3.6	0.03*
	CP3	-4.3±7.6	2.0±4.7	0.13
	CP4	-5.9±7.1	1.9±6.4	0.11
	P3	-4.6±7.2	-2.8±2.6	0.73
	P4	-7.5±6.6	0.4±4.7	0.04*

*adjusted $p < 0.05$. **adjusted $p < 0.005$

Table 3: Comparison of Mean ERD percentage between HC and ALS during the imagination interval of the RMI task (0 to 5 sec).

Frequency Band	*Channel*	*HC (ERD%)*	*ALS (ERD%)*	*p-value*
μ-Band	FC3	-32.5±18.4	-12.9±18.8	0.09
	FC4	-33.7±17.9	-7.2±9.2	0.03*
	C1	-34.4±19.9	-15.7±13.9	0.11
	Cz	-32.5±17.4	-13.0±9.4	0.08
	C2	-39.4±14.9	-13.7±19.3	0.03*
	C3	-37.4±17.2	-16.0±21.3	0.13
	C4	-34.1±16.9	-14.0±14.8	0.06
	CP1	-36.6±15.8	-11.8±13.5	0.03*
	CP2	-34.1±18.2	-10.1±17.9	0.03*
	CP3	-40.4±14.6	-14.3±12.9	0.03*
	CP4	-33.6±19.3	-15.5±15.6	0.09
	P3	-36.9±10.9	-13.2±5.0	0.004**
	P4	-28.1±21.8	-14.1±14.6	0.18
β-Band	FC3	-29.1±11.5	-14.7±12.0	0.07
	FC4	-28.0±12.7	-12.4±11.4	0.06
	C1	-28.5±14.2	-17.7±12.3	0.13
	Cz	-29.1±15.6	-18.8±14.0	0.15
	C2	-30.5±11.4	-13.1±10.8	0.03*
	C3	-33.1±16.1	-14.5 ±11.3	0.03*
	C4	-28.9±14.4	-12.6±11.1	0.06
	CP1	-29.9±14.7	-11.3±13.1	0.03*
	CP2	-29.0±10.1	-11.1±13.2	0.06
	CP3	-30.5±16.7	-13.0 ±11.1	0.06
	CP4	-26.9±11.9	-10.9±12.2	0.08
	P3	-28.9±11.5	-13.7±9.7	0.03*
	P4	-26.2±13.5	-14.1±9.3	0.09

*adjusted $p < 0.05$. **adjusted $p < 0.005$

For the LMI task, no significant differences between patients and HC were observed for any of the ERD/ERS features except during the imagination interval, when only one channel showed significantly ($p < 0.05$) reduced mean ERD in the μ band for patients prior to FDR correction: $ERD_{mean\text{-}Cz}$ (HC: -37.1±14.4%; ALS: -21.5±10.4%; p=0.04). The difference did not remain significant following FDR correction.

3.3 Topographic Correlation Analysis Results

Figure 5 illustrates averaged MI scalp topographies of the r-squared (r^2) values for each MI task (LMI/RMI) vs. rest within the μ and β bands to compare the topographical activation of MI task relative to rest condition for each group (ALS and HC). Higher correlation values reflect higher MI activity. Generally, higher activity was observed for both LMI and RMI for HC compared to ALS. For HC, MI topography illustrated bilaterally localized patterns for RMI and more central activity with contralateral localization for LMI in the μ band. For the β band, more diffused patterns with bilateral activity in motor and sensorimotor channels were observed for both RMI and LMI tasks. The activity was slightly more profound in the contralateral channels for all MI tasks in both bands. For ALS, MI activity was reduced in all channels with the exception of C3. MI r-squared correlation topography showed bilateral activity in μ band more prominent on the ipsilateral hemisphere for LMI. For the β band, the activity was more centrally focused, where Cz was a focus of activity for both LMI and RMI. Table 4 shows the correlation values for representative motor channels (C3, Cz, C4) for both HC and ALS in both the μ and β bands

