Neural Alterations During Use of a P300-based BCI by Individuals with Amyotrophic Lateral Sclerosis*

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Abstract— Recent work has demonstrated that P300-based BCI systems can provide long-term communication for individuals with amyotrophic lateral sclerosis (ALS). However, even individuals with a successful history of BCI home use, can experience substantial variation in their day-to-day P300-based BCI performance. Recent studies suggest that functional connectivity among frontal-parietal cortical network governs the generation of P300 components. This study aims to characterize the correlates of EEG spectral and functional connectivity that underlie these fluctuations in performance during use of the P300-based BCI speller at home. Our results suggest that increased frontal-parietal functional connectivity and frontal non-phase locked theta band power modulations are associated with unsuccessful performance. The identified neural patterns suggest possible conscious/unconscious error-related adaptation mechanisms that can be associated with the realization of uncertainty and response conflict. These findings provide new insights into the underlying mechanisms of BCI performance variation and can inform the development of more robust BCI systems.

I. INTRODUCTION

The visual P300-based BCI has been validated as a practical communication system for amyotrophic lateral sclerosis (ALS) patients in their homes. Although most current non-invasive BCI systems are not designed for long-term use, recent work by National Center for Adaptive Neurotechnologies (NCAN) and other groups has demonstrated the efficacy of P300-based BCI systems for long-term communication in individuals with ALS [1]. Effective and longitudinal use of P300-based BCIs was investigated in a study involving in-home installation of the system for 27 individuals diagnosed ALS [2]. In these studies, BCI systems were able to restore independent communication through direct selection. However, considerable performance variation within and across days of use were reported [3], in contrast to relatively stable performance for healthy users [4]. In these studies, system and classifier reliability are maintained via periodic inspection of the user's data collected during a routine copy-spelling calibration task. However, performance fluctuations are not well correlated with system reliability issues, e.g., high impedance. These variations, which have also been reported by other groups, may represent non-stationarities in the neural signals [5, 6].

Recently, pathological changes beyond the primary motor areas in patients with ALS have attracted the attention of many researchers and clinicians in the field [7]. Considering the nature of ALS as a multisystem disorder and the crucial role of cognitive functions in BCI performance, one possible explanation for BCI performance fluctuations could be associated with cognitive variations [8]. Previous work investigated EEG correlates of BCI performance across patients' groups [3, 9]. Features related to the P300 event-related potential (ERP) morphology and conventional spectral band power were reliably identified as predictors of P300-based BCI performance [9]. However, the focus of these studies was mainly to characterize the between-subject rather than within-subject variations. The P300-ERP is not a unitary phenomenon, and it involves underlying cognitive components and network dynamics that may lead to variations within patient groups; specifically, those with neurodegenerative disorders. In one of our prior studies, we observed that a top-down circuit with a strong information flow in healthy controls is impaired in ALS. This connection becomes weaker during unsuccessful sessions [10].

The present study attempts to provide insight into the neurophysiological differences at both local and network levels that might influence BCI performance variations in patients with ALS. While at the network level, coherence associations of longitudinal BCI performance variations were explored, at the local level, both evoked and induced spectral correlations were investigated. In contrast to most prior studies focusing on between-subject variations, we attempt to explore within-subject neural oscillatory changes and quantify the associations with successful versus unsuccessful runs. Characterizing discrepancies in performance levels of BCIs and applying proper strategies are imperative for prolonged usage of these systems.

II. MATERIALS AND METHODS

A. Subjects, Experimental Protocol, and Data Acquisition

The BCI-24/7 home system [1, 2] was used independently by nine ALS patients at home for a period of 2 to 10 months. This analysis focuses on the copy-spelling calibration, where the number of prescribed characters for each run varied between 10 to 20 for each run. For each run, BCI users were seated comfortably upright in their bed or their own wheelchair at a comfortable viewing distance (approximately 90 cm) from the system's monitor. The task was based on the

P300 oddball paradigm. The average number of runs for all users was 61 ± 29. Users' ALS revised Functional Rating Scale (ALS-FRS-R) scores ranged between 0 and 32 (median=12, std =12.83) on a 48-pt scale. All studies were approved by the Institutional Review Boards of New York State Department of Health, and Helen Hayes Hospital. EEG data was recorded from eight electrodes located at Fz, Cz, Pz, Oz, P3, P4, PO7, and PO8 [4]. The signals were amplified using a g.USBamp amplifier (g-tec Medical Technologies) with a reference and ground to the right and left mastoid, respectively, digitized at 256 Hz, and bandpass filtered at 0.5-30 Hz. The number of trials and the classifier required for online sessions were optimized for each user independently depending on the offline performance [4]. Online feedback was provided to the user for each selection and a threshold of 70% was used to categorize the performance during each run as successful (≥70%) or unsuccessful (<70%). The percentage of unsuccessful runs varies from 13% to 56% for different participants with an average of 32% across all subjects.

