

IMPACT OF EPILEPSY SURGERY ON DEVELOPING MINDS: HOW DO WE WEIGH THE CONSEQUENCES?

Cognitive Function in Preschool Children after Epilepsy Surgery: Rationale for Early Intervention

Freitag H, Tuxhorn I

Epilepsia 2005;46(4):561–567

PURPOSE: The detrimental effect of frequent early seizures on the cognitive potential of children is a significant clinical issue. Epilepsy surgery in childhood offers a good prognosis for seizure control and improved developmental outcome. We studied the postoperative outcome and the developmental velocity after surgery and analyzed risk factors for developmental delay in 50 consecutive preschool children treated surgically for severe epilepsy at ages 3 to 7 years.

METHODS: Pre- and postoperative developmental quotients (DQs) were analyzed with analysis of variance; stepwise linear regressions were performed on preoperative DQs and on a difference score between post- and preoperative DQs to determine risk factors for preoperative development and factors influencing postoperative development.

RESULTS: Of the 50 patients, 70% were retarded, with IQ <70; 16% were of average intelligence, with IQ ranging from 85 to 115. Age at seizure onset and extent of lesion were predictive variables for preoperative cognitive development. Six to 12 months after surgery (early post-

operative phase), 66% were seizure free (Engel outcome class I), 26% had substantial to worthwhile seizure reduction (classes II and III), and 8% were unchanged (class IV). Forty-one (82%) children showed stable velocity of development; three children showed gains of 15 IQ points; three had developmental decline (loss of 10 IQ points), which was transient in two children; and three children moved from not assessable to assessable. At last follow-up (6 months to 10 years after surgery), 11 children showed IQ/DQ gains of 15 IQ points. Gains in IQ were observed only in seizure-free children and were stable over time. Shorter duration of epilepsy was significantly associated with a postoperative increase in DQ.

CONCLUSIONS: (a) Substantial global mental delay is common in young children treated for epilepsy with surgery; (b) in most patients, postoperative development proceeded at a stable velocity; (c) catch-up development may occur but only in seizure-free patients; (d) substantial cognitive losses were noted in only one child; and (e) early seizure control stabilized developmental velocity in this patient cohort.

COMMENTARY

When deciding whether to proceed with epilepsy surgery, parents are universally concerned about the potential cognitive and behavioral affects on their child. The hope for improved function with removal of the nociferous cortex (1) pushes family and caregivers toward a decision for surgery, while the fear of cognitive losses results in surgical delays. Published series detail the prospect for either worsening or improvement, but many of these studies are limited by their methodology or scope (2–7). Common limitations include small sample size, lack of standardized testing, inadequate follow-up, and failure to account for potential risk factors for cognitive changes.

In the present study, Freitag and colleagues found that most preschool children continued along the same develop-

mental path that they were on preoperatively, while a minority of patients eventually made developmental gains. The finding is important to epilepsy specialists who care for young children. Although parents of preschool children (who are often just beginning to realize the extent of their child's cognitive problems) are understandably very concerned about developmental issues, preoperative counseling has been limited by the lack of prior studies in this age group. In their assessment of the effect of surgical timing on cognitive outcomes, the authors appropriately account for potentially confounding factors. The analysis is limited, to some extent, by the severe cognitive dysfunction making absolute quantification of cognitive deficits impossible in many of the patients. Nevertheless, the cohort is likely representative of young children undergoing surgery at most tertiary centers.

The tools used for analysis in this study are sweeping measures of development and cognition. The Bayley Scales of Infant Development I and II as well as the McCarthy Scales of

Children's Abilities were used in the multivariate analysis. These tests include a broad sample of cognitive and motor tasks. When children scored below 50 on IQ testing, ICD-10 criteria, such as cognitive testing, mobility, and continence were used to classify children as either moderately, severely, or profoundly retarded. It is certainly possible that patients remained stable or improved by these broad measures after the initial assessment, despite suffering limited neuropsychological deficits, such as language or visual-spatial disturbances. Prior studies that assessed older children undergoing temporal lobectomy suggest that the risk for focal cognitive deficits in children is lower than for adults, but still significant (8,9). Assessment of isolated deficits would have been complicated in this group of children, given the variable nature of the surgeries as well as the young age and prominent preoperative cognitive dysfunction of the patients. Practically speaking, the Bayley and McCarthy scales are probably reasonable measures of the day-to-day function that parents can expect from their children after surgery.

