Temporal pole epilepsy surgery-Sparing the hippocampus

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Bastien Herlin, MD[1,2,3], Claude Adam, MD[1], Marie-Odile Habert, MD, PhD[4,5], Bertrand Mathon, MD[3,6,7], Stéphane Clemenceau, MD[6], Vincent Navarro, MD, PhD[1,3,7] *, Sophie Dupont, MD, PhD[1,2,3,7]*

[1]AP-HP Pitié-Salpêtrière Hospital, Epileptology Unit, Paris, France

[2] AP-HP Pitié-Salpêtrière Hospital, Rehabilitation Unit, Paris, France

[3] Sorbonne Université, Paris, France

[4] AP-HP Pitié-Salpêtrière Hospital, Department of Nuclear Medicine, F-75013, Paris, France

[5]Sorbonne Université, CNRS, INSERM, Laboratoire d'Imagerie Biomédicale, LIB, F-75006, Paris, France

[6]AP-HP Pitié-Salpêtrière Hospital, Neurosurgery Department, Paris, France

[7] Paris Brain Institute, ICM, INSERM, CNRS, Paris, France

* Equally contributed

Corresponding author:

Dr Bastien Herlin

Epileptology Unit, Pitié-Salpêtrière Hospital, 47, boulevard de l'Hôpital, 75013 Paris, France

Phone/FAX: (33) 1 42 16 03 01/1 42 16 03 03

Mail: bastien.herlin@aphp.fr

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Ethical statement

We confirm that we have read the Journal’s position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

Abstract:

Temporal pole epilepsy (TPE) is a poorly known and difficult to individualize subtype of temporal lobe epilepsy. Consequently, in drug-resistant TPE, there is still a debate on the need for a large surgical removal of the temporal pole and mesial temporal structures or a limited resection of the temporal pole. We reviewed all patients who underwent presurgical evaluation for drug-resistant epilepsy over a 17-year period, and report here 19 patients with proven drug-resistant temporal pole epilepsy who underwent a selective temporal pole resection with respect of mesial structures. Most (15) TPE patients exhibited seizures resembling mesio-temporal seizures, whereas the others exhibited nocturnal hyperkinetic seizures or an association of both seizure types. MRI revealed a temporal pole lesion in 58% of patients. Long-term postoperative outcome after a conservative surgery was excellent: 63% of patients were seizure-free (ILAE 1) at one-year post-surgery and 78% at 5 years. These results show that TPE has no specific electroclinical features but is a distinct type of temporal lobe epilepsy allowing a conservative surgery. Respecting the mesio-temporal structures is a valid surgical approach for drug-resistant temporal pole epilepsy.

Introduction:

The involvement of the temporal pole has already been substantiated in mesial temporal lobe epilepsy (MTLE), as assessed by intracranial recording of MTLE patients showing early propagation of the epileptic discharge arising from the hippocampus to the temporal pole[1], MRI temporal pole blurring frequently associated with hippocampal sclerosis (HS)[2], and temporal pole hypometabolism frequently found in FDG-PET of MTLE patients with HS[3]. Nevertheless, little is known about seizures that arise directly from the temporal pole. Many questions remain: are temporal pole seizures clinically distinct from MTL seizures? Are there any specific symptoms related to an epileptic discharge located in the temporal pole, or are symptoms due to secondary involvement of adjacent structures? If a surgery is considered for drug-resistant temporal pole epilepsy (TPE), what kind of resection should be proposed: anterior temporal resection involving the temporal pole, amygdala and hippocampus, or focal resection restricted to the temporal pole? [7]

To address these questions, we aimed to better characterize the electroclinical profiles of TPE patients and to demonstrate that TPE is a distinct subtype of TLE allowing a conservative surgical approach sparing the hippocampus. We therefore examined long-term postsurgical outcome of patients with drug-resistant TPE who underwent selective temporal pole resection.

Methods:

We selected all patients with drug-resistant TPE who underwent selective temporal pole resection between 2000 and 2017 at the Pitié-Salpêtrière Hospital (Paris, France) Epileptology Unit.

All patients underwent a standardized presurgical evaluation including a long-term video-EEG monitoring, a dedicated structural MRI and a neuropsychological assessment. All patients underwent the same imaging protocol on a 1.5T or 3T MRI depending on the year, including 3mm-thick coronal fluid-attenuated inversion recovery (FLAIR) and T2-weighted sequences, 3mm-thick axial T2 and T2* sequences, and volumetric pulse sequences (3DT1) reformatted in axial, sagittal and coronal planes.

