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CASE REPORT

Key Lesion Localization and Pre-Surgical Planning Using Magnetoencephalography in Patients with Medically Refractory Epilepsy Three Case Reports

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Abstract

Epilepsy is a common and debilitating disease affecting up to 50 million people worldwide. Nearly 30% of patients with epilepsy have disease refractory to treatment with medication alone. Even in medically refractory disease, neurosurgical resection can be curative when the epileptic focus is correctly identified. Several non-invasive techniques are available for epileptic focus localization and pre-surgical planning. These include electroencephalography (EEG), magnetic resonance imaging (MRI), and magnetoencephalography (MEG). Each of these techniques provides complementary information for precise lesion localization and targeted neurosurgical approach to minimize damage to important adjacent structures. We present three cases of medically refractory epilepsy. The cases show how the combination of EEG, MRI, and MEG allows for lesion localization and safe surgical planning in a variety of cases. They include epilepsy related to cortical dysplasia, grey matter heterotopia, and tumor recurrence. We emphasize the role of MEG and demonstrate how it can provide critical additional information which is not captured by conventional EEG and MRI alone.

Key Words: *Epilepsy; Magnetoencephalography; Magnetic resonance imaging; Magnetic source imaging*

Introduction

Epilepsy is a chronic debilitating neurologic disease affecting nearly 50 million people worldwide. Of those with epilepsy, nearly 80% live in low- and middle-income countries and many, go untreated and suffer from stigma and discrimination (WHO Fact sheet June 2019). Epilepsy is characterized by recurrent and unpredictable interruptions of normal brain function due to abnormal and excessive neuronal discharges [1]. While one third of patients with epilepsy have disease refractory to medication, neurosurgical treatment may be curative if the underlying epileptic focus can be correctly identified and removed [2]. For successful surgical treatment, comprehensive pre-surgical evaluation is important to localize the epileptic focus and to develop a precise surgical plan to minimize damage to important surrounding structures.

Currently, the "gold standard" for epilepsy lesion localization and pre-surgical planning is intracranial electroencephalography (iEEG); however, iEEG is invasive and is associated with morbidity

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(Burneo, 2006 #60). Several alternative non-invasive techniques are available and promising. These include video-electroencephalography (vEEG), magnetic resonance imaging (MRI), and magnetoencephalography (MEG). However, each technique has advantages and disadvantages [3].

Of the non-invasive techniques, MEG has shown particularly promising results. MEG is a technique that evaluates the small magnetic fields produced by neuronal electrical activity in the brain using extremely sensitive devices: "superconducting quantum interference devices" (SQUIDs). The data acquired from MEG can be combined with MRI data to produce a magnetic source image (MSI) which can be used to pinpoint the source of seizures. One benefit of MEG compared to other conventional imaging modalities is that no radiation or magnetic fields are emitted by the MEG scanner. Compared to other modalities, MEG has demonstrated high spatial and temporal resolution as well as high sensitivity. Spatial resolution of MEG has been reported as 2-3 mm compared to 7-10 mm for vEEG (Singh, 2014 #98), and sensitivity of MEG has been reported as requiring a minimum of 4 cm2 of cortical activity to detect an epileptic spike [4], whereas a minimum of 10 cm2 is required by vEEG [5]. Several prior studies have demonstrated MEG to accurately locate epileptic zones and have shown a high concordance with iEEG [6-8]. Finally, when used in the context of surgical planning, several studies have shown MEG to be associated with favorable post-surgical outcomes [9,10].

We present three cases in which the combination of MEG with vEEG and MRI provided complementary information for successful epileptic lesion localization and pre-surgical planning that may not have been possible without the added information obtained from MEG. The cases span a variety of causes for epilepsy including cortical dysplasia, grey matter heterotopia, and brain tumor recurrence.

