Insular lobe epilepsy

**Insular lobe epilepsy** (ILE) is an under-recognized cause of extratemporal epilepsy and explains some epilepsy surgery failures in children with drug resistant epilepsy.

Several lines of evidence have implicated the insula in the extended network involved in mesial temporal lobe epilepsy, and resections of the insula for epilepsy date back to the late 1940s \(^1\).

With advances in both surgical and diagnostic techniques, the functional and pathologic role of the insula in epilepsy is becoming increasingly clear.

The insula has long been implicated in the 30% failure rate after temporal lobe resections for medial temporal lobe epilepsy (MTLE).

Penfield \(^2\) noted the similarity between many of the symptoms of MTLE and those he found with insular stimulation, indicating that, in theory, insular seizures could be confused with MTLE seizures. Early surgeons often found residual postexcision spikes on their electrocorticograms arising from the insula after temporal lobe resection, confirming its epileptic potential. However, independent epileptogenicity was difficult to prove, and no difference in outcome was demonstrated when these additional areas were removed, whereas morbidity was high.

In addition, it has been extremely difficult to differentiate seizures that arise from the mesial temporal lobe and rapidly spread to the insula versus those that originate in the insula and then spread to the temporal lobe. Although the former might still be cured with a temporal lobectomy, the latter likely requires insular resection for successful outcome \(^3\).

**Diagnosis**

Positron emission tomography with 18\(^{\text{F}}\)fluorodeoxyglucose and \([11\text{C}]\)flumazenil-PET scans do show insular hypometabolism and decreased benzodiazepine-receptor binding in the insula in the majority of patients with MTLE, but this finding likely indicates frequent spread, rather than initiation \(^4\).

Subtraction ictal single-photon emission computed tomography coregistered to MRI (SISCOM), which should be more sensitive to ictal onsets, often demonstrates insular as well as medial and lateral temporal lobe hyperperfusion during MTLE \(^5\).

However, the technique also has poor temporal resolution and cannot always differentiate onsets from early spread. It would be interesting to perform SISCOM on a patient with proven insular onsets to see if this technique can identify these patients noninvasively. Thus, depth electrodes are currently the only method with adequate temporal resolution to define insular seizures, although their limitation is in spatial sampling. Only a limited number of depths can be placed, and the ictal-onset zone may not be adequately sampled.

The diagnosis of ILE usually requires invasive investigation with insular sampling; however, the location of the insula below the opercula and the dense middle cerebral artery vasculature renders its sampling challenging. Several techniques have been described, ranging from open direct placement of orthogonal subpial depth and strip electrodes through a craniotomy to frame-based stereotactic placement of orthogonal or oblique electrodes using stereo-electroencephalography principles.

Weil et al describe an alternative method for sampling the insula, which involves placing insular depth...
electrodes along the long axis of the insula through the insular apex following dissection of the sylvian fissure in conjunction with subdural electrodes over the lateral hemispheric/opercular region. The authors report the feasibility, advantages, disadvantages, and role of this approach in investigating pediatric insular-opercular refractory epilepsy.

The authors performed a retrospective analysis of all children (< 18 years old) who underwent invasive intracranial studies involving the insula between 2002 and 2015.

Eleven patients were included in the study (5 boys). The mean age at surgery was 7.6 years (range 0.5-16 years). All patients had drug-resistant epilepsy as defined by the International League Against Epilepsy and underwent comprehensive noninvasive epilepsy surgery workup. Intracranial monitoring was performed in all patients using 1 parasagittal insular electrode (1 patient had 2 electrodes) in addition to subdural grids and strips tailored to the suspected epileptogenic zone. In 10 patients, extraoperative monitoring was used; in 1 patient, intraoperative electrocorticography was used alone without extraoperative monitoring. The mean number of insular contacts was 6.8 (range 4-8), and the mean number of fronto-parieto-temporal hemispheric contacts was 61.7 (range 40-92). There were no complications related to placement of these depth electrodes. All 11 patients underwent subsequent resective surgery involving the insula.

Parasagittal transinsular apex depth electrode placement is a feasible alternative to orthogonally placed open or oblique-placed stereotactic methodologies. This method is safe and best suited for suspected unilateral cases with a possible extensive insular-opercular epileptogenic zone.

**Treatment**

The results of insular resection to treat pharmacoresistant epilepsy are rarely reported.

Gras-Combe et al., report 6 consecutive cases of right insular resection performed based on anatomoelectroclinical correlations provided by stereoelectroencephalography (SEEG).

Six right-handed patients (3 male, 3 female) with drug-resistant epilepsy underwent comprehensive presurgical evaluation. Based on video electroencephalographic recordings, they all underwent SEEG evaluation with bilateral (n = 4) or unilateral right (n = 2) insular depth electrode placement. All patients had both orthogonal and oblique (1 anterior, 1 posterior) insular electrodes (n = 4-6 electrodes). Preoperative magnetic resonance imaging findings were normal in 4 patients, 1 patient had right insular focal cortical dysplasia, and 1 patient had a right opercular postoperative scar (cavernous angioma). All patients underwent right partial insular corticectomy via the subpial transopercular approach.

Intracerebral recordings demonstrated an epileptogenic zone confined to the right insula in all patients. After selective insular resection, 5 of 6 patients were seizure free (Engel class I) with a mean follow-up of 36.2 months (range, 18-68 months). Histological findings revealed focal cortical dysplasia in 5 patients and a gliosis scar in 1 patient. All patients had minor transient neurological deficit (eg, facial paresis, dysarthria).

Insular resection based on SEEG findings can be performed safely with a significant chance of seizure freedom.

Weil et al., retrospectively reviewed the records of all pediatric patients who underwent insular cortical resections for intractable epilepsy at Miami Children's Hospital from 2009 to 2015. Presurgical
evaluation included video electroencephalography monitoring and anatomical/functional neuroimaging. All patients underwent excisional procedures utilizing intraoperative electrocorticography or extraoperative subdural/depth electrode recording.

Thirteen children (age range 6 months-16 years) with intractable focal epilepsy underwent insular-opercular resection. Seven children described symptoms that were suggestive of insular seizure origin. Discharges on scalp EEG revealed wide fields. Four patients were MRI negative (i.e., there were no insular or brain abnormalities on MRI), 4 demonstrated insular signal abnormalities, and 5 had extrainsular abnormalities. Ten patients had insular involvement on PET/SPECT. All patients underwent invasive investigation with insular sampling; in 2 patients resection was based on intraoperative electrocorticography, whereas 11 underwent surgery after invasive EEG monitoring with extraoperative monitoring. Four patients required an extended insular resection after a failed initial surgery. Postoperatively, 2 patients had transient hemiplegia. No patients had new permanent neurological deficits. At the most recent follow-up (mean 43.8 months), 9 (69%) children were seizure free and 1 had greater than 90% seizure reduction.

Primary insular seizure origin should be considered in children with treatment-resistant focal seizures that are believed to arise within the perisylvian region based on semiology, widespread electrical field on scalp EEG, or insular abnormality on anatomical/functional neuroimaging. There is a reasonable chance of seizure freedom in this group of patients, and the surgical risks are low.


