Epilepsy & Behavior 101 (2019) 106552

Contents lists available at ScienceDirect

Epilepsy & Behavior

journal homepage: www.elsevier.com/locate/yebeh

Parents' view of the cognitive outcome one year after pediatric epilepsy surgery

Christian Hoppe [a,*], Izabela Porębska [a], Kassandra Beeres [a], Robert Sassen [a], Stefan Kuczaty [a], Ulrike Gleissner [b], Michael Lendt [c], Christian E. Elger [a], Christoph Helmstaedter [a,c]

[a] Department of Epileptology, University of Bonn Medical Centre, Venusberg-Campus 1, FRG-53127 Bonn, Germany
[b] LVR-Klinik Bonn, Kinderneurologisches Zentrum, Waldenburger Ring 46, FRG-53119 Bonn, Germany
[c] St. Mauritius Therapieklinik, Strümper Str. 111, FRG-40670 Meerbusch, Germany

ARTICLE INFO

Article history:
Received 22 August 2019
Revised 6 September 2019
Accepted 8 September 2019
Available online 5 November 2019

Keywords:
Pediatric epilepsy surgery
Postsurgical neurocognitive outcome
Parental survey
Parental outcome rating
Neuropsychology

ABSTRACT

Objectives: The cognitive outcome of pediatric epilepsy surgery has mainly been examined on the basis of standardized tests. Here, we analyzed the outcome in six cognitive domains from the parents' view.
Methods: Included were consecutive surgical pediatric patients whose parents filled-in a comprehensive questionnaire on cognitive problems in children and adolescents (*Kognitive Probleme bei Kindern und Jugendlichen* (KOPKIJ); Gleissner et al. 2006) at the preoperative baseline (T1) as well as twelve months thereafter (T2). All children also underwent standard neuropsychological assessments at T1 and T2.
Results: Parents of 96 patients provided pre- and postoperative KOPKIJ data. Overall, 80% of the children became seizure-free at the follow-up. Group means indicated a strong positive effect of time on KOPKIJ and neuropsychological performance. We found postoperative improvements in five out of six cognitive domains (language, memory, executive functions, attention, school; unchanged: visuospatial abilities). Individually, improvements were twice as likely as declines. However, 33 patients (35%) experienced significant decline in at least one cognitive domain. Later onset of epilepsy resulted in better performance but had no effect on change scores. Seizure-free status, lower antiseizure drug load, and stronger drug reduction after surgery contributed to postoperative cognitive improvements as perceived by the parents; no other effects of clinical factors were obtained (e.g., localization/lateralization). Despite their similar outcome patterns, change scores as derived from parental ratings and neuropsychological assessment were not correlated.
Conclusions: Parents acknowledged the overall positive neurocognitive development after pediatric epilepsy surgery as previously shown by standardized tests. Seizure freedom and lower antiseizure drug load contributed to the beneficial cognitive outcome. Even if cognitive improvements outweighed declines, a risk for cognitive decline with impact on everyday functioning does exist.

1. Introduction

Epilepsy surgery comprises a series of resective and disconnective interventions for the treatment of severely disabling and otherwise therapy-refractory focal seizures in children and adults [1,2]. Therapeutic superiority over conservative drug treatment was shown by randomized controlled trials [2–6]. Unforeseen chronic neurosurgical complications are reportedly rare [7,8]. Consequentially, the neuropsychological outcome gains in importance for surgical decision-making. Several studies demonstrated cognitive safety of established surgical procedures on the basis of psychometric performance tests [8–16]. However, no common standard battery of sensitive measures was agreed on by experts so far, and unfortunately, the clinical and ecological validity of several measures in use was never proven [17]. Furthermore, the setting of a standardized assessment is artificial, especially for children, and because of the inherent time restrictions, psychometric tests might miss cognitive or mnestic deficits that occur on a different time scale only (e.g., delayed free recall after hours or days). Thus, one might legitimately ask whether the overall positive findings from psychometric surgical outcome research do actually mirror postoperative real life performance.

In the present study, we wanted to assess the real world cognitive outcome one year after surgery in one of the worldwide largest series of surgical children with epilepsy (Bonn, Germany). Parental questionnaires represent a well-established and frequently applied method for structured psychological screening and evaluation of children, especially their everyday behavior and performance [18–21]. Different parental surveys (and interviews) were already used for epilepsy and

* Corresponding author.
E-mail address: christian.hoppe@ukbonn.de (C. Hoppe).

https://doi.org/10.1016/j.yebeh.2019.106552
1525-5050/

epilepsy surgery outcome research (e.g., [22–26]); a tabular literature overview is given in Supporting Table S1. Sample sizes increased from case series in the 1990s to reasonable levels during the last decade, but most studies, especially recent ones, focused on behavior. The overall impression, especially from larger studies, is positive, i.e., parents acknowledged cognitive safety and stability of pediatric epilepsy surgery as obtained by psychometric tests in their children's daily life. Even a trend towards improved cognition and behavior becomes apparent. Studies comparing surgical patients versus nonsurgical controls demonstrated better development in surgical children. Seizure freedom and antiepileptic drug load (reduction) were positive predictors. A recent systematic review summarized studies on the emotional and behavioral development after epilepsy surgery in pediatric patients and confirmed the overall positive impression [27]. Two recent studies addressed the memory domain [28,29]. One study found no impact of surgery on everyday memory [28] while the other found decline after temporal lobe surgeries and improvement after frontal lobe surgeries [29].