Case Report

Case 1

A 60-year-old right-handed male with history of childhood seizures presented with refractory epilepsy. Although his seizures initially developed during childhood, his seizures subsided for a period but recurred when he was 36 years old. When his seizures recurred in adulthood, he was treated medically with phenytoin, but eventually his seizures became more difficult to control and he developed side effects related to medication use including tremor, dizziness, and irritability. At the time of presentation, the patient reported having up to 5 seizures a day. Studies including vEEG, MEG, and MRI were performed for further evaluation and for potential identification of a seizure focus (Figure 1). Initial vEEG demonstrated gross seizure lateralization to the left side of the brain but poor localization. Subsequent MEG demonstrated more specific seizure localization to the left temporal lobe and left superior temporal gyrus. Follow up MRI was performed and data from the MEG and MRI was combined to create MSI maps which demonstrated structural localization to the left superior temporal gyrus. Using the MSI structural localization, the MR images were reviewed and a subtle area of focal cortical dysplasia in the left superior temporal gyrus corresponding to the patient's seizure focus was identified which may not have been recognized using MR imaging alone.

Case 2

This was a 55-year-old right-handed female presented with a history of medication resistant seizures. She first started having seizures at age 50. Her seizures were controlled with lamotrigine for a period, but she began having breakthrough seizures despite medication use. At the time of presentation, she reported 1-3 seizures per month, often with a catamenial component. For further evaluation, vEEG, MRI, and MEG were performed (Figure 2). Initial vEEG demonstrated lateralization to the right hemisphere, but no clear localization. Subsequently, MRI was performed which demonstrated subependymal gray matter heterotopia along the right temporal horn and posterior body of the right lateral ventricle, compatible with the patient's seizure source. MEG was subsequently performed for confirmation of the seizure source and for surgical planning. Combining MEG and MRI data, MSI maps were created which confirmed the seizure source at the area of subependymal gray matter heterotopia. Using the combined MEG and MRI data, MSI functional maps of the nearby Wernicke's

