Brain-Computer Interfacing in Amyotrophic Lateral Sclerosis: Implications of a Resting-State EEG Analysis

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***Abstract*— Despite decades of research on EEG-based brain-computer interfaces (BCIs) in patients with amyotrophic lateral sclerosis (ALS), there is still little known about how the disease affects the electromagnetic field of the brain. This may be one reason for the present failure of EEG-based BCI paradigms for completely locked-in ALS patients. In order to help understand this failure, we have recorded resting state data from six ALS patients and thirty-two healthy controls to investigate for group differences. While similar studies have been attempted in the past, none have used high-density EEG or tried to distinguish between physiological and non-physiological sources of the EEG. We find an ALS-specific global increase in gamma power (30–90 Hz) that is not specific to the motor cortex, suggesting that the mechanism behind ALS affects non-motor cortical regions even in the absence of comorbid cognitive deficits.**

1. Introduction

Amyotrophic Lateral Sclerosis (ALS) is a surprisingly well-known disease given its relative rarity, associated with the names of American baseball players and British astrophysicists, and the dumping of ice water on one's head. Yet, despite decades of research and exhaustive characterization from a medical perspective [1], the electrophysiological effects of the condition remain very poorly characterized, possibly because for the majority of the history of ALS it has been considered a purely motor disorder. As such, the electroencephalographic (EEG) signal has been relied upon these intervening decades as the best non-invasive method of interacting with paralysed patients by brain output alone. ALS patients have been a fertile ground for Brain-Computer Interface (BCI) study–studies which, despite early success [2]–[4], have recently proved unable to maintain the rate of progress [5]. It is the aim of this study to help shed light on subtler effects of ALS on the recorded EEG, and thereby try to understand why recent BCI efforts have met such little success.

The resting-state frequency band analysis of ALS is limited to a single study done nearly twenty years ago, which reported that the power in the α-band (8–12 Hz) over the central cortex was significantly reduced in ALS patients as compared to healthy controls [6]. More recently, motor planning tasks have shown that ALS patients have a lower sensorimotor α-rhythm desynchronization [7], limiting frequency band findings to the central and sensorimotor cortex exclusively. Studies of Event-Related Potentials highlighted atypical responses in ALS patients to attentional tasks as well [8]. The paucity of these findings is suspicious in the light of alternate neuroimaging evidence gathered by MRI and PET scanning over the years which suggest marked functional changes in the motor cortex [9]–[11] as well as suggesting involvement by systems outside of it [12]. Given the increase in powerful artifact reduction and source separation techniques that have come to the fore since those studies, such as independent component analysis (ICA) [13], we expect to be able to gain more insight by revisiting the attempt to use quantitative EEG methods on ALS, and hopefully to find evidence that helps explain the current failure of late-stage ALS patients to communicate with EEG-based BCIs.

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2. Methods

A. Subjects and experimental data

Five minute resting-state recordings were taken from eight non-demented ALS patients using an actiCAP 124 channel active electrode system with QuickAmp amplifier (both provided by BrainProducts GmbH, Gilching,

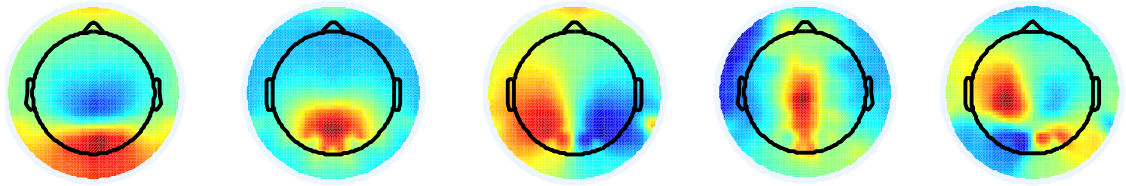

Fig. 1. Topographic plots showing the projections of the five cortical independent components isolated from the pooled patient and control data onto the electrodes

Germany) sampled at 500 Hz. One patient was excluded because of scores above the cutoff for fronto-temporal dementia on both the Edinburgh Cognitive Assessment Screen [14] and the ALS Fronto-Temporal Dementia (FTD) Questionnaire [15]. Electrodes were placed according to the extended 10-20 system, with the electrode P7P as the initial reference. All recordings were converted to common average reference and high-pass filtered at 0.1 Hz to remove drift artifacts. Data was then visually inspected for strong artifactual noise, which led to the invalidation of the recording from one more ALS patient. The data of the remaining six patients (cf. Table I) was then combined with 37 non-age-matched control subjects without known neurological deficits. For the recordings, subjects retaining command of their gaze were instructed to fixate on a point displayed on a monitor in front of them and relax. The study was approved by the ethics committee of the Max Planck Society and each subject gave informed consent in agreement with guidelines set by the MPS.

