LA-UR- 99-630

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CONF-990207- -

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Submitted to: SPIE Medical Imaging Conference
San Diego, CA
Feb. 20-26, 1999

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Bayesian Analysis of MEG Visual Evoked Responses

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ABSTRACT

We have developed a method for analyzing neural electromagnetic data that allows probabilistic inferences to be drawn about regions of activation. The method involves the generation of a large number of possible solutions which both fit the data and prior expectations about the nature of probable solutions made explicit by a Bayesian formalism. In addition, we have introduced a model for the current distributions that produce MEG (and EEG) data that allows extended regions of activity, and can easily incorporate prior information such as anatomical constraints from MRI. To evaluate the feasibility and utility of the Bayesian approach with actual data, we analyzed MEG data from a visual evoked response experiment. We compared Bayesian analyses of MEG responses to visual stimuli in the left and right visual fields, in order to examine the sensitivity of the method to detect known features of human visual cortex organization. We also examined the changing pattern of cortical activation as a function of time.

Keywords: MEG, Inverse Problem, MCMC

1. INTRODUCTION

The problem of estimating the current distribution in the brain from surface EEG or MEG measurements (the so-called electromagnetic inverse problem) is mathematically ill-posed; that is, it has no unique solution in the most general, unconstrained case.[1,2] Existing approaches to the electromagnetic inverse problem fall into two broad categories: (1) "few-parameter models" that use a restricted model for current in order to produce a well-posed inverse problem (i.e., those in which $M \ll N$, where M is the number of parameters to be estimated in the model and N is the number of recording sites); (2) and "many-parameter models" (i.e., those in which $M \geq N$) that use a mathematical criterion to select one "best" current distribution from among the many possible that also fit the data. A well-known example of the "few parameter" approach is the single- or multiple-dipole model,[3–5] in which the current is assumed to be represented by a few point-dipoles, the "order" of the model is estimated using Chi-square or related statistical techniques, and the best-fitting values of the dipole parameters (locations, orientations, and magnitudes) are estimated using non-linear numerical minimization techniques. A well-known example of the "many-parameter" approach is the "minimum-norm linear inverse",[6–8] in which the problem is under-determined (because $M \geq N$) and a strictly mathematical criterion is used to select among the many solutions that fit the data equally well; in the case of the minimum-norm approach the mathematical criterion is the solution that minimizes the sum of squared current strengths.

We have recently demonstrated the first steps of a new probabilistic approach to the electromagnetic inverse problem,[9] based on Bayesian inference.[10,11] Unlike almost all other approaches to this problem, including other recent applications of Bayesian methods,[12,13] our approach does not result in a single "best" solution to the problem. Rather, we estimate a probability distribution of solutions upon which all subsequent inferences are based. This distribution provides a means of identifying and estimating the likelihood of features of current sources from surface measurements that explicitly emphasizes the multiple solutions that can account for any set of surface EEG/MEG measurements. Furthermore, we have implemented this approach using a general neural activation model that allows a variable number of extended regions of activation and can incorporate a great deal of prior information on neural current such as information on location, orientation, strength and spatial smoothness. Thus, our approach incorporates much of the information about active regions being fairly sparse and focal that multiple dipole models achieve while not being so restrictive as to require them to consist of a fixed number of point sources. In addition, the resulting under-determined inverse problem is adequately addressed through the sampling of the full posterior probability distribution. This results in much more realistic, robust inferences about neural activation from electromagnetic data.

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2. OUTLINE OF ANALYSIS METHOD

Our analysis method is based on Bayesian inference. Bayesian inference (BI) is a general procedure for constructing a (posterior) probability distribution for quantities of interest from the measurements given (prior) probability distributions for all of the uncertain parameters—both those that relate the quantities of interest to the measurements and the quantities of interest themselves. The method is conceptually simple, using basic laws of probability, making its application even to complicated problems relatively straightforward. The posterior probability distribution is often too complicated to be calculated analytically, but can usually be adequately sampled using modern computer techniques, even in problems with many parameters. A more detailed discussion of Bayesian inference can be found elsewhere.[11]

