■ Case vignette

Epileptic Disord 2022; 24 (6): 1116-1119

Epileptic Disorders

The challenge of epilepsy surgery and intraoperative neurophysiological monitoring in an underweight young infant

Rivus Ferreira Arruda[1,a], Ianne Lucena Arruda[1,a], Rayanne MB. Silveira[1], Talita HM. Sarti[2], Laura MFF. Guilhoto[1], Henrique Carrete Júnior[3], João Norberto Stavale[4], Jose Eduardo Peixoto-Santos[5], Ricardo Silva Centeno[2], Mirian SB. Guaranha[1], Elza Márcia T. Yacubian[1]

[1] Epilepsy Research and Treatment Unit, Department of Neurology and Neurosurgery, Universidade Federal de São Paulo (UNIFESP), São Paulo, SP, Brazil

[2] Neurosurgery Discipline, Department of Neurology and Neurosurgery, Universidade Federal de São Paulo (UNIFESP), São Paulo, SP, Brazil

[3] Adult Diagnostic Imaging Discipline, Department of Diagnostic Imaging, Universidade Federal de São Paulo (UNIFESP), São Paulo, SP, Brazil

[4] Department of Pathology, Universidade Federal de São Paulo (UNIFESP), São Paulo, SP, Brazil

[5] Neuroscience Discipline, Department of Neurology and Neurosurgery, Universidade Federal de São Paulo (UNIFESP), São Paulo, Brazil

Received April 28, 2022;
Accepted July 11, 2022

[a]These authors contributed equally

• **Correspondence:**
Jose Eduardo Peixoto-Santos
Department of Neurology and Neurosurgery,
Universidade Federal de São Paulo, Brazil
<peixoto.santos@unifesp.br>

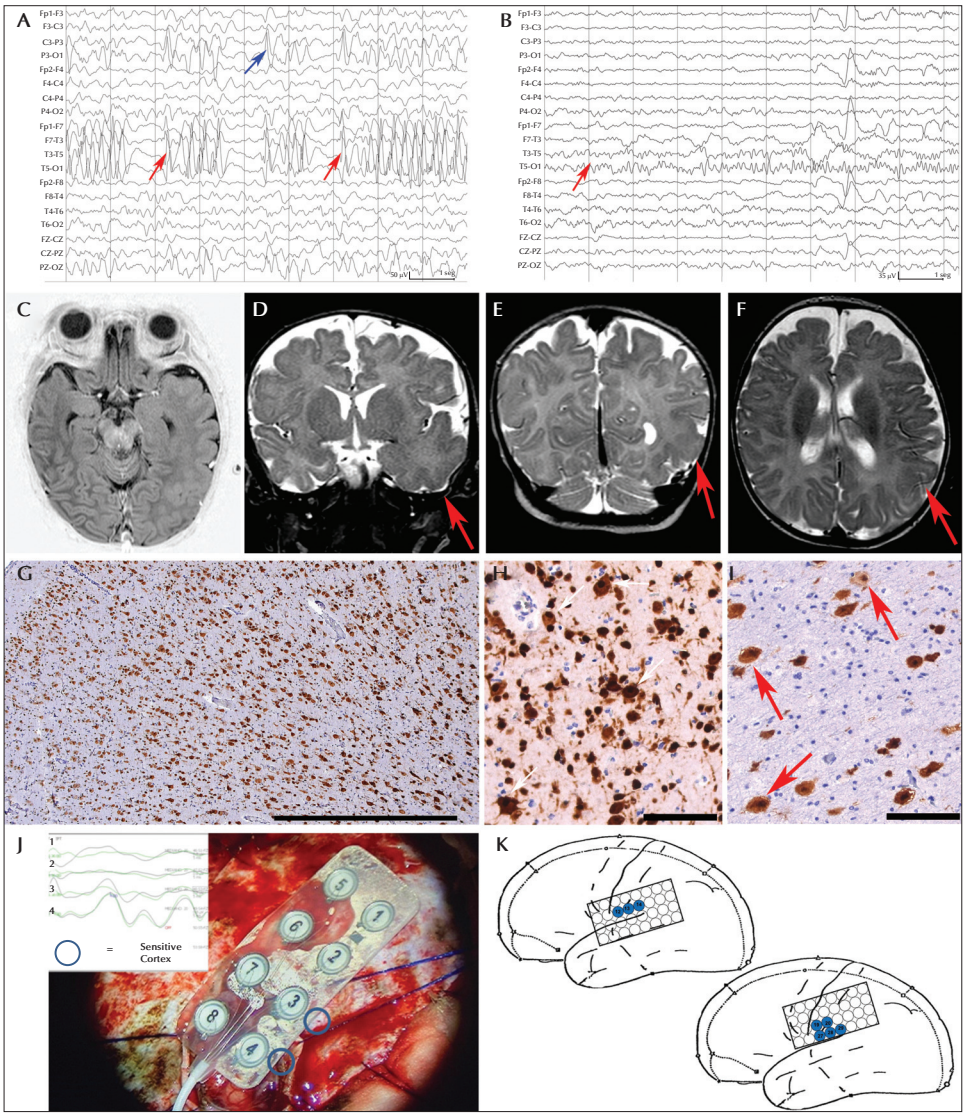
doi:10.1684/epd.2022.1481

A two-month-old female with seizures since the 15th day of life and recurrent status epilepticus (SE) was admitted to the intensive care unit. Seizure semiology included oral automatisms, right eye and head version, bilateral blinking, and asymmetric tonic posturing with right extension and left flexion of the upper limbs, lasting for 40 seconds. She presented with 30 seizures/day, which were pharmacoresistant to phenytoin, phenobarbital, carbamazepine, clobazam, and levetiracetam (*supplementary table 1*).

