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# Parent-reported symptoms of ADHD in young people with epilepsy before and two years after epilepsy surgery

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ABSTRACT

The aim was to compare parent-reported symptoms of attention-deficit/hyperactivity disorder (ADHD) before (baseline) and two years after pediatric epilepsy surgery (follow-up). The parents of 107 children who underwent epilepsy surgery completed surveys including the Conners 10-item scale at baseline and follow-up. Changes in scores between baseline and follow-up were compared using paired sample *t*-test. Factors associated with changes in scores were analyzed using linear regression. Features of ADHD were significantly reduced at follow-up ($p < 0.001$). Items with the greatest reduction were items focusing on core aspects of the diagnostic criteria for ADHD. Fewer children were in the at-risk range for ADHD on the Conners 10-item scale at follow-up but this did not reach statistical significance (49% vs. 43%; $p = 0.481$). Factors independently significantly associated with improvement in ADHD symptoms on multivariable analysis were higher baseline scores ($p < 0.001$), seizure-free status ($p = 0.029$), and right-sided surgery ($p = 0.031$). Children who undergo epilepsy surgery have a high rate of ADHD symptoms. Parent-rated symptoms of ADHD improved at 2-year follow-up after epilepsy surgery. All children undergoing epilepsy surgery should undergo assessment for ADHD at baseline and follow-up.



## 1. Introduction

Epilepsy surgery in children is successful with respect to seizure reduction and/or freedom [1] and improved quality of life [2] provided that there is appropriate selection of candidates. There is also evidence that at least some children have gains in global cognition [3,4]. The picture is less clear with regard to behavioral and psychiatric functioning. Some studies have indicated no change [5–8] while others have indicated improvements in at least some domains of behavioral functioning [9,10].

As well as recurrent unpredictable epileptic seizures, children with epilepsy are at increased risk for a range of behavioral and emotional difficulties. These difficulties often have a greater impact on health-related quality of life (HRQOL) [11,12] than the epileptic seizures. Attention-deficit/hyperactivity disorder (ADHD) is defined by Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria as a persistent pattern of inattention and/or hyperactivity–impulsivity that interferes with functioning or development [13]. It is the most frequent behavioral diagnosis in children with epilepsy [14,15] with one in three children with 'active' epilepsy fulfilling DSM-IV diagnostic criteria for a diagnosis of ADHD in a population-based sample [15]. Children with epilepsy more often have symptoms of inattention than symptoms of hyperactivity–impulsivity [16,17]. ADHD is also a common diagnosis in pediatric epilepsy surgery candidates [5,7].

In children undergoing epilepsy surgery, high rates of neuropsychiatric comorbidity have been noted both before surgery and after surgery [5–7]. In the majority of studies, follow-up times have been short, typically 12 months or less, and study samples have been small. Additionally, there are limited data on features of ADHD using standardized instruments. Knowledge of the impact of epilepsy surgery on symptoms of ADHD will add to an understanding of the broad psychosocial impact of epilepsy surgery.

The purpose of the current study was to describe parent-reported symptoms of ADHD in a sample of children undergoing epilepsy surgery. A second aim was to compare parental ratings on a standardized measure of ADHD before and two years after epilepsy surgery. A final aim was to consider factors associated with changes in parental ratings on the measures of ADHD and behavior.

## 2. Method

The study sample comprised all young people (≤19 years) who underwent presurgical evaluation from 1995 to 2014 at Queen Silvia

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Children's Hospital, Gothenburg and subsequently underwent surgery at Sahlgrenska University Hospital. Information is collected longitudinally for each patient and contains baseline information about epilepsy history, preoperative seizure types, mean monthly seizure frequency during the year preceding the presurgical investigation, antiepileptic drugs (AEDs), preoperative investigations, psychosocial data, surgical data, and histopathologic diagnoses. Two-year follow-up data cover seizure types and frequencies, AEDs, and psychosocial data.

Eligibility criteria were that the children underwent surgery as part of the epilepsy surgery program at Queen Silvia Children's Hospital in Gothenburg. Children were excluded if they were not residents of Sweden at the time of surgery.

