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BRAIN ACTIVATION MAP DURING BCI COMMUNICATION IN COMPLETE LOCKED IN STATE

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ABSTRACT: Nonverbal and verbal communications are completely lost in patients with complete motor paralysis, leaving no other means of communication except brain-computer interfaces (BCIs). BCIs translate the thought to generate control signal, by which an individual can control a spelling device or external mechanical and electrical devices for communication. Recently we developed a functional near infrared spectroscopy (*f*NIRS) based auditory BCI, which was used by four patients in completely locked-in state (CLIS) to answer "yes" and "no" to known and open questions. Patients used fronto-central oxygenation concentration measured with *f*NIRS to answer "yes" and "no", while electro-encephalographic (EEG) signal was used to detect any vigilance drop during BCI sessions. Here, we evaluated frontal-central cortical activation by applying general linear model (GLM) to the *f*NIRS data and EEG signal time-frequency analysis to explore the metabolic and neuroelectric processes occurring during "yes" and "no" questions presented to CLIS patients.

INTRODUCTION

Amyotrophic lateral sclerosis may cause an individual to be in complete locked-in state (CLIS), a condition in which the patient is fully conscious and aware of their surroundings but is unable to perform any kind of movement leaving them completely paralyzed without any means of communication [1-2]. In such a scenario brain computer interface is the only remaining direct communication pathway between patient's brain and an external device [3-4].

It has been demonstrated that all of existing BCI techniques such as P300 endogenous event-related potential, slow cortical potentials (SCP) [5], extracting different features in frequency domains of the electro-encephalographic signal (EEG) [6] and subdurally implanted electrodes on the surface of the brain [6-7] do not reach a sufficient level of success for communication purposes [5]. Based on the unreliability of the aforementioned BCI, *f*NIRS based auditory BCI was used for binary communication in four Amyotrophic Lateral Sclerosis (ALS) patients in CLIS. Patients were able to successfully answer simple "yes" and "no" questions using the developed BCI [6].

Patients performed several sessions of BCI spread over weeks to learn to answer "yes" and "no" to personal and open questions, as described in Chaudhary et al. (2017) [6]. Here we present the *f*NIRS activation results and EEG time-frequency results from one of the patient.

MATERIALS AND METHODS

The Internal Review Board of the Medical Faculty of the University of Tübingen approved the experiment reported in this study and the patient's legal representative gave informed consent for the study with permission to publish the results and show the face of patients in the publication. The study was in full compliance with the ethical practice of Medical Faculty of the University of Tübingen. The clinical trial registration number is ClinicalTrials.gov Identifier: NCT02980380.

Patient

The study was performed on four patients, but here we present the results of one patient whose details are below.

Patient (Female, 76 years old, CLIS) was diagnosed with bulbar ALS in 2010. She lost speech and capability to walk by 2011. She stopped communicating with eyes in August 2014 which was confirmed by eye movement recordings. Before the brain computer interface was introduced an attempt was made to communicate with the subtle twitch of eye-lid, which proved to be unreliable. The husband and caretakers declared no communication with her since August 2014.

Instrumentation

A continuous wave (CW) based *f*NIRS system, NIRSPORT (NIRX) was used to acquire *f*NIRS data while multi-channel EEG amplifier (Brain Amp DC, Brain Products, Germany) was used to record EEG data simultaneously. EEG signal was recorded only to check the drop of vigilance based on changes of EEG signal power in the low frequency bands.

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The 8 sources and 8 detectors *f*NIRS optodes, and 8 EEG channels that were placed on the patient's scalp encompassing mainly primary somatosensory cortex, primary, pre-motor and supplementary motor cortex, Broca's area and dorsolateral prefrontal cortex is shown in Fig. 1.

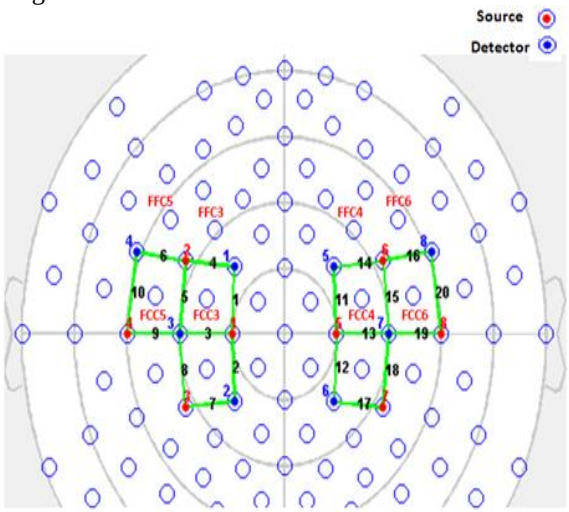

Figure 1: Source-detector layout in the fronto-central cortex with 10 source-detector pairs (channels) each on the left and right cortices and 8 EEG channels.

