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A case of auditory auras: application of general principles to define and localize the epileptogenic zone

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ABSTRACT – An illustrative case of auditory aura and complex partial seizures is presented to highlight challenges in the accurate localization of the epileptogenic zone. Application and interpretation of various diagnostic tools is discussed in this case using the North American approach to the localization of the epileptogenic zone. Whenever possible, the differences and similarities between the North American and the French/Italian approach for the localization of the epileptogenic zone are discussed.

Keywords: epileptogenic zone, epilepsy surgery, partial epilepsy, auditory aura, seizures

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The challenge of defining and localizing the epileptogenic zone is a key step in selecting patients for surgical treatment of epilepsy. Several general principles from two major approaches, the North American and French/Italian schools, guide us in evaluating epilepsy patients for surgery (Talairach *et al.* 1974, Rosenow and Luders 2001). However, the application of tests, their interpretation, and how they complement each other in defining the epileptogenic zone remains unique for each individual patient. We present an illustrative case with a seizure-free outcome after surgery in order to discuss the complex interplay of a variety of techniques that were used to localize and define the epileptogenic zone in this case. Whenever possible, we also discuss the similarities and differences in approach to this patient's pre-surgical evaluation using the North American and French/Italian schools of thought.

Case report

History

A 25-year-old, right-handed male presented for management of intractable seizures that had begun at the age of seven years. He had no prior illness or identifiable risk factors for epilepsy. The patient reported a consistent aura before most of his seizures, which was characterized by hallucinatory distortion of familiar sounds such as ringing, human crying or television sounds. Sounds were perceived in both ears. A few seconds later, he would lose

awareness, and witnesses reported the patient to be restless, moving and stiffening his trunk, and unresponsiveness for 1-2 minutes. He had 2-3 seizures a day; 25% of the episodes being followed by a generalized tonic-clonic seizure for an additional 2-3 minutes. After regaining awareness, he had marked difficulty in finding his words. He also usually felt exhausted and reported headache (no post-ictal deficit?). He had tried unsuccessfully several medications including phenytoin, carbamazepine, gabapentin, valproate, lamotrigine and levatiracetam as monotherapy or in various combinations. His physical and neurological examination results were within normal limits. He was a high school graduate, previously employed as a non-skilled factory worker. He sought disability services a year prior to our seeing him, and had stopped working because of the daily seizures.

Scalp-video EEG and pre-surgical work-up

Typical auras followed by complex partial seizures and secondarily generalized, tonic-clonic seizures were recorded. In one seizure, he was noted to have right-hand dystonia (before secondary generalization) and post-ictal aphasia (naming, comprehension, and repetition). Interictal EEG using scalp and sphenoidal electrodes, showed sharp waves in the left anterior temporal region *(figure 1)* Ictal EEG showed a 6-7Hz, left temporal sharp rhythm that developed and evolved 8-17 seconds after the patient announced his aura (*figures 2, 3*). A high resolution brain MRI, including three dimensional, T1-weighted, thin coronal volume acquisition images, T2-weighted and FLAIR (fluid attenuated inversion recovery) coronal sequences were normal. Brain FDG-PET (fluorodeoxyglucose positron emission tomography) showed significant hypometabolism in the left temporal pole, mesial temporal structures, and extending up to the mid-lateral temporal region *(figure 4)*. Ictal SPECT (single photon emission computed tomography) was attempted unsuccessfully. Speech and memory lateralization by intra-carotid amobarbital injection revealed left hemispheric speech and equal, bilateral memory representation. Neuropsychological evaluation showed an average, full scale IQ (FSIQ) score of 101 with average verbal (immediate verbal score 97, delayed verbal score 97) and visual (immediate visual score 102, delayed visual score 108) memory scores. The patient was presented in the epilepsy management conference. A diagnosis of left temporal epilepsy was agreed upon. It was thought that the possibility of lateral neocortical epilepsy could not be ruled out because of the auditory aura and atypical seizure semiology for mesial temporal seizures. Invasive monitoring over the left mesial and lateral temporal regions was suggested to further define and localize the epileptogenic zone.

Invasive video EEG evaluation with sub-dural arrays

To further define the location of the epileptogenic zone in the left temporal region, the patient underwent left craniotomy for placement of sub-dural arrays. Sub-dural arrays (*figure 5*, see inset brain cartoon) were placed over the left lateral temporal region (plate A, 4x11 electrodes), perirolandic and upper sylvian bank (plate B, 5x8 electrodes), left frontal opercular region (plate C, 4x4 electrodes), orbito-frontal region (plate D, 4x4 electrodes), and basal

