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Risks and benefits of epilepsy surgery in a pediatric population: Consequences for memory and academic skills

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ABSTRACT

We examined benefits and risks for memory and academic functioning associated with epilepsy surgery in a pediatric population. A total of 46 patients with intractable seizures and a single seizure focus were divided into four groups according to focus localization: right temporal, left temporal, frontal, and parietal/occipital region. Pre- and postsurgery performance measures were compared across groups and with a fifth group of patients that had intractable seizures but did not undergo surgery. Both groups with temporal lobe epilepsy showed significant declines in memory test scores, while performance of the group with frontal lobe epilepsy improved. These changes were mirrored in parental reports of everyday memory. Consistent with other pediatric studies, no lateralized material-specific declines in the groups with temporal lobe epilepsy were found. When memory improved, the improvement was associated with decreases in seizure frequency and the number of anticonvulsant medications. Presurgical performance was the best predictor of declines in memory test performance. Deterioration of academic test scores in the group that did not have surgery exemplified a potential risk of living with seizures and antiepilepsy medication.

1. Introduction

Epilepsy syndromes have been associated with a wide range of cognitive problems that include decreased overall intelligence, memory, and executive functions. Cognitive dysfunction may arise from the following: (a) disruption caused by the seizure events themselves, (b) iatrogenic effects of antiepileptic drugs (AEDs), or (c) underlying neuropathology that produces the seizures [1]. Surgical intervention is associated with cognitive risk for adults, although the risks for the pediatric population are less well-known [2]. Much of the extant research has focused on the risk for loss of cognitive function. There may, however, be cognitive benefit due to reduced seizure burden and reduced need for anticonvulsant medication [3]. Any reasoned decision about surgical intervention should involve an estimate of both the potential functional risks and the potential benefits of the procedure.

Cognitive outcome data have come primarily from studies of temporal lobectomy performed on adults. These studies indicate a clear risk for a decline in the ability to learn new verbal information after anterior temporal lobectomy in the language-dominant hemisphere, with less certain risk for diminished learning of visual–spatial material following lobectomy in the nondominant hemisphere, although variability related to moderating variables has been reported [4–6]. There have been fewer studies of the impact of temporal lobectomy on memory in the pediatric population, and the available findings have been less consistent. Many pediatric studies of temporal lobectomy have reported either no change in memory function from pre- to postassessment [7–9] or improvements in function [9–14]. Even when pediatric studies have found a significant decline in memory following surgery, the results have not shown the lateralized, material-specific declines that have been reported with adults [9,15–18]. Studies with adults also suggest that the effects of a temporal lobectomy are more evident on tests that assess learning of semantically unrelated material, particularly under the demands of delayed recall [4].

Though some surgical interventions for epilepsy involve frontal lobe resections, the cognitive consequences of this type of resection have not been as well-studied as have temporal lobe resections in either adults or younger patients. There is reason to believe that frontal lobe resections would result in memory deficits, although the characteristics of those memory problems may differ from those of mesial temporal lobe

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resections [19]. Poor memory test performance after a frontal lobe resection is more likely to reflect executive deficits such as inefficient encoding or search strategies as opposed to the failure to consolidate information that is commonly seen after a temporal lobe resection. The existing data are too limited to warrant clear conclusions about decline in memory following frontal lobe resections [7,20].

Because most studies of the cognitive consequences of epilepsy surgery have relied exclusively on standardized psychological tests to assess outcomes, little is known about whether improvements or declines in test performance after surgery are noticed in a patient's day-to-day activities, which typically include everyday memory and learning as well as academic performance. The impact of temporal lobe resections on subjective assessments of memory has been investigated with adults [21] and younger patients [22,23], but these studies have not found either positive or negative effects of temporal lobectomies on subjective reports of memory. Likewise, limited attention has been given to the impact of surgery on the acquisition of academic skills [9,15,24]. There is evidence that reading and math skills are impacted by memory in young people with epilepsy and, therefore, may be affected by a decline in memory skills [25]. Conversely, one might expect better academic test performance with increased alertness due to reduction of seizure frequency and anticonvulsant medication. Again, the available are too limited to draw any definitive conclusions.

The current study was conducted to help clarify the potential risks and benefits of surgery for memory and scholastic functions in pediatric patients. To this end, we asked a number of specific questions: (1) Are there nonspecific effects of epilepsy surgery, regardless of resection site? We did not have an explicit hypothesis in this regard, given a balance of reasons to expect changes in either direction. (2) Are patients who have frontal and temporal lobe resections particularly vulnerable to decline in memory function? We expected that these two groups would experience more declines than would patients with other resection sites. (3) Are functional risks greater with temporal lobe resections than with frontal lobe resections? We expected that the groups with temporal lobe epilepsy would exhibit more declines than patients with frontal lobe resections given that most memory tests require the types of skills supported by the hippocampal memory system and that these declines would be most evident on delayed recall memory tests. (4) Is there evidence of lateralized, material-specific memory deficits after temporal lobe resections? (5) What are the consequences, if any, of different resections for academic skills? As noted above, the extant literature offers little reason to propose specific hypotheses with respect to this question.

