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High-Frequency Spectral Changes in Dorsolateral Prefrontal Cortex for Potential Neuoroprosthetics

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Abstract— **Dorsolateral Prefrontal Cortex (DLPFC) has been associated with goal encoding in primates. Thus far, the majority of research involving DLPFC, including all electrophysiology studies, has been performed in non-human primates. In this paper, we explore the possibility of utilizing the cortical activity in DLPFC in humans for use in Brain-Computer Interfaces (BCIs). Electrocorticographic signals were recorded from seven patients with intractable epilepsy who had electrode coverage over DLPFC. These subjects performed a visuomotor target-based task to assess DLPFC's involvement in planning, execution, and accomplishment of the simple motor task. These findings demonstrate that there is a distinct high-frequency spectral component in DLPFC associated with accomplishment of the task. It is envisioned that these signals could potentially provide a novel verification of task accomplishment for a BCI.**

I. Introduction

A Brain-Computer Interface (BCI) is a device that can decode human intent from the direct measurement of brain activity for purposes of communication and control [1]. This brain-derived control is dependent on the emerging understanding of cortical physiology as it pertains to cognitive encoding. Recently, the use of electrocorticography (ECoG) for BCI has gained attention as a promising platform for clinical applications [2]. Compared with electroencephalography (EEG), ECoG has been shown to have superior signal-to-noise ratio, immunity to artifacts, and spatial and spectral characteristics. [3]–[6]. High-frequency gamma activity in ECoG has been associated with numerous aspects of language and motor function in humans [2], [7]–[10]. Beyond the information content, these constructs should have a greater likelihood for long-term clinical recordings than single-unit neuron recordings or EEG [11], [12].

Currently, most ECoG-BCI research has utilized signals from primary motor cortex [2], [13]. Although a logical starting point, it has certain limitations because this area is very localized and tends to degrade in the individuals who would use BCI clinically (e.g., in Amyotrophic Lateral Sclerosis). Therefore, other potential neurophysiological substrates have been explored such as sensory cortex, ipsilateral motor intentions, and working memory [14]–[16]. Other studies have examined the attentional activity in prefrontal cortex involved with encoding of target information [17], [18]. In the context of a BCI, this physiology may provide a useful substrate for detecting when a goal has been achieved during active control [19].

Studies of DLPFC began when deficits were observed in lesioned primates and humans [20]–[23]. In primate models, individual neurons have shown increased firing rates during presentation and delay for a match-to-sample task in primate prefrontal cortex [24], [25]. Subsequent studies have also shown correlation to both directional and direction-agnostic response in these tasks [18], [26]–[28]. Similar task-dependent signals have been explored in human DLPFC primarily with fMRI [29], [30].

Canolty et al. have shown DLPFC to be active for lexical targets [31]. Early findings by Ramsey et al. have shown that DLPFC signals associated with working memory can be used as control features for BCI [15], [32]. In this study we examine cortical activity from seven subjects in DLPFC during a joystick-controlled center-out task. We demonstrate for the first time that changes within the power spectral density of a specific frequency band were distinguishable between the various stages of planning, execution, and task accomplishment. These spectral differences, most notably the very high frequency changes during task accomplishment, could provide additional control features to augment future neuroprosthetic devices.

II. Methods

A. Subjects and Paradigm

ECoG arrays were implanted over DLPFC in 7 subjects (ages 9-48 years of age, 2 male/5 female, 6 right handed/1 left handed) with intractable epilepsy for the clinical localization of seizure foci. The Talairach daemon program (talairach.org) and intra-operative clinical knowledge of the positions of certain electrode grids were used to approximate Brodmann areas. Electrodes in Brodmann areas 9 (25 electrodes) and 46 (21 electrodes) were classified within DLPFC. Figure 2 shows the superposition of all electrodes from the 7 subjects that were in DLPFC. The hand contralateral to the DLPFC electrodes was used to perform the task. Recording sessions were performed 2-6 days after implantation. All subjects were consented to perform study under IRB