In applying the methods of Bayesian inference to the EEG/MEG inverse problem we constructed a model for regions of activation which is intended to be applicable in evoked response experiments. There is both theoretical and experimental evidence that EEG and MEG recorded outside the head arise primarily from neocortex, in particular from apical dendrites of pyramidal cells.[14,7,8] We therefore constructed a model that assumes a variable number of variable size cortical regions of stimulus-correlated activity in which current may be present. Specifically, an active region is assumed to consist of those locations which are identified as being part of cortex and are located within a sphere of some radius r centered on some location w, also in cortex. There can be any number n of these active regions up to some maximum n_{max} and the radius can have any value up to some maximum, r_{max}. The goal, in our approach, is to determine the posterior probability values for the set of activity parameters $\boldsymbol{\alpha} = \{n, w, r\}$ which govern the number, location, and extent of active regions. A more detailed description of this method may be found elsewhere.[9]

3. ANALYSIS OF VISUAL EVOKED RESPONSE MEG DATA

To evaluate the feasibility and utility of the Bayesian approach with actual data, we analyzed MEG data from a visual evoked response experiment. We compared Bayesian analyses of MEG responses to visual stimuli in the left and right visual fields, in order to examine the sensitivity of the method to detect known features of human visual cortex organization. We also examined the changing pattern of cortical activation as a function of time.

3.1. Methods

Visual stimuli were black-white circular sinusoidal patterns, 1.0 degree in diameter, presented near the horizontal meridian at 6.2 degrees in the left and right visual fields. The stimulus duration was 250 ms and the average inter-stimulus interval was 1.0 s. One hundred epochs (from 100 ms before each stimulus to 400 ms after each stimulus) were averaged; bad channels were identified and removed before data analysis. The variance of the noise was estimated by calculating the variance of the pre-stimulus epoch. Figure 1 presents the field distributions for these data at a few latencies.

A source was defined as a pattern of current bounded by a spherical shell of variable radius centered on cortex. Currents were confined to cortex and had an orientation prior probability distribution that was Gaussian with mean that was normal to the cortical surface and a standard deviation of 30°. Cortex was identified by segmenting gray matter regions from an anatomical MRI of the subject. The current strength was assumed to have a Gaussian distribution centered about zero, with a standard deviation of 8 nAm, consistent with the maximum current strength measurements by Okada.[15] The model was applied separately to the data for each visual field stimulus at 10 ms intervals from 110 ms to 160 ms post-stimulus. Ten thousand samples of the posterior probability were generated for each latency using a Markov Chain Monte Carlo (MCMC) technique.

3.2. Results

To illustrate the character of the results of our analysis a few of the samples from the right visual field stimulus data at 110 ms latency are shown in Fig. 2. All of the samples shown in Fig. 2 are among the 95% most probable and therefore fit both the data and the prior expectations quite well. Any of these could have produced the given MEG data, yet there are clearly vast differences among the samples. The number of active regions ranges from 2 to 5, the sizes of the regions vary greatly and the locations of the active regions vary nearly across the entire tagged region of the brain (when considering all the samples). This variability is a representation of the degree of the ambiguity of the inverse problem for these MEG data, even with the prior information present.