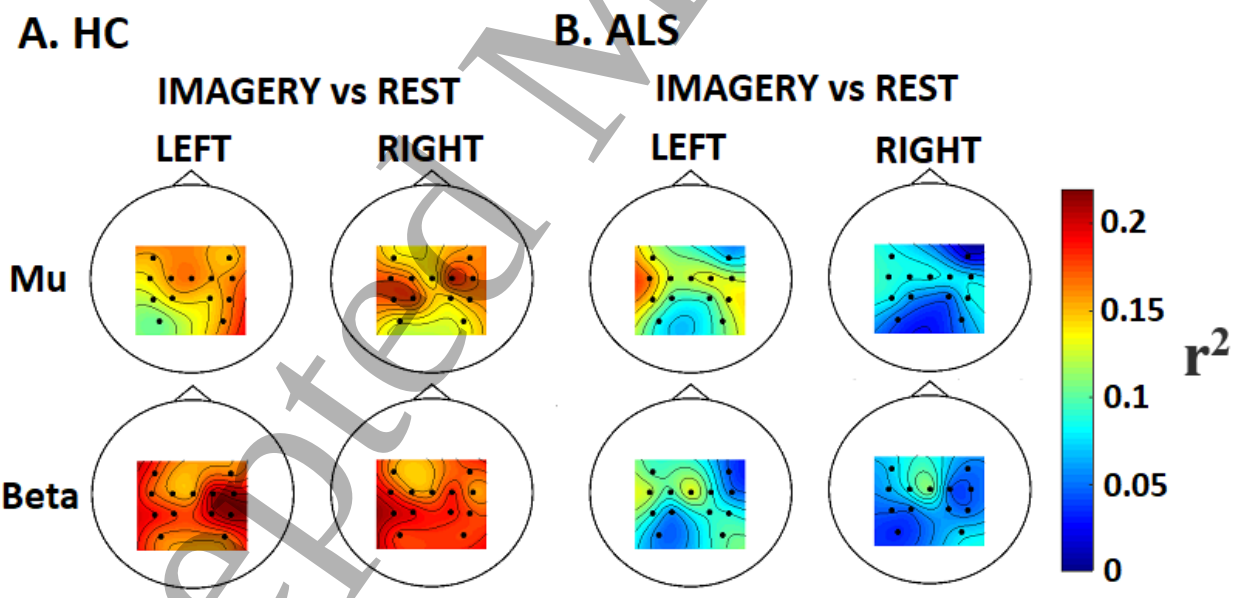

Figure 5: Averaged topographies of r^2 for the μ and β band motor imagination (MI) activity (i.e. averaged over frequencies within each band respectively). A. Left- and right-hand MI versus rest for controls. B. Left- and right-hand MI versus rest for ALS.

Table 4: Pearson Correlation Values Over Motor Channels.

Frequency Band	*Condition*	*Channel*	*HC (r^2)*	*ALS (r^2)*
μ-Band	Right	C3	0.17	0.09
	Right	C4	0.17	0.08
	Right	Cz	0.14	0.08
	Left	C3	0.14	0.16
	Left	C4	0.16	0.12
	Left	Cz	0.17	0.12
β-Band	Right	C3	0.19	0.06
	Right	C4	0.16	0.04
	Right	Cz	0.16	0.11
	Left	C3	0.17	0.12
	Left	C4	0.20	0.05
	Left	Cz	0.16	0.13

3.4 Correlations between ERD features and ALS clinical characteristics

Correlations between the quantified ERD/ERS features (i.e. ERD_{min}/ERS_{max}, ERD_{mean}/ERS_{mean}, and ERD_{onset} in both μ and β bands) and the analyzed ALS clinical scores (i.e. disease duration, ALSFRS-R-B and ALS-CBS) were examined. Overall, for the RMI task, particularly in the β band, during motor preparation, $ERD_{min\text{-}C2}$ was significantly negatively correlated (rho=-0.94; p=0.03) with ALS-CBS scores (i.e. worse cognitive function is correlated with less reduction in ERD). Similarly during motor preparation β band $ERD_{mean\text{-}CP1}$ and $ERD_{mean\text{-}CP2}$ were both significantly negatively correlated, respectively (rho=-0.88; p=0.03) and (rho=-0.85; p=0.04), with the ALSFRS-R-B (i.e., worse bulbar dysfunction is correlated with less ERD reduction during preparation). During motor imagination, β band $ERD_{min\text{-}CP4}$ was significantly negatively correlated (rho=-0.97; p=0.01) with the ALSFRS-R-B, in addition to $ERD_{mean\text{-}CP4}$ (rho=-0.88; p=0.03) and $ERD_{mean\text{-}FC3}$ (rho=-0.85; p=0.04) in the same band which also were significantly negatively correlated (i.e. worse bulbar dysfunction is correlated with less ERD reduction during imagination). No significant correlations were observed within the μ band or during the post-imagination interval.

