Published in final edited form as:

J Clin Neurophysiol. 2007 June ; 24(3): 215–231. doi:10.1097/WNP.0b013e3180556095.

Concordance Between Routine Interictal Magnetoencephalography and Simultaneous Scalp Electroencephalography in a Sample of Patients with Epilepsy

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Summary

Both electroencephalography (EEG) and magnetoencephalography (MEG) localize epileptiform activity but may yield different results. This discordance may arise from different detection capabilities or from different data collection and interpretation techniques. Comparisons of MEG and EEG have focused on detection of individual spikes. However, side-by-side comparisons of results as used in the clinical setting is lacking. In this report, we present our empirical comparison. We reviewed 58 simultaneous MEG-EEG recordings (35 paired-sensors, 23 whole-head) from a diverse epilepsy population, comparing previous clinical MEG interpretations with new blinded EEG interpretations, noting lobar concordance of readers' judgments of regional abnormalities. A second-pass unblinded analysis, using all available clinical data, assessed the relative contribution and plausibility of the results of each technique. Concordance was high (85%) overall. Discordance was sometimes caused by constraints imposed by MEG dipole fitting techniques. Even when results of the techniques did not match, MEG often disambiguated the clinical scenario, especially when combined with imaging information. Thoughtful analysis of combined MEG-EEG datasets, beyond algorithm-based interictal spike detection, can help guide clinical decision-making even when concordance between techniques is imperfect. In some cases, EEG and MEG are synergistic and provide complementary information.

Keywords

Magnetoencephalography; Electroencephalography; Epilepsy; Concordance

Magnetoencephalography (MEG) and electroencephalography (EEG) are both neurophysiological techniques used in the evaluation of people with epilepsy to record interictal epileptiform discharges that give clues to location of onset of seizures (eg, Minassian et al., 1999). This can help clarify an individual's seizure type and epilepsy syndrome (Proposal for revised classification of epilepsies and epileptic syndromes;

Commission on Classification and Terminology of the International League Against Epilepsy, 1989) and may also indicate whether resective surgery is a treatment option. MEG is not limited by conductivity issues, as is EEG, and is thought to be more sensitive to tangential sulcal sources. As MEG has developed as a technology, source modeling techniques have grown in tandem, making it possible to perform single dipole analysis and then to superimpose results on anatomic MRI images (this is known as magnetic source imaging, or MSI). EEG, by contrast, is in routine clinical practice visually inspected; computer-aided source analysis is not part of standard practice in most EEG laboratories. For a review of technical and practical matters surrounding the use of EEG and MEG in epilepsy, see Barkley et al. (2003).

Because of these differences in measurement and analysis techniques, it is to be expected that the results of routine scalp EEG and MEG will not be identical. This discordance between results may in part be due to conductivity issues. Some investigators have attempted to minimize this variable by comparing MEG results with electrocochleography (ECoG) in the same patients (Nakasato et al., 1994; Oishi et al., 2002). Under these conditions, with issues of conductivity minimized, it has been suggested that spike-to-spike concordance depends on the location of spike origin, MEG being more sensitive for lateral convexity versus deep basal temporal sources (Oishi et al., 2002). Intracranial recordings are typically performed after MEG has already been performed, and, in fact, MEG may have value in planning intracranial electrode placement. Thus, it is of practical value to know the concordance between scalp EEG and MEG.

Most investigators have attempted to answer this question by looking at spike-to-spike concordance. Lin et al. (2003) found a 78.3% concordance rate in mesial and lateral temporal lobe epilepsy and suggested that MEG was better at detecting lateral temporal spikes not seen on EEG. Yoshinaga et al. (2002) studied seven patients with intractable focal epilepsy: Although three had clear spikes apparent on both EEG and on MEG, two had EEG spikes only and two had MEG spikes only, but this discordance could be resolved by using averaging techniques or estimated dipoles for nonspike MEG patterns. The use of a higher-density scalp array, improved EEG analytic tools, and back-averaging EEG on MEG spikes also improved EEG-MEG spike concordance in a case reported recently (Rodin et al., 2004). More recently, the special case of EEG-MEG spike concordance when polymicrogyria changes cortical sulcation was addressed, with concordance seeming to depend on orientation of sources: MEG was limited in its ability to detect spike onset for radial sources, though such spike onsets were clearly demonstrated on simultaneous EEG; MEG showed propagated spikes after a lag from EEG spike onset (Bast et al., 2005).

As Baumgartner pointed out in his 2004 review, “a ‘fair’ head-to-head comparison between the two techniques performed in a clinical setting with a comparable number of channels and comparable source localization techniques is ... urgently needed (p. 1064)” (Baumgartner, 2004), and the recent study of Scheler et al. (2006) comparing MEG and EEG source localizations begins this important work. We would also point out that we are lacking head-to-head comparisons of the results of MEG and of a comprehensive visual analysis of a simultaneous scalp EEG, as they are performed in typical clinical situations. Past studies, as we review above, have focused on spike-by-spike concordance between the

two techniques and/or between MEG and ECoG. However, EEG readers do more than detect and localize spikes when approaching a record, and the judgment that a record reveals a focal abnormality is made on a variety of grounds, including focal slowing or focal loss of normal background rhythms (though these focal abnormalities are of course nonspecific and do not in themselves mean that a region is epileptogenic). Therefore, in our study, rather than focusing exclusively on the ability of each technique to capture an individual spike, we took a broader view, assessing the frequency and nature of discordance and concordance between the global interpretation of scalp EEG and of simultaneous MEG as they are performed in the clinical setting. We proceeded without the use of special EEG source localization techniques or high-density EEG recording, as we were seeking to compare MEG with EEG as performed in most outpatient EEG settings.

