PAPER

Magnetoencephalographic spike sources associated with auditory auras in paediatric localisation-related epilepsy

I S Mohamed, H Otsubo, E Pang, S H Chuang, J T Rutka, P Dirks, S K Weiss, O C Snead

J Neurol Neurosurg Psychiatry 2006;**77**:1256–1261. doi: 10.1136/jnnp.2005.083089

See end of article for authors' affiliations

Correspondence to: H Otsubo, Division of Neurology, Department of Pediatrics, The Hospital for Sick Children, 555 University Avenue, Toronto, ON M5G 1X8, Canada; hiroshi.otsubo@sickkids.ca

Received 3 November 2005
Revised 6 June 2006
Accepted 21 July 2006
Published Online First 4 August 2006

Objective: To characterise magnetoencephalographic spike sources in paediatric patients with auditory auras and recurrent localisation-related epilepsy.

Methods: Six patients (four boys and two girls (ages 7–14 years) were retrospectively studied. All patients had auditory auras as part of their initial seizure manifestation, including four patients who underwent previous brain surgery. Scalp video electroencephalography and magnetoencephalography (MEG) were carried out in six patients, intraoperative electrocorticography in three patients and extraoperative intracranial video electroencephalography in one patient. MEG auditory-evoked fields (AEFs) were studied in four patients.

Results: Three patients had elementary auditory auras, one had complex auditory aura and two had both complex and elementary auras. All six patients had clustered MEG spike sources with coexisting scattered spike sources. MEG clusters were localised in the superior temporal gyrus with surrounding scatters in four patients (two left and two right); two patients had scattered spikes in the superior temporal gyrus in addition to clustered MEG spike sources in the left inferior and middle frontal gyri or parieto-occipital region. AEFs were located within an MEG cluster in one patient and within 3 cm of a cluster in two patients. Surgical resection, including the regions of MEG clusters, was carried out in four patients. Three of four patients who had previous surgeries were seizure free at 2 years after excision of the MEG cluster region.

Conclusions: MEG spike sources clustered in the superior temporal gyrus in six patients with auditory auras. These spike sources were in close proximity or seemed to engulf the magnetic AEF. Areas with MEG spike sources contained the residual or recurrent epileptogenic zone after incomplete cortical excision for lesional epilepsy.

Auditory auras are considered to be reliable indicators of temporal-lobe seizure onset.[1–4] Epileptic auditory phenomena include elementary and complex auras. Elementary auditory auras are simple sounds, such as buzzing or ringing, provoked either by direct cortical stimulation of the medial part of Heschl's gyrus or by spontaneously elicited epileptic discharges involving the primary auditory cortex.[3 5] Complex auditory auras can be hallucinations or illusions of sounds. The auditory hallucinations consist of elaborate phenomena of music or voices, whereas the illusions consist of modifications of intensity, tonality or resonance of surrounding voices. Unlike elementary auditory auras, which have a focal origin on the auditory cortex, complex auditory hallucinations and illusions tend to be elicited from more widespread areas involving the planum temporale or the lateral part of the superior temporal gyrus.[3 5]

Magnetoencephalography (MEG) localises the sources of intraneuronal electric currents that contribute to extracranial magnetic fields. MEG analysis uses an equivalent current dipole (ECD) model overlaid on to magnetic resonance images to localise sources of interictal epileptiform discharges. This technique can provide unique information about epileptogenic zones as reflected by interictal epileptiform discharges in patients with neocortical localisation-related epilepsy secondary to lesions.[6 7] As magnetic fields are comparatively unaffected by the different electrical conductivities of the brain, cerebrospinal fluid, skull and skin, MEG can non-invasively and accurately localise the residual epileptic spike sources in patients with recurrent seizures, even in the presence of skull defects after brain surgery.[8 9]

In a previous article,[10] we reported on the significance of ear plugging as a behavioural manifestation of auditory auras in three patients. We now report on the localising value of MEG spike sources in six patients with localisation-related epilepsy and auditory auras as the initial manifestations of their seizures. To our knowledge, this is the first report of MEG spike sources associated with auditory auras in paediatric patients with epilepsy.

