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Fast oscillations associated with interictal spikes localize the epileptogenic zone in patients with partial epilepsy

Adrian G. Guggisberg^{a,d,*}, Heidi E. Kirsch^{a,b}, Mary M. Mantle^a, Nicholas M. Barbaro^c, and Srikantan S. Nagarajan^a

^a Biomagnetic Imaging Lab, Department of Radiology, University of California San Francisco (UCSF), 513 Parnassus Ave S-362, San Francisco, CA 94143-0628, USA ^b Department of Neurology, University of California San Francisco (UCSF) ^c Department of Neurological Surgery, University of California San Francisco (UCSF) ^d Department of Neurology, University of Berne, Inselspital, 3010 Bern, Switzerland

Abstract

Although interictal epileptic spikes are defined as fast transient activity, the spatial distribution of spike-related high-frequency power changes is unknown. In this study, we localized the sources of spike-locked power increases in the beta and gamma band with magnetoencephalography and an adaptive spatial filtering technique, and tested the usefulness of these reconstructions for determining the epileptogenic zone in a population of 27 consecutive presurgical patients with medication refractory partial epilepsies. The reliability of this approach was compared to the performance of conventional MEG techniques such as equivalent current dipole (ECD) models. In patients with good surgical outcome after a mean follow up time of 16 months (Engel class I or II), the surgically resected area was identified with an accuracy of 85% by sources of spike-locked beta/gamma activity, which compared favourably with the accuracy of 69% found for ECD models of single spikes. In patients with a total of more than 50 spikes in their recordings, the accuracies increased to 100% vs. 88%, respectively. Imaging of spike-locked beta/gamma power changes therefore seems to be a reliable and fast alternative to conventional MEG techniques for localizing epileptogenic tissue, in particular if more than 50 interictal spikes can be recorded.

Introduction

Magnetoencephalography (MEG) is increasingly used in the presurgical management of patients with partial epilepsies refractory to combined pharmacotherapy. It has the advantage of being completely non-invasive and of offering a broad set of high-resolution analysis techniques. By recording the minute extracranial magnetic fields produced by brain current sources, it can trace field changes with a time resolution below 1 millisecond and permits the localization of sources with an accuracy of several millimetres (Wheless et al., 2004).

Furthermore, it also allows the assessment of the frequency content of neural oscillations. Thus,

*Correspondence: Adrian G. Guggisberg, Biomagnetic Imaging Lab, Department of Radiology, University of California San Francisco (UCSF), 513 Parnassus Ave S-362, San Francisco, CA 94143-0628, USA, Email: aguggis@gmail.com, Phone: +1 415 476 5093, Fax: +1 415 502 4302.

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it is ideal for the study of cerebral activity that changes rapidly over space, time, and frequency, such as epileptic discharges.

The most widely used MEG technique for localizing the epileptogenic zone in patients with partial epilepsy is visual identification of interictal spikes in the raw MEG and calculating the location and orientation of equivalent current dipoles (ECD) that best account for the observed magnetic field (Vrba et al., 2001; Wheless et al., 2004). Several studies have shown that this method can provide reliable and useful information in presurgical patients with partial epilepsy (Stefan et al., 2003; Wu et al., 2006; RamachandranNair et al., 2007), and have concluded that non-invasive MEG techniques might eventually partly replace invasive intracranial recording techniques (Pataria et al., 2004; Papanicolaou et al., 2005; Knowlton et al., 2006). However, the analysis procedures require that each dipole is manually reviewed and classified as either corresponding to a real spike or as corresponding to a non-epileptic origin, which can be time-consuming, requires trained and experienced scorers, and introduces a sizeable amount of subjectivity in the results.

