Stereotactic depth electrode investigation of the insula in the evaluation of medically intractable epilepsy

Clinical article

Atman Desai, M.D., Barbara C. Jobst, M.D., Vijay M. Thadani, M.D., Krzysztof A. Buijarski, M.D., Karen Gilbert, A.P.R.N., M.S., Terrance M. Darcey, Ph.D., and David W. Roberts, M.D.

Section of Neurosurgery and Department of Neurology, Dartmouth-Hitchcock Medical Center, Lebanon, New Hampshire

Object. The authors describe their experience with stereotactic implantation of insular depth electrodes in patients with medically intractable epilepsy.

Methods. Between 2001 and 2009, 20 patients with epilepsy and suspected insular involvement during seizures underwent intracranial electrode array implantation at the authors’ institution. All patients had either 1 or 2 insular depth electrodes placed as part of an intracranial array.

Results. A total of 29 insular depth electrodes were placed using a frontal oblique trajectory. Eleven patients had a single insular electrode placed and 8 patients had 2 insular electrodes placed unilaterally. One patient had bilateral insular electrodes implanted. Postoperative imaging demonstrated satisfactory placement in all but 1 instance, and there was no associated morbidity or mortality. Fourteen patients underwent a subsequent resection, involving the frontal lobe (9 patients), temporal lobe (4), or frontotemporal lobes (1), and of these, 11 currently have Engel Class I outcome. Two patients (10%) had seizures originating within the insula and another 5 patients (25%) demonstrated early specific insular involvement. Neither patient with an insular seizure focus went on to resection. All 5 of the patients with early specific insular involvement underwent an insula-sparing resective procedure with Engel Class I outcome in all cases.

Conclusions. Stereotactic placement of insular electrodes via a frontal oblique approach is a safe and efficient technique for investigating insular involvement in medically intractable epilepsy. The information obtained from insular recording can be valuable for appreciating the degree of insular contribution to seizures, allowing localization to the insula or clearer implication of other sites. (DOI: 10.3171/2010.9.JNS091803)

Key Words • depth electrodes • epilepsy surgery • epilepsy • insula • stereotaxy

Abbreviations used in this paper: EEG = electroencephalography; FLAIR = fluid attenuated inversion recovery; PET = positron emission tomography; SEEG = stereoelectroencephalography; SPECT = single photon emission computed tomography.

The concept of seizures arising within the insula was first proposed in the 1940s by Guillaume and Mazars,10 based on electrocorticographic recordings obtained intraoperatively in patients undergoing epilepsy surgery. Several years later, their findings were replicated by Penfield.20 There followed several decades of anecdotal reports of seizures associated with insular lesions,4,5,11,22 but perhaps owing to the hazardous surgical anatomy and poor outcomes reported with insular resection,25 there was little focused investigation of the role of the insula in ictal onset.

In the past decade, however, several groups have reported experiences with the use of insular recording electrodes in patients with medically intractable epilepsy.1,8,12–14,16,17,24 These studies have helped to characterize seizures that have an insular onset and have suggested at least comparable outcomes for insular resections compared with temporal or frontal resections in patients with these seizures. Furthermore, these studies have demonstrated several techniques and trajectories for placement of recording electrodes into the insula.

At our institution, implanted intracranial recording arrays for the investigation of medically intractable epilepsy are routinely employed. In patients with suspected insular involvement, insular depth electrodes are placed as part of the array. This study of our experience with insular depth electrodes was undertaken to evaluate their safety and efficacy in the diagnosis and treatment of patients with medically intractable epilepsy.

Methods

Selection Criteria

Between 2001 and 2009, 20 patients with medically refractory epilepsy, in whom possible insular involve-
Depth electrode investigation of the insula

ment during epileptic seizures was suspected, underwent intracranial electrode array implantation. All of these patients had either 1 or 2 insular depth electrodes placed as part of the intracranial array. The need for insular electrodes was determined on the basis of clinical seizure characteristics, video-EEG (scalp) recordings, MR imaging, ictal and interictal SPECT, and interictal PET scans.