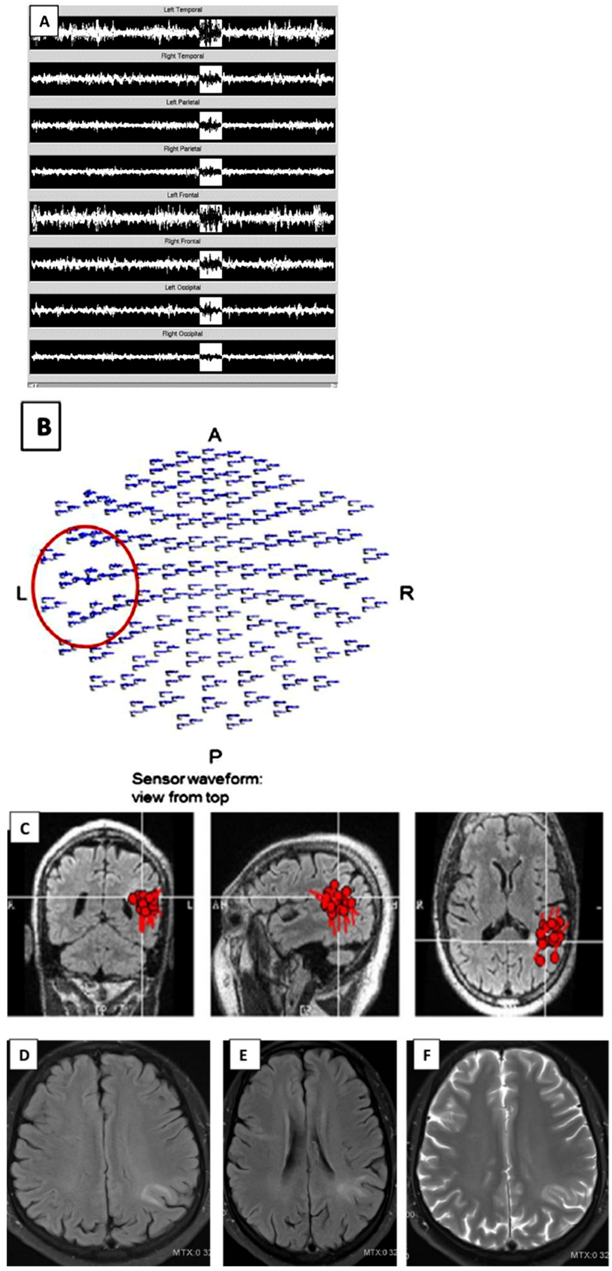

Figure 1) *(A)Initial vEEG demonstrates left-sided lateralization with corresponding epileptiform spikes in the left temporal and parietal regions. (B) Topologic map generated from MEG acquisition demonstrates lesion localization to the left superior temporal gyrus where there are corresponding epileptiform spikes. (C)MSI map, generated from combined MEG and MRI data, demonstrates structural localization to the left superior temporal gyrus with multiple epileptiform spikes (red dots) localizing to the left superior temporal gyrus. (D, E, F) Axial T1-weighted MR image demonstrates subtle cortical thickening and gray-white blurring in the left superior temporal gyrus compatible with focal cortical dysplasia, corresponding to the patient's seizure focus.*

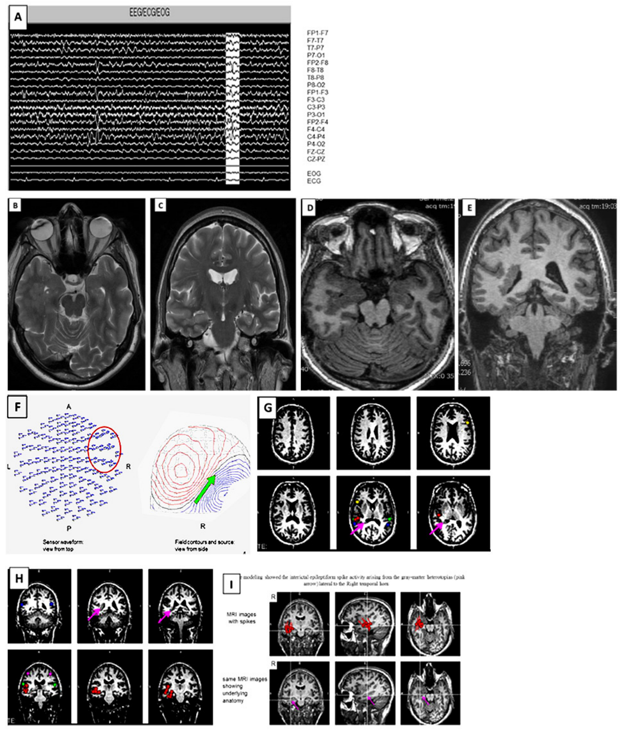

Figure 2) *(A) Initial vEEG demonstrates lateralization to the right hemisphere with epileptiform spikes in the right temporal and frontal lobes. (B), (C), are T2W MRI whereas (D), (E) are 3D Vol SPGR MRI showing extensive gray matter heterotopia along the temporal horn and posterior body of the right lateral ventricle-right ventricular heterotopia (curved arrows) with several adjacent areas of abnormal overlying cortex, in the right temporal and posterior frontal lobes. (F) demonstrates MEG raw with a right temporal spike. (G), (H) Key shows; Red-spikes, blue-wernicke's mapping, purple-median nerve response, green-auditory response, yellow-Broca's mapping. Stimulation of left and right median nerves(purple) elicited cortical responses with age-appropriate latency and distribution in the right and left postcentralgyri. The language mapping task indicated the receptive-language-specific cortex in the patient localized to the posterior aspect of the left and right superior temporal gyri (Wernicke's area-blue) whereas the expressive language-specific cortex (Broca's area-yellow) using picture naming localized appropriately to the left and right inferior frontal gyri. (I) shows abnormal spontaneous MEG recording. Frequent epileptiform spikes were observed during spontaneous MEG recordings when the patient was resting (46 spikes observed over 50 minutes). Source modeling showed the interictalepileptiform spike activity arising primarily from the prominent gray-matter heterotopias (red) lateral to the right temporal horn and the more-lateral associated heterotopic cortex; some spikes from the adjacent anterior right hippocampus; (purple arrows) and some spikes from the more posterolateral aspect of the right temporal lobe, some of which are close to the subtle heterotopic gray-matter of the infero-postero-medial right insula. No propagation of the spikes was observed.*

area, auditory response regions, and median nerve response regions were created which allowed for the development of a precise surgical plan to spare sparing these critical functional areas of the brain during surgery.