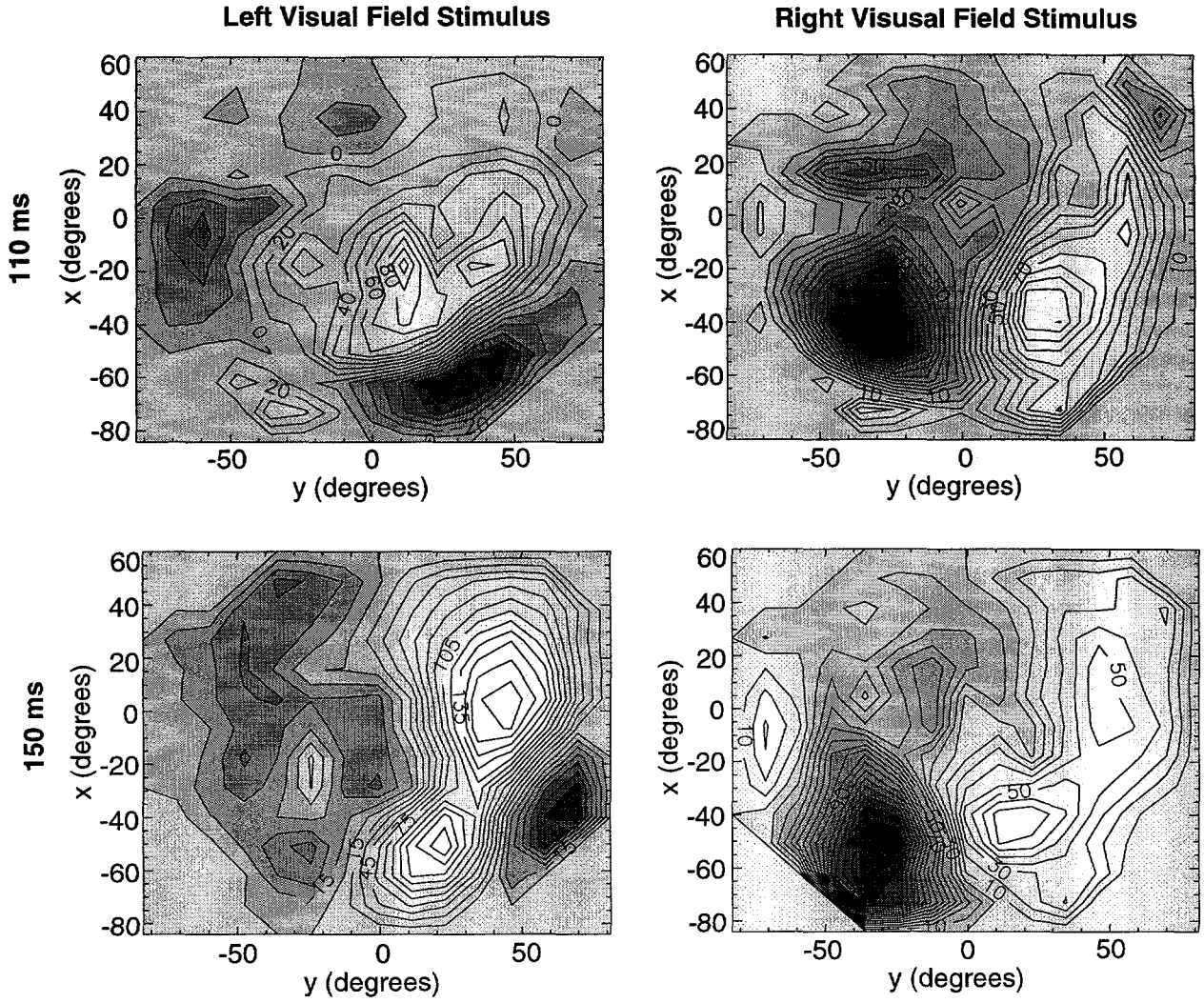

Figure 1. The field patterns for a few latencies of the MEG data shown in a top projection view with the subject facing up.

Despite the degree of variability among the samples in Fig. 2 a property common to all is apparent; namely an active region in the occipital region of the left hemisphere. A feature, such as this, common to all or most of the samples, is associated with a high degree of probability. This probability can be quantified because the samples are distributed according to the posterior probability distribution.

The top of Fig. 3 presents maximum intensity projections of the probability of activity for each voxel in the anatomical model for the left and right visual field stimuli at two different latencies following stimulus onset (110 and 150 ms, respectively). This probability distribution was constructed by calculating the fraction of MCMC samples in which each voxel had activity and is a marginalization of the full posterior probability distribution onto the space of anatomical voxels. The bottom of Fig. 3 presents the posterior probability marginalized onto the number of active regions for each latency and visual field combination.

For the left visual field stimulus, maximal probability of activation at 110 ms was located in the right (contralateral) hemisphere, centered upon the calcarine region. This pattern was reversed for the right visual field stimulus at 110 ms. In order to show this more clearly, regions which contained activity at a probability level of 95% were identified and are shown in greater detail in Fig. 4, which depicts relative probability of activation within these regions in three orthogonal slices through the calcarine region and a three-dimensional rendering of the occipital