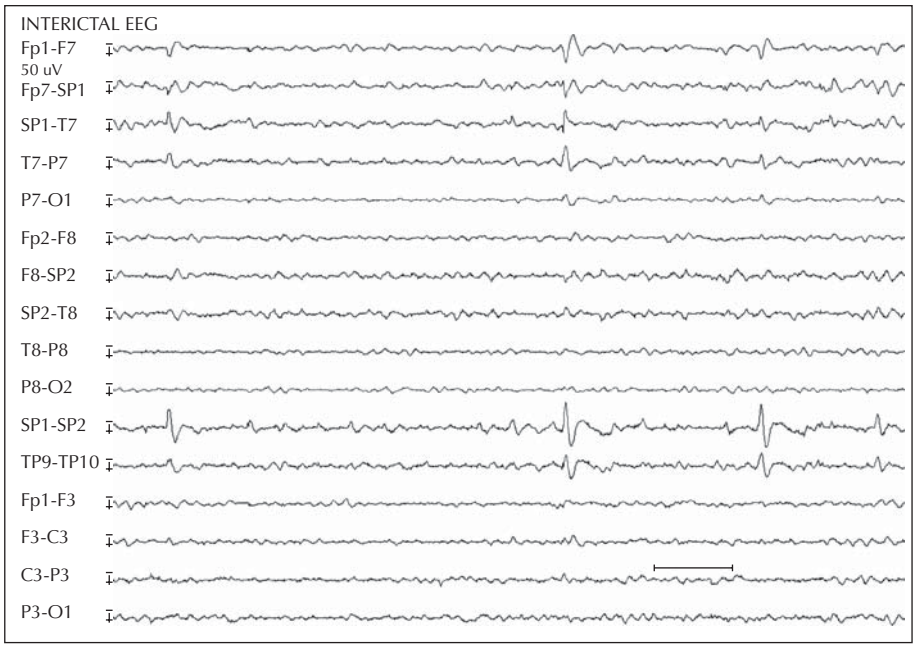

Figure 1. Interictal scalp record showing a sleep epoch with left temporal sharp waves at the left sphenoidal (Sp1) electrode.

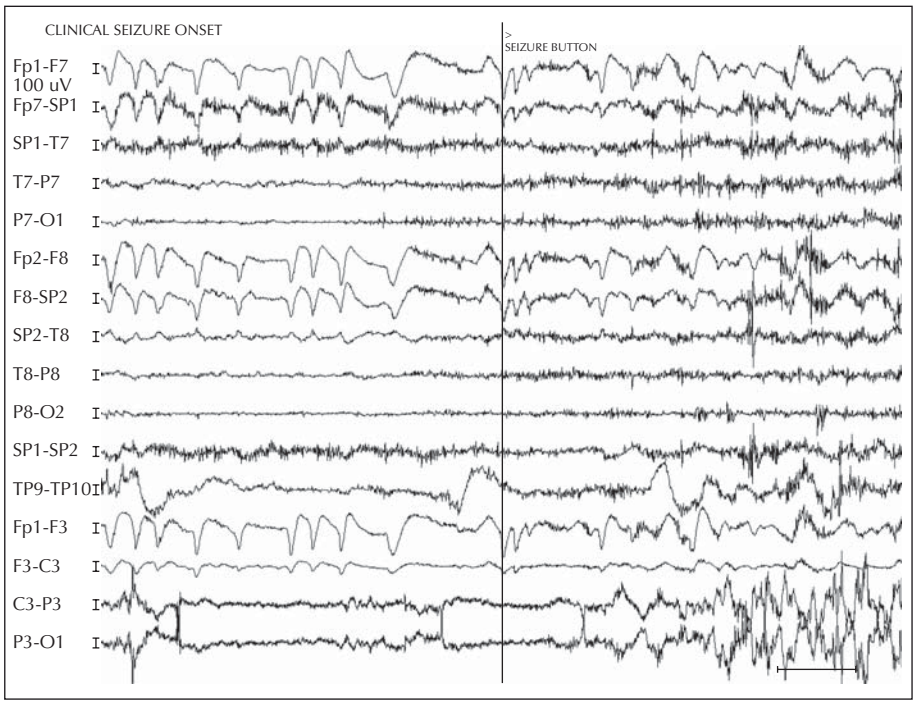

Figure 2. Ictal scalp EEG showing clinical onset when patient pushed (see marker) seizure button at the onset of auditory aura without any significant EEG change.

