

Ictal deafness in drug-resistant MRI-negative epilepsy

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ABSTRACT – Ictal clinical semiology indicates where the patient's seizure arises from and how it progresses. A patient's description of a focal sensory seizure may support a surgical decision even when MRI and PET abnormalities are absent. Ictal deafness is a focal auditory seizure characterized by suppression of hearing, presumably originating from the auditory cortex in the temporal lobe. However, the precise localization has not been confirmed with surgical cases. We present a case in which the region from where ictal deafness arose was confirmed by intracranial electroencephalography, with successful epilepsy surgery and review other published cases.

Key words: ictal deafness, Heschl's gyrus, epilepsy, epilepsy surgery, semiology, temporal lobe epilepsy

Patient details

A 20-year-old, right-handed woman had suffered with seizures since the age of six years, consisting of focal tonic seizures beginning in the right side of the face or right limbs and focal impaired awareness seizures with hypersalivation, followed by motor aphasia. These seizures occasionally evolved to bilateral tonic-clonic seizures. She was referred to our hospital four months after the onset of epilepsy. Her seizures occurred monthly despite medication with antiepileptic drugs (AEDs). The seizure frequency gradually increased at age 15 years despite administration of various AEDs, including carbamazepine, valproate, clobazam, levetiracetam, and topiramate. She

became aware of impaired hearing before the occurrence of these seizures at around the age of 19 years. She described the aura as *"sound became fainter and fainter, and finally disappearing"*. Her seizures were characterized by suppressed hearing (ictal deafness [ID]), followed by speech arrest, and then evolved into right facial tonic seizures. She could state verbally when the auditory symptoms would start. She had two or three seizures per week over the last six months under treatment with carbamazepine at 200 mg, levetiracetam at 2,000 mg, and clonazepam at 4 mg. History was normal for gestation, birth, and development, and there was no family history of neurological or epileptic disorders.

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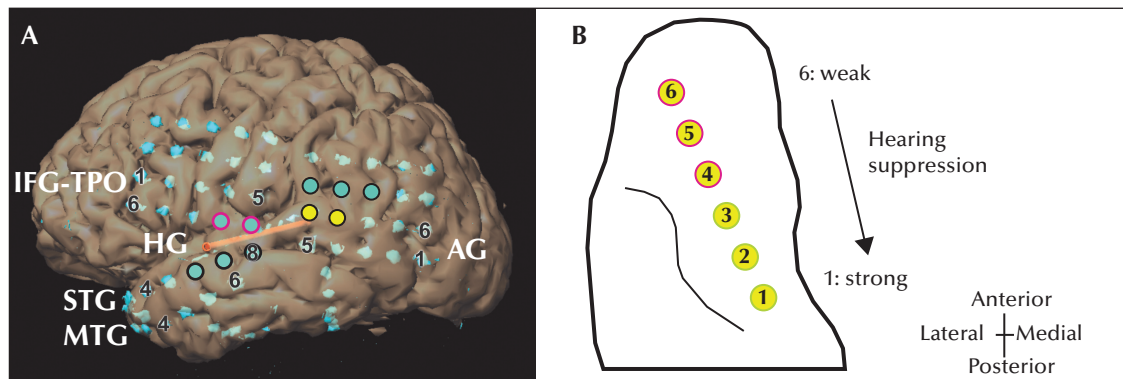


Figure 1. (A) Three-dimensional presentation of electrode locations on the patient's brain. Subdural strip and grid electrodes on the post-implantation CT scan are coloured blue. The trajectory of the depth electrode in Heschl's gyrus (HG) is shown as an orange line. The black circle indicates the site where language response was provoked by ECS. The electrode number is partly indicated. Anatomical information is represented as follows: IFG-TPO: inferior frontal gyrus and temporo-parietal operculum; STG: superior temporal gyrus; MTG: middle temporal gyrus; AG: angular gyrus. (B) Schematic illustration of the locations of the HG depth electrodes (numbered circles). The temporal lobe is viewed from above. Electrical stimulation of the electrodes provoked impairment of hearing in the ear contralateral to the stimulated hemisphere. Suppression was stronger in the posteromedial part of HG than in the anterolateral part. In both (A) and (B), the seizure onset zone and propagation are represented by coloured circles (magenta: seizure onset zone; green: propagation), and the area where the ECS elicited impairment of hearing is shown as a yellow circle.

Non-invasive investigations

Comprehensive pre-surgical evaluation was performed. A 3.0 Tesla magnetic resonance imaging (MRI) revealed no structural abnormality and fluorodeoxyglucose-positron emission tomography (PET-FDG) showed no local hypometabolism. Long-term video-EEG monitoring demonstrated interictal spikes in the left mid-temporal region and ictal onset from the left temporal area. Neurological examination revealed no abnormalities with no obvious auditory disturbance. Her intelligence and memory function were within normal range based on the Wechsler Adult Intelligence Scale, third edition, and Wechsler Memory Scale-Revised.