Here, we assessed the parents' view of the 12-month postoperative cognitive outcome in more detail by a standardized parental survey, *Kognitive Probleme bei Kindern und Jugendlichen* (KOPKIJ; i.e., *Cognitive Problems in Children and Adolescents*; [30]), which addresses cognitive everyday performance differentially in six functional domains: language, memory, attention, executive functions, visuoconstruction (including visuospatial abilities), and school (i.e., academic achievement). The KOPKIJ is generic in nature, and the items and scales have high face validity as they operationalize the usual demands in the daily life of children. Further motivation for the separate analysis of the surgical outcome on the basis of parental evaluations was provided by a recent cross-sectional study from our group, which obtained only low correlations between psychometrically based cognitive domain rating scores and conceptually related KOPKIJ domain ratings [31]. In the present surgical outcome study, both methodological approaches, objective and subjective, were combined allowing additional analyses of the correlations between change scores from parental versus psychometric evaluation.

2. Methods

2.1. Study design

This is a retrospective monocentric treatment outcome study in pediatric patients with therapy-refractory structural epilepsies who underwent different types of neurosurgery including standard and tailored resections of epileptogenic tissues as well as hemispherotomies. Parents were asked to rate cognitive problems in the daily life of their children by filling-in the KOPKIJ questionnaire before (T1) as well as twelve months after surgery (T2). All other data including neuropsychological test scores from T1 and T2 were taken from the patient records and anonymized before further processing. The study was approved by the local ethics committee of the Medical Faculty of the University of Bonn (Germany).

2.2. Patients

The KOPKIJ norms span the ages from 6 to 16 years. We included all surgical pediatric patients of this age (at the time of presurgical assessment) whose parents provided KOPKIJ data at T1 and T2; older age at T2 did not result in exclusion. To maximize the data basis, surveys obtained 9 to 23 months after baseline testing, respectively, were considered as 12-month follow-up data (T2). We recently reported the clinical characteristics and the neuropsychological outcome at the 12-month follow-up of the entire sample of surgical pediatric patients at our unit (n = 306) from which the sample of the present study was drawn [8,32].

2.3. Methods and measures

The KOPKIJ survey [30] was used to record parents' evaluations of their children's cognitive performance in daily life and at school. An English translation of the survey can be found in the supporting online material to [31]. Besides several more general questions (e.g., who filled in the questionnaire, academic achievement of mother and father, handedness of the child), the questionnaire comprises 100 items with a 4-stepped Likert scale (from 1 = never to 4 = always or nearly always) on the frequency of highly defined cognitive problems in six different domains ("language", "memory", "visuospatial abilities", "executive functions", "attention", and "school"). Parents are instructed to refer their answers to the past three months. The KOPKIJ was standardized in a normative sample of 352 healthy school children (aged 6–16 years). The manual provides percentiles (PR) for the raw score sums of each cognitive domain and the authors of the survey considered PR > 85 "salient". To facilitate statistical analyses and data description in the present study, PR were transformed into positively scaled standard values for each domain (i.e., higher values indicating higher performance; mean = 100, standard deviation = 10; cutoff for salient findings: standard value <90, equaling PR > 85). For regression analysis, we also calculated a KOPKIJ total score, which we defined by the arithmetic mean of the six domain standard scores. The test authors also reported reliability estimates, r_{tt}, for each domain on the basis of both the scales' internal consistencies as obtained in healthy children (i.e., Cronbach's α, range: 0.82–0.97; Table 2 in [30]) and test–retest correlations (range: 0.71–0.85; Table 9 in [30]) in a clinical sample of 55 children with epilepsy (median test–retest interval: 12 months). It might be of interest that the reanalysis of data from that former patient sample obtained no significant change over time from test to retest in any KOPKIJ domain score (data not shown). Given their higher sensitivity for change, we decided to use the slightly higher reliability estimates as obtained from the healthy controls.