Surgical Procedure

Twelve-contact depth electrodes (Ad-Tech Medical Instrumentation Corp.; contacts measuring 1.1 mm in outside diameter and 2.3 mm in length, with 6-mm on-center spacing) were placed in the insula as part of a larger intracranial array in all 20 patients. The electrodes were stereotactically implanted using a Leksell Model G stereotactic frame (Elekta AB) and a frontal oblique trajectory. The trajectory and placement were planned using preoperative MR imaging studies (T1-weighted, TE 3, TR 25, 256 matrix, 1.5-mm slice thickness, Gd enhanced) loaded onto a SurgiScope workstation (ISIS Intelligent Surgical Instruments and Systems). The placement and trajectory of the insular depth electrodes were planned to avoid internal vasculature, minimize violation of pial boundaries, maximize contacts residing within the insula, and coordinate with other electrodes in the array. The SurgiScope software was used to calculate stereotactic coordinates for electrode target and entry, and in-house software was used to determine the angles of the trajectory. The electrodes were placed through 4-mm linear incisions and 3/16-inch craniotomies using the bushings of the stereotactic frame as a drill guide. The dura was coagulated with electrocautery. An insertion cannula with a central stylet was placed through an appropriately-sized bushing and down the trajectory. The central stylet was then withdrawn, the depth electrode inserted, and the outer cannula removed. The electrode was secured to the scalp with a 2-0 silk suture, which also closed the incision. The stereotactic frame was then removed and the scalp re-prepared and draped for subdural strip and/or grid electrode placement through bur hole and craniotomy, respectively. Sterile dressings were applied. A high-resolution CT scan (512 matrix, 2.5 mm spacing) was obtained the evening of surgery, and that study was coregistered with the patient’s preoperative MR imaging to determine the angles of the trajectory. The electrodes were placed through 4-mm linear incisions and 3/16-inch craniotomies using the bushings of the stereotactic frame as a drill guide. The dura was coagulated with electrocautery. An insertion cannula with a central stylet was placed through an appropriately-sized bushing and down the trajectory. The central stylet was then withdrawn, the depth electrode inserted, and the outer cannula removed. The electrode was secured to the scalp with a 2-0 silk suture, which also closed the incision. The stereotactic frame was then removed and the scalp re-prepared and draped for subdural strip and/or grid electrode placement through bur hole and craniotomy, respectively. Sterile dressings were applied. A high-resolution CT scan (512 matrix, 2.5 mm spacing) was obtained the evening of surgery, and that study was coregistered with the patient’s preoperative MR imaging for assessment of electrode position. Patients were treated with prophylactic antibiotic therapy during the recording period.

Video-EEG Recording and Data Collection and Analysis

The patients were admitted postoperatively to the Epilepsy Monitoring Unit. Continuous stereo-electroencephalography recording through the intracranial electrodes with concomitant video recording of the patient was performed. Interictal and ictal EEG recordings, functional mapping, and video correlates were analyzed. Postoperative imaging was used to assess electrode position and aid interpretation. Recording was performed beginning the evening of surgery, with a goal of capturing at least 3 of the patient’s typical seizures. Antiepileptic medications were reduced or stopped, and hyperventilation, photic stimulation, sleep deprivation, and exercise on a stationary bicycle were performed in most cases to help provoke seizures.

Preoperative and postoperative clinical information on patients undergoing implantation of intracranial recording electrodes at our institution is logged prospectively into a computerized database. These records were reviewed, and patients with insular electrodes as part of the array were identified. The demographic characteristics; seizure history and semiology; scalp EEG, MR imaging, SPECT, and PET findings; operative procedures; intracranial electrode recordings; postoperative course; and seizure outcomes for this group were reviewed. Seizure outcome was graded according to the Engel classification system.

Results

Patient Population

The demographic and clinical features of the 20 patients included in this study are described in Table 1. The mean patient age was 36 years, with a range of 19 to 58 years. Seven patients were men and 13 were women. The mean period of video-EEG monitoring was 8.7 days with a range of 1–17 days. All patients underwent preoperative neuropsychological testing. All patients underwent preoperative MR imaging and ictal and interictal SPECT scans. Eleven patients underwent PET scans in addition. Two patients’ MR imaging scans showed insular abnormalities. In one of these patients, MR imaging showed increased T2 and FLAIR signal in the left insula and medial frontal lobe. In the other patient blurring of the gray-white junction was seen at the right insula and orbitofrontal regions. Nine patients had SPECT scans that demonstrated increased perfusion in the insula during seizures. The insula did not show hyper- or hypometabolism on PET studies performed in this group of patients.

Electrode Placement

In 19 of 20 cases, postoperative imaging demonstrated satisfactory electrode placement, with between 3 and 7 electrode contacts within the insula (mean 5.2, median 5, SD 0.76). In one case, the depth electrode intended for the insula was dislodged by the application of a frontal grid so that no contacts resided in the insula. In further analysis of seizures, this patient was not considered to have an insular electrode. There was no hemorrhage and no morbidity or mortality associated with placement of the insular electrodes.