Single epileptic spikes are defined as having a duration of less than 70 milliseconds (IFSECN, 1974), which corresponds to an oscillation frequency of greater than 7 Hz. Thus, epileptic spikes are mostly manifested in the alpha, beta, and gamma frequency bands of MEG recordings, and localizing sources of these higher-frequency activities seems to be a promising approach for localizing epileptogenic tissue. The more recently introduced adaptive spatial filtering techniques such as synthetic aperture magnetometry (SAM) indeed make it possible to reconstruct the sources of the spectral content of the electromagnetic brain activity (Van Veen et al., 1997; Vrba et al., 2001; Sekihara et al., 2001; Sekihara et al., 2004; Sekihara et al., 2005). However, high-frequency MEG activity is obviously not composed of epileptic spikes only, but also contains intrinsic, physiologic brain activity as well as noise. A reliable algorithm for localizing epileptic tissue therefore has to accomplish the task of separating these components. One solution that was previously proposed is based on the assumption that spikes have a greater kurtosis than physiologic activity (Robinson et al., 2004). SAM(g2) therefore combines spatial filtering of beta and gamma activity with a measure of excess kurtosis of the MEG signal, and allows the automatic creation of 3-dimensional images estimating the origin of spikes in the brain. Several studies (Robinson et al., 2004; Ukai et al., 2004; Kirsch et al., 2006) have demonstrated the usefulness of this method when there is a single spike focus and a good signal-to-noise ratio. However, as ECD, this method requires manual verification of all obtained localizations, which again is time-consuming and susceptible to subjective criteria.

Here, we propose a different approach that requires manual intervention at an early analysis stage, but then provides fully automated localization of epileptogenic tissue: in a first step, interictal epileptic spikes are manually marked in the MEG recordings, and then, the sources of spike-locked power changes in the beta and gamma bands are localized using an adaptive spatial filtering method. This study demonstrates the validity of this algorithm in a population of 27 consecutive patients with partial epilepsies, and compares it with the validity of established MEG based localizations of epileptogenic tissue. As gold standard for determining the correct location of the epileptogenic zone, we use the location of surgically resected tissue in patients that have a significant reduction in seizures after surgery.

Materials and Methods

Patients

All 27 patients with medically refractory partial epilepsy who were admitted to the Biomagnetic Imaging Lab for magnetic source imaging (MSI) between June 2004 and August 2006 and who met the following inclusion criteria were retrospectively included in the study: they had epilepsy surgery at the Department of Neurological Surgery, UCSF, after MSI, and they had

follow-up at the Department of Neurology, UCSF, for at least 2 months after surgery. All participants gave their written informed consent to participate in the experiments, all procedures were approved by the UCSF committee on human research, and all experiments were conducted according to the Declaration of Helsinki.

Structural images

Magnetic resonance imaging (MRI) was performed at 1.5 Tesla. The protocol typically included the following sequences: (1) a T1-weighted, 3D spoiled gradient-recalled echo in a steady state sequence with TR 34 ms, TE 3 to 8 ms, flip angle 30°; (2) a T2-weighted 3D fast-spin echo sequence with TR 3000 ms, TE 105 ms. Both sequences had a slice thickness of 1.5 mm, matrix 256×256×(108–140), and a field view of 260×260 mm with skin-to-skin coverage to include the nasion and preauricular points.

Recordings

The participants were lying with their eyes closed in a magnetically shielded room. Between 20 and 60 minutes of continuous, interictal, resting state MEG were recorded with a 275 channel whole-head CTF Omega 2000 system (VSM MedTech, Coquitlam, BC, Canada), using a passband of DC to 70 Hz and a sampling rate of 600 Hz. In addition, 19 electroencephalography leads were recorded according to the international 10–20 system. Some patients were sleep deprived, and reached various stages of sleep during the recordings.

Surgical procedures

After the MEG recordings, all patients underwent surgical interventions with the intention of improving the seizure-frequency. All surgeries were performed by the same surgeon (NMB) and used intraoperative electrocorticography (ECoG) to tailor the margins of resection, along with intraoperative and extraoperative direct cortical stimulation mapping of functional cortex, and extraoperative subdural ictal ECoG recording as needed (results noted in Table 1 as “ECoG Ictal Onset”). Anterior temporal lobectomies (denoted as “ATL” in Table 1) were done using tailored subpial dissection with en bloc removal of mesial structures when possible, using intraoperative electrocorticography and (for dominant resections) direct electrical cortical stimulation language mapping to determine the precise boundary of resection. In general, unless otherwise noted, dominant resections included the superior temporal gyrus back to 2.5–3 cm from the temporal tip, the middle temporal gyrus to 3.5–4 cm, and the inferior temporal gyrus to 3.5–5 cm depending on the results of language testing. Nondominant lateral cortical resections extended to 4–5 cm from the pole. Resections included the amygdala and the hippocampus to 2–3.5 cm.

