A System for Single-trial Analysis of Simultaneously Acquired EEG and fMRI

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***Abstract*— In this paper we describe a system for simultaneously acquiring EEG and fMRI and evaluate it in terms of discriminating, single-trial, task-related neural components in the EEG. Using an auditory oddball stimulus paradigm, we acquire EEG data both inside and outside a 1.5T MR scanner and compare both power spectra and single-trial discrimination performance for both conditions. We find that EEG activity acquired inside the MR scanner during echo planer image acquisition is of high enough quality to enable single-trial discrimination performance that is 95% of that acquired outside the scanner. We conclude that EEG acquired simultaneously with fMRI is of high enough fidelity to permit single-trial analysis.**

I. Introduction

Simultaneously acquired EEG and fMRI has the potential to yield high resolution spatio-temporal information about brain function. However, because of the low signal-to-noise and signal-to-inference ratios of these imaging modalities, most EEG and fMRI analysis methods estimate relevant activity through trial or event-locked averaging. However, averaging places a limit on the utility of EEG/fMRI, as it does not permit assessment of inter-trial variability critical for understanding the relationship between neural processing and variation in behavioral responses. Single-trial variability may arise as a result of changes in attention, adaptation, or habituation, as well as changes in the recording environment.

Our group has developed single-trial EEG analysis based on linear discrimination [1], [2] which enables one to relate response variability across trial/stimulus presentation to the underlying electrophysiological variability [3], [4], [5]. In this paper we present results which assess whether EEG acquired simultaneously with fMRI is of high enough quality to allow use of such single-trial techniques.

II. Materials and Methods

A. Subjects & Behavioral Paradigm

We collected simultaneous EEG/fMRI from 10 subjects. Informed consent was obtained from all participants in accordance with the guidelines and approval of the Columbia University Institutional Review Board.

An auditory oddball paradigm was used, with tones of frequency 350 Hz for standards and 500 Hz for oddballs, with stimulus intensity set to 85 dB. Auditory stimuli were presented through MR compatible headphones that do not contain any electronics that might add artifact to EEG. Tones were presented for XXX ms with an inter-stimulus-interval (ISI) chosen from a uniform distribution between 2 and 4 secs in increments of 200ms. The probability of a standard tone was 0.8, with the probability of an oddball tone being 0.2. Subjects were instructed to close their eyes during all experiments and the lights in the scanner room were off. Subjects were also instructed to press a button with the index finger of their right hand when they heard an oddball tone. There were a total of 50 oddball and 200 standard trials. Whole brain fMRI data were collected on a 1.5T scanner (Philips Medical System, Bothell, WA). Echoplanar data were acquired using 15 slices of 64 x 64 voxels with in-plane resolution of 3.125 mm, slice thickness of 8 mm and field of view (FOV) of 200 mm. Repetition time (TR) was set to 3000 ms with an echo time (TE) of 50 ms. Structural scans were performed using a T1-weighted spoiled gradient recalled (SPGR) sequence (XX slices; 256 x 256; FOV = 200 mm).

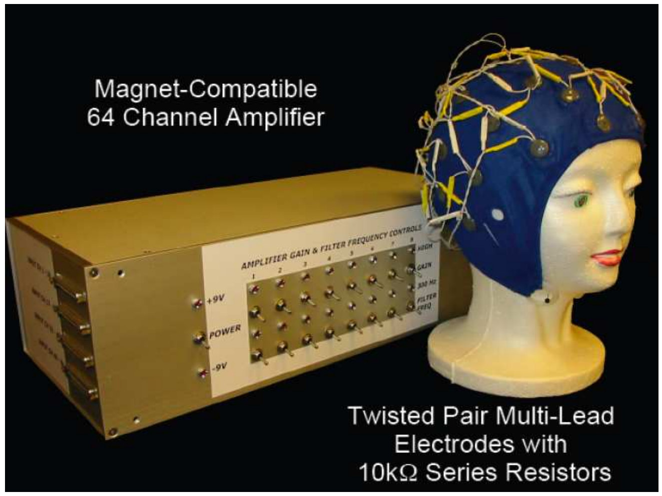

Fig. 1. Custom built MR compatible EEG system. The system includes a 64 channel high input impedance amplifier and a cap consisting of an array of bipolar, twisted pair Ag/AgCl electrodes.