PATIENTS AND METHODS

Patients

We retrospectively studied six patients (four boys and two girls), whose ages ranged from 7 to 14 years. All had auditory auras as initial manifestations of their seizures. All patients underwent magnetic resonance imaging (MRI), MEG and scalp video electroencephalography (EEG) during their presurgical evaluations at the Hospital for Sick Children, Toronto, Ontario, Canada, between 2001 and 2004. Three patients (numbers 2, 4 and 6) also underwent intraoperative electrocortigraphy (ECoG), and one patient (number 1) underwent extraoperative intracranial video EEG (IVEEG). Four patients (numbers 1–4) did not undergo an MEG study before their initial surgery but, owing to postoperative seizure

Abbreviations: AEF, auditory-evoked field; DNET, dysembryoplastic neuroepithelial tumour; ECD, equivalent current dipole; ECoG, electrocortigraphy; EEG, electroencephalography; FLAIR, fluid-attenuated inversion recovery; IVEE, intracranial video electroencephalography; MEG, magnetoencephalography; MRI, magnetic resonance imaging; MST, multiple subpial transection

recurrence, had MEG testing before their subsequent surgery. Parents of these paediatric patients gave informed consent for all procedures.

MRI procedures

MRI studies used a GE 1.5-T Signa Advantage 5.6 unit (GE Medical Systems, Milwaukee, Wisconsin, USA). The epilepsy protocol included the following sequences: sagittal T1-WI, axial and coronal dual-echo T2-WI, coronal fluid-attenuated inversion recovery (FLAIR) and coronal volumetric three-dimensional Fourier transform gradient echo.

EEG studies

All patients underwent prolonged scalp video EEG recordings. For the digital EEG, we placed 19 scalp electrodes according to the International 10–20 scalp–electrode system, with a single reference electrode. Additionally, we used subtemporal electrodes in two patients (numbers 5 and 6) and zygomatic and sphenoidal electrodes in one patient (number 4; BMSI System 4000 and 5000, Nicolet, Madison, Wisconsin, USA, and Stellate, Harmonie, Montreal, Quebec, Canada).

Simultaneous MEG and EEG recordings

MEG studies used a whole-head Omega 151-channel gradiometer system (VSM MedTech, Port Coquitalam, British Columbia, Canada). The details of MEG acquisition and analysis are as described previously.[11 12] We defined the MEG spike source location and orientation for each spike as that of a single ECD fit from the earliest phase of each spike meeting the criterion of a residual error of $<30\%$. We classified MEG spike sources into two groups according to their number and spatial contiguity: a cluster consisted of a localised group of $\geqslant 6$ spike sources with $\leqslant 1$ cm between adjacent sources; scatters consisted of groups of either <6 spike sources regardless of the distance between sources, or groups of spike sources with >1 cm between each spike source regardless of the number of spike sources in the group.

MEG auditory-evoked fields

We recorded MEG auditory evoked responses in four children (numbers 1, 2, 5 and 6). Each patient listened through plastic ear inserts to 1-kHz tones presented to one ear, while white noise was presented to the other ear. Both ears were tested. We signal averaged the recording and used a single ECD model to determine the orientation of the source of the averaged response.[13]

Magnetic source imaging, coregistration of MEG with MRI

Immediately after collection of MEG data, we carried out an axial three-dimensional fast-spoil gradient T1-weighted volume acquisition MRI (GE Medical Systems). We placed fiducial markers (Multi-Modality Radiographic Markers, IZI Medical Products, Baltimore, Maryland, USA) on the patients' preauricular points and nasion to indicate the exact position of the MEG localisation coils for MRI coregistration. Slices of 2-mm thickness and spacing were acquired in an axial plane, without angling, repetition time 11 ms, echo time 4 ms. We used a bandwidth of 15.63–32.15 with an acquisition number of 2. The fiducial markers were displayed on trigonal MRIs on the MRI Viewer program version 4.12.2. After coregistering MEG and MRI fiducial markers, we created an appropriate spherical model.

The MEG spike sources and auditory-evoked field (AEF) sources were mapped into the MRI pixels using the MARK VOXEL program (VSM MedTech).

Extraoperative IVEEG, intraoperative ECoG and surgical procedures

For patients 1–4, we carried out initial lesionectomy with intraoperative ECoG using a 4×5 surface electrode array (Ad-Tech, Racine, Wisconsin, USA) based on the concordant ictal scalp video EEG findings and neuroimaging abnormalities without MEG data. We extended the resection or carried out multiple subpial transections (MSTs) if the area of active spiking was close to eloquent cortex on the intraoperative ECoG.

At the second surgery, in patient 1 we carried out extraoperative IVEEG using a custom-made subdural grid array. We constructed the subdural grid based on three-dimensional MRIs, interictal and ictal scalp EEG results, MEG spike sources and clinical symptoms. We placed two depth electrodes in the left hippocampus.

