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Spectral Components of the P300 Speller Response In and Adjacent to the Hippocampus

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***Abstract*—Recent studies have demonstrated that the P300 Speller can be used to reliably control a brain-computer interface via stereotactic depth electrodes (SDEs) implanted in and adjacent to the hippocampus. The superior bandwidth and spatial resolution of intracranial signals compared to scalp electroencephalography (EEG) may provide better insight into the nature of the responses evoked by the P300 Speller. Furthermore, the signals acquired by SDEs provide a new glimpse at activity from deeper brain structures, with respect to well-established scalp-EEG characterization of the P300 Speller responses. This study examines the spatio-temporal progression of the P300 Speller response from SDEs in and adjacent to the hippocampus for six conventional frequency bands.**

Keywords-P300 Speller, hippocampus, electroencephalography

I. Introduction

A Brain-Computer Interface (BCI) is a device that uses brain signals to provide a non-muscular communication channel [33], particularly for individuals with severe neuromuscular disabilities. One of the most investigated paradigms for controlling a BCI is the P300 Speller [10]. Based on multiple scalp-recorded electroencephalogram (EEG) studies in healthy volunteers [13][15][19][27], and initial results in persons with physical disabilities [25][30][32], the P300 Speller has the potential to serve as an effective communication device for persons who have lost or are losing the ability to write and speak.

More recently, studies have shown that both intracranial electrocorticography (ECoG) and stereotactic depth electrodes (SDEs) can be used to reliably control the P300 Speller, with performance comparable to scalp EEG [6][16][17]. Intracranial signals have been shown to have superior signal-to-noise ratio, immunity to artifacts such as EMG, and spatial and spectral characteristics compared to EEG [5][11][28]. It is believed that a thorough characterization of the P300 Speller response properties from intracranial electrodes will also lead to improved scalp-EEG P300 performance.

Because the traditional control signal for the P300 Speller is an event-related potential (ERP), the majority of prior analyses have focused on low frequency features in the time domain. Bernat *et al.* (2007) [4] performed a time-frequency decomposition of P300 activity from scalp EEG and showed predictable time courses in the delta, theta, and alpha bands. The superior bandwidth and fidelity of intracranial recordings warrants a similar characterization of intracranial signals, particularly the new perspective provided by SDEs in and adjacent to the hippocampus.

This paper provides a preliminary spatio-temporal analysis of the P300 Speller responses recorded from electrodes in and adjacent to the hippocampus using the conventional delta, theta, alpha, beta, low-gamma, and high-gamma bands. In addition, theta-gamma coupling is examined. This work serves as a companion paper to our analogous study using ECoG signals [18].

II. Methodology

A. Subjects

Three subjects with medically intractable epilepsy who underwent Phase 2 evaluation for epilepsy surgery with temporary placement of SDEs to localize seizure foci prior to surgical resection were tested for the ability to control a visual keyboard using SDE signals. All three subjects were presented at Mayo Clinic Florida's multidisciplinary Surgical Epilepsy Conference where the consensus clinical recommendation was for the subject to undergo invasive monitoring primarily to localize the epileptogenic zone. The study was approved by the Institutional Review Boards of Mayo Clinic, University of North Florida, and Old Dominion University. All subjects gave their informed consent.

B. Electrode Locations and Clinical Recordings

Electrode (AD-Tech Medical Instrument Corporation, WI, USA) placements and duration of ECoG monitoring were based solely on the requirements of the clinical evaluation, without any consideration of this study. All electrode placements were guided intra-operatively by Stealth MRI neuronavigational system (Medtronics, Inc., MN, USA). Each subject had post-operative anterior–posterior and lateral radiographs to verify electrode locations. The interelectrode spacing along the arrays was 10 mm for Subject A and 5 mm for Subjects B and C. Approximate electrode locations are illustrated in Figure 1. By capturing seizures with an electrographic pattern typical for hippocampal onset seizures, the three most anterior right temporal contacts for Subject A and the five most anterior left temporal contacts for Subjects B and C were confirmed to be in or adjacent to hippocampal tissue. Aside from the most posterior electrodes for Subject A, it is highly probable that all electrodes were in or adjacent to hippocampal tissue. After electrode implantation, all subjects were admitted to an ICU room with epilepsy monitoring capability. Clinical data were gathered with a 64-channel clinical video-EEG acquisition system (Natus Medical, Inc., CA, USA).

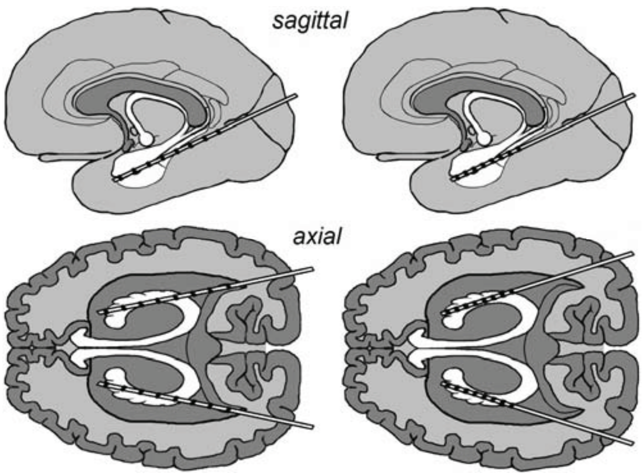

Fig 1. Approximate sagittal and axial electrode locations. Left column: Subject A, Right column: Subjects B & C.

