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Academic skills in the long term after epilepsy surgery in childhood

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ABSTRACT

Objective: We evaluated the progression of academic skills in a cohort of patients who underwent, or were considered for, epilepsy surgery in childhood, four to eleven years before. The few existing studies that have evaluated cognitive function in the long term after surgery have examined intelligence and memory.
Method: Participants were 97 patients with childhood-onset intractable epilepsy; 61 had undergone resective epilepsy surgery. Participants completed standardized tests of reading, spelling, arithmetic, and intelligence at baseline and, on average, 7 years after. Surgical patients were additionally assessed one year postsurgery.
Results: At baseline and long-term follow-up, 61% and 69% of patients, respectively, scored at least one standard deviation below normative data in at least one academic domain. Evaluation of change over time while controlling for IQ showed that arithmetic scores were lower at long-term follow-up in comparison with those at baseline among all patient groups, whereas reading and spelling scores remained unchanged. Few advantages were associated with seizure control. Multiple regression analyses found that older age at surgery, cessation of antiepileptic medications, improved IQ, and low baseline scores were independently associated with improvement in some academic domains among all patient groups.
Conclusion: We found that arithmetic scores were lower at long-term follow-up, suggesting a lack of ongoing development or deterioration in skills. Reading and spelling scores remained stable suggesting that patients made gains in abilities at a rate expected for their increase in age; this finding contrasts with recent short-term outcome studies identifying significantly lower scores over time in these areas.

1. Introduction

Low academic achievement – performance significantly below that of same-aged peers – in at least one of the core domains of reading, reading comprehension, spelling, and arithmetic, is prevalent in 62 to 72% of children with epilepsy [1–3]. Although such difficulties may be especially common among children with chronic seizures, there is a relatively high risk of academic problems among children with recent onset, uncomplicated, well-controlled, or "benign" epilepsies [4–7]. Low academic achievement has been associated with a myriad of direct and indirect factors, including epilepsy factors, such as seizure severity, age of onset, and side effects of medications and psychosocial factors, such as family environment, self-esteem, parental anxiety, attitudes towards epilepsy, and difficulties with school attendance [1,2,8–11]. In addition, cognitive deficits can contribute to poor academic performance and may additionally interfere with the development and attainment of academic skills [8,10,11]. Nonetheless, academic deficits can be differentiated from more generalized impairments in intelligence and cognition [2,7]. Furthermore, underachievement, defined as performance below what is expected based on the child's IQ, is prevalent in 28 to 48% of children with epilepsy [1–3].

Few studies have evaluated academic achievement following pediatric epilepsy surgery. Those studies that have examined academic skills have focused on short-term outcomes (on average one year after surgery), finding no significant postoperative change [12,13] or lowered scores in specific domains, such as reading [14], or across multiple domains, such as reading, arithmetic, and spelling [3]. Seizure control has not been found to be a significant contributor in these short-term outcome studies. The findings of lower scores after surgery in the latter study may be a result of the larger sample size of surgical patients (136 children) in comparison with those in previous reports which used fewer than 40 surgical patients. In terms of long-term follow-up studies of pediatric epilepsy surgery, the few studies that have evaluated cognitive outcomes have reported on intellectual [15–18] and memory functioning [18,19]. Other aspects of cognition, including academic achievement, have yet to be evaluated in the long term. Therefore, it is unknown whether academic skills improve or worsen in the long term following epilepsy surgery in childhood.

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The current study addressed this knowledge gap using a large sample of surgical patients evaluated at baseline and four to eleven years after epilepsy surgery in childhood. In addition, we evaluated, at similar time points, a group of patients with intractable childhood epilepsy who did not undergo epilepsy surgery. Comparing the outcomes of patients who underwent surgery with those who continued medication management allows for the examination of the possible causes of change following epilepsy surgery, whether it is a result of ongoing development of the child, seizure control, or the surgical intervention itself [12]. We evaluated academic skills using standardized measures of reading, spelling, and arithmetic and hypothesized that patients with controlled seizures would show an advantage in the long term.

2. Methods

2.1. Participants

All patients underwent evaluations to determine surgical candidacy between 2002 and 2009 at the Hospital for Sick Children in Toronto, Ontario, Canada. Prior to surgical evaluation, all patients had been unable to achieve adequate seizure control from at least two trials of antiepileptic drugs (AEDs). Patients who subsequently underwent surgery formed our surgical group; these patients had a clear unilateral seizure focus which did not involve the eloquent cortex. Exclusion criteria for the surgical group included hemispherectomy or corpus callosotomy procedures as these individuals tend to have marked neurological impairment and these procedures may be performed for reasons other than complete seizure control, such as alleviating drop attacks. Patients who declined surgery, or were not surgical candidates, formed our nonsurgical comparison group; patients with epilepsy syndromes that would not normally be treated with surgery or epilepsy associated with neurodegenerative disorders were excluded.

