Child's Nervous System (2019) 35:1189–1195
https://doi.org/10.1007/s00381-019-04067-6

ORIGINAL ARTICLE

EEG lateralization and seizure outcome following peri-insular hemispherotomy for pediatric hemispheric epilepsy

Ananth P. Abraham[1] · Maya Mary Thomas[1] · Vivek Mathew[1] · Karthik Muthusamy[1] · Sangeetha Yoganathan[1] · G. Edmond Jonathan[1] · Krishna Prabhu[1] · Roy Thomas Daniel[2] · Ari G. Chacko[1]

Received: 18 October 2018 / Accepted: 16 January 2019 / Published online: 30 January 2019
© Springer-Verlag GmbH Germany, part of Springer Nature 2019

Abstract

Objective To determine whether preoperative non-lateralizing scalp electroencephalography (EEG) influences seizure outcome following peri-insular hemispherotomy (PIH) in pediatric hemispheric epilepsy.

Methods Retrospective data was collected on all 45 pediatric patients who underwent PIH between 2005 and 2016. All underwent a basic pre-surgical evaluation consisting of detailed history and examination, neuropsychological assessment, MRI, and EEG. SPECT/PET, fRMI, or Wada testing were done in only eight patients. Seizure outcome was assessed using the Engel classification.

Results Among those who underwent hemispherotomy, 20 (44%) were females. Mean age at surgery was 8 ± 4.3 years and mean duration of symptoms was 5.2 ± 3.7 years. The most common etiologies of hemispheric epilepsy were hemiconvulsion-hemiplegia epilepsy syndrome, Rasmussen encephalitis, and post-encephalitic sequelae, together comprising 27 (60%) patients. Among the 44 patients with follow-up data (mean duration 48 ± 33 months), seizure freedom (Engel class I) was attained by 41 (93.2%). Anti-epileptic medications were stopped or decreased in 36 (82%). Seventeen (38.6%) patients had non-lateralizing EEG. Seizure outcome was not related to lateralization of EEG activity.

Conclusions PIH provides excellent long-term seizure control in patients despite the presence of non-lateralizing epileptiform activity, although occurrence of acute postoperative seizures may be higher. Routine SPECT/PET may not be required in patients with a non-lateralizing EEG if there is good clinico-radiological concordance.

Keywords Epilepsy surgery · Hemispherotomy · Peri-insular · EEG · Seizure outcome

Introduction

The hemispherotomy or functional hemispheric disconnection, first described by Rasmussen [1], is routinely used for children with intractable epilepsy due to hemispheric pathology. The different techniques of disconnection include the peri-insular hemispherotomy (PIH) [2], the vertical parasagittal hemispherotomy [3], and the trans-sylvian keyhole hemispherotomy [4]. The selection process for hemispherotomy in patients with hemispheric epilepsy needs to be focused on identifying a uni-hemispheric epileptic syndrome. The evaluation consists of a detailed history and clinical examination, high-resolution magnetic resonance imaging (MRI) of the brain and multiple scalp electroencephalograms (EEG), and video-EEG monitoring.

Non-lateralizing epileptiform (NLE) activity on preoperative scalp EEG, i.e., bilateral independent spiking, generalized discharges, and contralateral slowing, was believed to predict poor seizure control in such patients [5] leading to the utilization of interical/ictal single-photon emission computed tomography (SPECT) or positron emission tomography (PET) for further evaluation before proceeding with surgery [6]. Current recommendations even include invasive EEG monitoring techniques in select patients [7]. However, data from a few studies indicate that EEG findings are not always predictive of seizure outcomes [8–10]. At our institute, we routinely perform surgery despite the presence of NLE activity provided there is a definite hemispheric MRI abnormality with good

✉ Maya Mary Thomas
maya@cmcvellore.ac.in

[1] Department of Neurological Sciences, Christian Medical College, Vellore, Tamil Nadu, India

[2] Department of Neurosurgery, University Hospital of Lausanne, Lausanne, Switzerland

clinical correlation on preoperative evaluation. The aim of this study was to determine whether NLE activity on preoperative scalp EEG adversely affects seizure outcome.

Methods

Institutional Review Board approval was obtained for this retrospective study (IRB Min No: 10820 [Retro] dated 23rd August 2017). Electronic medical records of all patients who underwent PIH between January 2005 and December 2016 were reviewed. Follow-up data was obtained in 44 out of 45 patients.

Selection criteria

(1) Seizures refractory to anti-epileptic drugs (AED).
(2) Hemiparesis with significant weakness of distal musculature.
(3) Hemispheric pathology on MRI contralateral to hemiparesis.