Thus, our study is not intended to add to the growing literature comparing MEG and EEG spike-for-spike. Nor is it intended to be a fair comparison between the best scalp EEG source localization techniques (i.e., high density recording, realistic head modeling, and dipole analysis). Instead, it is meant to address the clinical question: “of what use is routine MEG compared to routine scalp EEG in the evaluation of patients with epilepsy?” We share this goal with Knake et al. (2006), who published a similar series recently, though they focused on patients undergoing presurgical workup. Our clinical impression has been that the two techniques—routine low-density EEG and routine MEG—are complementary, and we wanted to see if this impression was warranted. In addition, dipole modeling of EEG/MEG spikes alone misses valuable information contained in the record that can indicate a focal region of abnormal cortical function (e.g., focal slowing on EEG and MEG, or focal low voltage fast activity on MEG), and we wanted to understand how this information could be used to enhance the value of the modalities.

METHODS

We reviewed simultaneously recorded 21-channel scalp EEG and paired 37-channel MEG studies performed on 35 consecutive consenting patients with epilepsy referred from physicians both within and outside of UCSF between 2002 and 2003. We also reviewed simultaneous 21-channel scalp EEG and 275-channel whole cortex MEG studies from 23 consenting patients studied in 2004 and 2005. All studies included a minimum of 45 minutes of recording time. Though the recordings were intended to be interictal, if a seizure happened to be recorded, as it was in three cases, the ictal M/EEG was analyzed along with the rest of the record. The clinical MEG data had previously been analyzed by a single experienced technologist (M.M.) as follows: After the data were band-pass filtered between 1 to 70 or 3 to 70 Hz, spikes were chosen for analysis based on duration (<80 ms), morphology, and lack of associated artifact (e.g., ECG, EMG, EOG). Although the MEG readers had access to the simultaneous EEG to help distinguish spikes from artifact, they also selected spikes that met criteria but appeared only on MEG. Spike onsets were chosen, and corresponding dipoles were fit by using the commercial software supplied by the manufacturer (paired-sensor: 4-D Neuroimaging, San Diego, Calif; whole-head: CTF Systems, VSM, Port Coquitlam, BC); dipoles with >97% correlation and >95% goodness-of-fit were selected and superimposed on patients' MRI scans. Results of this MSI were also reviewed by the director of the laboratory (S.N.) and by the staff neuroradiologist who

would generate a clinical report. EEG data were separately analyzed retrospectively by a neurophysiologist (H.E.K.) blinded to MEG results, using visual inspection of data presented in longitudinal bipolar and transverse montages, and focal abnormalities and epileptiform discharges were noted. The identification of spikes was based on duration (<80 ms), morphology, field, and lack of associated artifact. Lobar localization of epileptiform discharges was made based on published descriptions of neurophysiologic-anatomic correlations (Homan et al., 1987; Jasper, 1958); that is, T3 spikes were judged to arise from the midportion of the left temporal lobe.

We then grouped these studies, on the basis of the EEG and MEG findings reported in the blinded analysis, into two groups, concordant and discordant. These groups were further subdivided as follows (based loosely on a similar schema used to rate spike concordance in MEG/EEG datasets (Lin et al., 2003) and modified by R. Knowlton [personal communication]):

- IA** Concordant, E+/M+: EEG and MEG results both showed epileptiform discharges in the same location (lobar concordance).
- IB** Concordant, E-/M-: There were epileptiform discharges found with either method.
- IC** Concordant, E+/M+ overlap: EEG and MEG both showed epileptiform discharges, but the locations of these were not 100% in agreement (e.g., one method suggested frontal and temporal foci, and the other suggested frontal only).
- IIA** Discordant, E+/M-: EEG showed epileptiform discharges but MEG did not.
- IIB** Discordant, E-/M+: MEG showed epileptiform discharges but EEG did not.
- IIIC** Discordant, E+/M+ no overlap: EEG and MEG both showed epileptiform discharges but in different locations with no overlap (e.g., one method suggested a frontal focus and one suggested a temporal focus).

Note that we did not compare individual spikes across modalities; concordance ratings were based on the overall conclusion taking the entire study (either EEG or MEG) into account. In the case of MEG, this was the clinical report, and in the case of EEG, this was the blinded EEG interpretation.

After this primary grouping analysis, we made a second unblinded pass through the data, comparing directly the MEG and EEG signals and incorporating the MSI and clinical data (as noted in Table 2, a through f) to place the results of the MEG and EEG within their clinical context. This enabled us to judge whether the discordance noted in the first pass analysis was true discordance—that is, based on actual differences in recorded signal—or pseudodiscordance—that is, based on differences in criteria for reporting patterns or in restrictions of source modeling.

RESULTS

First-pass concordance ratings are summarized in Table 1. Note that for three scans, there was artifact in the MEG recording, the EEG recording, or both such that concordance between the two methods could not be obtained. These cases are not included in the totals in Table 1.