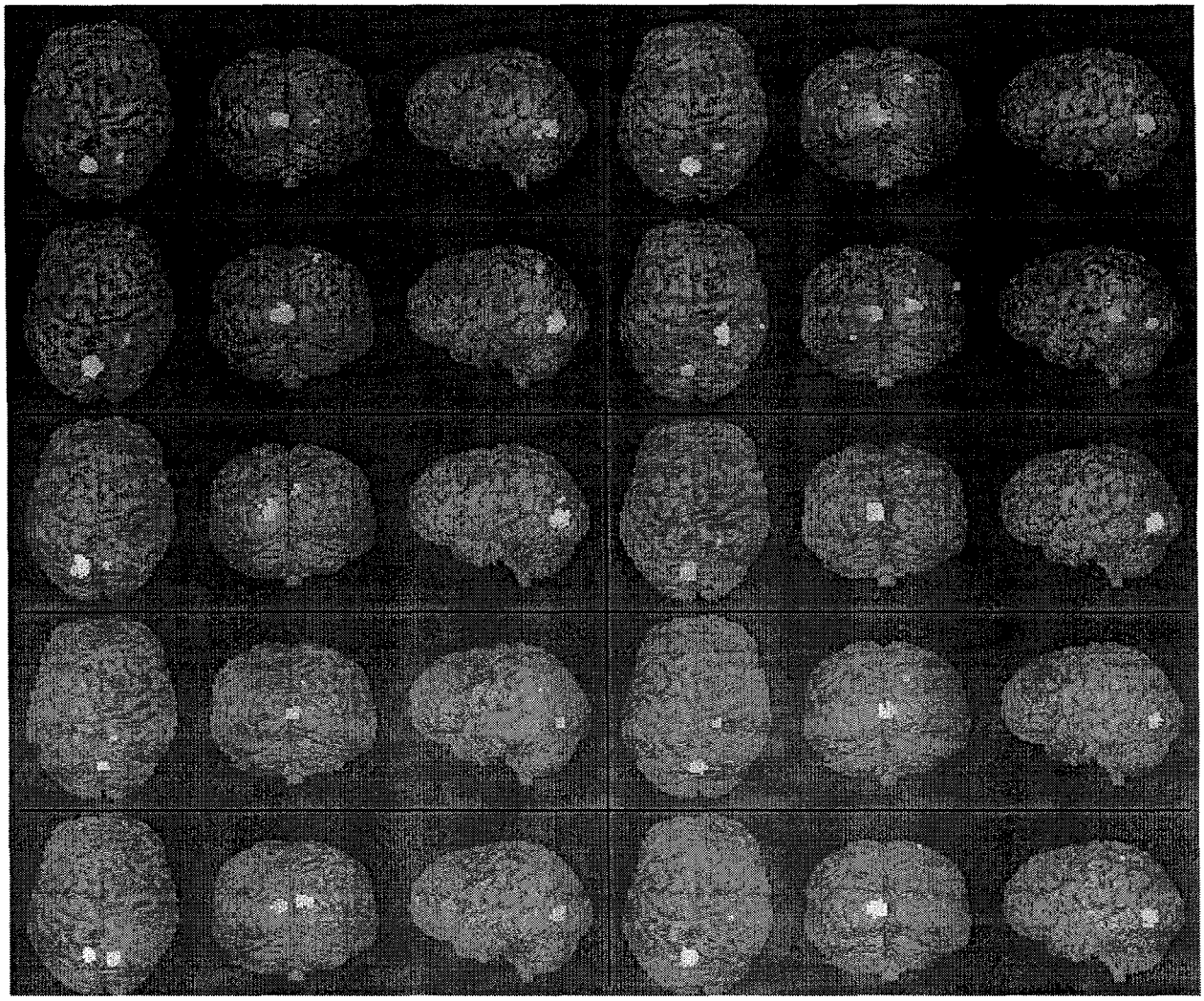

Figure 2. A few of the samples drawn from the posterior probability distribution for the right visual field stimulus data at 110 ms latency. Each panel shows 3 views of the maximum intensity projection of all of the active regions from a single sample. All of these samples could have produced the given MEG data set.

region. These results are consistent with expectations from anatomy, and from lesion, fMRI, and previous MEG studies. Although it is nice to see this agreement, it is not sufficient to justify this or any MEG inverse method based solely on whether it produces a result consistent with expectations. This is because any of the sets of active regions shown in Fig. 2 could have also been used to generate the same MEG data. Any robust and highly probable result or inference therefore should be consistent with the wide range of possible sets of active regions, as are the results in Fig. 4 by construction. This is a very important feature of BI which is necessarily missing from any other analysis method that only considers just one possible result, even if it happens to be the most likely result within a given model.