Signal analyses

A single-sphere (for ECD) and a multi-sphere (for adaptive spatial filtering) head-model were created for each patient, based on the structural MRI images. Co-alignment of structural and functional images was achieved by marking 3 prominent anatomical points (nasion and preauricular points) of the subject’s head in the MRI images, and localizing 3 magnetic fiducials attached to the same points before and after each MEG scan.

All recordings were reviewed by 3 experienced epileptologists/technicians, and the peak of all epileptic spikes was marked manually based on both the MEG and EEG recordings. The third reviewer made the final decision on which patterns were classified as epileptic spike.

In addition to the continuous recordings, spike-locked datasets were created starting 1 second before and ending 1 second after each spike, and corrected for baseline-offset using the first

700 milliseconds. Spikes with an interval of less than 1 second to the previous spike were excluded.

An equivalent current dipole model was fitted to the magnetic field recorded with the entire MEG sensor array during each single spike (ECDss). For each spike, the sampling point was used that yielded the model with the smallest residual variance. As a general rule, spikes with dipoles having greater than 10% residual variance were rejected. Spike topography, moment strength, and orientation were also considered for selection of ECDss.

In addition, an ECD was also calculated for the average of all spikes (ECDav) using the averaged, baseline-corrected, spike-locked datasets. A 1-dipole model was used for most patients, but the magnetic field map of 3 patients suggested the presence of 2 distinctive dipoles, and a 2-dipole model was used in these cases (patients 8, 9, 22).

For analysis of SAM(g2), the 2-minute MEG segments that showed the greatest amount of interictal epileptiform discharges and no muscle artefacts were selected, and subjected to estimation of excess kurtosis and band power between 20 and 70 Hz at each 5×5×5 mm volume element in the brain (Kirsch et al., 2006; Robinson et al., 2004). The data reported here includes all peaks of these SAM(g2) images without manual revision of locations in the source waveforms.

For the method proposed here (spike-locked adaptive spatial filter, SpiFi), we first assessed the time course and frequency pattern of spike-induced MEG changes by calculating a time-frequency transform for a subset of 19 equally spaced MEG sensors that were closest to the electrode positions in the international 10–20 system and thus covered the entire scalp. Overlapping time-windows of 200 milliseconds length were Hanning-windowed and Fourier-transformed, sliding the time window in 25 ms steps (short-time Fourier transform). The resulting power spectra of each time step were averaged over spike-epochs and log-transformed. Power changes at each time-frequency point were obtained by subtracting the mean baseline log-power spectrum from each spectral estimate (Zygierewicz et al., 2005). A dual-state adaptive spatial filter (Van Veen et al., 1997; Vrba et al., 2001; Sekihara et al., 2001; Sekihara et al., 2004; Sekihara et al., 2005) was then used to calculate source power changes in the beta and gamma frequency bands (~12–55 Hz) during the interictal spikes from the recordings of all MEG sensors. Based on the results of the time-frequency transforms, an active time window of 100 ms before to 100 ms after the spike peak and a baseline time window of 700 ms to 500 ms before the spike peak were selected for all subjects. The selection of the limits of the frequency band included for adaptive spatial filtering was found to be not critical: in all our subjects, a broad generic band of 12 to 55 Hz essentially yielded the same activation patterns as more narrow bands that were individually determined within the beta/gamma range based on time-frequency transforms. We report here the activations in the individually determined frequency bands, since they often showed greater power changes than activations in the generic band.

All source localizations were done with the dipole-fit and adaptive spatial filtering software provided by VSM MedTech (Coquitlam, BC, Canada), as well as custom in-house programs (Dalal et al., 2004).

Performance validation and statistical analyses

The surgical outcome was clinically assessed and classified according to the Engel criteria (Engel et al., 1993). For the purpose of this study, the Engel classes I and II were interpreted as good outcome (G), and the Engel classes III and IV as bad outcome (B). The results of all MEG studies were classified into one of the following 3 groups: MEG localization concordant with surgical resection site, i.e. within 2 centimetres of the limits of the resection area (c), MEG

localization discordant with surgical resection (d), or MEG non-localizing (n). The non-localizing group included all of the following cases: technical failure due to artefacts, no area localized due to insufficient spikes, diffuse or multi-focal (>2) localizations, localizations outside the brain, or localizations in the basal ganglia/cerebellum. If an MEG study showed 2 different foci, it was classified as concordant (c) if at least one of them was within 2 centimetres of the resection area. The location of surgical resection could be inspected in post-surgical MRIs or CTs in 13 patients, and was estimated from the detailed descriptions in the operation reports for the remaining patients. The data of the 25 patients with complete resections was used to calculate:

- the sensitivity of each MEG analysis technique as: # of Gc/# of (Gc+Gn+Gd);
- the accuracy as: # of Gc/# of (Gc+Gd);
- the positive predictive value as: # of Gc/# of (Gc+Bc).