In patients 2 and 4 (second surgery), and in patient 6 (first surgery), we carried out intraoperative ECoG. Along with preoperative scalp EEGs, MRIs and clinical symptoms, we used MEG spike-source distributions to determine the areas for craniotomy and trajectories for intraoperative ECoG. During surgery, we used the frameless stereotaxy system (Zeiss/SNN Neurosurgical Navigational System, Carl Zeiss, Toronto, Ontario, Canada) to correlate spikes sources localised by ECoG with those by MEG. We defined an epileptic zone as the place where synchronised spike discharges were seen at three or more ECoG electrodes.[11 12]

RESULTS

Clinical profiles

Three patients had elementary auditory auras, two had both elementary and complex auras, and one had a complex auditory aura only. Elementary auditory auras included stampeding elephants (patient 1), unbearable sounds (patient 2), buzzing sounds (patient 4), and rushing water (patient 5). Patient 3 probably had an elementary auditory aura because he tended to plug his left ear, but language delay prevented him from describing the sensation.

Three patients had complex auditory auras. Patient 6 presented with the auditory illusion of ''amplification of sounds in both ears'' that coexisted with the auditory hallucination of ''singing sounds''. Patient 2, in addition to presenting with an elementary auditory aura, experienced a complex aura when he asked his parents to stop talking during an auditory illusion of amplification of their voices. At age 7 years patient 4 heard the buzzing sounds of an elementary aura, and at age 11 years experienced additional auditory hallucinations of ''friends' voices talking around him''.

Two patients presented with sensory auras in addition to auditory auras: patient 5 had a tingling sensation in the left foot and patient 6 experienced a feeling of throat constriction. None of the patients had auditory reflex or musicogenic epilepsy.

Patients 1–4 had undergone previous surgeries, but their seizures persisted after the initial resection. Patient 1 underwent lesionectomy of a cystic tumour over the left angular gyrus and additional resection of the anterior part of the superior and middle temporal gyri with MST over the left angular and supramarginal gyri. Patient 4 received a lesionectomy with cortical excision of the posterior part of the superior temporal gyrus behind the vein of Labbe. Both patients had dysembrioplastic neuroepithelial tumours (DNETs) and were seizure free for 6 months after surgery. Patient 2 had Sturge–Weber syndrome, underwent resection of a left occipital angioma and was seizure free for 28 months after surgery. Patient 3 underwent a right anterior temporal lobectomy and amygdalohippocampectomy. We carried out MSTs on the posterior edge of the resection. Postexcisional ECoG showed residual spikes over the right temporo-occipital junction and diffuse spikes over the posterior portion of the middle and inferior frontal gyri. Surgery showed a dual

pathology of mesial temporal sclerosis and cortical dysplasia. His seizures recurred immediately after surgery.

MRI findings

In patients 1–4, MRI findings were compatible with their previous surgical resections. The MRI of patient 1 showed minimal linear dural enhancement along the previous resection site. In patient 2, the MRI showed residual leptomeningeal enhancement along the medial aspect of the left occipital lobe, consistent with a diagnosis of Sturge–Weber syndrome. The MRI of patient 3 showed extensive residual cortical dysplasia affecting the medial aspect of the right occipital lobe and the margins of the previous right temporal lobectomy. In patient 4, the MRI showed a small nodule of high-signal intensity on FLAIR just above the resection. Patient 5 had normal MRI findings. The right insula of patient 6 showed high-signal intensity on FLAIR sequences after an episode of complex partial status epilepticus. This abnormality disappeared on subsequent MRIs taken with surface coils.

Scalp video EEG findings

Ictal scalp video EEG showed left frontotemporal onset in patients 1 and 2, temporal onset in patient 4, right temporal onset in patients 3 and 6, and diffuse right hemispheric onset in patient 5. Three patients (numbers 1, 2 and 5) had ictal onset characterised by low-amplitude fast activity (up to 20 Hz). Five patients (numbers 1, 2, 3, 4 and 6) had rhythmic sharp waves or spike and wave discharges in the theta range.

More than one ictal onset pattern was present in patients 1–3. In patients 1 and 2, scalp video EEG recorded low-amplitude fast activity and rhythmic sharp waves at ictal onset in separate electroclinical seizures with similar semiology. Patient 3 had two ictal onset patterns: rhythmic right temporal sharp waves and diffuse right hemispheric attenuation. Scalp video EEG ictal onset zones and ictal characteristics did not correlate with elementary or complex auditory auras.

MEG findings

Table 1 lists the MEG findings, surgical procedures and postsurgical seizure outcomes. Figure 1 shows MEG spike sources and AEFs.

