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Different cortical involvement pattern of generalized and localized spasms: A MEG study

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Abstract

We report successful magnetoencephalography (MEG) recording in a child who had generalized epileptic spasms (ES) as well as ES involving legs only during the recording. MEG source localization results demonstrated that 1) the origin of the interictal epileptiform discharges and of both types of ES were the same, i.e. right parietal region, and 2) the two types of ES involved different cortical spread patterns, i.e. epileptic involvement localized to right parietal region in spasms of legs, and rapid diffuse involvement in generalized spasms. The MEG in this case provided new insight about the mechanisms of the two types of ES, i.e. both were generated from the same focus and, in generalized ES, abnormal excitation spread to cortical areas diffusely.

Keywords

Epileptic spasms; Magnetoencephalography; Single dipole analysis; Dynamic statistical parametric mapping

Introduction

The neurophysiological mechanism underlying intractable epileptic spasms (ES) is not yet fully understood. ES may arise from diffusely damaged immature brain [1], but evidence from successful epilepsy surgery suggests that ES are a peculiar form of secondarily generalized seizures originating from focal or multifocal abnormal cortex during a critical developmental period [2].

Magnetoencephalography (MEG) is a noninvasive technique that can determine the intracranial source responsible for extracranially measured magnetic fields, usually employing an equivalent current dipole (ECD) model [3]. MEG has better spatial resolution

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than electroencephalography (EEG) because the magnetic field is not affected by the differences of conductivity in the intervening tissue layers, whereas electrical source localization is made difficult (and sometimes inaccurate) by the necessity to account for these boundaries. When we are fortunate enough to capture a seizure during a MEG recording, investigation of the magnetic field manifestations at the beginning of the seizure can provide valuable information about the ictal onset zone.

Clinical MEG recordings are ordinarily limited to an hour or two, so it is unusual to record a seizure during MEG testing. In addition, the movement artifacts that occur frequently with seizure onset can be detrimental to the quality of MEG recording [4]. There are relatively few papers reporting ictal MEG [4], but the referral pattern at our epilepsy center yields ictal recordings in approximately 9% of our patients [5]. Our higher yield of MEG-recorded seizures than at most centers provides unique information and, to our best knowledge, this is the first report of ictal spasms recording during MEG.

We report successful MEG recording in a child who had generalized ES as well as ES involving the legs only. This recording has provided new insight into the different mechanisms producing the two types of ES.

Case report

A 2 $\frac{3}{4}$ year old boy began to have seizures at age 5 months, manifest initially by occasional head nods. His birth and development history had been unremarkable up to that time, and his family medical history was marked only by a maternal grandfather who had seizures only twice in his life. At the of age of 6-7 months, however, his development seemed to stagnate and he began to have 50-100 spells per day. EEG findings were compatible with hypsarrhythmia without a dominant side or a focus. A full investigation, including studies of blood cerebrospinal fluid disclosed no clear etiology. He was diagnosed with West syndrome and ACTH therapy was started. Although ACTH therapy had to be stopped due to hypertension and other side effects, valproic acid eliminated the spasms associated and normalized the EEG at age 9 months at least transiently. Spasms reappeared when he was approximately 1 year old, and have continued 25-50 times per day despite various antiepileptic medications. Nevertheless, his development has continued normally up to the time of examination.

The patient has had two types of ES; one involving legs only and manifest by a subtle flexion of both thighs and which did not disturb his daily life, and the other involving the head and all four extremities. MRI and positron emission tomography were negative. Simultaneous EEG and MEG were recorded and analyzed, for the most part according to the technical details described elsewhere [3], but also including continuous movement compensation [6]. Interictal epileptiform discharges (ED) were seen on the EEG with broad negativity involving the right posterior quadrant, and localization using ECD analysis on the MEG signals showed dipoles estimated over right parietal region (Fig. 1a). In addition to the interictal ED, our recording captured generalized ES as well as ES involving legs only. ES involving legs only was associated with a focal spike followed by slow wave discharge; a dipole analysis was applied to the spike component. The dipoles correlated with ES