Presurgical evaluation

All patients underwent a detailed presurgical evaluation. This included extensive history taking focusing on seizure semiology and temporal evolution as well as analysis of home videos provided by parents, neurological examination, neuropsychological assessment multiple EEGs (including at least one video telemetry), and high-resolution MRI. Four patients were subjected to either SPECT or PET. Two patients had functional MRI (fMRI), one underwent a Wada test and one had an etomidate speech and memory test (eSAM). EEG spikes, sharp waves, or seizures were considered as epileptiform activity while focal or generalized slowing was excluded. [9] All patients demonstrated epileptiform activity on EEG (multiple EEGs were required in some). Epileptiform activity on preoperative EEGs was deemed either non-lateralizing (NLE) or lateralizing (LE) based on the presence or absence of epileptiform discharges in the contralateral hemisphere, respectively. NLE activity was defined as ictal onset from the normal hemisphere, independent inter-ictal discharges from the normal hemisphere, or generalized or multifocal epileptiform activity.

Surgical technique

All 45 patients underwent PIH as described by Villemure et al. [2]. The fundamental principle of this technique is to achieve radical hemispheric tractotomy with minimal resection of brain tissue.

Seizure and functional outcomes

Seizure outcome was documented at each follow-up using the Engel classification [11]. Language function, motor power, and overall functional status of the patients were also recorded.

Statistical analysis

Data was stored in an electronic database and statistical analysis was done using SPSS (version 16.0; SPSS, Chicago IL, USA). Descriptive statistics were used for patient characteristics and surgical details. Chi-square was used for categorical variables and Student's *t* test or non-parametric test (Mann-Whitney) used for continuous variables as required.

Results

Demographic data

There were 20 females and 25 males in this series with a mean age of 8 years (SD 4.3, range 10 months to 17 years). The mean duration of symptoms was 5.2 years (SD 3.2). There were 11 patients with Rasmussen encephalitis (RE), 10 with hemiconvulsion-hemiplegia epilepsy syndrome (HHE), 6 with post-encephalitic sequelae (PES), 6 with post-stroke sequelae (PSS), 4 with hemimegalencephaly (HME), 3 with Sturge Weber syndrome (SWS), 3 with non-hypertrophic hemispheric cortical dysplasia (FCD), and 2 with post-traumatic sequelae (PTS). For the purpose of analysis, these were grouped into developmental (HME, FCD) and non-developmental (RE, HHE, PES, PSS, SWS, PTS) etiologies. Thirty-seven patients had a history of generalized seizures while 7 (15.9%) had purely focal motor seizures. Eighteen patients (40%) had more than one seizure type. Patients were on an average of three antiepileptic drugs (range 2 to 6). Seizure frequency ranged from 1 to 200 per day. Six patients were in epilepsia partialis continua at admission and six had a history of status epilepticus.

Operative details and complications

Surgery was on the left side in 25 and on the right side in 20 patients. The operating time ranged from 3.5 to 8 h (mean 5.4, SD 1.3). Blood loss ranged from 150 to 1000 ml and 33 (73%) of patients required a blood transfusion. Postoperative hospital stay ranged from 7 to 44 days with a mean of 15 days. Only four (8.9%) patients had major postoperative complications—two developed pyogenic meningitis and two developed symptomatic hydrocephalus requiring ventriculoperitoneal shunting (one of these patients also needed a subduroperitoneal shunt). One patient died a year later due to a respiratory illness. Minor

complications included aseptic meningitis in 14 (31.8%), urinary tract infections in 3 (6.8%), and pseudomeningoceles in 3 (6.8%).

Seizure and functional outcomes

Forty-four patients had returned for long-term follow-up after surgery (mean duration 48 months, SD 33.6). The patient who was lost to follow-up had HME. Freedom from disabling seizures (class I) was achieved in 41 (93.2%) patients. Seizure recurrence occurred in three patients of whom two (4.5%) had class II outcome and one (2.3%) had a class III outcome. The patients who did not attain class I outcomes had RE, SWS, and PTS. AED administration had been stopped in 6 (13.6%), decreased in 30 (68.2%), and remained the same in 8 (18.2%) patients at last follow-up.

Functionally, there was improved motor power at follow-up compared to the immediate postoperative period in 23 (52.3%) patients and in 16 there was no change, while in 5, this information could not be obtained from the medical records. Twenty (45.4%) patients were able to re-join school, two were being tutored at home, one had completed college, and one was working. Fifteen (34%) were still partially or completely dependent on caregivers. A few illustrative examples of patient outcomes have been depicted in Figs. 1, 2, and 3.