All patients had at least one cluster of MEG spike sources with additional groups of scattered MEG spike sources. The clusters were in the superior temporal gyrus in four patients (left, patients 1 and 4; right, patients 5 and 6 (fig 1A,D–F)). Patient 2 had an MEG cluster in the left posterior parietal and mesial occipital regions, and scattered sources in the left superior temporal gyrus (fig 1B). Patient 3 had an MEG cluster in the right inferior frontal gyrus, with additional scattered sources in the right superior temporal gyrus (fig 1C).

Orientations of the dipole moments in the superior temporal gyrus were uniformly vertical to the sylvian fissure in four patients (numbers 3–6 (fig 1C–F)) and randomly directed in the remaining two patients (numbers 1 and 2 (fig 1A,B)).

AEFs were elicited bilaterally in three patients (numbers 1, 5 and 6; fig 1A,E,F). The source locations of the AEFs were in the Heschl's gyrus contralateral to the tested ear, except in patient 1, where AEFs on the left, lesion-containing side seemed to be displaced inferiorly in the left superior temporal sulcus (fig 1A). In patient 2, only the right ear AEF was elicited. As MEG was carried out under general anaesthesia for patients 3 and 4, they did not have auditory testing. The AEF source was located in an MEG cluster in patient 6 (fig 1F) and in the scattered spike sources surrounding a cluster in patients 1 and 5 (fig 1A,E).

Surgical procedures and outcomes

Patients 1, 2 and 4 underwent reoperations for recurrent seizures. The surgeries resulted in complete freedom from disabling seizures at a follow-up of 2 (patient 1) or 3 years (patients 2 and 4).

In patient 1, extraoperative IVEEG showed two ictal onset patterns. Low-amplitude fast waves over the left superior temporal gyrus were associated with his typical auditory auras. A second ictal pattern consisted of low-amplitude fast waves, up to 50 Hz, over the left mid-temporal and posterior temporal regions and the left inferior frontal gyrus, with a rapid spread to the hippocampal electrodes, which were associated clinically with generalised tonic seizures. The IVEEG ictal onsets corresponded to the MEG cluster over the left posterior superior temporal gyrus and the scatters over the inferior frontal gyrus (fig 1A).

Patient 2 underwent surgical resection of the left posterior parietal and occipital regions containing clustered MEG spike sources (fig 1B). Post-excisional ECoG showed high-amplitude spike and wave discharges over the middle part of the superior temporal gyrus corresponding to the MEG scatters, and independently over the hippocampus. We carried out further excision of the mesial temporal structures and the anterior and middle part of the superior temporal gyrus. We carried out additional MSTs over the posterior part of the superior temporal gyrus. At 3 years follow-up, patient 2 was seizure free except for occasional auditory auras, which probably originated from residual posterior portions of the superior temporal gyrus or from adjacent areas.

Patient 4 underwent excision of the residual anterior portion of the left superior temporal gyrus corresponding to the MEG cluster, and the posterior temporal region surrounding the vein of Labbe corresponding to the MEG scatters (fig 1D). Post-excisional ECoG showed isolated spikes over the left inferior frontal gyrus. No additional resections or MSTs were carried out.

Pathological examination showed residual cortical dysplasia and DNET in patient 1, angiomatosis consistent with Sturge–Weber syndrome in patient 2 and no evidence of recurrence of DNET in patient 4.

Patient 6 was originally diagnosed with right temporal lobe epilepsy that was refractory to several drugs for epilepsy. At 10 months after her first seizure, she presented with complex partial status epilepticus that was refractory to high-dose suppressive treatment. In the absence of motor weakness or atrophic changes on MRI, the diagnosis of Rasmussen's encephalitis could not be verified without a pathological specimen. Intraoperative pre-excisional ECoG showed active epileptiform discharges at the anterior to middle portion of the inferior frontal gyrus as well as the superior temporal gyrus, and occasionally at the mesial temporal region as well. She underwent right anterior temporal lobectomy with cortical excision over the right inferior frontal gyrus based on ictal scalp video EEG onset from F8 and T4. MEG cluster in the superior temporal gyrus (fig 1F) and intraoperative ECoG pathology were consistent with chronic encephalitis. Although she was not seizure free after surgery, her typical seizures preceded by auditory auras completely disappeared at 10 months follow-up. Instead, she experienced seizures twice a day, consisting of facial twitching, drooling, pallor and altered consciousness. Repeat MRI showed progressive right hemispheric atrophy.

Patient 3 had MEG spike sources located over an extensive area of the right inferior, middle frontal and superior temporal gyri (fig 1C). As this patient had considerable developmental delay and was uncooperative for IVEEG, he was not considered to be a good surgical candidate. Patient 5 with normal MRIs still awaits IVEEG for epilepsy surgery.