At long-term follow-up, 152 individuals (92 surgical) were identified as possible candidates to participate in the study; 17 (6 surgical) could not be contacted, 2 (1 surgical) were deceased, and 36 (24 surgical) declined or were unable to participate because of distance. In sum, 97 individuals (61 surgical, 36 nonsurgical) completed a neuropsychological assessment at long-term follow-up. Participants were classified not only in terms of their surgical status but also in terms of whether or not their seizures had been controlled in the year prior to their participation in the study. When possible, patients who did not wish to participate were asked whether they had had seizures in the preceding year and if they were taking any AEDs.

2.2. Study design

As part of routine care, all patients had completed a neuropsychological assessment during the evaluation for surgical candidacy (baseline assessment), and surgical patients were additionally assessed one year following surgery (short-term follow-up). The baseline (for all participants) and short-term follow-up data (for the surgical patients) were extracted from patients' clinical records. For a variety of reasons (e.g., time constraints, poor cooperation), some patients had not completed all academic tests at baseline and/or short-term follow-up; for this reason, data were not available for all participants on all tasks. Four to eleven years after surgery or after the baseline assessment for nonsurgical patients, patients were contacted and offered a similar neuropsychological assessment as part of a larger project examining various cognitive, affective, behavioral, vocational/educational, and quality-of-life outcomes following surgery [17,20–23].

The study was approved by the Research Ethics Board of the Hospital for Sick Children, and informed consent/assent was obtained from patients and/or their parents. All cognitive assessments were conducted by experienced psychometricians or trained research assistants. Study data were managed and stored using REDCap [24].

2.3. Neuropsychological assessment

At each assessment, academic skills (single word reading and spelling and arithmetic) were measured using standardized tests: the Wechsler Individual Achievement Test (WIAT or WIAT-II) [25,26], the Wechsler Fundamentals Academic Skills (WFAS) [27], the Wide Range Achievement Test [28], or the Woodcock–Johnson Test of Achievement [29]. The WFAS was used almost exclusively during the long-term follow-up assessment for children and young adults; such homogeneity could not be ensured at baseline and short-term follow-up assessments since these assessments were completed for clinical purposes. Intelligence was assessed with the age-appropriate version of the Wechsler Intelligence Scales at each time point [30–32]. The results of the academic skills and intelligence tests are presented as standard scores (mean: 100; standard deviation: 15).

2.4. Statistical analyses

In examining demographic and epilepsy-related variables among the four patient groups, 2 (surgical status) × 2 (seizure status) analyses of variance (ANOVA), and χ^2 or Fisher's exact test were utilized. Change over time was evaluated with linear mixed effects models, using unstructured covariance matrix and a backwards selection model, such that higher order interactions were sequentially removed from the model if $p > .05$. Since all nonsurgical patients did not have data for the short-term follow-up, analyses were performed twice; first among surgical patients using seizure status and time (baseline, short-term and long-term follow-up) as fixed effects and second among all patients using surgical status, seizure status, and time (baseline and long-term follow-up) as fixed effects. Intelligence quotient was used as a time-varying covariate in each analysis. Sidak corrections were used for pairwise comparisons, and significant interactions were followed with simple effects analyses. We also evaluated change at the individual level using χ^2 or Fisher's exact test, as appropriate. In addition, to identify demographic and epilepsy-related variables associated with change in academic achievement from baseline to long-term follow-up, multiple linear regressions, using the enter method and pairwise deletion for missing variables, were conducted.

3. Results

Surgical patients who did not participate did not differ from participating surgical patients in baseline demographic, seizure, and cognitive variables and follow-up seizure status and AED use (all p values >.05). Similarly, there were no significant differences on these variables between nonsurgical patients who did and did not participate.

Among participating patients, the mean follow-up period was 7.04 years (SD: 2.22; range: 4.00 to 11.83 years), and for the surgical group, the mean age at surgery was 13.03 years (SD: 4.49; range: 4.25 to 18.83 years). Age at surgery was positively correlated with age at seizure onset ($r = .48$, $p < .001$). The proportions of surgical (54%) and nonsurgical (39%) patients who had no seizures in the 12 months preceding the long-term follow-up were not statistically different ($\chi(1) = 2.10$, $p = .15$). Table 1 shows the demographic and epilepsy characteristics of the four patient groups: 1) surgical seizure-free, 2) - surgical with seizures, 3) nonsurgical seizure-free, and 4) nonsurgical with seizures. Comparing the two subgroups who were seizure-free, it was found that those who had undergone epilepsy surgery had a higher proportion of the follow-up period seizure-free, compared with patients who did not undergo surgery- 92% and 51%, respectively ($p < .001$). Seizure-free patients had a shorter duration of life with seizures ($p < .001$) compared with those of other patient groups. Surgical seizure-free patients had a lower proportion of life with seizures ($p < .028$) and used fewer AEDs at long-term follow-up ($p < .001$) compared with those of other patient groups. A larger proportion of nonsurgical patients with continued seizures had a