Pediatric Epilepsy Column (Editorial)

Surgical advancements in pediatric epilepsy surgery: from the mysterious to the minimally invasive

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"*Men regard its nature and cause as divine from ignorance and wonder, because it is not at all like to other diseases. And this notion of its divinity is kept up by their inability to comprehend it.*"—Hippocrates, *On the Sacred Disease*, 400 BC

Nearly two and a half millennia ago, Hippocrates described epilepsy as "the sacred disease." His hypothesis that seizures arose from an organic, physical substrate that was not understood, rather than from the divine or supernatural, was ahead of his time. Yet, despite centuries of research and innovation, superstitions about epilepsy remain deeply embedded in local cultural traditions and belief systems throughout much of the world (1). More than 50 million people worldwide have epilepsy, making it the most prevalent serious chronic neurological disorder. Seizures disproportionately affect children: the incidence is higher in infancy compared with any other age group (1,2).

Our understanding of the pathogenesis of epilepsy and its impact on the developing brain as well as our armamentarium of anti-epileptic medications to treat seizures continue to evolve. Despite profound advancements, one fifth to one third of patients have disease that remains drug resistant. Seizures that persist despite trials of two properly selected medications are deemed by the International League Against Epilepsy criteria as drug-resistant epilepsy (DRE). Once these criteria are met, it is critical that children are referred for surgical evaluation because, at that point, the likelihood of medical control is extremely low (3). Further, early age of seizure onset and pharmacoresistance are risk factors for poor cognitive development (4), and seizure freedom after surgery is likely to rescue that downward trajectory. Unfortunately, at this time, most children with DRE still endure years of seizures before surgical evaluation, and epilepsy surgery remains among the most under-utilized therapies in modern medicine (5).

Recent advancements in the diagnosis and treatment of epilepsy are creating a paradigm shift in the surgical management of children with DRE and opening the door to a future of minimally invasive surgical therapy. High-resolution structural magnetic resonance imaging (MRI) and voxel-based morphometry algorithms allow quantitative analysis of brain structure to better identify malformations of cortical development (6). Resting-state functional MRI allows the identification of functional brain circuits and the analysis of connectivity without performing tasks. Through these techniques and many more, modern neuroimaging is rapidly evolving to identify previously undetectable lesions and map functionally eloquent neuronal circuits (6,7). The use of minimally invasive intracranial electroencephalography (EEG) recordings using stereotactic depth electrode placement, or stereo EEG (SEEG), facilitated by newly developed robotic technology to allow the efficient, accurate placement of multiple bilateral electrodes, is replacing large craniotomies for intracranial EEG recordings. Simultaneously, new computational algorithms are being developed to model three-dimensional epileptic networks based on interictal EEG data, potentially limiting the duration of electrode recordings required to map the epileptogenic zone (8,9).

Large subdural electrode arrays are still often required for cortical stimulation mapping of eloquent brain tissue,

especially in children who may not be able to tolerate task-based functional MRI. This is often the case in patients with epileptic lesions that border motor and language cortex, as well as for anatomic resections extending to primary cortex in non-lesional epilepsy. However, recent advancements in transcranial magnetic stimulation (TMS) are now facilitating mapping outside the operating room on an outpatient basis. TMS allows cortical stimulation mapping through the scalp, and functional maps may be imported into neuronavigation equipment in the operating room. These advances have the potential to significantly decrease the number of patients in whom multi-stage craniotomies are required for functional mapping of eloquent cortex (10,11).

Finally, the advent of MRI-guided laser interstitial thermal therapy (LITT) is quickly revolutionizing the surgical management of DRE in children. The stereotactic placement of cooled lasers of different sizes, followed by ablation of the epileptogenic zone monitored in real-time using MR thermography, has demonstrated promising efficacy in the management of deep epileptic foci in children such as hypothalamic hamartomas (12). LITT is now being used to treat a variety of epileptic lesions in children (13). Previously, minimally invasive diagnostics like SEEG were uncoupled with minimally invasive treatment approaches such as LITT. Many patients requiring SEEG have MRI-negative disease, and multi-stage craniotomies with cortical stimulation mapping and large anatomic resections were required to achieve seizure freedom.