DISCUSSION

MEG spike sources associated with auditory auras

MEG detected and localised spike sources in the superior temporal gyrus that were close to or engulfed the magnetic

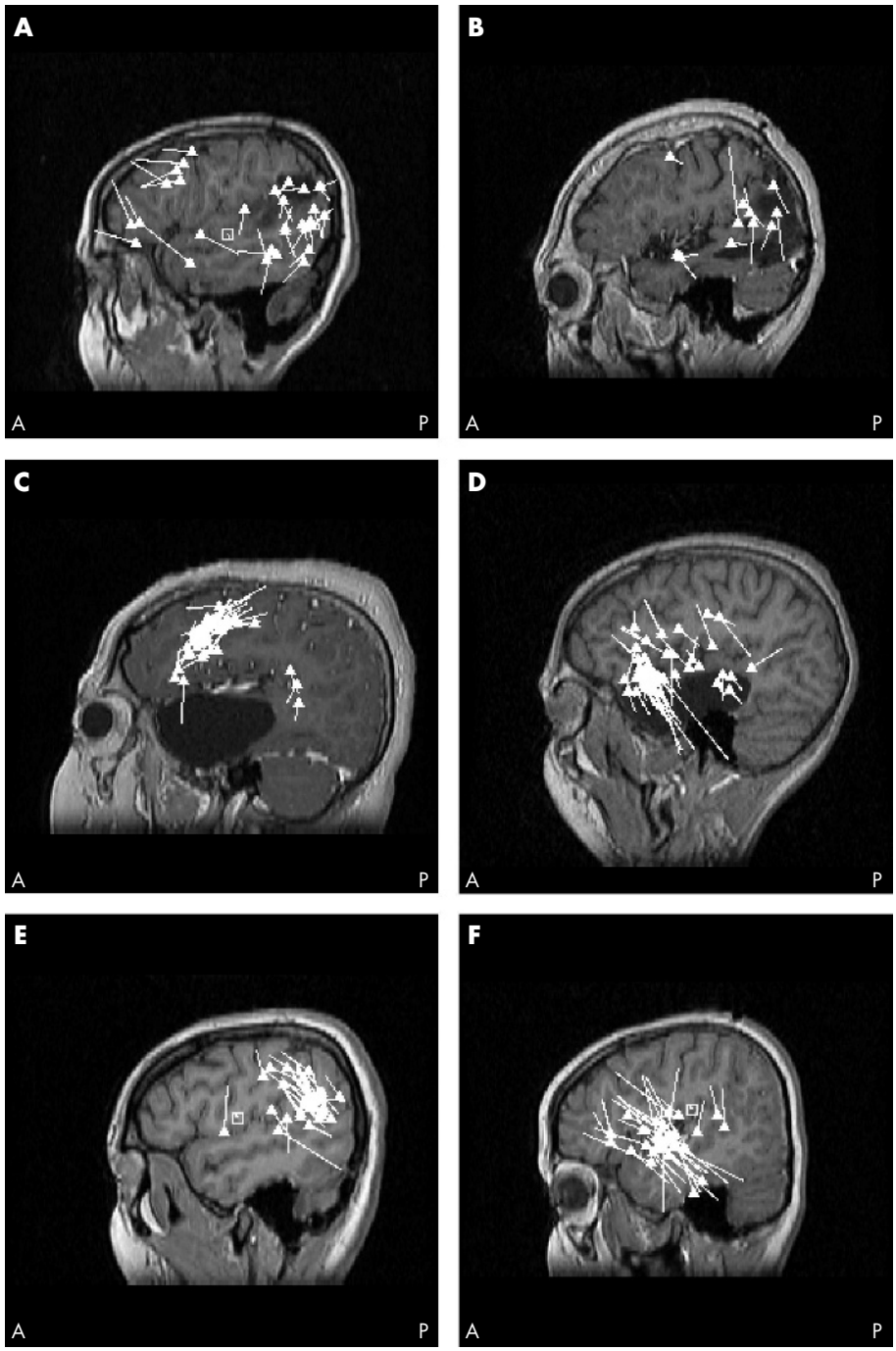

Figure 1 Sagittal magnetic resonance images showing magnetoencephalography (MEG) equivalent current dipoles of interictal spike sources (closed triangles, source localisations; tails, dipole moments) in all six patients. (A–F correspond to patients 1–6, respectively.) Patients 1, 4, 5 and 6 had clustered MEG spike sources involving the superior temporal gyrus. Auditory evoked responses (open squares) were elicited in patients 1, 5 and 6.

auditory field sources of six paediatric patients with auditory auras. In four of six patients, the MEG spike sources and auditory-evoked ECD orientations were predominantly directed vertically, to the sylvian fissure.

