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Magnetoencephalography with temporal spread imaging to visualize propagation of epileptic activity

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HIGHLIGHTS

- Our novel method can show the spatiotemporal spread pattern of epileptic activity.
- The reproducibility of its propagation pattern can be statistically confirmed.
- The pattern was compared with that of FDG-PET hypometabolism in clinical cases.

ABSTRACT

Objective: We describe temporal spread imaging (TSI) that can identify the spatiotemporal pattern of epileptic activity using Magnetoencephalography (MEG).
Methods: A three-dimensional grid of voxels covering the brain is created. The array-gain minimum-variance spatial filter is applied to an interictal spike to estimate the magnitude of the source and the time (Ta) when the magnitude exceeds a predefined threshold at each voxel. This calculation is performed through all spikes. Each voxel has the mean Ta (<Ta>) and spike number (N_{sp}), which is the number of spikes whose source exceeds the threshold. Then, a random resampling method is used to determine the cutoff value of N_{sp} for the statistically reproducible pattern of the activity. Finally, all the voxels where the source exceeds the threshold reproducibly shown on the MRI with a color scale representing <Ta>.
Results: Four patients with intractable mesial temporal lobe epilepsy (MTLE) were analyzed. In three patients, the common pattern of the overlap between the propagation and the hypometabolism shown by fluorodeoxyglucose-positron emission tomography (FDG-PET) was identified.
Conclusions: TSI can visualize statistically reproducible patterns of the temporal and spatial spread of epileptic activity.
Significance: TSI can assess the statistical significance of the spatiotemporal pattern based on its reproducibility.

Abbreviations: TSI, temporal spread imaging; ECDs, equivalent current dipoles; HPI, head position indicator; PCA, principal component analysis; MSI, magnetic source imaging.

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1. Introduction

Spencer (2002) presented the concept of epilepsy as a disorder of large neural networks which are connected functionally and structurally (the epileptic network). This suggests that broad regions of brain structures are related to epileptic activity as part of the epileptic network rather than a single localized region of seizure onset. This concept is supported by the evidence that the hypometabolic zone, as detected using fluorodeoxyglucose-positron emission tomography (FDG-PET), is usually larger than the structural lesion and epileptogenic zone and often extends beyond the temporal lobe in intractable temporal lobe epilepsy (TLE) (Savic et al., 1997; Arnold et al., 1996; Chassoux et al., 2004; Dupont et al., 1998). One hypothesis to explain the mechanism of extra-temporal hypometabolism in TLE is that frequent propagation of epileptic activity to the extra-temporal area may have impaired metabolism as part of the epileptic network. In support of this hypothesis, an animal study reported lesioning of the putative neural pathway prevented the epilepsy-induced hypometabolism in brain regions remote from an epileptic focus (Bruehl et al., 1998).

The investigation of propagation of epileptic activity can be helpful to understand the epileptic network. While electrocorticography (ECoG) with intracranial electrodes remains the gold standard method to monitor local propagation of epileptic activity, ECoG with intracranial electrodes is limited by spatial sampling and the invasiveness of neurological procedures. As magnetoencephalography (MEG) is noninvasive and can monitor the entire brain, it is superior to ECoG for investigating propagation of epileptic activity. In addition, high-resolution recordings of cortical function without attenuation or distortion by the skull or other intervening tissue layers below the scalp can be acquired by MEG. This advantage enables good accuracy of MEG to localize the source of epileptic activity (Knowlton, 2008). MEG analysis with a spatial filter approach, which does not assume a single site of generation, can visualize the spatiotemporal evolution of epileptic activity.