It is easy to see how LITT and SEEG may be used together in children with multifocal epilepsy, such as tuberous sclerosis complex. Leveraging multiple new technologies—including quantitative neuroimaging, robotic-assisted SEEG, outpatient functional mapping of eloquent cortex via TMS, and minimally invasive ablation with LITT—has the potential to usher in a new era of minimally invasive surgical treatment, with the result of shorter hospital stays and decreased morbidity. Through this series of articles on the evaluation, treatment paradigms, and emerging tools in the surgical management of pediatric epilepsy, we hope readers of *Translational Pediatrics* (*TP*) come to share not simply our passion about the power of surgery to cure epilepsy, but also our excitement about the future of the field. It is our hope that continued surgical innovation will change surgical treatment strategies for more and more children from large operations and brain resections to minimally invasive therapy. Undoubtedly, such innovation will help change the stigma associated with epilepsy surgery, allowing more children to realize a life without seizures, reach their full cognitive potential, and achieve functional independence.

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Footnote

Conflicts of Interest: The author has no conflicts of interest to declare.

References

1. Perucca E, Covanis A, Dua T. Commentary: Epilepsy is a global problem. Epilepsia 2014;55:1326-8.
2. Wilmshurst JM, Gaillard WD, Vinayan KP, et al. Summary of recommendations for the management of infantile seizures: Task Force Report for the ILAE Commission of Pediatrics. Epilepsia 2015;56:1185-97.
3. Kwan P, Arzimanoglou A, Berg AT, et al. Definition of drug resistant epilepsy: consensus proposal by the ad hoc Task Force of the ILAE Commission on Therapeutic Strategies. Epilepsia 2010;51:1069-77.
4. Berg AT, Zelko FA, Levy SR, et al. Age at onset of epilepsy, pharmacoresistance, and cognitive outcomes: a prospective cohort study. Neurology 2012;79:1384-91.
5. Engel J Jr. Why is there still doubt to cut it out? Epilepsy Curr 2013;13:198-204.
6. Kini LG, Gee JC, Litt B. Computational analysis in epilepsy neuroimaging: A survey of features and methods. Neuroimage Clin 2016;11:515-29.
7. Vadivelu S, Wolf VL, Bollo RJ, et al. Resting-state functional MRI in pediatric epilepsy surgery. Pediatr Neurosurg 2013;49:261-73.
8. Boido D, Kapetis D, Gnatkovsky V, et al. Stimulus-evoked potentials contribute to map the epileptogenic zone during stereo-EEG presurgical monitoring. Hum Brain Mapp 2014;35:4267-81.
9. Rummel C, Abela E, Andrzejak RG, et al. Resected brain tissue, seizure onset zone and quantitative EEG measures: towards prediction of post-surgical seizure control. PLoS One 2015;10:e0141023.
10. Narayana S, Rezaie R, McAfee SS, et al. Assessing motor

function in young children with transcranial magnetic stimulation. Pediatr Neurol 2015;52:94-103.
11. Babajani-Feremi A, Narayana S, Rezaie R, et al. Language mapping using high gamma electrocorticography, fMRI, and TMS versus electrocortical stimulation. Clin Neurophysiol 2016;127:1822-36.
12. Lewis EC, Weil AG, Duchowny M, et al. MR-guided laser interstitial thermal therapy for pediatric drug-resistant lesional epilepsy. Epilepsia 2015;56:1590-8.
13. Wilfong AA, Curry DJ. Hypothalamic hamartomas: optimal approach to clinical evaluation and diagnosis. Epilepsia 2013;54 Suppl 9:109-14.

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