Heschl's gyrus, located on the dorsal surface of the superior temporal convolution and partly buried in the sylvian fissure, represents the primary auditory cortex. Stimulation of Heschl's gyrus produces elementary tones in patients with epilepsy.[3 5] Functional MRI[14] and MEG[15 16] studies detect activation of the superior temporal gyrus during auditory hallucinations in patients with schizophrenia. To our knowledge, our findings are the first to report MEG spike sources in the superior temporal gyri of paediatric patients with localisation-related epilepsy and auditory auras.

MEG spike sources in our patients were not restricted to the areas anatomically shown by the previous studies to mediate the relevant auditory phenomenon: Heschl's gyrus for elementary auras and the lateral part of the superior temporal gyrus for complex auditory auras.[3 5] In patients 2 and 3, MEG scattered spike sources were localised to the auditory cortex, whereas MEG clusters were located in the neighbouring parieto-occipital region in patient 2 and inferior frontal gyrus in patient 3. Several possibilities could explain the lack of exact correlation between the location of MEG clusters and the type of auditory auras. The initial sensation of auras correlates with the first symptomatogenic brain area activated by the seizure, but does not necessarily represent the epileptogenic zone or the ictal onset zone.[17 18] Ictal onset discharges from silent areas of the temporal neocortex or neighbouring brain regions would not produce auras until these discharges spread to the symptomatogenic zone of the auras. This spread via axonal connections between the ictal onset zone and the ictal

Table 1 Magnetoencephalographic findings, surgical procedures and post-surgical seizure outcomes

	MEG									Surgery			
		Cluster (no of spike sources)		Scatter (no of spike sources)									
Patient	Total no of spike sources	Left	Right	Left	Right	Predominant dipole orientation	AEF	Correlation between AEF cluster	Previous surgery	Hemisphere	Excision	Removal of MEG spike sources	Postsurgical seizure outcome/ years
1	31	Posterior superior temporal gyrus (21)	—	Inferior and middle frontal gyri (8), anterior superior temporal gyrus (2)	—	Random	Left anterior superior temporal sulcus, right Heschl's gyrus	2.4 cm	Lesionectomy of DNET, anterior superior and middle temporal gyri	Left	Posterior superior temporal gyrus, mesial temporal structures; cortical excision inferior and middle frontal	Cluster, scatters	Seizure free/ 2
2	13	Posterior parietal region, mesial occipital region (8)	—	Superior temporal gyrus (3), cingulate gyrus (1)	Cingulate gyrus (1)	Random	Right Heschl's gyrus	NA	Lesionectomy of cavernoma in Sturge-Weber syndrome, occipital region	Left	Posterior occipital region, anterior & middle superior temporal gyrus mesial temporal structures	Cluster	No disabling seizures, occasional auditory auras/3
3	38	—	Inferior and middle frontal gyri (35)	—	Superior temporal gyrus (3)	Uniformly vertical to sylvian fissure	NA	NA	Temporal lobectomy, mesial temporal sclerosis, cortical dysplasia	—	—	—	—
4	47	Anterior superior temporal gyrus (44)	—	Rolandic region (2), posterior superior temporal gyrus (1)	—	Uniformly vertical to sylvian fissure	NA	NA	Lesionectomy of DNET, posterior superior temporal gyrus	Left	Anterior superior temporal gyrus, posterior middle temporal gyrus	Cluster	Seizure free/ 3
5	38	—	Posterior superior temporal, supramarginal, angular gyri (35)	Rolandic region (1), superior temporal gyrus (1)	Anterior superior temporal gyrus (1)	Uniformly vertical to sylvian fissure	Bilateral Heschl's gyri	1.8 cm	—	—	—	—	—
6	35	—	Superior temporal gyrus (31)	—	Inferior frontal gyrus (2), inferior temporal gyrus (2)	Uniformly vertical to sylvian fissure	Bilateral Heschl's gyri	AEF within cluster	—	Right	Inferior frontal gyrus, anterior temporal lobectomy	Cluster	No auditory auras, daily seizures/0.8

AEF, auditory evoked field; MEG, magnetoencephalographic; NA, not applicable, when MEG study was carried out under general anaesthesia, AEF was not carried out.

symptomatogenic zone ultimately leads to ictal manifestations.[19] Also, the distinction between different auditory phenomena might not be clear in children who have language impairment or developmental delays. In addition, the auditory cortex next to the surgical area could have been disorganised by the excision and gliosis in patients who underwent previous surgery.