In this paper we describe a newly developed method, temporal spread imaging (TSI), that can identify the spatiotemporal pattern of electrophysiological epileptic activity and assess the statistical significance of the pattern based on its reproducibility. First, a three-dimensional (3D) grid of voxels ($5 \times 5 \times 5$ mm) covering the whole brain is created for a patient. The array-gain minimum-variance spatial filter (Sekihara and Nagarajan, 2008) is applied to an interictal MEG spike to estimate the magnitude of the source activity as well as the time value, Ta, when the source activity exceeds a predefined threshold for the first time at each voxel. Then, this calculation is performed through all interictal MEG spikes. As a result, each voxel has two values: the mean Ta (<Ta>) and spike number (N_{sp}), which is the number of MEG spikes

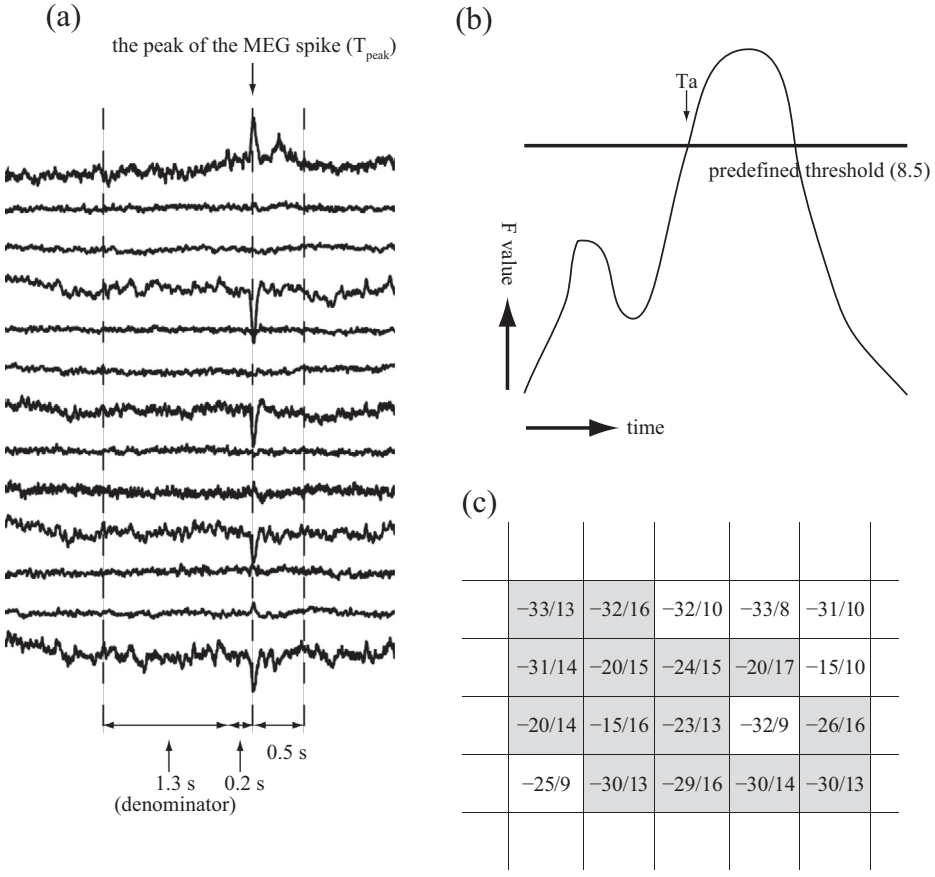

Fig. 1. Analysis by TSI. (a) MEG waveforms of "Spike Segment". The MEG spikes were cut to 2.0-s epochs (Spike Segment. 1.5-s period before a peak of the MEG spike (T_{peak}) and 0.5-s period after T_{peak}). F value from the source activity at every time and every voxel using 1.3-s epoch (−1.5 to −0.2 s relative to T_{peak}) as a denominator was calculated. (b) F value in a voxel. A time value, Ta (which was relative to T_{peak}), when the F value exceeded a predefined threshold (we used 8.5 in this study) for the first time in the "Analysis Window" was given to each voxel. (c) The mean Ta (<Ta>) and the "Spike Number" (N_{sp}). The figure shows each voxel has <Ta> (the value on the left side) and N_{sp} (the value on the right side) which is the number of the MEG spikes whose F value at the voxel exceeds the threshold (<Ta>/N_{sp}). The voxels where the power exceeds the threshold above the cutoff value for N_{sp} (N) through the analyzed spikes are shown on the patient's MRI by the color scale representing <Ta>. For example, if N is 12, the colored voxels are shown.