2Dimensional Inverse Imaging (2DII) of Epileptic Seizure

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Introduction

It is difficult to perform ictal vs. interictal MEG localization studies. MEG recordings of epileptic seizures are rare and are often accompanied by patient movements. However, during routine MEG recordings of a presurgical patient with epilepsy, a complex partial seizure was recorded with a whole head neuromagnetometer (4D Neuroimaging Magnes WHS2500). During seizure, the patient opened his eyes and stared without body movement [1]. The MEG data during seizure consisted of 15 Hz rhythmic activity that changed to 5 Hz spike and wave discharges of increasing amplitude during the first 700 milliseconds. The largest magnetic field amplitudes were from MEG sensors adjacent to the left temporal scalp.

Single equivalent current dipole (ECD) imaging indicated epileptic spike data peaks corresponded to focal source activity near the margin of a previous resection of the left temporal lobe [2]. However, these results are derived from a discontinuous series of single time slices in which the epileptic activity is dominated by a compact source that can be modeled as a single point current dipole. Thus, the ECD results do not adequately describe the full extent of the cortex involved. However, with the 2DII MEG imaging technique a complete sequence of whole brain images of the seizure event was produced [3,4]. These 2DII images included both focal and extended epileptic source activity as well as the ongoing background activity. Thus, it was possible to determine if the change from rhythmic to spike and wave activity involved the recruitment of other cortical regions or involved dynamic changes in a single regional structure. In addition, the analysis is enhanced when 2DII results are displayed as 3-dimensional false color images that can be rotated to any orientation.

The focal cortical activity initiating the onset seizure event was imaged with the 2DII technique and the subsequent spread of activity was assessed. Also, prior focal activity at this seizure initiation site was observed in 2DII images even though it was not detected by the single ECD technique [2].

Methods

147 channels of MEG data were acquired at a rate of 500 Hz. These data were filtered 0.1 to 100 Hz during acquisition and subsequently digitally filtered 3 to 100 Hz, 60 Hz notch. A 146 second MEG/EEG recording containing the seizure plus two ten minutes recordings of spontaneous MEG/EEG were acquired. All 147 channels of MEG data were utilized to generate 2DII whole cortex images of neuronal activity. 2DII images were examined to determine the initial seizure site and high activity sites that might be responsible for continuing seizure activity. 4D Neuroimaging software was used to generate single equivalent current dipole (ECD) source solutions. For ECD solutions, only 64 channels of MEG sensor data were used to enhance localization accuracy of left temporal sources.

Results

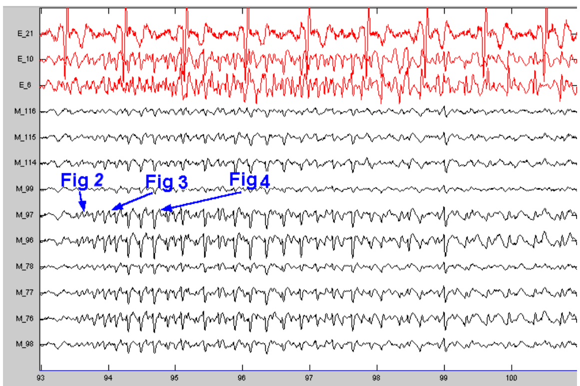


Figure 1 MEG (black) and EEG/EKG (red) for a time window of data that included the seizure.

In Figure 1 the seizure is easily detected in these channels of MEG data recorded from the left temporal region of the patient's scalp. Sequences of 2DII cortical source images were generated for seizure initiation, wave form transition and maximal seizure time windows. For the color code of all 2DII figures, red corresponds to the maximum grid point source amplitude of the image. The minimum 2DII source amplitude displayed is colored blue and corresponds to 15 percent of the maximum amplitude. During the first 250 milliseconds of measurable seizure activity, (93.48 to 93.73 sec.), the MEG recordings consisted of 15 Hz. rhythmic activity. The sequence of 2DII images is dominated by the activity of a compact region of the lower temporal cortex adjacent to a previous resection. In Figure 2, the average of a sequence of 130 2DII image summarizes the source activity during the initial rhythmic discharge phase of the seizure. The site of initiation is also the center of greatest activity in this figure, (the compact red region of the lower temporal cortex). The amplitude of seizure activity is relatively low, so concurrent cortical activity unrelated to the seizure is visible.

The peak amplitude of the seizure data increased in the next 230 milliseconds and included the transition to an epileptic spike and wave pattern. The average of 124 2DII images for this time segment, (93.73 to 93.96 sec.) is shown in Figure 3. Concurrent brain activity unrelated to the seizure is visible in some of the individual 2DII images. However, this low amplitude activity does not attain the image threshold for inclusion in this composite image. Only activity in the right frontal and midline cortex is sufficiently large and persistent to be included in the composite 2DII image. The superior right cortical source is involved in the seizure event. This conclusion is based on a review of the full sequence of 2DII images simultaneously with the contour maps of MEG data. The mid-line source structure could be real or an artifact of the 2DII imaging technique.

