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Automatic Localization of Epileptic Zones Using Magnetoencephalography

Xiang, J[1], Holowka, S[1], Qiao, H[2], Sun, B[2], Xiao, Z[3], Jiang, Y[4], Wilson, D[1], Chuang, S[1]
[1]MEG Lab, Department of Diagnostic Imaging, The Hospital for Sick Children, Toronto, ON, Canada; [2]MEG Lab, Tiantan Hospital, Beijing, China; [3]EEG Lab, Chongqing Medical University, Chongqing, China; [4]Laboratory of Neuropsychology, National Institute of Mental Health, Bethesda, MD, USA

Corresponding Author: Jing Xiang, Department of Diagnostic Imaging, The Hospital for Sick Children,
555 University Avenue, Toronto, ON, Canada, M5G 1X8.
Phone: +1-416-813-7646; Email: Jing.Xiang@sickkids.ca

ABSTRACT

Conventional visual identification of epileptic spike is a challenging problem in the clinical application of magnetoencephalography (MEG). More importantly, the conventional method has problems of detecting other abnormalities such as high frequency oscillation in the human epileptic brain. The objective of this study was to develop a new approach using magnetic spectral analysis and spatial filtering. Twelve patients with seizure have been studied with a whole cortex MEG system. Fifteen epochs were recorded for each patient; each epoch was 120 seconds. Neuromagnetic spectrum was analyzed using a new method called accumulated spectrogram. Focal increases of spectral power were localized using synthetic aperture magnetometry (SAM). The MEG results were then compared with clinical findings. Focal increases of spectral power have been identified in all patients (12/12, 100%). The locations of the focal increases of spectral power were in agreement with dipole locations of spikes in 9 patients (9/12, 75%). A comparison between MEG results and clinical findings indicated that SAM revealed focal epileptic activities in two patients when dipole fitting failed. The results suggest that epileptic regions could be quantitatively identified and accurately localized using accumulated spectrogram and SAM. In comparison to visual identification of spike, the new approach is objective and sensitive, and provides the possibility of analyzing much wider frequency bands.

KEY WORDS

Magnetoencephalography (MEG), Epilepsy, Synthetic aperture magnetometry (SAM), Spectrogram, Spike.

INTRODUCTION

MEG is one of the most important advances made in the past decade in the management of seizure disorders and has developed to the point that it has now entered routine clinical application [Barkley, 2003]. The combination of functional data derived from magnetoencephalographic recordings co-registered with structural magnetic resonance imaging (MRI) is called Magnetic Source Imaging (MSI). MSI decreases the risk of morbidity associated with epilepsy surgery and enhances the probability of postsurgical seizure control. In current practice, MEG epileptiform signals are visually identified. After representative epileptic spikes have been marked, they are localized by fitting to an equivalent current dipoles (ECD) model. This method is labor-intensive, time-consuming, subjective and requires considerable skill to minimize errors. Newly developed multichannel and high sampling rate MEG recording techniques have provided the ability to ask and partially answer questions that were previously beyond our capability. Our previous studies have showed that focal increases of spectral power can be accurately localized with magnetic spatial filtering technique, such as SAM [Xiang, 2003]. Therefore, it would be very interesting to use spectral analysis and spatial filtering technique to study epileptiform activities. The objective of this study is to combine two new methods, magnetic frequency transform and spatial filtering techniques, to form a new systematic approach to identifying the neuromagnetic activation associated with epilepsy. Building on our previous studies, this study focuses on the localization of pediatric seizures.

METHODS

Twelve children with epilepsy (6 girls and 6 boys, aged 6 – 17 years, with a mean age of 10 years) were studied. A 151-channel whole cortex CTF OMEGA system was used for recordings (CTF Systems Inc., Port Coquitlam, Canada). MEG measurements were performed in a magnetically shielded room (MSR) with a total system-white-noise level below 10 fT/√Hz. The localization of the subject's head relative to the sensor array was measured using three small coils affixed to the nasion and pre-auricular points. Sleep deprivation was used to provoke epileptic discharges. Data were recorded with noise cancellation of third order gradients. The sampling rate of data acquisition was 625 Hz. Each epoch was 120 seconds; fifteen epochs were recorded for each patient. The head position was measured before and after each epoch. To ensure accurate source localization, the movement of the patient's head was limited in 5 mm. If patient's head moved more than 5 mm during the recording, the datum set was marked as bad and another additional epoch would be recorded. Three-dimensional MRI, 3D-SPGR sequence, was obtained for each subject using a Signa Advantage (GE Medical System, Milwaukee, USA).