If necessary, further examinations were performed to delineate the epileptogenic focus including FDG-PET, interictal-ictal SPECT, and intracranial EEG recording (sEEG).

All surgeries were done at the Pitié-Salpêtrière Hospital Neurosurgery Department. For the surgery, the patient is positioned supine, with the shoulder elevated, and the head turned about 75° contralaterally while being extended to make the zygomatic arch the highest point of the operative field. Scalp incision is a small curvilinear shape that starts at the superior border of the zygomatic arch just in front of the tragus, extends to the superior temporal line and anteriorly to the hairline. The temporalis muscle is incised via a curvilinear incision and retracted anteriorly. Two burr holes are placed on each side of the sphenoid wing. A small temporal craniotomy is fashioned to expose the superior and middle temporal gyri, and the sylvian fissure. The sphenoid wing is flattened with a rongeur to allow adequate exposure to the anterior part of the temporal pole. The dura is opened in a semicircular fashion and reflected over the temporalis muscle. Using an ultrasonic aspirator, a cortectomy is made about 3 cm from the temporal tip in the dominant hemisphere and 4 cm from the temporal tip in a non-dominant hemisphere. Identifying the temporal horn of the ventricle marked the medial extent of the resection. Intraoperative MRI or electrophysiology were not used.

Epilepsy surgery outcome was assessed using ILAE classification at 1, 3 and 5 years after surgery.

All the patients gave their informed consent to the use and publication of data related to their epilepsy at the time of video-EEG.

Results:

Clinical characteristics

Nineteen patients (15 males, 4 females) were identified. Demographic and clinical data are summarized in table 1. In most cases, TPE started during childhood (median age at first seizure: 13 years ± 8) and median age at surgery was 25 years ± 10. Preoperative average seizure frequency was 37 per month (min 1/month, max 150/month). All patients had antiepileptic drug polytherapy, ranging from 2 to 4 antiepileptic drugs (mean: 2.5 drugs).

Patients with TPE experienced different seizure types. 15 patients had seizures resembling mesio-temporal seizure, starting with rising epigastric sensation, déjà-vu, or feeling of fear, followed by loss of awareness and gestural or swallowing automatisms. Two patients had nocturnal hyperkinetic seizures and two patients had both diurnal MTLE-type seizures and nocturnal hyperkinetic seizures. 8 of 19 patients also had focal seizures evolving to bilateral tonic-clonic seizures.

Neuropsychological assessment was normal in 7 patients. 8 patients had episodic memory impairment compatible with the lateralization of their epilepsy (visual memory deficiency for patient with right-sided TPE, verbal memory deficiency for patient with left-sided TPE), and 4 patients had both visual and verbal episodic memory impairment. 8 patients also exhibited signs of frontal dysfunction (attention impairment, dysexecutive syndrome).

Imaging and electrophysiological characteristics

Brain MRI was performed at 1.5T in 2 patients and 3T in 17 patients. It showed a temporal pole lesion in 11 of 19 patients (Table 1).

Ten patients, including the 8 patients with normal MRI, had an FDG-PET. It showed a unilateral temporopolar hypometabolism in all patients, associated with an ipsilateral mesio-temporal hypometabolism in 3 patients and an orbitofrontal hypometabolism in 4 patients.

Ten patients had an interictal-ictal SPECT. It showed a predominant temporopolar hyperperfusion in 3 patients, and a more diffuse hyperperfusion pattern (ipsilateral temporopolar, mesiotemporal and orbitofrontal hyperperfusion) in 7 patients.

Examples of imaging finding are shown in figure 1.

Seven of 8 patients with a normal MRI had intracranial EEG recording, assessing that the seizure onset zone was located in the temporal pole. Clinical and electrophysiological data are summarized in Table 2. For all patients, the epileptic discharge spread to the ipsilateral hippocampus and amygdala during the first seconds after seizure onset. For two patients, it secondarily spread to the ipsilateral orbitofrontal cortex. Symptoms associated with an epileptic discharge strictly located to the temporal pole were indistinguishable from MTLE symptoms. Electrical stimulations on temporal pole electrodes (n=5 patients) elicited the same MTLE symptoms in three patients. Spreading to the ipsilateral hippocampus was associated with loss of awareness, while spreading to the orbitofrontal cortex was associated with motor manifestations.

