# A Cognitive Brain-Computer Interface for Patients with Amyotrophic Lateral Sclerosis

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***Abstract*—Brain-computer interfaces (BCIs) are often based on the control of sensorimotor processes, yet sensorimotor processes are impaired in patients suffering from amyotrophic lateral sclerosis (ALS). We devised a new paradigm that targets higher-level cognitive processes to transmit information from the user to the BCI. We instructed five ALS patients and eleven healthy subjects to either activate self-referential memories or to focus on processes without mnemonic content, while recording a high-density electroencephalogram (EEG). Both tasks are likely to modulate activity in the default mode network (DMN) without involving sensorimotor pathways. We find that the two tasks can be distinguished from bandpower modulations in the theta- (3–7 Hz) and alpha-range (8–13 Hz) in fronto-parietal areas, consistent with modulation of neural activity in primary nodes of the DMN. Training a support vector machine (SVM) to discriminate the two tasks on theta- and alpha-power in the precuneus, as estimated by a beamforming procedure, resulted in above chance-level decoding accuracy after only one experimental session. Therefore, the presented work could serve as a basis for a novel tool which allows for simple, reliable communication with patients in late stages of ALS.**

***Index Terms*—EEG; brain-computer interface; brain-machine interface; ALS; locked-in.**

## I. Introduction

The usage of brain-computer interfaces (BCIs) in patients suffering from late-stage amyotrophic lateral sclerosis (ALS) holds the promise enabling communication. This mission has proven to be very challenging in the final stages of the disease, as BCIs are often based on motor- and sensory processes, such as the volitional modulation of sensorimotor rhythms [1], [2]. However, patients suffering from ALS show degeneration of neurons in the primary motor cortex [3], and impairment in their ability to modulate these rhythms in later stages of the disease. Visual speller systems require subjects to fixate on target stimuli, which also fails due to impaired oculomotor control [4]. For the same reason, patients are unable to make use of the covert attention paradigms which rely on fixating on a spot [5]. Tactile [6] and auditory [7] BCIs have only been tested on healthy subjects and patients in earlier stages of the disease. Their usefulness for establishing a reliable communication with completely locked-in patients remains unclear. Therefore, we propose a novel approach that incorporates non-sensorimotor-related higher level brain functions that may be spared in ALS.

Higher-level brain functions can be incorporated into BCIs by training subjects via neurofeedback to self-regulate neural activity in cortical areas that subserve higher functions [8]. One major issue with this approach is the amount of training that is needed to modulate activity above chance-level. The need for extensive training decreases the feasibility of the system, especially for patients in later stages of the disease.

Recent studies have discussed mental tasks as an alternative to motor imagery to improve BCI performance for disabled users [9]. Here, we propose a novel cognitive strategy to facilitate the manipulation of activity in the default mode network (DMN), a large-scale cortical network that is involved in self-referential processing [10] and is connected to the degree of consciousness [11]. Based on these properties of the DMN, we instructed subjects to alternate between self-referential thoughts, which activate the DMN [12], and focusing on their breathing, which deactivates the DMN because it is devoid of self-referential mnemonics [13]. The current study investigates the hypothesis that this strategy elicits bandpower changes in the electroencephalogram (EEG) over areas consistent with the DMN which are sufficiently strong to enable above chance-level decoding accuracies in healthy subjects and patients with ALS, without any subject training.

## II. Methods

### A. Experimental Paradigm

Healthy subjects were placed in a chair approximately 1.25m away from a 17” LCD screen with a resolution of 1280x1024 pixels and a 60 Hz refresh rate. The background of the screen was black, with a white fixation cross appearing in the centre. Prior to the experimental session, two five-minute resting state EEGs were recorded. Subjects were asked to let their mind wander and to either keep their eyes open in the first resting-state and closed in the second one. After the resting-state sessions, subjects performed three experimental blocks with brief intermissions. Each experimental block consisted of ten

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trials in which the participants were asked to "remember a positive experience" and ten trials in which the participants were asked to "focus on their breathing", in pseudo-randomized order. Each trial began with $5.5 \pm 0.50$ seconds rest, followed by instructions that were given acoustically and visually to indicate which of the two cognitive tasks should be performed. After 60 seconds, the trial ended and the next trial started. To ensure comprehension, both cognitive tasks were explained to participants in a briefing before the experiment.

For ALS patients, the experimental paradigm remained the same;however, they were only asked to perform one experimental block.