Residual auditory auras

Four patients who previously underwent lesionectomies or temporal lobectomies retained auditory auras. Patients 1 and 2 had MEG clusters with random ECD orientations in the superior temporal gyrus, and patients 3 and 4 had scattered spike sources with ECD orientations directed vertically to the sylvian fissure in the superior temporal gyrus. MEG spike sources in patients 3–6 were uniformly vertical to the sylvian fissure. The orientation of some of the spike ECDs resembled those of auditory-evoked ECDs.

MEG can accurately identify N100m of the magnetic auditory field in the posterior temporal auditory cortex on the supratemporal plane.[13 20] N100m presents a vertical orientation to the temporal plane in children.[20 21] ECDs in benign rolandic epilepsy show a similar orientation to somatosensory fields evoked by median nerve stimulation.[22] This similar orientation is possibly the result of closely located generators arising from the same neuronal plane.

The MEG spike sources in the superior temporal gyrus in our patients with residual auditory auras may be related to the generators of initial epileptic symptoms in the auditory cortex.

Recurrent or residual epileptogenic zone on MEG

Before undergoing MEG, patients 1–4 had lesionectomies but continued to have intractable epilepsy. In all four patients, MEG showed residual spikes located at the asymmetrical margins of the previous resections. MEG precisely localised the residual or recurrent epileptogenic zones on the post-surgical brain structures.

Compared with scalp EEG, MEG source localisation is less affected by tissue conductivity. Postoperative subdural scarring, bone defects, arachnoid adhesions and shifting of normal brain will affect the accuracy of scalp EEG localisation.[23] Experiments analysing distortion caused by the skull on EEG and MEG signals have used human craniums and swine skulls with holes drilled to mimic the human fontanel. These studies found signal distortion on EEG but lack of distortion on MEG.[24–26] Hence, compared with EEG signals, MEG signals are less likely to be distorted by postoperative skull defects as evidenced by these human and animal studies.[24–26] Furthermore, extraoperative IVEEG using subdural electrodes is less effective in detecting recurrent or residual epileptogenic zones after brain surgery. Epileptic discharges of differing amplitudes coexist in the unresected part of the cortex and the cortex affected by the resection, which is covered by gliotic tissues secondary to subdural scarring and arachnoid adhesions. Lower-amplitude epileptogenic spike discharges beneath the gliosis might be ignored or masked by misleading, relatively higher-amplitude, more prominent epileptic discharges on the unaffected brain surface. MEG is, however, a unique valuable tool for identifying the extent of residual or recurrent epileptic spike sources at the border of a previous resection.[8 9] Three patients in our study who underwent further resection of areas containing MEG spike sources became seizure free.

This paper provides the first report of MEG spike sources compared with AEF in patients with epilepsy with auditory aura. These cases also show the utility of MEG for localising the epileptogenic zone in a subset of patients with epilepsy with residual or recurrent seizures after previously failed epilepsy surgery.

ACKNOWLEDGEMENTS

We thank Mrs Carol L Squires for her editorial assistance.

Authors' affiliations

I S Mohamed, H Otsubo, E Pang, S K Weiss, O C Snead, Division of Neurology, The Hospital for Sick Children, Toronto, Ontario, Canada
S H Chuang, Division of Diagnostic Imaging, The Hospital for Sick Children
J T Rutka, P Dirks, Division of Neurosurgery, The Hospital for Sick Children

Competing interests: None.

Ethical approval: This study was conducted using protocols approved by the Hospital for Sick Children Research Ethics Board.