Electrode Arrays

Eleven patients had a single insular electrode placed and 8 patients had 2 insular electrodes placed unilaterally (anterior and posterior). One patient had bilateral insular electrodes placed. The insular electrodes were in all cases part of larger intracranial arrays, which included between 4 and 14 separate electrodes. The arrays comprised various combinations of depth, strip, and grid electrodes. A total of 154 electrodes were placed in the 20 patients (mean 7.7 ± 2.5 per patient). Of these a total of 36 electrodes (mean 1.8 ± 2.1 per patient) were depth electrodes.
TABLE 1: Characteristics of patients with insular depth electrodes

<table>
<thead>
<tr>
<th>Pt No.</th>
<th>Age (yrs), Sex</th>
<th>Description of Seizure</th>
<th>MRI Findings</th>
<th>Interictal PET &amp; Ictal SPECT Findings</th>
<th>Days†</th>
<th>Ictal EEG Recordings (early activity)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>46, M</td>
<td>gastric aura, subjective recognition of seizure, minor oral &amp; hand automatisms, never completely loses contact, recovers quickly</td>
<td>rt temporal region of encephalomalacia</td>
<td>PET: normal; SPECT: normal</td>
<td>3</td>
<td>rt subtemporal origin, w/ early spread to rt hippocampus &amp; insula, then diffuse spread</td>
</tr>
<tr>
<td>2</td>
<td>49, F</td>
<td>abrupt onset, bilateral hand automatisms, laughter/vocalization, grimacing, &amp; rocking in bed; rapid return to baseline</td>
<td>incr FLAIR signal lt insula &amp; medial lt frontal lobe</td>
<td>PET: NP; SPECT: incr ictal perf lt medial frontal region</td>
<td>13</td>
<td>It medial parasagittal origin w/ spread to ant insula &amp; lt lat frontal convexity, then diffuse bilateral spread</td>
</tr>
<tr>
<td>3</td>
<td>19, F</td>
<td>awakens, eyes staring to rt, oral automatism, rt hand twitching, tonic posturing, clonic movements</td>
<td>normal</td>
<td>PET: normal; SPECT: incr perf lt ant temporal lobe &amp; rt orbitofrontal region</td>
<td>9</td>
<td>It orbitofrontal origin, spread to lt occipitotemporal electrode followed by rt occipitotemporal electrode, followed by lt ant temporal convexity, &amp; then diffuse spread</td>
</tr>
<tr>
<td>4</td>
<td>45, M</td>
<td>awakens, grabs groin, rocking motions of body, automatisms of lt leg &amp; arm, then dystonia of rt arm &amp; leg, w/ or w/o secondary generalization</td>
<td>normal</td>
<td>PET: normal; SPECT: incr activity on lt temporal lobe, lt insula, lt frontal pole</td>
<td>14</td>
<td>no seizures recorded</td>
</tr>
<tr>
<td>5</td>
<td>21, F</td>
<td>arouses from sleep, frenetic automatisms in bed, then rapid recovery</td>
<td>normal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>49, F</td>
<td>arouses from sleep, sniffs, generalized rigidity, moans; lt face, arm, &amp; leg automatisms followed by rt dystonias &amp; postictal dysphasia</td>
<td>normal</td>
<td>PET: normal; SPECT: incr perf lt temporal regions, lt more than rt</td>
<td>8</td>
<td>some seizures originating in rt &amp; some originating in lt hippocampus</td>
</tr>
<tr>
<td>7</td>
<td>36, M</td>
<td>staring, slight clumsiness, gagging, coughing</td>
<td>lt hippocampus w/ reduced vol &amp; incr FLAIR signal</td>
<td>PET: decr metabolism ant temporal lobe; SPECT: incr perf ant medial lt temporal lobe &amp; insula &amp; lt basal ganglia &amp; thalamus</td>
<td>4</td>
<td>origin in lt hippocampus, spread to lt insula &amp; lt temporal convexity</td>
</tr>
<tr>
<td>8</td>
<td>25, F</td>
<td>oral automatisms w/ secondary generalization w/ head turning to rt nausea, déjà vu, retching</td>
<td>lt frontal region w/ incr FLAIR signal</td>
<td>PET: normal; SPECT: normal</td>
<td>8</td>
<td>origin in lt hippocampus w/ spread to lt temporal convexity</td>
</tr>
<tr>
<td>9</td>
<td>44, F</td>
<td>nausea, déjà vu, retching</td>
<td>normal postop changes following rt selective amygdalohippocampectomy</td>
<td>PET: NP; SPECT: incr perf lt temporal region superior &amp; pst to previous resection</td>
<td>12</td>
<td>possible origin in rt temporal convexity but difficult to tell apart from interictal spikes</td>
</tr>
<tr>
<td>10</td>
<td>58, F</td>
<td>arouses from sleep, chewing, tongue protrusion, opens eyes, cries/screams, agitated, rocking, lt hand automatisms, rt hand dystonias</td>
<td>lt hemisphere encephalomalacia</td>
<td>PET: hypometabolic lt hemisphere; SPECT: incr perf of lt temporal lobe</td>
<td>9</td>
<td>origin in lt hippocampus, spread to mesial temporal lobe</td>
</tr>
<tr>
<td>11</td>
<td>19, M</td>
<td>intense indescribable &quot;aura&quot; w/ limb weakness (lt worse than rt)</td>
<td>normal postop changes following previous resection of rt temporal lesion</td>
<td>PET: NP; SPECT: normal</td>
<td>17</td>
<td>origin in rt insula (ant &amp; pst electrodes)</td>
</tr>
</tbody>
</table>