### 2.1. Outcome measures

Parents of all children were asked to complete surveys focusing on child behavior, quality of life, and parental expectations of surgery at the time of presurgical evaluation (baseline) and two years postoperatively (follow-up). The questionnaires were distributed by the epilepsy nurse and were self-administered. Respondents did not receive payment for participating.

The parental survey included the Conners 10-item [18], which consists of ten statements for which a parent rates the child's behavior on a 4-point Likert scale, ranging from '0 — not at all true' to '3 — very much true'. The scale has been found to discriminate well between children with and without ADHD in a Swedish sample [19]. The scale constitutes a two-factor structure: a restless/impulsive behavior dimension and an emotional lability dimension — with a high correlation between the two [19,20]. With respect to cutoff scores for at-risk status for parental ratings of children, Landgren and collaborators [21] used a cutoff of 10 in their study of 6-year-old children with developmental disorders, and this cutoff is used in the current study. The Connors 10-item scale has been used in a community sample of children as young as 3 years of age [20]; although, no data was provided on the instrument's validity in this study. A validation study with 5- to 16-year-old children suggests that younger age is associated with higher scores [22]. Additionally, there is evidence that the Conners 10-item scale is less valid in students with recognized special education needs yielding a significant number of false positives and false negatives in this population [23].

### 2.2. Child characteristics

Information about the children before and two years after surgery was also collected, including age at surgery, gender, age of seizure onset, seizure frequency, use of AEDs, intellectual functioning, type of surgery, and laterality of surgery.

Seizure outcome was graded as seizure-free (seizure-free with or without auras during last year of follow-up), ≥75% reduction, 50–74% reduction, and 0–49% reduction in seizure frequency or increased seizure frequency. For patients who were not seizure-free at the two-year follow-up, the mean monthly seizure frequency in the last year of follow-up was reported. For the purposes of this study, two categories were compared: seizure-free vs. nonseizure-free equivalent to Engel Class I vs. Engel Class II to Engel V outcome.

Data on cognitive functioning were based on results of assessment using relevant Wechsler scales or in the case of low functioning children the Griffiths Developmental scales.

### 2.3. Ethics

The study was approved by the University of Gothenburg Regional Board of Medical Ethics, and informed consent was obtained from all parents.

## 3. Statistical analysis

Descriptive statistics were used to describe characteristics of the children.

Mean (M) scores are reported for Conners 10-item scale at baseline and at follow-up. Chi-Square or *t*-test analyses were carried out to compare the characteristics of the children whose parents responded and children whose parents did not respond with respect to gender, age at surgery, age of epilepsy onset, change in AEDs, change in Full Scale Intelligence Quotient (IQ) (FSIQ) score, and seizure outcome.

Changes in Conners 10-item scale scores between baseline and follow-up were tested using paired sample *t*-test. Given the uncertainty of the validity of the Conners 10-item scale in children under 6 years of age and children with moderate, severe, or profound intellectual disability the paired sample *t*-test were rerun after excluding children 5 years and under and children with an IQ score < 50. Differences between the proportions of cases (Possible/Probable) versus noncases of ADHD respectively at baseline and follow-up were calculated using McNemar's analysis. Standardized Response Mean (SRM) was calculated as the difference between mean values divided by the standard deviation of change scores; SRM magnitude was interpreted against the criteria suggested by Cohen for effect sizes: trivial (0 to <0.2), small (≥0.2 to <0.5), moderate (≥0.5 to <0.8), and large (≥0.8) [24]. Differences between those at-risk and not at-risk on the Conners 10-item scale with respect to changes in Conners total score were calculated with an independent *t*-test.

Linear regression was used to identify factors associated with change (Δ) in scores on the Conners 10-item scale. The predictors in the model were gender, age at time of epilepsy surgery in years, age of seizure onset in years, seizure outcome status (seizure-free vs. nonseizure-free), baseline FSIQ, change in FSIQ, change in AEDs, surgery type (temporal lobe vs. other), lateralization (left vs. right), and presurgery ADHD symptoms (i.e., score on Conners at baseline). All predictors were first tested in a univariable manner. Factors significant at the $p < 0.200$ were entered in multivariable modeling.

