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ORIGINAL ARTICLE

Decision-making in temporal lobe epilepsy surgery based on invasive stereo-electroencephalography (sEEG)

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Abstract

In medical refractory temporal lobe epilepsy (TLE), the epileptogenic zone can be difficult to identify and therefore difficult to treat, especially in the absence of clear MRI pathologies and specific results from presurgical evaluation. Invasive monitoring with stereo-electroencephalography (sEEG) is a tool for a better determination of the epileptogenic zone. Here, we investigate the impact of sEEG on decision-making in temporal lobe epilepsy surgery. We reviewed patients with TLE who underwent further investigation with sEEG in our epilepsy unit. We examined specifically how sEEG findings influenced our decision regarding indication for a surgical procedure and resection volume. From 2013 to 2017, we performed 152 temporal resections in epilepsy patients. Twenty-one of these patients were designated for further preoperative investigation with sEEG due to incongruent findings in presurgical evaluation. Six patients were implanted bitemporally. In five cases, the hypothesis for the epileptogenic zone and localization had to be changed due to sEEG findings and resulted in a different tailored resection than intended. In three cases, sEEG findings led to the cancelation of the originally intended temporal resection as the epileptogenic zone was not definable or bilateral. In another three cases, the prognosis for reduction of seizures postoperatively had to be reduced due to the sEEG findings. However, the resection was performed after interdisciplinary discussion and informed consent of the patient. The examination by sEEG led to a change of plan for further treatment in 13 patients (61.9%) suffering TLE in total. Invasive monitoring with sEEG electrodes had a strong impact on decision-making for further treatment in patients suffering from temporal lobe epilepsy with incongruent findings in presurgical examination designated for epilepsy surgery. This applies to resection volumes as well as to prediction of seizure outcome.

Keywords Temporal lobe epilepsy (TLE) · Epilepsy surgery · Stereo-encephalography (sEEG) · Bilateral

Introduction

Refractory temporal lobe epilepsy (TLE) is generally a domain of epilepsy surgery due to good seizure outcome. Invasive diagnostic is seldom necessary [1]. However, when the combination of preoperative clinical and diagnostic data is incongruent or relevant MRI features are missing, invasive monitoring like stereo-electroencephalography (sEEG) becomes necessary. This is also the case when lateralization is questionable or bilateral seizure onset is assumed. Furthermore, sEEG is a useful tool to discriminate between the different mesial subtypes described by Bartolomei et al. [2, 3]. The goal of sEEG is to delineate the epileptogenic zone in a clinically useful way [4]. Surgical planning must take into account not only the epileptogenic zone but also the eloquent cortex areas all of which can be determined by sEEG. Recently, guidelines for the indication and use of sEEG were published [5]. A number of studies already describe the seizure outcome after sEEG recording [6, 7]. However, there is hardly any data on how the immense amount of data obtained from sEEG exploration is influencing daily practice in an

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appropriate way and how this affects our surgical planning in TLE. In this paper, we present an approach to interpreting sEEG data in TLE and the consequences that can be drawn from it.

Methods

All patients suffering from pharmaco-resistant TLE who were designated for further invasive monitoring by stereo- electroencephalography between June 2013 and December 2017 were included for evaluation. Patients had already undergone evaluation, performed at our Epilepsy Center, comprised of history of seizure, semiology, video electroencephalography (EEG) monitoring, 3 Tesla magnetic resonance imaging (MRI), neuropsychological testing, and partially single photon emission computed tomography (SPECT) and/or positron emission tomography (PET); language lateralization was determined by functional transcranial Doppler sonography [8]. MRI involved a T2-weighted space dark fluid, a T1-weighted magnetization-prepared rapid gradient-echo (MP-RAGE), and a FLAIR volume dataset. Likewise, a T2-weighted turbo spin echo (TSE) coronal, a T1-weighted turbo inversion recovery (TIR) coronal, and a proton density (PD)/T2-weighted axial dataset were acquired. Planning of sEEG trajectories and electrode implantations were performed by WH and JAK in cooperation with ML and TM at the University Medical Center Hamburg-Eppendorf. All patients received a postoperative MRI during their hospital stay. The patients were followed up through clinical investigations and EEG at our Epilepsy Center. Seizure outcome was evaluated according to the ILAE classification system whereby class 1–4 were defined as improvement [9]. Analysis of correlative clinical data was conducted retrospectively by chart review. Informed consent for clinical data evaluation was provided by all patients. The indication for surgical treatment was set in an interdisciplinary presurgical conference with epileptologists, neurosurgeons, and neuropsychologists. Qualitative variables are outlined as numbers and percentages. Statistical analysis of the data was performed by a univariate analysis (Fisher's exact test) to examine correlations between the parameters using IBM® SPSS® Statistics 22 (IBM Corporation, Armonk, NY, USA). Our epilepsy data register is approved by the local ethic committee at the medical council of the state of Hamburg (Ethik-Kommission der Ärztekammer Hamburg – PV-4585).