Plan

A surgical plan of Right temporal lobectomy was made.

Case 3

A 55-year-old right-handed male presented with medically refractory epilepsy after multiple surgeries and treatments related to a brain tumor. Originally, he was diagnosed with a right parieto-occipital ependymoma which was surgically excised followed by whole brain radiation. Years later, he returned with increasing headaches at which time a brain MRI demonstrated a cyst in the previous area of resection. A porencephalic cyst fenestration was performed, but the patient continued to have seizures. Follow up MRIs eventually demonstrated new areas of suspicious enhancement in the right parietal and occipital regions and the patient underwent thermo-ablation of the enhancing regions. After thermo-ablation, he continued to have seizures approximately 6 times per day which lasted from several minutes to 1.5 hours. Given the extensive areas of post-treatment changes, it was difficult to discern the exact location of the seizure focus by MR imaging alone. Therefore, vEEG, MRI, and MEG were performed to precisely locate the seizure focus and to map adjacent functional areas (Figure 3). As expected, initial vEEG demonstrated lateralization to the right hemisphere. Follow up MRI and MEG showed localized epileptiform spike activity arising from the right temporo-occipital junction corresponding to an area suspicious for tumor recurrence. A surgical plan was developed for resection of the right temporo-occipital seizure focus at the area suspicious for tumor recurrence. The additional information provided by MEG allowed for precise identification of the true seizure focus among extensive areas of post-procedural change which could have potentially contributed to seizure, and MEG allowed for a surgical plan sparing the important adjacent functional region.

Plan

Right temporo-occipital surgical resection of the lesion was suggested with a plan to spare the functional areas.

Discussion

We present three cases which highlight how the combination of EEG, MRI, and MEG allows for precise lesion localization and pre-surgical planning in patients with medically refractory epilepsy who require surgical intervention. These cases exemplify how EEG, MRI, and MEG are complimentary tools, and how the added information from MEG can allow for precise lesion localization and allow for tailored surgical approaches that spare important surrounding functional regions which may not be achievable using vEEG and MRI alone.

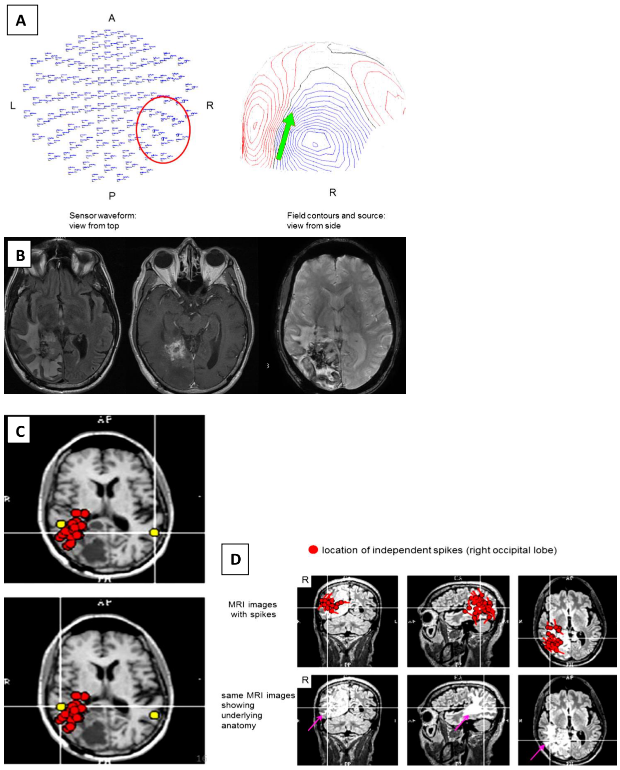

Figure 3) *(A) Topologic map generated from MEG acquisition demonstrates seizure focus localization to the right temporo--occipital region where there are corresponding epileptiform spikes. (B) T2 FLAIR, T1 W with contrast and T2-GRE demonstrate vasogenic edema in the right temporo-occipital region with a region of enhancement in the right temporo-occipital region as well as central cavitation which may be related to tumor recurrence and/or post thermal-ablation changes. (C) and (D) are axial MSI maps that demonstrate multiple epileptiform spikes (red dots) localizing to the right temporo-occipital region at the area suspicious for tumor recurrence. Key: Red-spikes, blue-Wernicke's mapping, purple-median nerve response, green-auditory response, yellow-Broca's mapping.*