TABLE I
ALS PATIENT DATA

Patient	Age	Sex	ALSFRS-R
ET	51	F	12
GV	75	M	42
LEK	56	F	0
GH	58	M	39
LS	63	M	33
HR	81	M	23

B. Data processing

To attenuate non-cortical artifacts in the EEG, we pooled the recorded data across all subjects and separated it into independent components (ICs) based on the SOBI algorithm [16]. Five cortical processes were isolated from the resulting ICs by manual filtering for clear dipoles in the induced electrode topology, an inverse power law relationship in the frequency transform, and clear α-band activity in the source time series, as corresponds to previously determined criteria [**?**], [17] (Figure 1). The power spectra of each cortical source was computed for each subject at the following frequency bands: 1–4 Hz (δ), 4–8 Hz (θ), 8–14 Hz (α), 20–30 Hz (β), 30–50 Hz (γ_{low}), and 50–90 Hz (γ_{high}). A discrete Fourier transform (DFT) in conjunction with a Hann window was computed over the length of the session for each source, and the amplitudes of the resulting frequency series were averaged over the frequency windows to produce resting-state log-bandpower estimates for each source at each frequency band. The estimates were then averaged to create a global cortical estimate for each subject.

C. Statistical analysis

To check for significant interactions of the condition and band range on the computed log-bandpower, a two-way unbalanced ANOVA was computed. The condition (ALS or healthy control) was not significantly related to bandpower measurements, but the choice of band ($p < 0.001$) and the interaction between band and condition ($p < 0.05$) were. To investigate this significant interaction, we then computed a permutation-based two-tailed t-test to see which mean differences in bandpower were significant.

3. RESULTS

We found that global bandpower was significantly enhanced in the high γ-range (two-tailed permutation test, $p = 0.03$ uncorrected) (Figure 3) when averaged over all cortical ICs in ALS patients as compared to healthy controls. However, IC time series as recreated by SOBI are constrained to be of unit variance, which does not reflect how they are represented on the electrode level. To better understand the spatial differences in bandpower, we reprojected the cortical components to