Magnetic spikes were identified and classified by an experienced MEG expert and a neurologist using the CTF DataEditor program. The dipole source location corresponding to each spike was estimated individually using the CTF DipoleFit program with the single dipole model. We used spectral analyses to identify frequency abnormalities and used SAM to localize the abnormalities. The analysis time window was same as the epoch length. All recorded MEG data were transformed to spectrogram with Fourier Transform. Since each epoch only has 120 seconds and may have no spike, all fifteen epochs (total of 30 minutes) from each patient were accumulated as one accumulated spectrogram (ASM). The accumulation procedure included two steps. The first step was to normalize each channel for each frequency band according to the averaged spectral power from all measuring channels [Xiang, 2002]. The second step was to recursively add all data from one patient onto one spectrogram.

A realistic head model was produced from each subject's MRI, and multiple spheres were used in SAM analysis. The region of interest (ROI) was set to include the whole brain with a 2.5 mm voxel resolution. SAM Z value was calculated from the changes in spectral power in each voxel of all 120 seconds recording and normalized by the variance. We calculated one SAM image for each epoch (one datum set); total of 15 SAM images were computed and an averaged SAM image was produced. The volume of an epileptic region was calculated by using a software called magnetic source locator (MSL) [Xiang, 2003]. The distribution of spectral power was displayed on individual MR images. A SAM peak was defined when a focal Z value was higher than 5. We considered as focal any region which was smaller than 5 cm in diameter. MSL automatically co-registered dipoles and SAM peaks with MRI using the three fiducial points for each patient. An epileptic region confirmed clinically by ECoG was firstly identified and marked on MRI, and then the distance on the MRI between the dipole and/or SAM peak and the epileptic region were quantitatively measured and compared.

RESULTS

Focal increases of spectral power have been identified in all patients (12/12, 100%). All 15 datasets with spikes were found in 8 children, 9 to 14 datasets with spikes were found in the other 4 children. Therefore, all the children in this study had MEG spikes in at least 9 datasets. In spectrogram, we identified focal increases of spectral power. All 15 datasets with a focal increase of spectral power were