B. Simultaneous EEG and fMRI acquisition

We used a custom-built 64 channel magnet-compatible differential amplifier with a bipolar electrode EEG cap [6]. The EEG cap includes in-line 10 kΩ surface mount resistors and copper leads. Leads for bipolar electrode pairs were twisted for their entire 10 ft. length. The cap consists of a 43 Ag/AgCl scalp electrode montage including left and right mastoids. All input impedances were $< 20k\Omega$. The MR compatible amplifier included matched radio-frequency

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(RF) filters, a 4^{th} order Butterworth low-pass filter (125 Hz), with 10k gain for the EEG channels and 2k gain for the electocardiogram (ECG) channels. All channels were sampled at 1kHz. Analog-to-digital conversion of the EEG was synchronized to the MR scanner clock to enable removal of gradient artifacts. EEG sampling was synchronized to the MR imager clock by sending a transistor-transisitor logic (TTL) pulse each repetition time (TR) to a field programmable array (FPGA) card (National Instruments, Austin, TX), programmed to emit a pulse train that resets each TR.

C. EEG pre-processing

A software-based 0.5 Hz high-pass filter was used to remove DC drift. Gradient artifacts were then removed by aligning data to the start of each TR and subtracting the mean across TRs. A ten-point (10 ms) median filter was then applied to eliminate the minimal remaining RF and muscle artifacts. Software based 60 Hz and 120 Hz (harmonic) notch filters are applied to remove line noise artifacts. All filters were designed to be linear-phase to prevent delay distortions.

Ballistocardiogram (BCG) artifacts were then estimated by using principal component analysis (PCA) to find the first two principal components across bipolar EEG channels that have been low-pass filtered at 4 Hz. The sensor weights derived from PCA were applied to the original EEG (not filtered at 4 Hz), and this BCG estimate was projected into each electrode and subtracted from the data. Motor response and stimulus events recorded on separate channels are delayed to match latencies introduced by digital filtering of the EEG.

Figure 2 A & B shows an example EEG data before and after preprocessing. Figure 2 C & D shows the power spectrum for a subject with data collected inside (IS) vs. outside (OS) the MR scanner before and after artifact removal. Note the gradient artifacts are removed (peaks at 5Hz and harmonics) and there is significant attenuation of the ballistocardiogram (at approx. 1.5 Hz and harmonics).

D. EEG analysis

We used single-trial analysis of the EEG to discriminate between the two experimental conditions: presentation of a standard tone versus presentation of an oddball tone. Logistic regression was used to find an optimal projection for discriminating between the two conditions over a specific temporal window [1], [2]. Specifically, we defined a training window starting at a post-stimulus onset time τ, with a duration of δ, and used logistic regression to estimate a spatial weighting vector $\mathbf{w}_{\tau\delta}$ which maximally discriminates between sensor array signals $\mathbf{X}$ for the two conditions:

$$\mathbf{y} = \mathbf{w}_{\tau,\delta}^T \mathbf{X} \tag{1}$$

where $\mathbf{X}$ is an N x T matrix (N sensors and T time samples). The result is a “discriminating component” $\mathbf{y}$ which is specific to activity correlated with one condition while minimizing activity correlated with both task conditions. We use the term “component” instead of “source” to make it clear that this is a projection of all the activity correlated with the underlying source. For our experiments, the duration of the training window (δ) was 50 ms and the window onset time (τ) was varied across time from 250 - 500 ms. We used the re-weighted least squares algorithm to learn the optimal discriminating spatial weighting vector $\mathbf{w}_{\tau,\delta}$ [7].

