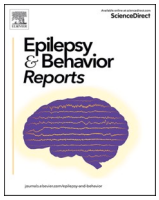
Epilepsy & Behavior Reports 27 (2024) 100689

Contents lists available at ScienceDirect

Epilepsy & Behavior Reports

journal homepage: www.elsevier.com/locate/ebcr



# Hemispherectomy for dominant hemisphere Rasmussen's Encephalitis – how late is too late?

James Butler [a,b,*], Aayesha Soni [b,c], Roger Melvill [a]

[a] Constantiaberg Mediclinic, Cape Town, South Africa
[b] Division of Neurology, Department of Medicine, University of Cape Town, Cape Town, South Africa
[c] Neuroscience Institute, University of Cape Town, South Africa

ARTICLE INFO

*Keywords:*
Epilepsy surgery
Rasmussen's
Dominant hemisphere
Cognitive function
Adult-onset

ABSTRACT

It is unclear whether a dominant hemispherectomy/hemispherotomy in someone with Rasmussen's Encephalitis (RE) may produce a satisfactory outcome when performed over the age of 40 years. Important questions include whether RE may continue to evolve three decades after onset, and whether a hemispherectomy may adequately shift language function when performed in older ages. Two cases illustrate seizure, language, motor and functional outcomes after dominant hemispherotomies. The cases were selected from an epilepsy surgery database of procedures performed at a private hospital in Cape Town, South Africa, spanning the period 1998–2023. A man in his 40s with epilepsy since childhood and dominant hemisphere RE partially regained impaired comprehension and ambulation, while expressive language function did not recover post-hemispherotomy. By contrast, a young teenage patient with dominant hemisphere RE demonstrated considerable recovery of expressive and receptive language and ambulation post-surgery. Both remain seizure-free. These two cases demonstrate that a dominant hemispherotomy, when performed on a quadragenarian, may produce a satisfactory, albeit inferior, functional outcome in comparison to when performed in childhood. RE may cause progressive neurological dysfunction in the late thirties and older and should be considered in patients presenting with functional decline decades after disease onset.

## 1. Introduction

A hemispherectomy, especially in the dominant hemisphere, is constrained by the potential for permanent loss of eloquent function [1]. Hence, someone with medically intractable, unihemispheric epilepsy with severe disease-related language and motor dysfunction of the contralateral hand, but with normal contralateral hemispheric functioning, is a good candidate for a hemispherectomy [2]. This is especially the case when the unihemispheric disorder is progressive, predicting more loss of function, and the patient is young, affording maximal opportunity for neural plasticity and shift of function [3,4]. For these reasons, hemispherectomies are generally performed in children, while a small number of adult hemispherectomies have been reported [1,5,6]. Hemispherectomies, an older surgical procedure involving the entire *en bloc* removal of the cerebral hemisphere, has now largely been replaced by hemispherotomies which is partial cortical removal and has fewer complications. We describe two cases of dominant *peri*-insular hemispherotomies for patients with RE. As per our knowledge, our first case is the oldest documented patient to have received a dominant hemispherotomy for RE, with a satisfactory functional outcome recorded.

## 2. Results

**Case 1:** In 2019, a right-handed man in his 40s presented with medically refractory seizures. His seizures started at the age of nine years, when he had a focal to bilateral tonic-clonic seizure (FBTCS), followed by a right Todd's paresis and transient aphasia. He then had frequent FBTCS in association with declining academic performance, which compelled termination of schooling at the age of 14 years. At the age of 16 years, he started working at the mines, doing manual work. He did not disclose his condition to his employers and his career came to an end when he had a seizure with a right Todd's paresis and transient aphasia whilst at work.

His perinatal and developmental histories were normal. He had recurrent lower limb deep vein thromboses for 14 years prior to

* Corresponding author at: Division of Neurology, Department of Medicine, University of Cape Town, Cape Town, South Africa.
*E-mail address:* drjtbutler@gmail.com (J. Butler).

https://doi.org/10.1016/j.ebr.2024.100689
Received 21 March 2024; Received in revised form 20 June 2024; Accepted 20 June 2024
Available online 21 June 2024

presentation, which necessitated the use of an anticoagulant (warfarin). There was no history of major illnesses, family history of seizures, febrile seizures, or traumatic brain injuries.

