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Predictors of intellectual functioning after epilepsy surgery in childhood: The role of socioeconomic status

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ABSTRACT

Objective: The objective of this study was to evaluate the association between socioeconomic status and intellectual functioning in children with medically refractory epilepsy, before and after resective epilepsy surgery. Family environment is a strong contributor to cognitive development in children and has been recently shown to play a significant role in intellectual outcome after surgery in children with epilepsy.
Methods: One hundred children who had undergone resective epilepsy surgery and completed preoperative and postoperative assessments of IQ as part of clinical care were included in the study. We evaluated the impact of epilepsy-related variables, income quintile, and residence location on IQ.
Results: Greater improvements in IQ after surgery were associated with an older age at surgery ($\beta = .235$, $p = .018$). Higher IQ scores at follow-up were associated with an older age of seizure onset ($\beta = .371$, $p < .001$), older age at surgery ($\beta = .356$, $p < .001$), unilobar epileptogenic focus ($\beta = .394$, $p < .001$), and mesial temporal sclerosis ($\beta = .338$, $p = .001$) or tumor ($\beta = .457$, $p < .001$) in comparison with malformation of cortical development; age at seizure onset did not remain as a significant predictor in multivariable regression analysis. Income quintile, residence location, seizure control, and antiepileptic medication use were not significant predictors.
Conclusions: Epilepsy-related variables were the strongest predictors of IQ and postoperative change in IQ. We were unable to identify a significant association between IQ and socioeconomic status. Future research should evaluate the impact of multiple aspects of family environment.

1. Introduction

Although there is a huge range of variability in intellectual functioning among children with epilepsy, spanning from <1st percentile to >99th percentile, children with epilepsy are at a high risk of cognitive impairment [1]. Population-based studies find that the distribution of intelligence quotient (IQ) scores are negatively skewed, where 24–35% of children with epilepsy have an IQ < 50 and 21–40% have an IQ < 70, in comparison with <0.1% and 2% of the general population, respectively [2–4]. Poor cognitive functioning represents a main area of concern for children with epilepsy and their parents [5] and is associated with a number of poor outcomes including quality of life and long-term educational/vocational outcomes [6,7]. Previous studies have extensively focused on identifying patient- and epilepsy-related variables that contribute to deficits in intellectual functioning, frequently finding an association with age at seizure onset, etiology, number of antiepileptic drugs (AEDs), duration of epilepsy, and frequency of seizures [3,8,9].

Little is known about the contributing role of family environment on intellectual functioning among children with epilepsy, despite a well established relationship in the general population [10–12]. Of the few studies that have evaluated the relationship between family environment and intellectual functioning, parental education has been associated with higher IQ scores but is not protective against cognitive declines [13], whereas socioeconomic status has not been associated with IQ [2]. Little is known about the role of family environment on cognitive development after epilepsy surgery. Meekes et al. [14] reported that higher parental education was associated with greater improvements in IQ following epilepsy surgery in childhood, suggesting that, following surgery, the child may develop in accord with what would be expected based on the education of their parents. It is important to evaluate whether other aspects of the family environment, which are amenable to intervention, also contribute to cognitive development after epilepsy surgery in childhood. Past studies that have evaluated postoperative intellectual functioning have focused on patient- and epilepsy-related variables and

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found few changes in the short term [15]. In this study, we investigated one aspect of the family environment, that of socioeconomic status. The aim was to evaluate whether socioeconomic status, operationalized as family income and residence location, was associated with change in IQ following resective epilepsy surgery in childhood, as well as preoperative and postoperative IQ scores.

2. Methods

2.1. Patients

We performed a single-center, retrospective, health record analysis of all patients that underwent resective epilepsy surgery at 18 years of age or younger between January 1st, 2001 and December 31st, 2013 at the Hospital for Sick Children. Exclusion criteria included multiple surgeries, nonresective surgeries such as corpus callosotomy and vagus nerve stimulator insertions, or hemispherectomies, as these individuals tend to have marked neurological impairment. As part of clinical care, patients had undergone a neuropsychological assessment preoperatively and, on average, one year after surgery. There were 235 children meeting study criteria; however, some patients were excluded because of missing IQ scores; 15 were too young for IQ testing at the time of surgery, 65 did not have preoperative and postoperative IQ scores, 45 did not have postoperative IQ scores, and 10 did not have preoperative scores. There were 100 children who met study criteria and were included in the current study.

2.2. Study measures

This study was approved by the Research Ethics Board of the Hospital for Sick Children, and study data were managed and stored using REDCap [16]. Intelligence quotient scores, assessed using the Wechsler intelligence scales [17,18], are presented as standard scores (mean: 100; standard deviation: 15). The intelligence testing was completed by a trained psychometrist as part of clinical care preoperatively and, on average, one year after surgery. Patient- and epilepsy-related variables were obtained from the patients' medical charts including postal code, sex, age at seizure onset, age at surgery, etiology, duration of seizures from onset to epilepsy surgery, number of preoperative and postoperative antiepileptic medications, side and location of surgical resection, preoperative seizure frequency, and postoperative seizure outcome. Etiology was classified as malformation of cortical development, mesial temporal sclerosis, tumor, vascular, or other. Postoperative seizure outcome was classified using ILAE classification [19]. We compared patients who were completely seizure-free with no auras (ILAE 1) with patients with persistent seizures (ILAE 2–6); we also compared patients who showed postoperative seizure improvement (ILAE 1–4) with patients that showed no improvement, classified as less than 50% reduction in seizures (ILAE 5–6).