For the LMI task, significant correlations were mainly observed in the β band. During motor preparation, $ERD_{mean\text{-}C3}$ and $ERD_{min\text{-}C3}$ were both significantly positively correlated, respectively, (rho=0.98; p=0.005) and (rho=0.92; p=0.02), with disease duration (i.e. longer disease duration is

correlated with less ERD reduction during the preparation period). During motor imagination, $ERD_{mean\text{-}FC4}$ was significantly negatively correlated (rho=-0.97; p=0.01) with ALSFRS-R-B, in addition to $ERD_{mean\text{-}C3}$ (rho=-0.85; p=0.04), $ERD_{mean\text{-}CP2}$ (rho=-0.97; p=0.01), $ERD_{mean\text{-}CP4}$ (rho=-0.97; p=0.01), $ERD_{mean\text{-}P4}$ (rho=-0.85; p=0.04), and $ERD_{min\text{-}CP4}$ (rho=-0.85; p=0.04) which also were significantly negatively correlated (i.e. worse bulbar dysfunction is correlated with less ERD reduction during imagination). As for the cognitive functions, there were no significant correlations between any of the ERD/ERS features with the ALS-CBS for LMI. Figure 6 illustrates correlations between the representative feature ERD_{mean} and the bulbar subscore (ALSFRS-R-B) for both RMI and LMI tasks and for four representative channels (FC3, FC4, CP1, and CP4) in which the correlations were significant, although the significant values did not survive after FDR correction. The significant correlations observed between other channels and ALS clinical scores (ALS-CBS, ALSFRS-R-B, and disease duration) for both RMI and LMI can be found in Figures 1 and 2 in the Supplementary document.