The discrimination vector $\mathbf{w}_{\tau,\delta}$ can be seen as the orientation (or direction) in the space of the EEG sensors that maximally discriminates between standard versus oddball tone trials. The time dimension defines the time of a window (relative to the either the stimulus or response) used to compute this discrimination vector. Given a fixed window width (50 ms in this case), sweeping the training window from the onset of auditory tone to the earliest response time represents the evolution of the discrimination vector across time. Within a window, at a fixed time, all samples are treated as independent and identically distributed to train the discriminator. Once the discriminator is trained, it is applied across all time so as to visualize the projection of the trials onto that specific orientation in EEG sensor space. A “discriminating component” is defined as one such discrimination vector, with its activity visualized by projecting the data across all time onto that orientation. We call this visualization a discriminant component map. For instance, for recurring components, one would expect activity trained during one window time to also be present at another time. We find that discrimination performance is better in bipolar space than re–referenced space. Therefore, discrimination is performed with bipolar data and scalp projections are re–referenced to visualize results.

We quantified the performance of the linear discriminator by the area under ROC, referred to as A_z, with a leave-one-out approach [8]. We used the ROC A_z metric to characterize the discrimination performance while sliding our training window from stimulus onset to response time (varying τ). Finally in order to assess the significance of the resultant discriminating component we used a bootstrapping technique to compute an A_z value leading to a significance level of $p = 0.01$. Specifically we computed a significance level for A_z by performing the leave-one-out test after randomizing the truth labels of our oddball and standard trials. We repeated this randomization process 100 times to produce an A_z randomization distribution and compute the A_z leading to a significance level of $p = 0.01$.

III. Results

In the auditory oddball task inside the scanner, participants correctly responded to 97.6% $\pm$ 2.1% of oddball tones and 99.8% $\pm$0.4% of standard tones. Outside the scanner, participants correctly responded to 97.6% $\pm$ 3.4% of oddball tones and 99.8% $\pm$ 0.4% of standard tones. Inside the scanner, response times for correctly identified oddball tones ranged from 265–973 ms, mean response time of 475 $\pm$ 109 ms (s.e.m. = 57 ms). Outside the scanner, response times for ranged from 266–2294 ms, mean response time of 496 $\pm$ 172 ms (s.e.m. = 83 ms).