All tests were two-tailed, and a 5% significance level was used throughout.

All analyses were conducted using IBM SPSS version 25 (Chicago, IL, U.S.A.).

## 4. Results

The total number of children who were operated on and meet eligibility criteria was 137 (see Fig. 1). This included two children who had undergone surgery on two separate occasions longer than two years apart. The parents of nine children did not fill in the surveys at baseline or follow-up. Nine parents filled in the survey at baseline but not at follow-up, and six parents filled in the survey at follow-up but had not filled in the survey at baseline. One child died before the 2-year follow-up and five children were of adult age at follow-up and were not seen for follow-up at the pediatric department. This left a total of 107 parents who completed the surveys. In the case of reoperations within two years, we took the survey two years after the most recent operation.

There was not a significant difference between those who completed surveys and those who did not for seizure outcomes ($p = 0.220$), change in AEDs ($p = 0.253$), child age ($p = 0.096$), age of epilepsy onset ($p = 0.858$), child gender ($p = 0.092$), or change in child IQ ($p = 0.292$).

The mean IQ score at baseline (68.35) for the children where there were data available at baseline and follow-up ($n = 98$) was significantly higher than mean IQ score at follow-up (64.30) ($p < 0.001$). Sixty-three (64%) children had a lower IQ score at follow-up while 29 (30%) children had an improved IQ score, and 6(6%) had an unchanged IQ.

Table 1 shows the data on the children whose parents completed surveys at baseline and follow-up.

Table 2 shows the mean scores and scores in the at-risk range on the Conners 10-item scale before and after surgery.