Surgery outcome

Histopathological findings were consistent with imaging findings for the 11 MRI-positive patients. For the 8 MRI-negative patients, histopathological analyses showed slight cytoarchitectural alterations (neuronal heterotopia or non-specific gliosis) in 6 patients and no anomalies in 2.

Surgery outcome was assessed using ILAE classification at 1, 3 and 5 years after surgery (Figure 2).

At 1 year after surgery, 12 patients (63%) were seizure-free (ILAE 1) and 2 patients (11%) had only auras with no other seizure (ILAE 2). The 5 remaining patients had at least 4 seizures per year with a 50% reduction of their baseline seizure frequency (ILAE 4).

Several patients had further improvement between the first and the third year after surgery. Therefore, at 3 years after surgery, 15 patients (79%) were classified ILAE 1, and only 2 were still ILAE 4.

At 5 years after surgery, one patient was lost during follow-up (he was ILAE 1 at 1 and 3 years). For the 18 remaining patients, 14 patients (78%) were classified as ILAE 1. Their antiepileptic medications were gradually decreased: at 5 years, 9 patients were on antiepileptic drug monotherapy and treatment was discontinued in 5 patients.

All patients had a neuropsychological assessment 1 year after surgery. It showed identical results in comparison with the pre-operative neuropsychological assessment in 13 patients, slight worsening of episodic memory in 4 patients (verbal episodic memory worsening after left TPE surgery in 3 patients, and visual episodic memory worsening after right TPE surgery in one patient), and improvement of executive functions in 2 patients.

Discussion:

Our study pointed two major findings: TPE has no specific electroclinical feature, and a conservative resection sparing the hippocampus is a viable surgical approach for drug-resistant TPE.

Electroclinical features

Some previous studies reported that most TPE patients exhibited nocturnal hyperkinetic seizures[5,7,9,10]. In our study, nocturnal hyperkinetic seizures was found in 4 of 19 patients, i.e. 21%, which is higher than usually found in TLE (6% in Staack's cohort[7]). Most of our patients had focal seizures with impaired awareness mimicking MTLE seizures. The only distinctive features of TPE compared with MTLE were the higher seizures frequency (37/month in TPE, vs 6/month in our MTLE cohort[6]), and the absence of febrile seizure during childhood (0/19 TPE patients). TPE may thus mimic either MTLE or frontal lobe epilepsy, certainly depending of the preferential spreading of the epileptic discharge. A fast spreading to the ipsilateral mesio-temporal structures was found in all patients who underwent sEEG, which was associated with MTLE symptoms, and the nocturnal hyperkinetic seizures might be related to the spread to the frontal lobe.

TPE is a rare subtype of temporal lobe epilepsy, accounting for only a small number of TLE patients: over the same period, in our centre, 308 patients had a surgery for drug-resistant MTLE[5], including 214 associated with hippocampal sclerosis and 94 associated with other etiology (focal cortical dysplasia, DNET…). However, TPE is hard to identify and individualize. In our cohort, MRI-negative TPE patients underwent sEEG with implantation scheme sampling the mesial temporal structure (hippocampus and amygdala), enabling us to assess that the seizures indeed started from the temporal pole and secondarily spread to the mesial temporal structure. On the other side, some MRI-negative patients might have been

falsely identified as MTLE instead of TPE if we missed a temporal pole onset during sEEG due to an insufficient sampling of the temporal pole.

Surgical approach and postoperative outcome

Our study is the first one reporting postoperative outcome of patients with drug-resistant TPE after a conservative surgery sparing the mesial temporal structures. In the only other cohort of patients with temporal pole epilepsy, Wang et al[12] reported 8 patients who underwent a surgery, 6 of which had anterior temporal lobectomy including amygdalo-hippocampectomy, and only 2 had a conservative surgery.

The excellent surgical outcome in our cohort (79% patients ILAE I at 3 year after surgery and 78% at 5 years) is similar to the best results of MTLE surgery. In a 2015 Cochrane meta-analysis[13], 69% of patients were Engel class I (which approximately correspond to ILAE 1 and 2) at 1 year after temporal lobe surgery, and 74% in case of hippocampal sclerosis. In our previously published cohort of MTLE patients[5], seizure outcome after surgery was classified Engel I in 83.7% patients at 8.7 years.