- I** Concordant studies: In 27 of the 33 analyzed paired-sensor cases (82%), and 20 of the 22 analyzed whole-head cases (91%), the EEG and MEG findings were concordant.
- IA** E+/M+: Table 2a: for 28 cases, there was agreement as to the lobe(s) involved.
- IB** E-/M-: Table 2b: for eight cases, no clearly epileptiform abnormalities were seen on either modality.
- IC** E+/M+ overlap: Table 2c: for 11 cases, EEG and MEG identified the same lobe but one modality might indicate an additional focus. In two of these (cases 10 and 41), EEG showed a bilateral pattern that MEG suggested was secondary bilateral synchrony, and in three EEG had bilateral findings (bitemporal in case 49, bioccipital in cases 15 and 48) that on MEG appeared to arise from a unilateral focus. In four cases (cases 16, 21, 30, and 54) MEG findings overlapped EEG findings and MSI results were able to better define the epileptiform discharges relative to a structural lesion that in one case (case 16) was large and probably caused misleading EEG localization due to volume conduction. In one recording (case 32) made during multifocal status epilepticus, there was EEG evidence of ongoing multifocal seizures. MEG showed ongoing multifocal spikes corresponding to EEG, but when these spikes were selected, only those arising from the right frontocentral region could be modeled as arising a single equivalent current dipole with acceptably low error.
- II** Discordant studies: In 6 of the 33 analyzed paired-sensor cases (18%) and 2 of the 22 analyzed whole-head cases (9%), the EEG and MEG findings were discordant.
- IIA** E+/M-: Table 2d: In five cases, EEG showed focal epileptiform discharges not apparent using MEG alone; in a sixth case (case 31), a corresponding potential abnormality (regional low voltage fast activity versus. muscle artifact) was visible on MEG, but there were no MEG spikes that met criteria for source modeling.
- IIB** E-/M+: Table 2e: In one case (case 33), MEG detected spikes that were apparent only as a sharp transient or a wicket spike rather than as a clear epileptiform discharge on EEG (in this case MEG agreed with ictal onset from scalp telemetry and with PET result).
- IIIC** E+/M+ no overlap: Table 2f: In one paired-sensor case (case 35), there was a weak EEG finding (single sharp wave), whereas MEG found clear spikes that localized on MSI to a lesion in the other hemisphere.

Unblinded second-pass analysis was then done using clinical data and side-to-side comparisons of the datasets.

Representative Cases

Here, we present cases from each category (except for the E-/M- category) along with illustrative figures for six of the cases.

IA. Concordant, E+/M+

Case 17: Case 17 was an 18-year-old man with cortical dysplasia and symptomatic intractable complex partial seizures. MRI shows abnormal thickening and coarsening of gyri of the right hemisphere with a shallow right Sylvian fissure. EEG showed profuse runs of spike and slow wave discharges maximal at T4 > C4. Paired-sensor MEG showed spikes in the right temporal and central region. On MSI, the MEG spikes localized, clearly and consistently, to the deep cortex in the inferior aspect of the dysplasia. See Fig. 1.

Case 23: Case 23 was a 15-year-old girl with choroid plexus papilloma resection in infancy, now with intractable complex partial seizures with left head turn followed by asymmetric tonic posturing and left sided clonic activity. MRI showed large area of cystic encephalomalacia in the right posterior quadrant. In the past, long-term video-EEG monitoring showed ictal onset from the posterior left temporal region.

EEG showed bursts and runs of polyspike and slow wave discharges from right central regions and from right posterior temporal regions, along with several brief subclinical seizures from the same area. Paired-sensor MEG showed spikes from the same region. On MSI, these mapped to the rim of the encephalomalacia, including the deep rim. Subsequent extraoperative ECoG with a grid of subdural electrodes placed over the posterior quadrant and across the mouth of the cyst showed onset around the mouth of the cyst but could not document seizure propagation, perhaps because the seizure spread to involve the deep rim of the cyst in a manner that could not be recorded by subdural electrodes. After extensive excision of these regions, including the deep sources only revealed by MSI, she was seizure-free. See Fig. 2.

Case 53: Case was a 21-year-old man with intractable complex partial seizures. MRI was normal except for a Rathke's cleft cyst. Interictal EEG in the past showed generalized spike and slow wave discharges. Ictal scalp recordings were either nonlocalizing or showed left frontal/frontocentral onset. EEG showed left frontal sharp waves on EEG that were better seen on whole-head MEG and had excellent dipole fits. He also had more generalized bursts on EEG and MEG that could not be reliably modeled for MSI. See Fig. 3.

IC. Concordant E+/M+ Overlap

Case 10: Case 10 was a 13-year-old girl with simple partial seizures involving the sensation of "turning" followed by motor features involving the left arm. MRI was normal except for a slight enlargement of the right choroidal fissure consistent with a small arachnoid cyst. EEG demonstrated 3 to 4 Hz spike and slow wave complexes with a maximum/lead from the right frontal region (F4) and significant secondary bilateral synchrony as well as rare spike and

slow wave complexes only seen at Fp2-F4. Paired-sensor MEG showed spikes in the same regions. On MSI, these were clearly shown to have a single right frontal source. The MSI thus strengthens the impression of secondary bilateral synchrony and helped to identify the source more precisely, aiding presurgical decision making. See Fig. 4.

Case 30: Case 30 was a 25-year-old woman with symptomatic partial seizures since age 8, consisting of drooling, abdominal sensations, and left hand weakness. MRI showed cortical dysplasia in the right perirolandic region. Prior long-term video-EEG monitoring showed ictal onset that appeared to be generalized and nonlateralizing, whereas interictal discharges were usually generalized with a right-hemispheric emphasis, but there were also rare bihemispheric independent discharges. EEG showed bilateral independent polyspike and slow wave complexes arising from temporal regions, right (T4/T6) more frequent than left (T3/T5). Paired-sensor MEG showed frequent bilateral independent discharges, but only the right hemispheric spikes met analysis criteria, so the results were rated as E+/M+ overlap rather than fully matched. However, on MSI, when the spikes meeting criteria were modeled, they localized to regions surrounding the area of cortical dysplasia. Thus, although EEG and MEG results were only overlapping, MSI was more consistent with the imaging abnormality and thus helped add weight to the dysplasia as the source of seizures. See Fig. 5.