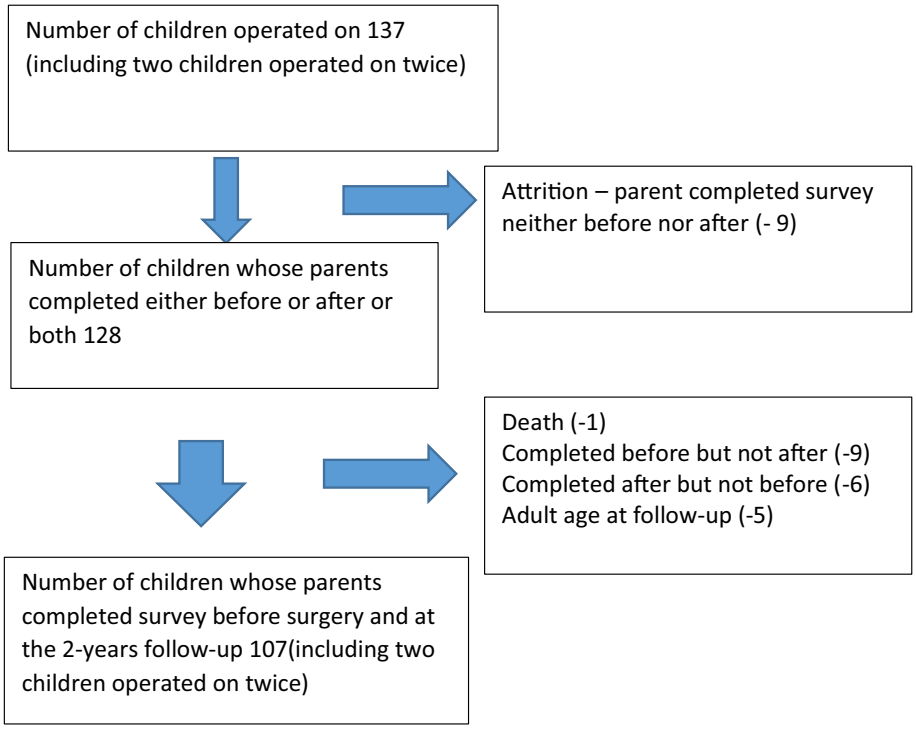



**Fig. 1.** Children who underwent surgery Gothenburg 1995–2014.

**Table 1**
Data on the children whose parents completed surveys before and two years after epilepsy surgery (n = 107).

| | |
|---|---|
| Gender (m/f) | 52/55 |
| Age at surgery in years — mean (range) (SD) — parent-reported | 9.7 (1.5–19) (4.8) |
| Age at epilepsy onset in years - mean (range) (SD) | 3.9 (0–17) (4.2) |
| Total AEDs before — mean (range) (SD) | 2.3 (0–5) (1.1) |
| No AED | 1 |
| Monotherapy | 27 |
| Polytherapy | 79 |
| Total AEDs after — mean (range) | 1.7(0–4) (1.1) |
| No AED | 17 |
| Monotherapy | 25 |
| Polytherapy | 63 |
| Missing | 2 |
| Type of surgery | |
| Temporal lobe resection | 38 |
| Frontal lobe resection | 19 |
| Parietal lobe resection | 9 |
| Occipital Lobe resection | 4 |
| Multilobar resection | 1 |
| Hemispherotomy | 9 |
| Disconnection of hamartoma | 6 |
| Corpus callosotomy | 18 |
| Multiple subpial transection | 2 |
| Insula | 1 |
| Cognitive functioning at baseline | |
| IQ ≥70 | 53 |
| IQ 50–69 | 18 |
| IQ <50 | 36 |
| Cerebral palsy | 20 |
| Seizure outcome at 2-year follow-up | |
| Seizure-free | 48 |
| ≥75% reduction in seizure frequency | 22 |
| 50–74% reduction in seizure frequency | 12 |
| 0–49% reduction in seizure frequency | 19 |
| Increased seizure frequency | 5 |
| Missing | 1 |

### *4.1. Scores on Conners 10-item scale*

The mean group scores on the Conners 10-item scale were significantly lower at the 2-year follow-up ($p < 0.001$; SRM = 0.38 (small)). The mean group scores on the Conners 10-item scale were also significantly lower at the 2-year follow-up when only children 6 years and older at baseline (n = 77) were included ($p < 0.001$; SRM = 0.52 (medium)) and when only children with an IQ ≥ 50 (n = 67) were included ($p < 0.001$; SRM = 0.46 (small)). At baseline, 48.5% of children scored in the at-risk zone on the Connors-10 while at follow-up the corresponding figure was 43.1%. This difference was not significant ($p = 0.481$). Eleven children (11%) who scored in the at-risk zone at baseline did not score in the at-risk zone at follow-up while seven children (7%) who scored outside the at-risk zone at baseline scored in the at-risk zone at follow-up.