### *B. Experimental Data*

The study was conducted at the Max Planck Institute for Intelligent Systems in Tübingen, Germany. Eleven healthy subjects (eight male and three female, mean age $29.3 \pm 8.3$ years) and five ALS patients (cf. Table I) were recruited from the local community and in cooperation with the University Clinics Tübingen. Participants received 12 Euro per hour for their participation. One healthy subject was excluded due to noisy recordings. Another healthy subject and patient ET were excluded due to technical disturbances during the experiment, resulting in an unequal amount of trials per condition. This left nine healthy subjects and four patients for the final analysis. All participants were naive to the setup. They were informed by the experimenter about the procedure and signed a consent form to confirm their voluntary participation in advance. The study was approved by the ethics committee of the Max Planck Society.

TABLE I
ALS PATIENT DATA

| Patient | Age | Sex | ALSFRS-R[1] | Impairment |
|---|---|---|---|---|
| GN | 54 | M | 48 | Mild limb impairments |
| GV | 75 | M | 42 | Mild limb impairments |
| HR | 81 | M | 23 | No limb functionality |
| ET | 51 | F | 12 | Locked-in, eye-movements |
| LEK | 59 | F | 0 | Residual eye-movements |

[1]Revised amyotrophic lateral sclerosis functional rating scale [14]

A 124-channel EEG was recorded at a sampling frequency of 500 Hz using actiCAP active electrodes and a QuickAmp amplifier (provided by BrainProducts GmbH, Gilching, Germany). Electrodes were placed according to the extended 10-20 system with the left mastoid electrode as the initial reference. All recordings were converted to common average reference. The application was realised with the BCI2000 and BCPy2000 toolboxes [15].

### *C. Data Analysis*

We performed an offline analysis on the acquired data to identify confounding EMG activity, to analyse the cortical distribution of the induced effect, and to investigate differentiability of the activity-patterns associated with self-referential thoughts and focus on breathing.

*1) Preprocessing:* To compare healthy subjects and patients with the same amount of trials, we focused on the first block in our main analysis. We restricted our analysis to the time-window of 6 to 60 seconds per trial, as instructions were given in the first few seconds of each trial. To capture the effect of self-referential processing, we restricted our analysis to the $\alpha$ and $\theta$-frequency bands (3Hz$\sim$16Hz, lower and upper $\alpha$ limit individually adjusted for each subject based on the resting-state data, the lower $\theta$ limit was fixed at 3Hz), as self-referential processing correlates with $\theta$ and $\alpha$ spectral power [16]. The individual $\alpha$-band for each subject was determined by overlapping the spectral power of eyes open and eyes closed resting states [17]. The lower and upper boundary of the individual alpha band was set at the intersection point of the two curves corresponding to the power spectra of the resting states.

*2) Attenuation of EMG artifacts:* EEG recordings are likely to be contaminated by scalp-muscle artifacts [18]. Therefore, subjects may have been able to involuntarily influence the EEG signal by altering the tonus of their scalp muscles. In order to identify such EMG confounds, we employed independent component analysis (ICA) [19]. The continuous data of one session was first reduced to 64 components by principal component analysis, and then separated into independent components using the SOBI algorithm [20]. We then sorted the ICs according to their neurophysiological plausibility [21], manually inspected the topography, spectrum, and time-series of each component, and rejected those for which at least one of the following criteria applied: (1) Components displayed a monotonic increase in spectral power starting around 20 Hz. This is characteristic for muscle activity. (2) Eye-blinks were detectable in the time series. (3) The topography did not show a dipolar pattern. (4) The time series seemed to be contaminated by other sources of noise, like bad impedance, large spikes, and 50 Hz line noise. As discussed in [22], it is unreasonable to expect a complete removal of artifacts using ICA, but careful application is a useful means of rejecting the most dubious results on the scalp.

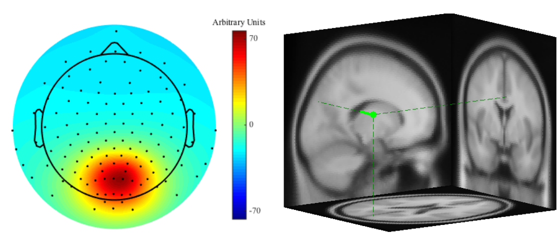


Fig. 1. Topography of sources that represent the precuneus targeted by the beamforming procedure.