(continued)
<table>
<thead>
<tr>
<th>Pt No.</th>
<th>Age (yrs), Sex</th>
<th>Description of Seizure</th>
<th>MRI Findings</th>
<th>Interictal PET &amp; Ictal SPECT Findings</th>
<th>Days†</th>
<th>Ictal EEG Recordings (early activity)</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>26, M</td>
<td>aura of “odd feeling,” some gastric sensation, oral automatisms, lip-smacking &amp; staring, occasional tongue biting/incontinence</td>
<td>lt frontal operculum 1-cm cavernoma, lt mesial temporal sclerosis</td>
<td>PET: decr activity lt ant temporal lobe; SPECT: incr activity lt temporal lobe</td>
<td>1</td>
<td>origin lt hippocampus</td>
</tr>
<tr>
<td>13</td>
<td>37, F</td>
<td>confusion, generalized seizures</td>
<td>normal</td>
<td>PET: normal; SPECT: incr activity lt pst temporal region &amp; lt ant insula</td>
<td>12</td>
<td>origin lt frontal convexity, then diffuse spreading (displaced insular electrode)</td>
</tr>
<tr>
<td>14</td>
<td>23, F</td>
<td>nocturnal lt arm &amp; leg shaking, no loss of consciousness</td>
<td>normal</td>
<td>PET: hypometabolism bilat medial parietal lobes; SPECT: incr activity rt temporal, frontal, &amp; insular regions</td>
<td>7</td>
<td>origin rt medial frontal region</td>
</tr>
<tr>
<td>15</td>
<td>34, M</td>
<td>aura of gastric sensation, “funny feeling,” then rt hand dystonia &amp; oral alimentary automatisms w/ secondary generalization</td>
<td>rt hippocampus w/ reduced vol</td>
<td>PET: hypometabolism rt parietal lobe; SPECT: incr perf rt frontal &amp; insular cortex</td>
<td>6</td>
<td>rt frontal origin, then generalization</td>
</tr>
<tr>
<td>16</td>
<td>35, F</td>
<td>staring, aphasia, often preceded by indescribable sensation, then generalized tonic phase, then confusion</td>
<td>bilat migration disorder</td>
<td>PET: NP; SPECT: incr perf rt insula &amp; frontal operculum</td>
<td>7</td>
<td>rt frontal convexity origin, early spread to lt frontal</td>
</tr>
<tr>
<td>17</td>
<td>53, F</td>
<td>distortion of reality, fear, then vocalizes, agitation, bilat automatisms, worse in arms, than legs</td>
<td>blurring of gray-white junction at rt insula &amp; orbitofrontal cortex</td>
<td>PET: NP; SPECT: incr perf rt insula &amp; orbitofrontal cortex</td>
<td>13</td>
<td>origin in rt medial frontal region, then spread to rt insula, &amp; then rt lat frontal region &amp; medial temporal region</td>
</tr>
<tr>
<td>18</td>
<td>27, F</td>
<td>brief stiffening, head turns to rt, heavy breathing, subjective electrical sensation</td>
<td>normal postop changes following previous rt frontal resection</td>
<td>PET: NP; SPECT: incr uptake rt basal ganglia, insula, pst lat frontal lobe</td>
<td>6</td>
<td>diffuse origin</td>
</tr>
<tr>
<td>19</td>
<td>40, M</td>
<td>perception of a bad taste, followed by oral &amp; lt hand automatisms, then rt hand dystonia, w/ confusion &amp; aphasia</td>
<td>normal postop changes following previous rt temporal resection</td>
<td>PET: NP; SPECT: incr activity in lt insula</td>
<td>7</td>
<td>origin in lt insula</td>
</tr>
<tr>
<td>20</td>
<td>24, F</td>
<td>arouses from sleep, then rocks back &amp; forth &amp; is confused; develops bilat hand &amp; leg automatisms</td>
<td>normal postop changes following previous lt medial frontal resection</td>
<td>PET: NP; SPECT: incr perf in lt anterolateral frontal lobe</td>
<td>9</td>
<td>origin in lt medial frontal lobe, then generalization</td>
</tr>
</tbody>
</table>

* Ant = anterior; decr = decreased; incr = increased; NP = not performed; perf = perfusion; pst = posterior; Pt = Patient.
† Days refers to number of days of monitoring.
that were placed in sites other than the insula. Up to 8 of these electrodes were placed in each case, and these included occipitotemporal electrodes, medial frontal electrodes, posterior temporal electrodes, and electrodes targeting specific areas of scarring seen on preoperative MR imaging (1, frontal).

A total of 49 strip electrodes (range 0–5, mean ±1.10) and 41 grid electrodes (range 0–4, mean ±1.05) were placed. Thirteen patients received bilateral arrays, and 7 patients received unilateral arrays.