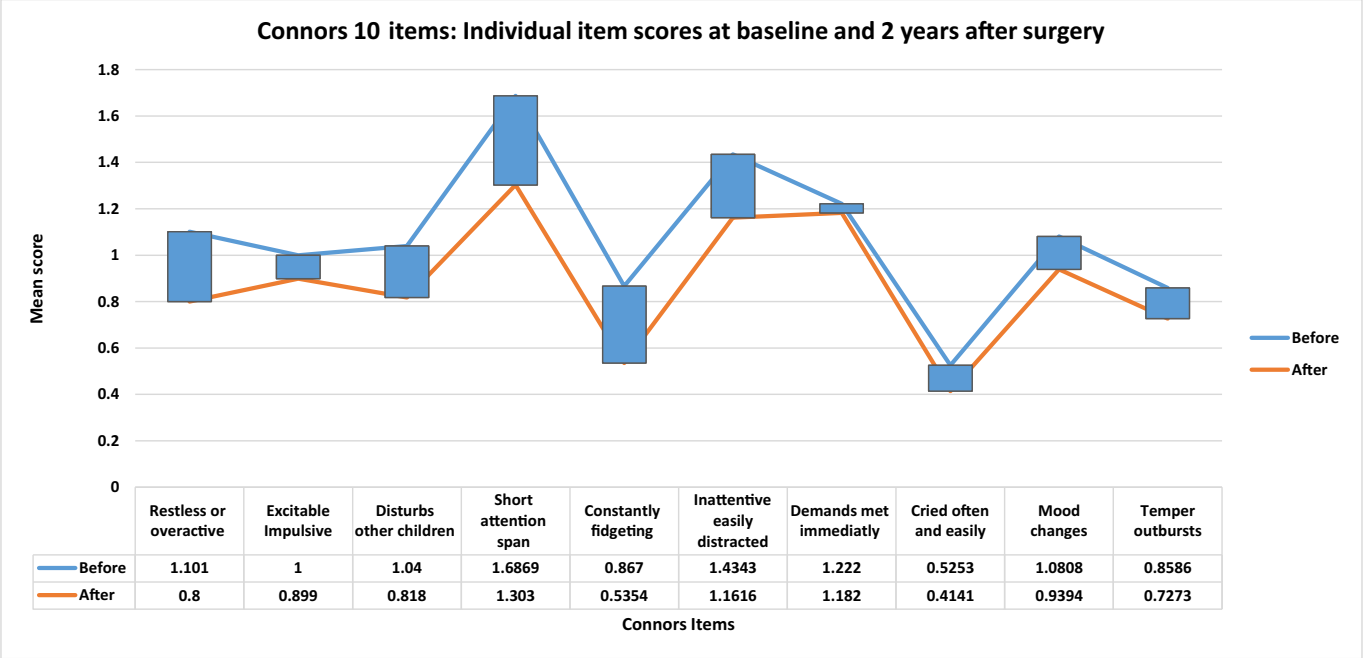
Fig. 2 shows individual items scores on the Conners 10-item scale at baseline and at follow-up. Mean item scores were lower at follow-up for all items. The greatest difference for items before and after surgery was in order of magnitude of difference: 'short attention span', 'constantly fidgeting', 'restless overactive', and 'inattentive easily distracted' (see Fig. 2).

Those at-risk on the Conners 10-item scale at baseline showed significantly greater improvements in Connors 10-item scale score compared with those not at-risk at baseline ($p < 0.001$).

**Table 2**
Scores on the Conners 10-item scale at baseline and 2-year follow-up.

| | Baseline | 2-year follow-up | p |
|---|---|---|---|
| Conners 10-item scale Mean total score (SD) (n = 99)* | 10.53 (8.11) | 8.58 (6.99) | <0.001 |
| Conners — proportion over 10 point cutoff# | 50 (48.5%) (n = 103) | 44 (43.1%) (n = 102) | 0.481 |

*#Ninety-nine patients had Conners 10-item scale completed before and after; 3 patients had Conners 10-item scale completed before but not after; 4 patients had Conners 10-item scale completed after but not before; 1 patient did not have Conners 10-item scale fully completed before or after.




| | Restless or overactive | Excitable Impulsive | Disturbs other children | Short attention span | Constantly fidgeting | Inattentive easily distracted | Demands met immediatly | Cried often and easily | Mood changes | Temper outbursts |
|---|---|---|---|---|---|---|---|---|---|---|
| Before | 1.101 | 1 | 1.04 | 1.6869 | 0.867 | 1.4343 | 1.222 | 0.5253 | 1.0808 | 0.8586 |
| After | 0.8 | 0.899 | 0.818 | 1.303 | 0.5354 | 1.1616 | 1.182 | 0.4141 | 0.9394 | 0.7273 |

**Fig. 2.** Mean scores on the Conners 10-item scale before and two years after epilepsy surgery.

### *4.2. Regression analysis*

The results of regression analysis are in Table 3.

The factors significantly associated with postoperative improvement in ADHD symptoms (lower scores on the Conners 10-item scale) were higher baseline scores, seizure outcome, and laterality. Higher scores on the Conners 10-item scale at baseline were significantly associated with greater improvement in ADHD symptoms ($p < 0.001$). Seizure freedom was also associated with a greater improvement in ADHD symptoms ($p = 0.019$). Additionally, right-sided surgery was also associated with a greater reduction in ADHD symptoms ($p = 0.031$).