Case 15: Case 15 was a 2.5-year-old girl with linear sebaceous nevus syndrome and infantile spasms. MRI showed a smaller right hemisphere with enlarged perivascular spaces. Prior MR spectroscopy and PET suggested metabolic abnormalities of the right posterior quadrant. EEG showed multifocal spikes arising independent from left and right posterior quadrants; generalized spike and slow wave discharges in sleep, whereas paired-sensor MEG suggested that these were from the right posterior regions. MSI showed dipoles localizing to the posterior parietal-occipital regions of the right hemisphere. Thus, although EEG and MEG results could be rated as concordant, E+/M+ overlap, we saw on second-pass analysis that MEG suggested a unilateral source in a region that was abnormal by multiple imaging methods. Thus, as for the previous case (case 30), although EEG and MEG results were only overlapping, MSI was more consistent with the imaging abnormality. See Fig. 6.

IIA. Discordant E+/M–

Case 30: Case 30 was a 10-year-old girl with simple partial seizures during which she felt unable to move. MRI showed a heterotopia lateral to the temporal horn of the left lateral ventricle. EEG showed focal low-voltage, high-frequency activity (versus focal muscle artifact) in the left posterior temporal derivations. Paired-sensor MEG showed low-voltage, high-frequency activity in the same area. Because the source of this activity could not be modeled as described above, this case was rated as M–. However, both datasets did show the regional abnormality that corresponded to the MRI lesion. The first pass rating of E+/M– did not capture the fact that the datasets agreed, although dipoles could not be modeled for MEG and would not have been able to be modeled for EEG had we attempted to do so.

IIB. Discordant E-/M+

Case 33: Case 33 was a 25-year-old woman with simple partial seizures consisting of fear, garbled speech, and clonic movements of the right arm. MRI (without surface coil) was normal; PET showed reduced uptake in the left thalamus compared with the right. Previous long-term video-EEG monitoring showed ictal onset from the right temporal lobe. EEG showed sharp transients (but not sharp waves or spikes) in the left frontocentral region and a single burst of left temporal wicket rhythm. Paired-sensor MEG showed sharp and slow waves that mapped to the left posterior temporal region on MSI.

IIC. Discordant E+/M+ No Overlap

Case 35: Case 35 was a 32-year-old woman with complex partial and secondarily generalized seizures. MRI and PET were normal. EEG showed a single sharp wave phase-reversing at P3. Paired-sensor MEG showed spikes maximal in the right parietal region that on MSI map to the right posterior parietal gray-white junction.

The cases in categories IA and IC (pictured in the figures) are examples of cases that on secondary unblinded analysis, using both datasets, yielded richer information when the EEG and MEG/MSI datasets were combined. They illustrate that the use of both datasets together can be complementary and that this characteristic of the data was not conveyed adequately by labeling the cases as “concordant” or “discordant.” For example, MEG/MSI could clarify the relation of a particular EEG pattern to a structural lesion, or, as mentioned above, might offer support for an apparently generalized EEG pattern being the result of secondary bilateral synchrony from a single focus.

DISCUSSION

In this series of heterogeneous patients with epilepsy, MEG and EEG results were most often concordant in a first-pass analysis. Concordance was higher for the whole-head system, in line with a previous report that concordance may be higher when more sensors are used (Stefan et al., 2003). In some of the cases in which concordance was not absolute but in which the results of the two methods overlapped, the different results may have been related to the presence of a large lesion that distorted cortical anatomy and made EEG localization difficult (using visual analysis only), whereas the relation between the lesion and MSI dipoles was often very useful. In one case, MEG revealed spikes that were not clearly epileptiform on routine low-density scalp EEG with visual analysis alone; this superiority may be due to the MEG’s theoretically superior spatial resolution.

Sometimes when EEG revealed focal epileptiform abnormalities and MEG did not, this discordance was attributable to the different criteria used for judging EEG and MEG: That is, abnormalities seen on EEG may have also been apparent on MEG, but not as spikes that could be used for convincing source models. This is supported by a pattern that we noticed: there were six times as many EEG+/MEG– cases as there were EEG–/MEG+ cases, and this discrepancy may be an artifact of the fact that only spikes meeting certain criteria could render a case “MEG+,” whereas the significance of other MEG patterns is not yet fully known. Choosing MEG spikes arbitrarily, based on criteria developed for EEG spikes, and

failing to attend to other features of the MEG record is limiting. The neurophysiology community should pursue the development of a validated dictionary for visual analysis, presenting EEG patterns with corresponding MEG patterns found in the same patients. Techniques for modeling the sources of “patchy” or regional MEG features (such as focal slowing or focal low-voltage fast activity), though computationally intensive, should be pursued.

In addition, common analysis techniques only allow MEG spikes that can be modeled as single stationary dipoles, so that solutions are computationally tractable, but this limitation forces us to accept limited solutions that do not reflect the true source of epileptiform activity. As was pointed out in a recent editorial (Lesser, 2004), we lack an understanding of how EEG and MEG spikes are related in terms of morphology, specificity, usefulness, and relation to underlying pathophysiology. For now, performing simultaneous EEG with MEG should be considered routinely to gain this experience; as pointed out by several groups cited above, EEG spikes can also be used to find MEG spikes by, for example, averaging techniques (e.g., Rodin et al., 2004; Yoshinaga et al., 2002), thereby maximizing the sensitivity of a study.

Our second-pass unblinded analysis suggested that simple division of results of these two technologies into “concordant” and “discordant” fails to capture the richness of the data gathered. In some cases in which MEG spikes were concordant with EEG focality on first pass, it was able to go beyond EEG, though the use of source modeling and MSI, adding significant value to the clinical picture. In “discordant” cases, often examination of the discordance itself pointed to a factor that was important to understanding the case—in other words, the discordance was not random but made sense within the context of the entire dataset. Often, the two datasets were synergistic, providing information that enriched and disambiguated the clinical scenario beyond expectations of the terms “concordant” or “discordant.” For example, EEG might show bilaterally synchronous occipital spikes that are only seen unilaterally on MEG and whose dipoles localize to a unilateral posterior quadrant lesion on MSI. In such a case, although first-pass analysis indicated that the results of the two studies are not perfectly concordant, it was clear on unblinded review of the dataset that the results are consistent with the underlying pathology as viewed through the lenses of different techniques.