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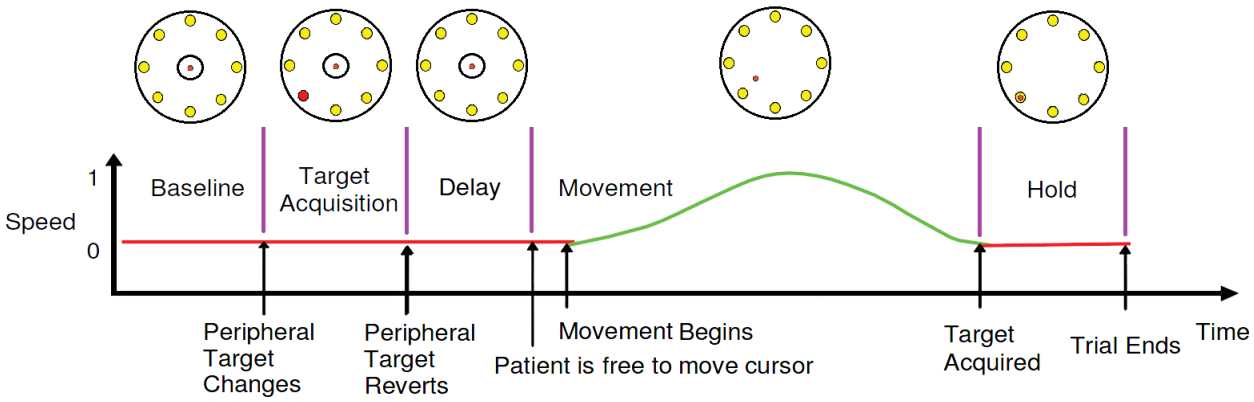

Fig. 1. The five periods of center-out task. The circular figures above each period indicate an example of what the subject observes on the monitor during the corresponding period.

approved by Washington University, accordingly at no time was clinical care compromised by this study.

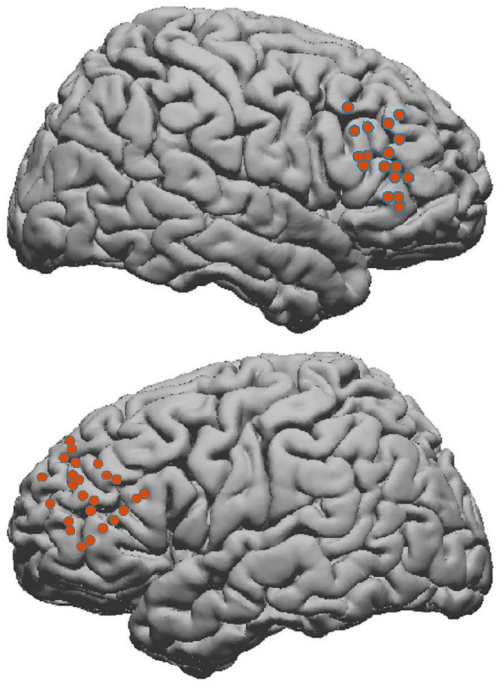

Fig. 2. The superposition of the DLPFC electrodes for the 7 subjects. Electrodes in Brodmann areas 9 and 46 were considered in DLPFC.

ECoG signals were recorded as the subjects performed a modified center-out task. The task had 8 targets placed radially and equidistant (45 degrees apart) around a center starting point to be of maximum diameter on the 15-inch LCD display as illustrated in Figure 1. There were 5 designated periods to the task; baseline (300 ms), encoding (500 ms), delay (300, 400, or 500 ms), movement (500 ms - 1500ms), and holding (300 ms). A baseline was collected prior to the subject encoding for the target. The desired target was then highlighted in red. A delay period followed the target encoding period, where the subject held the target in memory. Delay periods were added to the task in order to be able extract target encoding features without potentially confounding movements, as done in the delay match-to-sample task from the traditional monkey paradigms [33]. At the end of the delay period a ring surrounding the cursor disappeared, prompting the subject to move the cursor to the appropriate target using the joystick (i.e. movement period). Once the subject reached the target they held the cursor on the target until the end of the trial. The sequence was repeated and with the desired targets presented in a randomized order. All subjects were presented each of 8 targets 5 times over 2 runs for a total of 80 movements for each subject. Any error trials were not repeated and removed from further analysis.

