Optimizing the Detection of Subtle Insular Lesions on MRI When Insular Epilepsy Is Suspected

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ABSTRACT

SUMMARY: Insular epilepsy is underdiagnosed and accounts for a number of failed operations. Identifying insular target lesions on MR imaging can help guide intracranial electroencephalography and improve the outcome of surgery. In this study, we present a novel method of exploring the insular region for subtle lesions on 3D MR imaging by MPR postprocessing of slices in oblique reference planes. Using this method, we retrospectively reviewed presurgical MRIs that were initially considered to have normal findings in 7 pediatric patients with intractable insular epilepsy. Insular epilepsy was confirmed in these patients on stereo-electroencephalography and histopathology. The MPR postprocessing method we describe helped detect subtle insular lesions in all 7 patients.

ABBREVIATIONS: FCD = focal cortical dysplasia; SEEG = stereo-electroencephalography

Refactory epilepsy of the insula is one of the most challenging forms of epilepsy to diagnose and treat for a number of reasons. Due to the position of the insula situated at the crossroads of several lobes, the clinical semiology of insular seizures often orients toward a frontal, parietal, or temporal lobe origin. Furthermore, because the insula is covered by the opercular folds, its electrical activity is partly shielded from scalp electroencephalography. Several authors have shown that the ictal discharge in insular seizures could mimic frontal, temporal, central, or parietal seizure-onset zones, misleading the diagnosis.

When insular epilepsy is suspected, stereo-electroencephalography (SEEG) is often required to accurately locate the ictal onset zone. The proper positioning of these intracranial electrodes depends on the ability of MR imaging to define a target lesion. When MR imaging is unable to define a lesion, the chances of a successful operation are significantly reduced.

Because the insula covers a small surface area of the brain and its cortex forms discrete gyri oriented in an oblique sagittal plane, it may be difficult to identify its architecture and its limits on MR imaging viewed in standard orthogonal planes (sagittal, axial, and coronal).

In this retrospective study of 7 pediatric patients who underwent an operation for refractory insular epilepsy, we show how MPR postprocessing of high-resolution 3D-T1WI and 3D-T2WI can help identify subtle insular lesions that were initially missed on presurgical MR imaging but were subsequently identified on SEEG and histopathology.

METHODOLOGY

Local regional ethics approval was obtained for this retrospective study.

Case Selection

Of the 293 patients who had undergone focal resection for refractory epilepsy in our institution between January 2009 and December 2016, we selected those with insular epilepsy on the basis of SEEG results (30 patients; 10%). Of these patients, we excluded those MRIs positive for insular lesions (11 patients). Among the remaining cases, apparently “nonlesional,” we excluded those whose presurgical MRIs were performed with insufficient resolution (maximum voxel size of 1 mm³) (12 patients).

Seven patients were retained in our study, 4 boys and 3 girls with a mean age at the time of presurgical MR imaging of 8.6 years (range, 3–14.7 years).

Imaging Acquisition and Analysis

MR imaging was performed on a 3T Ingenia scanner (Philips Healthcare, Best, the Netherlands) using a 32-channel head coil. All of the scans were obtained with the patient under general anesthesia, as is routine in our institution for children younger than 7 years of age or for patients with difficulty in remaining calm for the duration of the examination.
FCD of the insula, the peri-insular sulci, the opercula, or other structures surrounding the insula. These signs included cortical thickening, increased cortical T2WI signal, blurring of the gray/white matter junction, abnormal white matter signal extending from the cortex to the ventricular surface, the transmantle sign, and abnormal gyral and/or sulcal patterns, including shallow sulci or broad gyri (pachygyria), and sulci or gyri with an unusual form (dysmorphic or irregular gyral pattern).

RESULTS

The clinical and radiologic data are summarized in Tables 1 and 2, respectively.

The 7 patients selected for our study underwent an operation at an age of 8.6 years (range, 3–13 years). SEEG was performed in all patients before the operation and demonstrated an ictal onset zone within the insula in all patients. MR imaging was performed at a maximum of 3 months before the operation and showed subtle abnormalities involving the insula in all patients. One patient had FCD limited to the insula, and 6 had FCD involving the adjacent structures as well.