EEG channels locations were FFC5, FFC3, FFC4, FFC6, FCC5, FCC3, FCC4 and FCC6. Four electrodes were used to acquire the vertical and horizontal EOG, the result of EOG is presented in Chaudhary et al. (2017) [6].

Experiment Design

Patients were presented an auditory paradigm consisting of two kind of yes/no sentences: questions with known answers for training and feedback sessions (i.e. known question) and with unknown answers for the open question sessions (i.e. open question). Known questions were based on the life of patient and its answer is known by family members, caretakers and the experimenters (e.g. "Are you from Germany?"), while open questions can only be answered by the patient (e.g. "Do you have pain?").

In each training and feedback session patients listened to 10 true and 10 false known questions which are presented randomly. Patients were asked to think "ja, ja, …" (German for "yes") and "nein, nein, …" (German for "no") for 15 seconds, during the inter stimulus interval (ISI), until they heard the next sentence after an average interval of 5 seconds rest, as shown in Fig. 2. After the end of each training session, change in oxy-hemoglobin features corresponding to "yes" and "no" thinking was extracted and fed to the Support Vector Machine (SVM) classifier to differentiate between "yes" and "no" answers. After successful training (i.e. the classification accuracy of training sessions was greater than the threshold of 65%) [8] patients were presented with feedback session. During this session they were always provided with an auditory feedback of their answers at the end of the response time (i.e. "Your answer was recognized as yes" or "Your answer was recognized as no"). In this paper we performed the analysis using 16 training, 6 feedback sessions and 1 open question session performed by the patient over a period of several days.

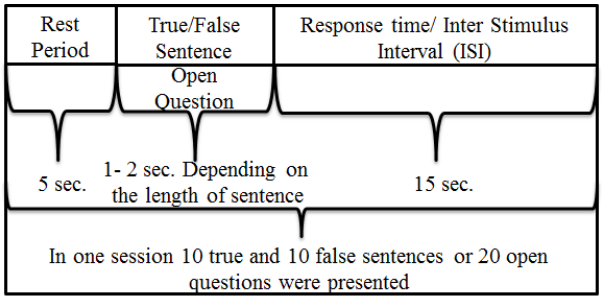

Figure 2: The auditory brain computer interface paradigm used for communication in CLIS patient.

Online fNIRS signal processing

The *f*NIRS data acquired online was normalized, filtered using a bandpass filter between 0.01-0.3 Hz and processed using the Modified Beer-Lambert law to calculate the relative change in concentration of oxy-(O_2Hb) and deoxy-hemoglobin (RHb).

The mean of relative change in O_2Hb across each channel was used as feature to train the SVM model through a 5-fold cross-validation procedure.

Since the classification accuracy as documented by (Chaudhary et al, 2017) [6] was higher for the mean of relative change in O_2Hb across each channel, the SVM model generated using O_2Hb was used to provide online feedback for known as well as open questions sessions.

EEG signal processing

Each EEG-channel was referenced to an electrode on the right mastoid and grounded to the electrode placed at Fz location of the scalp. Electrode impedances were kept below 10 kΩ and the EEG signal was sampled at 500 Hz. The signals were band pass filtered using a finite impulse response filter with a bandpass of 0.5–30 Hz and the filter order 8250 of EEGLAB [9]. As in complete locked state patients there is no eye movement [6], there is no EOG artifact contamination in EEG signal.

Offline and general linear model (GLM) analysis of fNIRS signal

Signal processing of *f*NIRS signals and the GLM analysis was done with nirsLAB (v2014.05). The *f*NIRS signal was bandpass filtered between 0.01-0.3 Hz. The Modified Beer–Lambert law was used to quantify the changes in the concentrations of O_2Hb and RHb from the absorption of near-infrared light. A statistical parametric mapping method (SPM)[10-11]was employed to extract dynamic features from hemodynamic responses and map this information to head-space models. The regressors are four conditions, "yes" question presentation, "no" question presentation,

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"yes" question ISI, and "no" question ISI, while the dependent variable was oxy hemoglobin (O2Hb). A canonical HRF with a time-series of stimulus onsets was convolved [11].