Two patients with incomplete surgical resection (see Table 1) were excluded from this analysis. The analysis techniques were tested for an association with the site and outcome of the epilepsy surgery by subjecting the corresponding contingency tables to Fisher-Freeman-Halton tests.

Results

Table 1 gives an overview of the clinical profiles, surgical procedures, and MEG localizations of all patients. The included patients had a mean age of 38 years (range 17–67), 17 were women. They suffered from seizures of various types and due to different focal pathologies for a mean duration of 27 years (4–54). After epileptic surgery, patients were followed up for an average of 16 months (2–30). Nineteen patients (70.4%) had a good post-surgical outcome as defined by an Engel class I (seizure-freedom) or II ($>85\%$ reduction in seizure frequency).

Interictal epileptic spikes were associated with a short lasting, transient power increase in a relatively broad frequency band ranging from delta to beta and sometimes gamma rhythms (Figure 1A and 1C). The beta rhythms started to increase earlier than low-frequency rhythms, which is in agreement with the shape of spikes and their subsequent slow waves. In addition, high-frequency power changes were typically more focal than low frequency changes (see Figure 1A and 1C).

Figure 1 shows the sources of spike-locked beta/gamma activity of 2 typical patients, and demonstrates that they were generally in agreement with the locations of spike ECD (Figure 1B) and with the surgical resection site (Figure 1B and 1D).

Figure 2 shows that, overall, the method proposed here had a superior sensitivity, accuracy, and positive predictive value than ECD models and uncorrected SAM(g2): the sensitivity for ECDss, ECDav, uncorrected SAM(g2), and SpiFi was 47%, 37%, 32%, and 58%, respectively; the accuracy 69%, 64%, 40%, and 85%; the positive predictive value 82%, 88%, 100%, and 100%. In patients with more than 50 spikes, i.e., where sufficient data for calculation of the adaptive spatial filter weighting matrix was available, the sensitivity, accuracy, and positive predictive value of SpiFi was 90.9%, 100%, and 100%, respectively, which is also superior to the values of all traditional methods. In patients with rare spikes, i.e. with insufficient data for the spatial filter, the proposed approach showed the expected poor performance, but all traditional methods had only marginally better results. Figure 2 also shows that SpiFi outperformed traditional spike localization methods in patients with neocortical as well as in patients with mesiotemporal epilepsies.

The localizations of the method proposed here showed a significant association with the site of surgery and the post-surgical outcome ($p < 0.033$), which was not the case for all traditional methods ($p > 0.27$).

Discussion

This is the first study to demonstrate that the transient increase in beta and gamma power accompanying interictal epileptic spikes can be used to reliably localize the epileptogenic zone in presurgical patients with medically refractory partial epilepsy. In our patient population, the sensitivity and accuracy of this approach compared favourably with the performance of traditional ECD models. The reliabilities reported here might appear lower than values reported in larger populations (Stefan et al., 2003), which we attribute to differing definitions of sensitivity and accuracy and the more severe criteria for concordance of MEG results with the surgical resection site used in this study. The positive predictive value for good post-surgical outcome was similarly high for our method as previously reported for traditional MEG techniques (RamachandranNair et al., 2007).

The enhanced overall performance of the technique introduced here can be explained with its inherent technical advantages:

1. Unlike ECD models of single spikes, SpiFi makes use of the combined information of all interictal spikes recorded from a patient for localizing the epileptogenic zone, which makes the results more robust. In particular, the localizations can be expected to be correct even in the case of a low signal-to-noise ratio, and even if a minority of the MEG field changes classified as epileptic spikes are in reality of non-epileptic origin. This is illustrated in Figure 1D, where the single ECD were localized diffusely throughout the brain, whereas the average power changes in the beta/gamma band correctly identified the surgically removed epileptogenic zone.
2. Unlike ECD models, which assume that the observed MEG field is produced by a few point sources and therefore yield misleading results if the source of epileptic spikes has a larger extension (Kobayashi et al., 2005), adaptive spatial filters as used in the proposed approach calculate source power at each volume element in the brain and thus potentially allow thousands of dipoles to be the sources of MEG activity. This seems to be particularly beneficial when several heterogeneous spikes originating from a source with relatively large extension are averaged, since our results show that adaptive spatial filtering provides more reliable localizations than ECD models of the averaged spike field (see Table 1, patients 4, 5, 6, 14, 19; ECDav). Averaging the interictal spike waveforms in sensor space necessarily assumes that the underlying sources are reliably arising from similar locations. Source location variability leads to systematic error in reconstructions, and may reduce the reliability of localization. In contrast, SpiFi can be considered as performing averaging in source space, and therefore, inhomogeneity in location of individual spikes causes spatial blur in reconstructions.
3. A common technical problem of MEG recordings are low frequency artefacts originating from non-removable metal such as dental fillings in the patient's body (Stefan et al., 2003). ECD models on single spikes cannot be used in this case, and even averaging across spikes often does not remove the high-amplitude artefacts. The example of patient 4 (Table 1) shows that SpiFi is still able to correctly localize the epileptogenic zone in these cases, due to the spatial filtering method and also because it only uses the high-pass filtered data that is not affected by the typical low-frequency artefacts caused by metals.

4. Unlike SAM(g2), SpiFi makes use of the highly reliable classification skills of epileptologists and technicians at an early analysis stage, and then provides valid localizations without further manual interventions. This study shows that the excess kurtosis used by SAM(g2) to separate spikes from other high frequency rhythms, has a comparatively lower performance. SAM(g2) therefore requires extensive manual verification of its results at a later analysis stage, which then improves its performance reported here (Kirsch et al., 2006). However, the required revision of source waveforms fits less smoothly into the clinical routine procedure of reviewing the raw data than the marking of spikes used in the proposed approach.

In addition to being accurate and sensitive, SpiFi has the practical advantage of being computationally faster than ECD models and SAM(g2) and of reducing the work-load for MEG technicians.

On the other hand, the method introduced here has the disadvantage that the adaptive spatial filter used for source reconstruction requires a sufficient amount of recording time for a valid estimation of the sensor covariance and therefore of the sensor weighting matrix (Van Veen et al., 1997). With the settings used in this study, at least 50 to 60 spikes were necessary for reliable localizations. In patients with rare interictal events, the method performed poorly and worse than conventional methods (Figure 2).

We may thus conclude that source reconstruction of spike-locked beta and high-gamma activity with adaptive spatial filters is a reliable and fast alternative for localizing the epileptogenic zone in patients with partial epilepsy who have a sufficient amount of interictal spikes in their recordings.

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Figure 1.

MEG results in 2 typical patients. **A, C.** Short-time Fourier transforms reveal transient power increases time-locked to the peak of interictal epileptic spikes at 0 seconds in a broad frequency band ranging from delta to gamma rhythms, with high-frequency changes being more focal than low-frequency changes. **B, D.** An adaptive spatial filter localizes spike-locked beta and gamma power increases (squares in upper row) to the zone that was later surgically resected (lower row), and, in case of patient 5, to the area of clusters of corresponding ECD (yellow dots). Images are presented in neurological convention (left is left). *ECDss* refers to equivalent current dipoles of single spikes; *SpiFi*, spike-locked dual-state adaptive spatial filtering in the beta/gamma frequency band.

Figure 2.

The sensitivity, accuracy, and positive predictive value as defined in the Method section are shown for conventional MEG analysis techniques and for the new method introduced here. *ECDss* refers to equivalent current dipoles of single spikes; *ECDav*, ECD of averaged spikes; *SAM(g2)*, synthetic aperture magnetometry and excess kurtosis; *SpiFi*, spike-locked dual-state adaptive spatial filtering in the beta/gamma frequency band.