In fact, careful examination of both datasets, moving between them and integrating them with MRI images, allowed a deeper appreciation of the nature and source of epileptiform activity. In some cases, this appreciation meant that a patient could be considered for epilepsy surgery, or at least for invasive monitoring, because the MEG had been performed. In the cases in which MEG confirmed secondary bilateral synchrony (such cases have also been reported by Tanaka et al., 2005), this helped target ECoG; when MEG suggested that epileptiform activity localized to an edge of a large lesion, this could either guide the placement of chronic intracranial electrodes or allow for lesionectomy with intra-operative ECoG. In some cases, such as case 23 (Fig. 2), MEG-guided surgery directly by revealing epileptiform activity deep within a cavitary lesion that could not, therefore, be recorded using implanted electrodes. Combined computational approaches to data analysis are under

development (e.g., Fuchs et al., 1998) and should help users combine datasets quantitatively and objectively in the future.

Acknowledgments

Part of this work was funded by NIH DC004855 to S.S.N. and by K23 NS047100 to H.E.K.

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FIGURE 1.

Paired-sensor MEG, simultaneous scalp EEG, and MSI for case 17. Dipoles in this and following figures are shown as triangles with vector tails indicating orientation and strength (proportional to length).

FIGURE 2.
Paired-sensor MEG, simultaneous scalp EEG, and MSI for case 23.

FIGURE 3.

Whole-head MEG, EEG, and MSI for case 53. Top panel: Left frontal and temporal MEG channels (left column and top of right column), ECG, and EEG (bottom of right column) for left frontal spikes (marked with gray dashed vertical cursors) along with MSI showing left frontal dipoles. Bottom panel: Left frontal and temporal MEG channels, ECG, and EEG for generalized spike and slow wave bursts that could not be reliably modeled for MSI.

FIGURE 4.

Paired-sensor MEG and simultaneous scalp EEG and MSI for case 10; the same epoch of MEG and EEG (limited to bilateral temporal longitudinal bipolar montage) is shown at normal (left) and increasingly expanded time scales (marked with blue cursor to show lead/lag).

FIGURE 5.
Paired-sensor MEG, simultaneous scalp EEG, and MSI for case 30.

FIGURE 6.
Paired-sensor MEG, simultaneous scalp EEG, and MSI for case 15.

TABLE 1**First-Pass Concordance Ratings**

Rating	Number and Percent of Cases (paired-sensor)	Number and Percent of Cases (whole-head)	Number and Percent of Cases (both scanners)
IA. Concordant E+/M+	17 (52%)	11 (50%)	28 (51%)
IB. Concordant E-/M-	3 (9%)	5 (23%)	8 (15%)
IC. Concordant E+/M+ overlap	7 (21%)	4 (18%)	11 (20%)
Total concordant	27 (82%)	20 (91%)	47 (85%)
IIA. Discordant E+/M-	4 (12%)	2 (9%)	6 (11%)
IIB. Discordant E-/M+	1 (3%)	0	1 (2%)
IIC. Discordant E+/M+ no overlap	1 (3%)	0	1 (2%)
Total discordant	6 (18%)	2 (9%)	8 (15%)
Total analyzed	33	22	55

Note that columnar percentages may not add to 100% because of rounding.

TABLE 2A

Type IA cases (E+/M+ Concordant)

Type of Study	Case No.	Age	Sex	Seizure Type/Risk Factors	Neuroimaging	Video-EEG (scalp)	EEG	MEG/MSI
PS	2	13	m	CPS with head turn to right and right arm flexion; known cortical dysplasia s/p one resection without improvement	MRI: right frontoparietal resection cavity		Right centroparietal semirhythmic slowing; multifocal spikes right and left centroparietal	Multifocal spikes right and left centroparietal
PS	3	16	f	Brief CPS with staring; longer SPS with limb shaking, stiffening, salivation	MRI: normal; PET: possible left mid temporal hypometabolism	Ictal onset: right frontal	Right frontal and central spike and slow and polyspike and slow waves	Right frontal-central spikes
PS	4	36	f	SPS with clonic movements and sensory changes right hand and face; known left frontoparietal grade 2 astrocytoma, s/p resection	MRI: left frontoparietal resection cavity with peripheral rim of T2 prolongation involving the parenchyma deep to the cavity		Left temporal spikes; irregular left temporal slowing	Left temporal spikes
PS	5	20	m	CPS with flexion at waist, bilateral arm shaking, bilateral leg stiffening; history of head trauma	MRI: extensive bilateral white matter disease with multiple foci of chronic hemorrhage and mild hydrocephalus ex vacuo	Ictal onset: right temporal onset; interictal: bilateral independent temporal spikes	Right temporal spikes	Right temporal sharp waves
PS	6	46	m	SPS with fear; CPS	MRI normal		Left central and frontal spikes; bifrontal spikes; independent right frontal spikes; bilaterally synchronous frontal sharp waves	Multifocal spikes, left central and frontal; bifrontal
PS	8	32	m	SPS with right arm clonic activity	MRI: mild cerebellar atrophy, otherwise normal; SPECT: hot spot in left frontal lobe but in raw data but subtraction SPECT not confirmatory		Occasional left frontal/central sharp waves in sleep	Left frontal/central sharp waves; cluster of three spikes seen in left mid frontal lobe
PS	9	39	m	SPS with left hand tingling; CPS with 'zoning out'; drop attacks	MRI: focal area of cortical dysplasia in the right posterior perisylvian region		Right temporal and central polyspike and slow wave complexes; increased beta activity diffusely	Spikes and polyspikes in the right midtemporal region and the posterior perisylvian region (adjacent to malformation)
PS	12	40	m	CPS with staring and sweating	MRI: small mesial frontoparietal cavernous malformation with associated developmental venous anomaly; some mild T2 hypointensity in left	Ictal onset: left temporal	Left frontocentral sharp and slow waves; left central-temporal slowing	Left parietal spikes