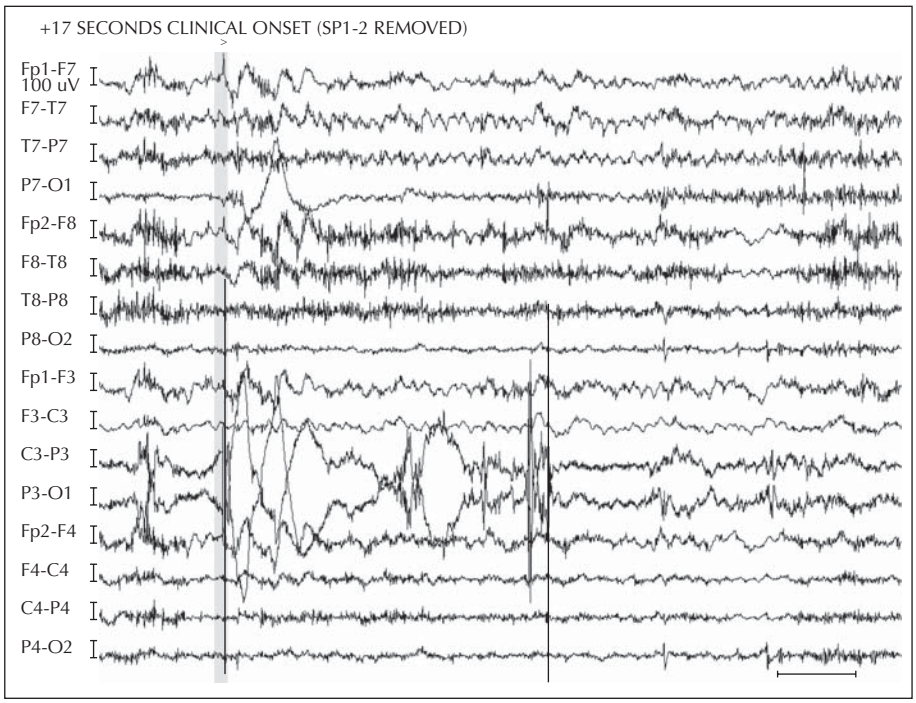

Figure 3. Ictal scalp EEG showing clinical onset when patient pushed (see marker) seizure button five seconds later, left temporal seizure pattern was noted.

temporal regions extending from the mesial to lateral surface covering the anterior (plate E, 1x6 electrodes), mid- (plate F, 1x6 electrodes), and posterior (plate G, 1x6 electrodes) basal temporal regions. Sub-dural arrays were co-registered with three dimensional brain MRI images to localize accurately the relationship of the electrodes to the major anatomical surface landmarks.

Video EEG recording identified a much wider area of interictal and ictal onset as shown in *figures 5-11*. Interictal epileptiform discharges were noted independently over the left lateral anterior and mid temporal regions *(figure 5)* and the parahippocampal gyrus overlying the mesial structures (*figure 6).* Ictal onset was diffuse over the lateral surface of the left temporal lobe during typical complex partial seizures (*figures 7, 8*). During two auditory auras that lasted for 1 minute without evolving into a motor seizure, ictal EEG seizures began and remain localized over the left para-hippocampal gyrus (*figures 9, 10*). Cortical mapping was also done by electric stimulation (Grass stimulator, 50Hz, 1-15mamp, bipolar and biphasic stimulation) over the A and C plate and eloquent areas for speech and language were identified *(figure 11)*. During brain mapping, patient reported his typical auditory auras at two electrodes and had a complex partial seizure at one electrode (stimulation intensity = 5-6 mamp) over the mid-portion of the superior temporal gyrus *(figure 11)*. The patient was discussed again in the epilepsy surgery management conference. After discussion of benefits, risks and alternatives with the patient and family (see discussion) it was decided to proceed with the resection of the anterior and mid-left superior temporal gyrus avoiding of Wernicke's areas *(figure 12)*.

Post-operative evaluation

Histopathology of the resected brain tissue showed findings of neuronal heterotopia, architectural disorganization, neuronal cytomegaly and dysmorphic neurons. Post-operative brain MRI performed six months after surgery *(figure 12)* showed surgical resection with no new findings of concern. The patient reported no change in his memory, speech and language function for routine activities. Neuropsychological testing at six months showed no significant change in visual (immediate score 121, delayed score 129) and verbal (immediate score 102, delayed score 105) memory scores. The patient reported no auras or seizures at his two year follow-up visit. He was able to come off two medications and is currently on carbamazepine monotherapy.

Discussion

This patient illustrates some of the many challenges in the accurate localization of the epileptogenic zone. Using the North American approach (refer to article by Lüders *et al.* 2006), *table 1* summarizes the contribution of each test in the localization of various cortical zones in this patient. The patient's history, video EEG evaluation combined with scalp EEG and brain PET suggested the location of the epileptogenic zone to be in the left temporal lobe, most likely in the mesial temporal regions. However, there were several unusual findings in this patient, which meant that this was not a straightforward, surgical treatment of mesial temporal lobe epilepsy. The unusual findings included a consistent auditory aura, absence of mesial temporal sclerosis or any other structural abnormality in the mesial structures on brain MRI, average memory scores with no neuropsychological deficits suggesting dominant hippocampal dysfunction, and suggestion of dominance (memory and language) in the left hemisphere based on his right-handedness, post-ictal aphasia, and intracarotid amobarbital test. Sometimes, differentiation between mesial temporal lobe epilepsy (MTLE) and neocortical lateral temporal lobe epilepsy (NTLE) is not easy (Andermann 2003, Burgerman *et al.* 1995) This is especially true in patients like ours, where the brain MRI fails to show a structural lesion. Brain FDG-PET is known to show a much wider region of hypometabolism, but may not help in the differentiation of MTLE and NTLE as in our patient, where FDG-PET showed global, left, temporal hypometabolism-.(Hajek *et al.* 1993) Although in our patient, the eventual resection (after invasive subdural evaluation) was a subset of the area that was hypometabolic on the FDG-PET, the standard anterior temporal lobe resection including the mesial structures as suggested by FDG-PET, would have posed an unacceptably high risk of post-operative, verbal memory deficits, and the posterior margins of a standard resection may not have reached the final resection. The mesial temporal lobe contains certain highly epileptogenic structures, and it is well known that scalp-recorded epileptogenic discharges and seizures may appear falsely to be originating from the temporal lobe even though they are due to lesions located outside the temporal lobe in the lateral, mid-to-posterior lateral temporal lobe, parieto-occipital regions or even the frontal lobe (Lee *et al.* 2003, Andermann 2003, Pacia *et al.* 1996).