## 5. Discussion

This is to our knowledge the first study to evaluate parent-reported symptoms of ADHD before and after pediatric epilepsy surgery. Nearly half the children who underwent surgery were rated as having symptoms of ADHD in the at-risk zone before surgery. Symptoms of ADHD reduced significantly at the 2-year follow-up. Factors significantly associated with improvements in symptoms of ADHD included a higher score on the Conners 10-item scale at baseline, seizure-free status at follow-up, and having had right-sided surgery.

Consistent with previous studies of children with epilepsy, a high proportion of the children were reported to have significant symptoms of ADHD. Nearly half of the children with epilepsy scored in the at-risk range on the Conners 10-item scale. Sherman et al. [17] reported that 71% of children with severe epilepsy scored in the at-risk range a measure of ADHD (ADHD inattentive 34.5%, ADHD combined type 34%, ADHD hyperactive impulsive 2.5%) while Dunn et al. [25] reported that 38% of children with chronic epilepsy were at-risk for ADHD. The two items with the highest mean score on the Conners 10-item scale before surgery were 'short attention span' and 'inattentive easily distracted' highlighting that children in this study, consistent with previous studies [15,16,20], mostly have difficulties with inattention as opposed to hyperactivity–impulsivity. ADHD is often not diagnosed in children with epilepsy despite the presence of impairing symptoms [15,26], and this was also the case in our study. Despite the high number of children scoring in the at-risk range, only 10 (9%) children had a diagnosis of ADHD at baseline.

Symptoms of ADHD had improved significantly at the 2-year follow-up. Although previous studies of functioning before and after surgery have not used ADHD specific measures, improvements in parent-rated

**Table 3**
Regression analysis of factors associated with change in Connors score.

| | Univariable regression | p | Multivariable regression | p |
|---|---|---|---|---|
| Gender | −0.949 (−2.998 to 1.101) | 0.745 | N/A | N/A |
| Age at surgery | −0.071 (−0.292 to 0.150) | 0.524 | N/A | N/A |
| Age of epilepsy onset | −6.782 (−0.251 to 0.250) | 1.000 | N/A | N/A |
| Change in IQ | −0.022 (−0.103 to 0.059) | 0.587 | N/A | N/A |
| Baseline IQ | −0.010 (−0.045 to 0.024) | 0.557 | | |
| Change in AEDs | 0.199 (−1.096 to 0.698) | 0.661 | N/A | N/A |
| Seizure outcome | 1.665 (−0.356 to 3.685) | 0.105 | 2.388 (0.408 to 4.368) | 0.019 |
| Temporal vs. rest | 0.857 (−1.263 to 2.978) | 0.424 | NA | NA |
| Frontal vs. rest | −0.469 (−3.136 to 2.198) | 0.728 | NA | NA |
| Laterality | −2.707 (−4.937 to −0.477) | 0.018 | −2.122 (−4.040 to −0.204) | 0.031 |
| Conners 10-item scale baseline score | −0.329 (−0.438 to −0.220) | <0.001 | −0.356 (−0.474 to −0.237) | <0.001 |

N/A as not in final model.

attention have been noted on the attention subscale of the Child Behavior Checklist (CBCL) [27] in one study with a mean follow-up of 6 years [28], but not in a study with a follow-up period of 12 months [8]. A possible reason for this is that longer follow-up time allows for a greater chance of change [8]. In our study, there was a reduction in the proportion of children in the at-risk range, but this was not significant. This echoes previous studies suggesting that change in numbers of children with epilepsy reaching diagnostic criteria for behavioral disorders after epilepsy surgery is not significant [5–7]. Despite this lack of a significant reduction in the proportion of children in the at-risk range, the improvement in symptoms at follow-up was significant and likely results in improved functioning at least based on parental report. However, ADHD symptoms are still very frequent in children after epilepsy surgery and parents should be informed about that at presurgical counseling.

