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IDENTIFICATION OF MULTIPLE SOURCES

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INTRODUCTION

Neuromagnetic measurements and associated modeling procedures must be able to resolve multiple sources in order to localize and accurately characterize the generators of visual evoked neuromagnetic activity. Van Essen (1985) has identified at least 11 areas in the macaque, throughout occipital, parietal, and temporal cortex, which are primarily or entirely visual in function. The surface area of the human occipital lobe is estimated to be 150-250cm^2. Primary visual cortex covers approximately 26cm^2 while secondary visual areas comprise the remaining area. For evoked response amplitudes typical of human MEG data, Okada (1984) estimates that a two-dipole field may be statistically distinguishable from that of a single dipole when the separation is greater than 1-2cm. Given the estimated expanse of cortex devoted to visual processes, along with this estimate of resolution limits, it is likely that MEG can resolve sources associated with activity in multiple visual areas.

Brenner et al. (1981) and Okada (1983) noted evidence for the existence of multiple sources when presenting visual stimuli in a half field; however, they did not attempt to localize them. We have examined numerous human MEG field patterns resulting from different visual field placements of a small sinusoidal grating which suggest the existence of multiple sources. The analyses we have utilized for resolving multiple sources in these studies differ depending on whether there was evidence of 1) synchronous activation of two spatially discrete sources or 2) two discrete asynchronous sources. In some cases we have observed field patterns which appear to be adequately explained by a single source changing its orientation and location across time. This situation is examined in detail in a separate paper (George, Aine, Medvick and Flynn, this volume).

METHOD

Vertical sinusoidal gratings (2° x 2°) of either 1 or 5 cycles per degree (cpd) were randomly presented to different locations in the visual field (e.g., central field, right field along the horizontal meridian, lower left and right quadrants) while subjects maintained central fixation. Rastered images were generated by microcomputer and displayed on a rear-projection screen with a video projector. Background and grating intensity parameters were selected to produce equal average luminance in stimulus and background. The interstimulus interval was randomized with an average presentation rate of one per second. Stimulus duration was 100 msec in some cases and 400 msec in others.

Experiments were conducted in an aluminum and mumetal magnetically shielded chamber. Neuromagnetic responses from 6 right-handed subjects were monitored with a 7-channel SQUID-coupled gradiometer system while subjects counted the number of stimuli. Data were obtained over occipital and parietal cortical areas (42-112 sensor locations) while subjects lay prone on a table. A hole through the table permitted the subject to view the screen, via a system of mirrors, while allowing experimental access to the occipital and parietal regions of the head. In some cases, left hemisphere recordings were made while subjects lay on their right side; these data sets were kept separate from the posterior recordings to prevent possible confounds due to small differences in the retinal image. Experiments were replicated at least three times at each placement of the dewar resulting in averages containing at least 75 individual responses.

Field maps were constructed from amplitudes measured from the mean prestimulus baseline at 10 msec intervals. A least squares procedure (single dipole model) was applied to neuromagnetic distributions demonstrating two or more extrema of opposite polarity to estimate the location and orientation of the equivalent current dipole. A 2-dipole model was applied to the data, after initial screening with a single dipole model, if the single dipole model did not account for much of the variance *and* there was evidence of three or more peaks in the field distributions. In many cases, the residual fields obtained from the single dipole model (i.e., the difference between the empirical and theoretical field patterns) contained a dipolar field pattern. When the 2-dipole model was not appropriate for the data, the routine collapsed into a single dipole fit (characterized by two *strong* antiparallel sources at the same location) and/or the percent of variance accounted for by the model was not significantly better than that achieved by a single dipole fit.

RESULTS

Figure 1 displays neuromagnetic field distributions for two subjects when central and right visual fields were stimulated. These distributions illustrate effects of two discrete synchronous sources. The evoked field maps for subject GM were constructed from field

