

Child Neurology: Functional Evaluation of the Dominant Hemisphere Using Magnetoencephalography Prior to Hemispherectomy

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Abstract

Rasmussen encephalitis is a devastating progressive inflammatory disorder that leads to debilitating neurologic deficits and intractable epilepsy. Surgical treatment of the dominant hemisphere has been attempted with hesitation, given the lack of effective diagnostic tools to determine the potential functional deficits from disconnection procedures.

Introduction

We present the case of a 15-year-old adolescent boy with Rasmussen encephalitis (RE), right hemiparesis, profound aphasia, and recurrent status epilepticus, who underwent language assessment using magnetoencephalography (MEG) before urgent hemispherectomy for epilepsy partialis continua. Cortical responses in the passive auditory task were localized to the left and right hemispheres at latencies of 200 and 380 ms, respectively, from the stimulation onset. The current density reconstruction analysis showed the sources at 380 and 200 ms in the right and left temporal-parietal junctions, respectively. These findings confirmed that the patient's language was represented bilaterally. Other tests conventionally used to assess cortical language function were not attempted, given his poor functional status and ongoing seizures. The left functional hemispherectomy resulted in seizure freedom and significantly improved language function.

The MEG-based evaluation of the language function could provide valuable information regarding cortical language organization before hemispherectomy in patients with RE. Such an approach of mapping the eloquent cortical functions can be used in other structural and autoinflammatory disorders of the brain, especially in patients who cannot participate in the conventional diagnostic modalities designed to assess critical brain functions such as language and memory.

The clinical features and pathophysiology of RE, a progressive autoinflammatory disease of the cerebral hemisphere, were initially described in 1958.¹ Drug-resistant epilepsy and progressive hemiplegia have become hallmarks of this syndrome, while functional hemispherectomy has been the only definitive treatment approach to alleviate seizures and prevent the progressive functional deterioration in RE. Given that most patients with RE are children and adolescents, the concern for disruption of the critical cortical functions in the developing brain during a disconnection procedure has limited the availability of hemispherectomy, especially in patients with RE in the dominant hemisphere.² The available noninvasive approaches to map the eloquent cortical functions before disconnection procedures, including fMRI and the Wada test, may be tolerated only by a few pediatric patients with advanced RE. Moreover, invasive procedures such as the Wada carry an increased risk of strokes, encephalopathy, allergic reactions, and carotid artery dissections.³ Therefore, newer noninvasive tools for the assessment of these patients are urgently needed.⁴

MEG has emerged as a valuable tool to assist in the localization of seizure focus before hemispherectomy for drug-resistant epilepsy; however, this technique has not been previously reported

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Glossary

ASD = antiseizure drugs; MEG = magnetoencephalography; RE = Rasmussen encephalitis.

for use in functional mapping of patients with RE.⁵ We provided the description of the clinical course and evaluation of a 14-year-old adolescent boy with an advanced RE who underwent MEG to assess his language function before urgent hemispherectomy for refractory focal motor status epilepticus. Despite the ongoing seizures during the MEG, the novel passive listening paradigm was successfully applied during the study and allowed an accurate assessment of this receptive language function. A successful disconnection procedure has led to postoperative seizure freedom and improved language function.

Case Report

A 14-year-old, right-handed adolescent boy who presented to the ambulatory clinic at our epilepsy center in 2013 was the product of a full-term pregnancy that was complicated by prolonged labor, fetal distress, and hypoxia at birth, leading to moderate developmental delays. He was initially evaluated at age 9 years after he developed seizures, which consisted of prolonged tonic-clonic events and frequent focal motor seizures characterized by right facial twitching and clonic movements of the ipsilateral upper and lower extremities. At his initial evaluation, he had a normal neurologic examination with intact cognitive and language function; his brain MRI was unrevealing. Despite being treated with 3 antiseizure drugs (ASDs), within 6 months, he developed refractory focal epilepsy and recurrent status epilepticus, requiring frequent hospitalizations to the intensive care unit. In addition to ASDs, the patient received treatment with vagal nerve stimulator, corticosteroids, and intravenous immunoglobulin for presumed autoimmune encephalitis; however, the immunotherapies allowed only temporary improvement of seizures.