Results

Out of 152 surgical candidates suffering temporal lobe epilepsy, 21 (13.8%) patients were designated for investigation by sEEG. In our center, patients selected for sEEG have undergone non-invasive investigations consisting of seizure history, semiology, video-EEG, MRI, and neuropsychological exam. In a second step, functional imaging like PET and SPECT are conducted. If the collected results are still incongruent, sEEG is advised (Fig. 1). Bilateral implantation was mostly indicated for patients with temporal seizures with no clear lateralization in semiology and a bilateral pathological EEG, and in patients with a temporal lesion and an incongruent EEG finding. sEEG planning required a hypothesis for the individual epileptogenic zone which was established during presurgical conference. Localization and number of electrodes are summarized in Table 1. The results of presurgical evaluation are summarized in Table 2. Our analysis showed that the hypothesis regarding the epileptogenic zone was confirmed more frequently in patients with bilaterally implanted electrodes than in patients with only unilateral implantation (85.7% vs. 28.6%, $p = 0.024$). Using a non-parametric Kursal-Wallis test, we found no significant association between surgical outcome (significant reduction of seizure frequency, ILAE class I) and the number of implanted electrodes ($p = 0.260$).

MRI abnormalities were found in 11 patients. This includes hippocampal sclerosis ($n = 4$), cavernoma ($n = 1$), heterotopia ($n = 1$), residual lesions ($n = 4$), and hemosiderin ($n = 1$). The detection of a lesion in 3-T MRI showed no correlation with the probability of a confirmed hypothesis (Fig. 2; $p = 0.055$, regression analysis).

Seventeen patients (81%) were found eligible for surgery after sEEG. Based on the sEEG results, we were able to define four different groups based on the original hypothesis (Fig. 1). Group I is defined by the confirmation of the preliminary hypothesis through sEEG ($n = 8$, 38.1%). No further investigation is needed, and the planned surgery is carried out. Groups II–IV are characterized by their divergence from the original hypothesis. Group II ($n = 6$, 28.6%) is characterized by a different epileptogenic zone than expected which leads to a different tailored surgical resection. Group III ($n = 4$, 19.0%) has a main epileptogenic zone but also at least one recorded epileptogenic focus distant from it. Surgery will be suggested as planned but with a declined prognosis. Group IV ($n = 3$, 14.3%) shows a bitemporal or indefinable seizure onset zone. No epilepsy surgery will be performed. Examples are presented in Figs. 3 and 4. Hence, 13 patients (61.9%) received a different treatment than initially planned. Nine patients showed a significant reduction in seizure frequency after epilepsy surgery after 1 year. In three of them, sEEG did not confirm the original hypothesis. Histological work-up revealed hippocampal sclerosis (HS; $n = 3$), focal cortical dysplasia (FCD; $n = 5$), tumor ($n = 2$), and gliosis ($n = 1$). No histological diagnosis correlated with an increased use of sEEG. These results are summarized in Table 3.

Seizure outcome was evaluated according to the ILAE classification and mean follow-up was 18 months. ILAE class 1 was found in 75.0% of patients in group I, 33.3% of patients