Pre-operatively, he had weekly seizures at the minimum. His most frequent seizure type consisted of a cephalic sensation followed by amnesia and a staring appearance, head deviation to the left, and often abduction of the right shoulder and flexion of the right elbow. He also had epilepsia partialis continua (EPC) of the right fingers, dysphasic seizures and FBTCS, with several admissions in the preceding year for status epilepticus (SE). Over the preceding two years language functioning declined markedly and he had been severely depressed and socially isolated for a few years. He was treated for his mood disorder. He was right-handed until 2017, when progressive clumsiness of the right hand (first noticed in 2014), forced him to become left-handed. At the time of admission to hospital the right hand was no longer of any use to him. At this time of assessment, he concurrently used five anti-seizure medications (ASMs), namely carbamazepine, levetiracetam, clobazam, phenytoin and clonazepam.

On examination he had a marked receptive and expressive dysphasia, right visual extinction, and markedly impaired right fine finger movements and weakness of the right upper limb. Mild upper motor neuron weakness of the right lower limb was noted. He had a spastic, right hemiplegic gait.

The neuropsychologist found him difficult to test because of "limited speech". On formal testing, his scores were impaired in all domains, except visual memory and visuo-spatial function (Table 1).

Long-term video and scalp electroencephalogram (EEG) monitoring showed a marked asymmetry of alpha rhythms, better developed over the right than the left hemisphere. Frequent theta and intermittent rhythmic delta waves in the left fronto-temporal area and multifocal spikes and seizures were seen over the left hemisphere, consistent with clinical and video evidence of multifocal seizures originating in the left hemisphere (Fig. 2). These occurred at a frequency of 20–30 events per day. EPC exhibited no EEG correlate.

Magnetic resonance imaging (MRI) of the brain revealed atrophy of the entire left cerebral hemisphere and cerebral peduncle, with evidence of progression when compared to previous scans, and FLAIR hyperintensity in the thinned *peri*-Sylvian cortex and postcentral gyrus (Fig. 1). A functional MRI (fMRI) was performed, which suggested left-hemisphere language dominance, while motor mapping showed that right foot tapping produced increased signal within anatomically typical areas of the left hemisphere, with assisted right finger tapping represented ipsilaterally.

The case was discussed extensively with the family, where all therapeutic options were explored. It was postulated that, in the absence of surgery, he had an elevated mortality attributable to his medically refractory seizure disorder. The need for the continued use of warfarin increased his risk of bleeding from an intracranial haemorrhage consequent upon a seizure with falling. The excess mortality attributable to medically refractory epilepsy is substantially reduced by successful surgery [7]. Given the trajectory of language and motor function over the preceding three years, in the absence of surgery, these functions likely would continue to deteriorate. His and his mother's quality of life would remain severely impaired by continued, frequent seizures, the risk of recurrent SE, the continued need for a multitude of ASMs and multiple hospital admissions (with its associated risks) and the greater risks of seizures with advancing age. There is evidence that medically refractory epilepsy is associated with an accelerated loss of cortex elsewhere in the brain at a rate that is double that of peers. This process could be arrested by successful surgery [8]. Surgery could effect a seizure-free state, allowing the weaning of ASMs, with possible benefits for cognition, mood, and energy levels. While it could not be guaranteed, there was a good chance that he would be able to walk again, albeit with greater difficulty. He likely would not be able to speak, while comprehension would be severely impaired immediately after surgery and probably would improve, albeit imperfectly. Reading and writing

**Table 1**
Results of pre-operative formal neuropsychological testing in multiple domains, including the tests performed and their interpretation for Case 1.

