INSULAR SEIZURES: HAVE WE BEEN MISSING THE BOAT?

Clinical Manifestations of Insular Lobe Seizures: A Stereo-electroencephalographic Study

Isnard J, Guenot M, Sindou M, Mauguiere F

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PURPOSE: In this study, we report the clinical features of insular lobe seizures based on data from video and stereoelectroencephalographic ictal recordings and direct electric insular stimulation of the insular cortex performed in patients referred for presurgical evaluation of temporal lobe epilepsy (TLE).

METHODS: Since our first recordings of insular seizures, the insular cortex has been included as one of the targets of stereoelectroencephalographic electrode implantation in 50 consecutive patients with TLE whose seizures were suspected to originate from, or rapidly to propagate to, the perisylvian cortex. In six, a stereotyped sequence of ictal symptoms associated with intrainsular discharges could be identified.

RESULTS: This ictal sequence occurred in full consciousness, beginning with a sensation of laryngeal constriction and paresthesiae, often unpleasant, affecting large cutaneous territories, most often at the onset of a complex partial seizure (five of the six patients). It was eventually followed by dysarthric speech and focal motor convulsive symptoms. The insular origin of these symptoms was supported by the data from functional cortical mapping of the insula by using direct cortical stimulations.

CONCLUSIONS: This sequence of ictal symptoms looks reliable enough to characterize insular lobe epileptic seizures. Observation of this clinical sequence at the onset of seizures on video-EEG recordings in TLE patients strongly suggests that the seizure-onset zone is located not in the temporal but in the insular lobe; recording directly from the insular cortex should occur before making any decision regarding epilepsy surgery.

COMMENTARY

Like the lost island of Atlantis, the human insula lies submerged beneath the parietal, frontal, and temporal opercular cortices, buried under a tangled web of middle cerebral artery branches. Although surface expeditions with grid and strip electrodes fail to record its mysteries, more adventurous surgical explorers have often found themselves drowning in high morbidity rates (1,2). Anatomically, the insula has extensive connections with the limbic system, including the amygdala, entorhinal cortex, cingulate gyrus, and hippocampus (3). Several lines of evidence have implicated the insula in the extended network involved in medial temporal lobe epilepsy, and resections of the insula for epilepsy date back to the late 1940s (1). With recent 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) (2,4). Penfield (4) 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 (2). 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.

Fortunately, French epileptologists and neurosurgeons have generally favored the use of depth electrodes over the surface grids commonly used in other parts of the world. These electrodes can be advanced safely through the overlying operculum into the insula; with the help of image-guided navigation to avoid the overlying vasculature, they can be stereotactically

placed in predetermined regions of the insula. By using several lines of evidence, including ictal semiology, cortical stimulation, and response to surgical ablation, Isnard et al. have shed further light on the mysteries of the insula. First, a comprehensive lexicon of the functional behaviors elicited with stimulation of the insula is presented, including somatosensory, viscerosensitive, auditory, dysarthric behaviors, and sensations of unreality or body movement. Their descriptions are not quite as evocative as the prose of Penfield, who wrote in 1954: "On the insula there appears to be representation of the gastrointestinal tract as judged by the fact that stimulation here produces various types of abdominal sensation such as nausea, umbilical sensation, borborygmi, belching, and the desire to defecate"(5). Second, correlations between ictal symptoms and insular discharges revealed several fascinating facts. Although obvious in retrospect, the authors point out that if seizures spread to the insula from the mesial temporal lobe, patients' reports of their symptoms are inconsistent and unreliable because their consciousness is affected. Thus, only patients with seizures arising in the insula can provide such information. Although the majority (86%) of the 50 MTLE seizures reported in this paper did spread to the insula, only 10% actually arose from the insula (in this selected group of patients with semiologic evidence of insular involvement). Notably, laryngeal discomfort or perioral and hemisensory paresthesias were quite specific for insular involvement, as was eventual spread to motor areas.

The authors are able to characterize insular onsets in the following set of symptoms—memorization of which may benefit all epileptologists. A fully conscious patient with laryngeal discomfort, dyspnea, unpleasant perioral or somatic paresthesias, and dysarthric speech, followed by somatomotor symptoms, implies an insular onset. The final proof is in the response to surgery. The authors provide both positive and negative evidence, that is, two patients who underwent only insular ablation were cured, whereas two who underwent only temporal ablation had persistent seizures.

Although the authors' arguments are convincing, further data from noninvasive imaging studies would be helpful. Positron emission tomography with ^{18}[F]fluorodeoxyglucose and [^{11}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 (6). 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 (7). 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.

How safe is surgery in the insula? The early reports of 20% morbidity are clearly overestimates of current morbidity rates. In the last few years, several reports of surgery in the insula have appeared in the literature, mainly for low-grade gliomas. In the era of frameless stereotactic navigation and intraoperative MRI, surgery in the insula is becoming increasingly common and safe (8,9). One recent report of seizure outcome after removal of insular tumors demonstrated an 82% Engel I outcome with 45% transient and no long-term morbidity in a series of 11 patients (8). Now that Isnard et al. have elegantly illustrated how to identify insular seizures by semiology, epileptologists and epilepsy surgeons should be more aggressive about localization with depth electrodes and even surgical resection within the insula, encouraged by the results reported in neurosurgical oncology. We hope that additional cases of successful surgery to treat insular epilepsy will soon appear in the literature to lend further support to the authors' limited, but encouraging series.

by Theodore H. Schwartz, MD, FACS

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