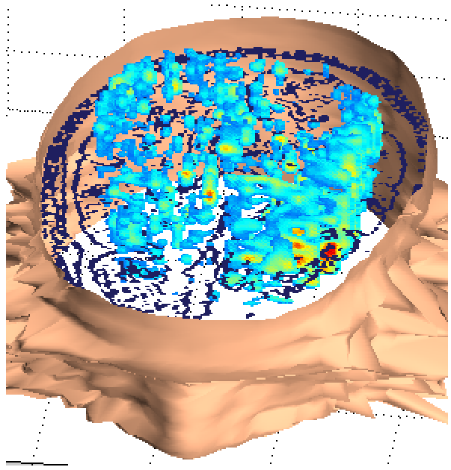


Figure 2: Average 2DII image of brain activity during the first 200 milliseconds. The largest red region corresponds to the initial focal source and most active seizure site. Other concurrent cortical activity is included with the left hemisphere exhibiting greater activity. External distortion of the patient skull is due to artifacts in the MRI data used to generate the 3D surface.

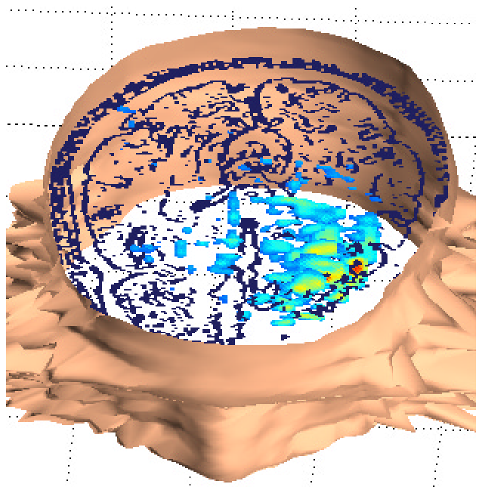


Figure 3: The average of 124 2DII images corresponding to a window of MEG data containing the transition to spike and wave activity. Concurrent brain activity in super right frontal and mid-line cortex is low amplitude relative to the primary seizure site. Nevertheless, these right frontal structures are likely involved in the seizure. The initial focus, (see Figure 2), remains the site of greatest activity.

After 1.2 seconds the amplitude of the MEG recordings is at maximum amplitude. In Figure 4, maximal spike and wave activity, (94.64 to 94.64 sec.), is summarized as the average of 104 sequential 2DII source images. In this figure, the same cortical structures seen earlier in Figure 3 are present. The main seizure site is slightly enlarged and the anterior right frontal cortex is slightly more active.

The same 2DII analysis was performed on the MEG data, 101.27 to 101.66 sec), at the end of the seizure. This composite 2DII image looked very similar to initial seizure image in Figure 3. Thus, this sequence of 2DII cortical activation images demonstrate a single stationary site was the site of initial seizure activity as well as the most active cortical site during the entire seven second seizure event. In addition, these 2DII results shows seizure activity occurred throughout the left temporal cortex as well as a small region of the right superior frontal cortex.

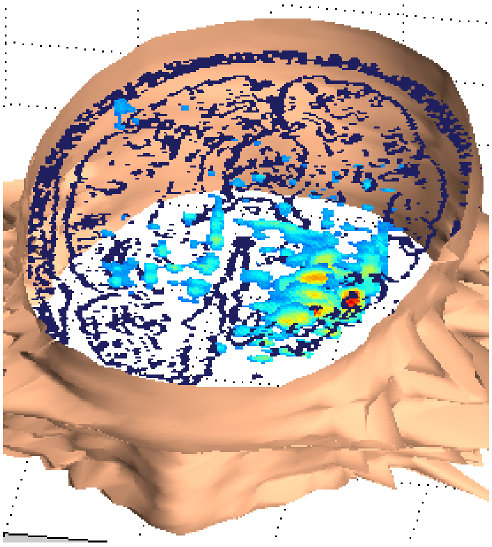


Figure 4: The average of 104 2DII images corresponding to a MEG data segment of maximum amplitude spike and wave seizure activity, (1.2 seconds after seizure onset). The left temporal lobe cortex involved in the seizure is slightly enlarged in the posterior direction. In addition, the right frontal and mid-line cortical involvement is increased, relative to the previous data in Figure 3.

In contrast to these 2DII findings, the single ECD analysis did not demonstrate the existence of a stationary primary site of activity [2]. At the start of the seizure, the correlation of the best single ECD results was less than 0.89. At later time points, the best correlation of the data to the ECD results was 0.96 and the source locations of the best eight ECD solutions were scattered throughout the lower temporal lobe near the border of the previous resection rather than at a single site. In addition, both 2DII and single ECD techniques were applied to the time series MEG recordings of interictal spike activity [2]. Activity of the primary seizure focus was observed in interictal MEG data, Figure 5. However, the location of interictal epileptic activity determined with the single ECD technique differed from the primary seizure site and the previous ictal source locations.