| Domain | Test | Raw Score | %tile / SS | Interpretation |
|---|---|---|---|---|
| **Fine motor speed and dexterity** | Grooved Pegboard | DH (Left) = 97 s<br>NDH (Right) = unable to complete | <1st<br>– | Severely defective<br>– |
| **Processing Speed** | Symbol Search | 15–0 error = 15 | SS = 5 | Borderline |
| **Attention & Working memory** | Digit span | LDSF = 2 (consistent) LDSB = 3 (inconsistent) | <1st<br>10th | Severely defective<br>Borderline |
| | Trail-making test | TMTA = 51 s<br>TMTB = 177 s | 19th<br>4th | Low average<br>Borderline |
| **Visual-Perceptual** | RCFT – copy | 32 | 50th | Average |
| | Clox 1 | 15 | NA | Intact |
| | Clox 2 | 15 | NA | Intact |
| **Language** | Boston Naming Test | 40 (international norms) | <1st | Severely defective |
| | Category Fluency | 15 | SS = 1 | Severely defective |
| | Colour naming | 69 s | SS = 1 | Severely defective |
| | Word reading | 38 s (0 errors) | SS = 1 | Severely defective |
| **Memory** | | | | |
| Verbal | RAVLT List learning | Trial I-V = 31 (2,5,7,8,9) | 4th | Borderline |
| | Retention | 7 | 19th | Low average |
| | Delay | 3 | 3rd | Defective |
| | Recognition | 11tp – 7fp = 4 | <1st | Severely defective |
| | Distractor list | 4 | 13th | Low average |
| | Logical Memory | Immediate recall = 22 Delayed recall = 12 | SS = 5<br>SS = 6 | Borderline<br>Borderline |
| Visual | Rey complex figure | Immediate recall = 22 Delayed recall = 19 | 54th<br>31st | Average<br>Average |
| **Executive Function** | | | | |
| Verbal Fluency | Letter Fluency (FAS) | 7 | SS = 1 | Severely defective |
| Nonverbal Fluency | Nonsense designs | 1 correct – 4 error | NA | (8–10 expected) |
| Inhibition | Colour-Word inhibition | 88 s | SS = 2 | Severely defective |
| | Colour-word inhibition errors | 1 | SS = 10 | Average |
| Cognitive flexibility | Colour-word switching | 164 s | SS = 1 | Severely defective |
| | Colour word switching errors | 14 | SS = 1 | Severely defective |
| | Verbal fluency switching condition | 6 | SS = 1 | Severely defective |
| | Switching accuracy | 3 | SS = 1 | Severely defective |
| Planning | NAB Mazes | 5 | 1st | Defective |
| Abstract reasoning | Similarities | 12 | SS = 5 | Borderline |

Abbreviations: RCFT- Rey complex figure test; RAVLT- Rey auditory verbal learning test; NAB- neuropsychological assessment battery; LDSF- longest digit span forward; LDSB- longest digit span backward.

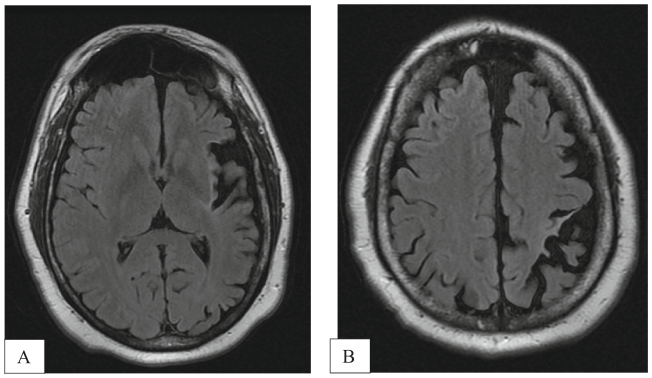



**Fig. 1.** Pre-surgical axial MRI brain of patient 1 showing moderate left cerebral hemispheric atrophy, most severe within the left insular cortex, parietal lobe, and temporal operculum. There are enlarged left parafalcine subarachnoid spaces due to the unilateral left-sided atrophy. There are apparent increases in the left hemispheric sulcal spaces compared to the scan done 7 years earlier, consistent with the history of clinical progression.