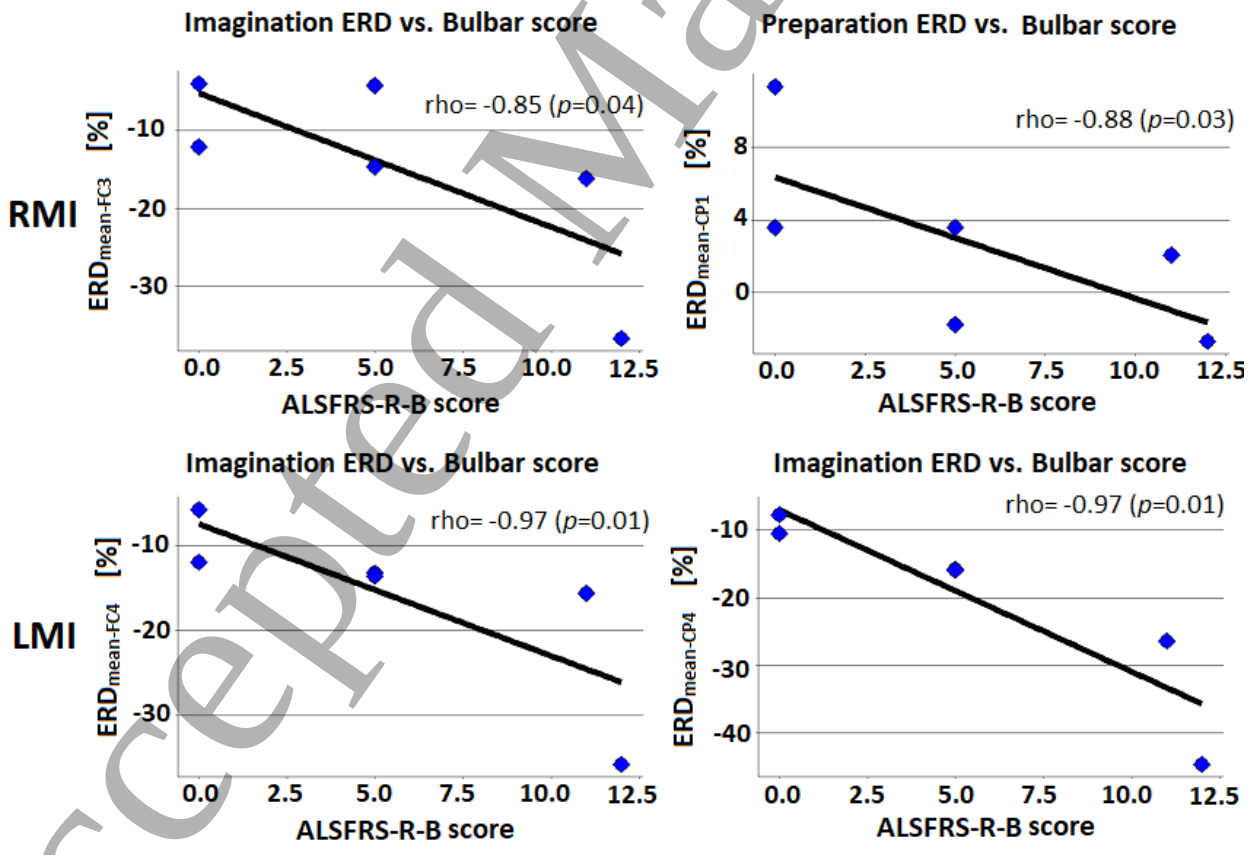

Figure 6: Significant correlations between representative ERD/ERS features in the β band and clinical measures of ALS progression.

4. Discussion

This study investigated the impact of ALS on the functional state of the cortical sensorimotor areas involved in MI by exploring abnormalities in the magnitude and timing of ERD/ERS oscillations in the μ (8-12 Hz) and β (13-25 Hz) rhythms. Due to the deterioration of muscle control in ALS patients, and considering the importance of their motor dysfunctions, more studies are required to quantify the features of MI rather than focusing on the characteristics of ME. In this study, ERD/ERS features of MI tasks (ERD_{min}, ERD_{mean}, ERS_{max}, and ERD_{onset}) were extracted to quantify the dynamics of ERD/ERS oscillations over the scalp using thirteen channels covering the premotor and sensorimotor areas while the experimental paradigm consisted of three main MI task-related intervals including preparation, imagination, and post-imagination. Our results show that ALS patients have an overall reduced mean and minimum ERD during the preparation and imagination activities in both the μ and β bands compared to HC. However, our results did not identify significant differences in post-imagination ERS activities between the two groups for both RMI and LMI in either the μ or β bands. There were also no significant differences between the two groups during preparation for the LMI task. The ERD reduction for ALS patients is consistent with previous studies on ERD during MI in ALS patients (Kasahara et al. 2012). Previous studies involving direct ME reported inconsistent results. Riva et al. (2012) reported no changes in ERD amplitudes for ALS patients during ME but a significantly reduced post-ME ERS in the β frequency band. Bizovičar et al. (2014), reported significantly reduced ERD in β frequency band only during the preparation of ME which contradicted a study by Proudfoot et al. (2017) in which an increased β desynchronization for patients during actual motor preparation was observed. Nevertheless, it is difficult to directly compare the result reported in Proudfoot's study with previous EEG findings as this MEG study adopted a "Go-NoGo" ME protocol (De Kleine and Van der Lubbe 2011) to study motor preparation, which may bias the observed patterns given associations between β band modulation during motor preparation and the response uncertainty and inhibitory control involved in this type of protocol (Huster et al. 2013; Tzagarakis et al. 2010). Another factor might be considered in this respect is that the sample of ALS patients considered for this study had an average disease duration of 6.5 years, longer than the 23.7 months in Proudfoot et al. (2017). This might suggest that the observed reduced ERD in this study may be a feature related to later stages of the disease in contrast with earlier enhanced ERD observed in

Proudfoot et al. (2017). Longitudinal studies with ALS patients are ultimately required to verify this hypothesis though.