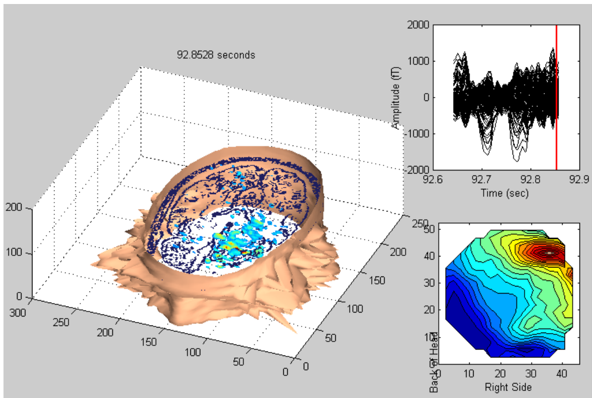
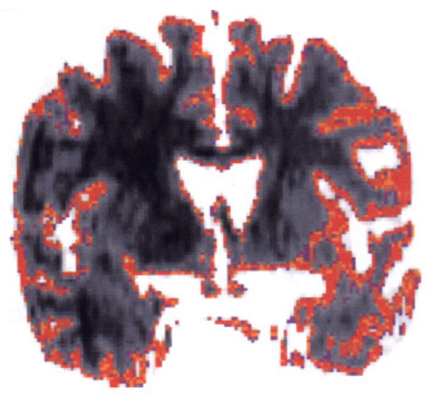


Figure 5: Near the end of a segment of MEG data prior to seizure, the primary epileptic focus is active in the 2DII source activity image. External distortion of the patient skull is due to artifacts in the MRI data used to generate the 3D surface. The data segment and the top view contour plot of the MEG data are included.

Discussion

Sequential Analysis of the 2DII images indicates that this seizure event was initiated and driven by the activity of a single cortical site. Further, the extent of the cortex involved in the seizure remained the same throughout the full seven-second event. Therefore, changes in the epileptic source dynamics observed in the MEG data were due to local parameter changes of neuronal response rather than an expanded seizure circuit. These 2DII results and conclusions are supported by the MRI results

[5]. In Figures 2,3,4, the primary seizure site is near the border of the previous surgical resection. In addition, comparisons of MRI pixel intensities of cortical gray mater demonstrate abnormalities throughout the left temporal region involved in the seizure event. In Figure 6, the red MRI amplitude range corresponds to cortical surface pixels in the normal right hemisphere. However, the temporal lobe cortex that was not removed is not normal. The entire cortical gray mater in the left temporal cortex has red MRI intensities.



right **left**

Figure 6: MRI asymmetry of cortical gray mater for a narrow band of pixel intensities is displayed in red false color. In the normal right hemisphere these pixel intensities correspond to a narrow band of surface cortex.

The 2DII cortical activation images and the single ECD source localization results are consistent with one another. However, this report demonstrates the need to image the full extent of cortical activity in order to observe the embedded activity of epileptic foci. In addition, both the stability of the 2DII solutions and accuracy was enhanced by using the MRI volumetric data to construct a cortical model of 2940 grid locations matching the cortical gray mater of the patient.

The 2DII cortical activation images in this report are useful for assessing the cortical structures involved in a seizure event. However, the time sequence of individual 2DII images must be analyzed to determine the underlying connections and verify that cortical activation at one site leads to activation of other sites. This is a significantly more difficult problem that will likely involve neural network modeling, state space formulation of these networks and optimal control theory [6,7,8].

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References

1. P. Kotagal, Complex Partial Seizures With Automatisms, in The Treatment of Epilepsy: Principles and Practice, E. Wyllie, Ed. Baltimore: Williams & Wilkins, 1996, 385-400.
2. S.M. Bowyer, K. Mason, B.J. Smith, G.L. Barkley, Epileptic Seizure Localized by Whole Head MEG, *this volume.*
3. Moran J.E., Tepley N., Two Dimensional Inverse Imaging (2DII) of Current Sources in Magnetoencephalography, *Brain Topography.* 12 no. 3 , 2000, 201-217.
4. J.E. Moran, N. Tepley, Two Dimensional Inverse Imaging (2DII) applied to large array magnetoencephalographic data, in Recent Advances in Biomagnetism, T Yoshimoto et. al. Eds. , Tohoku University Press, Sendai, 1999 ,270-273
5. A. Palmini, M.C. Sam, G,D, Cascino, MRI in the Evaluation of Epilepsy Surgery, in The Treatment of Epilepsy: Principles and Practice, E. Wyllie, Ed. Baltimore: Williams & Wilkins, 1996, 385-400.
6. P.D. Wasserman, Neural Computing: Theory and Practice, Van Nostrand Reinhold, New York, 1989, 43-75
7. D.M. Wiberg, Theory and Problems of State Space and Linear Systems, Schaum's Outline Series, McGraw-Hill, New York, 1971, 164-202.
8. J.G. Proakis, D.G. Manolakis, State-Space System Analysis and Structures in Digital Signal Processing Principles,Algorithms, and Applications 3rd Edition, Prentis Hall, New Jersy, 1996, 539-556.