Subsequent evaluation in our patient by subdural arrays suggested a wider area of irritative and ictal-onset zone in the left mesial and lateral temporal lobe extending from the anterior pole to the mid-posterior temporal regions over the superior and middle temporal gyrus. Using the North American concept of defining the irritative and actual seizure-onset zones with the subdural evaluation, the best estimate of the epileptogenic zone was that it was located somewhere in the left temporal lobe. The patient did not undergo the three dimensional stereotactic EEG, but applying the French/Italian view point to the subdural evaluation, left mesial temporal structures were at least the part of early seizure spread and were in the epileptogenic zone. It is possible that invasive recording from three dimensional stereotatically-placed electrodes at various points in the left temporal lobe could have better defined

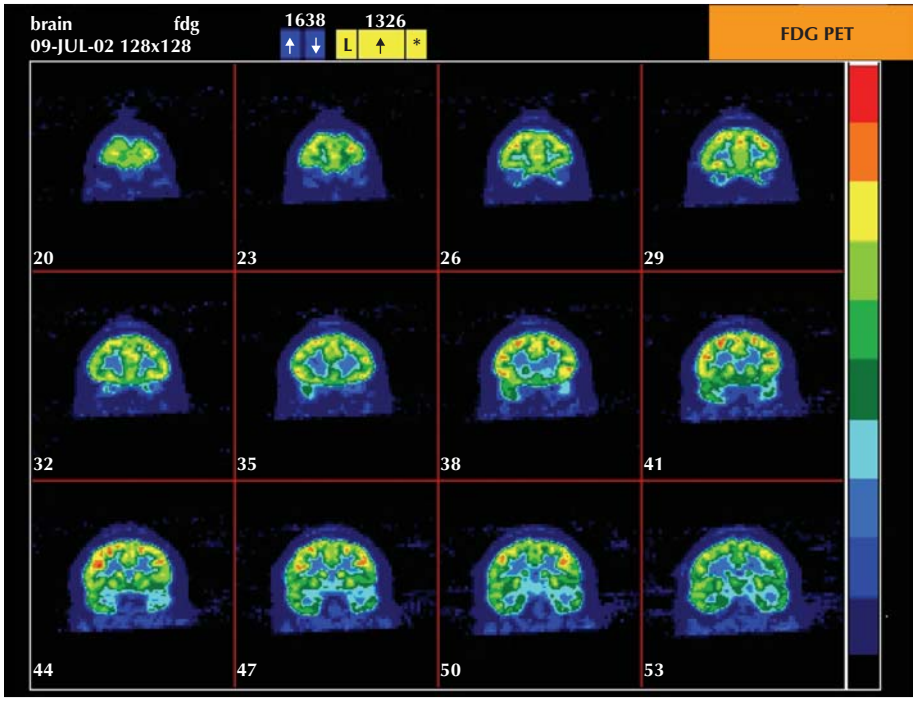

Figure 4. Brain FDG-PET coronal slices showing left temporal hypometabolism in the left temporal pole, mesial temporal structures and extending in to the lateral superior and middle lateral temporal lobe (slices 32-53 in the bottom two rows).