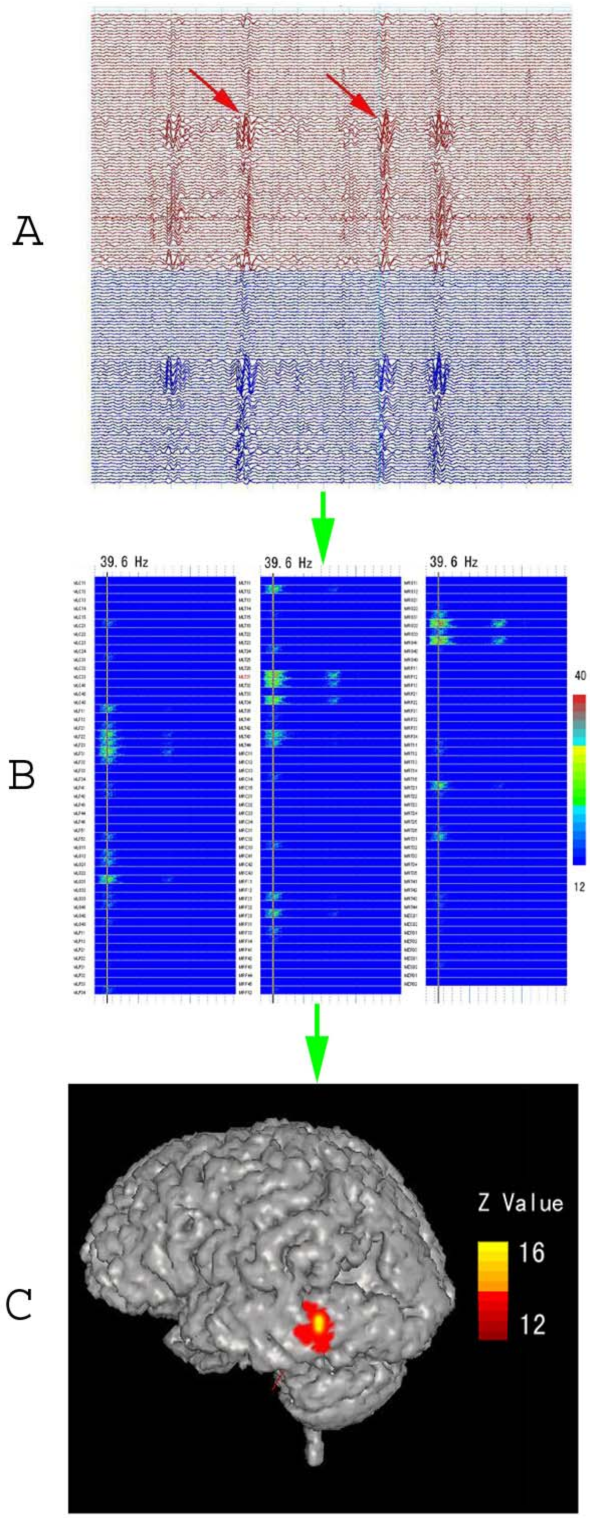

Figure 1. Flowchart of the developed method for localization of epileptic regions. (A) Time domain waveforms show epileptic spikes. The arrows are pointing to spikes. (B) Spectrogram shows focal increases of spectral power (indicated by yellow). Each column is a different set of channels. (C) Magnetic source image (MSI) shows an epileptic region estimated by SAM. A, B and C are the same data.

found in 9 children; 9 to 14 datasets with focal increase of spectral power were found in 3 children. In comparison with time-domain waveform, spectrogram has similar sensitivity but showed more focal abnormalities in the MEG data. One focal increase of spectral power was identified in 7 children; two focal increases were identified in 4; and more than two focal increases were identified in the other 2. In comparison with single epoch spectrogram (or spectrogram), accumulated spectrogram showed much clearer focal increase of spectral power. Fig. 1 shows an example of spikes and focal increases of spectral power in a typical case. The accumulated spectrogram showed a focal increase of spectral power in all children.

All 15 SAM images (each epoch had one SAM image) showed that a focal increase of spectral power were found in 6 children; 9-14 SAM images showed a focal increase were found in the other 6. To enhance the focal increases of spectral power across all SAM images, an averaged SAM image was produced for each patient. In comparison to single SAM image, the averaged SAM image showed much clearer focal increase of spectral power. The exact location of focal increase of spectral power was defined by overlapping averaged SAM image onto individual MRI. The locations of SAM peaks were in agreement with the dipoles in 9 children (9/12, 75%). One child did not have a clear dipole cluster, but averaged SAM image showed a clear epileptic focus. Interestingly, dipoles around the center of SAM peak were found in 4 children who had single epileptic focus. In three children who had multiple epileptic foci, the SAM showed more foci than dipole clusters and the dipole clusters tending to be in the middle of two SAM peaks. The comparison of MEG results and clinical findings indicated that SAM accurately localized epileptic regions in 91% (11/12) of children with localization related seizures. There were one or more additional focal increases of spectral power in SAM images which did not have corresponding clinical evidences in 2 children.

DISCUSSION

The primary results indicate that accumulated spectrogram is a new approach, which can quantitatively describe the epileptiform paroxysms. In comparison with conventional visual identification of spikes, accumulated spectrogram provides a quantitative way to identify the increase of spectral power including conventional spike (15 – 70 Hz). Our results have demonstrated that channel normalization could cancel most of the background activity and highlight focal increases of spectral powers. However, channel normalization is not enough to produce a good spectrogram with high correlation between focal increase of spectral power and spike. Therefore, we further developed accumulated spectrogram to accumulate more than one spectrogram. Once focal increase of spectral power was found, spatial filtering technique was applied to localize the focal increases of spectral power. To get the whole picture of the entire recording for each patient, we developed a new tool to average SAM images for all 15 epochs. Our results indicate that averaged SAM image provides a better solution for identifying epileptic foci.

The present method yielded very plausible equivalent sources for the patients that showed a structural lesion on MRI. Our previous study indicates that SAM can delineate the functional area of the somatosensory cortex [Xiang, 2003]. According to the data from this study, SAM has the potential to localize and delineate the epileptic region. According to our data, using accumulated spectrogram and averaged SAM images, subtle epileptic activity could be identified. In comparison with the conventional visually identifying spikes, the current method has the following advantages: (1) it is objective; the focal increases of spectral power can be quantitatively described. (2) the current method opens a door to analyze much wider frequency ranges; the frequency can be as high as 500 Hz, which goes beyond the convention spike and sharp wave (15 – 70 Hz). (3) According to our data, the shape and extent of an epileptic focus can be visualized. We consider that the combination of spectral analyses and spatial filtering techniques have the potential to make a breakthrough in the clinical applications of MEG in epilepsy.

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