EEG (*figure 1A, B*) revealed depressed rhythms and quasi-continuous interictal spikes on the left temporo-occipital lobes, rare spikes in the parietal region, and a high frequency of focal seizures in the left posterior temporal region. Brain MRI (*figure 1C-F*) showed thick gyri, blurring, and white matter T2 hypointensity in the left temporo-occipital region reaching the lower angular and supramarginal gyri, and an enlarged lateral ventricle and Sylvian fissure. Thus, our hypothesis was hemimegalencephaly with a left temporal seizure onset zone.

We chose a staged surgery for this young, low-weight (4.3 kg/second percentile) infant. The first procedure, a left temporal lobectomy, reduced seizures to 5-8/day, prevented SE and improved development slightly. Histopathology revealed a type IIA focal cortical dysplasia (*figure 1G-I*). At five months of age, seizures increased, accompanied by disorganised EEG background and frequent left temporo-occipital discharges.

At 10 months, we performed intraoperative neurophysiological monitoring (IONM)-guided (*figure 1J-K*) left periinsular posterior functional quadrantotomy involving the remaining MRI visible lesion and the irritative zone. The central sulcus was identified through the median somatosensory evoked response phase-reversal technique, with right median nerve stimuli (12-mA, 200-µS pulses at 4.87 Hz) and extradural somatosensory evoked potentials registered via a 4×2 strip. N20 corresponding to primary sensory areas was recorded at contacts 3 and 4. We used the short-train stimulation technique (seven anodal, 25-mA, 0.5-mS pulses at 250 Hz) with grid contacts and a ball-tip monopolar probe in the motor cortex but failed to obtain any motor response. Electrocorticography (ECoG) revealed an irritative zone reaching the central sulcus.



■ **Figure 1.** Summary of the IONM-guided staged surgerical procedure and diagnostics. (A) On surface EEG, abundant interictal spikes are seen in the temporo-occipital region (red arrow on T3-T5/T5-O1); these changes were also seen less frequently in the parieto-occipital region (blue arrow on P3-O1). (B) The ictal recording showing onset in the left posterior temporal region, as indicated by the red arrow. (C) Pre-surgical 3 Tesla MRI showing increased volume of temporo-occipital regions in inversion-recovery. Note the gradient of change, with a more marked abnormal cortex in the anterior than the posterior region, while in the anterior temporal lobe, all regions are affected; in the occipital lobe, only the lateral cortex is affected. (D-F) T2-weighted images showing the increased volume and blurring of the grey-white matter junction in the left temporal region (red arrow in (D), which extends to the left occipital lobe (red arrow in (E). This lateral pathology seemed to reach the inferior parietal cortex, as some of the angular/supramarginal gyrus seemed abnormal (red arrow in (F). G-I) Histopathological evaluation of NeuN immunostaining reveals cortical disorganization, with a lack of cortical layering (G) and the presence of large, dysmorphic neurons in the grey matter (white arrows in (H) and deep white matter (red arrows in I). J) Localization of the left central sulcus (and consequently the sensitive cortex just behind) by IONM during the second surgery showing phase reversal in somatosensory evoked potentials at Contacts 3 and 4. (K) Intraoperative electrocorticography (ECoG) was used to safely delimit the anterior margin of surgical resection according to the region of discharges. The bar in (G) indicates 500 µm, and (H-I) indicates 100 µm.

At 19 months, she was still on antiseizure medications (*supplementary table 1*) and was classified as Engel Class Id on topiramate reduction. The Denver-II test at 18 months showed equivalent age for language, gross motor, fine motor/adaptive, and personal/social skills at 10, 9, 9, and 8 months, respectively. She could stand on her own and walk with support and verbalize single words, and developed left-handed dominance.

Epilepsy surgery in infants up to three months is rarely described, as shown by a recent multicentric review of 64 cases [1]. Although mortality is a concern in infants, two studies showed no mortality in surgery [1, 2], and 11 described rare mortality [1]. Permanent morbidity of early interventions is also rare, and the most frequent surgical risk is blood loss, while hydrocephalus is a common complication [1-3]. Nevertheless, as uncontrolled seizures impair neurodevelopment and brain plasticity, early surgery is protective [3, 4]. In infants, hemispheric and focal procedures are similar regarding seizure control and surgical complications, which are also comparable to surgery in older children [1, 5].