Two additional features of these results should be noted. First, although maximal probability of activation at the 110 ms latency was indeed located in the opposite hemisphere, there exists sizable probability for activity in the ipsilateral hemisphere near the mid-line. Second, the extent of the 95% probability regions shown in Fig. 4 is indicative of both the extent of estimated activation and the degree of error or uncertainty in that estimate even allowing for the possibility of different numbers of active regions of variable extent.

Second, as shown in Fig. 5, analyses at other latencies suggest a progressively increasing number of probable

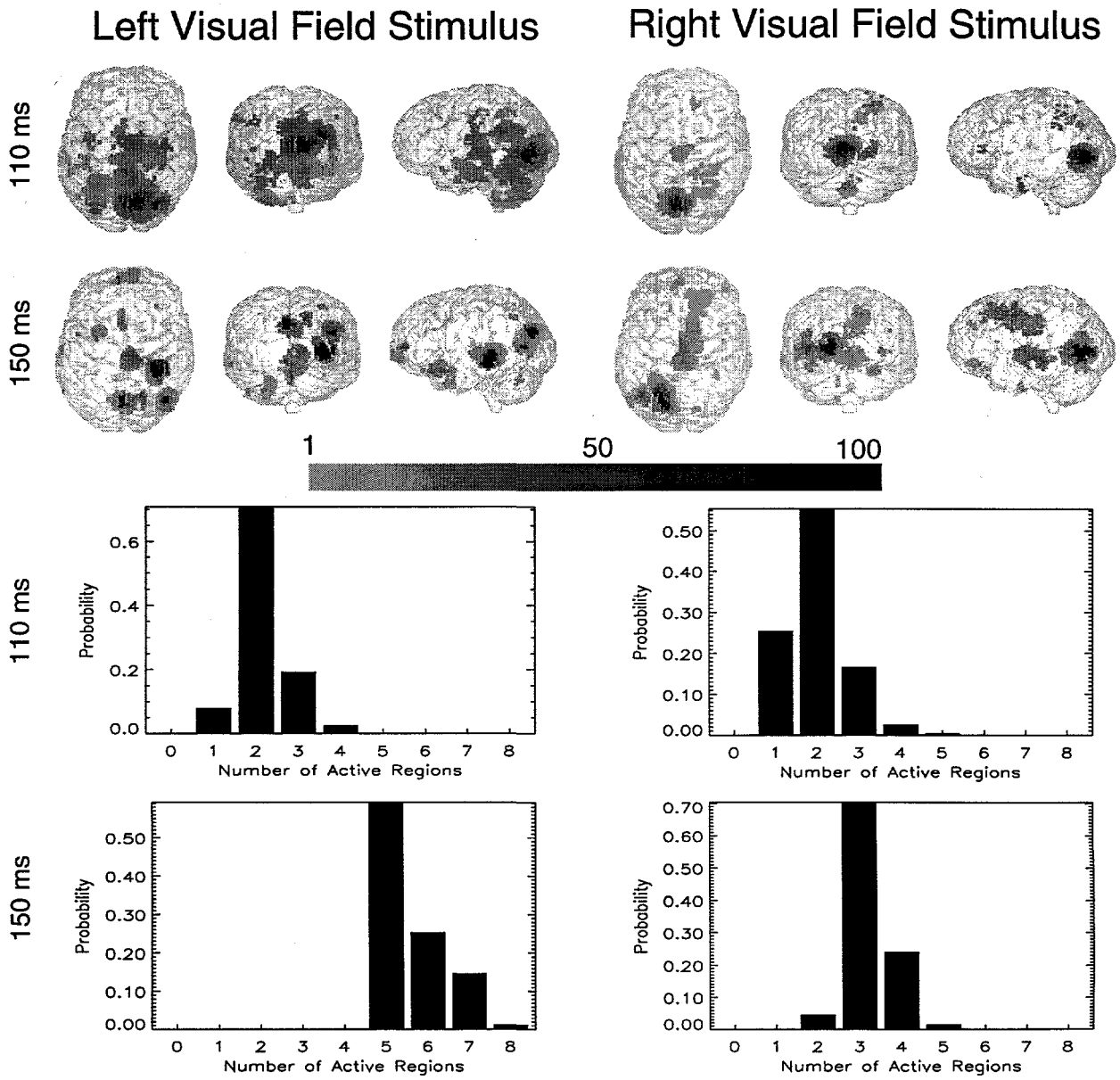

Figure 3. Posterior probability distributions for the MEG data shown in Fig. 1, marginalized onto anatomical location and onto number of active regions. The probability of activation as a function of location distributions are shown as maximum intensity projections over surface renderings of anatomy in the top half of the figure. The color bar shows the mapping between shades of grey and probability. The distributions for the number of active regions are shown in the bottom half of the figure. These results show evidence for activation contralateral to the stimulus at both 110 ms and 150 ms latencies.