In general, large μ band amplitudes have been assumed to be associated with deactivated cortical areas that are "idle" or not currently involved in sensory, motor, or cognitive information processing (Pfurtscheller 1992; Pfurtscheller and Neuper 1994; Pfurtscheller et al. 1996). Hence, the μ ERD (the decrease or blocking of the μ band) of the underlying neural populations has been interpreted as an increase of cortical excitability and an indicator of the functional recruitment of the cortical areas involved in the processing of sensory, motor, and cognitive information (Pfurtscheller and Berghold 1989; Pfurtscheller and Klimesch 1992). In this context, reduced ERD for ALS patients may be interpreted as a signature of reduced cortical activation during MI due to motor cortical degeneration. Furthermore, a dysfunction in imagery-specific cortical synchronization may be explained by a dysfunction in sensory-motor coupling in the somatosensory cortex (Aguilera et al. 2013). This is consistent with previous functional magnetic resonance imaging (fMRI) results (Stanton et al. 2007) where ALS patients showed reduced cortical activation during MI tasks. Their study concluded that ALS-specific cortical reduction during MI can be attributed to potential cognitive deficits that might make the MI tasks more challenging for these patients. However, they did not report cognitive evaluation for the ALS patients, only that all subjects found the task straightforward and had no attentional problems during the task. Another explanation they offered for the reduction of ERD during MI was the potential disruption of the prefrontal-parietal network involved in the MI due to the ALS extra-motor pathology that involves prefrontal regions according to neuroimaging and neuropathological studies (Abrahams et al. 2000; Ludolph et al. 1992; Woolley et al. 2010; Abrahams et al. 2004; Ellis et al. 2001). However, they did not report any clinical correlations with the decrease of cortical activity during the MI task.

In another study by Kasahara et al. (2012), it was suggested that ERD decrease in ALS may be due to neuronal loss from the progression of the disease based on a quantitative EEG (QEEG) study in the resting state. Their study reported that ALS bulbar deficits were significantly correlated with smaller ERD magnitudes. The authors speculated that this might be due to a possible correlation between bulbar deficits and cognitive dysfunction due to fatigue and lack of attention. However, the study did not include a cognitive evaluation for the ALS patients to verify this potential relationship and its effect on the reported ERD patterns in these patients.

In this study, we found the minimum ERD (ERD_{min}) and the mean ERD (ERD_{mean}) were significantly negatively correlated with the bulbar subscale (ALSFRS-R-B) for participants with ALS in the β band during imagination in the premotor, motor, and sensorimotor areas for both RMI and LMI tasks, which is consistent with the study conducted by Kasahara et al. (2012). However, interestingly, we did not find any significant correlation between the bulbar subscale (ALSFRS-R-B) and cognitive test scores (ALS-CBS). In fact, the patients with most bulbar dysfunction (ALSFRS-R-B=0) had the highest ALS-CBS scores. Hence, we could not verify that our observed ERD abnormality and the associations with the bulbar dysfunction are due to cognitive issues such as attention and concentration that might arise from the bulbar deficits in our ALS sample group. Moreover, our patients reported no difficulties or attentional problems during the task. Hence, the relationship between bulbar dysfunction and reduced ERD in ALS needs further investigation. However, a plausible explanation may be based on the neuropathological features of bulbar deficits in ALS. Evidence from recent studies (Cooper 2006; Shellikeri et al. 2017) suggests that brain regions which are highly associated with speech and language deficits (i.e. Broca and Wernicke areas) in bulbar-onset ALS also play a functional role in the human "mirror neuron system" (MNS) (Acharya and Shukla 2012) which may be also activated throughout MI (Garrison et al. 2010; Carvalho et al. 2013). It also has been demonstrated that Broca's area contains a motor representation of hand actions (Binkofski and Buccino 2004). We speculate a potential involvement of MNS deficits in the reduced ERD patterns, especially for ALS patients with bulbar dysfunction. MNS system impairments have been discussed in relation to various neurological disorders (i.e. autism spectrum disorders, schizophrenia, Alzheimer's and Parkinson's disease) (Vivanti and Rogers 2014; Mehta et al. 2014; Farina et al. 2017; Pohl et al. 2017). However, research in mirror neuron network activation for ALS patients is scarce (Eisen et al. 2015). Nevertheless, interestingly, it has been proposed that suppression of both the μ and β frequency bands can be used to index the human mirror neuron system (Hobson and Bishop 2016; Hobson and Bishop 2017), which may support our interpretation.

The contrast between MI and ME results remains controversial. One possible explanation of why significantly reduced ERD was observed during preparation of ME and MI but not during ME might be related to the fact that ME preparation and motor imagination activate the same cortical areas and underlying neural networks (Pfurtscheller et al. 1997; Munzert et al. 2009). Comparisons between ME and MI of hand movements suggest a partial overlap of neural networks associated with both while concluding that these networks may be partly distinct (Gerardin et al.