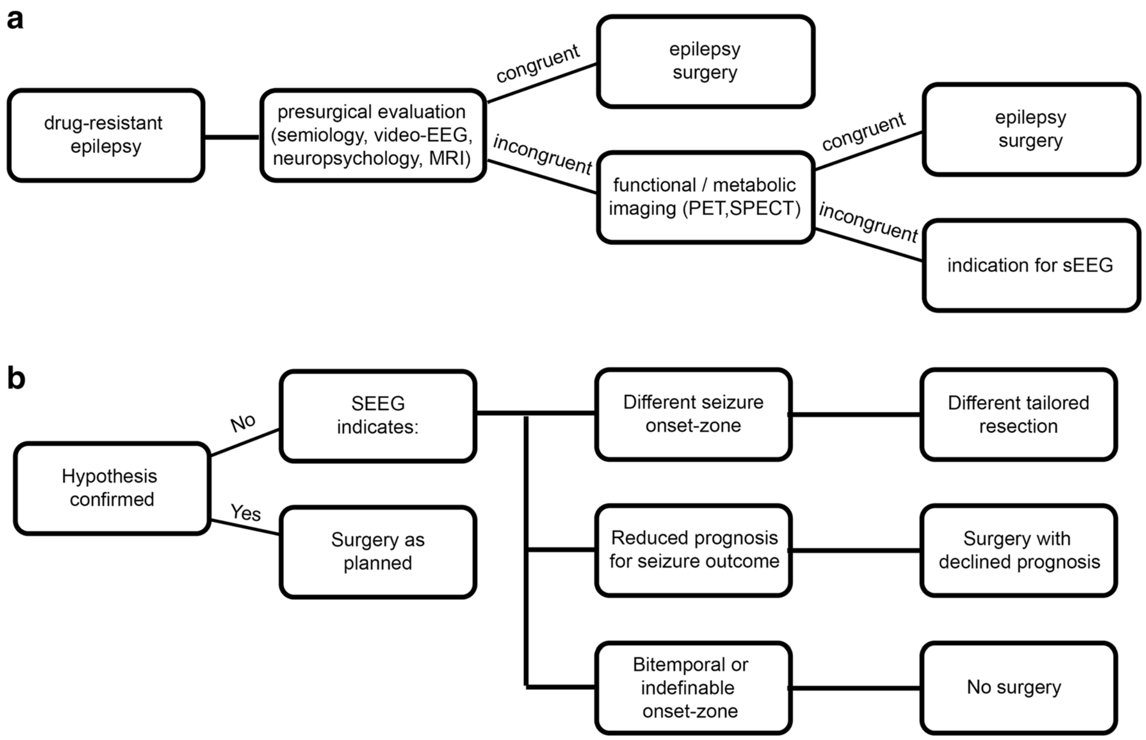

Fig. 1 Flow-chart illustrating the consecutive steps in the work-up for epilepsy surgery (**a**). Decision-tree. Group I ("surgery as planned"): *n* = 8, ILAE 1: 75.0%; group II ("diff. tailored resection"): *n* = 6, ILAE 1: 33.3%; group III ("declined prognosis"): *n* = 4, ILAE 1: 25.0%; group IV ("no surgery"): *n* = 3 (**b**)

Table 1 Distribution of sEEG electrodes in our cohort (−: no, +: yes; *l* left, *r* right)

Patient (group)	Bilateral	Temporal	Insular	Frontal	Parietal	n (l/r)
1 (III)	+	+	−	−	−	4/4
2 (I)	+	+	−	−	−	4 l,4 r
3 (II)	−	+	−	−	−	5 l
4 (I)	−	+	+	+	−	8 r
5 (IV)	−	+	+	−	−	7 r
6 (II)	−	+	−	−	−	7 r
7 (II)	−	+	+	−	−	8 l
8 (I)	−	+	−	−	−	5 r
9 (I)	+	+	−	−	−	3 l/5 r
10 (III)	−	+	−	+	−	7 l
11 (I)	+	+	+	−	−	6 r/2 l
12 (II)	−	+	+	+	−	9 l
13 (I)	+	+	−	−	−	2 r/3 l
14 (III)	−	+	−	−	−	6 r
15 (III)	−	+	+	−	−	7
16 (I)	+	+	−	−	−	4 r/2 l
17 (II)	−	+	−	−	−	7 l
18 (II)	−	+	+	−	−	6 r
19 (IV)	+	+	−	+	+	5 l/1 r
20 (IV)	−	+	+	−	−	7
21 (I)	−	+	+	−	−	7 l

in group II, and 25.0% of patients in group III. Group IV patients were all designated to deep-brain stimulation in the course (Table 4). One patient showed an intracerebral hemorrhage after sEEG explantation. In our own cohort of TLE, patients treated by surgery without prior sEEG evaluation 71.1% achieved ILAE class 1.

Discussion

There are several series evaluating the role of sEEG in different types of epilepsy in the literature [11, 12]. We focused on temporal lobe electrodes only in order to achieve as homogenous a cohort as possible. A rate of resection of 81.0% after sEEG recordings is comparable to others [6]. Of those, 12 patients (57.1%) were treated differently or were confronted with a declined seizure prognosis in the course of sEEG recordings which led to a logic step-by-step treatment-decision pattern for results in stereo-electroencephalography in temporal lobe epilepsy. Four groups based on the sEEG findings and the initial seizure-hypothesis could be established. The first group, group I, is characterized by the confirmation of the hypothesis by sEEG. Groups II–IV are distinguished by sEEG findings incongruent to the initial hypothesis and thereby leading to different treatment strategies. Furthermore, patients can be advised individually according to sEEG results. This could already be shown for frontal lobe epilepsies [13].