In our recent evaluation of the neuropsychological surgical outcome of the entire sample of pediatric patients at our unit [32], we used a standardized method for summarizing (or condensing) age-normed standardized scores from single tests into higher-order categorical neuropsychological scores for eight cognitive domains that were "intelligence", "motor function" (i.e., manual coordination), "attention", "verbal memory", "figural memory", "language", "visuoconstruction" (including visuospatial abilities), and "behavior" (single test assignments are shown in [32], Table 1); of note, the "behavior" domain refers to the *Child Behavior Checklist* [33] that is a parental questionnaire as well. Domains were evaluated on a 5-stepped Likert scale according to the following definitions: 0 = strongly impaired (i.e., at least two of the test scores for the respective function were smaller than mean [M]–2 standard deviations [SD]); 1 = impaired (i.e., at least two respective test scores were smaller than M–1 SD); 2 = borderline (i.e., one test score smaller than M–1 SD or at least two test scores roughly equaling M–1 SD); 3 = average (i.e., a maximum of one test score roughly equals M–1 SD while all other scores were average at least); 4 = above average (i.e., at least two test scores were larger than M + 1 SD).

2.4. Statistics

Effects of time (T1 vs. T2) on KOPKIJ scores and neuropsychological scores were tested by multivariate repeated measures analysis of variance (ANOVA) and post hoc univariate t-tests for paired samples. The size of the multivariate time effect was estimated by partial η^2; effect sizes were classified as follows: $\eta^2 > 0.01$ small, >0.06 medium, and >0.14 large [34]. Group mean differences (e.g., clinical factors) were tested by t-tests for independent samples or the χ^2-test, respectively. Single sample t-tests were run to test differences between sample mean KOPKIJ domain standard scores and the normative mean (i.e., 100). To determine statistically significant changes of KOPKIJ scores over time in individual patients, we calculated critical differences at the 95% confidence limit (two-sided) for each domain sum score using the

Table 1
Patient characteristics and clinical outcome.

Children, number	96
Sex, number (%)	
Male	46 (48)
Female	50 (52)
Handedness, number (%)	
Right	70 (73)
Left	20 (21)
Ambidextrous	6 (6)
Age at T1, mean (SD; range) years	11.1 (3.1; 4.9–17.4)
Age at seizure onset, mean (SD; range) years	5.5 (3.8; 0.0–15.0)
Duration of epilepsy at T1, mean (SD; range) years	5.6 (3.3; 0.5–14.7)
Test intelligence, mean (SD; range)	87 (20; 26–137)
Antiseizure drugs at T1, number (%)	
Off-drug	0 (0)
Monotherapy	28 (30)
Polytherapy	67 (70)
KOPKIJ at T1 filled in by, number (%)	
Mother	66 (70)
Father	18 (19)
Both	11 (12)
Surgery	
Interval from T1 to surgery, mean (SD; range) months	1.9 (2.4; 0.0–11.1)
Side, number (%)	
Left	58 (60)
Right	38 (40)
Site, number (%)	
Temporal	43 (45)
Frontal	24 (25)
Other cortical	16 (17)
Hemispherotomy/multilobectomy	13 (14)
Type, number (%)	
Lesionectomy/partial resection	66 (69)
Hemispherotomy/multilobectomy	13 (14)
Lobectomy	9 (9)
Selective amygdalohippocampectomy	8 (8)
Etiology, number (%)	
Tumor	29 (30)
Migration/maturation disturbance	23 (24)
Hippocampal sclerosis	19 (20)
Other	25 (26)
Clinical outcome one year after surgery (T2):	
Interval from surgery to T2, mean (SD; range) months	12.1 (1.9; 9.0–19.0)
Seizure-free (Engel IA), number (%)	77 (80)
Antiseizure drugs, number (%)	
Off-drug	5 (6)
Monotherapy	60 (67)
Polytherapy	25 (28)
Change of number of antiseizure drugs from T1 to T2, number (%)	
Reduced	49 (51)
Unchanged	42 (44)
Increased	5 (5)

T1, baseline; T2, 12-month follow-up.

reliability estimates, r_{tt}, from the KOPKIJ's normative sample as mentioned above. Critical differences were defined by $CD_{(1-\alpha)\%} = z_{\alpha/2} * SD * \mathrm{sqrt}(2 * (1 - r_{tt}))$. On the basis of $CD_{95\%}$, individual three-stepped categorical change scores (declined/unchanged/improved) were calculated for each domain. Change of neuropsychological test performance from T1 to T2 was defined by any change of the categorical neuropsychological domain score. Correlations of performance and change scores were tested with Pearson's product–moment correlations and shown as color-coded correlation matrices; effect sizes were classified as follows: r > 0.1 small, >0.3 medium, and >0.5 large [34]. All correlating sociodemographic and clinical factors were considered for stepwise multiple linear regression modeling of the KOPKIJ total score at T2 as well as two KOPKIJ change scores (namely, number of domains declined, number of domains improved). The significance level for all statistical tests was set to $p < 0.05$, two-sided. Effect sizes were evaluated according to Cohen [34]. All statistics were performed with the German edition of IBM SPSS Statistics 24.