Hypothesis

Based on the ictal symptom, we hypothesized that her seizures initially originated from the left auditory cortex and propagated to the surrounding regions, first to the language area and then to the left facial motor cortex, before losing awareness. The scalp EEG findings support this hypothesis. Her normal cognitive function and imaging studies indirectly suggest the presence of a mild or focal epileptogenic lesion.

Invasive investigations

Pre-surgical evaluation was performed with intracranial electrodes. A depth electrode was inserted along Heschl's gyrus (HG) postero-medially using the frameless stereotactic system (VarioGuide®, Brainlab,

Germany) (Reddy *et al.*, 2010). Subdural strip and grid electrodes were arrayed at the temporo-parietal area surrounding HG, including the inferior frontal gyrus, temporo-parietal operculum, superior temporal gyrus (STG), middle temporal gyrus, and angular gyrus (*figure 1A, B*). The locations of the contacts were identified using automatic fusion images based on postoperative thin-slice computed tomography and preoperative MRI (*figure 2*). Two events of sudden hearing impairment were recorded

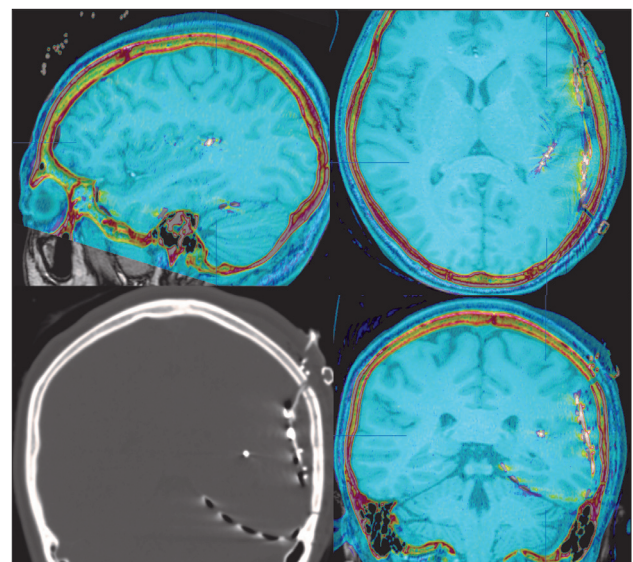


Figure 2. Thin-slice computed tomography (CT) after electrode implantation and automatic fusion images between postoperative CT and preoperative MRI demonstrating the depth electrodes located in HG.

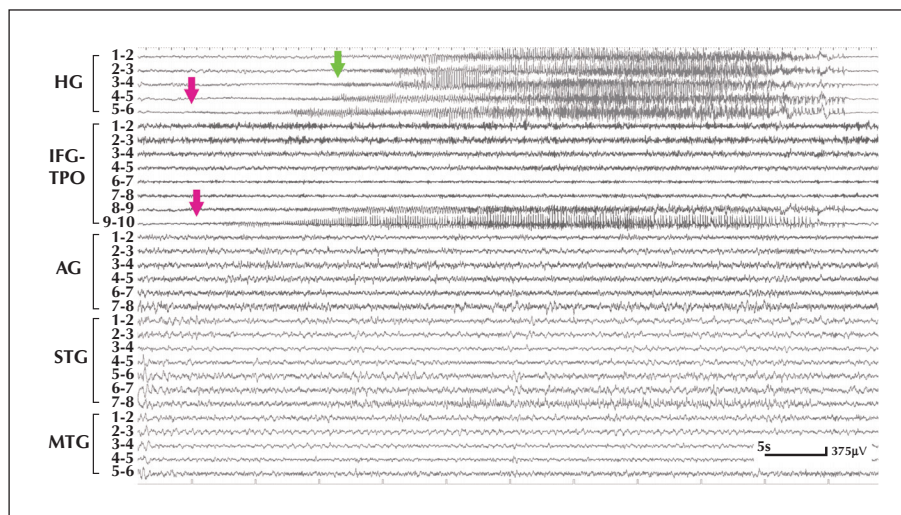


Figure 3. Intracranial EEG recordings during ictal deafness. Ictal discharges were observed in the HG and the posterior superior temporal gyrus (IFG-TPO and STG in this figure). Note that early ictal EEG change started in the lateral half of HG (HG 5-6 and IFG-TPO 9-10 [magenta arrow]) and then propagated to the medial half of HG (HG 1-3 [green arrow]).

during video-EEG monitoring. Intracranial EEG demonstrated the beginning of ictal discharges in the lateral half of HG and part of the posterior STG (*figure 3*). Interictal discharges were observed in the left middle temporal area. Functional mapping with electrical cortical stimulation (ECS) (biphasic square pulses; frequency: 50 Hz; pulse width: 0.3 ms; stimulation intensity: 1-10 mA; duration of each stimulation: 2 s) reproduced language responses in the posterior STG and suppression of hearing in HG. The patient reported stronger hearing impairment at the medial part of HG. Bipolar stimulation at 2 mA at contacts HG1 and 2 elicited complete deafness, but no or mild hearing suppression was provoked at contacts HG3 to 6. The patient consistently reported predominant hearing impairment in the right (contralateral) ear (*figure 1B*).