Residence location and income were determined by linking the patient's postal code with Statistics Canada Census data from 2011 [20]. Since few patients resided in smaller population centers (12 in rural areas, 9 in small population centers [1000 to 29,999 people], and 8 in medium population centers [30,000 to 99,999]), residence location was categorized as large urban population center (≥100,000 people) or smaller population center (<100,000 people). Household income was inferred from dissemination area income levels; dissemination area is the smallest geographic unit from Census Canada data comprised of one or more neighboring blocks of houses. Dissemination area income levels are based on the median income per single-person equivalent in a dissemination area obtained from the 2011 census [21]. Income levels are ranked and assigned by Census Canada to one of five groups (approximately 20% of the population in each group) ranked from lowest to highest to generate income quintiles.

2.3. Statistical analyses

Analyses were conducted using IBM SPSS Statistics version 23.0 (IBM Corp. Armonk, NY, U.S.A.). Simple linear regressions were used to evaluate the relationship between patient- and epilepsy-related variables with change in IQ, postoperative IQ, and preoperative IQ. Next, significant predictor variables were evaluated using multivariable linear regression, using the enter method. Since preoperative IQ and postoperative IQ in the short term following surgery are similar and associated with the same epilepsy-related variables, we did not include preoperative IQ as a predictor of postoperative IQ in multivariable regressions in order to maintain a focus on the patient-, epilepsy-, and socioeconomic status-related predictors of postoperative IQ and change in IQ.

3. Results

One hundred children (mean age at surgery: 12.86 ± 4.17 years; range: 3.59 to 18.53 years) were included in the study; 47 (47%) were female. The age of epilepsy onset ranged from 0.12 to 17.00 years, and the duration from epilepsy onset to surgery ranged from 0.28 to 17.99 years. The mean follow-up period from surgery to the postoperative IQ assessment was 1.15 years and ranged from 6 months to 3.40 years (only two patients were seen after two years, and only 3 patients were seen in less than 9 months). The mean preoperative IQ was 84.13 ± 17.95, ranging from 36 (<0.01st percentile) to 120 (91st percentile), and the mean postoperative IQ was 82.61 ± 17.84, ranging from 36 (<0.01st percentile) to 114 (82nd percentile). There were six patients that declined in at least one standard deviation postoperatively, two patients that improved in at least one standard deviation, and 92 patients that scored within one standard deviation of their preoperative score. Accordingly, preoperative IQ was a strong predictor of postoperative IQ ($B = 0.90$ (95% CI: 0.81; 0.98), $\beta = .904$, $p < .001$). Table 1 presents descriptive data of the patient-, epilepsy-, and socioeconomic status-related variables for all participants. Independent samples *t* tests or χ^2 analyses indicated that there were no significant differences (all *p* values >.12) in these variables and preoperative IQ scores among the children who were included in the study and those who were not included because of missing IQ scores.

Simple linear regressions predicting change in IQ showed that an older age at surgery was significantly associated with greater improvement in IQ ($\beta = .235$, $p = .018$). Other variables examined, including seizure status, income quintile, and residence, were not significant predictors (see Table 2). Simple linear regressions predicting postoperative IQ showed that higher IQ scores were associated with an older age of seizure onset ($\beta = .371$, $p < .001$), older age at surgery ($\beta = .356$, $p < .001$), unilobar epileptogenic focus ($\beta = .394$, $p < .001$), and mesial temporal sclerosis ($\beta = .338$, $p = .001$) or tumor ($\beta = .457$, $p < .001$) in comparison with malformation of cortical development; see Table 2. In multivariable regression, all predictors remained significant ($.229 \leq \beta \leq .341$, $p \leq .016$) with the exception of age at seizure onset ($p = .059$; see Table 3). With respect to preoperative IQ, univariable and multivariable linear regression results were similar to analyses predicting postoperative IQ (see Tables S1 and S2). The assumptions of residual normality, linearity, and homoscedasticity were evaluated in the multivariable regression models, and no violations were detected. In addition, among the predictor variables, there was no evidence of multicollinearity or influential outliers.

There was a trend ($p = .054$) between lower income quintile and higher postoperative IQ scores in simple linear regression; therefore, an exploratory set of analyses was conducted to compare the patients in the highest and lowest income quintiles. Independent samples *t* tests, χ^2, or Fisher's exact test compared these groups across the patient- and epilepsy-related variables presented in Table 1. A greater number of patients in the lowest income quintile had a unilobar epileptogenic focus (94%), in comparison with patients in the highest income quintile