For the two patients classified ILAE 4 at 5 years, a missed mesiotemporal onset of the seizure might be considered, but they had both benefited from presurgical sEEG, sampling temporal pole, hippocampus and amygdala, that did assess an onset in the temporal pole. Another hypothesis might be a second epileptogenic focus not recorded during sEEG. The patients were proposed a second presurgical evaluation, but they declined it.

Temporal lobe resections sparing the hippocampus have a cognitive benefit compared with resections including the hippocampus, such as a benefit in verbal learning performance in resections within the dominant hemisphere[10], but they can still be associated with a decline in memory performances. Wagner et al[11] demonstrated that any resection within the

temporal lobe might lead to a secondary hippocampal atrophy, and thus a memory decline. This could explain the slight worsening of episodic memory seen in 4 of our patients at one year post-surgery. Nevertheless, as the majority of our patients (13/19) did not show any neuropsychological worsening after surgery, we recommend to spare the hippocampus in temporal pole epilepsy.

Limitation of the study

The main limitation of our study is the lack of a comparative group. In our centre, we favoured the most conservative surgical approach, therefore no TPE patient underwent anterior temporal resection including the mesial structures.

Conclusion

TPE is a specific epileptic syndrome with electroclinical features resembling MTLE, except for a higher seizure frequency and the absence of febrile seizure during childhood. TPE must be differentiated from MTLE, and may require intracranial EEG in the absence of MRI lesion. TPE is accessible to a conservative resective surgery, sparing the mesial temporal structures, with a good surgical outcome both in terms of seizure freedom and memory outcome.

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Tables and figures:

Table 1. Summary of patient demographic, clinical and paraclinical data

Gender	M : 15 / F : 4
Epilepsy risk factor	Febrile seizure during childhood: 0/19 Prematurity: 2/19 (10.5 %) Familial history of epilepsy: 0/19 Cranial trauma: 0/19
Age at 1st seizure: median (minimum-maximum), years	13 (3-33)
Age at surgery: median (minimum-maximum), years	25 (17-50)
Seizure frequency: median (minimum-maximum)	37/month (5/month - 10/day)
Epilepsy lateralisation	Left: 11 (58 %) / Right: 8 (42 %)
MRI findings	Normal MRI: 8 /Temporal pole lesions: 11 *Cystic lesion: 3* *Cortical dysplasia: 3* *Tumoral lesion: 4* *Cerebral cavernous malformation: 1*
Interictal scalp EEG findings	Homolateral temporal spikes: 19/19 (100 %) Contralateral temporal spikes: 4/19 (21 %) Homolateral frontal spikes: 3/19 (16 %)
Histopathology	Focal cortical dysplasia: 3 DNET: 3 Ganglioglioma: 2 Dermoid cyst: 1 Ependymal cyst: 1 Arachnoïd cyst: 1 Neuronal heterotopia: 2 Gliosis: 4 No anomaly: 2

Table 2. Clinical and electrophysiological data during seizures and electrical stimulations for the 7 TPE patients who underwent sEEG.

Patients	**Seizure onset**	**Early spreading (1 to 10 seconds after seizure onset)**	**Late spreading (more than 10 seconds after seizure onset)**	**Electrical stimulation**
Patient 1 Histology: neuronal heterotopia	Anterior temporopolar fast discharge	Ipsilateral hippocampus	No late spreading	Temporal pole stimulation: feeling of fear or joy Hippocampus stimulation: feeling of fear or joy
	No symptom	Feeling of anxiety and fear, followed by loss of awareness	NA	
Patient 2 Histology: gliosis	Mesial temporopolar fast discharge	Ipsilateral amygdala, hippocampus, and mesial temporo-basal cortex	Ipsilateral orbitofrontal cortex	Temporal pole stimulation: not practiced (technical issue) Hippocampus stimulation: triggers an amygdalo-hippocampal rhythmic discharge, associated with paleness and aphasia
	Gustatory hallucination, memory recall	Loss of awareness	Contralateral arm dystonia, contralateral tonic head deviation	
Patient 3 Histology: neuronal heterotopia	Basal temporopolar and anterior temporopolar fast discharge	Ipsilateral hippocampus	Ipsilateral fronto-insular areas	Temporal pole stimulation: triggers a focal seizure with the same electrical pattern and the same symptoms than spontaneous seizure Hippocampus stimulation: triggers an asymptomatic temporopolar fast discharge
	Tachycardia, feeling of « adrenaline rush »	Loss of awareness	Shout, bilateral upper limbs hyperkinetic movements	
Patient 4 Histology: no anomaly	Anterior temporopolar onset with fast involvement (200ms) of ipsilateral temporo-basal cortex and	Ipsilateral hippocampus, then contralateral hippocampus	No late spreading	Not done