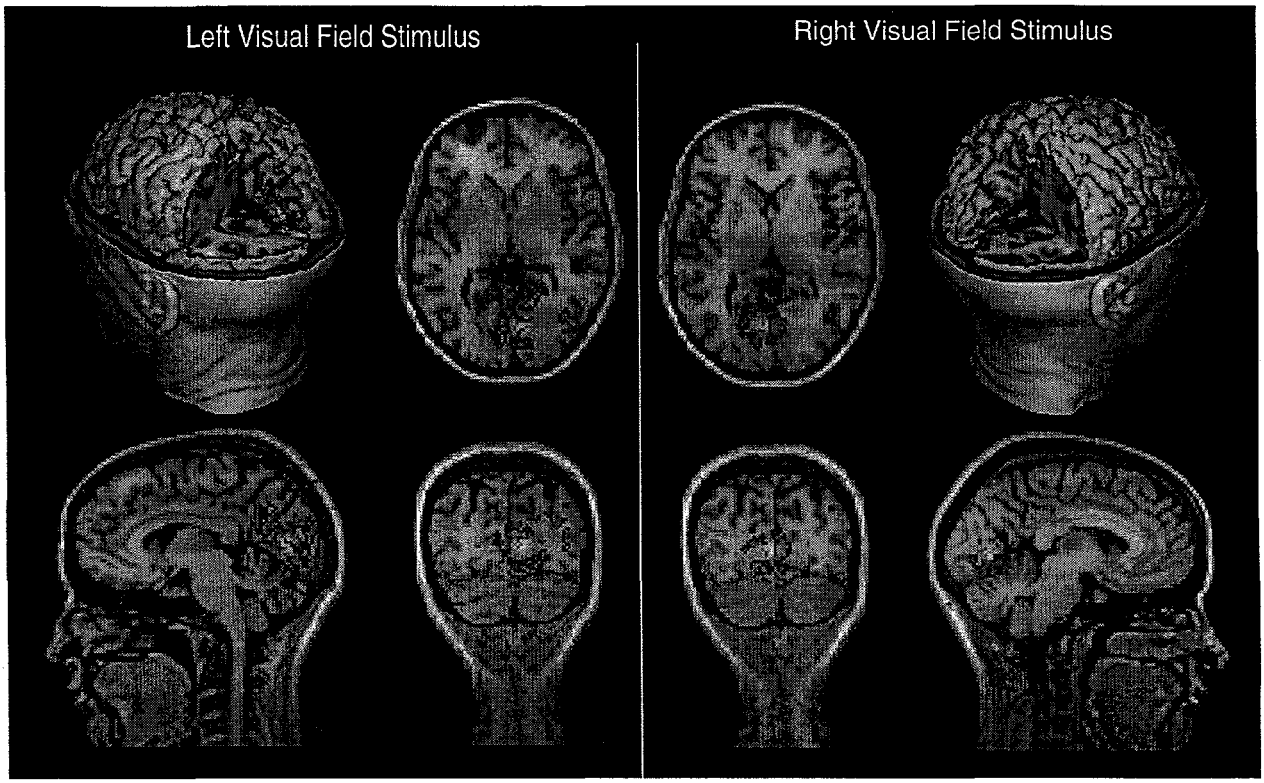

Figure 4. Four views of a region that was found to contain activity at a 95% probability level for both a left and a right visual field stimulus, at 110 ms latency. The two-dimensional views show the probable regions of activity within the anatomical MRI data. The horizontal and coronal views are from the top and from the back of the subject, respectively; the sagital views are from the left for the left visual field stimulus panel and from the right for the right visual field stimulus panel. The three-dimensional views are useful for showing the location of the regions relative to other brain structures. These results indicate that the probability of activity is maximal in the calcarine region of the hemisphere contralateral to the visual field stimulated.