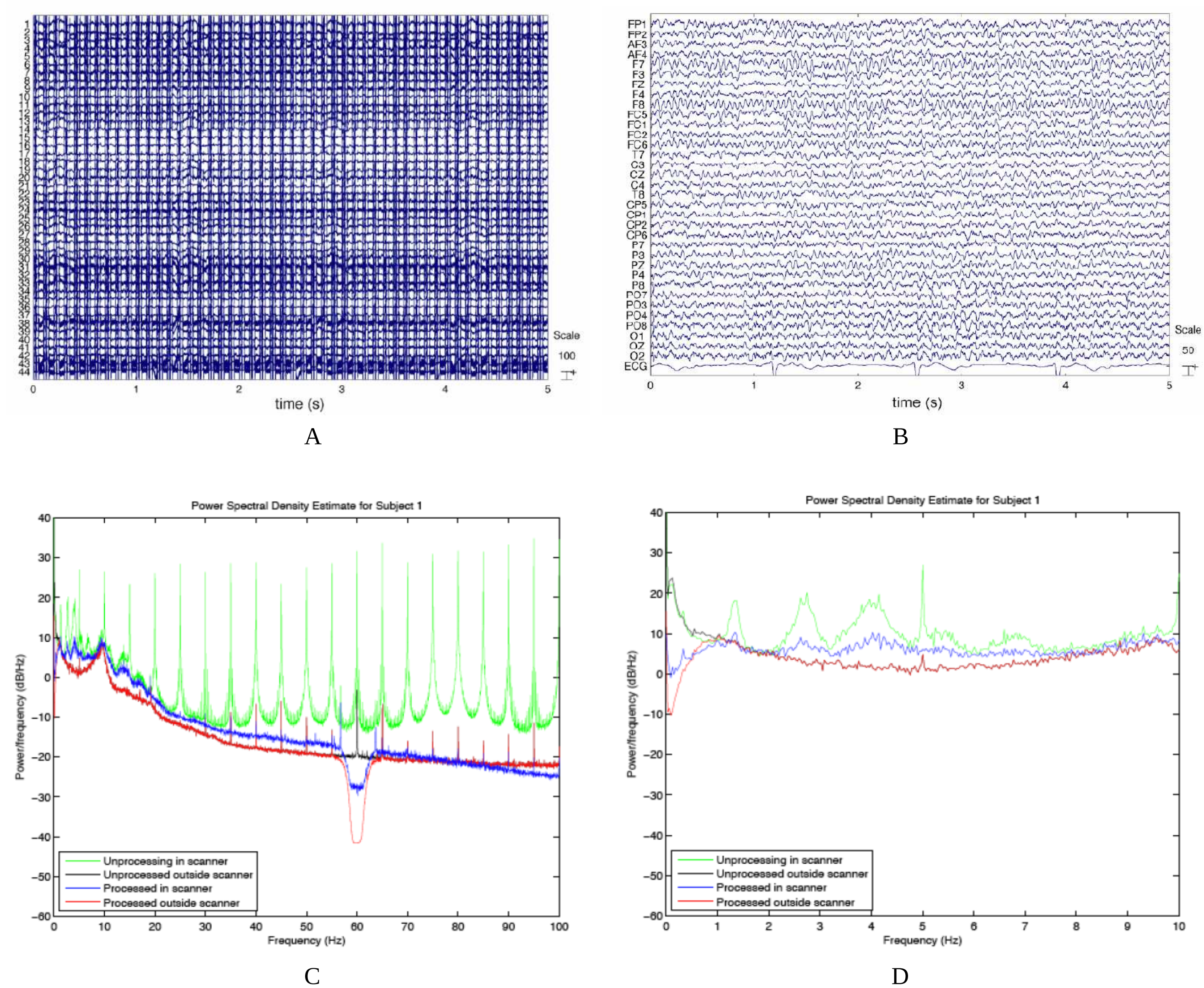

Fig. 2. Artifact removal from EEG acquired in a 1.5T MR Scanner. (A) Unreferenced EEG acquired during fMRI acquisition(echo planar imaging) and (B) same EEG after referencing and artifact removal including removal of ballistocardiogram, gradient artifacts and high frequency and 60Hz noise. (C) Example power spectrum of EEG acquired inside and outside the MR scanner during acquisition. Power spectrum from 0 to 100Hz for (green) EEG acquired in the scanner (black) EEG acquired outside the scanner but before filtering (red) EEG acquired outside the scanner and filtered (blue) EEG acquired inside the scanner with artifact removal and filtering. (D) Same as left but zoomed on frequencies 0-10Hz.

Figure 3 shows results for comparing single-trial discrimination for inside (IS) vs. outside (OS) the MR scanner. Note that the single-trial performance is not significantly degraded inside the scanner and that the average across the 10 subjects is well above the 90%. For this auditory oddball protocol, the 250-500ms interval post stimulus is most relevant, given the P300 activity that is present in trial-averaging. We see both for IS and OS Az values peak during this interval and that fidelity of IS vs OS is maintained at 95%. Note that across all time and all subjects the mean ratio is 94% (10 subjects). During the physiologically relevant interval for this experiment (250-500ms, during the time of the P300) the ratio of inside to outside the scanner Az was 95%.

IV. Discussion

In this study we describe how EEG acquired simultaneously with fMRI, is of high enough signal quality to permit extraction of single-trial discriminating components. Focus in this paper has been how how a combination of hardware design, signal processing and machine learning can reduce MR induced artifacts in the EEG to the point where there is minimal difference from EEG acquired outside the MR scanner. Our current and future research will use this system to couple trial-to-trial electrophysiological variability with hemodynamic changes in order to provide an accurate picture of spatio-temporal cortical networks, particularly those associated with visual discrimination and perceptual decision making [3], [5].

References

[1] L. Parra, C. Alvino, A. Tang, B. Pearlmutter, N. Young, A. Osman, and P. Sajda, "Linear spatial integration for single-trial detection in encephalography," *Neuroimage*, vol. 17, pp. 223–230, 2002.

[2] L. Parra, C. Spence, A. Gerson, and P. Sajda, "Recipes for the linear analysis of EEG," *Neuroimage*, vol. 28, no. 2, pp. 326–341, 2005.