C. BCI Data Acquisition

All subjects performed BCI testing between 24-48 hours after electrode implantation. Testing was performed only when the subject was clinically judged to be at cognitive baseline and free of physical discomfort that would affect attention and concentration. Testing was performed at least six hours after a clinical seizure. Stimuli were presented and the ECoG data were recorded using the general-purpose BCI system BCI2000 [29]. All electrodes were referenced to a scalp vertex electrode, amplified, band pass filtered (0.5–500 Hz), digitized at 1200 Hz using 16-channel g.USB amplifiers (Guger Technologies, Graz, Austria), and stored. A laptop with a 2.66 GHz Intel Core 2 Duo CPU, 3.5 GB of RAM, and Windows XP was used to execute BCI2000. The signals for the BCI experiments were acquired concurrent with the clinical monitoring via a 32-channel electrode splitter box (AD-Tech Medical Instrument Corporation, WI, USA).

D. Task, Procedure, and Design

The experimental protocol was based on the protocol used in an EEG-based P300 Speller study [15]. Each subject sat in a hospital bed about 75 cm from a video monitor and viewed the matrix display. The task was to focus attention on a specified letter of the matrix and silently count the number of times the target character flashed, until a new character was specified for selection. All data was collected in the copy speller mode: words were presented on the top left of the video monitor and the character currently specified for selection was listed in parentheses at the end of the letter string as shown in Figure 2. Each session consisted of 8-11 experimental runs of the P300 Speller paradigm; each run was composed of a word or series of characters chosen by the investigator. This set of characters spanned the set of characters contained in the matrix and was consistent for each subject and session. Each session consisted of between 32-39 character epochs. A single session lasted approximately one hour. One to three sessions were collected for each subject, depending on the subject's physical state and willingness to continue.

Fig. 2: The 6x6 matrix used in the current study. A row or column intensifies for 100 ms every 175 ms. The letter in parentheses at the top of the window is the current target letter "D." A P300 should be elicited when the fourth column or first row is intensified. After the intensification sequence for a character epoch, the result is classified and online feedback is provided directly below the character to be copied.

E. Data Analysis

The first uncorrupted session from each subject was used for the analysis. The band-power was determined for six frequency bands: delta (0-3 Hz), theta (4-7 Hz), alpha (8-12 Hz), beta (13-30 Hz), low-gamma (31-70 Hz), and high-gamma (71-200 Hz). The band-power was computed by forward and reverse filtering each channel with a precise FIR filter to produce zero-phase distortion. The resulting channel values were then squared and smoothed using the same zero-phase approach to extract the band-power envelope.

For each channel, 800 ms segments of data following each flash were extracted for the analysis. Each segment was divided into non-overlapping 100 ms partitions and the average band-power for each of the six frequency bands was computed for each partition. The average band-power was then correlated with the binary target labels (i.e., target or non-target flash) and the resultant p-values were computed, where the p-value corresponds to the hypothesis that the correlation between the band-power and the task is zero. All activity having a significance level of $p = 0.05$ or better was labeled as statistically significant and all other activity was labeled as not statistically significant. The results were compared across subjects to reveal the common spatio-temporal activations. To examine theta-gamma relationship as indicated in several recent studies [1][7][22], the identical procedure was performed by correlating the theta band-power with the low and high gamma band-powers, respectively.

III. RESULTS

Figure 3 illustrates the statistically significant activations for the six frequency bands over the 100 ms increments (centered on the values provided on the x-axis). Each individual 15 X 2 vertical grid represents the relative electrode position from anterior (top) to posterior (bottom) in spacing increments of 5 mm. The left and right hemispheres are represented by the left and right columns, respectively. Note that not all positions are common across subjects based on the different electrode spacing for Subject A. The statistically significant activations are color-coded by subject and pairs of subjects. There were no activations common among all three subjects, although there are several adjacent activations that may be considered common based on the relative imprecision of the electrode position estimates.