**Video-EEG Recording**

The ictal EEG findings of the 20 patients in the study are summarized in Table 1. Nineteen patients had clinical seizures with video and EEG correlation and analysis possible. Two patients (10%) had interictal and ictal recordings consistent with insular onset. Functional mapping was performed in both patients. The first patient, with right insular onset, was found to have replication of his typical aura of rapidly progressive malaise and subjective left arm and leg weakness with stimulation of the right insular electrode contacts. In the second patient, in whom seizure onset appeared to be in the left insula and frontal operculum, functional mapping showed language participation within this entire region. Five additional patients (25%) demonstrated early, specific insular involvement during seizures. In these patients abnormal ictal activity was seen specifically within the insular electrodes (sometimes in conjunction with other sites) subsequent to activation of an initial seizure onset zone elsewhere.

**Resective Procedures**

On the basis of data obtained from video-EEG monitoring, resection was performed in 14 of 20 patients. The resection was of the frontal lobe in 9 patients (3 right, 6 left) and of the temporal lobe in 4 patients (1 right, 3 left). A right-sided frontotemporal resection was performed in 1 patient. Histopathological examination revealed mesial temporal sclerosis in 3 cases, focal cortical dysplasia in 2, and changes suggestive of posttraumatic encephalomalacia in another. In the remaining 8 cases, histopathological analysis did not show any abnormal tissue with increased epileptogenic potential.

All 5 patients who had demonstrated early specific insular involvement in their seizure development went on to undergo an insula-sparing resective procedure. This was based upon the ictal recordings suggesting secondary insular involvement but not insular origin. One of these patients had a right frontal resection, 2 a left frontal resection, 1 a right temporal resection, and 1 a left temporal resection.

Six patients did not undergo resection after electrode placement. This group included both patients found to have insular seizure onset. One patient had seizures originating within the right insula and was offered resection but declined further surgery. One patient with seizures originating in the left insula was also found to have language participation within the seizure onset zone and went on to undergo vagal nerve stimulator placement. In the remaining 4 patients, a resectable seizure focus was not identified. Two went on to undergo placement of a vagal nerve stimulator. Another patient went on to participate in the NeuroPace responsive stimulation trial. The final remaining patient did not undergo any further surgery.

**Outcomes**

In all 20 cases, clinical follow-up is on-going (mean 36.4 months, range 7–92 months, median 32.5 months). Of the 14 patients who underwent resection, the outcome currently is Engel Class I in 11 and Class III in 3. Mean follow-up for this group is 32.9 months (range 7–67 months, median 31 months). One patient who underwent a right medial frontal resection developed a supplementary motor area syndrome that resolved within 1 week of surgery. Another patient who underwent a right selective amygdalohippocampectomy was found to have a partial left upper quadrantanopsia following surgery. No other patients undergoing a resection had a new neurological deficit after surgery.

In all 5 patients with early insular involvement but not onset who underwent an insula-sparing resection, outcome is all currently Engel Class I (follow-up: mean 23.7 months, range 8–67 months, median 21 months).

**Illustrative Cases**

**Case 1: Insular Seizure Focus**

This 40-year-old man (Patient 19, Table 1) presented with recurrence of seizures after a left anterior temporal lobectomy at another hospital 13 years earlier. An ictal subtraction SPECT demonstrated increased perfusion in the left insula. His MR imaging showed expected postoperative changes only. His seizures consisted of a perception of a bad taste, followed by oral and left hand automatisms, with development of right hand dystonia and aphasia. Ictal scalp EEG showed no clear changes at ictal onset.

He was admitted for implantation of an intracranial electrode array and video-EEG monitoring. He underwent placement of 2 left insular depth electrodes (anterior and posterior), a left temporal 4 x 8 contact subdural grid electrode, a left subtemporal 4 x 8 contact grid electrode, and a left frontal 4 x 8 contact grid electrode (Fig. 1).

Video-EEG monitoring revealed onset of rhythmic epileptiform activity from both left insular depth electrodes (Fig. 2). The patient underwent functional mapping and was found to have language participation within the insula and adjacent frontal lobe. Resection of the seizure onset zone was therefore not possible. His electrodes were removed without complication. He went on to undergo vagal nerve stimulator placement. At 92 months’ follow-up he has no seizures (Engel Class I outcome).

**Case 2: Secondary Insular Involvement**

This 49-year-old woman (Patient 2, Table 1) presented with medically intractable seizures that involved an abrupt onset of bilateral hand automatisms, vocalization, grimacing, and laughter. Magnetic resonance imaging revealed an area of increased T2 signal intensity in the left insula and left medial frontal lobe. Ictal subtraction SPECT showed in-
creased perfusion in the left frontal lobe during seizures. She was admitted for video-EEG monitoring and underwent placement of left anterior and left posterior insular depth electrodes, accompanied by 2 left medial frontal depth electrodes, 2 left frontal convexity 1 × 8 contact strip electrodes, 2 right medial frontal depth electrodes, and 2 right frontal convexity 1 × 8 contact strip electrodes (Fig. 3).

