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Implanted medical devices or other strong sources of interference are not barriers to magnetoencephalographic recordings in epilepsy patients

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HIGHLIGHTS

- Patients with implanted medical devices (e.g. VNS) can routinely undergo satisfactory MEG recording.
- Artifacts can be removed from MEG data and epileptic spikes can be localized by filtering with spatiotemporal signal space separation (tSSS).
- The effect of spatiotemporal signal space separation (tSSS) on dipole fitting is to either improve the statistical parameters of the fit (44%) or to make a source localization possible when otherwise no fit could have been made (28%).

ABSTRACT

Objective: Localization accuracy in magnetoencephalography (MEG) recordings is highly dependent on signal to noise ratio, which is difficult to control.
Methods: We have post-processed our data in order to reduce noise to a level permitting adequate source localization with equivalent current dipole methods. In 30 consecutive epilepsy patients, MEG was recorded using a whole-head MEG system consisting of 204 planar gradiometer and 102 magnetometers, with simultaneous EEG. Data were reviewed to identify interictal spikes. The initial analysis was done after employing a spatiotemporal signal space separation (tSSS) method. A total of 18 dipole clusters in 15 patients were reanalyzed without tSSS, to compare the number, goodness of fit, and locations of acceptable dipoles before and after processing.
Results: In 8 of 18 clusters, although acceptable dipole clusters were captured before processing, there was a clear improvement of all parameters with tSSS. In another 5 clusters, all from patients with vagus nerve stimulators, there were few or no acceptable dipoles before processing, but sufficient dipole clusters were obtained with tSSS.
Conclusion: In contrast to volunteer research subjects, clinical patients cannot be expected to cooperate as fully, and their MEG data are likely to include more interference. This study demonstrates that processing the MEG data with a method to eliminate artifact arising from outside the brain significantly improves the data.
Significance: In some cases, this improvement can mean the difference between satisfactory dipole fits vs no possible localization.

1. Introduction

As a result of several advantages, magnetoencephalography (MEG) has established itself as a part of the non-invasive presurgical epilepsy evaluation (Knake et al., 2006; Knowlton et al., 2009; Sutherling et al., 2008). In the clinical setting, where each electroencephalography (EEG) electrode must be individually affixed to the scalp, EEG sensor placement according to the International 10-10 pattern or higher densities can become impractical, yet whole-head MEG systems easily comprise hundreds of sensors. For source modeling MEG requires primarily knowledge of the inner skull boundary, whereas EEG source modeling requires more accurate knowledge of all of the boundaries (inner skull, outer skull, scalp) and their conductivity ratios (Hamalainen and Sarvas, 1989). Thus the combination of better sensor coverage and simpler

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physics yields clinically better localization abilities for MEG (Nakasato et al., 1994). In addition, MEG and EEG have each been shown to detect epileptiform abnormalities in a complementary fashion (Iwasaki et al., 2005; Wheless et al., 1999), and therefore both modalities are often recorded simultaneously.

One of the difficulties in obtaining good MEG recordings is that the magnetic signals produced by the brain are much weaker than environmental interference. Because localization accuracy is highly dependent on the signal to noise ratio (SNR), it is critical to suppress as much as possible any magnetic interference that is not coming from the patient's brain. Sources of external interference include artifacts from other electronic equipment, nearby movement of equipment and patient gurneys, construction activity, etc. Conventional methods to remove these artifacts include magnetically shielded rooms, gradiometers, signal space projection, etc. (Tesche et al., 1995).

However, there are also sources of interference that are internal to the patient, such as implants (vagus nerve stimulator (VNS), pacemakers), metallic debris from neurosurgical procedures (drill-bit filings), and dental work (fillings, braces), all of which produce large artifacts that do not yield to the traditional methods noted above. Although conventional ensemble averaging is employed to improve SNR in most mapping and cognitive-related protocols, averaging of interictal activity is not desirable during spontaneous MEG recordings in epilepsy patients, and alternative methods of noise reduction are sought.