likely would not be possible. The patient repeatedly expressed the view that he could no longer continue living as he was, that he was deteriorating and that, mindful of the trade-offs, he strongly wanted to have surgery. The patient's mother agreed, noting that even prior to assessment she had expected him to continue to decline neurologically, that he had a very poor quality of life and that she was worried that he would die in the ensuing years. They understood that trials of other ASMs and vagus nerve stimulation were unlikely to produce a seizure-free state. The option of a more limited resection, preceded by intracranial recordings, was considered but dismissed, as there was a clear history of ongoing, progressive decline of language and right-hand motor function (strongly predictive of active disease in these areas) and seizure semiology and EEG findings implicated primary motor hand and language areas in the left temporal, parietal and frontal regions. The patient felt that nothing short of seizure-freedom would help his depression.

A diagnosis of RE was made, and a left *peri*-insular hemispherotomy was performed. The surgical technique included a central craniotomy flap, followed by resection of the frontal operculum. A corpus callosotomy, including the genu and splenium, was performed from within the lateral ventricle. After this, the superior temporal gyrus, amygdala, hippocampal head and tail were resected followed by a superior and frontal disconnection extending to the temporal horn and sphenoidal wing, respectively. The insular cortex was only resected where it was possible to reach the tissue between the M2 vessels. Histology demonstrated isolated T-lymphocytes, denoting possible encephalitis.

Post-operatively he was globally aphasic and right hemiplegic, but within seven days was able to open and close his left hand and eyes to command. Six months later he was able to walk a few metres with a stick and ankle–foot orthosis.

Five years later, he remains seizure-free, using only one ASM (carbamazepine) at a very low dose, after ASMs had been sequentially and slowly weaned. His family report a markedly improved mood and affect, independent eating, and use of the toilet. He can partially manage his own bank account. To communicate, he can draw to express himself (post-operative formal neuropsychology testing was not performed as he lives far away in a small town). He is unable to produce spontaneous speech, but he can repeat some words. His mother reports that he can sing along to his favourite songs. He executes 2 and 3 step commands correctly and correctly points to various body parts and objects in the room. Praxis is intact. He walks around the house with an orthosis and a stick. (Video 1) The patient's family are very happy with his overall functional outcome and well-being. To the examiner, the change in his affect is as striking as it is to the family.

**Case 2:** A right-handed pre-teen girl, previously well, presented with an 18-month history of medically refractory seizures and progressive neurological dysfunction implicating the left hemisphere. This included a monoparesis of the right upper limb, drooling and dysphasia. ASMs that had been trialed at this point included sodium valproate, topiramate, lamotrigine, levetiracetam and clonazepam.

The semiology was predictive of multifocal left hemispheric seizures occurring at a frequency of up to 50 times per day. Long-term video and scalp EEG monitoring revealed an asymmetry of alpha rhythms and fronto-central beta, diminished in amplitude on the left, persistent theta and delta over the entire left hemisphere and multifocal left hemispheric spikes (Fig. 3). There were multifocal left hemispheric seizures that occurred every few minutes. The MRI brain showed progressive atrophy and hyperintensities in the left hemisphere (images unavailable as digital records not available at the time). A WADA test revealed left hemispheric language functioning. Pre-operative formal neuropsychology testing was deferred as she was drooling, poorly attentive and un-cooperative, with frequent seizures occurring every hour. A diagnosis of RE was made and a defunctioning left hemispherotomy was performed, using the same technique as described above. Histology supported the diagnosis, with neuronal loss and astrocytosis, perivascular chronic inflammatory infiltrates, and microglial aggregates with overt neuronophagia indicative "of an inflammatory polioencephalopathy". Post-operatively she was hemiplegic and globally aphasic.

Over the following two years, her right lower limb function and language progressively improved, especially in respect of comprehension. When seen eight years later, she had undertaken an independent airplane journey and only had a mild hemiparetic gait. The patient could express herself well, with the recovery of comprehension exceeding the recovery of expressive language. She remains seizure-free and medication free 20 years after her surgery (Video 2).