B. Power Analysis

A time-frequency decomposition of the EEG data was performed via a complex Morlet wavelet convolution using a set of wavelets ranging from 1 to 30 Hz and a variable number of cycles (3 to 10). For each run, all trials of EEG data were extracted within 1200 ms (200 ms pre-stimulus and 1000 ms post-stimulus). Evoked power was obtained by averaging all trials for each run and then convolving with the set of wavelets. For induced power, the average of all trials was subtracted from each trial and convolution was performed. The resulting power was averaged across all the trials. The final power values were normalized to the baseline power in the range of -200 to -50 ms pre-stimulus and an average over delta [1-3 Hz], theta [4-8 Hz], alpha [9-13 Hz], and beta [14-30 Hz] frequencies, respectively, was computed.

C. Coherence Analysis

Coherence is a bi-variate and non-causal connectivity measure that can provide a basic understanding of neural oscillations at the network level. For this analysis, we used coherence to assess how the frontal-parietal network, crucial for underlying cognitive functions involved in P300 tasks, is synchronized, and how the network differs across runs. Briefly, coherence was calculated based on magnitude squared of the normalized cross spectrum at a specific frequency between two signals as below:

$$C_{xy}(f) = \left| \frac{S_{xy}(f)}{\sqrt{S_{xx}(f)S_{yy}(f)}} \right|^2 \qquad (1)$$

where $C_{xy}(f)$ is the coherence at each frequency bin, $S_{xy}(f)$ denotes the cross-spectral density between channels x and y, $S_{xx}(f)$, and $S_{yy}(f)$ denote auto-spectral densities at frequency f at each channel respectively. In this analysis, to explore the entire coherence of successful and unsuccessful runs, coherence was calculated once over the entire run and denoted as total coherence (i.e., TC). It was also computed once over the trials to explore event-related coherence (ERC) dynamics post-stimulus. The parameter N

in equation (1) is the maximum time in the case of TC analysis, and maximum trial in the case of ERC analysis.

TC was calculated for the entire run using a set of Hanning windows with a length of 1 second and 0.5-second overlap in frequencies ranging between 1-30 Hz. The average coherence was obtained over all windows. ERC was calculated based on power and phase values obtained from Wavelet time-frequency decomposition similar to the previous section. A non-parametric Wilcoxon signed rank test (α=0.05) was used to assess the statistical significance of the difference of the power and coherence measures between successful and unsuccessful runs.

III. RESULTS

Fig. 1 (top) illustrates the time-frequency plots of induced and evoked power differences between unsuccessful and successful runs at the frontal channel (Fz). The analysis shows an enhanced induced and suppressed evoked power in the theta band for unsuccessful runs relative to successful runs. Fig. 1 (bottom) illustrates the time evolution of both induced and evoked theta power. For unsuccessful runs, the theta induced power was enhanced significantly in the window of 0-270 ms post-stimulus (p-value = 0.02), while the theta evoked power was significantly suppressed within the window of 190-500 ms post-stimulus (p-value = 0.01), the period of interest for relevant P200/P300 components.

Fig. 2 illustrates the TC barplots at four specified frequency bands between the frontal (Fz) and each of the other locations. The analysis shows a significant increase of frontal (Fz)-parietal (P3, Pz, PO7, and PO8) delta coherence in unsuccessful runs, with average mean and standard deviation of 0.29 ± 0.08 and 0.24 ± 0.05 for unsuccessful and successful runs respectively (P<0.02). Similarly, a significant increase of theta connectivity in unsuccessful runs for the frontal-central (Fz-Cz) connection, having a mean and standard deviation of 0.76 ± 0.06 and 0.74 ± 0.07 for unsuccessful and successful runs respectively, was observed (P = 0.02). The frontal-parietal connection (Fz-Pz), having a mean and standard deviation of 0.42 ± 0.08 and 0.37 ± 0.1 for unsuccessful and successful runs respectively, was also found to be statistically significant (P = 0.03).

Fig. 3 (top) illustrates the time-frequency ERC difference between unsuccessful and successful runs between Fz and Cz. Similar to the TC Fig. 3 (bottom), at this connection, a general increase of coherence in delta and theta ranges was observed for unsuccessful runs relative to successful runs. However, the obtained ERC was only significant in the delta range (p-value = 0.01) and no significant ERC differences were observed in any other connections and at any other frequency bands.