The most commonly observed MR imaging features of insular FCD in our study were insular and peri-insular blurring, found in 6 of the 7 patients, and an abnormal gyral pattern of the insula, found in all 7 patients. On the basis of these features, 1 radiologist found insular FCDs in all 7 patients, and the other radiologist found in all 7 patients. On the basis of these features, 1 radiologist found insular FCDs in all 7 patients, and the other radiologist found insular FCD in 6 of the 7 patients. Neither radiologist found such anomalies in the contralateral insula. The rate of interobserver agreement for the detection of insular dysplasia was almost perfect, with a $\kappa$ score of 0.86.

The presurgical MR imaging, CT–MR imaging coregistration with SEEG electrodes in place, and postsurgical MR imaging of 2 types of patients are shown: one with an isolated insular lesion (patient 1, Fig 3) and one with an insular lesion extending into the peri-insular sulcus (patient 3, Fig 4).

DISCUSSION

To our knowledge, this is the first clinical report to describe a method for analyzing MRIs to improve the detection of subtle insular lesions in patients with drug-resistant epilepsy.

In the few studies that have reported insular epilepsy surgery in children, negative findings on MRIs are common, and little attention is given to imaging considerations. Lesion identifi-
cation on MR imaging increases a patient’s chances of complete resection, which is an essential prognostic factor of successful epilepsy surgery.\textsuperscript{10-12}

In this study, 6 of the 7 detected lesions were classified as FCD on histopathologic analysis according to the Blu¨mcke classification.\textsuperscript{13} The 1 case in which no FCD was found (patient 3) may be attributed to the small size of the surgical samples due to the surgical constraints in this region. Those constraints might explain why 2 patients were not seizure-free after the operation (patients 4 and 6).

The MR imaging sequences we chose to analyze are in keeping with the recommended international consensus guidelines for imaging infants and children with recent-onset epilepsy.\textsuperscript{14} Apart from high-resolution 3D-T1WI and 3D-T2WI sequences, there is no consensus on the use of other types of sequences in the clinical setting. Furthermore, it is necessary to use both T1WI and T2WI sequences to detect FCDs in a young pediatric population because maturation of subcortical white matter appears at different ages on T1WI and T2WI, becoming isointense to cortex at times.\textsuperscript{15} Beyond 24 months, subcortical white matter maturation is usually complete and FCDs can be detected on both T1WI and T2WI.

The use of MPR postprocessing helped to identify the gyral pattern of the insula and the pattern of the peri-insular sulcus. It also improved the detection of abnormal cortical signal, thickening, and blurring of these structures. All 7 patients were

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**Table 1: Clinical data**

| Patient | Sex | Age at Seizure Onset (yr) | Neurologic Status before Surgery | Age at Last Surgery (yr) | Topography of Resective Surgery | Postsurgical Deficit | Pathology | FU Duration (yr) | Engel\textsuperscript{a} |
|---------|-----|--------------------------|---------------------------------|--------------------------|---------------------------------|---------------------|-----------|-----------------|-----------------|
| 1       | M   | 2.5                      | LH, Special education           | 13.0                     | Posterior Ins and posterior Op, + frontal Disc | 0                   | FCD IIa   | 4.2             | I               |
| 2       | M   | 3.2                      | RH, MoMR                       | 6.2                      | Posterior Ins and STG           | Negative            | FCD Ib    | 4.2             | I               |
| 3       | F   | 3.5                      | RH, Normal cognitive function   | 14.7                     | Anterior Ins + frontal Disc     | 0                   | FCD IIa   | 2.3             | III             |
| 4       | F   | 0.8                      | RH, MoMR                       | 3.0                      | Anterior Ins + frontal Disc     | 0                   | FCD IIa   | 0.9             | I               |
| 5       | M   | 0.4                      | Left hemiparesis SMR, ASD       | 6.1                      | Anterior Ins + frontal Disc     | 0                   | FCD IIa   | 3.0             | III             |
| 6       | F   | 2.0                      | LH, MiMR                       | 7.6                      | Posterior Ins and parietal Op, temporal Op | 0                   | FCD IIb   | 1.8             | II              |
| 7       | M   | 1.0                      | LH, MoMr, ASD                   | 9.7                      | Anterior Ins and Inferior Frontal | 0                   | FCD IIb   | 4.2             | I               |

Note: —LH indicates left-handed; RH, right-handed; MoMR, mild mental retardation; MoMR, moderate mental retardation; SMR, severe mental retardation; ASD, autism spectrum disorder; Op, operculum; Ins, insula; STG, superior temporal gyrus; Disc, disconnection; FU, follow-up; yr, year.