## 3. Discussion

Upper age limits for performing a dominant hemispherectomy have not been established; rare patients have been reported to have had surgery in the teens [3,4]. The largest case series of 47 adults reports satisfactory outcomes following non-dominant hemispherectomy, but no dominant cases were performed [6]. A systematic review of adult hemispherectomies reported left hemisphere surgeries, however these surgeries were of uncertain or non-dominance [5,6,9–13]. This included a cohort of 25 adults aged 18–39 years (median = 20), of whom 15 had left hemispherectomies. Remarkably, all patients had an improvement in full-scale, verbal and performance IQ, as well as quality of life (QOLIE-31) after surgery [10]. Given these outcomes and uncertain language dominance, the language outcomes are difficult to apply to an adult considering a dominant hemispherectomy. A man in his 50s, who sustained a severe asymmetric traumatic brain injury at the age of five years, unexpectedly had a partial decline in language function after a satisfactory left amobarbital test and left hemispherectomy [14]. Another patient in their 20s had a "permanent dysphasia" after left hemispherectomy for a vascular malformation [12].

Our first case demonstrated unprecedented late radiological and clinical progression of RE which was noted 32 years after onset, leading to the outcome of a dominant hemispherotomy in his 40s. The partial recovery of posterior language function, with permanent loss of already limited anterior language function, parallels the pattern seen in children following dominant hemispherectomy, albeit considerably less in extent [15]. Case two demonstrated more substantial recovery of posterior language function than anterior language function. Compared to case one, she also showed considerably greater recovery of motor function for the contralateral lower limb. In both cases, ambulation recovered, but the extent and speed of recovery of gait in case two was considerably better than case one.

Aetiology, reflected in contralateral radiological and EEG abnormalities and intellectual development, and age at disease onset are proposed as determinants of post-surgical outcomes [7,16,17]. The