*3) Pattern Classification:* Because the precuneus is a hub of the DMN [23], we aimed a linearly constrained minimum variance (LCMV) beamforming algorithm [24] at this region. First, the subject-specific covariance matrix $\Sigma \in \mathbb{R}^{N \times N}$ of the resting state recording with $N = 124$ EEG channels was computed. Then, the beamformer was computed by solving the LCMV-optimization problem

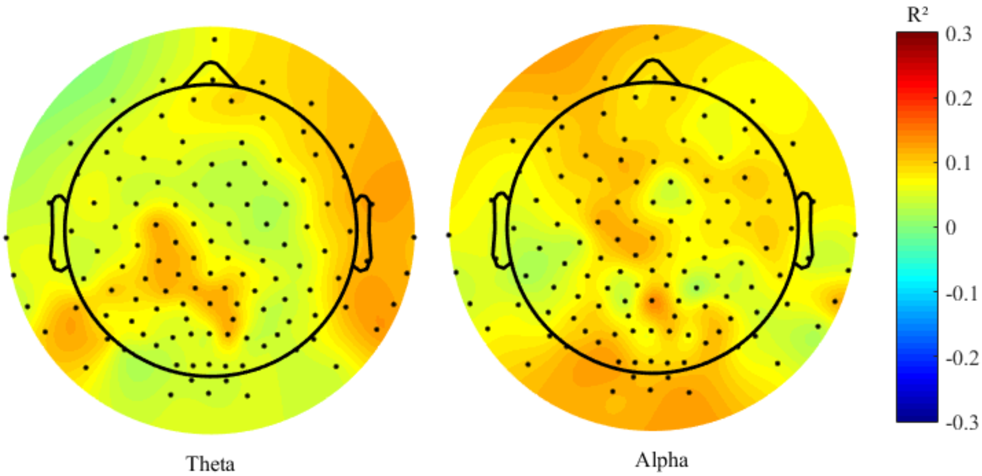


Fig. 2. Average cortical $R^2$-maps for $\theta$ and $\alpha$-bandpower across all patients.

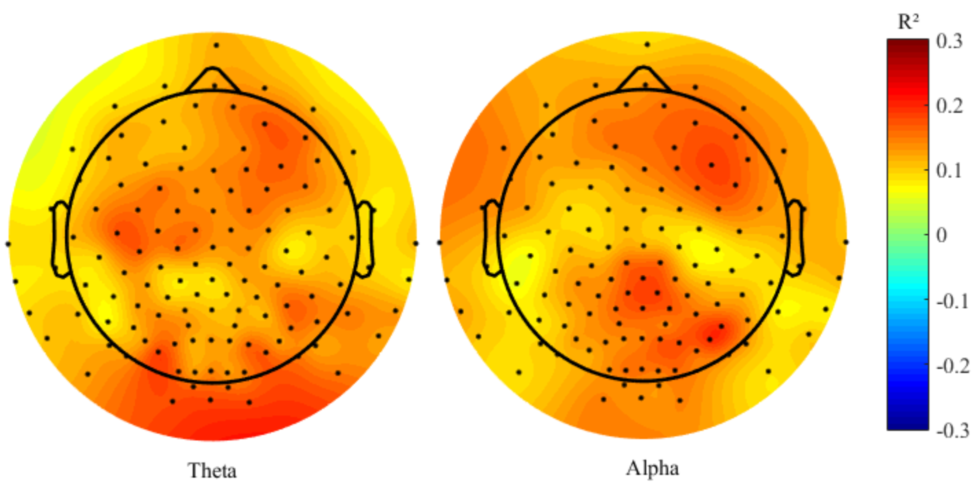


Fig. 3. Average cortical $R^2$-maps for $\theta$ and $\alpha$-bandpower across all healthy subjects.

$$\mathbf{w}^* = \text{argmin}\left\{\mathbf{w}^T \Sigma \mathbf{w}\right\} \text{ s.t. } \mathbf{w}^T \mathbf{a} = 1$$

with $\mathbf{a} \in \mathbb{R}^N$ being the scalp topography based on a subset of sources in a forward model that represents the precuneus (cf. Figure 1 and [8]). The resulting spatial filter $\mathbf{w}^*$ was then applied to the EEG data $\mathbf{x}[t] \in \mathbb{R}^N$ to obtain a 1D signal $y[t] = \mathbf{w}^{*T}\mathbf{x}[t]$ from the target area, in which the variance of all sources outside this area is optimally attenuated. For each trial, we windowed the resulting current density estimate in the precuneus with a Hann window, performed a DFT and averaged over the combined $\theta$- and $\alpha$-range to get a log-bandpower estimate for the trial. This served as our one-dimensional feature space.

We then employed a support vector machine (SVM) with a linear kernel to estimate the accuracy in discriminating the activity-patterns of both tasks based on the combined $\theta$ and $\alpha$ bandpower as described above. We employed a leave-one-trial-out cross-validation procedure within each subject. The optimal regularisation parameter for each training-set was determined in an inner loop and afterwards used in an outer loop to determine the classification accuracy. To test the null-hypothesis $H_0$: median classification-accuracy = 0.5 (chance-level), we used a Wilcoxon signed-rank test, given the classification-accuracy value of each subject.