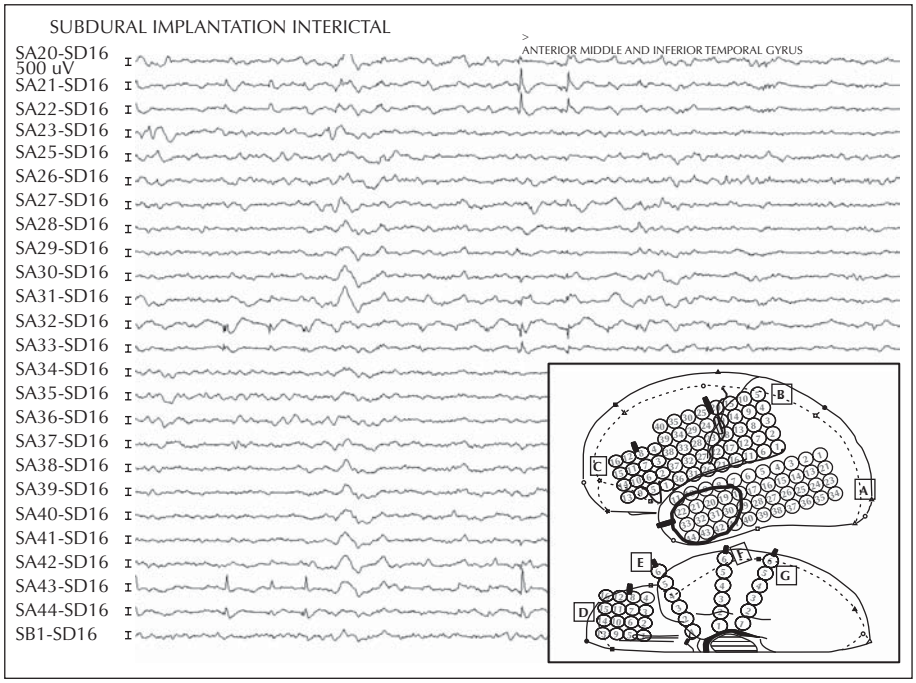

Figure 5. Electrocorticography showing distribution of interictal discharges recorded from the implanted subdural electrodes in the left anterior lateral region. Inset brain cartoon shows corresponding regions inside the circle.

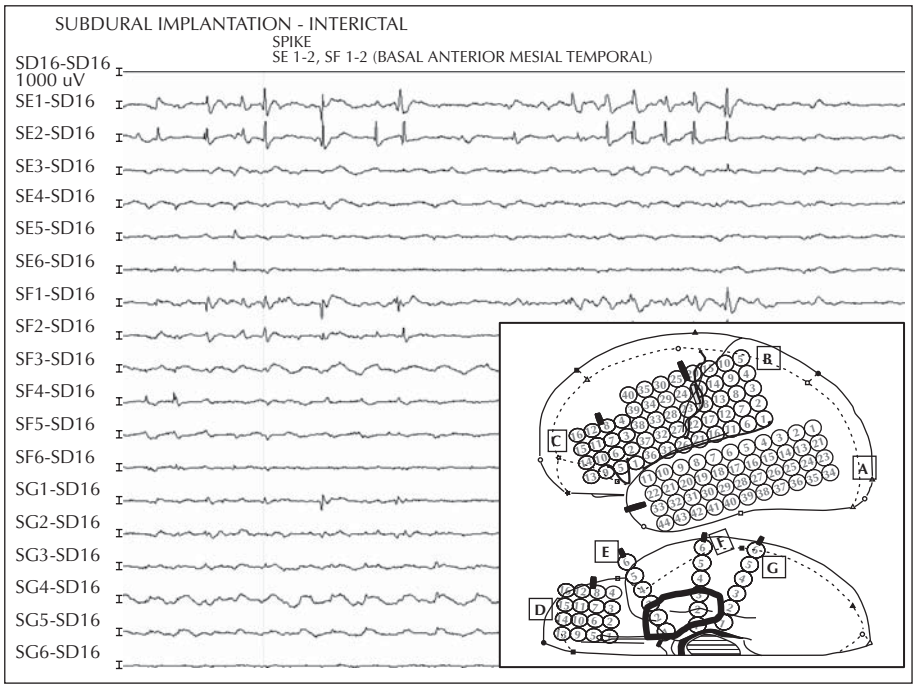

Figure 6. Electrocorticography showing distribution of interictal discharges recorded from the implanted subdural electrodes in the basal anterior mesial temporal region. Inset brain cartoon shows corresponding regions inside the circle.