Ictal recording showed left medial frontal parasagittal seizure origin with early propagation to the anterior insula and left lateral frontal convexity, prior to more diffuse spread (Fig. 4). The patient underwent a left medial frontal resection and has Engel Class I outcome at 11 months’ follow-up.

Case 3: No Insular Involvement. This 23-year-old woman (Patient 14, Table 1) presented with medically intractable seizures that involved sudden arousal from sleep at night followed by dystonic posturing of both arms. The results of an MR imaging study were unremarkable. A PET study revealed hypometabolism within bilateral medial parietal lobes. Ictal SPECT showed increased perfusion within the right insula and frontotemporal lobes. She was admitted for video-EEG monitoring and underwent placement of a right insular depth electrode, accompanied by anterior and posterior interhemispheric 3 × 8 contact grid electrodes, right lateral and medial frontoparietal convexity 4 × 8 contact grid electrodes, and a right 1 × 8 contact parietal strip electrode (Fig. 5).

Ictal recording showed fast sharp discharges originating in the right medial frontal region at seizure onset (Fig. 6). No electrical involvement of the insula was seen. The patient underwent a right medial frontal resection and has Engel Class I outcome at 44 months’ follow-up.

Discussion

The use of intracranial EEG to investigate seizure onset in patients with medically intractable epilepsy is well established. Until recently, however, there was little reported literature on how this strategy could be best used to safely and accurately characterize the role of the insula in seizure origin. Our present study, evaluating the use of depth electrodes placed stereotactically using a frontal oblique trajectory in 20 consecutive patients with medically intractable epilepsy and suspected insular involvement, demonstrated the technique to be both safe and useful for localizing and clarifying the role of the insula in seizure onset. Patients were selected on the basis of a combination of ictal SPECT, interictal PET, MR imaging, scalp EEG, and seizure semiology. Using this approach, specific seizure origin within the insula was found in 2 (10%) of 20 patients. Although neither of these patients underwent further surgery, localization of the seizure focus to the insula was of value in avoiding surgery in eloquent cortex, avoiding surgery in regions other than the seizure focus, and guiding further management. A further 5 patients (25%) were found to have specific, early involvement of the insula during their seizures, secondary to onset in a separate site. This enabled insula-sparing resections with good outcomes in terms of seizure control and absence of neurological deficits. In the remaining 13 patients, shown to be without insular involvement in their...
seizures, exclusion of the insula helped support and confirm seizure onset in other regions.

Previous Reports of Direct Insular SEEG Recording

The role of the insula in seizure onset has received increasing interest over the past decade, during which time several groups have published reports documenting the use of intracranial monitoring electrodes implanted into the insula using a variety of methods to investigate seizure onset (Table 2).

In 2000, Isnard et al. reported on 21 patients who underwent insular electrode placement for seizure monitoring; in 2 of these patients the seizures were found to have an insular onset and failed to improve after temporal resection. In 2004, the same group reported on 50 patients who underwent insular recording and described a specific insular seizure syndrome in 6 of these patients, with good results from insular resection. In 2006, Ryvlin et al. reported on 3 patients with nocturnal frontal lobe epilepsy who underwent intracranial electrode recording and were found to have an insular onset to their seizures, although none underwent further surgery. In 2008, Afif et al. described recording from the insula using anterior and posterior oblique trajectories; using this method the authors were able to demonstrate specific insular origin of seizures in 5 of 30 patients and only secondary involvement in 10 further patients. In 2009, Malak et al. reported their experience with insular resections for patients with insular epilepsy. Five of 7 patients had insular onset documented by intracranial recording. Good seizure outcomes were obtained in all of these patients.

Patient Selection and Diagnostic Yield

Previous reports have tended to select patients for insular recording on the basis of clinical seizure characteristics, scalp EEG recordings (with or without video correlation), MR imaging, SPECT and PET imaging and describe in approximately 10%–20% of patients with insular recording electrodes, a seizure onset zone specifically within the insula. The patients in the present study were selected because of suspected insular onset based upon results from these same evaluations (Table 3).
Depth electrode investigation of the insula

Fig. 6. Illustrative Case 3: no insular involvement seen (Patient 14). An EEG recording demonstrating localization of seizure onset to the right anterior interhemispheric electrodes (RAI, solid arrow), with no early discharge within the right insular electrode (RID).

tracranial EEG recording subsequently demonstrated insular onset in 2 of 20 patients, consistent with the previous literature. The issue of optimal patient selection criteria for insular electrode implantation for SEEG, however, remains unanswered.

Surgical Technique

Patients in the present study had depth electrodes placed stereotactically using an image-guided, frame-based transfrontal oblique trajectory planned to minimize pial violations. All patients underwent postoperative imaging and no hemorrhage associated with the insular electrodes was seen. This strategy enabled satisfactory electrode placement in all cases, with the exception of one in which the postoperative scan obtained on the evening of surgery revealed that the electrode had migrated distally and no longer resided within the insula. We do not know if this migration occurred during surgery or in the early postoperative period. There was no morbidity or mortality associated with the placement of the insular depth electrodes in our experience.