It may be comforting for parents to know that all but two of the children who initially lost ground, with time, caught up to their preoperative baseline, usually by 2–3 years after surgery. The authors note that this subset of patients had good seizure control after surgery, but they do not speculate that the improved seizure control was the reason for the eventual developmental improvement. Although statistical analysis on the two patients who worsened after surgery is not feasible, it would have been helpful if the authors had commented in greater detail on their clinical course. For example, these two patients, who worsened and did not eventually return to baseline developmental levels, had tumors. Were the tumors completely removed? Was radiotherapy used?

It is especially interesting that patients were much more likely to exhibit improvement after several years than at 6–12 months. The authors imply that seizure control was likely the reason for continued improvement, since improvement was noted only in patients who became seizure-free. On the basis of the multivariate analysis, we know that the underlying pathology and preoperative cognitive function did not predict improvement. To shed light on potential factors that might account for improvement in this group, it would have been interesting if the authors had provided information on pertinent events that transpired in the years after surgery. For example, did the patients' seizure control allow for adjustments in their medication regimens? Did the seizure improvements allow the child to move into an improved educational environment?

On the basis of their finding that the duration of epilepsy is negatively related to the probability of cognitive improvement, the authors conclude that surgery should be considered as an appropriate early intervention for these patients. Their findings are in keeping with those of other investigators (2). Whether this association is truly a causal relationship is uncertain, as the authors note. Similar questions in adults have led to a multi-

center trial to assess the effects of early surgical intervention. It should be remembered that the multivariate analysis in the Freitag et al. study included only patients performing well enough on standardized tests to allow for valid scores (approximately the top half). Thus, the relatively modest association between short epilepsy duration and cognitive improvement after surgery may not be present in preschool children with more severe cognitive dysfunction.

So how will these findings help in counseling parents of preschool children who need epilepsy surgery? According to this study, parents of young children can be told that the risk for global cognitive decline is very low and that some young children who undergo successful operations will eventually have a modest improvement, especially if they have not had a protracted course. Certainly, the hope for cognitive improvement should not be overstated. Parents can be informed that if improvement occurs, it may not manifest for years. Perhaps, the most important fact that the clinician can offer parents is that developmental decline, especially permanent decline, is extremely rare. Thus, regardless of hopes and fears regarding potential cognitive outcomes, the decision whether or not to perform surgery should not be centered on this issue.

by Paul A. Garcia, MD

References

1. Penfield W, Jasper H. *Epilepsy and the Functional Anatomy of the Human Brain*. Boston: Little, Brown and Company, 1954.
2. Bourgeois M, Sainte-Rose C, Lellouch-Tubiana A, Malucci C, Brunelle F, Maixner W, Cinalli G, Pierre-Kahn A, Reiner D, Zerah M, Hirsch JE, Goutieres F, Aicardi J. Surgery of epilepsy associated with focal lesions in childhood. *J Neurosurg* 1999;90(5):833–842.
3. Bjornaes H, Stabell KE, Henriksen O, Roste G, Diep LM. Surgical versus medical treatment for severe epilepsy: Consequences for intellectual functioning in children and adults. A follow-up study. *Seizure* 2002;11(8):473–482.
4. Pulsifer MB, Brandt J, Salorio CF, Vining EP, Carson BS, Freeman JM. The cognitive outcome of hemispherectomy in 71 children. *Epilepsia* 2004;45(3):243–254.
5. Smith ML, Elliott IM, Lach L. Cognitive, psychosocial, and family function one year after pediatric epilepsy surgery. *Epilepsia* 2004;45(6):650–660.
6. Wyllie E, Comair YG, Kotagal P, Raja S, Ruggieri P. Epilepsy surgery in infants. *Epilepsia* 1996;37(7):625–637.
7. Korkman M, Granstrom ML, Kantola-Sorsa E, Gaily E, Paetau R, Liukkonen E, Bowman PA, Blomstedt G. Two-year follow-up of intelligence after pediatric epilepsy surgery. *Pediatr Neurol* 2005;33(3):173–178.
8. Westerveld M, Sass KJ, Chelune GJ, Hermann BP, Barr WB, Loring DW, Strauss E, Trenerry MR, Perrine K, Spencer DD. Temporal lobectomy in children: Cognitive outcome. *J Neurosurg* 2000;92(1):24–30.
9. Miranda C, Smith ML. Predictors of intelligence after temporal lobectomy in children with epilepsy. *Epilepsy Behav* 2001;2(1):13–19.