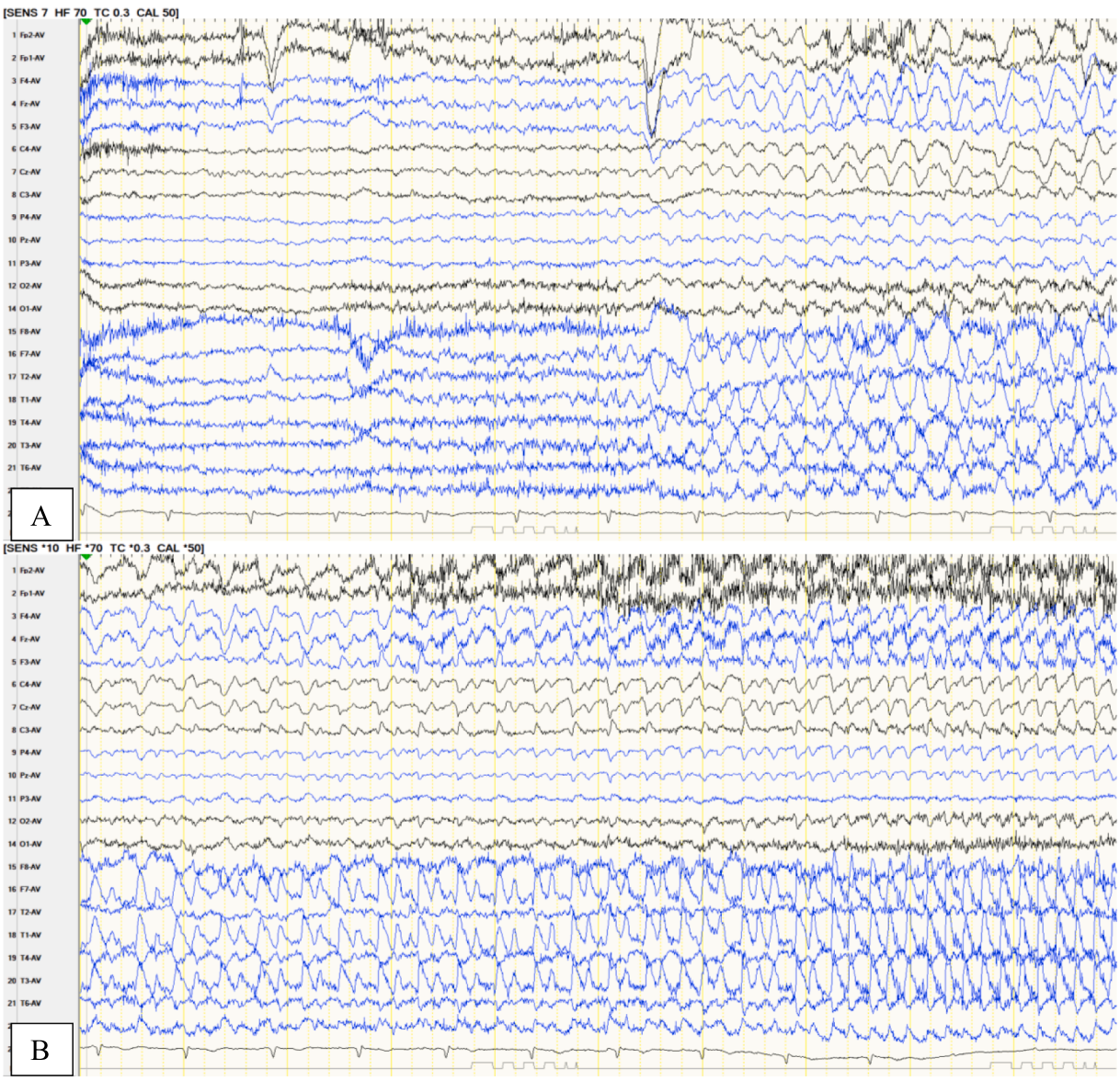



**Fig. 2.** Two images of long-term video EEG monitoring of patient 1- in panel A there is minimal rhythmic low amplitude theta frequency discharge at M1-F7-T3, evolving in the same derivations. On video, he looks to the right and fidgets immediately after the seizure starts and he then suddenly turns his head to the left, prompting his mother to recognize the seizure, remove the cup from his hand and push the trigger button. He moves his fingers and toes to command post-ictally. EEG in panel B demonstrates the evolution of the EEG seizure in the left hemisphere.

benefits and risks of a dominant hemispherectomy were carefully weighed for case one. Probable loss of function after surgery included expressive more than receptive language function and further weakening of the right leg. Given the progressive deterioration of language function in the preceding two years, there was a strong likelihood that, even in the absence of surgery, he would lose more language function. Surgery was associated with a substantial probability of a seizure-free state and reduced mortality associated with his condition. Surgery could markedly reduce the risk of injuries, including fractures and subdural haemorrhages (in the setting of continued anticoagulation use), and avoid the emotional burden and financial costs of repeated hospitalisations for SE. Similarly, adverse effects on frequent subclinical and clinical seizures, and five ASMs in high doses for right hemispheric function could be averted. He was severely depressed and there was the potential that this could be reversed. After extensive counseling, the patient and family were adamant about having the surgery.

It has been suggested that criteria for hemispherectomy in adults list seizures in the dominant hemisphere as a contraindication to surgery [5]. The first case reported here lost more language function after dominant hemispherotomy than the second, but the patient and his family's happiness with the outcome reflects his pre-operative dire condition, their grasp of trade-offs, realistic expectations of possible outcomes and gains associated with surgery. A lateral defunctioning hemispherotomy was the preferred technique of the neurosurgeon. Some recent evidence suggests that a vertical approach may produce better seizure outcomes [18].

## 4. Conclusion

These two cases demonstrate that a dominant hemispherotomy performed on a quadragenarian with RE may produce a satisfactory outcome, but a better outcome may occur after surgery in the early teenage years. RE may cause indolent, progressive neurological dysfunction well into adult life and should be considered in patients presenting with otherwise unexplained functional decline decades after onset.