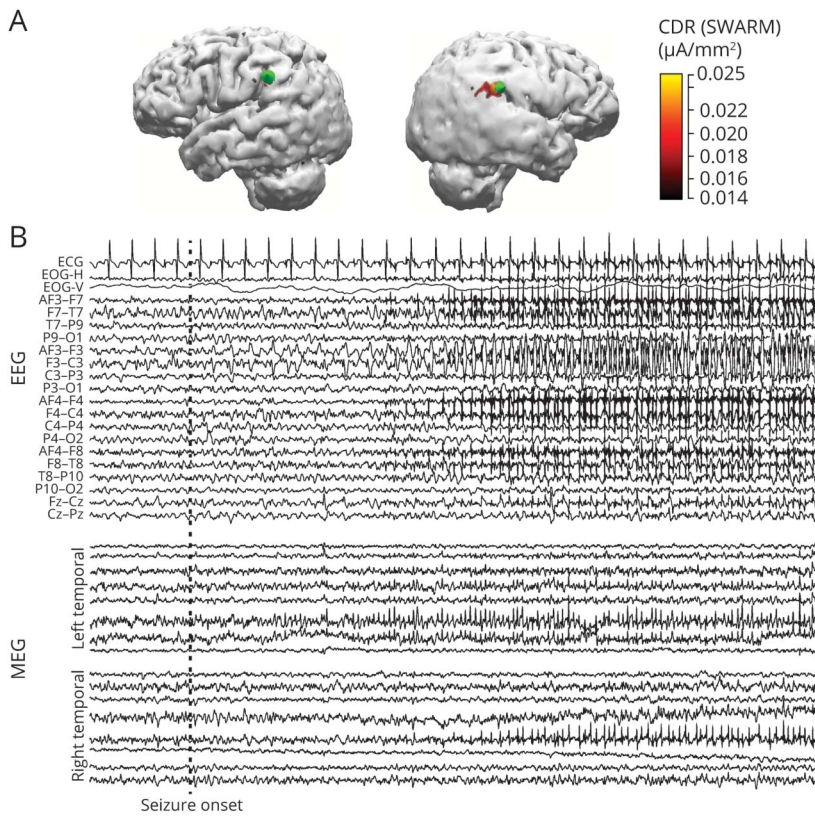
Within 12–18 months from seizure onset, the patient developed expressive and receptive aphasia, followed by right hemiparesis. His brain MRI revealed new signal hyperintensity in the left frontal inferior lentiform nucleus on a T2 sequence suggestive of possible inflammation. The open brain biopsy revealed patchy perivascular and parenchymal lymphocytic inflammation with microglial nodule formation, neuronophagia, astrocytic gliosis, and subpial gliosis suggestive of RE. Given the presence of independent epileptiform discharges and seizures in both hemispheres, corpus callosotomy was initially offered as palliative treatment, but it was declined by his parents because of the concern for cognitive deterioration. Twenty-four months after the diagnosis of RE, the patient developed *epilepsia partialis continua*, characterized by nearly continuous twitching of the right facial muscles and right upper and lower extremities. Seizures had impaired his ability to receive nutrition and led to rapid deterioration of his cognitive and motor functions. His assessment then

revealed moderate expressive and receptive aphasia and right hemiparesis. His MRI revealed moderate cortical atrophy in the left hemisphere. After a repeated discussion at the multidisciplinary epilepsy case conference, urgent functional hemispherectomy was recommended. His language function was assessed using the MEG-based passive auditory language paradigm. During the passive listening task, MEG cortical responses were recorded using the 306-MEG channel whole-head system (Neuromag, Helsinki, Finland), and the EEG data were recorded using a 60-channel prefabricated cap (Easy Cap, Germany). The patient was presented with 100 single-word audio clips from popular cartoons, and the words were delivered every 2 seconds spoken forward (words) and backward (nonwords). We created this paradigm using both forward and backward verbal stimuli to be able to specifically compute the differential average between these 2 stimuli addressing the semantic information and subtracting similar, but nonsemantic, auditory parameters. This difference wave form was then submitted for source localization analysis, the standardized low-resolution brain electromagnetic tomography-accurate minimum-norm method implemented in CURRY software (Compumedics Neuroscan, Charlotte, NC).

The source localization analysis revealed the receptive language function in the left posterior middle temporal gyrus at 200 ms and in right angular gyrus at 380 ms, further confirming the bilateral representation of language (Figure 1A). The reliability of these findings was unaffected by ongoing seizure activity during the test (Figure 1B). Given that the patient was unable to tolerate fMRI or the Wada test, the MEG findings were the only quantitative data available to prognosticate the potential language impairment after the proposed left hemispherectomy.