Comparison of patients based on preoperative EEG activity

Among the 44 patients who were followed up, 17 (38.6%) had NLE activity on preoperative scalp EEG. There were no statistically significant differences in patient characteristics between those who had LE and NLE activity (Table 1). Table 2 shows the patient age and pre-operative clinical details. Again, there were no significant differences between those who had LE and NLE activity. Among the 17 patients with NLE activity, only 4 had preoperative SPECT/PET done and none of these patients had recurrence of seizures. Among the remaining 13 patients with NLE activity, one had recurrence of seizures (Engel class III). This was not statistically significant ($p = 1.0$). Table 3 compares the seizure outcomes and requirement of AEDs at follow-up with preoperative EEG activity. Although there was a trend towards more acute postoperative seizures (seizures ≤ 1 week after surgery) in the NLE activity group, statistical significance was not reached in this study.

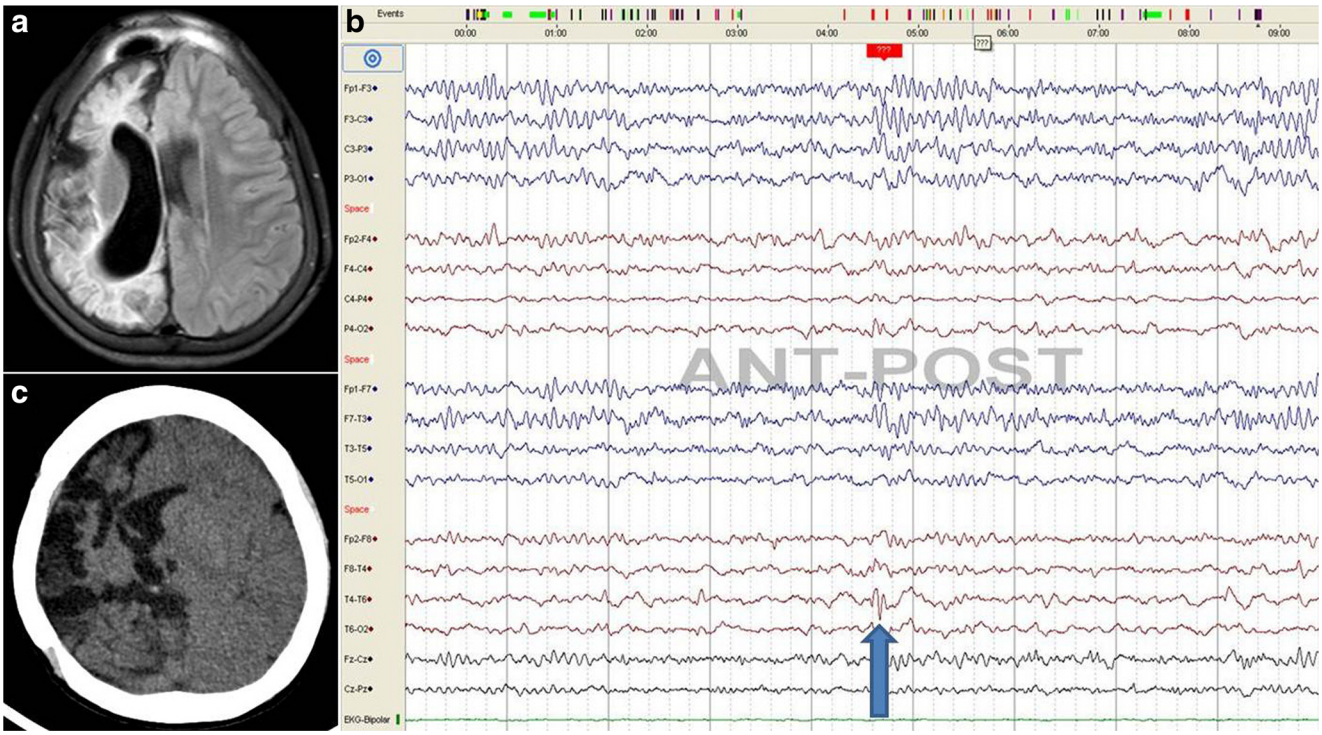

Fig. 1 **a** MRI, **b** preoperative EEG, and **c** postoperative CT scan of a 10-year-old boy with right-sided Rasmussen encephalitis. He presented with recurrent episodes of left focal motor seizures with secondary generalization since the age of 4 years. His preoperative sleep EEG showed loss of normal sleep pattern in the right hemisphere with spike discharges (arrow) localized to the right temporal region and was therefore classified as lateralizing. Postoperatively, he became seizure free till last follow-up 21 months after surgery. He had also made significant functional gains and was being home tutored