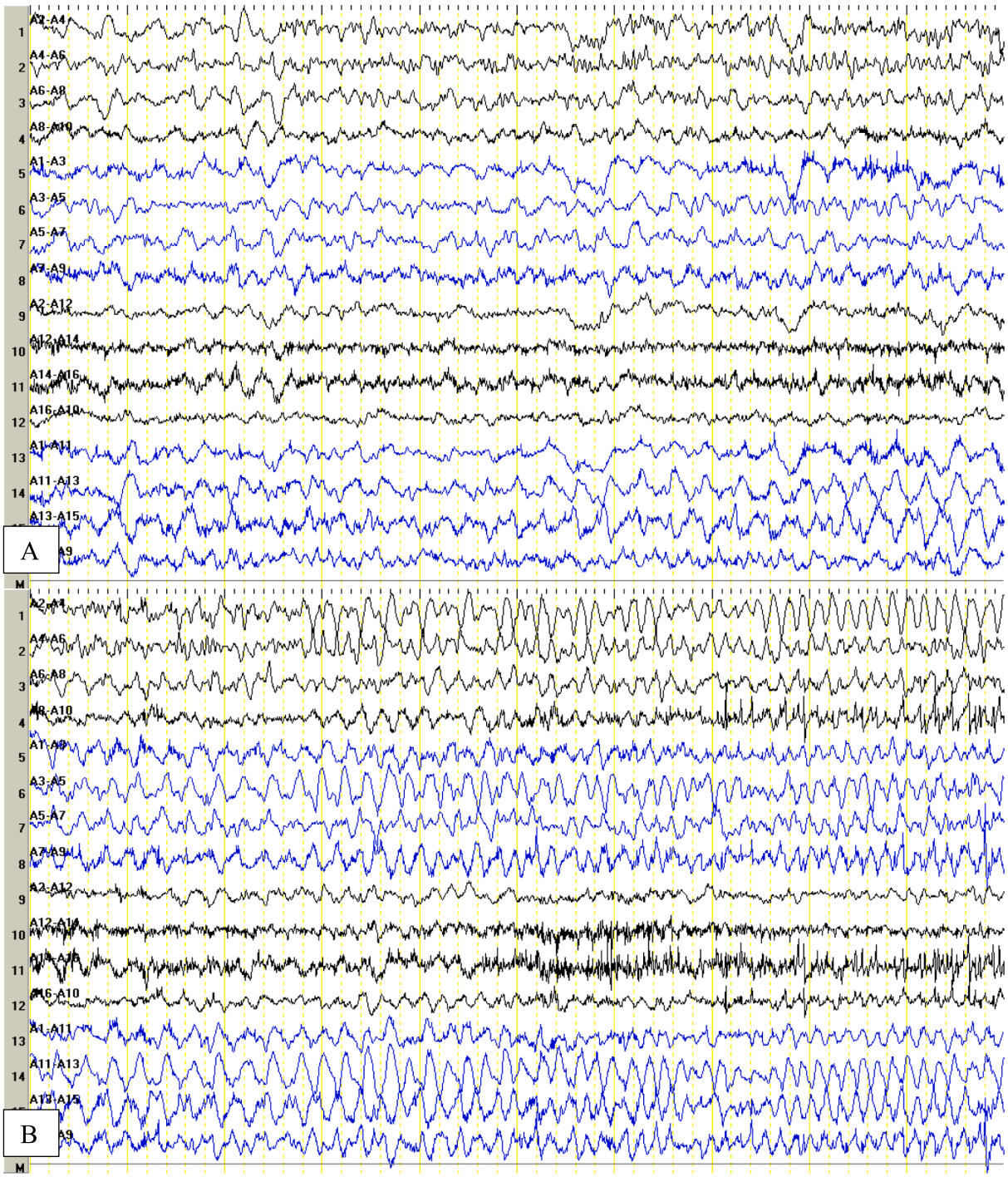



**Fig. 3.** Patient 2: Bipolar anterior to posterior montage, right hemisphere in black, left hemisphere in blue, parasagittal derivations in the top half, temporal derivations in lower half of the 10-second epochs. There is an evolving seizure, initially associated with arousal from stage 2 sleep, at T3, becoming progressively more widespread in the left hemisphere. There is an asymmetry of F-waves and V-waves during the first few seconds in panel A. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

## CRediT authorship contribution statement

**James Butler:** Writing – original draft, Supervision, Resources, Methodology, Investigation, Data curation, Conceptualization. **Aayesha Soni:** Methodology, Investigation, Writing – original draft, Writing – review & editing. **Roger Melvill:** Writing – review & editing.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Acknowledgements

Nil.