Type of Study	Case No.	Age	Sex	Seizure Type/Risk Factors	Neuroimaging	Video-EEG (scalp)	EEG	MEG/MSI
PS	13	23	f	SPS with fear, gripping sensation in chest; CPS with left hand posturing	frontal-parietal white matter consistent with venous ischemia frontal-parietal white matter consistent with venous ischemia MRI: possible cortical dysplasia in left superior frontal region	Ictal onset: poorly localized but on occasion preceded by right frontal sharp waves	F3 sharp waves	Sharp waves from left frontal perisylvian regions
PS	14	32	f	SPS with anxiety loneliness, CPS with mumbling and neck posturing; history of childhood meningitis with residual left hemiparesis	MRI: high T2 signal in right insular region, mild enlargement of the temporal horn of right lateral ventricle and mildly diminished size of right hippocampus	Ictal onset: Right anterior to mid temporal; interictal: right temporal spikes	F8 spikes and sharp transients	Spikes from right inferior frontal lobe
PS	17	18	m	Intractable seizures	MRI: abnormal thickening and coarsening of gyri on right with shallow right Sylvian fissure		Profuse runs spike and slow waves right hemisphere	Right hemisphere spikes
PS	19	40	m	SPS with clonic activity of left face and neck; known right frontal glioma status post 2 resections	MRI: right frontal mass lesion extending from cortical surface to ventricular margin; adjacent cystic cavity	Ictal onset: right central	Right central slowing and breach rhythm; C4 sharp and slow waves	Spikes at posterior edge of frontocentral lesion
PS	22	16	m	CPS; history of head trauma	MRI: right mesial temporal sclerosis; right posterior frontal and parietal encephalomalacia	Ictal onset: right hemisphere	F4>T4 spikes and sharp waves; slowing on right; asymmetric spindles (seen better on left than on right)	Multifocal right hemisphere spikes plotted to right insula (not to hippocampus)
PS	23	15	f	CPS with left head turn then asymmetric tonic posturing and left sided clonic activity; choroid plexus papilloma resected in early childhood	MRI: large right posterior quadrant resection cavity	Ictal onset: right posterior temporal	Bursts and runs of polyspike and slow wave discharges broadly over F4-C4-P4 and also T6>T4; several brief seizures from same area	Spikes surrounding cavity
PS	25	6	m	Autism; possible Landau Kieftner variant	MRI: one study showed right parietal patchy subcortical lesion not seen on recent study	Profuse right frontocentral spike and slow wave discharges with frequent secondary bilateral synchrony; more recently EEG only mildly slow	C4 sharp wave	Right frontal sharp wave near posterior Sylvian fissure
PS	26	16	m	CPS with right head turn and right arm extension	MRI: abnormally oriented right parietal sulcus with possible thickening of cortex and blurring of gray-white junction	Ictal onset: bursts of rhythmic activity in right parasagittal region (C4-P4); interictal: C4-P4 maximum sharp waves and bursts of low voltage fast activity	Profuse runs of right centroparietal spike and slow and polyspike and slow wave runs; right hemisphere slowing	Frequent spikes seen in right parietal region near lesion on MRI, seen individually or in 2- to 3-second trains

Type of Study	Case No.	Age	Sex	Seizure Type/Risk Factors	Neuroimaging	Video-EEG (scalp)	EEG	MEG/MSI
WH	37	8	f	Epilepsia partialis continua of right leg progressing to right arm	MRI: normal	Continuous left frontocentral epileptiform activity	Profuse spiking left frontocentral region	Continuous central spikes near left toe region on somatosensory mapping; excellent dipole cluster
WH	38	12	m	Intractable nocturnal tonic seizures	MRI and PET normal	Interictal spikes left centroparietal; ictal poorly localizing but suggestive of left central onset	Bursts of left central spikes/polyspikes phase reversing at C3/P3	Left parietal spikes
WH	39	39	f	Intractable complex partial seizures	MRI: normal; PET with left temporal hypometabolism	Left temporal ictal onset	In sleep, frequent spikes with a broad field but phase reversing at F7	Left temporal spikes with broad field
WH	40	38	f	Intractable complex partial seizures	MRI: right mesial temporal sclerosis	Interictal: frequent left anterior temporal spikes; 2 seizures with left temporal onset and two with poorly lateralized onset	Irregular slowing over left temporal region; spikes maximal at F7	Left temporal spikes
WH	42		m	Refractory absence and generalized tonic-clonic seizures thought consistent with inherited generalized epilepsy	MRI: left MTS; PET: left posterior mesial temporal hypometabolism, small area of hypometabolism left occipito-parietal	None; past EEGs have shown bursts of generalized spike and slow wave	Left anterior temporal sharp waves	Left anterior temporal spikes
WH	43	46	m	Intractable CPS status post radiosurgery of right frontal AVM with no change in seizures	MRI: AVM inferior to head of right caudate	Ictal onset: diffuse right hemisphere changes maximal over right frontal and temporal regions	Occasional broad sharp waves seen over right hemisphere, maximal at F8; independent left hemisphere spikes maximal at F7; independent spikes seen at FP1 and less frequently FP2	Bilateral independent and simultaneous right and left frontal and right and left temporal spikes
WH	44	6	f	Landau Kleffner syndrome	MRI: normal		Frequent independent bitemporal spikes, with broader field over the right, and phase reversal at C3-T3 over the left	Bilateral perisylvian spikes
WH	51	54	m	Intractable CPS	MRI: left MTS	Ictal onset left temporal	Rare left hemisphere spikes with a broad field and phase reversal at F7	Left anterior temporal spikes
WH	52	33	f	Intractable CPS	MRI: right MTS	Ictal onset: right temporal	Irregular slowing over right frontotemporal region; spikes isopotential at F8-T4	Right temporal spikes
WH	53	21	m	Intractable CPS	MRI: normal except for Rathke's cleft cyst	Two seizures nonlocalizing and one with left frontocentral onset; interictal frequent generalized polyspike and slow wave	Left frontal sharp waves and spikes; generalized spike and slow waves left maximal	Generalized spike and slow wave complexes maximal on left with poor dipole fits; left frontal spikes with good dipoles