Offline Time-Frequency analysis of EEG signal

Offline Time-Frequency analysis of EEG signal was done using Short-Term Fourier Transform to identify low frequencies power spectra alteration during response time (ISI interval). This analysis served to exclude the slow-wave sleep state during BCI sessions.

RESULTS

In order to investigate the activated areas of brain, GLM coefficients were interpolated to elucidate activation in the fronto-central brain region of the patient during "yes" vs. "no" thinking as shown in Fig. 3. Fig. 3 shows the activation map for the change in the concentration of O_2Hb for "yes" vs. "no" responses ($p<0.05$) across the 23 sessions performed by the patient. Fig. 3 explicates significant differences between "yes" and "no" response in the left fronto-central brain region of the patient.

The GLM coefficients for "yes" and "no" response over all the sessions performed by the patient are shown in Fig. 4, which shows the *f*NIRS channels with greatest contrast between "yes" and "no" response.

Fig. 5 and Fig. 6 illustrate the time frequency decomposition of EEG signal for all EEG channels during "yes" and "no" response, respectively. Fig. 5 and Fig. 6 elucidate that the dominant frequencies during "yes" and "no" thinking are the ones in the high theta and low alpha bands.

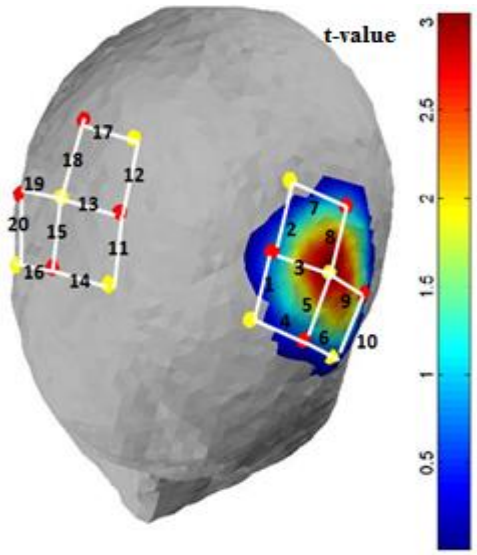

Figure 3: Activation map of change in oxy-hemoglobin across 23 sessions performed by the patient. (Contrast, "no" response > "yes" response, $p<0.05$, O_2Hb)

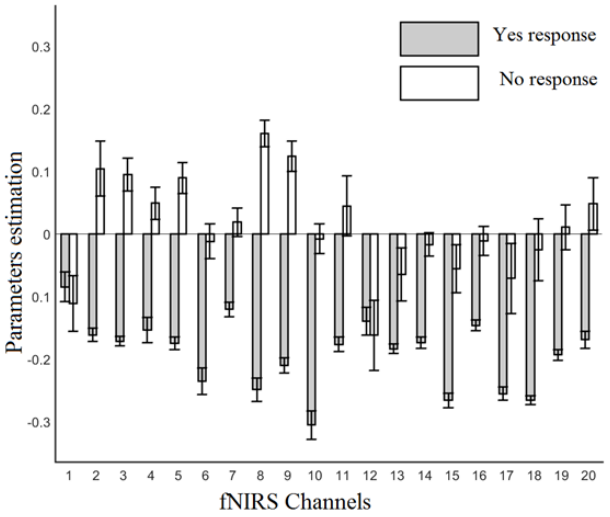

Figure 4: GLM coefficients for "yes" and "no" responses over all the sessions performed by the patient. In the Fig. y-axis is the GLM coefficient after normalization and x-axis is the *f*NIRS channels. Grey block represents the "yes" response and white block represents the "no" response.