*Use of Artifical Intelligence*

Generative artificial intelligence has not been used in the preparation of this manuscript.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ebr.2024.100689.

## References


[1] Lopez AJ, Badger C, Kennedy BC. Hemispherotomy for pediatric epilepsy: a systematic review and critical analysis. Childs Nerv Syst 2021;37(7):2153–61.
[2] Kurwale NS, Bapat D, Jagtap SA, et al. Predicting seizure outcomes and functional outcomes after hemispherotomy: are we any better? Childs Nerv Syst 2023.
[3] Borne A, Perrone-Bertolotti M, Jambaque I, et al. Cognitive outcome after left functional hemispherectomy on dominant hemisphere in patients with Rasmussen encephalitis: beyond the myth of aphasia. Patient Series. J Neurosurg Case Lessons 2022;4(22).
[4] Bulteau C, Grosmaitre C, Save-Pedebos J, et al. Language recovery after left hemispherotomy for Rasmussen encephalitis. Epilepsy Behav 2015;53:51–7.
[5] Schusse CM, Smith K, Drees C. Outcomes after hemispherectomy in adult patients with intractable epilepsy: institutional experience and systematic review of the literature. J Neurosurg 2018;128(3):853–61.
[6] McGovern RA, Moosa ANV, Jehi L, et al. Hemispherectomy in adults and adolescents: seizure and functional outcomes in 47 patients. Epilepsia 2019;60(12):2416–27.
[7] Granthon C, Tranberg AE, Malmgren K, et al. Reduced long-term mortality after successful resective epilepsy surgery: a population-based study. J Neurol Neurosurg Psychiatry 2024;95:249–55.
[8] Galovic M, de Tisi J, McEvoy AW, et al. Resective surgery prevents progressive cortical thinning in temporal lobe epilepsy. Brain 2020;143:3262–72.
[9] Steinhoff BJ, Staack AM, Bilic S, et al. Functional hemispherectomy in adults with intractable epilepsy syndromes: a report of 4 cases. Epileptic Disord 2009;11(3):251–7.
[10] Liang S, Zhang G, Li Y, et al. Hemispherectomy in adults patients with severe unilateral epilepsy and hemiplegia. Epilepsy Res 2013;106(1–2):257–63.
[11] Cukiert A, Cukiert CM, Argentoni M, et al. Outcome after hemispherectomy in hemiplegic adult patients with refractory epilepsy associated with early middle cerebral artery infarcts. Epilepsia 2009;50(6):1381–4.
[12] McClelland S, Maxwell RE. Hemispherectomy for intractable epilepsy in adults: the first reported series. Ann Neurol 2007;61(4):372–6.
[13] Schramm J, Delev D, Wagner J, et al. Seizure outcome, functional outcome, and quality of life after hemispherectomy in adults. Acta Neurochir (Wien) 2012;154(9):1603–12.
[14] Loddenkemper T, Dinner DS, Kubu C, et al. Aphasia after hemispherectomy in an adult with early onset epilepsy and hemiplegia. J Neurol Neurosurg Psychiatry 2004;75(1):149–51.
[15] Boatman D, Freeman J, Vining E, et al. Language recovery after left hemispherectomy in children with late-onset seizures. Ann Neurol 1999;46(4):579–86.
[16] Moosa AN, Jehi L, Marashly A, et al. Long-term functional outcomes and their predictors after hemispherectomy in 115 children. Epilepsia 2013;54(10):1771–9.
[17] Bajer C, Hofer W, Pieper T, et al. Correlates of intellectual development before and after hemispherotomy: an analysis of 75 children and adolescents. Epileptic Disord 2020;22(5):571–81.
[18] Chen JS, Harris WB, Wu KK, et al. Comparison of hemispheric surgery techniques for pediatric drug-resistant epilepsy: an individual patient data meta-analysis. Neurology 2023;101(4):e410–24.