Surgery and outcome

Based on the results of intracranial EEG recording and electrical cortical stimulation, resection of the lateral half of Heschl's gyrus and a small part of the superior temporal gyrus was performed (*figure 4*). Subsequently, the patient has been seizure-free for one year and four months, except for a single episode of breakthrough seizures upon AED (clobazam) withdrawal at five months after surgery (International League Against Epilepsy Class 3). Histopathological examination revealed focal cortical dysplasia type IIa (*figure 5*). Her auditory acuity and neuropsychological test scores were stable at one year after surgery and she was able to find employment postoperatively. Her ability to listen to music and sing songs (karaoke) did not change after surgery.

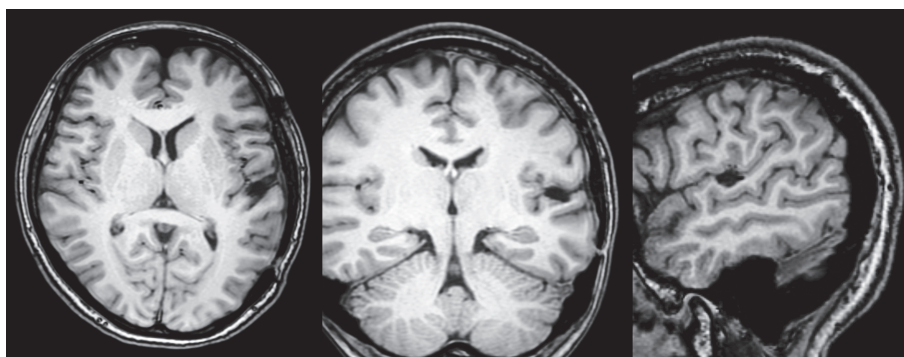


Figure 4. Postoperative MRI showing removal of the anterolateral part of HG by surgery.

Table 1. Summary of cases with ictal deafness

Author	Patient No.	Dominant side of ID symptom	Seizure symptoms other than ID	IED localization	Imaging abnormality (modality)	Epileptogenic side	Treatment	Sz outcome
Ghosh et al., 2001	1	Bil	R face clonic > R body clonic Sz, FIAS	L T, P	Calcification at L T, P (CT)	L	Phenytoin	Free
	2	R	Hyperkinetic Sz	L T	Normal (CT)	L	CBZ	Free
	3	Bil	Weakness of R lower limb with or without R lower limb clonic Sz	L T, P, O	Ring enhanced lesion at L P, T, O (CT)	L	CBZ	Free
Florindo et al., 2006	4	NR	NR	Bil (L>R)	L T, P dysplastic lesion	L	NR	NR
	5	NR	NR	L T	L T vascular lesion (MRI)	L	NR	NR
	6-8	NR	NR	L T	Normal (MRI)	L	NR	NR
Shahar et al., 2010	9	NR	NR	L T, P, O	Normal (MRI)	L	NR	NR
	10	NR	FIAS, Focal to bilateral tonic Sz	Bil	Normal (MRI)	Unknown	VPA	Free
	11	NR	Eye deviation to L, L hand clonic Sz, FIAS	R T	Normal (MRI), R T hypometabolism (FDG-PET)	R	CBZ, LEV, CZP, LTG	Worthwhile improvement
Present case	12	R	R face or R body tonic Sz, FIAS	L T	Normal (MRI), FDG-PET	L	CBZ, VPA, LEV, CLB, TPM, Surgery	Rare (without ID)

ID: ictal deafness; IED: interictal epileptiform discharge; Sz: seizure; Bil: bilateral; R: right; NR: not reported; FIAS: focal impaired awareness seizure; L: left; T: temporal; P: parietal; O: occipital; CT: computed tomography; MRI: magnetic resonance imaging; FDG-PET: fluorodeoxyglucose-positron emission tomography; CBZ: carbamazepine; VPA: valproate; LEV: levetiracetam; PHT: phenytoin; CZP: clonazepam; LTG: lamotrigine; CLB: clobazam; TPM: topiramate.