B. Data Analysis

Data were collected using g.USB amplifiers (g-tec Medical Engineering) at a sampling rate of 1200 Hz. The 60-Hz line interference and harmonics were filtered using notch filters. The power spectrum was computed over 100 ms windows using an autoregressive model based on the maximum entropy method with an model order of 30 [34]. The spectrum for each channel was divided into 5-Hz frequency bins, which were normalized by subtracting the mean of the entire trial. Differences in mean power between the baseline state, delay, and hold periods were compared using a Student's t-test to identify significant changes between these periods. The spectral variation for each DLPFC electrode, frequency bin, and trial was computed by subtracting the mean of the trial over all tasks periods from each task period and computing the resulting standard deviation.

III. Results

Cortical changes were observed in DLPFC that were distinct in frequency band and period of the task. Figure 3 illustrates the broad-band high-frequency changes observed at one electrode site in primary motor cortex and one electrode site in DLPFC. Consistent with previous studies, the motor site showed a maximal relative change between 100-150 Hz, which occurred solely during the movement period

[10], [35]. However, for DLPFC site, a higher frequency range 150-250 Hz was found predominantly during the Hold period. When cortical changes are aggregated across all seven subjects, higher frequency changes are again present. The most substantial changes occur during the Hold period. Figure 4A shows, for each frequency bin, the the number of electrodes that have a significant difference between Baseline and Hold periods based on the t-test. Figure 4B shows the spectral variation averaged over all DLPFC electrodes and all subjects for each task period. Distinct spectral characteristics are observed in each of the task periods. A substantial change in spectral variation above 150 Hz is observed during the Hold task, peaking near 250 Hz. This peak is attenuated during the Movement period and suppressed during the Delay period.

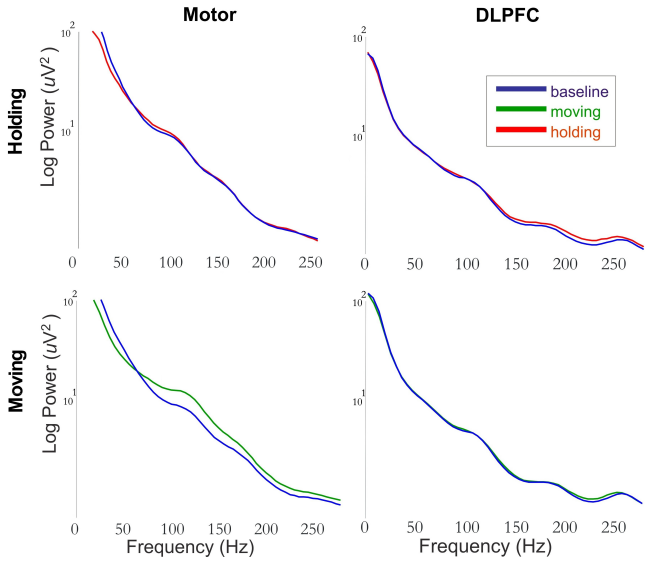

Fig. 3. Average log-power spectra across all trials for a selected primary motor electrode site and a DLPFC electrode site for Holding vs. Baseline and Moving vs. Baseline for a representative subject. The differences are most prominent below 120 Hz for the motor electrode and above 160 Hz for the DLPFC electrode. During movement, the motor electrode shows much broader tuning including in the high frequency-band. There is negligible difference in activation between Baseline and Movement for the DLPFC electrode.

