Editorial

Corpus Callosotomy: Editorial

Ayataka Fujimoto 1,* and Tohru Okanishi 2,

1 Comprehensive Epilepsy Center, Seirei Hamamatsu General Hospital, Hamamatsu 430-8558, Japan
2 Division of Child Neurology, Department of Brain and Neurosciences, Faculty of Medicine, Tottori University, Yonago 683-8503, Japan; tokanishi@tottori-u.ac.jp
* Correspondence: afujimotoscienceacademy@gmail.com

Since corpus callosotomy (CC) was first reported in 1940 [1,2], this surgical technique has become one of the most recognized epilepsy surgeries [3]. While this method was temporarily viewed in a negative light, meaning few studies on CC were performed between the 1970s and 2000s, the number of CCs performed and the number of papers published on CC have increased in recent years [4].

One reason why CC is not often performed is because CC is a palliative rather than a radical therapy [5]. This is probably because when considering open cranial surgery for intractable epilepsy, the mainstream process is generally to identify the epileptic focus and perform epileptic focus resection to radically eliminate the source of epileptic seizure. In addition, permanent higher brain function disorders might arise after CC, such as split-brain syndrome [6]. We have performed many CCs and have never experienced typical split-brain phenomena or memory impairment [7]. In addition, temporary postoperative disturbance of consciousness [4] and postoperative chemical meningitis [8] are factors that may cause anxiety for all medical personnel and caregivers involved in the postoperative management of patients who have undergone CC. These reasons might lead to hesitation in proceeding with CC.

However, if the epileptic focus is not identified from stereotactic electroencephalography (SEEG) or intracranial electrode placement following focal resection, is it sufficient to simply remove the electrode? Even though vagus nerve stimulation (VNS) is available as a palliative treatment, VNS therapy for drop attacks can be enhanced by adding VNS therapy to CC [9], but whether this is sufficient to control seizures is unclear. In fact, inadequate efficacy of VNS has been reported [10].

Many studies have compared CC and VNS therapy, but what these methods have in common is simply that they are palliative therapies. In terms of drop attacks, clinicians need to consider whether the drop attack represents epileptic spasm (ES), atonic seizure, or bilateral tonic seizure. However, the efficacy of CC and VNS therapy is often reported without clearly distinguishing among seizure types. Since the mechanisms underlying CC and VNS therapies are completely different, direct comparison between these methods is not appropriate.

The effect of CC on the “drop attack” is marked [2]. ES is found mainly in West syndrome, and adrenocorticotropic hormone (ACTH) therapy is the core treatment. However, if the response to ACTH therapy or anti-seizure medications is insufficient, surgical treatment, such as CC or radical surgery, is considered. The rate of seizure resolution by CC with respect to ES varies, but is reported to be 25–79%. Conversely, the rate of seizure resolution with radical surgery, including cortical resection, lobectomy, and hemispherical disconnection, is 61–83% [11–20]. The major difference in patient backgrounds between the two surgical options was that 83–100% (mean, 94%) of patients with radical surgery had brain lesions, as shown by magnetic resonance imaging (MRI). Radical surgery is usually performed on a single hemisphere of the brain, and has been considered to have been performed on patients that show signs of lateralization preoperatively. The fact that radical surgery has been performed based on not only MRI, but also nuclear medicine
examinations (including positron emission tomography), has been reported [21], along
with 70 cases that underwent radical surgery based only on MRI without invasive EEG
monitoring [22].

In terms of CC, 0 to 65% (mean, 17%) of cases have brain lesions, less than with radical
respective surgery. As a preferable prognostic factor for CC, “no brain lesions” have been re-
ported [20]. Therefore, in the selection of CC for intractable ES, on the one hand, the absence
of structural factors is considered a positive factor. On the other hand, successful cases
have also been described with bilateral widespread polymicrogyria, cortical/subcortical
tubers in tuberous sclerosis complex, and diffuse atrophy [11,13,15,20]. Since selecting a
radical operation is difficult for such lesions, CC may be indicated.

In a group of patients with West syndrome without brain lesions, who showed pre-
dominantly ES, but also had some tonic seizures, ES was more effectively controlled by
CC than tonic seizures [10]. CC is less effective in Lennox-Gastaut syndrome than in West
syndrome [23]; therefore, CC may be necessary during the West syndrome stage or the
ES-only stage. After CC, if epileptogenicity is lateralized to one hemisphere and clinically
focal (asymmetric) ES is exhibited, radical surgery might be considered, and the seizure
resolution rate in such cases is 43–71% [11,14,15,18,24].