Table

Clinical data, MRI, EEG, MEG findings, surgical procedures, pathology, and post-surgical outcomes of all 27 patients included in the study. MEG localizations in bold letters were considered concordant with the operation site, localizations in italic letters were considered discordant. Underlined letters correspond to patients that had more than 50 interictal spikes in their recordings

Nr	Age	Sex	Seizures	MRI	VEEG	ECog	MEG	ECDss	ECDav	SAM(g2)	SpilFi	Site	Type	Comp	Pathology	Outcome
			Type	Dur [yr]	Ictal Onset	Ictal Onset	Spikes [nr]									FU [mth] SzFr [mth] Engel
Good Outcome																
<i>mesiotemporal</i>																
1	40	M	CPS	36	MTS R	R-T	-	34	R-T-a	nl	nl	R-T	ATL	yes	MTS	18 IA 18
2	32	F	CPS	27	MTS L	L-T	-	50	nl	nl	nl	L-T	ATL	yes	MTS	20 II 19
3	46	F	CPS	42	MTS R	R-T	-	17	nl	nl	nl	R-T	ATL	yes	MTS	19 IB 19
4	41	M	CPS/2GS	8	atrophy hippo R	L-T	-	<u>73</u>	artefact	nl	<u>L-T-s/L-F-dl</u>	L-T	ATL	yes	MTS	24 IB 24
5	67	F	CPS	48	MTS L	L-T	-	<u>108</u>	<u>L-T-a</u>	<u>L-F-vm/L-T-a</u>	<u>L-T-a</u>	L-T	ATL	yes	MTS	18 IA 18
6	45	F	SPS	43	atrophy hippo L+R	R-T	-	<u>72</u>	<u>R-T-a/R-F-vm</u>	<u>L-T-i</u>	<u>R-T-a</u>	R-T	ATL	yes	MTS	12 IA 12
7	44	F	CPS	41	MTS L	L-T	-	10	R-T	nl	nl	L-T	ATL	yes	MTS	11 IA 11
8	55	M	CPS	53	atrophy hippo L, infarct MCA L-TP	L-T	-	<u>71</u>	<u>L-T-i</u> nc*	<u>R-P-ps</u>	<u>L-T-i</u>	L-T	ATL	yes	MTS	21 II 16
9	30	F	CPS	29	MTS L	nl	L-T-m	<i>R-T-m</i>	<i>R-T-m/L-P-a*</i>	<i>R-T-m</i>	<i>R-T-m</i>	L-T-m	AHE	yes	MTS	10 IA 10
10	20	M	CPS/NCSE	15	residual hippo L	-	-	<u>56</u>	<u>L-F-dl</u>	<u>L-T-pl</u>	nl	L-T-m	Re – AHE	yes	MTS	7 IA 7
<i>neocortical</i>																
11	31	F	CPS/2GS	10	normal	L-T-p	L-T-pi	0	nl	<i>L-O/R-O</i>	nl	L-T-i	CorE	yes	CD	21 IA 21
12	27	F	CPS/2GS	4	lesion L-T-i	L-T	-	39	<u>L-T-a/L-F-vl</u>	<u>L-T-i</u>	<u>L-T-i</u>	L-T + L-T-i	ATL/CorE	yes	Gloma/CD	19 II 15
13	23	F	CPS/2GS	17	infarct MCA L-TP	L-T-a	L-T-pi	<u>117</u>	<u>L-T-pi</u>	<u>L-T-pi</u>	<u>L-T-pi</u>	L-T	ATL	yes	Ischemia	21 II 0
14	54	F	CPS	36	gray matter-heterotopia R-T-p	R-T	-	<u>78</u>	<u>R-T-pm</u>	nl	<u>R-T-pm</u>	R-T-p	CorE	yes	Gliosis	7 IA 7
15	35	F	CPS	30	EM L-T-I, atrophy hippo L	L-T	L-T-i	<u>82</u>	<u>L-T-s</u>	<u>L-T-s</u>	<u>L-T-s</u>	L-T + L-T-i	ATL	yes	Gliosis	3 IA 3
16	46	M	CPS	5	AVM R-F-vm	R-T	-	<u>51</u>	nl	<u>L-F-dl/L-T-m</u>	<u>R-F-vm</u>	R-F-vm	CorE	yes	AVM	25 II 0
17	24	F	CPS	16	lesion L-P-p, MTS L	L-T-p	L-P-p	36	<i>L-P-a</i>	L-P-p	<i>L-T-s</i>	L-P-p	CorE	yes	CD	2 IA 2
18	17	M	CPS	17	EM R, atrophy hippo R	R-F-a	-	<u>240</u>	R-F-d	R-F-d	R-F-d	R	Re – HemE	yes	CD/scar	9 IB 9
<i>unknown</i>																
19	34	M	CPS/2GS	9	normal	R-T-a	-	<u>69</u>	<u>R-T-m</u>	<u>L-F-dl/R-F-dl</u>	<u>R-T-a</u>	R-T	ATL	yes	Gliosis	15 IA 15
Bad Outcome																
<i>mesiotemporal</i>																
20	60	F	CPS	54	MTS R	nl	-	1	artefact	nl	nl	R-T	ATL	yes	MTS	30 IV 6
21	37	F	CPS/2GS	7	MTS L	L	L-T-pi	0	nl	nl	nl	L-T-pi	CorE	yes	Gliosis	13 IV 0
22	37	M	CPS	34	MTS L	L-T	-	31	nl	<i>L-T-s/L-F-vm*</i>	<i>R-M</i>	L-T	ATL	no	Gliosis	8 III 0