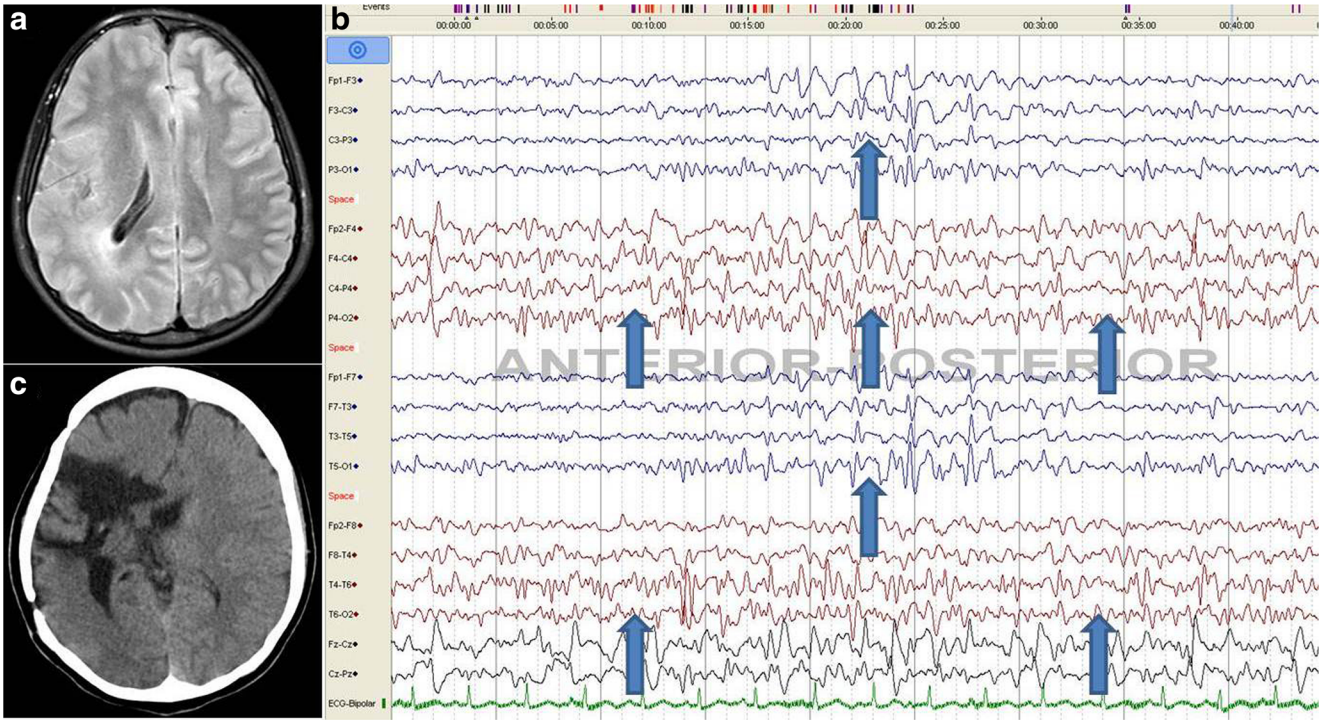

Fig. 2 **a** MRI, **b** preoperative EEG, and **c** postoperative CT scan of a 10-year-old girl with refractory left focal motor seizures for 9 years. The right cerebral hemisphere is larger than the left, with polymicrogyria, suggestive of hemimegalencephaly. Her EEG showed multifocalinterictal spike discharges (arrows) in both cerebral hemispheres, right more than left. Although her EEG was classified as non-lateralizing, there was good clinico-radiological concordance. At 26-month follow-up after right hemispherotomy, she was seizure free and was enrolled in the third grade at school

Discussion

Hemispheric disconnection

Hemispherotomy for drug-resistant hemispheric epilepsy, once thought to be quite morbid and fraught with complications, has evolved tremendously over the last four decades thanks to concerted global efforts. Essentially, the functional hemispherotomy disconnects the seizure focus, preventing electrical activity from spreading to the contralateral hemisphere [1]. Complications have decreased due to less invasive and more functional resections while good seizure, cognitive, and functional outcomes have remained high [6, 12–17]. Reported seizure-free outcomes have ranged from 50 to 90% [15, 17]. In a meta-analysis of 56 studies, it was found that the pooled seizure free rate was 73% [18]. In our study, 93% of patients were seizure free (Engel class I) at follow-up which is one of the highest reported in literature. We attribute this primarily to our focused presurgical evaluation and careful patient selection for PIH. However, the fact that the majority of our patients had non-developmental etiologies causing their epilepsy may have also contributed. While younger age of seizure onset and developmental cortical malformations are known to have a strong association with poor seizure-free outcomes, multifocal epilepsy or non-lateralization has also been reported to be associated with poorer seizure-free outcomes. In the above-mentioned meta-analysis [18], lateralization of inter-ictal and ictal EEG findings appeared to significantly improve seizure outcome (inter-ictal: OR 1.66, 95% CI 1.03–2.67, $p = 0.04$; ictal: OR 1.88, 95% CI 1.15–3.07, $p = 0.01$).