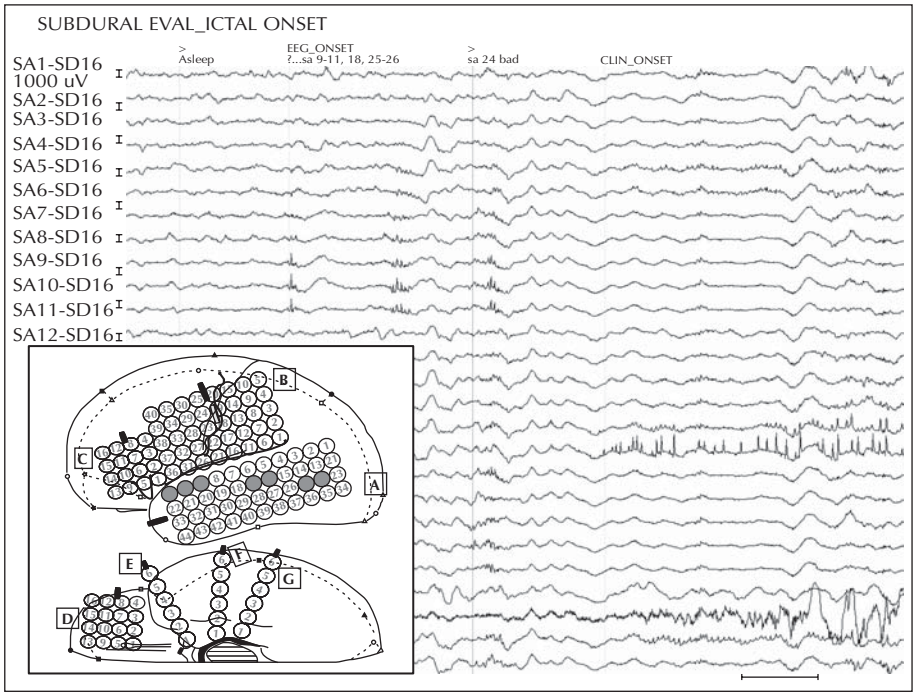

Figure 7. Electrocorticography showing a poorly localizable ictal onset zone over the lateral temporal convexity during a typical complex partial seizure at the onset into the seizure. Inset brain cartoon shows corresponding regions at the darkened (filled in) electrodes.

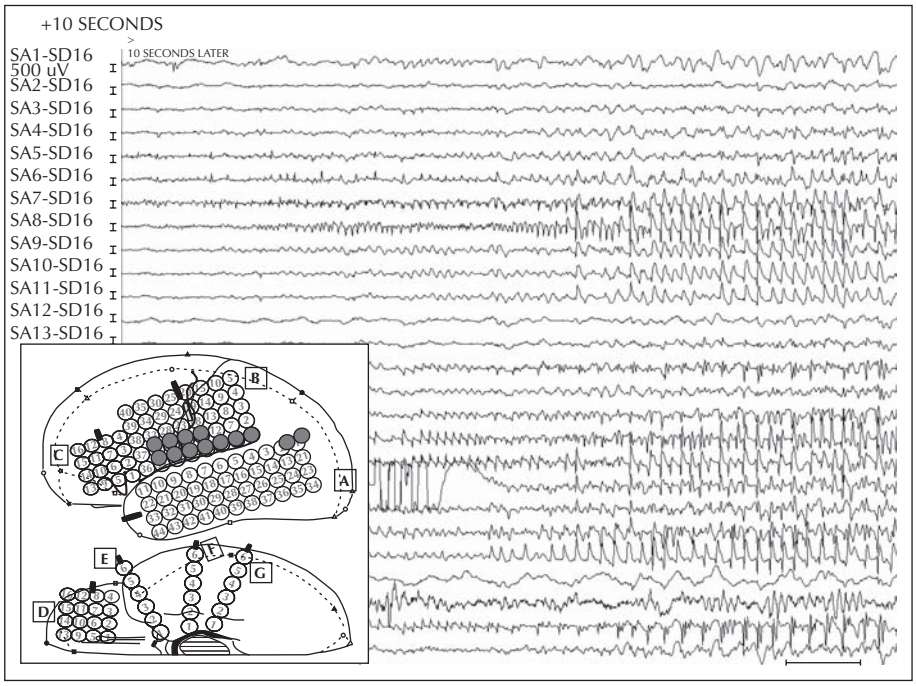

Figure 8. Electrocorticography showing a poorly localizable ictal onset zone over the lateral temporal convexity during a typical complex partial seizure at 10 seconds into the seizure. Inset brain cartoon shows corresponding regions at the darkened (filled in) electrodes.