Type of Study	Case No.	Age	Sex	Seizure Type/Risk Factors	Neuroimaging	Video-EEG (scalp)	EEG	MEG/MSI
WH	56	5	m	Congenital right middle cerebral artery stroke and intractable complex partial seizures	MRI: large area of encephalomalacia involving the right temporal, frontal, and parietal regions	Interictal: prominent irregular slowing and frequent, sleep activated, interictal spike discharges from the right occipital area; no seizures captured	Obiteration of normal posterior basic rhythm on the right, with a suppressed background over the right posterior quadrant with very frequent bursts of high-voltage polyfrequency activity and spikes from that region	discharges and multifocal spikes with left central predominance (F3-C3) discharges and multifocal spikes with left central predominance (F3-C3) discharges and multifocal spikes with left central predominance (F3-C3) Spikes medial and lateral to the occipital horn of the right lateral ventricle

PS, Paired-sensor; WH, whole-head; SPS, simple partial seizures; CPS, complex partial seizures.

TABLE 2B

Type IB cases (E-/M-)

Type of Study	Case No.	Age	Sex	Seizure Type/Risk Factors	Neuroimaging	Video-EEG (scalp)	EEG	MEG
PS	1	51	m	SPS with left sided clonic activity; known right frontal oligodendroglioma	MRI: high to mid right frontal convexity mass without enhancement		Left central-parietal breach	No spikes
PS	11	44	m	SPS with right leg weakness, involuntary right arm movement, blinking	MRI: cortical dysplasia extending to the left ventricular surface of the posterior left frontal lobe		Right temporal wicket	No spikes
PS	24	45	f	CPS with altered awareness, staring, lip smacking, dysphasia	MRI: large area of remote hemorrhage and hemosiderin staining within left posterior temp lobe	Ictal onset: left temporal	Left temporal breach	No spikes
WH	36	9 mo	m	Intractable seizures and mild delay	MRI: hypothalamic hamartoma	Ictal EEG normal	Normal	No spikes
WH	45	28	m	Intractable complex partial seizures	MRI: increased signal intensity in the posterior body and tail of the left hippocampus	Ictal onset left posterior temporal region	Normal	No spikes
WH	46	31	f	Intractable complex partial seizures	MRI: normal	Ictal onset left posterior temporal region	Normal	No spikes
WH	55	19	m	Intractable SPS with rocking	Normal	Ictal onset with diffuse slowing	Normal	No spikes
WH	57	46	f	Intractable CPS	MRI: normal except for mild cerebellar atrophy; PET: normal	Interictal: right frontal spikes and independent bitemporal spikes L = R; ictal pattern nonlateralizing	Normal	No spikes

PS, Paired-sensor; WH, whole-head; SPS, simple partial seizures; CPS, complex partial seizures.

TABLE 2C

Type IC Cases (E+/M+ Overlap)

Type of Study	Case No.	Age	Sex	Seizure Type/Risk Factors	Neuroimaging	Video-EEG (scalp)	EEG	MEG
PS	21	18 mo	m	SPS with left head and eye deviation, left arm tonic posturing; history of perinatal intraparenchymal hemorrhage of right temporal lobe	MRI: extensive post-hemorrhagic periventricular leukomalacia of the right hemisphere; PET: large defect in corresponding area	Ictal onset: right hemisphere (broad)	Right hemispheric slowing and loss of detail maximal in the posterior quadrant; right posterior quadrant spikes; bursts of more generalized polyspike-and-slow-wave discharges bilateral frontocentral	Frequent spikes seen anteriorly, posterior and superior to area of T2 prolongation within right temporal lobe as well as in white matter adjacent to right lateral ventricular horn
PS	7	7	f	Landau Kleffner syndrome	MRI: left inferior temporal cortical dysplasia	Continuous spike and slow wave in sleep with a dipole oriented parasagittal negative/temporal positive; at times unilateral discharges seen more frequently on the right; no distinct seizures	Broad bilateral spike and slow waves without clear laterality; independent right and left midtemporal discharges	Generalized spike and slow wave but higher amplitude and lead on left
PS	10	13	f	SPS of 'turning' and clonic movements of left arm	MRI: slight asymmetrical enlargement of right choroidal fissure, likely a small arachnoid cyst		Occasional bursts of 3- to 4- Hertz spike-wave, broadly distributed but with a right frontal maximum	Occasional right frontal spikes
PS	15	2	f	Linear sebaceous nevus syndrome and infantile spasms	MRI: giant perivascular spaces throughout right hemisphere; smaller right hemisphere; MR spectroscopy: right posterior parieto-occipital focus; PET: diffuse hypometabolism of right hemisphere with relative sparing of frontal lobe and basal ganglia	Ictal onset: generalized electrodecremental	Multifocal spikes arising independently from left and right posterior quadrants; generalized spike and slow wave discharges in sleep	Spikes in right posterior parietal and occipital region
PS	16	32	F	Intractable CPS	MRI: dysplasia of left hippocampus and amygdala; bilateral periventricular heterotopic gray matter; large schizencephalic cyst replacing posterior left frontal lobe, left parietal lobe, and posterior left temporal lobe		Bilateral occipital spikes, both synchronous and independent, left > right; bilateral independent anterior temporal spikes	Bilateral independent temporal spikes; left temporal spikes localize to middle cranial fossa on rim of large cyst