Table 2 Results of diagnostics during presurgical evaluation. (sEEG indicates where seizures were recorded by sEEG; EEG indicates where epileptic potentials were recorded by scalp EEG; MRI: −: no morphological changes, +: morphological changes; SPECT: possible seizure zone evaluated after ictal and interictal SPECT; *Amy* amygdala, *HC* hippocampus, *r* right, *l* left)

Patient (group)	sEEG	EEG	MRI	SPECT
1 (III)	Temporal post r	r/l temporal	−	Temporal r
2 (I)	r	l temporoanterior	+	Temporal r
3 (II)	HC	l temporal	+	/
4 (I)	Temporal lat r	r temporal	−	Temporal r
5 (IV)	Lat neocortical	r hemisph.	−	Temporal r
6 (II)	Temp	r frontal	+	/
7 (II)	Amy, HC	r/l temporal	−	Temporal l
8 (I)	Amy, HC	r temporal	+	/
9 (I)	Amy r, HC r	No focus	+	/
10 (III)	Ci	l temporal	−	Temporal l
11 (I)	HC r/l	r frontal	+	/
12 (II)	l		+	/
13 (I)	HC head l	r/l temporal	+	/
14 (III)	HC tail lat	Temporal bilat.	−	Temporal r/l
15 (III)	Temporal dors	No focus	+	/
16 (I)	Bilat.	Partly r temporal	−	Temporal bilat.
17 (II)	Amy, HC	l temporoanterior	+	/
18 (II)	r		−	Temporal r
19 (IV)	Bilat.	l frontal	−	Indiff.
20 (IV)	Insular, temporopar.	l frontal	+	Indiff.
21 (I)	HC l	l temporal	−	Temporal l

The classification in four different groups is not only feasible for patient communication but also for communication between the different specialties in epilepsy surgery as proposed by the ILAE routinely [14]. Sindou et al. already addressed the influence of sEEG on TLE surgery but did not clearly define the resulting subgroups [15].

The use of bilateral sEEG electrodes in TLE correlated positively with the confirmation of the hypothesis. This seems odd at first glance, since bilateral sEEG might suggest a very vague hypothesis. On the other hand, bilateral electrodes can contribute to a much more precise picture of the course of seizure development by ruling out a contralateral propagation and thereby lead to a better prediction regarding successful epilepsy surgery [16, 17]. Bilateral recording might also lead to a better seizure outcome in otherwise poorly to localize epilepsy [18]. Temporal lesions visible on MRI did not contribute to a higher percentage of confirmed hypotheses. This can be explained by a mismatch of the lesions' localization and the additional findings during diagnostic evaluation, pointing to a different organized epileptogenic zone

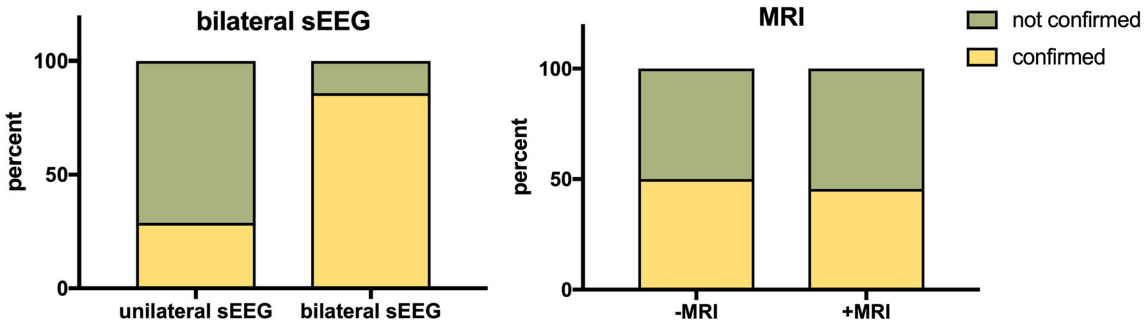

Fig. 2 In bilateral sEEG recordings ($n = 7$), confirmation of the hypothesis was significantly higher than in unilateral recordings ($n = 14$), $p = 0.024$. The existence of a negative ($n = 10$) or positive ($n = 11$) MRI was independent from the confirmation of the hypothesis