Magnetoencephalography (MEG), provides a new non-invasive tool for epilepsy localization [11]. Prior studies have shown that MEG is useful for brain mapping and subsequent lesion localization (Colon, 2018 #114). Our case series, however, highlights individual scenarios where the lesion may be completely missed on MRI, functional information allows for surgical sparing, and discrete epileptic foci can be isolated from a background of abnormality.

The most common pathologic entity encountered in patients with intractable temporal lobe epilepsy is mesial temporal sclerosis. The other major group of pathologies in which MRI has made enormous contributions to epilepsy is in malformations of cortical development (MCDs). [11]. Focal lesions such as focal cortical dysplasia (FCD) are common developmental pathologies in children with extratemporal lobe seizures and recognition of these lesions can have an important bearing on the management and prognosis. MRI can accurately define diffuse malformations such as lissencephaly, band heterotopia, and periventricular nodular heterotopia as seen in figure 2.

MEG is superior to EEG, in such a way that unlike electrical potentials measured with EEG, which are attenuated in strength and spatially blurred by tissues between brain and scalp surface, magnetic fields are minimally affected by intervening tissue layers [12]. The main advantage of MEG over EEG is based on greater precision and accuracy of the observed signal at the scalp such that it allows cerebral sources to be modeled more simply; and this in turn allows for more clinically usable and reliable localization of brain activity [13]. The clinical applications of MEG depend mostly on the ability to estimate the dipole source, which provides noninvasive information on the normal or abnormal function of discrete cortical areas.

The Video EEG Monitoring Test allows the patient to be constantly monitored over a video screen so that brainwave activity during the time a seizure or spell is occurring. The synchronous display of the ictal v EEG pattern aids in confirming a seizure disorder, classify seizure type, assess seizure frequency and precipitating factors, and for surgical localization (Cascino, 2002 #100) however MEG MRI has better precision. In all three cases presented above, v EEG helped in lateralization to the hemisphere in question and poor localization however, MEG MRI showed lesion localization because it has better precision. MEG has better resolution than EEG, but the combination of MEG with MRI (MSI) is what gives the best localization. MEG is also reliable for localization of spike sources in patients with no lesion visible on MRI, as seen in case 1, on T1W images, where no lesion was shown, and in cystic lesions (post-traumatic encephalomalacia with prior surgical resection) in which MRI localization is ambiguous, as seen in case 3, and in patients with lesions of undetermined significance as seen in case 2 of heterotopia. The most important difference between MEG and EEG is the accuracy of source localization.

In a large study, Magnetic source imaging (MSI) [14] demonstrated a sensitivity of 89% for lobar localization and the results for extratemporal cases being even superior to those with temporal lobe surgery. MSI supplied additional information in 35% and information crucial to final decision making in 10% {Stefan, 2003 #99}. MSI is increasingly useful in surgical planning for tumors or other epileptogenic lesions, such that costly invasive procedures and postoperative neurological deficits can be minimized; this was demonstrated in all the three-case series whereby lesion localization was done for surgical planning thus sparing the functional areas.

With the above advantages and the fact that MEG is noninvasive, it is a very fundamental investigation in epilepsy however, the main limitation is the financial cost.

Conclusion

These case series demonstrate how the combination of MEG with conventional non-invasive seizure evaluation tools including vEEG and MRI allow for critical additional information to be captured which can greatly impact treatment and patient morbidity, information which may not be captured by conventional methods alone. The magnetic source imaging allows for better image localization and precision in brain mapping thus allowing for sparing of the functional areas during surgery.

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