2000). This distinction could lead to speculation that ERD reduction is only observed in ME preparation and MI-task related activities (i.e. preparation and imagination) in ALS due to a potential disruption in the underlying cortical neural networks associated with ME preparation and MI versus ME.

Moreover, we verified the hypothesis that ALS patients have delayed ERD onset. Our results indicated a significantly delayed ERD onset latency for μ band in the contralateral sensorimotor area to the MI and β band in the ipsilateral premotor area to the MI. However, these results did not retain significance after FDR correction for multiple comparisons. Further validation of the hypothesis is therefore required with larger sample size. Delayed ERD onset has been studied and consistently found over the sensorimotor regions contralateral to self-paced movement in other motor neuron diseases such as Parkinson's Disease (PD). In Multiple Sclerosis (MS), delayed ERD onset latency was significantly correlated with more severe measures of brain damage suggesting that MS-related pathology disrupts the underlying neural connections of preparation for ME (L. Leocani et al. 2005). The latency of ERD is generally accepted to reflect the dysfunction of cortical networks involved in motor preparation (Leocani and Comi 2006).

Our results indicate significantly decreased ERD patterns for ALS patients versus HC and consider the dynamics of these discrepancies over space and time in three MI task-related intervals (i.e. preparation, imagination, and post-imagination). As mentioned, the underlying neural networks and cortical activations of ME preparation and MI are similar (Munzert et al. 2009), but we also consider the preparation for MI which occurs before the imagination cue onset. During MI preparation, the significant decrease of μ ERD was only in the contralateral hemisphere. This topography is consistent with the ERD dynamics during ME preparation which begin contralaterally around two seconds before movement onset (Pfurtscheller and Lopes da Silva 1999). In the β band, the significant decrease of ERD is bilateral over the sensorimotor and parietal regions during preparation. During imagination, the significant ERD decrease shifts bilaterally towards the premotor-parietal areas in both frequency bands. Interestingly, these dynamics are consistent with other neuroimaging studies (i.e. fMRI and magnetoencephalography [MEG]) investigating the neural networks underlying MI (Gerardin et al. 2000; Hétu et al. 2013). These studies highlight prefrontal and premotor-parietal MI networks, lateral premotor activation during MI, and consistent activation of the parietal cortex largely prevailing in the left hemisphere. These neural dynamics reflect higher cognitive functions during MI such as preparation, intention, and adjusting postural representations during imagination. The spatiotemporal dynamics of the

significant ERD reduction of ALS suggest that these patients have a disruption in the underlying MI neural networks activated throughout two main stages of the task (preparation and imagination); no significant changes were found for the post-imagination interval. Another interpretation of the involvement of the parietal regions could be related to the fronto-parietal ERD patterns observed for elderly subjects as opposed to more central patterns for younger ones, though this pattern was reported in ME rather than MI (Derambure et al. 1993). It should be noted that the most significant differences between ALS and HC were found for the RMI task in our patient samples. For LMI, the significant difference was central in the motor area and only during the imagination activity. Whether this could be explained by the underlying MI network being predominant in the left hemisphere requires further investigation.

Comparison of the time-frequency maps of MI for HC versus ALS patients reflected a significant power reduction relative to the baseline, in both the μ and β bands during the imagination period in HC. However, despite an overall relative power reduction in ALS, this pattern was not significant for these patients. This can explain our findings of reduced suppression of ERD patterns for ALS patients relative to HC. Worth noting is that no appreciable ERS was observed for either HC or ALS patients. This may be explained by the fact that ERS is generally more consistent for ME rather than MI. It has been speculated that post-ME ERS is related to the deactivation of primary motor cortex neurons, which are argued to be more involved in ME rather than MI (Pfurtscheller et al. 1997)

Comparisons between MI topographic activities illustrated more prominent activity for healthy participants, bilaterally localized in the μ band and more contralateral in the β band. For ALS, the activity was reduced in almost all the channels with an ipsilateral localization in the μ band and a slight central localization in the β band. It has been previously reported that sensorimotor ipsilateral activity is more prominent for ALS patients during ME tasks compared to HC, but this was not observed for MI tasks (Poujois et al. 2013).