The fact that there was a significantly greater reduction in symptoms in the at-risk group compared with those not at-risk indicates that not only do symptoms of ADHD reduce at the group level but also that those with the highest scores experience the greatest reduction. Only eleven children (11%) moved from out of the at-risk zone for ADHD on the Conners 10-item scale at follow-up while seven (7%) moved into the at-risk zone at follow-up. Like previous studies [5–7], the current study indicates that there is individual variation with respect to changes in behavioral functioning after pediatric epilepsy surgery. This makes it difficult to predict the outcome in individual cases.

Seizure-free outcome at follow-up was significantly associated with improvement in ADHD symptoms. A greater improvement in behavioral symptoms for those with seizure freedom after surgery has been noted by Lendt et al. [10] with respect to total scores on the CBCL suggesting that seizure freedom can contribute to an improvement in behavior for at least some children. Children operated on in the right hemisphere experienced a greater improvement in symptoms at follow-up than children operated on in the left hemisphere. A previous study by Law et al. [8] also noted a similar improvement on total competence scale of CBCL for patients operated on in the right hemisphere. An effect of laterality however has not been noted in other studies where it has been considered [10,28]. Differences between studies are perhaps reflective of measures used in assessment of behavior, sample composition, sample size and follow-up time. None of the other epilepsy-related factors were associated with change in symptoms. Research in the population with childhood epilepsy suggests that symptoms of ADHD and other behavioral disorders are present prior to onset of seizures [29] emphasizing that these children often have underlying brain dysfunction that lead to both behavioral problems and seizures and that treating seizures per se can only bring limited improvements in behavior [30].

## 6. Implications for practice and future research

The high level of ADHD symptoms, potential for improvements in symptoms, and low level of children with preoperative ADHD diagnoses highlights the need to assess for ADHD in children undergoing epilepsy surgery at baseline and follow-up. Although surgery brought about some improvements in symptoms, the children with significant symptoms of ADHD are likely to benefit for consideration of methylphenidate, which is effective and well-tolerated in this population [31] highlighting the benefits of identification and subsequent treatment. This like many other studies considering symptoms of ADHD in children with epilepsy employed parent-report only, and in future research studies it will be useful to ask teachers and the young people where appropriate, given that there can be significant differences regarding level of symptoms between different raters [32]. Qualitative interviews with parents and the young people may also help elucidate the impact of the change in level of symptoms on everyday functioning. The significantly greater improvement in symptoms for children operated on in the right hemisphere needs replication and further investigation.

## 7. Strengths and limitations

Strengths of the current study include the use of standardized parental measure of ADHD symptoms and the sample size that is one of the largest to date to consider aspects of behavior before and after pediatric epilepsy surgery. We also considered a wide range of factors including demographics, epilepsy-related factors, aspects of surgery factors, and child IQ.

There are a number of limitations that also need to be considered. We did not have a nonsurgery control group with which to compare behavior at baseline and at 2-year follow-up. Also, the age range and ability of children is quite wide. The validity of the Conners-10 scale is uncertain in children under 6 years of age and in children with moderate, severe, or profound intellectual disability. However, after excluding the younger children and children with IQ < 50 our analysis did not alter our main findings, and age and cognitive ability were not found to be significant predictors of change score in the regression analysis.

We did not use diagnostic interviews or clinical diagnosis with respect to Diagnostic and Statistical Manual of Mental Disorders (DSM)/International Classification of Diseases (ICD) criteria when considering ADHD. We did not have information on family or environmental factors that can influence child behavior. We employed parent-report only and did not ask the child themselves or teachers. The Conners 10-item scale contains only ten questions, and instruments with wider coverage of ADHD symptoms may be better in understanding the impact of surgery on the full range of ADHD symptoms.

## 8. Summary

This research adds to the understanding of the impact of epilepsy surgery on young people. While there are improvements in features of ADHD at follow-up, many children who have undergone surgery still have significant features of ADHD at follow-up. This is important to take into consideration when counseling the parents and children preoperatively. Seizure freedom and focus in the right hemisphere are associated with greater improvement in symptoms.

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*Conflicts of interest*

The authors have no conflicts of interest. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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