Various alternative approaches for placement of insular electrodes have also been described. The stereotactic orthogonal, or transpercular, approach as described by Talairach and Bancaud has been frequently reported. This approach requires multiple electrodes for sufficient coverage, in addition to detailed visualization of the middle cerebral artery, sylvian fissure, and sulcal vasculature to allow for safe insertion of electrodes to provide for adequate sampling. Other groups have also had success placing insular recording electrodes under direct visualization after splitting of the sylvian fissure. At present, all of our insular depth electrodes are placed stereotactically, using a fixed frame and preoperative MR imaging. Determination of targets and trajectory has been performed on our stereotactic treatment planning workstation so as to avoid vascular structures identified on high-resolution, contrast-enhanced MR imaging. We have not encountered any instance of vascular injury. Prior to this patient cohort we had placed strip electrodes over the insular cortex using this method but were not satisfied with the coverage. More recently, the use of oblique trajectories to target depth electrodes to the insula has been described, most notably by Afif et al., who used a frame-based stereotactic approach and incorporated both transfrontal and transparietal trajectories. These oblique approaches have been facilitated by advances in stereotactic planning, visualization, and trajectory determination.

Insular Involvement During Seizures

Investigation of the seizure focus in suspected frontal or temporal lobe epilepsy often necessitates consideration of the role of the insula, given its central location and numerous connections to the orbitofrontal and cingulate cortices, and temporohippocampal structures. Afif et al. reported good outcomes with insula-sparing resections of the frontal and temporal lobes in patients in whom the insula was identified as a site of secondary seizure propagation and in those who had no insular involvement. Conversely, Isnard et al. reported persistence of insular-onset seizures after temporal lobectomy. Therefore, when insular involvement is suspected in frontal, temporal, frontotemporal, or actual insular epilepsy, it is important to determine the precise seizure focus and clarify the role of the insula.

Previous reports have suggested clinical features common to seizures with insular origin on SEEG. These seizures are simple partial in nature, with common features being laryngeal discomfort, dysphonia, paresthesias, and somatomotor symptoms. The 2 patients in our study in whom insular onset was found both remained conscious and in contact with the environment during their seizures, which thus also belonged to the category of simple partial seizures. One patient had an intense generalized discomfort with weakness and tingling over the contralateral face and body. The second patient had a perception of a bad taste, accompanied by oral and left hand automatisms, followed by right hand dystonia and aphasia. The appearance of aphasia in the latter patient and its absence in previously reported insular lobe seizures may be partly accounted for by language function within this patient’s insular seizure zone, demonstrated by functional mapping, or possibly due to early involvement in the seizure of adjacent language cortex.

Relatively little is understood about the function of the insula, although several investigators have suggested that it may play a role in secondary sensory processing, language and motor control, or higher autonomic control, and as a component of the limbic system. The seizure characteristics of our patients with insular onset seizures, and those of patients in the aforementioned studies, are in keeping with this concept.

Study Limitations

Our findings should be interpreted within the limitations of our study. It is a retrospective analysis and is
limited to a single institution. A large range in patient follow-up exists, with a small but significant number (6 of 20) followed up for less than 2 years. In addition, of the 2 patients discovered to have an insular focus for their seizures, neither went on to undergo a resective procedure. Therefore, this study cannot answer to what extent insular depth electrodes can be used to define a safely resectable seizure focus within the insula. Furthermore, in all cases a frontal oblique trajectory and the same 12-contact electrode with 6-mm spacing was used. Thus it remains unclear whether different trajectories or electrodes can be used with similar results. In our study, selection for the placement of insular depth electrodes was based upon a combination of factors, including seizure history and