	amygdala			
	Loss of awareness, hand and oral automatisms	Loss of awareness, hand automatisms, polypnea, tachycardia	NA	
Patient 5 Histology: no anomaly	Temporopolar fast discharge, with fast spreading (200ms) to the ipsilateral external temporal cortex	Ipsilateral amygdala and hippocampus	No late spreading	Temporal pole stimulation: triggers a fast discharge associated with a feeling of seizure onset (nausea, feeling of strangeness) Hippocampus stimulation: cough, nausea
	Head and eye contralateral tonic deviation, nausea	Loss of awareness, hand and oral automatisms	NA	
Patient 6 Histology: gliosis	Basal temporopolar fast discharge	Ipsilateral inferior temporal cortex and hippocampus	No late spreading	Temporal pole stimulation: triggers an asymptomatic fast discharge Hippocampus stimulation: nausea (not recognized by the patient as a symptom of its seizure)
	Loss of awareness, motor and oral automatisms	Ipsilateral hand automatisms, contralateral upper limb dystonia	NA	
Patient 7 Histology: gliosis	Temporopolar fast discharge	Ipsilateral inferior temporal cortex	Ipsilateral hippocampus	Temporal pole stimulation: palpitation and rising epigastric sensation, followed by an asymptomatic temporal pole post-discharge Anterior hippocampus stimulation: fear and rising epigastric sensation
	Rising epigastric sensation	Loss of awareness, gestural automatisms	Loss of awareness, gestural automatisms	

Figure 1. Example of preoperative assessment in an MRI-negative patient. A: FDG-PET showing left temporopolar (white arrow) and orbitofrontal hypometabolism. B: subtraction ictal SPECT coregistered with MRI (SISCOM) showing left anterior temporal hyperperfusion. C: Normal preoperative axial and sagittal T1 MRI. D: Postoperative axial and sagittal MRI showing left temporal pole resection (red arrow) with preservation of left mesial temporal structures (blue arrow)

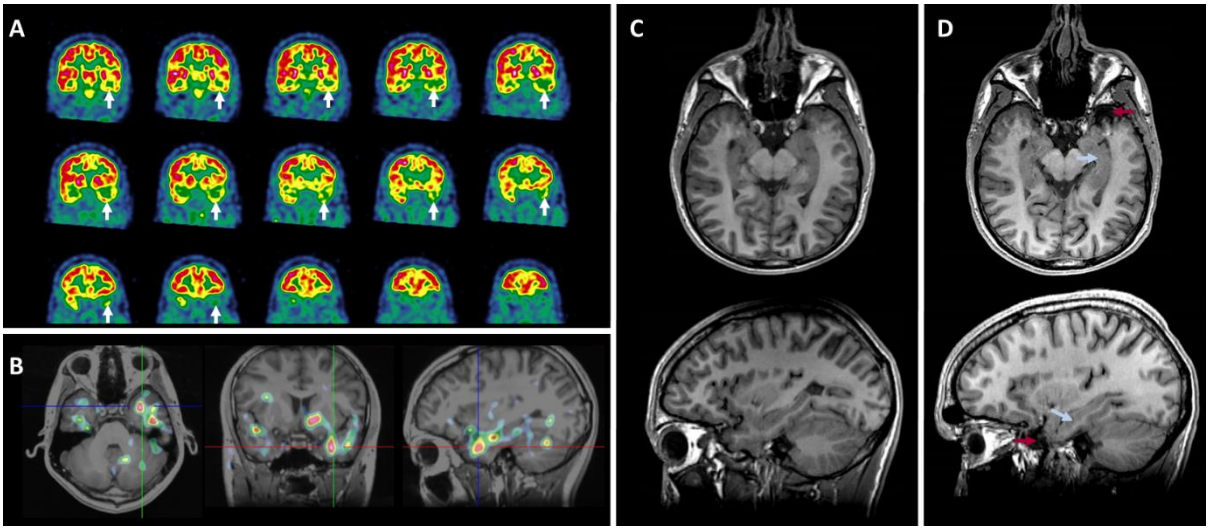

Figure 2. Surgery outcome at 1, 3 and 5 years, using ILAE classification