Utilization of magnetoencephalography (MEG) in pre-surgical workup of patients with hypothalamic hamartoma

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Background & Objective

Hypothalamic hamartomas (HH) are classically associated with gelastic seizures but there can be a wide spectrum of seizure types[1]. There is clear evidence supporting the epileptogenicity of the HH, however focal seizures arising from neocortex have also been seen. Surgical resection of the HH results in seizure freedom rates of 50-60% with some patients having a partial improvement and others having interval development of focal neocortical seizures [2–4]. This would seem to support the concept of secondary epileptogenicity in this patient population[5].

It is currently unclear which patients will have cessation of seizures with resection of their HH and which will have secondary sites of epileptogenicity. In most centers, the pre-operative work up of HH patients mainly relies on the use of MRI and EMU monitoring [6]. However, EEG monitoring in HH patients produces highly variable results and is often non-localizing or normal [5,6]. At our institution in patients who had evidence of seizures or potential epileptogenicity outside the HH, we have utilized MEG.

MEG is not routinely used in HH patients and has not been endorsed as part of the traditional workup in HH patients in the ILAE guidelines [6]. However, MEG offers superior spatial and temporal resolution in detecting neocortical epileptogenic activity [7,8]. In this study, we present our institutional experience in utilization of MEG in a cohort of HH patients.

Methods

We performed a retrospective review of patients at Texas Children's Hospital with intractable epilepsy secondary to non-syndromic HH, who had MEG performed and underwent laser ablation or resection of the HH. Patients included in this study underwent a pre-operative workup including EMU monitoring, MEG and MRI scans. Patients with clearly identified MRI radiographic abnormalities distinct from the HH were excluded from this study. Patients had a minimum of three month follow-up from the time of surgical procedure.

Case 5

Clinical course: 4-year 8-month-old male with a history of hypothalamic hamartoma and multiple refractory seizures since birth. At one week of age he developed generalized tonic-clonic (GTC) seizures lasting 10-20 seconds followed by post-ictal lethargy. At one year of age, he developed gelastic seizures with unprovoked laughing followed by agitation for 10 seconds. Both seizures occurred in succession with GTCs occurring before the gelastic seizures more than 50% of the time. At two years of age, he underwent an MRI which revealed the presence of a hypothalamic hamartoma. Pre-operative workup included EEG & MEG which revealed generalized spikes without a clearly identified cluster. He underwent stereotactic laser ablation of the hypothalamic hamartoma at age 3. Post-operatively, the gelastic seizures stopped immediately while the GTC seizures gradually decreased over two months. At last follow-up, he was seizure free for eight months.

MEG findings: Scattered spikes without a clearly identified cluster.

Outcome: Seizure free

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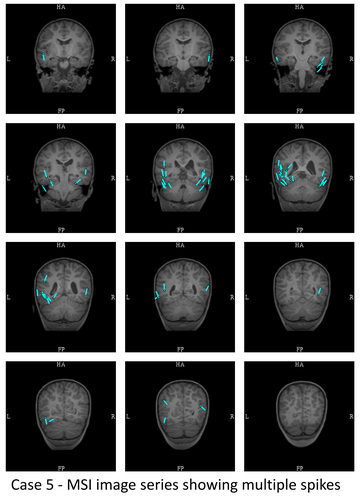
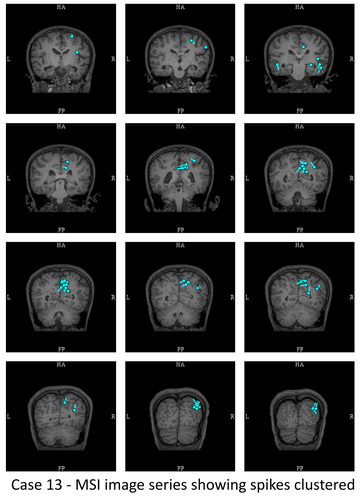
Table 1 – Individual Patient Results