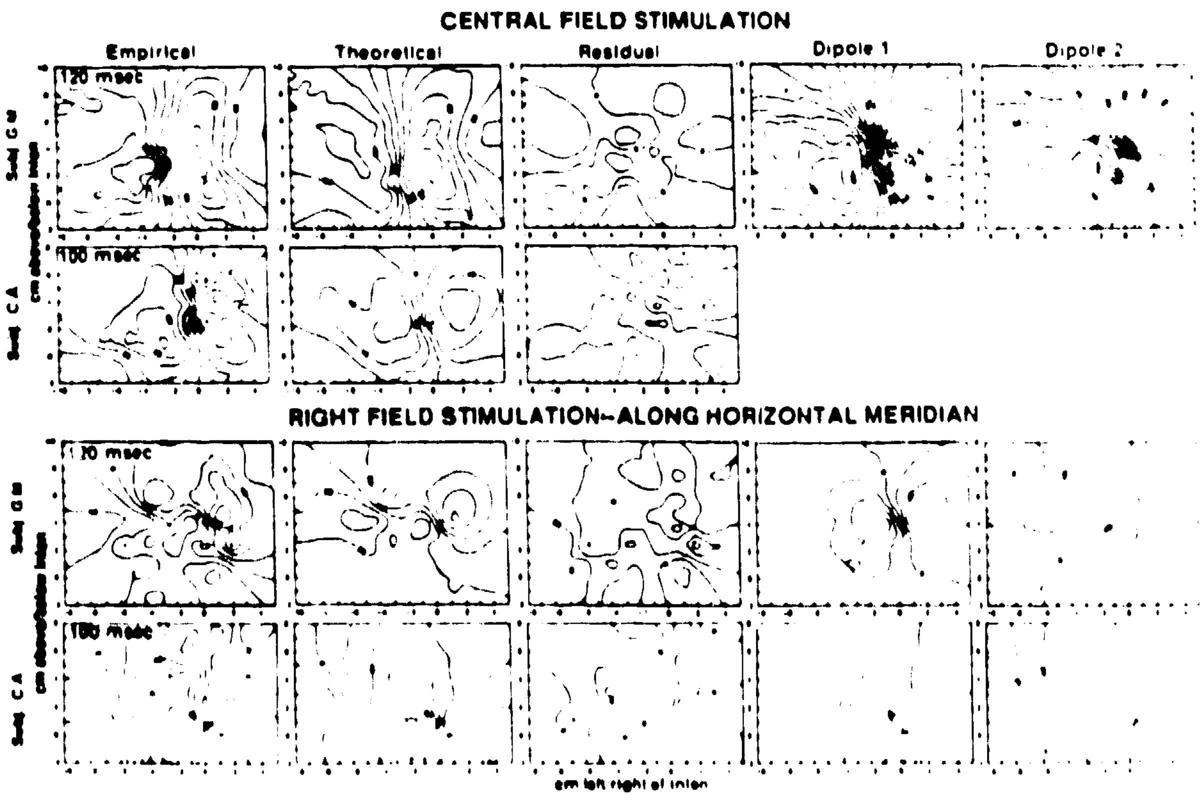

Figure 1. Field distributions for two subjects when a small sinusoidal grating was presented to the central visual field (top rows) and centered 7° along the horizontal meridian (bottom rows). The inion is at x=0, y=0 in these x-y surface plots

measurements at 120 msec poststimulus. Maps at 100 msec are illustrated for subject CA. The measured (empirical) field distributions are shown in the first column. Theoretical distributions calculated from a 2-dipole model are illustrated in the second column (except CA's central data was calculated from a single dipole model). Residual fields are illustrated in the third column and component dipole fields of a 2-dipole model (Dipole 1 and Dipole 2) are shown in the remaining columns. The calculated source locations for GM's central field data reveal two sources. Dipole1 and Dipole 2 suggest left and right hemisphere sources separated by 1.5-2cm with opposing orientations. Because these component dipoles exhibit greater field strengths than the empirical data or resultant 2-dipole theoretical model, it appears that significant cancellation occurred between hemispheres. Note also that elongated peaks seen in empirical fields (e.g., GM's central data) are often indicative of interacting fields. Two sources could not be resolved in CA's central data (second row): the two putative sources were fit as one weak source, possibly reflecting their close proximity and significant cancellation.

The field distributions shown in the bottom two rows of Figure 1 are similar to data presented by Okada when a 1 cpd grating was presented in a hemicircle of 5^o radius in the right visual field (1983; Fig. 12.9.4, pp. 447). These data suggest the existence of two synchronous sources in the left hemisphere: one source located close to the midline (Dipole 1) and an additional source located more laterally (Dipole 2). In GM's data, the positive peak of the midline source and the negative peak of the lateral source have effectively cancelled each other in the empirical data. Consequently, the empirical data displays an imbalance in the midline extrema (x=-2, y=3). In contrast, the negative fields from the lateral and midline source in CA's data have summated and are reflected in the empirical data as a strong negative peak (x=-2, y=1) along with two weak positive peaks. Although the empirical field distributions for subject GM and CA look dissimilar, an examination of the component dipoles reveals significant similarities across subjects. In both cases, the more lateral source for the right field data was 4-6cm from midline.