The patient underwent an uncomplicated functional hemispherectomy of the left hemisphere, which led to immediate seizure resolution. The histopathologic examination of the sections from the left frontal operculum and temporal lobe revealed diffuse microglial activation with scattered microglial nodules (Figure 2A), neuronophagia, and marked reactive subpial astrogliosis with regions of neuronal dropout and mild laminar disorganization, consistent with the diagnosis of longstanding RE. There was also patchy leptomeningeal, perivascular, and parenchymal chronic inflammation, consisting of predominantly T cells with increased CD8-positive T cells (Figure 2B). At his follow-up in epilepsy clinic at 1 month after surgery, his examination revealed an improvement in facial weakness, an antigravity strength in the right upper and lower extremities, a moderate improvement in expressive aphasia and significant improvement in receptive aphasia.

Figure 1 Magnetoencephalography and Surface Electroencephalography Data



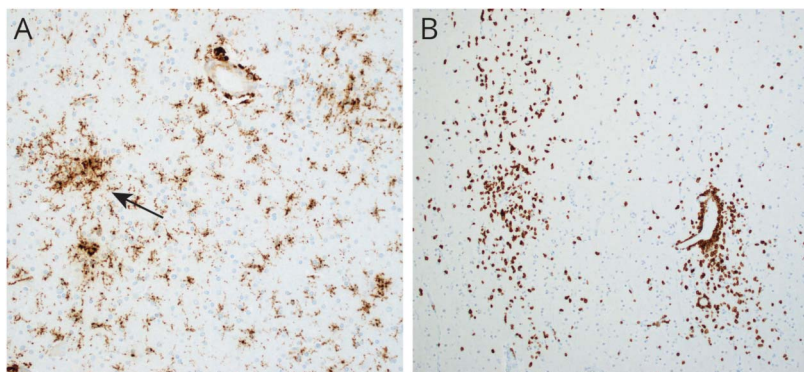
(A) Magnetoencephalographic (MEG) mapping of the language using the standardized low-resolution brain electromagnetic tomography (sLORETA)-accurate minimum-norm (SWARM). The maximum of SWARM activity (green arrow) was detected at on average 200 and 380 ms from the onset of auditory stimuli in the left and right hemispheres, respectively. Color scale represents the SWARM values. (B) Surface EEG and corresponding MEG data of a typical motor seizure that occurred during language mapping. The MEG waveforms represent ictal onset in the left temporal channels.

Discussion

We described a patient with RE in refractory status epilepticus, who had interictal activity in bilateral hemispheres, who underwent urgent hemispherectomy following the assessment of language function using the MEG. Previous studies have shown that dominant hemispherectomy is associated with significant worsening of the motor, memory, and language functions, and the tool to predict these deficits are limited.⁶ While numerous studies have explored the role of

MEG in language mapping, there is paucity in literature focusing specifically on its role in the pediatric surgical epilepsy population.⁷ With our case report, we were able to establish the need for such noninvasive assessment of language in presurgical evaluation of a pediatric patient, and interestingly, the MEG-based language mapping in our patient was accurate despite the ongoing seizure activity during the test. Seizures would preclude the completion of the task during other conventionally used procedures for mapping such as fMRI, the Wada test, or intracranial EEG.

Figure 2 Histopathologic Findings in Rasmussen Encephalitis



(A) Diffuse microglial activation and scattered microglial nodules (CD68 $\times 200$) with foci of neuronophagia. (B) Perivascular and intraparenchymal lymphocytic inflammation (CD3 $\times 100$).

While intracranial EEG monitoring is the most used approach for motor cortical mapping, historically, hemispheric language dominance has been determined using intracarotid amobarbital procedure, or often referred to as the Wada. Both these modalities remain invasive, and intracranial EEG is restricted to the areas where the electrodes are implanted. With the advent of newer noninvasive functional modalities such as fMRI and MEG, there has been renewed interest in exploring these tools to assess language, motor, and memory-related networks in the brain.^{7,8}

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Spriha Pavuluri, MD	Department of Neurological Sciences, University of Nebraska Medical Center, Omaha, NE	Drafting/revision of the article for content, including medical writing for content; major role in the acquisition of data; study concept or design; and analysis or interpretation of data

Appendix (continued)

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Olga Taraschenko, MD, PhD	Department of Neurological Sciences, University of Nebraska Medical Center, Omaha, NE	Drafting/revision of the article for content, including medical writing for content; major role in the acquisition of data; study concept or design; and analysis or interpretation of data

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