Type of Study	Case No.	Age	Sex	Seizure Type/Risk Factors	Neuroimaging	Video-EEG (scalp)	EEG	MEG
PS	30	25	f	SPS/CPS with drooling, abdominal sensations, left hand weakness	MRI: cortical dysplasia in right peritrolandic region	Ictal onset: generalized, nonlateralized; interictal: generalized spikes with right hemispheric emphasis but also rare independent hemispheric discharges	Polyspike and slow waves seen bilaterally and independently in right and left midtemporal regions, right slightly more frequently	Clear left hemisphere spikes seen on MEG did not meet criteria for analysis; independent right hemisphere spikes and generalized spikes mapped to right parietal cortical dysplasia, to the medial right temporal lobe (mid and posterior), to the right hippocampus, and to the right parahippocampal gyrus
PS	32	10	m	Prolonged status epilepticus following encephalitis of unknown etiology	MRI: progressive atrophy and increased T2 signal in both hippocampi	Ongoing multifocal seizures	Multifocal seizures arising independently and sequentially from the right frontal, left frontal, right posterior quadrant	Frequent multifocal spikes throughout recording, but only one group of right frontocentral spikes could be modeled with low error
PS	34	11	f	SPS/CPS with left sided clonic jerks; Rasmussen encephalitis	MRI: progressive atrophic changes and white matter loss in right frontal regions		V-waves skewed to left; single sharp wave left parasagittal	Multifocal independent spikes in bilateral central-parietal regions
WH	41	7	f	Intractable symptomatic localization related epilepsy	MRI: focal cortical dysplasia of right frontal region; PET: normal	Outside VET: generalized and bifrontal spike and wave discharges, maximal on the right	Profuse bifrontal spikes and polyspikes occurring singly, in bursts, and in prolonged runs; higher amplitude on right than on left	Bursts of moderate to high voltage spike activity bifrontal with right frontal predominance; dipoles clustered in right superior middle frontal gyri as well as anterior aspect of Sylvian fissure
WH	48	3	m	Language regression	MRI: 5 mm heterotopic focus of gray matter next to the trigone of left lateral ventricle; possible tiny area of heterotopic gray matter next to posterior horn of right lateral ventricle		Frequent high voltage independent bilateral occipital spikes, higher in amplitude on the right	Right occipital spikes
WH	49	20	m	Intractable CPS	MRI: left MTS	Ictal onset: bursts of high amplitude, sharply contoured activity over right and left temporal regions	Independent bitemporal sharp waves often followed by a burst of high voltage rhythmic theta	Left temporal spikes
WH	54	39	f	Intractable CPS status post resection of left temporal AVM	MRI: resection cavity	Ictal onset independently from left and right temporal regions	Frequent T3 spikes; left temporal breach	Independent spikes in the bilateral mesial and lateral temporal lobes, bilateral insula, and anterior to the resection cavity in the left frontotemporal region

TABLE 2D

Type IIA Cases (E+/M-)

Type of Study	Case No.	Age	Sex	Seizure Type/Risk Factors	Neuroimaging	Video-EEG (scalp)	EEG	MEG/MSI
PS	20	17	f	CPS	MRI normal	No clear EEG correlate	Single sharp and slow wave at F3	No spikes
PS	28	26	f	SPS/CPS with "ticking" in left face followed by right eye deviation, loss of vision, emesis	MRI normal; SISCOM: left posterior quadrant focus	Ictal onset: left posterior quadrant	T5 sharp waves in sleep	No spikes
PS	29	30	m	CPS with prominent salivation	MRI: bilateral, symmetric, diffuse subtle T2 hyperintensity of the white matter consistent with toxic or metabolic disease; PET: left temporal hypometabolism	Ictal onset: left frontal; interictal: left temporal spikes	Single broad left hemisphere spike; single T3 sharp wave	No spikes
PS	31	10	f	SPS with inability to move	MRI: Left posterior temporal periventricular heterotopia		High frequency low voltage activity in left temporal region	No spikes
WH	50	21	f	Intractable CPS	MRI: abnormal left hippocampal head and anterior body	Interictal generalized spike-wave discharges skewed towards the left; ictal onset nonlocalizing	Single T3 sharp wave	No spikes
WH	58		f	Meningoencephalitis and intractable complex partial seizures	MRI: Left frontal encephalomalacia and left MTS; PET: nonlocalizing	Interictal: bitemporal spikes; ictal pattern nonlateralizing	Rare right temporal sharp waves	No spikes

SPS = simple partial seizures, CPS = complex partial seizures.

TABLE 2E

Type IIB Cases (E-/M+)

Type of Study	Case No.	Age	Sex	Seizure Type/Risk Factors	Neuroimaging	Video-EEG (scalp)	EEG	MEG/MSI
PS	33	25	f	SPS with fear, garbled speech, clonic movement of right arm	MRI: normal (no surface coil); PET with reduced uptake left thalamus compared with right	Ictal onset: left temporal	Left frontocentral sharp transients; burst of left wicket rhythm	Left posterior temporal sharp and slow waves

SPS, Simple partial seizures.

TABLE 2F

Type IIC Cases (E+/M+ No Overlap)

Type of Study	Case No.	Age	Sex	Seizure Type/Risk Factors	Neuroimaging	Video-EEG (scalp)	EEG	MEG/MSI	Type of Study
PS	35	32	f	CPS with head turn to left	MRI and PET normal		P3 sharp wave	Spikes localizing to posterior right parietal gray-white junction	Discordant E+/M+ no overlap

CPS, Complex partial seizures.