Nr	Age	Sex	Seizures	Dur [yr]	MRI	VEEG		ECoG		MEG		Surgery			Pathology		Outcome			
						Ictal Onset	Ictal Onset	Ictal Onset	Spikes [nr]	ECDss	ECDav	SAM(g2)	SpiFi	Site	Type	Comp	FU [mth]	Engel [mth]	SzFr [mth]	
23	32	F	CPS	23	residual hippo L	L-T	-	-	46	<u>L-T-I</u>	<i>L-M-i</i>	<i>L-F-dl</i>	nl	L-T	Re – ATL	yes	MTS	25	III	0
24	36	F	CPS	26	normal	L-T	L-T-m	L-T-m	33	<i>L-M</i>	<i>L-M</i>	nl	nl	L-T	ATL	yes	MTS	26	III	1
<i>neocortical</i>																				
25	24	M	SPS	14	EM R-PT	R	-	-	<u>232</u>	<u>R-P-p</u>	<u>R-P-p</u>	<u>R-P-p</u>	<u>R-P-p</u>	R-P-p	CorE	no	Gliosis	18	IV	1
26	45	F	CPS	33	diffuse atrophy L	L	L-F/L-TP	L-TP	<u>54</u>	<u>L-T-m</u>	<u>L-T-m</u>	<u><i>L-T-ds</i></u>	<u><i>L-T-ds</i></u>	L-F-vm/L-T-m	CorE/HE	yes	CD	12	IV	0
27	52	M	CPS/2GS	44	mass effect R-T-p	R-FT	R-T-pi	R-T-pi	0	nl	nl	nl	nl	R-T	Re – ATL	yes	Gliosis	19	III	2

Abbreviations: All locations are reported according to the format: Side-Lobe-sublobe, with L referring to left; R, right; F, prefrontal; T, temporal; M, motor and premotor; P, parietal; O, occipital; a, anterior; p, posterior; m, medial/mesial; l, lateral; v, ventral; d, dorsal; s, superior; i, inferior. **Sex:** F refers to female; M, male. **Seizures:** SPS, simple partial seizures; CPS, complex partial seizures; 2GS, secondary generalized seizures; NCSE, non-convulsive status epilepticus; Dur, duration; yr, years. **MRI,** magnetic resonance imaging: MCA, middle cerebral artery; MTS, mesio-temporal sclerosis; hippo, hippocampus; EM, encephalomalacia; AVM, arterio-venous malformation. **VEEG,** video-electroencephalography. **ECoG,** electrocorticography. **MEG,** magnetoencephalography: ECDss, equivalent current dipole models of single spikes; ECDav, equivalent current dipole model of averaged spikes; SAM(g2), synthetic aperture magnetometry and excess kurtosis analysis; SpiFi, spike-locked dual-state adaptive spatial filtering in the beta/gamma frequency band; nl, non-localizing; nc, not in the cerebral cortex; *, a 2-dipole model was used to localize averaged spikes in these patients. **Surgery:** CorE, corticectomy; ATL, anterior temporal lobectomy; AHE, amygdalo-hippocampectomy; HE, hippocampectomy; HemE, hemispherectomy; Re-, redo-operation after previous intervention; Comp, complete. **Pathology:** CD, cortical dysplasia; MTS, mesio-temporal sclerosis; AVM, arterio-venous malformation. **Outcome:** FU, total follow up time; mth, months; SzFr, time seizure-free after operation.