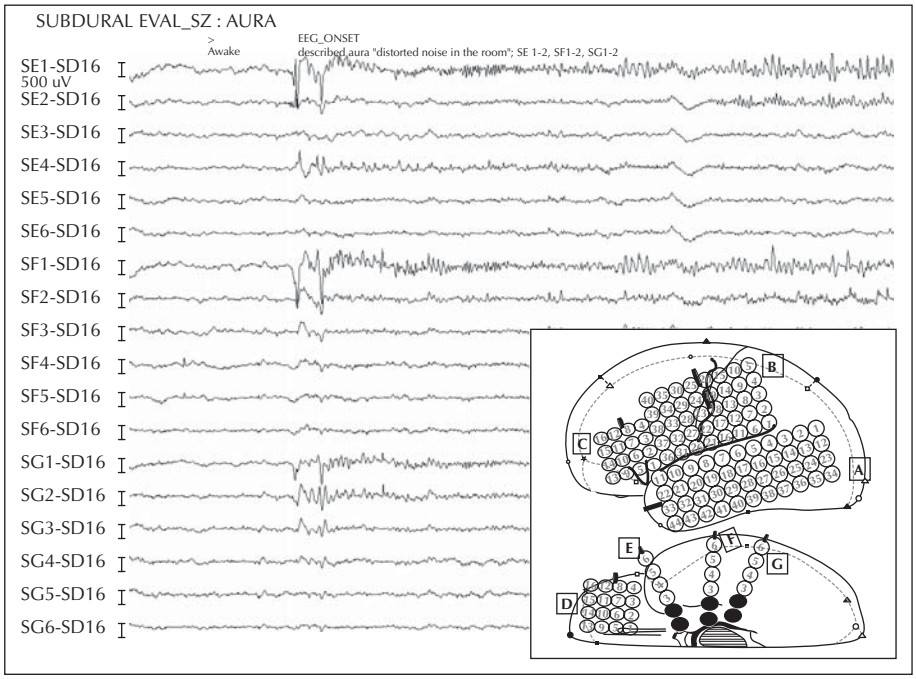

Figure 9. Electrocorticography showing focal ictal onset at the left mesial basal temporal lobe during a typical prolonged auditory aura. Inset brain cartoon shows corresponding regions at the darkened (filled in) electrodes.

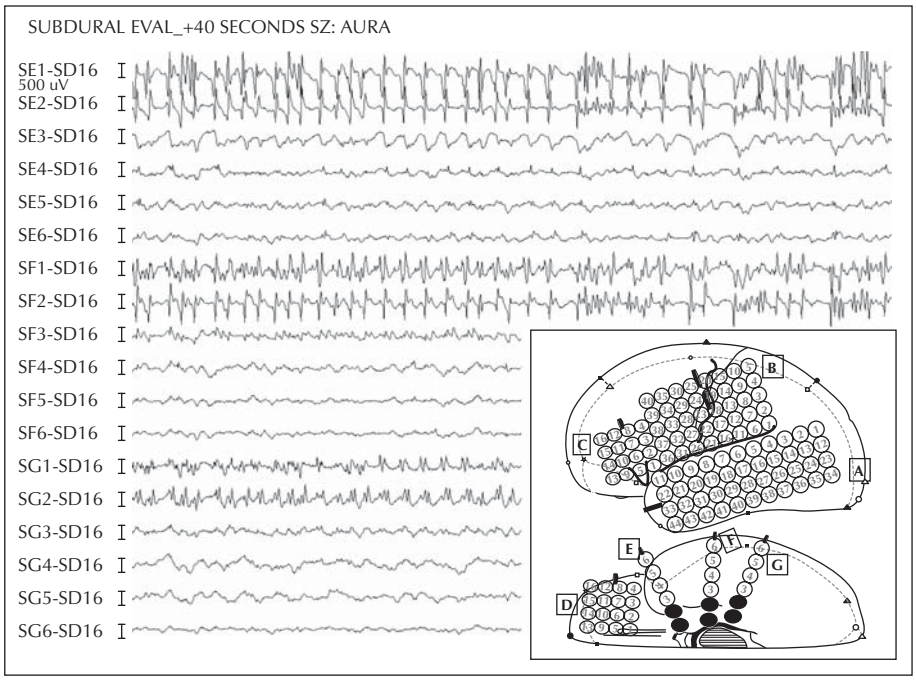

Figure 10. Electrocorticography showing seizure spread at the left mesial basal temporal lobe during a typical prolonged auditory aura. Inset brain cartoon shows corresponding regions at the darkened (filled in) electrodes.