Based on advanced analyses for presurgical EEG, less power and less connectivity of
high-gamma activities on presurgical scalp EEG recordings [14] and lower phase lags in
ictal slow and gamma waves among bilateral hemispheres [17] have been associated with
favorable seizure outcomes after CC.

Okanishi and Fujimoto have reported that ES can be categorized as follows: (1) focal-
onset ES; (2) potentially focal-onset ES; (3) generalized onset/bilateral focal-onset ES with
low callosal modulation; and (4) generalized onset. The generalized onset occurs in the
pathology of ES with high callosal modulation. Among these, CC is highly effective against
generalized onset ES. Pathologies in which the corpus callosum is strongly involved in the
development of ES and bilateral synchronization are often observed in generalized onset
ES. In a pathology where a seizure starts from one hemisphere, but clinically manifests as
generalized ES via the corpus callosum, CC may lead to lateralization and focal ES. In such
cases, subsequent radical surgery might be indicated [2].

Funding: This research received no external funding.

Conflicts of Interest: The author declares no conflict of interest.

References
1. Van Wagenen, W.P.; Herren, R.Y. Surgical division of commissural pathways in the corpus callosum: Relation to spread of an
epileptic attack. Arch. Neurol. Psychiatry 1940, 44, 740–759. [CrossRef]
2. Okanishi, T.; Fujimoto, A. Corpus callosotomy for controlling epileptic spasms: A proposal for surgical selection. Brain Sci. 2021,11, 1601. [PubMed]
3. Uda, T.; Kunihiro, N.; Uamba, R.; Koh, S.; Kawashima, T.; Ikeda, S.; Ishimoto, K.; Goto, T. Surgical aspects of corpus callosotomy. Brain Sci. 2021, 11, 1608. [CrossRef] [PubMed]
4. Nozaki, T.; Fujimoto, A.; Ichikawa, N.; Baba, S.; Enoki, H.; Okanishi, T. Higher intelligence may be a risk factor for postoperative transient disturbance of consciousness after corpus callosotomy. Epilepsy Behav. 2021, 115, 107617. [CrossRef] [PubMed]
5. Asada, R.; Mizuno, S.; Yu, Y.; Hamamoto, Y.; Anazawa, T.; Ito, D.; Kitagawa, M.; Hasegawa, D. Corpus callosotomy in 3 cavalier King Charles Spaniel dogs with drug-resistant epilepsy. Brain Sci. 2021, 11, 1462. [CrossRef]
6. Pinto, Y.; de Haan, E.H.F.; Lamme, V.A.F. The split-brain phenomenon revisited: A single conscious agent with split perception. Trends Cogn. Sci. 2017, 21, 835–851. [CrossRef]
7. Hayashi, M.; Fujimoto, A.; Enoki, H.; Niimi, K.; Inenaga, C.; Sato, K.; Homma, K.; Arakawa, T.; Okanishi, T. The Fornix May Play a Key Role in Korsakoff’s Amnesia Secondary to Subcallosal Artery Infarction. Brain Sci. 2021, 12, 21. [CrossRef]
8. Fujimoto, A.; Hatano, K.; Nozaki, T.; Sato, K.; Enoki, H.; Okanishi, T. Postoperative Pneumocephalus on Computed Tomography Might Predict Post- Corpus Callosotomy Chemical Meningitis. Brain Sci. 2021, 11, 638. [CrossRef]
9. Hatano, K.; Fujimoto, A.; Yamamoto, T.; Enoki, H.; Okanishi, T. Effects of Vagus Nerve Stimulation following Corpus Callosotomy for Patients with Drug-Resistant Epilepsy. Brain Sci. 2021, 11, 1395. [CrossRef]
10. Okanishi, T.; Fujimoto, A.; Nishimura, M.; Kanai, S.; Motoi, H.; Homma, Y.; Enoki, H. Insufficient Efficacy of Vagus Nerve Stimulation for Epileptic Spasms and Tonic Spasms in Children with Refractory Epilepsy. Epilepsy Res. 2018, 140, 66–71. [CrossRef]
11. Ono, T.; Baba, H.; Toda, K.; Ono, K. Callosotomy and Subsequent Surgery for Children with Refractory Epilepsy. *Epilepsy Res.* 2011, 93, 185–191. [CrossRef]

12. Obuki, T.; Kim, H.D.; Luan, G.; Inoue, Y.; Baba, H.; Oguni, H.; Hong, S.C.; Kameyama, S.; Kobayashi, K.; Hirose, S.; et al. Surgical versus Medical Treatment for Children with Epileptic Encephalopathy in Infancy and Early Childhood: Results of an International Multicenter Cohort Study in Far-East Asia (The Face Study). *Brain Dev.* 2016, 38, 449–460. [CrossRef]