Non-lateralizing epileptiform activity

The finding of contralateral scalp EEG activity in the presence of uni-hemispheric structural disease is a recognized phenomenon [9, 10]. Garzon et al. [8] postulated three hypotheses, possibly interdependent, to explain the paradoxical lateralization of ictal EEGs. The first was that interictal epileptiform discharges generated in the diseased hemisphere are unable to synchronize and develop into ictal rhythms due to a lack of a critical mass of cortical and subcortical connections. However, a rapid spread to the structurally normal hemisphere occurs to produce a clinical seizure and is detected on the contralateral scalp electrodes. The second was that the increased distance in an atrophied cerebral hemisphere between the epileptogenic zone and the scalp electrodes could result in an asymmetric ictal pattern with reduced amplitude ipsilateral to the lesion. Also, the very high frequency low amplitude ictal rhythms that precede this pattern may not be captured by the sampling and filter settings which are routinely employed. Lastly, the

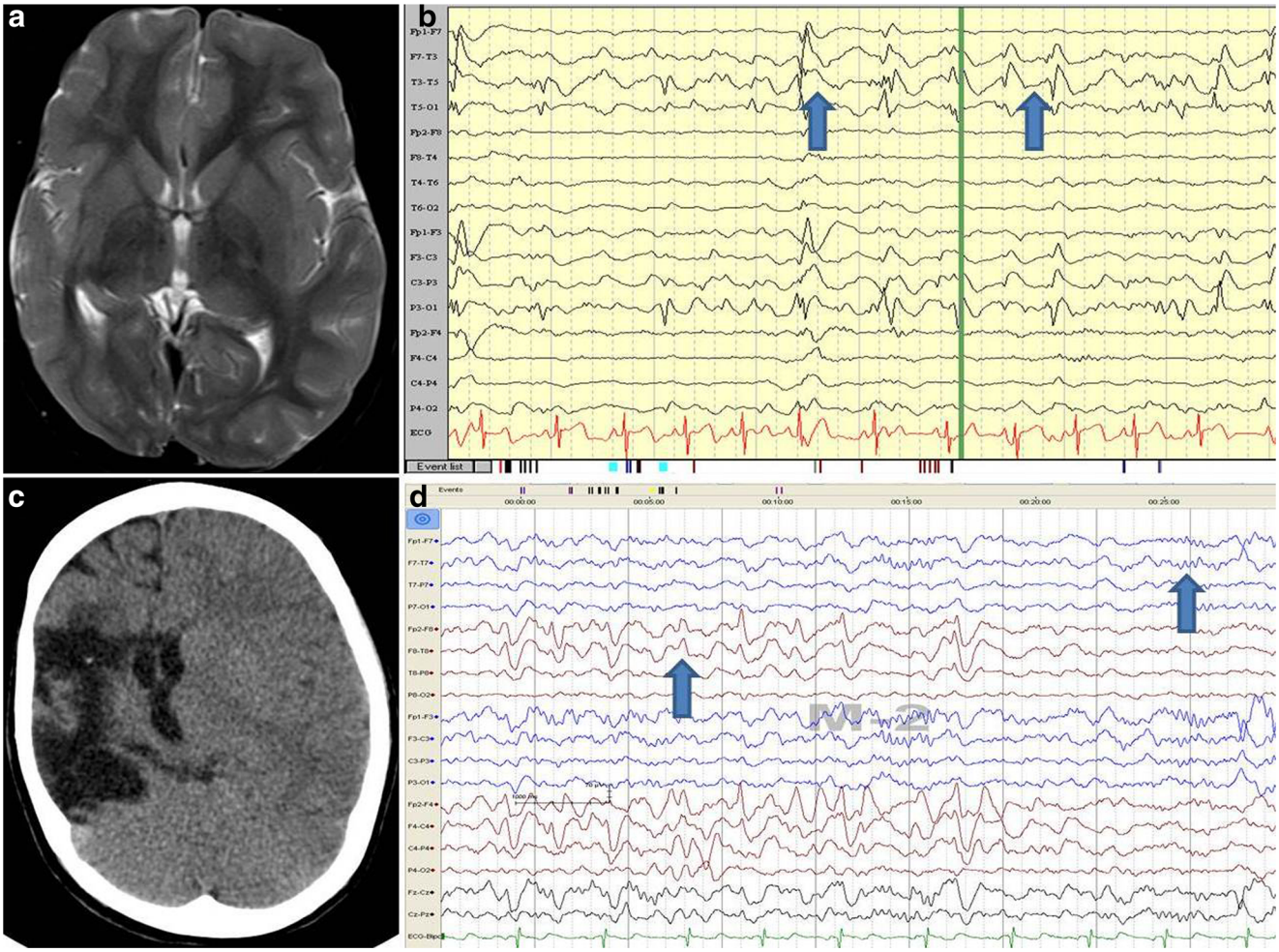

Fig. 3 The preoperative **a** MRI and **b** EEG along with the postoperative **c** CT scan and **d** EEG of a 7-year-old girl with right hemispheric dysplasia. In children with long-standing hemispheric pathology resulting in parenchymal volume loss, epileptiform activity may not be picked up by the ipsilateral leads causing the preoperative EEG to show only contralateral abnormalities (arrows in **b**), as is noted in this patient. As a result, differentiating between transmitted epileptiform activity from the diseased hemisphere and independent inter-ictal discharges from the normal hemisphere can often be difficult. However after surgery as seen in the postoperative sleep EEG, there is normal background activity with sleep spindles on the left side while from the right hemisphere, there are intermittent sharp wave discharges in a background of slow waves (arrows in **d**)

Table 1 Comparison of patients with lateralizing and non-lateralizing EEGs (categorical variables)

		Lateralizing ($n = 27$)	Non-lateralizing ($n = 17$)	p value
Gender	Male	14 (51.8%)	11 (64.7%)	0.40
	Female	13 (48.2%)	6 (35.3%)	
Surgery side	Right	10 (37%)	10 (58.8%)	0.16
	Left	17 (63%)	7 (41.2%)	
Etiology	Developmental	3 (11.1%)	3 (17.6%)	0.66
	Non-developmental	24 (88.9%)	14 (82.4%)	
Seizure type	Focal only	6 (22.2%)	1 (5.9%)	0.22
	Generalized	21 (77.8%)	16 (94.1%)	
Pre-op SE	Yes	3 (11.1%)	3 (17.6%)	0.66
	No	24 (88.9%)	14 (82.4%)	
Pre-op EPC	Yes	4 (14.8%)	2 (11.8%)	1.0