REFERENCES

1 **Maillard L**, Vignal JP, Gavaret M, *et al*. Semiologic and electrophysiologic correlations in temporal lobe seizure subtypes. *Epilepsia* 2004;**45**:1590–9.
2 **Ebner A**. Lateral (neocortical) temporal lobe epilepsy. In: Wolf P, eds. *Epileptic seizures and syndromes*. London: John Libbey, 1994:375–82.
3 **Penfield W**, Perot P. The brain's record of auditory and visual experiences: a final summary and discussion. *Brain* 1963;**86**:595–696.
4 **Williamson PD**, Wieser HG, Delgado-Escueta AV. Clinical characteristics of partial seizures. In: Engel J Jr, eds. *Surgical treatment of the epilepsies*. New York: Raven Press, 1987:101–20.
5 **De Graaf JB**, Liegeois-Chauvel C, Vignal JP, *et al*. Electrical stimulation of the auditory cortex. In: Luders H, Noachtar S, eds. *Epileptic seizures: pathophysiology and clinical semiology*. New York: Churchill Livingstone, 2000:228–36.
6 **Otsubo H**, Ochi A, Elliott I, *et al*. MEG predicts epileptogenic zone in lesional extrahippocampal epilepsy: 12 pediatric epilepsy surgery cases. *Epilepsia* 2001;**42**:1523–30.
7 **Stefan H**, Schnider S, Feistal H, *et al*. Ictal and interictal activity in partial epilepsy recorded with multichannel magnetoencephalography: correlation of electroencephalography/electrocorticocography, magnetic resonance imaging, single photon emission computed tomography, and positron emission tomography findings. *Epilepsia* 1992;**33**:874–87.
8 **Kirchberger K**, Hummel C, Stefan H. Postoperative multichannel magnetoencephalography in patients with recurrent seizures after epilepsy surgery. *Acta Neurol Scand* 1998;**98**:1–7.
9 **Baumgartner C**, Pataraia E, Lindinger G, *et al*. Neuromagnetic recordings in temporal lobe epilepsy. *J Clin Neurophysiol* 2000;**17**:177–89.
10 **Clarke DF**, Otsubo H, Weiss S, *et al*. The significance of ear plugging in localization-related epilepsy. *Epilepsia* 2003;**44**:1562–7.
11 **Iida K**, Otsubo H, Matsumoto Y, *et al*. Characterizing magnetic spike sources by using magnetoencephalography-guided neuronavigation in epilepsy surgery in pediatric patients. *J Neurosurg* 2005;(Pediatrics 2), **102**:187–96.
12 **Holowka SA**, Otsubo H, Iida K, *et al*. Three-dimensionally reconstructed magnetic source imaging and neuronavigation in pediatric epilepsy: technical note. *Neurosurgery* 2004;**55**:1266/E1244–E1248.
13 **Pang EW**, Gaetz W, Otsubo H, *et al*. Localization of auditory N1 in children using MEG: source modeling issues. *Int J Psychophysiol* 2003;**51**:27–35.
14 **Dierks T**, Linden D, Jandl M, *et al*. Activation of Heschl's gyrus during auditory hallucinations. *Neuron* 1999;**22**:615–21.
15 **Ropohl A**, Sperling W, Elstner S, *et al*. Cortical activity associated with auditory hallucinations. *Neuroreport* 2004;**15**:523–6.
16 **Ishii R**, Shinosaki K, Ikejiri Y, *et al*. Theta rhythm increases in left superior temporal cortex during auditory hallucinations in schizophrenia: a case report. *Neuroreport* 2000;**11**:3283–7.
17 **Schulz R**, Luders H, Tuxhorn I, *et al*. Localization of epileptic auras induced by stimulation by subdural electrodes. *Epilepsia* 1997;**38**:1321–9.
18 **Norman K**. Epileptic auras. In: Wyllie E, eds. *The treatment of epilepsy principles & practice*. Philadelphia: Lippincott Williams & Wilkins, 2001:299–308.
19 **Spencer SS**. Neural networks in human epilepsy: evidence of and implications for treatment. *Epilepsia* 2002;**43**:219–27.
20 **Nakasato N**, Yoshimoto T. Somatosensory, auditory, and visual evoked magnetic fields in patients with brain diseases. *J Clin Neurophysiol* 2000;**17**:201–11.
21 **Ozaki I**, Jin YC, Suzuki Y, *et al*. Dynamic anterolateral movement of N100 m dipoles in evoked magnetic field reflects activation of isofrequency bands through horizontal fibers in human auditory cortex. *Neurosci Lett* 2002;**329**:222–6.
22 **Lin YY**, Shih YH, Chang KP, *et al*. MEG localization of rolandic spikes with respect to SI and SII cortices in benign rolandic epilepsy. *Neuroimage* 2003;**20**:2051–61.
23 **Awad IA**, Nayel MH, Luders H. Second operation after the failure of previous resection for epilepsy. *Neurosurgery* 1991;**28**:510–18.
24 **Flemming L**, Wang Y, Caprihan A, *et al*. Evaluation of the distortion of EEG signals caused by a hole in the skull mimicking the fontanel in the skull of human neonates. *Clin Neurophysiol* 2005;**116**:1141–52.
25 **Okada Y**, Lahteenmaki A, Xu C. Experimental analysis of distortion of MEG signals by the skull. *Electroenceph Clin Neurophysiol* 1999;**110**:230–8.
26 **Barth DS**, Sutherling W, Broffman J, *et al*. Magnetic localization of a dipolar current source implanted in a sphere and a human cranium. *Electroenceph Clin Neurophysiol* 1986;**63**:260–73.