IV. DISCUSSION

In contrast to prior work, this study provides an initial investigation of within-subject variations in brain functional patterns associated with BCI performance fluctuations. The network analysis elucidated a significant pattern of increased connectivity in the frontal-parietal and frontal-central network in delta and theta frequency bands for runs with unsuccessful performance. We speculate that the observed increase of top-down synchronization may be interpreted in
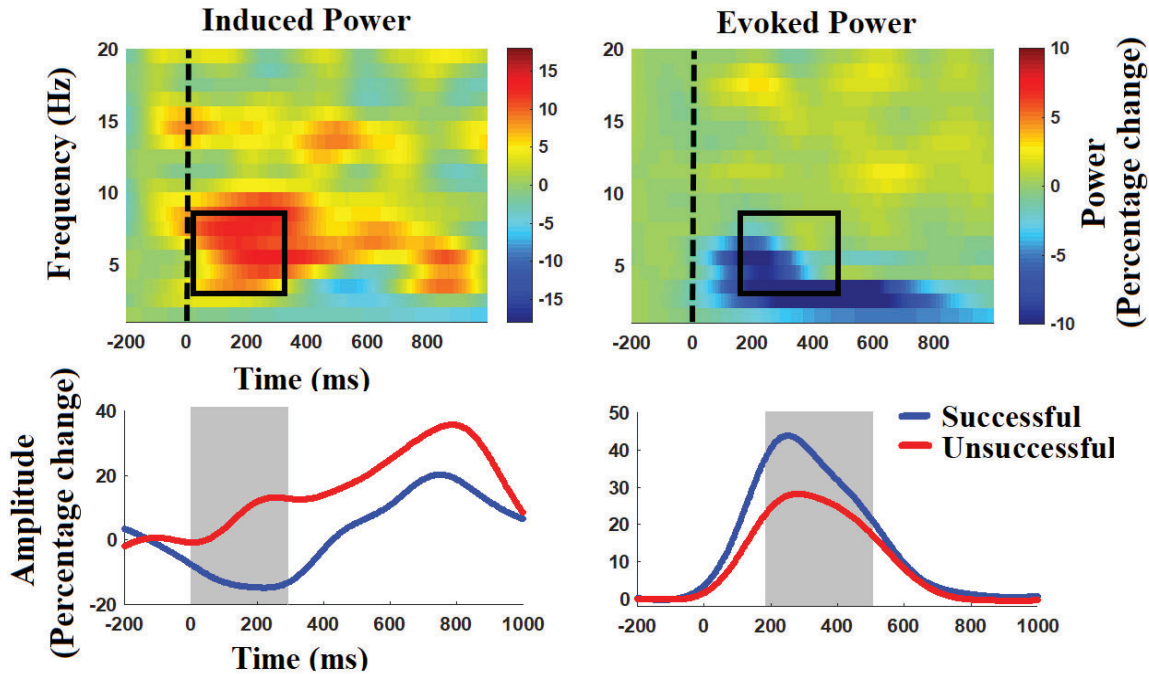
Figure 1. Top: time-frequency map difference (unsuccessful - successful) of induced power (left) and evoked power (right) for channel Fz. Bottom: temporal dynamic of induced (left) and evoked (right) theta power at channel Fz. Blue curves show successful runs and red curves show unsuccessful runs.

light of the role of the medial frontal cortex (MFC) mechanisms in detecting errors and subsequent performance adaptation as opposed to an increase of attention or target detection mechanism. In a study done by Cohen et al. [11], an enhanced top-down synchronization was observed on trials following unconscious and conscious errors and was identified as behavioral performance predictors. This interpretation is consistent with previous studies suggesting that the amplification of cortical responses to task-relevant information may be considered a prefrontal cognitive control mechanism for conflict/error processing which may occur in absence of conscious awareness [12, 13].

The P300 has been recognized as a composite phenomenon reflecting an information processing cascades of cognitive processes [14]. The importance of theta- and delta-band connectivity, at top-down connections, are highlighted for the contribution of stimulus detection and response selection processes that may underlie the P300 components [15]. Interestingly, various studies revealed that the enhancement of activity in regions involved in task-relevant stimulus processing may be related to error signaling and conflict detection [16]. A plausible interpretation of our network analysis reveals that increased top-down synchrony in poor runs is associated with a post-error adaptation mechanism in the spelling task whether consciously in the case of misspelled character and incorrect feedback, or unconsciously in the case of reasons related to the patient's cognitive state during the task. However, this hypothesis needs to be further investigated via studies involving multivariate network analysis to verify if it is indeed a top-down MFC-driven control mechanism. Besides, since the observed patterns related are not specific to ALS [17, 18], future investigations may involve comparison with healthy users.