	No	23 (85.2%)	15 (88.2%)	

EPC epilepsia partialis continua, *SE* status epilepticus

spatial orientation of the ictal onset rhythms as dipoles, either parallel to the surface or obliquely, in the mesial frontal or mesial parieto-occipital head regions, could cause paradoxical localization of epileptiform activity to the contralateral hemisphere. Previous studies have concluded that scalp EEG abnormalities in contralateral or bilateral hemispheres do not, in isolation, predict poorer seizure outcome following hemispherotomy [9, 10].

The results of our study reaffirm that NLE activity is not associated with poorer seizure outcomes. Although the incidence of acute postoperative seizures was higher in the NLE group, this was not statistically significant. Patient selection for surgery contributed greatly to the good seizure and functional outcomes in our series. A meticulous presurgical assessment of the patient begins with basic or phase 1 evaluation including a detailed

Table 2 Comparison of patients with lateralizing and non-lateralizing EEGs (continuous variables)

	Lateralizing ($n = 27$)	Non-lateralizing ($n = 17$)	p value
Median age in years (IQR)	9.0 (4.0, 12.0)	7.0 (4.0, 10.0)	0.4 *
Median duration of symptoms in years (IQR)	4.0 (2.0, 8.0)	4.0 (1.7, 8.0)	0.9 *
Median frequency of seizures per day (IQR)	4.0 (3.0, 12.0)	10.0 (3.5, 16.0)	0.3 *
Mean number of AED (SD)	3.02 (0.8)	3.11 (0.9)	0.7

*The p value from Mann-Whitney t test

AED anti-epileptic drugs, *IQR* inter-quartile range, *SD* standard deviation

history and examination, neuropsychological evaluation, MRI, and EEG(s). Traditionally, in the event of NLE, it has been recommended to proceed with phase 2 investigations such as interictal/ictal SPECT/PET or invasive EEG using strip or subdural grid electrodes in select patients [7]. There is a growing trend to routinely employ these additional investigations; however, it must be remembered that in developing countries including India, resources are limited and the cost-benefit ratio of any additional investigation must always be kept in mind. Only four of our patients with NLE activity underwent SPECT/PET. These were patients who had bilateral neurological deficits, only contralateral epileptiform activity on EEG, or contralateral MRI abnormalities in addition. The remaining 40 patients had a well-defined uni-hemispheric structural abnormality on MRI with good clinical correlation and hence did not undergo any additional testing. In fact, only 8 out of 44 patients required any form of ancillary testing apart from MRI and scalp EEGs.