regions of activation, in both the ipsilateral and contralateral hemispheres, over the latency region from 110 to 240 ms following stimulus onset. There was also evidence for the contralateral calcarine region reactivating near 170 *ms*. Regions of highest probability in each case were located in parieto-occipital and temporo-occipital regions of the hemisphere contralateral to the visual field stimulated. These results are consistent in general terms with MEG and fMRI evidence of multiple regions of extra-striate activity although additional work is needed to obtain a definitive comparison of Bayesian inference, multiple-dipole, and fMRI estimates of activity in such experiments.

It will be of considerable interest to explore the time dependence of the Bayesian inference analyses in relation to evidence for multiple, functionally organized areas of striate and extra-striate visual cortex and to examine the value of temporal prior information (not included in the current activation model) in the form of, for example, temporal covariance constraints. In addition, the Bayesian approach provides a natural means for incorporating information from other functional imaging modalities such as PET or fMRI.[16–18] The latter can be readily achieved with the Bayesian framework and with this activity model by assigning prior probabilities to possible locations of active regions based on results from the other modality or modalities. Such a Bayesian formulation of multi-modality integration would yield an inherently probabilistic result in which the quantity estimated would be the probability of activation as a function of both space and time.

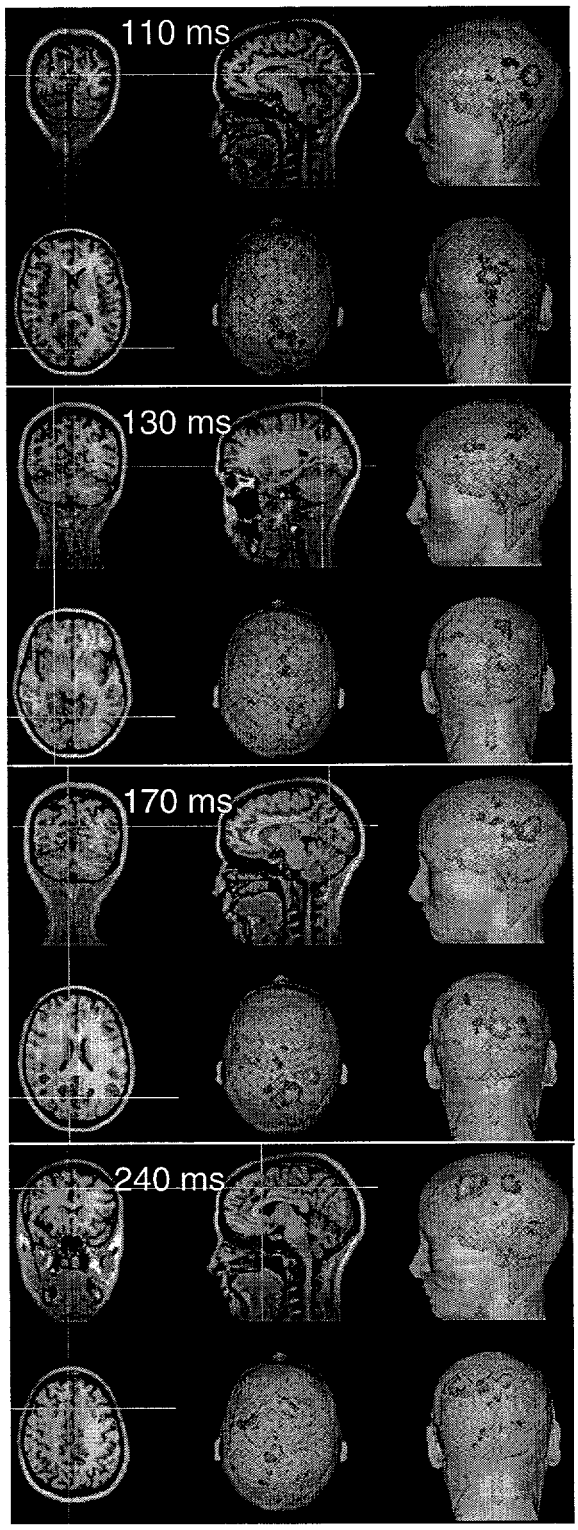

Figure 5. Results from four latencies of the left visual field data.

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