Our analysis also revealed significant correlations between the considered clinical scores (i.e. disease duration, ALSFRS-R-B, and ALS-CBS) and the extracted ERD/ERS features. In general, reduced ERD were correlated with worse bulbar functions (ALSFRS-R-B), worse cognitive functions (ALS-CBS) and longer disease duration. Interestingly, the correlations were found in the β band, which highlights the potential relevance of this band to ALS-specific abnormalities. As discussed before, our results were consistent with the previous study regarding correlation with bulbar functions. For RMI, worse cognitive functions were correlated with less preparatory ERD.

This might emphasize the effect of ALS on MI preparation and/or ME preparation as previously discussed. These results indicate that ERD features are sensitive to ALS disease progression and highlight the importance of quantifying the neural dynamics of MI for these patients.

5. Limitations & Future Directions

The statistical power of this study is limited by the low number of ALS patients recruited. This is due to the relative difficulty of recruiting and recording from ALS patients. Thus, a further expansion of our exploratory study is needed with a larger sample size, in order to strengthen the statistical power of our analysis. In addition, this study did not take into account differences in gender, age, medication type, or dosage. The heterogeneity in the ALS patient group involved in this study adds another limitation to our work. Future research should involve a larger sample of ALS patients that also permits subgroup analysis of EEG differences due to demographic factors, including disease duration, age, and gender. Although the ALS-CBS test was employed for the evaluation of cognitive functions, we could not evaluate the information and retrieval (fluency) section of the test which is more associated with bulbar functions and communication abilities. The reported ALS-CBS scores represented only an evaluation of attention, concentration, and tracking sections of the test and our cognitive profiles need more investigation.

Another limitation associated with the MI protocols is that there is generally no systematic way to assess whether participants are, in fact, performing the task. However, as the participants with ALS had reached a complete loss of motor control, MI is one of the most suitable endogenous responses to explore underlying motor functions in these patients. Also, worth noting is that during the first session of the recordings, our patients demonstrated the ability to use a BCI system application, the P300 speller (Schalk and Mellinger 2010), or eye-tracker, to answer a few simple questions which demonstrated their capability in following the instructions.

The importance of characterizing ALS-specific changes in sensorimotor oscillations can also have an impact on enhancing current MI-based BCI systems' performance. Considering our outcomes which indicate significantly reduced oscillations in ALS patients, these dynamics should be taken into account in future MI-BCI studies. Applying adaptive signal processing and machine learning algorithms might be considered as a potential solution to compensate for disease-specific abnormalities. Future studies might also involve integrating other types of neuroimaging modalities, such as functional near-infrared spectroscopy (fNIRS), to complement EEG in a hybrid manner—this can reveal hidden dynamics of abnormal motor functions undetectable using EEG

alone (Naseer and Hong 2015). Besides these neuroimaging modalities, if portable, they might compensate for the observed weak ERD patterns as an input to the BCI system through complementary neural features such as blood oxygenation levels

Future research directions could also involve exploring the hypothesized ALS-specific mirror neuron system dysfunction and identifying the role it may play in the disease diagnosis and prognosis. Moreover, further research is needed to investigate the dynamics of the underlying MI neural networks using higher-order analysis including functional and effective connectivity.

6. Conclusion

This study investigated the electrophysiological abnormalities of ALS cortical motor functions by quantifying ERD/ERS features of MI in frequency, time, and space. Overall, our results indicate that ALS patients have decreased ERD relative to HC, which results from reduced cortical activation during MI and might be attributed to cortical degeneration and disease progression. Furthermore, the results indicate that ALS patients have delayed ERD onset over the sensorimotor and premotor areas which can result from dysfunction of the underlying cortical networks involved in motor preparation. Our statistical analysis of comparing the extracted ERD/ERS features during each interval between ALS and healthy controls, demonstrated discrepancies in the topography of the significant reduction of the mean ERD, illustrating a dynamic ERD reduction for ALS time and space. In accordance with previous MI ALS studies, a negative correlation was found between reduced ERD for ALS and bulbar dysfunction which is speculated to be associated with deficits in the mirror neuron system activated through MI tasks. The spatio-spectral-temporal quantification of the dynamics of ERD/ERS in μ and β frequency bands could potentially capture progressive ALS-specific abnormalities and might serve as EEG markers to guide diagnosis and prognosis procedures.

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