Case	Age (yrs)	Gender	Seizure types	Duration of epilepsy (yrs)	MEG	EEG	Surgery	Outcome
1	2	F	gelastic, complex partial	6	-	+	SLA	Seizure free
2	3	M	gelastic	1.5	-	-	SLA	Seizure free
3	3	M	gelastic, partial	2	+	+	SLA x2	Ongoing seizures
4	3	M	gelastic	3	+	+	SLA	Ongoing seizures
5	4	M	gelastic, tonic	3	-	-	SLA	Seizure free
6	5	M	gelastic, tonic	2.5	-	-	SLA	Seizure free
7	6	M	gelastic, complex partial	3	+	+	L ATL, SLA	Seizure free
8	8	F	gelastic, complex partial	6	+	+	SLA x2	Seizure free
9	9	F	gelsatic, GTC	5	-	-	SLA	Ongoing seizures
10	9	M	gelsatic, GTC, complex partial	4	+	-	SLA	Ongoing seizures
11	10	M	gelsatic, GTC	9	-	+	SLA	Ongoing seizures
12	10	F	gelastic	9	+	+	SLA	Ongoing seizures
13	11	M	gelastic, tonic	7	+	+	SLA x2	Ongoing seizures
14	12	F	gelastic, tonic	6	+	+	SLA	Ongoing seizures
15	13	F	gelastic	12	-	-	SLA	Seizure free
16	13	F	gelastic, GTC, complex partial	7	-	-	SLA	Ongoing seizures
17	14	M	gelastic, GTC, absence	12	+	+	SLA	Seizure free
18	16	F	gelastic, GTC	5	+	+	SLA	Ongoing seizures

SLA: stereotactic laser ablation



Case 5 - MSI image series showing multiple spikes without a clear cluster.



Case 13 - MSI image series showing spikes clustered in right lateral occipital and parietal lobes.

Case 13

Clinical course: 11-year male with global developmental delay, intractable focal epilepsy, and a hypothalamic hamartoma. He began having unprovoked GTC seizures at age 3 that were refractory to medications. Within a year, he developed gelastic seizures with worsening GTC frequency. At age 7, he was found to have a hypothalamic hamartoma on MRI and subsequently underwent the first stereotactic laser ablation of the hamartoma at an outside hospital. He significantly improved post-operatively but began experiencing worsening seizures within six months. He presented to TCH at age 10 and underwent a second laser ablation of the hamartoma. Pre-operative workup included EEG & MEG which revealed spikes clustered in the right lateral occipital and right interhemispheric parietal lobes. At six months follow-up, he no longer had gelastic seizures but continued to have tonic and complex partial seizures with little change in frequency.

MEG findings: Spike clusters in right lateral occipital and right interhemispheric parietal lobes.

Outcome: Ongoing complex partial and tonic seizures, without gelastic seizures.

Results

A total of 18 patients were included (8 F, 10 M) with an average age of 8.2 years old (range 3-16). All patients had at least three months of follow-up from surgery (range 4-32 months). Ten patients had a positive MEG study that identified a source of focal (or multifocal) neocortical epileptogenicity. Of these patients, seven patients (70%) had ongoing seizures after surgical treatment of their hypothalamic hamartoma. Eight patients had a negative MEG study, of which three patients (37.5%) had ongoing seizures. The result was not statistically significant ($p = 0.34$).

Conclusions

We present our institutional experience of MEG in the presurgical workup of hypothalamic hamartomas. While no statistically significant findings were present, likely due to our small sample size, there does seem to be a suggestion that patients with a negative MEG result were more likely to be seizure free post-operatively, while those with a positive MEG result were more likely to have ongoing seizures. We would propose that in cases where there is evidence of more extensive epileptogenicity than the HH, a MEG may be a worthwhile study to better characterize the extent of epileptogenicity and potentially stratify patient outcomes. Further studies on a larger scale and of a prospective nature will be essential to validate these findings.

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