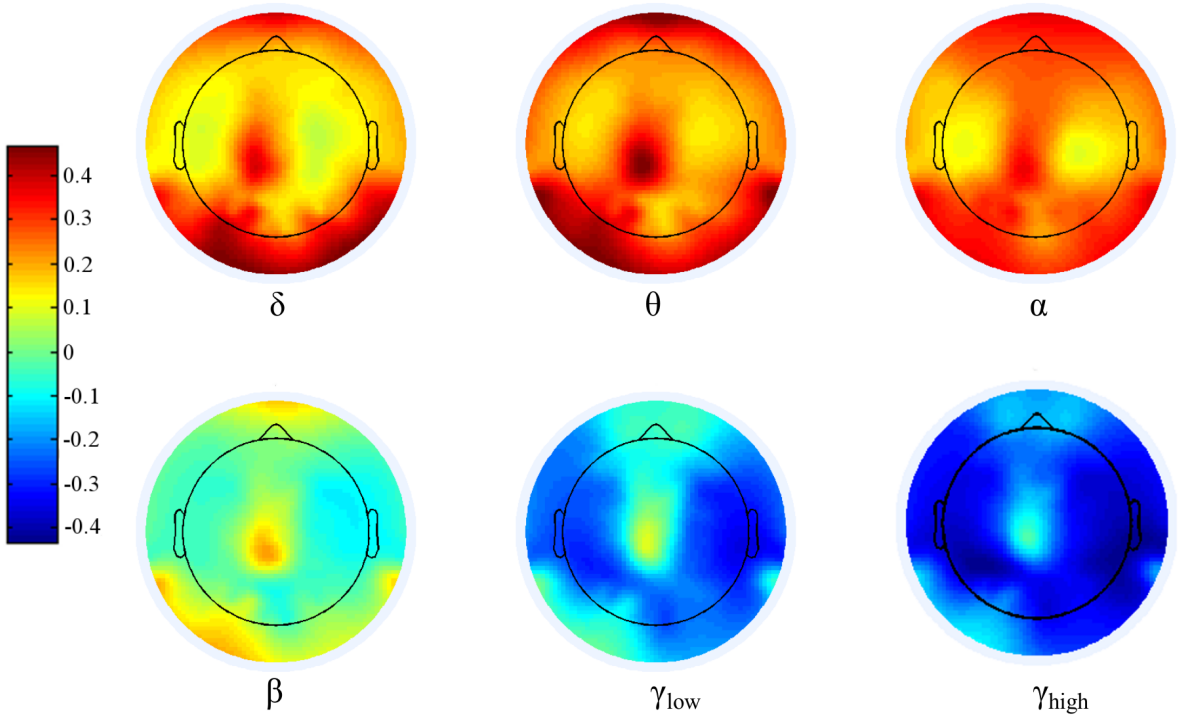

Fig. 2. Topological plots of the difference in mean log-bandpower between control and ALS patients (red, higher power in controls) for each frequency band.

the electrodes and looked at spatial differences in mean bandpower between ALS patients and controls (Figure 2). There is a broad trend of higher bandpower in the γ-range, but also a peak of lower α-power in the central area for ALS patients.

4. Discussion

Our data indicate that ALS is associated with bandpower changes that span the whole spectrum of the brain's electromagnetic field. Consistent with previous work from 1998 [6], we find a decrease in bandpower over central areas. In contrast to the results by Mai et al. , however, we find this decrease to be most pronounced in the θ- rather than in the α-band. This may be a result of a slowing of brain rhythms in ALS, for which we did not correct in our analysis. In addition to the work of Mai et al., we find a marked increase in bandpower in the γ-range outside of central areas. As such, changes to the brain's electromagnetic field in the ALS appear more widespread than it is commonly assumed. Changes in γ-power have been linked to various neurological disorders (for a more comprehensive review, see [18]). Interestingly, γ-oscillations are substantially reduced in the only

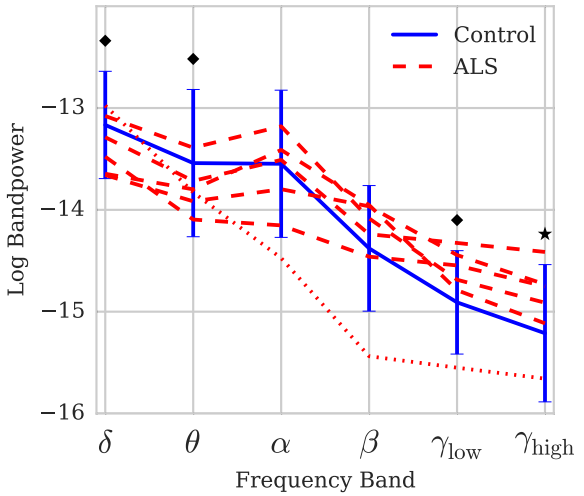

Fig. 3. Plot showing mean cortical bandpowers in control subjects (blue) with 95% confidence interval versus the mean cortical bandpowers in each ALS patient (red). Star correspond to bands with significant differences in mean ($p < 0.05$ uncorrected) between ALS and healthy controls, diamonds to differences approaching significance ($p < 0.10$). The dotted red line corresponds to the frequency bands of the patient with ALSFRS-R score 0.

patient in our study with an ALSFRS-R of zero. If this finding can be reproduced in a larger patient population, it may suggest a nonlinear relationship between γ-power and disease progression.

Given that success in BCIs for ALS patients becomes worse as the disease progresses, and these BCIs are mostly focused on lower frequency oscillations, it is possible that the reduced bandpower of these rhythms in the disease is also decreasing the range of their variability. This may be an explanation why voluntary modulation of these rhythms becomes more difficult to detect. Gamma-power, on the other hand, increases in resting-state frequency, putting it forth as a possible candidate for BCIs more robust to progression of the disease [19].

Despite the exciting nature of possible conclusions, we note that our study has been carried out on a small number of patients only. In addition, the control population was not age-matched to the ALS population. Previous research suggests that increased age is correlated with decreases in resting-state δ-, θ- [20] and α-power [20], [21]. Intriguingly, however, age has only been linked with decreases in γ-power across both the frontal- [21] and occipital [22] cortex. As such, our observation of increased γ-power in ALS is unlikely to be a result of age as a confounding variable.

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