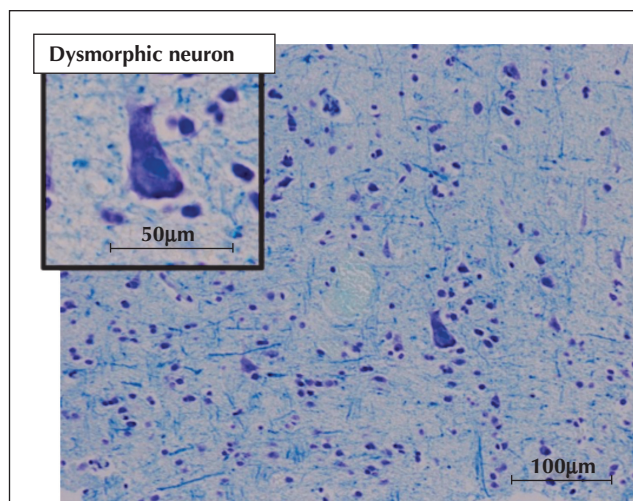


Figure 5. Histopathological examination of the surgical sample of HG revealed cortical dyslamination and dysmorphic neurons.

Discussion

Our patient presented with refractory seizures that initiated with ID, and intracranial EEG localized the seizure onset zone to the anterolateral part of HG. Partial removal of HG led to seizure improvement without auditory deficits. This outcome suggests that ID can arise from the anterolateral half of HG.

Ictal deafness was first described as a type of negative or inhibitory auditory seizure which is relatively rare, with an estimated prevalence of 0.1% (6/8,000) among epilepsy patients (Florindo *et al.*, 2006). Only 11 cases have been reported (*table 1*). The characteristics of these cases indicate that ID can arise from the temporal lobe.

The present case suggests that ID arises from the anterolateral part of HG. Previous electrical cortical stimulation studies support this conclusion (Sinha *et al.*, 2005; Fenoy *et al.*, 2006). Electrical cortical stimulation of HG, especially the anterolateral part of HG, can provoke suppression of hearing (Fenoy *et al.*, 2006). In our study, electrical cortical stimulation of HG also evoked the same phenomenon, but more easily at the posteromedial part of HG. Functional localization of suppression of hearing in HG may differ between patients because of the possible functional re-organization of the auditory system in patients with epilepsy (Sinha *et al.*, 2005).

The reported cases of ID are summarized in *table 1*. Florindo *et al.* (2006) suggested that ID may have lateralizing value because all nine previous cases (three reported by Ghosh *et al.* [2001] and six by Florindo *et al.* [2006]) had occurred in patients with a left temporal lesion. The present case supports this conclusion. In contrast, Shahar *et al.* (2010) reported a case of ID arising from the right temporal area. Furthermore, ECS

investigation elicited suppression of hearing by stimulation of the right HG in two thirds of patients (Fenoy *et al.*, 2006). Further case experience is necessary to confirm the lateralizing value of ID. The present case further suggests that the epileptogenic side may be lateralized and localized contralaterally to HG on the side of predominant suppression of hearing (Ghosh *et al.*, 2001; Sinha *et al.*, 2005).

The sequelae of HG resection are poorly understood. Removal or damage to the right side of HG may cause amusia (Russell and Golfinos, 2003; Terao *et al.*, 2006). Recently, removal of the right anterolateral part of HG was reported to be possible without auditory deficits (Nagahama *et al.*, 2018). In our case, removal of the left anterolateral part of HG caused no auditory or cognitive dysfunction. Therefore, the left part of HG or the anterolateral part of HG may be resectable with relatively low risk of postoperative auditory dysfunction. Further case experience with specific details of the extent of removal are necessary to validate these suggestions.

The present case is the first report of a patient who underwent epilepsy surgery for drug-resistant epilepsy with ID. Although a single breakthrough seizure on AED withdrawal indicates incomplete resection of the epileptogenic zone, the control of her weekly seizures and focal EEG findings still suggest that ID can arise from the anterolateral part of HG. This ictal symptom is rare but may have localizing value, and good seizure outcome can be achieved after removal without auditory deficits. □

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TEST YOURSELF



(1) Where does ictal deafness originate from in focal epilepsy?

- A. Parietal operculum
- B. Angular gyrus
- C. Heschl's gyrus
- D. Supramarginal gyrus

(2) Which of the following is not correct?

- A. Electrical stimulation to Heschl's gyrus may not reproduce impairment of hearing in epilepsy patients.
- B. Ictal deafness is a rare form of auditory seizures, with an estimated prevalence of 0.1% (6/8,000) among epilepsy patients.
- C. Predominant impairment of hearing can occur in the ear contralateral to the epileptogenic side.
- D. Removal or damage to Heschl's gyrus can cause amusia.

(3) Which part of Heschl's gyrus may be resectable with relatively low risk of postoperative auditory dysfunction? (two answers)

- A. Left
- B. Right
- C. Posteromedial
- D. Anterolateral

Note: Reading the manuscript provides an answer to all questions. Correct answers may be accessed on the website, www.epilepticdisorders.com, under the section "The EpiCentre".