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>No. of Pts</th>
<th>Pt Selection for Insular Electrodes</th>
<th>Method of Electrode Placement</th>
<th>No. of Electrodes Placed w/in Insula</th>
<th>Electrode Contacts Placed w/in Insula</th>
<th>Complications†</th>
<th>Patients w/ Localization of Seizure Focus to the Insula</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isnard et al., 2000</td>
<td>21</td>
<td>scalp video-EEG, PET, ictal subtraction SPECT, MRI</td>
<td>frame-based stereotactic orthogonal traj w/ telangiography</td>
<td>65 total (mean 3.1, range 2–5)</td>
<td>NP</td>
<td>NP</td>
<td>2/21 (9.5%)</td>
</tr>
<tr>
<td>Isnard et al., 2004</td>
<td>50</td>
<td>scalp video-EEG</td>
<td>frame-based stereotactic orthogonal traj w/ telangiography</td>
<td>144 total (mean 2.9, range NP)</td>
<td>NP</td>
<td>NP</td>
<td>6/50 (12%); onset solely in insula in 5/50 (10%)</td>
</tr>
<tr>
<td>Ryvlin et al., 2006</td>
<td>3</td>
<td>NP</td>
<td>1 frame-based stereotactic orthogonal traj w/ telangiography, 2 w/ oblique traj; ant vs pst traj details &amp; stereotactic methodology NP</td>
<td>3 total (mean 1)</td>
<td>mean 5, range 2–7</td>
<td>NP</td>
<td>3/3 (100%); description of larger cohort undergoing recording NP</td>
</tr>
<tr>
<td>Afif et al., 2008</td>
<td>30</td>
<td>clinical seizure characteristics, scalp video-EEG</td>
<td>frame-based stereotactic oblique traj w/ telangiography; majority transfrontal</td>
<td>35 total (mean 1.2)</td>
<td>mean 7.5, range NP</td>
<td>none reported</td>
<td>5/30 (18%); onset solely w/in insula in 2/30 (6.7%)</td>
</tr>
<tr>
<td>Malak et al., 2009</td>
<td>7</td>
<td>scalp video-EEG, PET, ictal subtraction SPECT, MRI</td>
<td>1 w/ orthogonal, frame-based stereotactic traj w/ telangiography; 6 w/ depth electrodes placed under direct visualization</td>
<td>total no. NP, 2 insular electrodes per pt in most cases</td>
<td>2 contacts for all insular electrodes</td>
<td>1 patient w/ transient leg weakness</td>
<td>7/7 (100%); description of larger cohort undergoing recording NP</td>
</tr>
<tr>
<td>Park et al., 2009</td>
<td>6</td>
<td>scalp video-EEG, MRI, PET, ictal subtraction SPECT in 3/6</td>
<td>1 w/ strip electrode placed under direct visualization; 2 w/ depth electrodes placed w/ frame-based stereotactic oblique transparietal traj; 3 w/ depth electrodes placed under direct visualization w/ aid of image guidance</td>
<td>3 depth electrodes per pt when placed under direct visualization; otherwise 1 per pt</td>
<td>strip electrode w/ 2 contacts; stereotactic depth electrodes w/ 2 contacts each; directly placed depth electrodes w/ 4 contacts each</td>
<td>none reported</td>
<td>6/6 (100%); description of larger cohort undergoing recording NP</td>
</tr>
<tr>
<td>Present study</td>
<td>20</td>
<td>clinical seizure characteristics, scalp video-EEG, PET, ictal subtraction SPECT, MRI</td>
<td>frame-based stereotactic oblique transfrontal traj</td>
<td>29 total (mean 1.45, range 1–2)</td>
<td>mean 5.2, range 0–7, median 5, SD 0.76</td>
<td>none</td>
<td>2/20 (10%)</td>
</tr>
</tbody>
</table>

* NP = not provided; traj = trajectory(ies).
† Complications arising from insular electrode implantation.
Depth electrode investigation of the insula

TABLE 3: Summary of criteria for patient selection for insular depth electrodes

<table>
<thead>
<tr>
<th>Criteria for Patient Selection</th>
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</thead>
<tbody>
<tr>
<td>seizure semiology w/ “insular-onset characteristics” (for example, simple partial, laryngeal discomfort, dysphonia, paresthesias &amp; somato-motor symptoms)</td>
</tr>
<tr>
<td>scalp EEG w/o clear localization of ictal origin, w/ early involvement of frontal &amp;/or temporal leads</td>
</tr>
<tr>
<td>structural or signal abnormality of insula on MRI</td>
</tr>
<tr>
<td>perfusion abnormality of insula on ictal subtraction SPECT imaging</td>
</tr>
<tr>
<td>hypometabolic abnormality of insula on PET imaging</td>
</tr>
</tbody>
</table>

features, MR imaging, video scalp EEG, ictal subtraction SPECT, and PET scans. Strictly defined inclusion criteria were not used, and given the small number of patients with seizures that were eventually found to be of insular origin, this study cannot determine which characteristics provide the best indication for proceeding with insular electrode placement. Finally, given the small number of patients involved, we are unable to show whether more contacts or more than 1 depth electrode within the insula provides a diagnostic advantage, however intuitive this may appear.

Conclusions
Stereotactic placement of insular electrodes via a frontal oblique approach is a safe and effective technique for investigating insular involvement in medically intractable epilepsy. This technique localized seizure origin within the insula in 10% of cases and demonstrated early specific involvement after onset in a separate site in a further 25% of cases. Such information is valuable for appreciating the degree of insular contribution to seizures, allowing localization to the insula, or more clearly implicating other sites.

Disclosure
The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Desai, Roberts. Acquisition of data: Gilbert, Darcey, Thadani, Bujarski. Critically revising the article: Desai, Jobst, Roberts, Thadani, Bujarski. Reviewed final version of the manuscript and approved it for submission: all authors.

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