Since inception of our MEG laboratory, we have post-processed our MEG data in order to reduce magnetic noise to a level that permits visual spike identification and allows adequate source localization of individual spikes with equivalent current dipole (ECD) methods. Signal space separation (SSS) and its temporal extension (spatiotemporal signal space separation, tSSS) are new tools reported by Taulu and colleagues. The SSS method (which has a longer history) divides raw MEG data into two linearly independent subspaces: one for the neuromagnetic signals from internal space including the brain, and the other for artifact signals from external space (Taulu and Kajola, 2005; Taulu et al., 2004, 2005). However, ferro-magnetic objects relatively close to the internal space (such as VNS) impair the performance of the SSS algorithm, because these artifacts will be partially picked up by the expansions in both subspaces.

The more recent tSSS method can also remove these strong artifacts which come from nearby sources by implementing the following: First, the data are divided into short segments, typically 4 s. Then, a unique decomposition of the measured signal vector with separate components for the internal and external signals is obtained within each segment. Signal components from both the internal and external spaces that are temporally correlated are considered to be artifacts and then removed (Taulu and Hari, 2009; Taulu and Simola, 2006). What remains are those signals that are temporally uncorrelated, which should theoretically be from brain. In this study, we compared the results with and without these post-processing methods, and we systematically evaluated the clinical usefulness of tSSS.

2. Methods

2.1. Patients

In our study of the effectiveness of tSSS, we included 30 patients with intractable epilepsy consecutively evaluated in the MEG laboratory. From the population of 30 patients, all patients ($N = 15$, 50%) who had shown at least one cluster of dipoles during routine clinical analysis (which always included tSSS processing) were selected for further study. A total of 18 clusters were obtained from these 15 patients. Reasons for exclusion of the other patients ($N = 15$, 50%) were: (i) fewer than 5 epileptiform discharges recorded ($N = 14$), (ii) widespread dipole sources with no evidence of clustering ($N = 1$).

2.2. Recordings/Acquisition settings

Spontaneous MEG and EEG were simultaneously recorded for 30–40 min. The patients were made comfortable and encouraged to relax in a magnetically shielded room. Usually the recording included both wakefulness and sleep.

MEG data were acquired with a system consisting of 204 planar gradiometers and 102 magnetometers (Neuromag, Helsinki, Finland) (Ahonen et al., 1993), while a minimum of 21 scalp EEG electrodes were placed according to the international 10-20 system, augmented by bilateral anterior temporal electrodes. All channels were sampled at 1000 Hz and bandpass-filtered between 0.1 and 330 Hz. Measurements of head position inside the sensor helmet were done at least every 10 min. The waveforms of every channel were reviewed manually to identify interictal spikes.

2.3. Post-processing/Experimental groups

The initial routine MEG analysis of epileptiform sources was carried out after tSSS processing. A correlation limit of 0.98 was used, and all of the other tSSS settings were left at the vendor's default settings. Then, the patients showing at least one cluster of dipoles with tSSS were reanalyzed without tSSS, both before and after SSS processing. Thus, experimental groups included three different post-processing methods: no SSS – gradiometer data before any processing, SSS – gradiometer data after processing only with SSS, and tSSS – gradiometer data after processing with tSSS.

2.4. Spike identification

The MEG data from each of the three processing groups were inspected together with the EEG data for interictal spikes. The MEG and EEG data from each processing group was reviewed separately and blindly, i.e. in three passes. The original sources identified clinically were used only to determine inclusion or exclusion from the study; the experimental passes were blind to these original dipole fits. Ipsilateral ear reference, longitudinal, and transverse bipolar montages were used for reviewing the EEG data, and spikes were identified using conventional EEG criteria. MEG spikes were deemed acceptable if the spike amplitude was double or larger than the background activity, and a clear physiological dipolar pattern was seen in the magnetic field distribution around the spike peak. Except for the differences in post-acquisition processing, we followed our customary clinical procedure.

2.5. Dipole fitting

After spikes were manually identified, their sources were localized using a single ECD model. When multiple peaks were prominent, the earliest peak was used for source analysis. The acquired data were low-pass filtered at 60 Hz. High-pass filtering was used at appropriate settings between 2 and 8 Hz to extract the spike component from the slower background activity. The ECD model was fitted to the patient's spherical head model using the recorded signals from a total of 204 planar gradiometer channels. Each interictal discharge was analyzed individually i.e. without averaging. Only one dipole source was chosen for each interictal discharge. The spike source was represented by the dipole with the highest goodness-of-fit (GOF) and lowest confidence volume. For the purposes of this research study, dipole fits were accepted as valid if