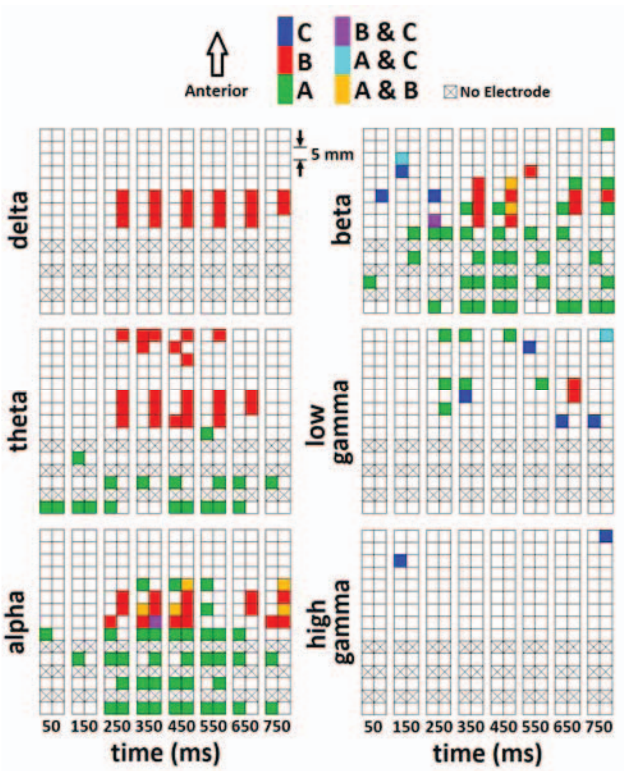

Fig. 3: The statistically significant activations for the six frequency bands over the 100 ms increments (centered on the values provided on the x-axis). Each individual 15 X 2 vertical grid represents the relative electrode position from anterior (top) to posterior (bottom) in spacing increments of 5 mm. The left and right hemispheres are represented by the left and right columns, respectively. The statistically significant activations are color-coded by subject and pairs of subjects.

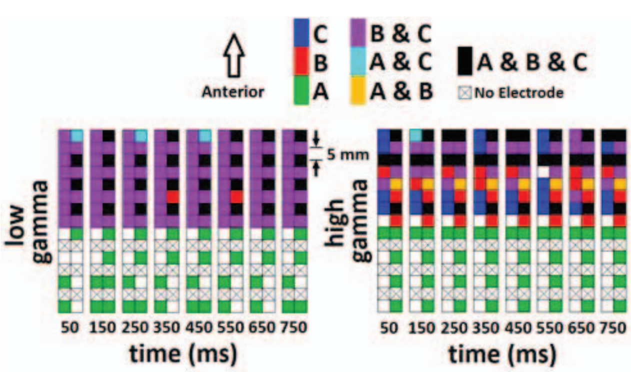

Fig. 4: The statistically significant correlations between the theta and low/high gamma band-powers. The format is identical to that described in Figure 3.

Figure 4 illustrates the statistically significant correlations between the theta and low/high gamma band-powers. In this case there are correlations that are common among all three subjects.

IV. Discussion

This work represents a first attempt to analyze and interpret the P300 Speller response from SDEs in terms of the conventional neural frequency bands. Although it is difficult to directly compare neocortical and hippocampal activations in terms of location, the temporal and spectral characteristics illustrated in Figure 3 are generally in correspondence with our prior ECoG study [18], showing much of the significant activity in the theta, alpha, and beta bands after 250 ms. The P300 Speller is a variation of the classical oddball paradigm [9], which requires both an attentional and memory component. Delta and theta frequency activities have been related to oddball target responses [1][3], and alpha reductions have been associated with increased cognitive processing during the oddball task [34]. One possible interpretation is that the strong oscillatory theta and alpha activity is associated with working memory [12][31]. Additionally, the amplitude of gamma activity correlates with memory load in hippocampus [34]. Sustained oscillatory activity in the beta band frequency was seen in n-back memory tasks with the highest memory load [7].

Recent studies of ECoG [7][22] and hippocampal [1] activity indicates phase–amplitude coupling between theta and gamma oscillations during memory encoding and maintenance. This is a possible explanation for the prevalent correlation between theta and gamma activity illustrated in Figure 4.

Two studies in the 1980s using SDE in epilepsy surgery patients suggested that the medial temporal lobe contributes to the generation of the P300 [14][22]. However, other workers found that patients with bilateral hippocampal lesions did not exhibit P300 abnormalities relative to controls [26] and that the hippocampus does not directly contribute to the P300 waveform [24]. Our current and previous work [17] supports the earlier findings by demonstrating that brain signals from electrodes in or near medial temporal lobe can be used to control a visual P300 speller. Because different electrode contact points within the same SDE array detect different brain signals after a visual target stimulus, the signals likely represent near-field potentials in the temporal lobe rather than a high amplitude far-field potential.

Subject A was left hemisphere dominant for both language and memory. Subject B was dominant for language in the right hemisphere, and had bilateral memory functioning albeit with greater representation in the right hippocampus. Subject C was dominant for language on the left and had bilateral memory albeit with better functioning on the left. For all three subjects, statistically significant activations in the various frequency bands occurred more often on the side of language dominance and greater memory representation. Although our sample size is small and the findings preliminary, the results suggest that the temporal lobe supporting working memory and/or language is important in P300 generation. More subjects are needed to confirm this observation. Equally important will be the results obtained in subjects with language and memory residing in opposite hemispheres. Those results will indicate whether language cortex or neural substrates underlying memory are more important to P300 generation.

Acknowledgment

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