involving just the legs were located in the same area as those of the interictal ED (Fig. 1b). For those ES involving the whole body (Fig. 1c), the MEG showed a focal spike followed by diffuse fast wave discharges, which then became obscured by movement artifacts within 200 msec. For these widespread discharges dynamic statistical parametric mapping algorithm (dSPM) analysis was applied to the initial more focal spike. dSPM was employed because ECD analysis is not appropriate for the non-dipolar field distributions associated with these diffuse discharges, and the source distribution model inherent to dSPM is known to be useful to represent characteristics of a whole-brain magnetic field [7,8]. This algorithm employs a noise-normalized minimum norm estimate producing an F-distributed estimate of the cortical current to statistically identify the locations where current dipolar strength is increased relative to the noise level [9]. The dSPM map of the initial phase of ictal onset (time point #1 in Fig. 1c) showed the most prominently activated onset area in the right parietal region. The later phase of the seizure, approximately 100ms later, of late phase of ictus (time point #2 in Fig. 1c), showed expansion of the activated area on the dSPM map. At the therapeutic strategy team meeting, it was agreed that seizures came from right parietal region, and the patient has since been treated continuously with medication.

Discussion

In this patient, source localization employing ECD analysis placed the epileptic activity responsible for the interictal ED and the ictal ES involving the legs in the identical area, i.e. the right parietal region. This suggests that the ES involving the leg were secondarily generalized seizures originating from the area where the interictal ED were generated. Tanoue et al. evaluated two cases with peculiar spasms involving unilateral leg [10]. From their observation using EEG, MRI and SPECT, they concluded that focal spasms result from focal epileptic activity from primary motor cortex. Our case supports their observation and with the high spatial accuracy of MEG provides more convincing evidence for a focal source of ED associated with localized ES.

Although the prominent regions of activation are both in the right parietal area, ictal MEG recordings of the two types of ES showed different patterns of cortical excitation.

The generalized spasms had much more diffuse activation in multiple cortical areas. We speculate that both types of spasms were generated from the same region but that the generalized ES involved more diffuse cortical spread than the ES involving legs only. About the mechanism of cortical involvement in spasms, Asano et al. studied the pattern of ES using electrocorticography [11]. They evaluated 62 patients; in 42 there was a leading spike prior to the spasm, and in the other 20 no leading activity preceded the spasm. They found that in the patients with the leading spike, resection of cortex creating the spike was significantly related to good seizure prognosis. Their observation is consistent with implication from our dSPM results that the right parietal region was responsible for the generalized spasms. Recently, Nariai et al. showed that ictal propagation to the sensorimotor cortex was associated with prominent body jerking in patients with epileptic spasms [11]. They evaluated 636 epileptic spasms seen in 11 children with electrocorticography and assessed the spatial and temporal characteristics of ictal high frequency oscillations (HFOs) in relation to the onset of spasms. They showed that ictal motor symptoms, or spasms, were

related to the presence of HFOs in the Rolandic cortex [12]. The observations from MEG in our case are consistent with their ECoG finding; i.e. generalized spasms represent diffuse cortical spread involving the Rolandic cortex, whereas spasms involving legs only would be related with preservation of the Rolandic cortex.

MEG recordings during ictal spasms have not been previously reported most likely because successful recordings can only be accomplished when movement is subtle or absent[4]. In our patient, even the generalized spasms were associated with only subtle head movements, and continuous head position monitoring compensated for this subtle motion [6]. This case demonstrates how MEG can be used as a tool for non-invasive evaluation of the neurophysiological profile of ES.

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Fig. 1.

EEG and MEG waveforms (top) and source analysis of (a) interictal epileptiform discharge (ED), (b) epileptic spasm (ES) involving legs, and (c) generalized ES (bottom). For the localized discharges in (a) and (b), single equivalent current dipole analysis was applied, and in (c) dynamic statistical parametric mapping (dSPM) was applied due to the widespread, non-dipolar magnetic field pattern.

(a and b, bottom) Waveform and contour maps: Arrows on the contour maps indicate the estimated dipole at the time point indicated by the broken line on the waveform. Solid lines indicate efflux of magnetic field from the brain surface, and dotted lines indicate magnetic field influx. MRI: The circle represents the dipole location and the bar shows the orientation.

(c, bottom) dSPM maps during the ictus at two timepoints (#1 and #2) approximately 100 ms apart. The whiter the color, the more significant is the activation.

Both the dipole localized from the interictal ED and the dipole related to the ES of legs only are localized to the right parietal region. The dSPM map of the early part of the generalized ictal ES (#1) showed the most prominent activation in the same right parietal region (dotted circle), while widespread cortical activation is seen in the map of the late phase (#2).