\textsuperscript{a} Engel Surgical Outcome Scale.

**Table 2: Review of presurgical MRIs in patients with intractable insular epilepsy with no initial detection of insular lesions**

| Patient No. | Insula | Gyral Pattern | Blurring | Peri-Insular Sulcus | Blurring | Surrounding Structures | Blurring |
|-------------|--------|---------------|----------|---------------------|----------|------------------------|----------|
| 1           | R      | Supernumerary ALG | +        | –                   | –        | –                      | –        |
| 2           | R      | Poorly defined AL | +        | Irregular anterior portion of SPS | –        | Anterior SPS           | –        |
| 3           | R      | Hypoplasia PL    | –        | –                   | –        | Hypoplasia STG         | STG, HG  |
| 4           | R      | Irregular AL     | –        | Irregular anterior portion of SPS | –        | –                      | –        |
| 5           | R      | Irregular AL     | –        | –                   | –        | Frontal opercula, orbitofrontal |
| 6           | L      | Thick PL         | –        | –                   | –        | HG, temporal stem      | –        |
| 7           | L      | Poorly defined AL | +        | Poorly defined APS  | –        | –                      | –        |

Note: —ALG indicates the anterior long gyrus; R, right; L, left; SPS, superior peri-insular sulcus; PL, posterior lobule; IPS, inferior peri-insular sulcus; STG, superior temporal gyrus; HG, Heschl gyrus; AL, anterior lobule; APS, anterior peri-insular sulcus; –, normal; +, present; –, absent.

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**FIG 3.** Patient 1. Isolated insular lesion. Oblique sagittal view parallel to the base of the insula. A, T1WI oblique sagittal view shows an unusual gyral pattern of the posterior lobule of the right insula, which shows 3 gyri (arrow). B, T1WI oblique sagittal view shows a normal gyral pattern of the contralateral insula. C, T2WI oblique sagittal view shows blurring of the most anterior long gyrus of the right insula (arrow). D, T2WI oblique sagittal view shows no blurring of the contralateral insula. E, T2WI oblique sagittal view with SEEG electrodes (ictal onset zone around electrode OP). OM, OP, IP, TP, and TS indicate the names of depth electrodes. F, FLAIR sagittal view of the right insula after an operation.
but no study has shown and should not be considered an indication of dysplasia. A retrospective study design was the most suitable for a preliminary study. As insular epilepsy is a rare condition in our experience, a retrospective design was chosen. A total of 1584 MRIs, were found to be epileptogenic on SEEG recordings. The insular sulcus, stressing the importance of a systematic analysis of these associations with localized gray/white matter blurring is suggestive of FCD. Asymmetry of the insular gyral pattern between the 2 hemispheres in the same patient is common. Of FCD. Asymmetry of the insular gyral pattern between the 2 hemispheres in the same patient is common and should not be considered an indication of dysplasia. A retrospective study design was chosen. A total of 1584 MRIs, were found to be epileptogenic on SEEG recordings. The insular sulcus, stressing the importance of a systematic analysis of these associations with localized gray/white matter blurring is suggestive of FCD. Asymmetry of the insular gyral pattern between the 2 hemispheres in the same patient is common.

In all 7 patients on MRIs initially considered to have negative findings. This highlights the importance of a rigorous imaging technique and analysis by experienced radiologists to reduce the number of so-called “negative” cases.

When exploring refractory epilepsy, the following criteria should be met to optimize the chances of detecting subtle insular lesions on MR imaging: The radiologist must have a good understanding of the gross anatomy of the insula and its surrounding structures. MR imaging sequences must include high-resolution 3D-T1WI and 3D-T2WI to detect signal anomalies at various stages of myelination in the young pediatric population. Images should be reconstructed in oblique planes using an MPR algorithm to improve the identification of the gyral pattern of the insula and the pattern of the peri-insular sulcus.