While other studies have clearly demonstrated the utility of SPECT and PET in epilepsy surgery [19, 20], their role in the pre-surgical evaluation of patients with hemispheric epilepsy may be overestimated. Wada testing or fMRI should be reserved for patients with left hemispheric epilepsy who have relatively well-preserved language function and are of suitable age to undergo the procedure. Even among these patients, if the seizures are disabling and/or progressively worsening, PIH will be indicated regardless of the fMRI or Wada test findings. This leaves only a small minority of patients in whom these investigations are truly indicated.

Also, procedures like strip/subdural grid electrode placement and Wada testing are invasive and not without risk [21, 22]. Out study therefore brings to the fore an important observation that NLE activity on scalp EEG does not mandate any additional investigations, provided there is good clinico-radiological concordance.

Good seizure control results in improvement in functional status of patients following hemispherotomies [23]. Many children are able to attend school and become more independent for their activities of daily living [24]. In our study, 66% of patients had satisfactory functional outcomes and most had improvement in motor power at follow-up. Results, similar to ours, have been reported from other centers in India [6, 16, 24]. Both short-term and long-term gains in cognitive function following surgery have been reported earlier from our institution. [24] Quality of life scores in epilepsy (QOLIE) were similar for vertical parasagittal hemispherotomy and PIH (80 and 87%) in a study by Panigrahi et al. [16].

Table 3 Outcomes after peri-insular hemispherotomy by preoperative EEG activity

		Lateralizing ($n = 27$)	Non-lateralizing ($n = 17$)	p value
APOS (≤ 1 week following surgery)	Yes	1 (3.7%)	4 (23.5%)	0.07
	No	26 (96.3%)	13 (76.5%)	
Anti-epileptic drugs at follow-up	Same	5 (18.5%)	3 (17.6%)	0.83
	Decreased	19 (70.4%)	11 (64.8%)	
	Stopped	3 (11.1%)	3 (17.6%)	
Seizure outcome	Engel class I	25 (92.6%)	16 (94.1%)	1.0
	Engel class II/III	2 (7.4%)	1 (5.9%)	

APOS acute postoperative seizures

Conclusions

PIH provides excellent long-term seizure control in patients with drug-resistant hemispheric epilepsy despite the presence of preoperative NLE activity, although occurrence of acute postoperative seizures may be slightly higher. This study shows that SPECT/PET, and other phase 2 tests like Wada test and invasive EEG monitoring are not required in pediatric patients with NLE activity, if there is strong clinico-radiological correlation on phase 1 pre-surgical evaluation.

Compliance with ethical standards

The authors report no conflict of interest. The datasets generated for the study are available from the corresponding author on reasonable request.

Disclosure A portion of this study was presented as a podium presentation at the 66th Annual Conference of the Neurological Society of India in December, 2017.

Conflict of interest None.