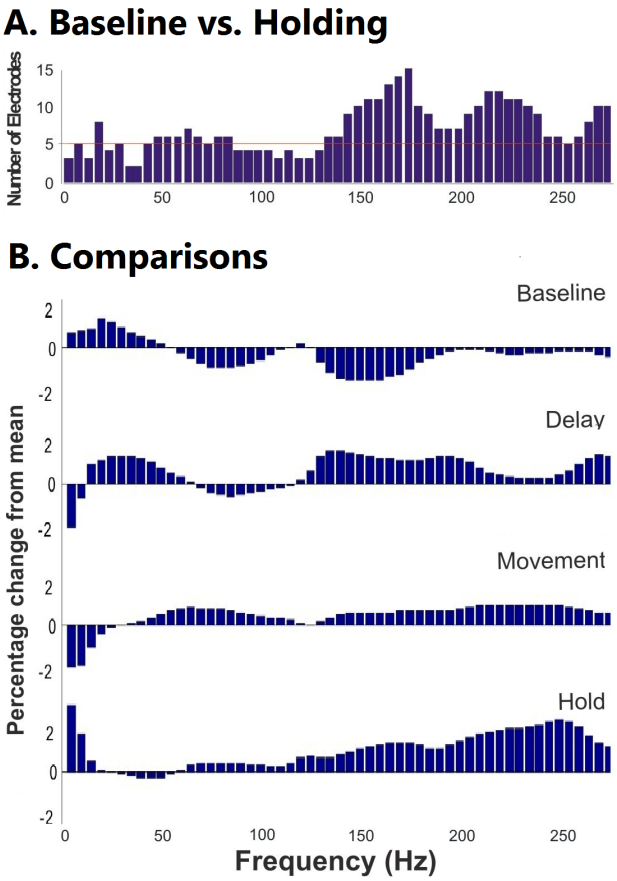

Fig. 4. (A) The number of electrodes showing statistically-significant changes based on at t-test in a given frequency band between the Baseline and Hold periods. The red line represents the number of electrodes that would be statistically significant by chance, such that electrodes numbers greater than the red line are statistically significant ($p<0.05$). (B) Percent deviation from the mean for all electrodes across all subjects. The mean spectra was taken for each electrode on each trial then the percent deviation was computed. It is clear that each task period exhibits distinct spectral activity.

IV. Discussion

This is the first study to examine human cortical physiology in DLPFC and its association with various stages of task execution and accomplishment. The study demonstrates a unique cortical physiology that has distinct spectral characteristics associated with task achievement. The high-frequency spectral change in DLPFC is statistically significant and shows similar changes across all subjects.

These findings are consistent with previous findings showing that DLPFC is associated with goal orientation and achievement [27], [36]. Our study differs in that the recordings used larger ECoG electrodes rather than microelectrodes. In spite of possible increased neural population noise due to larger electrodes, we find that cortical activations have distinct spectral characteristics depending on the phase of the task. Additionally, the signals in DLPFC seem to be in a higher frequency bands than the signals identified previously with ECoG in motor cortex. This spectral difference in more anterior frontal regions may be due to a different columnar organization than described classically with the more somatopically organized motor cortex and, as a result, may have different neural ensemble dynamics that are better represented in the higher-frequency scales.

These DLPFC attention-related signals may provide an important non-motor signal that can augment current applications in BCI. Specifically, distinct from motor signals which encode execution of a task, DLPFC may provide a signal that encodes the accomplishment of a task. These signals could be useful to indicate if user has navigated over a desired target, and thus facilitate its selection. Additionally, for other cognitive operations in the frontal lobe

(e.g. working memory), it may be worthwhile to examine higher frequency changes beyond those traditional high-gamma rhythms typically associated with motor intentions.

This study is a preliminary ECoG evaluation of DLPFC using a target- based delay match-to-sample task. Additional studies need to be conducted to further substantiate this phenomenon. furthermore, this signal will need to be used in a closed-loop BCI task to assess its potential utility for actual neuroprosthetic application. In summary, this study demonstrates that DLPFC in humans exhibits distinct spectral changes during different intervals of a center-out task that could provide useful information for enhancing future neuroprosthetic device control.

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