Despite proper analysis of the insular region on presurgical MRI, the full extent of certain forms of FCD still escapes detection. Further advances in the detection of these subtle lesions may be expected in light of the technologic progress being made in MR imaging research using ultra-high-field-strength (7T) scanners to improve spatial resolution as well as the possible contribution of advanced MR imaging techniques such as arterial spin-labeling and diffusion tensor imaging.

**REFERENCES**

1. Isnard J, Guénat M, Sindou M, et al. Clinical manifestations of insular lobe seizures: a stereo-electroencephalographic study. Epilepsia 2004;45:1079–90 CrossRef Medline
2. Nguyen DK, Nguyen DB, Malak R, et al. Revisiting the role of the insula in refractory partial epilepsy. *Epilepsia* 2009;50:510–20 CrossRef Medline

3. Levitt M, Ojemann J, Kuratani J. Insular epilepsy masquerading as multifocal cortical epilepsy as proven by depth electrode. *J Neurosurg Pediatr* 2010;5:365–67 CrossRef Medline

4. Dylgjeri S, Taussig D, Chipaux M, et al. Insular and insulo-opercular epilepsy in childhood: an SEEG study. *Seizure* 2014;23:300–08 CrossRef Medline

5. Colombo N, Tassi L, Galli C, et al. Focal cortical dysplasias: MR imaging, histopathologic, and clinical correlations in surgically treated patients with epilepsy. *AJNR Am J Neuroradiol* 2003;24: 724–33 Medline

6. Mellerio C, Labeyrie M, Chassoux F, et al. Optimizing MR imaging detection of type 2 focal cortical dysplasia: best criteria for clinical practice. *AJNR Am J Neuroradiol* 2012;33:1932–38 CrossRef Medline

7. Colombo N, Salamon N, Raybaud C, et al. Imaging of malformations of cortical development. *Epileptic Disord* 2009;11:194–205 CrossRef Medline

8. Weil A, Le N, Jayakar P, et al. Medically resistant pediatric insular-opercular/periSylvian epilepsy, Part 2: outcome following resective surgery. *J Neurosurg Pediatr* 2016;18:523–35 CrossRef Medline

9. Perry M, Donahue D, Malik S, et al. Magnetic resonance imaging-guided laser interstitial thermal therapy as treatment for intractable insular epilepsy in children. *J Neurosurg Pediatr* 2017;20:575–82 CrossRef Medline

10. Hauptman J, Mathern G. Surgical treatment of epilepsy associated with cortical dysplasia: 2012 update. *Epilepsia* 2012;53(Suppl 4):98–104 CrossRef Medline

11. Rowland N, Englot D, Cage T, et al. A meta-analysis of predictors of seizure freedom in the surgical management of focal cortical dysplasia. *J Neurosurg* 2012;116:1035–41 CrossRef Medline

12. Englot D, Raygor K, Molinaro A, et al. Factors associated with failed focal neocortical epilepsy surgery. *Neurosurgery* 2014;75:648–55; discussion 655; quiz 656 CrossRef Medline

13. Blümcke I, Thom M, Aronica E, et al. The clinicopathologic spectrum of focal cortical dysplasias: a consensus classification proposed by an ad hoc Task Force of the ILAE Diagnostic Methods Commission. *Epilepsia* 2011;52:158–74 CrossRef Medline

14. Gaillard W, Chiron C, Cross J, et al; ILAE, Committee for Neuroimaging, Subcommittee for Pediatric. Guidelines for imaging infants and children with recent-onset epilepsy. *Epilepsia* 2009;50:2147–53 CrossRef Medline

15. Barkovich AJ. Normal postnatal brain development. In: Barkovich AJ, Pediatric Neuroimaging. 2nd ed. New York: Raven Press; 1995:20–35

16. Türe U, Yaşargil D, Al-Mefty O, et al. Topographic anatomy of the insular region. *J Neurosurg* 1999;90:720–33 CrossRef Medline

17. Varnavas G, Grand W. The insular cortex: morphological and vascular anatomic characteristics. *Neurosurgery* 1999;44:127–36; discussion 136–38 CrossRef Medline

18. Augustin J. The insular lobe in primates including humans. *Neur Res* 1985;7:2–10 CrossRef Medline

19. Naidich T, Kang E, Fatterpekar G, et al. The insula: anatomic study and MR imaging display at 1.5T. *AJNR Am J Neuroradiol* 2004;25:222–32 Medline