13. Baba, H.; Toda, K.; Ono, T.; Honda, R.; Baba, S. Surgical and Developmental Outcomes of Corpus Callosotomy for West Syndrome in Patients without MRI Lesions. *Epilepsia* 2018, 59, 2231–2239. [CrossRef]

14. Baba, S.; Vakorin, V.A.; Doesburg, S.M.; Nagamori, C.; Cortez, M.A.; Honda, R.; Ono, T.; Toda, K.; Nishimoto, H.; Ebihara, T.; et al. EEG Before and after Total Corpus Callosotomy for Pharmacoresistant Infantile Spasms: Fast Oscillations and Slow-Wave Connectivity in Hypsarrhythmia. *Epilepsia* 2019, 60, 1849–1860. [CrossRef]

15. Okanishi, T.; Fujimoto, A.; Okanari, K.; Baba, S.; Ichikawa, N.; Nishimura, M.; Enoki, H. Corpus Callosotomy for Drug-Resistant Spasms Associated with Tuberous Sclerosis Complex. *Epilepsy Behav.* 2019, 98, 228–232. [CrossRef]

16. Kanai, S.; Oguri, M.; Okanishi, T.; Itamura, S.; Baba, S.; Nishimura, M.; Homma, Y.; Maegaki, Y.; Enoki, H.; Fujimoto, A. Symmetry of Ictal Slow Waves May Predict the Outcomes of Corpus Callosotomy for Epileptic Spasms. *Sci. Rep.* 2019, 9, 19733. [CrossRef]

17. Oguri, M.; Okanishi, T.; Kanai, S.; Baba, S.; Nishimura, M.; Ogo, K.; Himoto, T.; Okanari, K.; Maegaki, Y.; Enoki, H.; et al. Phase Lag Analyses on Ictal Scalp Electroencephalography May Predict Outcomes of Corpus Callosotomy for Epileptic Spasms. *Front. Neurol.* 2020, 11, 576087. [CrossRef]

18. Uda, T.; Kuki, I.; Inoue, T.; Kunihiro, N.; Suzuki, H.; Uda, H.; Kawashima, T.; Nakajo, K.; Nakanishi, Y.; Maruyama, S.; et al. Phase-Amplitude Coupling of Interictal Fast Activities Modulated by Slow Waves on Scalp EEG and Its Correlation with Seizure Outcomes of Disconnection Surgery in Children with Intractable Nonlesional Epileptic Spasms. *J. Neurosurg. Pediatr.* 2021, 27, 572–580. [CrossRef]

19. Pinard, J.M.; Delalande, O.; Chiron, C.; Soufflet, C.; Plouin, P.; Kim, Y.; Dulac, O. Callosotomy for Epilepsy after West Syndrome. *Epilepsia* 1999, 40, 1727–1734. [CrossRef]

20. Iwasaki, M.; Uematsu, M.; Hino-Fukuyo, N.; Osawa, S.; Shimoda, Y.; Jin, K.; Nakasato, N.; Toiminaga, T. Clinical Profiles for Seizure Remission and Developmental Gains after Total Corpus Callosotomy. *Brain Dev.* 2016, 38, 47–53. [CrossRef]

21. Liu, Y.; Zhou, W.; Hong, B.; Wang, H.; Lin, J.; Sun, Z.; Wang, S. Analysis of Surgical Strategies for Children with Epileptic Spasms. *Epileptic Disord.* 2021, 23, 85–93. [CrossRef] [PubMed]

22. Erdemir, G.; Pestana-Knight, E.; Honomichl, R.; Thompson, N.R.; Lachhwani, D.; Kotagal, P.; Wyllie, E.; Gupta, A.; Bingaman, W.E.; Moosa, A.N.V. Surgical Candidates in Children with Epileptic Spasms Can Be Selected without Invasive Monitoring: A Report of 70 Cases. *Epilepsia* 2021, 176, 106731. [CrossRef] [PubMed]

23. Camfield, P.; Camfield, C. Long-Term Prognosis for Symptomatic (Secondarily) Generalized Epilepsies: A Population-Based Study. *Epilepsia* 2007, 48, 1128–1132. [CrossRef] [PubMed]

24. Baba, S.; Okanishi, T.; Nozaki, T.; Ichikawa, N.; Sakakura, K.; Nishimura, M.; Yonekawa, T.; Enoki, H.; Fujimoto, A. Successful Hemispherotomy in a Patient with Encephalopathy with Continuous Spikes and Waves during Sleep Related to Neonatal Thalamic Hemorrhage: A Case Report with Intracranial Electroencephalogram Findings. *Brain Sci.* 2021, 11, 827. [CrossRef]