Tuberous sclerosis: Localizing the epileptogenic tuber with synthetic aperture magnetometry with excess kurtosis analysis

Leonides Canuet^{a,b,*}, Ryouhei Ishii^a, Masao Iwase^a, Ryu Kurimoto^a, Koji Ikezawa^a, Michiyo Azechi^a, Mari Wataya-Kaneda^c, Masatoshi Takeda^a

^a Departments of Clinical Neuroscience and Psychiatry, Osaka University Graduate School of Medicine, Osaka, Japan ^b Department of Neurology, "Saturnino Lora" Provincial Hospital, Santiago de Cuba, Cuba ^c Department of Dermatology, Osaka University Graduate School of Medicine, Osaka, Japan

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Abstract

The hallmark of tuberous sclerosis is the presence of multiple cortical tubers. Identifying the epileptogenic tubers is difficult and often requires invasive intracranial electroencephalograph (EEG) monitoring. We report on a patient with tuberous sclerosis upon whom the novel magnetoencephalography (MEG) technique of synthetic aperture magnetometry (SAM) with excess kurtosis (g2) analysis was performed for localization of the epileptogenic tuber. Simultaneous electroencephalography (EEG) was also performed. MEG data, as analyzed by SAM(g2), were superimposed on the patient's MRIs. In the fluid attenuated inversion recovery MRIs, several tubers and subependymal nodules could be identified, with the largest tubers being located in the right frontal and left anteriotemporal regions. Despite multiple cortical lesions existing, the SAM(g2) analysis may be clinically useful for the accurate identification of epileptogenic tubers in patients with tuberous sclerosis.

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1. Introduction

Multimodality neuroimaging has improved the detection of epileptogenic foci, allowing an increasing number of individuals to be evaluated for surgery.¹ However, because localization of epileptic foci remains challenging, there is an urgent need to improve the methods by which epileptogenic tubers are detected. Synthetic aperture magnetometry $(SAM)^{2,3}$ with excess kurtosis $(g2)^{4,5}$ is a recently developed analysis technique that transforms magnetoencephalography (MEG) data into a functional image of spike-like activity, giving the source waveforms for those locations. This technique seems to be appropriate for localizing epileptogenic tubers in tuberous sclerosis. In the current study we illustrate the value of the combination of MEG and SAM(g2) for the accurate interictal localization of an epileptogenic tuber in a patient with focal epilepsy as a symptom of tuberous sclerosis.

2. Clinical presentation

A 29-year-old female patient was diagnosed with tuberous sclerosis, in accordance with the revised clinical diagnostic criteria for tuberous sclerosis complex.⁶ Symptomatic focal epilepsy was also diagnosed, with age of onset being 14 years. After epilepsy appeared, the patient was followed up at the outpatient clinic of psychiatry, Osaka University Hospital, Japan. The patient experienced frequent partial complex seizures, suggestive of a temporal focus. Seizures were characterized by behavioral arrest and staring, usually accompanied by fear, nausea, mild cyanosis, and, rarely, secondary generalized seizures. Previous electroencephalography (EEG) recordings often showed bilateral epileptic discharges in the temporal regions. The patient underwent an MEG measurement using a 64-channel whole head magnetometer (NeuroSQUID Model 100, CTF Systems Inc., Port Coquitlam, BC, Canada). The data sample rate was 250 Hz per channel. To assist in spike detection, simultaneous EEG data were recorded using 19 electrodes (International 10-20 system). MEG demonstrated clear spike activity over the left temporal region (Fig. 1).

MEG data were analyzed by using synthetic SAM(g2). This functional imaging analysis technique combines a three-dimensional functional image of excess kurtosis, g2, considered a measure of spike-like activity, and the estimation of source waveforms at the coordinates identified in the functional image by SAM virtual sensors. The presence of spike activity yields a large positive kurtosis, whereas normal cortical activity exhibits a small kurtosis, and noise

^{*} Corresponding author. Present address: Department of Psychiatry, Osaka University Graduate School of Medicine, Yamadaoka 2–2, D-3, Suita City 565–0871, Japan. Tel.: +81 6 6879 3051; fax: +81 6 6879 3059.

E-mail address: leocanon2002@yahoo.com.mx (L. Canuet).

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Fig. 1. Magnetoencephalography (MEG) waveforms and topographic maps. Frequent sharp waves were identified on the MEG recording. Threedimensional whole-head topographic maps show the corresponding source localization of this epileptic activity over the left anterior temporal region.

has an excess kurtosis of zero. Epileptic activity was imaged by SAM(g2) for the 20–70 Hz frequency band, which is known to provide optimal image contrast for interictal spike activity.