Figure 2 illustrates that multiple sources can be resolved in MEG data by a careful examination of the temporal characteristics of neuromagnetic field patterns. This sample also demonstrates the existence of multiple sources without relying on modeling procedures. In the neuromagnetic field maps for this subject, the dominant feature from

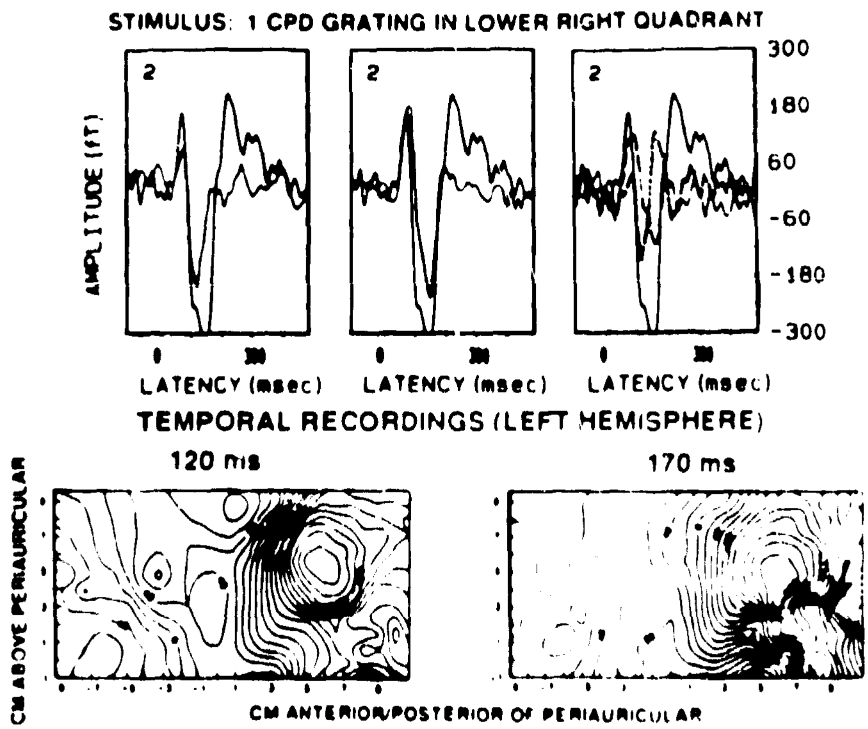

Figure 2. Sample neuromagnetic waveforms and field distributions demonstrating effects of overlapping fields. The left periauricular is at x=0, y=1 in the x y surface plots

120-170 msec was a high amplitude region of negative flux spanning left occipital and parietal regions (see the 120 msec field map below). The top row of this figure compares waveforms from selected regions to illustrate the temporal asynchrony at different sites. The first two columns of the top row suggest that a broad negative peak seen in some waveforms around 120-170 msec is a composite of at least two different sources. The first column shows a weaker negative peak which correlates with the first half of the broad negative wave. The second column similarly reveals a second weak negative peak which correlates with the second half of the broad negative wave. The third column shows two different waveforms superimposed on the broad negative wave. At some locations, the 170 msec peak inverted in polarity while the first half of the negative wave (120 msec) remained the same polarity (negative). Such observations clearly suggest the existence of at least two discrete sources. The bottom row of the figure illustrates the field distributions at 120 and 170 msec. The 120 msec field map shows a small positive peak at x=1, y=9 and a much larger negative peak at x=6, y=5; the arrow represents the approximate location of the equivalent current dipole. The field distribution at 170 msec reveals a different source location (arrow). Although cortical responses for stimuli near the midline could not be mapped while the subject was lying on his side, another data set collected from the posterior region of the head corroborated the existence of the 170 msec source.

DISCUSSION

When large regions of the head surface are mapped, complex neuromagnetic field patterns suggest the existence of multiple sources. We have found that an examination of the temporal characteristics of sources proves to be invaluable in differentiating between multiple sources. When two sources are separated in time and space (e.g., Figure 2) temporal correlations between peaks allow proper coupling between positive and negative peaks. Multiple synchronous sources which may have overlapping fields may be resolved by multiple simultaneous dipole fits. For example, three extrema can be identified in the 120 msec field pattern of Figure 2 but one of the peaks is of greater magnitude than the other two and reflects overlap of two discrete sources. Finally, when complex field patterns are reduced to component sources, similarities across subjects may be more apparent than in the field distributions themselves (refer to right field dipole sources in Figure 1). Slight differences in the orientation of the dipole due to differences in cortical geometry may cause significantly different field distributions across subjects even when the source locations are similar.

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