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

References

1. Rasmussen T (1983) Hemispherectomy for seizures revisited. Can J Neurol Sci 10:71–78
2. Villemure JG, Mascott CR (1995) Peri-insular hemispherotomy: surgical principles and anatomy. Neurosurgery 37:975–981
3. Delalande O, Bulteau C, Dellatolas G, Fohlen M, Jalin C, Buret V, Viguier D, Dorfmüller G, Jambaqué I (2007) Vertical parasagittal Hemispherotomy: surgical Pocedures and clinical long-term outcomes in a population of 83 children. Oper Neurosurg 60:19–32. https://doi.org/10.1227/01.NEU.0000249246.48299.12
4. Schramm J, Kral T, Clusmann H (2001) Transsylvian keyhole functional hemispherectomy. Neurosurgery 49:891–900 discussion 900-901
5. Carmant L, Kramer U, Riviello JJ, Helmers SL, Mikati MA, Madsen JR, Black PML, Lombroso CT, Holmes GL (1995) EEG prior to hemispherectomy: correlation with outcome and pathology. Electroencephalogr Clin Neurophysiol 94:265–270
6. Chandra PS, Padma VM, Shailesh G, Chandreshekar B, Sarkar C, Tripathi M (2008) Hemispherotomy for intractable epilepsy. Neurol India 56:127–132
7. Tripathi M, Ray S, Chandra PS (2016) Presurgical evaluation for drug refractory epilepsy. Int J Surg 36:405–410. https://doi.org/10.1016/j.ijsu.2016.10.044
8. Garzon E, Gupta A, Bingaman W, Sakamoto AC, Lüders H (2009) Paradoxical ictal EEG lateralization in children with unilateral encephaloclastic lesions. Epileptic Disord 11:215–221. https://doi.org/10.1684/epd.2009.0264
9. Greiner HM, Park YD, Holland K, Horn PS, Byars AW, Mangano FT, Smith JR, Lee MR, Lee KH (2011) Scalp EEG does not predict hemispherectomy outcome. Seizure 20:758–763. https://doi.org/10.1016/j.seizure.2011.07.006
10. Wyllie E, Lachhwani DK, Gupta A, Chirla A, Cosmo G, Worley S, Kotagal P, Ruggieri P, Bingaman WE (2007) Successful surgery for epilepsy due to early brain lesions despite generalized EEG findings. Neurology 69:389–397. https://doi.org/10.1212/01.wnl.0000266386.55715.3f
11. Engel J Jr, Van Ness PC, Rasmussen TB (1993) Outcome with respect to epileptic seizures. In: Engel J Jr (ed) Surgical treatment of the epilepsies, 2nd edn. Raven, New York, pp 609–621
12. Villemure J-G, Daniel RT (2006) Peri-insular hemispherotomy in paediatric epilepsy. Childs Nerv Syst 22:967–981. https://doi.org/10.1007/s00381-006-0134-3
13. Daniel RT, Joseph TP, Gnanamuthu C, Chandy MJ (2002) Hemispherotomy for Paediatric hemispheric epilepsy. Stereotact Funct Neurosurg 77:219–222. https://doi.org/10.1159/000064609
14. Kestle J, Connolly M, Cochrane D (2000) Pediatric peri-insular hemispherotomy. Pediatr Neurosurg 32:44–47
15. Thomas SG, Chacko AG, Thomas MM, Babu KS, Russell PSS, Daniel RT (2012) Outcomes of Disconnective surgery in intractable pediatric hemispheric and subhemispheric epilepsy. Int J Pediatr 2012:1–7. https://doi.org/10.1155/2012/527891
16. Panigrahi M, Krishnan SS, Vooturi S, Vadapalli R, Somayajula S, Jayalakshmi S (2016) An observational study on outcome of hemispherotomy in children with refractory epilepsy. Int J Surg 36:477–482. https://doi.org/10.1016/j.ijsu.2015.05.049
17. Basheer SN, Connolly MB, Lautzenhiser A, Sherman EMS, Hendson G, Steinbok P (2007) Hemispheric surgery in children with refractory epilepsy: seizure outcome, complications, and adaptive function. Epilepsia 48:133–140. https://doi.org/10.1111/j.1528-1167.2006.00909.x
18. Hu W-H, Zhang C, Zhang K, Shao XQ, Zhang JG (2016) Hemispheric surgery for refractory epilepsy: a systematic review and meta-analysis with emphasis on seizure predictors and outcomes. J Neurosurg 124:952–961. https://doi.org/10.3171/2015.4.JNS14438
19. Chandra PS, Vaghania G, Bal CS, Tripathi M, Kuruwale N, Arora A, Garg A, Sarkar C, Diwedi R, Malviya S, Padma V, Tripathi M (2014) Role of concordance between ictal-subtracted SPECT and PET in predicting long-term outcomes after epilepsy surgery. Epilepsy Res 108:1782–1789. https://doi.org/10.1016/j.eplepsyres.2014.09.024
20. Stamoulis C, Verma N, Kaulas H, Halford JJ, Duffy FH, Pearl PL, Treves ST (2017) The promise of subtraction ictal SPECT co-registered to MRI for improved seizure localization in pediatric epilepsies: affecting factors and relationship to the surgical outcome. Epilepsy Res 129:59–66. https://doi.org/10.1016/j.eplepsyres.2016.11.020
21. Hamer HM, Morris HH, Mascha EJ, Karafa MT, Bingaman WE, Bej MD, Burgess RC, Dinner DS, Foldvary NR, Hahn JF, Kotagal P, Najm I, Wyllie E, Luders HO (2002) Complications of invasive video-EEG monitoring with subdural grid electrodes. Neurology 58:97–103
22. Loddenkemper T, Morris HH, Möddel G (2008) Complications during the Wada test. Epilepsy Behav 13:551–553. https://doi.org/10.1016/j.yebeh.2008.05.014
23. Moosa ANV, Jehi L, Marashly A, Cosmo G, Lachhwani D, Wyllie E, Kotagal P, Bingaman W, Gupta A (2013) Long-term functional outcomes and their predictors after hemispherectomy in 115 children. Epilepsia 54:1771–1779. https://doi.org/10.1111/epi.12342
24. Thomas SG, Daniel RT, Chacko AG, Thomas M, Russell PSS (2010) Cognitive changes following surgery in intractable hemispheric and sub-hemispheric pediatric epilepsy. Childs Nerv Syst 26:1067–1073. https://doi.org/10.1007/s00381-010-1102-5