SAM(g2) images were superimposed on T_1 -weighted MRIs, and compared with the patient's fluid-attenuated inversion recovery (FLAIR) MRI slices, as FLAIR has proved to be more sensitive for detection of cortical tubers than conventional T_1 - and T_2 -weighted images.⁷ The FLAIR MRI sequences revealed several cortical tubers distributed widely in the brain, and subependymal nodules (Fig. 2). The largest cortical tubers were located in the right frontal and left anterior temporal regions.

Despite the patient having multiple and bihemispheric cortical lesions, the SAM(g2) images clearly showed a single large tuber and surrounding epileptogenic tissue in the left anterior temporal cortex (Fig. 3). This finding was consistent with the seizure semiology, and with that of the simultaneous EEG, even though several MEG epileptic spikes without corresponding EEG spikes were observed.



Fig. 2. Fluid attenuated inversion recovery (FLAIR) axial MRI. Widespread cortical tubers were visualized. (A) Subependymal nodules can also be seen. (B–C) Large tubers were identified in the right frontal and left temporal regions. The arrow indicates the location of the epileptogenic tuber in the left anterior temporal cortex.



Fig. 3. Synthetic aperture magnetometry with excess kurtosis [SAM(g2)] images superimposed on the three plane T1-weighted MRI. Epileptic activity was imaged by SAM(g2) in the left anterior temporal region that corresponded with the location of a large tuber and surrounding epileptogenic tissue.

3. Discussion

To date, accurate localization of small and widespread epileptogenic lesions is still challenging. MRI cannot be used to determine whether a tuber has epileptic activity, and it is often unable to detect all tubers.⁸ SPECT often fails to detect epileptic foci in tuberous sclerosis.⁹ Ictal-EEG monitoring has an important role in identification of the primary epileptogenic zone in patients with multiple brain lesions, and it has been used with functional neuronavigation for the removal of epileptogenic lesions.¹⁰ Nevertheless, invasive EEG monitoring with intracranial electrodes is generally required. Hence the interest in applying the recently developed MEG analysis technique, SAM(g2), in tuberous sclerosis.

Several studies^{9,11} have shown that MEG is of value in the noninvasive localization of interictal spike sources in partial epilepsy, including tuberous sclerosis. Most of these studies have used dipole analysis. This method is laborintensive and time-consuming, as it requires the manual identification of spikes and considerable skill to minimize errors. Although SAM(g2) has not yet been extensively used in symptomatic epilepsy, SAM automated analysis appears to offer improved detection of irritable zones and beneficial volumetric and frequency descriptions compared to conventional dipole modeling.²

Our findings are consistent with those of other investigations,¹² which have provided evidence suggesting that large tubers correlate better with the EEG foci than small tubers; our SAM(g2) findings revealed that the epileptic activity in this patient arose from a large tuber and surrounding tissue. However, a large tuber involving the right frontal area failed to exhibit epileptogenicity. Frontal tubers have been reported to have the weakest correlation with epileptogenic foci.¹³

SAM(g2) analysis was a useful tool for localizing the epileptogenic tuber in this patient. This suggests that the combination of the brain anatomical data provided by MRI with the functional images of MEG and SAM(g2) analysis may help identify epileptogenic zones, and differentiate between epileptogenic and nonepileptogenic tubers in patients suffering from tuberous sclerosis. This may be particularly important when evaluating intractable epileptic patients for surgical treatment. Further application of SAM(g2) in large samples of patients with tuberous sclerosis and other focal epilepsies with multiple brain structural lesions may confirm this argument.

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Primary intracranial low-grade fibromyxoid sarcoma (Evans tumor)

Kagan Tun^{a,*}, Ozlem Ozen^b, Erkan Kaptanoglu^a, Oktay Gurcan^a, Ethem Beskonakli^a, Bulent Celasun^b

^a Department of Neurosurgery, Ankara Numune Education and Research Hospital, Ankara, Turkey ^b Department of Pathology, Baskent University, Ankara, Turkey

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Abstract

Low-grade fibromyxoid sarcoma was first described in 1987 as a rare soft tissue neoplasm characterized by a bland and deceptively benign histological appearance but with aggressive behavior. A 20-year-old male patient presented with a recent history of headache and seizure. A right frontal mass was detected on MRI and he was operated upon to remove the intracranial mass. Histological examination revealed mildly atypical fibroblastic cells embedded within a myxoid matrix. Nuclear atypia and pleomorphism were minimal, and necro-

^{*} Corresponding author. Present address: Haymana yolu, Karsıyaka mah. Gorkem Sitesi, 355 sok. No: 8, 06830 Golbasi, Ankara, Turkey. Tel.: +90 312 4840933.

E-mail address: kagantun@yahoo.com (K. Tun).