Regarding surgical approaches, two reviews showed no difference between lateral and vertical hemispheric disconnection in seizure control and morbidity rates, although blood loss was reduced for the latter [6, 7]. Only complete disconnection was associated with differences in seizure control when comparing vertical vs. lateral and structural vs. functional hemispheric procedures [6, 8]. For hemispheric pathologies, in particular, reoperation is sometimes needed, but overall, seizure control was reported to be similar following hemispheric surgery and focal procedures in young patients [1, 2]. Our experience reinforces the minimal risks of staged surgery with lateral disconnection. In this case, manageable blood loss occurred in both procedures, without any permanent morbidity.

The IONM allows for safe removal of the epileptogenic zone close to eloquent areas, decreases postoperative deficits, and improves outcomes [5, 9]. Although some believe IONM has limited use in younger children, we show that it is feasible, however, signals and responses differ according to the child's age [10]. Moreover, in children, an ECoG-based surgical plan is less successful when ECoG-based change of the surgical procedure is indicated but not achievable [5]. Our case reinforces the difficulties in performing IONM, as we had the additional challenge of stimulation through the dura, and, as expected, obtaining motor evoked potential was impossible. Still, somatosensory evoked potentials led to location of the central sulcus , and ECoG allowed for surgical margin definition. Thus, we highlight the importance of IONM and staged surgery for small infants with epilepsy. ■

Supplementary material.
Supplementary data accompanying the manuscript are available at www.epilepticdisorders.com.

Acknowledgements and disclosures.
We thank Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP, grants #16/17882-4 and #21/01098-0) and Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq, grant #422911/2021-6) for the financial support. We thank Carolina de Oliveira Gigek and Andreia Fabiana do Vale Franco for the skilful technical assistance in immunohistochemistry. We also thank the Laboratório Multiuso de Patologia Molecular, for the use of the Autostainer Link 48 System.
None of the authors declare any conflicts of interest.

References

1. Roth J, Constantini S, Ekstein M, Weiner HL, Tripathi M, Chandra PS, *et al*. Epilepsy surgery in infants up to 3 months of age: safety, feasibility and outcomes: a multicenter, multinational study. *Epilepsia* 2021; 62: 1897-906.

2. Roth J, Carlson C, Devinsky O, Harter DH, Macallister WS, Weiner HL. Safety of staged epilepsy surgery in children. *Neurosurgery* 2014; 74: 154-61.

3. Guan J, Karsy M, Ducis K, Bollo RJ. Surgical strategies for pediatric epilepsy. *Transl Pediatr* 2016; 5: 55-66.

4. Ramantani G. Epilepsy surgery in early life: the earlier, the better. *World Neurosurg* 2019; 131: 285-6.

5. Lesko R, Benova B, Jezdik P, Liby P, Jahodova A, Kudr M, *et al*. The clinical utility of intraoperative electrocorticography in pediatric epilepsy surgical strategy and planning. *J Neurosurg Pediatr* 2020; 26: 533-42.

6. Lopez AJ, Badger C, Kennedy BC. Hemispherotomy for pediatric epilepsy: a systematic review and critical analysis. *Childs Nerv Syst* 2021; 37: 2153-61.

7. Cossu M, Nichelatti M, De Benedictis A, Rizzi M. Lateral *versus* vertical hemispheric disconnection for epilepsy: a systematic review and meta-analysis. *J Neurosurg* 2021; 136: 1627-37.

8. González-Martínez JA, Gupta A, Kotagal P, Lachhwani D, Wyllie E, Lüders HO, *et al*. Hemispherectomy for catastrophic epilepsy in infants. *Epilepsia* 2005; 46: 1518-25.

9. Borggraefe I, Tacke M, Gerstl L, Leiz S, Coras R, Blümcke I, *et al*. Epilepsy surgery in the first months of life: a large type IIb focal cortical dysplasia causing neonatal drug-resistant epilepsy. *Epileptic Disord* 2019; 21: 122-7.

10. Bidkar PU, Thakkar A, Manohar N, Rao KS. Intraoperative neurophysiological monitoring in paediatric neurosurgery. *Int J Clin Pract* 2021; 75: e14160.

TEST YOURSELF

(1) Why is aggressive treatment of pharmacoresistant focal epilepsy, including surgery if necessary, important during the first few months of life?

A. Surgical complications are less frequent in low-birth-weight infants.
B. This improves health-related quality of life and enhances cognitive development compared to conservative treatment.
C. Intraoperative monitoring is easier to perform the lower the age and weight of the patient.
D. The three previous alternatives are wrong.

(2) Considering the recording of somatosensory evoked potentials, which of the following waves corresponds to the primary sensory area?

A. N13
B. P14
C. N18
D. N20

(3) What is the importance of intraoperative neurophysiological monitoring (IONM) in epilepsy surgery?

A. IONM prevents surgical complications.
B. The possibility of a second surgical intervention is avoided with IONM.
C. IONM is easier to perform the lower the age and weight of the patient.
D. IONM aids in the localization of neural structures and enables surgeons to preserve the functional neural structures leading to a decreased incidence of postoperative neurological deficits and better patient outcomes.

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