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Failed epilepsy surgery: It is not too late

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Dear Sir

I was pleased to read the recent report by Ryzí and colleagues entitled “Long-term outcomes in patients after epilepsy surgery failure” (Ryzí et al., 2015). While resective surgery results in seizure freedom in one-half to two-thirds of patients of patients with focal neocortical (FNE) or mesial temporal lobe epilepsy (TLE), respectively, significant room for progress remains (Englot and Chang, 2014; Spencer and Huh, 2008). Meticulous scrutinization of surgical failures is essential if we are to increase seizure freedom rates with initial surgical treatment, and understand the potential for further clinical improvement with additional intervention.

From a group of nearly 300 surgical patients, Ryzí et al. studied 34 individuals with the worst (Engel class IV) seizure profile after the first post-operative year, examining long-term seizure outcomes with further treatment. At last follow-up, improved outcome (Engel I–III) was seen in 22 (65%) of these individuals, including 8 (24%) patients who achieved seizure freedom (Engel I). Furthermore, a progressive decrease in seizure frequency was observed over time in the cohort. Treatment after initial failed surgery included repeat resection in 6 (17%) individuals, which resulted in Engel I outcome in 4 of these cases. Other patients were not deemed to be candidates for reoperation, given lack of a single identifiable seizure onset zone or risk of neurological deficit. It would be interesting to know the authors’ hypotheses regarding reasons for failed epilepsy surgery in this cohort, the number of patients who received detailed re-evaluation for potential repeat surgery (including new long-term invasive or noninvasive electrographic monitoring), and the results of these evaluations.

Our group at the University of California, San Francisco also recently examined failed epilepsy surgery and the results of further post-operative intervention in our patient

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Conflict of interest

The author has no personal financial or institutional interest in any of the medications, materials, or devices described in this article.

population. In a series of 138 resections for FNE, detailed reevaluation in 36 of the 47 patients with persistent seizures revealed that 26 (72%) surgical failures were likely due to insufficient resection of the seizure onset zone, while 10 (28%) cases involved an additional epileptogenic region distal from the surgical site (Englot et al., 2014b). As in the study by Ryzí and colleagues, reoperation was pursued in a subset (16) of patients, resulting in seizure freedom in the majority (63%) of those cases. In our series of 241 patients who received resection for TLE, 13 re-operations were pursued after an initial failed surgery, with 7 (54%) individuals achieving Engel I outcome (Englot et al., 2013). Furthermore, patients with persistent post-operative seizures nevertheless experienced improved seizure profile after surgery, similar to the observation of Ryzí et al. Finally, we reported similar results in our surgical cohort of 110 pediatric patients, and observed that unrecognized hemispheric epilepsy syndromes may underlie a number of failed focal resections in this age group (Englot et al., 2014a).

Perhaps surprisingly, Ryzí et al. also report that 16 (47%) of 34 patients with Engel IV outcome one year after resection ultimately achieved an improved seizure profile (Engel I–III) with further adjustment to medical therapy but no additional surgery. These included 3 (9%) individuals who progressed from Engel IV to Engel I outcome. It would be interesting to learn the authors' thoughts regarding this significant post-operative clinical improvement with medication change alone. Could these patients have been better medically optimized prior to resection, or is it presumed that surgery altered their seizure networks such that previously ineffective medication regimens might have new benefit? In surgically naïve patients, Kwan and Brodie have described poor response to further antiepileptic drug (AED) trials after the failure of two regimens (Kwan and Brodie, 2000), although Schiller and Najjar did observe a more graded pattern of medication failure, with a minority of patients successfully achieving seizure freedom with new AEDs after failing two agents (Schiller and Najjar, 2008). Also, as the authors note, randomized-controlled trials of surgical vs. medical treatment in intractable TLE have demonstrated poor response rates to continued AED therapy alone (Engel et al., 2012; Wiebe et al., 2001). While the authors discuss the “running down phenomenon” – a term introduced by Rasmussen to describe post-operative improvement in seizures after initial surgical failure (Rasmussen, 1970) – the opposite is more commonly described, namely late seizure recurrence after early post-operative seizure freedom (de Tisi et al., 2011; Najm et al., 2013).

Ryzí et al. should be applauded for both excellent surgical results, and for their critical examination of surgical failures in the treatment of intractable focal epilepsy. The authors close their discussion with a call for prospective investigation into failed epilepsy surgeries. Given that seizure freedom is the greatest predictor of quality of life in this patient population, continued optimization of epilepsy surgery outcomes represents a critical goal.

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