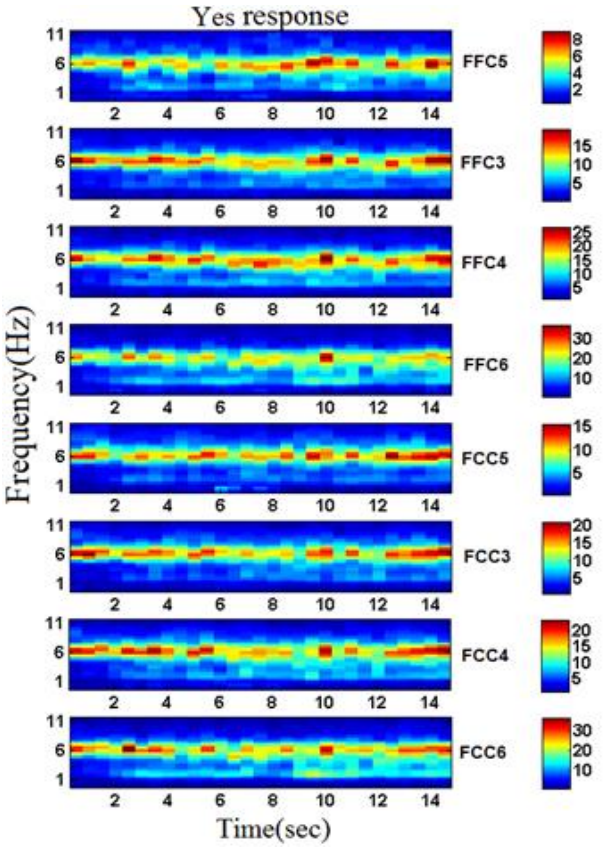

Figure 5: Time-Frequency decomposition for "yes" responses

DISCUSSION AND CONCLUSION

In patients completely motionless over years with restricted vision because of eye-muscle paralysis and drying of the cornea and likely reduced afferent input from the sensorimotor system reduced vigilance

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measured with EEG and a fragmented sleep-wake cycle was documented by Ramos et al. (2011) [7]and Soekadar et al. (2013) [12]. De Massari et al. (2013) [13] have shown that reduction of P300 amplitude across the BCI paradigm presentation predicted negative performance, again suggesting excessive loss and excessive variation of wakefulness and attention as a major limiting factor for BCI applications in such severely compromised patients. As it can be seen from time-frequency analysis the patient had a reduced EEG frequency band (around 6-7 Hz) compared to healthy population and almost no activity in the low frequency bands. These findings suggest that the patient was not in the sleep state, i.e., the patient was awake, mentally thinking yes or no.

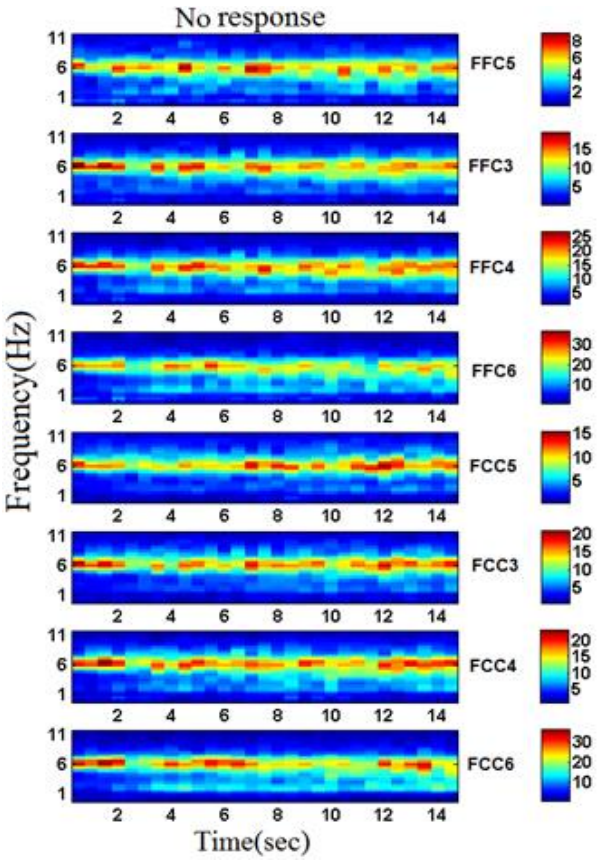

Figure 6: Time-Frequency decomposition for "no" responses

On the other hand, *f*NIRS signal showed significant difference ("no" response > "yes" response, $p<0.05$) between "yes" and "no" thinking in left hemispheres, see Fig. 3. The activation was more pronounced in the left hemisphere when compared with the right hemisphere, also shown in Fig. 4 the difference between "yes" and "no" response in the *f*NIRS channels placed on the left hemisphere of fronto-central brain region.

This suggests that in CLIS condition processing of "yes" and "no" response involves different neural substrates, in a similar manner as reported in healthy population [14]. Our result also suggests that, although the patient entered the complete locked in state from 2014, the high level cognitive functions (such as language comprehension, semantic processing and stimuli discrimination) are preserved.

Here we have presented the results from one out of four patients enrolled for this study; currently we are working on the detailed data analysis of the remaining three patients.

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