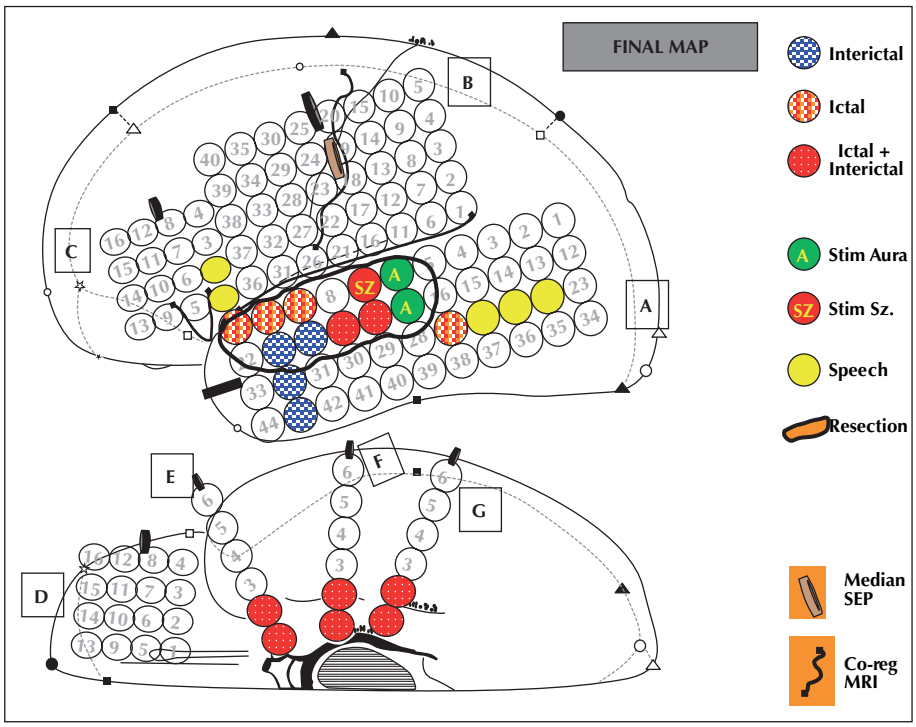

Figure 11. Final map generated after invasive evaluation using subdural array and planned resection of brain under the electrodes inside the circle. SEP = Central sulcus localization by somatosensory evoked potentials; Stim Sz. = seizures recorded after electric stimulation of electrodes; Stim aura = Auditory auras recorded after electric stimulation of electrodes; Co-reg MRI = Central sulcus localization by coregistered magnetic resonance imaging.

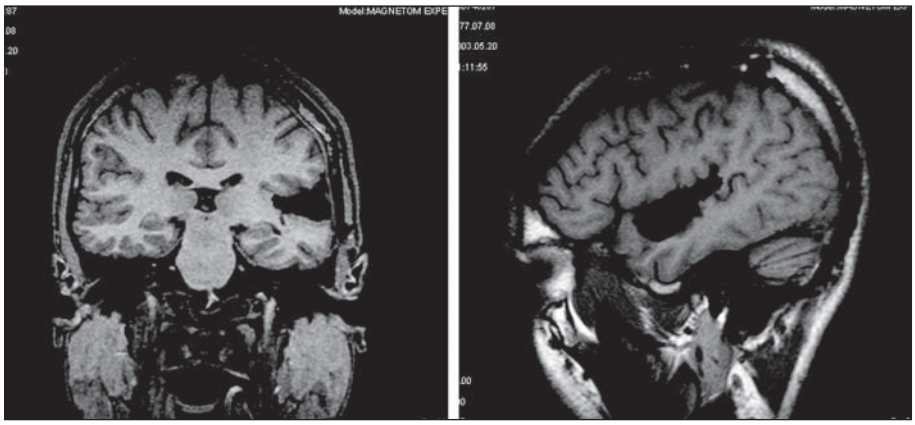

Figure 12. Post-operative brain MRI showing coronal and sagittal T1 weighted images after resection of the anterior and middle portion of the left superior temporal gyrus.

Table 1. Contribution of each test in the localization of various cortical zone in a patient.

Tests/observations used		Cortical Zones Defined in the Presurgical Evaluation				
		Irritative zone	**Ictal onset zone**	**Symptomatogenic zone**	**Functional Deficit Zone**	**Epileptogenic Lesion**
Seizure history/video evaluation						
	Aura	-	-	STG (auditory) or temporal (psychic) aura	-	-
	Right hand dystonia	-	-	Left hemisphere	-	-
	Post ictal aphasia	-	-	Dominant language hemisphere	-	-
Examination						
	Clinical exam	-	-	-	None	-
	Neuropsychological	-	-	-	None	-
Neuroimaging						
	Brain MRI	-	-	-	-	None
	Brain PET	-	-	-	Left temporal (mesial and lateral)	-
Scalp EEG						
	Interictal	Left temporal	-	-	-	-
	Ictal	-	Left temporal (likely mesial)	-	-	-
Electrocorticography (subdural arrays)	Interictal	Left mesial and lateral temporal		-	-	-
	Ictal	-	Left mesial and lateral temporal	-	-	-
	Aura/seizures on electrical stimulation	-	Left mid superior temporal gyrus	-	-	-

Abbreviations: MTS=mesial temporal structures; STG=superior temporal gyrus; '-'= not applicable.

the ictal-onset zone. Notably in this particular case, the only way to record Heschl's gyrus was to place a depth electrode inside it. Similarly, the only way to record the T1-T2 sulcus was to use depth electrodes rather than grids or strips that only record the cortical surface and cannot give access to the depths of the sulcus. During electrical stimulation of the brain for mapping eloquent cortex, the patient had a typical auditory aura and seizure over the mid-superior temporal gyrus close to the anatomical location of Heschl's gyrus. Although this finding was not incorporated in the localization of the epileptogenic zone, it implies a close relationship of the epileptogenic zone with the surface area being stimulated under the electrode. A similar analogy was used by Sir Victor Horsley and his colleagues when epilepsy surgery was first performed in 1886 (refer to article by Lüders *et al.* 2006). After discussion with the patient of the two surgical alternatives of standard, left temporal lobe resection versus a limited resection of the mid-portion of the superior temporal gyrus, it was decided to perform a limited resection of the superior temporal gyrus including the area under the electrodes that had led to the stimulation-induced seizures.

Conclusion

The epileptogenic zone is a useful theoretical concept in the evaluation of patients for surgical treatment. Accurate definition and localization of the epileptogenic zone should be individualized in each patient based on the critical interpretation of all available data. □

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