To answer these questions, we examined pre- and postsurgical memory functions in four groups of patients with intractable seizures who underwent a focal resection: a group with left temporal lobe seizures, a group with right temporal lobe seizures, a group with frontal lobe seizures, and a group with occipital/parietal seizures. We also included a control group with intractable seizures who were evaluated twice without intervening surgery. In addition to objective memory tests, we expanded our outcome measures to include assessments of parental perceptions of everyday memory and assessment of academic skills, which presumably would be impacted by any change in memory function. Finally, we examined the impact of a number of specific demographic and seizure-related factors that might further explain either improvements or declines in function.

2. Methods

2.1. Participants

Participants in this study were selected from the pool of pediatric patients who received baseline neuropsychological testing between 2005 and 2012 as part of an evaluation to determine suitability for surgical intervention for intractable epilepsy at Texas Children's Hospital in Houston. Seizures in all patients in this pool had not responded to trials of at least two anticonvulsants. Seizure foci and brain pathology were identified by prolonged video-EEG monitoring, by MRI, and, for some patients, by positron emission tomography or subdural grid recordings. Some parents were Spanish speaking, but patients were invited to participate if they were fluent in English and were being educated in classes conducted in English.

Only patients with a Full-Scale IQ of 70 or greater, and aged between 6 and 18 years at the time of initial evaluation, were considered for participation. Patients were excluded from study participation if they had multiple seizure foci or a progressive neurological disorder. After these exclusions, the initial baseline sample consisted of 102 eligible patients, 75 of whom had surgery. Of the 102 eligible patients, 56 returned for a second evaluation and were compared with the 46 patients who did not return. Returning and nonreturning patients did not differ significantly in the first (baseline) assessment on any of the demographic, seizure-related, or cognitive measures used in the study.

The final sample of 56 patients was classified into four surgical groups and one nonsurgical group. Patients in each of the surgical groups underwent surgery between the first and second neuropsychological assessments. The groups and group sizes were as follows: left temporal lobe epilepsy (L-TLE, $n = 16$), right temporal lobe epilepsy (R-TLE, $n = 12$), frontal lobe epilepsy (FLE, $n = 10$), and parietal or occipital lobe epilepsy (Other, $n = 8$). With the exception of one patient in the group with R-TLE, surgical intervention for the two groups with temporal lobe epilepsy involved mesial temporal structures. The fifth group comprised 10 nonsurgical control patients with various seizure foci (R-TLE, $n = 1$; L-TLE, $n = 3$; FLE, $n = 6$). Some patients within this nonsurgical group eventually received surgery, and some, consequent to the family's decision, did not. The time between evaluations for the patients who did not receive surgery ranged from 1 to 5 years with an average of 2.9 years.

Etiologies within the group with L-TLE were cortical dysplasia ($n = 5$), tumor ($n = 4$), mesial temporal sclerosis (MTS, $n = 4$), hydrocephalus ($n = 1$), MTS plus cortical dysplasia ($n = 1$), and MTS plus tumor ($n = 1$). Etiologies within the group with R-TLE included cortical dysplasia ($n = 2$), tumor ($n = 5$), MTS ($n = 2$), cortical dysplasia plus MTS ($n = 2$), and neurocysticercosis ($n = 1$). Etiologies within the group with FLE included cortical dysplasia ($n = 7$), tumor ($n = 2$), and encephalitis/infection ($n = 1$). Etiologies of the Other group consisted of cortical dysplasia ($n = 6$) and tumor ($n = 2$), and etiologies of the No Surgery control group consisted of cortical dysplasia ($n = 5$), tumor ($n = 1$), and MTS ($n = 1$). Etiology was unknown for 3 patients in the No Surgery group.

2.2. Procedure

Patients were referred for a neuropsychological evaluation as part of a routine workup for epilepsy surgery. All patients were either referred or invited to return for a second assessment irrespective of whether they previously had surgery. A standard neuropsychology test battery was administered at both visits. Parents completed the Everyday Verbal Memory Questionnaire and a questionnaire concerning demographic and seizure-related information at each visit. Seizure frequency was assessed over the three months prior to each assessment. Informed consent from the parent and assent from the child were obtained at the time of the first visit. The study was approved by the Institutional Review Board for Baylor College of Medicine.

2.3. Measures

2.3.1. Full-Scale IQ

Intellectual functioning was assessed with an age-appropriate version of the Wechsler intelligence test: Wechsler Intelligence Scale for Children — 4th Edition [26], Wechsler Adult Intelligence Scale — 4th Edition [27], or Wechsler Adult Intelligence Scale — 3rd Edition [28].