*4) Spatial Distribution:* To further investigate the spatial distribution of the effect, we computed the coefficient of determination ($R^2$) for every subject and channel to evaluate the average difference in band-power in $\alpha$ and $\theta$ bands induced by the two tasks.

## III. RESULTS

Table II and III show the accuracy of the classification of the beamformed, combined $\alpha$ and $\theta$-bandpower as described above for the ALS patients and healthy subjects, respectively. A one-tailed Wilcoxon signed-rank test rejected the null-hypothesis of a median classification accuracy on chance-level (50%) at $p < 0.001$ for the combined subject groups.

Figures 2 and 3 show the $R^2$-values on a topographic plot for the combined $\alpha$ and $\theta$-bandpower in patients and healthy subjects. A higher $R^2$-value depicts a higher percentage of variance explained by the experimental conditions. It can be seen that the observed modulation centres around the parietal as well as the prefrontal cortex, especially in the $\alpha$-band.

TABLE II
CLASSIFICATION ACCURACY FOR PATIENTS

| GV | LEK | GN | HR |
|---|---|---|---|
| 70% | 65% | 75% | 65% |

TABLE III
CLASSIFICATION ACCURACY FOR HEALTHY SUBJECTS

| S1 | S2 | S3 | S4 | S5 | S6 | S7 | S8 | S9 |
|---|---|---|---|---|---|---|---|---|
| 85% | 45% | 80% | 90% | 80% | 55% | 70% | 55% | 70% |

## IV. DISCUSSION

The current study aimed to show that the employed cognitive strategy modulates activity in the precuneus, and that this modulation can be differentiated above chance level without any subject training. Using a linear kernel SVM, we were able to successfully classify both patterns with an average decoding of 70% and 68.75% for the healthy subjects and ALS patients respectively. We further investigated the spatial distribution of the effect by looking at $R^2$ values for each EEG channel in the $\theta$- and $\alpha$-range. Larger $R^2$ values can mostly be seen around parietal and prefrontal areas, consistent with modulation of neural activity in primary nodes of the DMN. Additionally, $\alpha$ and $\theta$-bands show slightly different spatial patterns, which may indicate that both bands are involved in different cognitive processes. Most importantly, we found all four ALS patients in various stages of disease progression to be capable of self-modulating activity in the targeted areas without extensive training.

However, one has to be careful when interpreting these results in terms of communication. All data was analysed offline employing a cross-validation as a way of obtaining prediction-errors that are nearly unbiased [25]. This method cannot be employed during online use. Online, a classification accuracy $\geq$ 70% is usually considered necessary for communication. Similarly, according to Müller-Putz et al. [26], a classification accuracy of 70% is needed for 10 trials and two classes to reject the null-hypothesis in an online setting with $p < 0.05$. Additionally, 20 trials per participant limit the interpretability of individual classification results. Future research could therefore investigate the use of different decoding models, such as a multitask learning approach [27]. This method may allow for offline training on multiple subjects in multiple sessions, and could then be employed for online classification. Due to a larger set of training data, it may also allow for a comparison with unrestricted feature derivation on sensor-level.

While subjects effectively modulated activity in the precuneus, we found a large variability in bandpower differences on an individual level. One reason for this could be the choice of the non-self-referential condition. Focusing on breathing has been shown to decrease overall activity in the DMN, but it also increases synchronisation within the DMN [28]. These two effects may be difficult to separate when investigating EEG bandpower-values, as an increase in synchronisation can lead to an increase in spectral-power, indistinguishable from the self-referential activation. A potential solution to this problem could be the choice of a different non-self-referential strategy. One candidate could be a verbal spelling task, as verbal execution has been found to lower DMN activity [29].

The successful implementation of this novel cognitive strategy has a number of implications for further development of BCI systems for ALS patients. First, recordings were conducted with an 124-channel wet-electrode EEG system. Such conventional EEG systems are often only accessible in clinical environments. They are not very cost-efficient or portable. Also, nursing staff or family members of the ALS patient may not have the necessary expertise to setup such a conventional EEG system for online-communication. To create a communication method that is available to everyone, it would be beneficial to transfer the paradigm to a commercially available, less expensive, and portable EEG system. As the effects were very pronounced with this strategy, it could help to stabilise the effect in a way that it can still reliably be detected with such a low-density, low-cost system. Second, extensive training can be very exhausting for the patients, especially during later stages of the disease. Therefore, the training time needs to be reduced to make the system more applicable. Our strategy may achieve this by providing initial guidance for the use of the system. Last, the strategy is relatively easy to understand and to employ which may help to further simplify the task and make it more appealing. This would open opportunities for easily conductible studies. Most importantly, it could serve as a basis for an easy-to-use novel tool which allows simple, reliable communication with completely locked-in ALS patients.


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