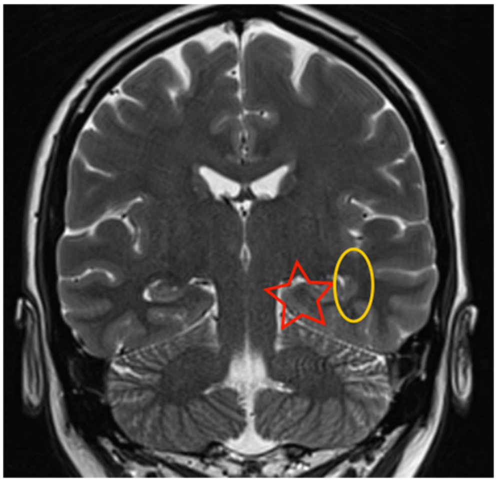

Fig. 3 Group II example: MRI revealed a paraventricular heterotopia left (yellow ellipse). sEEG on the other hand diagnosed a clear seizure zone in the left hippocampus (red star). Both pathologies were then resected. The functional coupling between these lesions has already been described [10]

comparable to the temporal plus epilepsies [19]. On the other hand, MR seemed to have an impact on outcome while narrowly missing statistical significance. Structural lesions in drug-resistant epilepsy are generally associated with a favorable seizure outcome after surgery [20]. An impact on confirmation of the hypothesis or seizure outcome could not be established due to the heterogeneous findings.

Seizure freedom in 75.0% of group I patients is comparable to seizure outcome after epilepsy surgery without preceding invasive sEEG and also to our own cohort of TLE patients treated by surgery where 71.1% achieved ILAE class 1. This supports that a strong pre-implantation hypothesis is crucial for the patients.

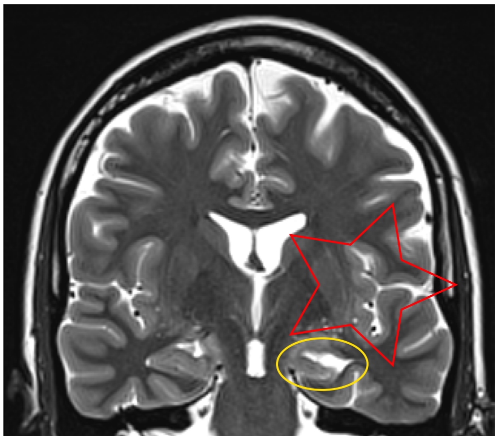

Fig. 4 Group IV example: MRI suggested a left-sided hippocampal sclerosis (yellow ellipse). sEEG detected different epileptic foci temporoparietal and insular but not hippocampal. Hence, no surgery was recommended (red star)

Table 3 Outcome data after evaluation by sEEG. (−: hypothesis not confirmed; +: hypothesis confirmed; Surgery: −: no, +: yes; previous surgery: −: no, +: yes; prognosis: +: unchanged, −: changed; histology: *FCD* focal cortical dysplasia, *HS* hippocampal sclerosis)

Patient (group)	Hypothesis confirmed	Surgery	Previous surgery	Prognosis	Histology
1 (III)	+	+	−	−	
2 (I)	+	+	−	+	HS
3 (II)	−	+	−	+	
4 (I)	+	+	−	+	
5 (IV)	−	−	−	+	
6 (II)	−	+	+	+	FCD
7 (II)	−	+	−	+	FCD
8 (I)	+	+	+	+	Tumor
9 (I)	+	+	−	+	HS
10 (III)	+	+	−	−	FCD
11 (I)	+	+	−	+	HS
12 (II)	−	+	−	+	
13 (I)	+	+	−	+	
14 (III)	−	+	+	−	FCD
15 (III)	−	+	−	−	
16 (I)	+	−	−	+	
17 (II)	−	+	+	+	Tumor
18 (II)	−	+	+	+	
19 (IV)	−	−	−	+	FCD
20 (IV)	−	−	−	+	
21 (I)	+	+	−	+	Gliosis

TLE is predisposed to sEEG due to the densely folded nature of the temporal lobe. Subdural grid electrodes would not be able to record adequately the temporomesial structures and carry a greater risk for perioperative morbidity [21, 22].

This data presents a comprehensible tool for decision-making in TLE after sEEG. This paradigm is important and useful for giving advice to the patient and/or guardian during the process of finding the right treatment strategy. Furthermore, it helps to assess the seizure outcome for the patient which is perhaps one of the most important facts to discuss with the individual when decisions regarding epilepsy surgery have to be made.

Table 4 Percent of patients showing ILAE 1 in the different sEEG groups I–IV

Group	ILAE 1 (%)
I	75.0
II	33.3
III	25.0
IV	–

Conclusion

We could show that investigation by sEEG has a strong impact on daily decision-making regarding further treatment in TLE for patients with incongruent findings in presurgical evaluation. The sEEG results helped to tailor personalized therapy regimens and to identify patients where epilepsy surgery would be without benefit.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

For this type of study, formal consent is not required.

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