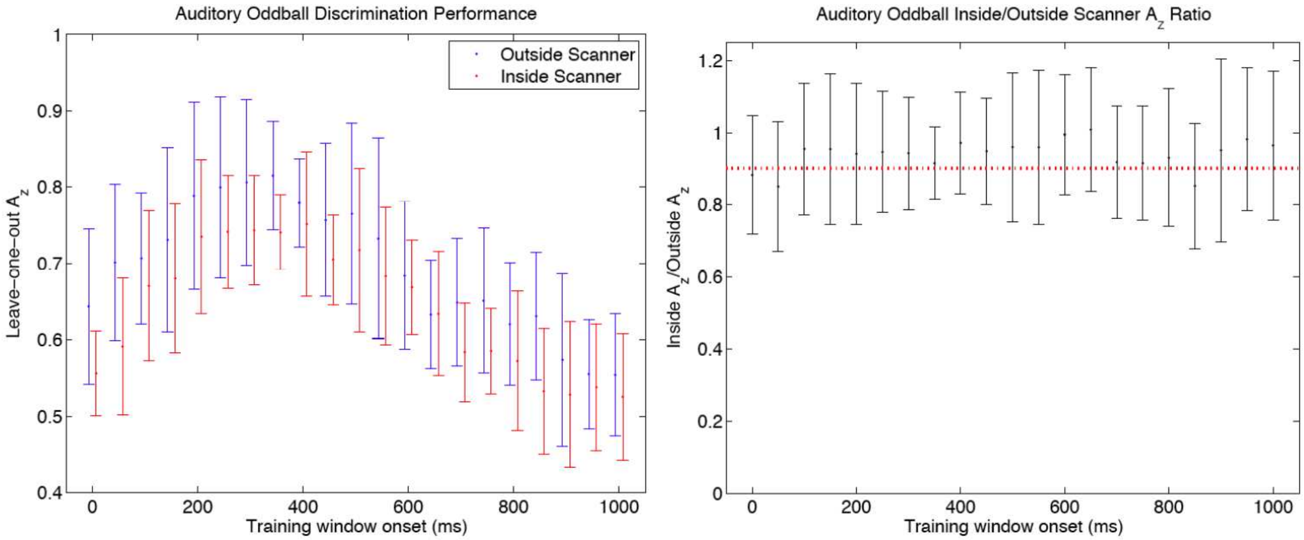

Fig. 3. Comparison of single-trial linear discrimination of EEG acquired inside vs. outside the MR scanner during an auditory oddball task. (A) Plotted is the leave-one-out (LOO) area under the ROC curve (Az) for linear discriminators (discriminating EEG for auditory oddball vs distractor trials) with a training window length of 50ms and shifted in increments of 50ms in time from 0ms (tone onset) to 1000ms. (blue) EEG acquired outside the scanner and (red) inside the scanner, using the paradigm described in Milestone 2. Note the increase in LOO Az from 200ms to 500ms, indicative of a P300 single-trial signature. (B) Ratio of discriminability (Az) for inside vs. outside the scanner. Red dashed line is 90% and shown are means (dots) and standard errors across subjects.

[3] A. Gerson, L. Parra, and P. Sajda, “Identifying the cortical origins of response time variability using single-trial analysis of the cortical origins of response time variability during rapid discrimination of visual objects,” *Neuroimage*, vol. 28, no. 2, pp. 326–341, 2005.

[4] M. Philiastides and P. Sajda, “Temporal characterization of the neural correlates of perceptual decision making in the human brain,” *Cerebral Cortex, doi:10.1093/cercor/bhi130,* vol. 16, no. 4, pp. 509–518, 2006.

[5] M. G. Philiastides, R. Ratcliff, and P. Sajda, “Neural representation of task difficulty and decision making during perceptual categorization: a timing diagram,” *Journal of Neuroscience*, vol. 26, no. 35, pp. 8965–8975, 2006.

[6] R. Goldman, A. Gerson, M. Cohen, T. Brown, and P. Sajda, “Simultaneous eeg and fmri for event related studies,” in *11th Annual OHBM Meeting*, Toronto, CANADA, 2005.

[7] M. Jordan and R. Jacobs, “Hierarchical mixtures of experts and the EM algorithm,” *Neural Computation*, vol. 6, pp. 181–214, 1994.

[8] R. Duda, P. Hart, and D. Stork, *Pattern Classification*. New York: Wiley, 2001.