Our local oscillatory analysis indicated an increase of induced (non-phase locked) theta power in the frontal channel (Fz) for unsuccessful runs. These results support recent cognitive models proposing that medial frontal theta power may be associated with the realization of uncertainty, response conflict, the need for behavioral change, or adaptation [17]. The situation of an error in case of spelling task may be interpreted in the context of distraction, uncertainty, and conflict detection which may elicit higher theta power [17]. Our analysis of non-phase locked theta modulations ensures that the observed activity is not related to the visual ERP components but rather reflects the inherent conflict-related neural oscillations midfrontal power [18], which supports our hypothesis for increased frontal-parietal synchronization.

One of the concerns attributed to our analysis, is that the volume conduction effect was not considered into our analysis. Future investigations should consider spatial filtering and other connectivity analysis to address this problem. Merging other neuroimaging techniques including functional-near infrared spectroscopy (fNIRS) should also provide a better insight into a more comprehensive understanding of our findings. Studying the implicit causes of potential variations in ALS patient's performance is considered an open question. In addition to disease-specific neurophysiological interpretations such as altered patterns of hyper-connectivity in resting state EEG, the possible non-motor deterioration can add another dimension to the possible reasons for performance variations.

Investigating performance variation in individuals with neurodegenerative disease is highly important for designing robust and practical BCI systems that can accommodate patients' communication needs over long periods of time.
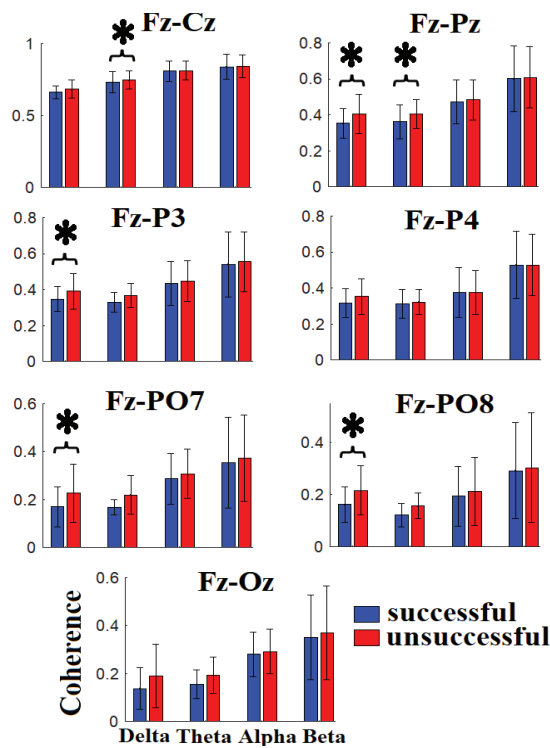
Figure 2. Total coherence (TC) between frontal channel (Fz) and all the other locations. Red and blue bars indicate the coherence for unsuccessful and successful runs respectively. An asterisk (*) indicates a statistically significant change after correction.
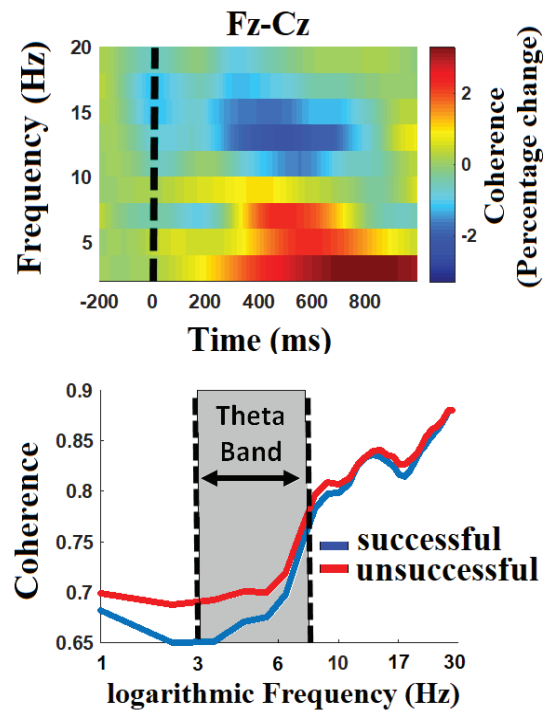
Figure 3. Top: event-related coherence (ERC) difference (unsuccessful - successful) between Fz-Cz. Bottom: total Fz-Cz coherence (TC) for successful (blue) and unsuccessful (red) runs.

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