3. Results

3.1. Patient characteristics

Parents from a total of 96 surgical patients provided the required KOPKIJ data at T1 and T2. The sociodemographic and clinical characteristics of the included patients are shown in Table 1.

At T1, the children were 11.1 years old on average (at T2, 5 patients were already older than 16 years). Mean epilepsy duration at T1 was 5.6 years. More than two-thirds of the patients were on antiseizure drug polytherapy before surgery. As regards the prevalence of atypical handedness (27%), mean intelligence (IQ 87), antiseizure drug load, sites, and types of surgery as well as etiology, the sample was representative for the entire population of surgical children at our unit [32].

3.2. Clinical outcome

On average, surgery took place 2 (range: 0–11) months after T1 and the surgery-to-T2 interval was 12 (9–19) months. The clinical outcome at T2 was excellent (Table 1): 80% of the surgical patients were seizure-free; the antiseizure drug load was reduced in most patients (55%); and most patients (67%) were on monotherapy. The outcome in this sample fully matched the clinical outcome in the entire surgical population at our unit [32].

3.3. Cognitive outcome: group level

A total of 75 KOPKIJ surveys (78.1%) were filled-in by mothers or by mothers and fathers together (Table 1). In 34 cases (35.4%), the parent filling-in the KOPKIJ changed from T1 to T2. However, no systematic effect of the person who filled-in the questionnaire (mothers vs. fathers) was obtained on any score at any time (t-tests; Supporting Table S2A). Furthermore, the educational levels of both parents (separately and combined) were not correlated with KOPKIJ domain scores at T1 (Supporting Table S2B).

Table 2 shows the group means of the KOPKIJ domain standard scores at T1 and T2.

All group mean scores at T1 and T2, except the "executive functions" score at T2, were below the normative mean value of 100 (multiple

Table 2
Performance scores.

	n	T1	T2	t[a]	p[a]
KOPKIJ scores, means (SD)					
- Language	96	89.3 (21.0)	93.5 (17.2)	−2.68	0.009
- Memory	96	89.6 (18.0)	94.3 (15.0)	−3.55	0.001
- Visuospatial	95	93.9 (14.4)	95.1 (14.9)	−1.34	0.184
- Executive functions	95	93.6 (13.5)	97.7 (12.1)	−3.83	0.000
- Attention	95	83.2 (16.6)	89.2 (15.0)	−4.36	0.000
- School	72	93.1 (14.0)	95.0 (14.1)	−3.94	0.000
Neuropsychological rating scores, means (SD)					
- Intelligence	65	2.2 (1.3)	2.2 (1.3)	−0.84	0.402
- Motor function	69	2.4 (0.9)	2.8 (0.8)	−3.51	0.001
- Attention	77	2.3 (1.2)	2.5 (1.2)	−1.85	0.069
- Verbal memory	79	2.0 (1.3)	2.1 (1.4)	−1.14	0.259
- Figural memory	75	2.4 (1.2)	2.8 (1.2)	−2.90	0.005
- Language	78	1.9 (1.3)	2.3 (1.3)	−3.75	0.000
- Visuospatial	75	2.5 (1.1)	2.8 (0.9)	−2.70	0.009
- Behavior	93	1.4 (0.8)	1.8 (1.0)	−3.48	0.001

T1, baseline; T2, 12-month follow-up. KOPKIJ standard scores are normally distributed (mean 100, standard deviation 10). Neuropsychological rating scores: 0-strongly below average, 1-below average, 2-borderline, 3-average, 4-above average.

[a] Post hoc univariate t-tests for paired samples.

single-sample t-tests, p's < 0.05; data not shown) indicating greater cognitive problems in daily life in study patients than healthy controls before and after surgery. At T1, two-thirds of the patients showed below-average scores in the "attention" domain; one-third had below-average scores in the other five cognitive domains (i.e., about twice as much as in the normative sample of healthy controls); and 73 (76%) patients had a below-average score in at least one domain.

At T2, the mean KOPKIJ scores had descriptively improved in all domains, and the percentage of below-average scores was reduced from two-thirds to one-half in the "attention" domain and from one-third to one-quarter in the "visuospatial abilities" and the "executive functions" domain; 61 (64%) patients had below-average scores in at least one domain. Accordingly, multivariate repeated measures ANOVA obtained a significant main effect of time (T1 versus T2; Wilk's lambda = 0.79, F = 2.91, p = 0.014); partial η^2 was 0.212 indicating a large effect [34]. Post hoc univariate analyses by t-tests for paired samples found significant improvements in all KOPKIJ domains except of "visuospatial abilities" (nonsignificant trend, p < 0.10).

Table 2 also shows the neuropsychological scores obtained from testing at T1 and T2. On average, the patients scored at "2–borderline"; "behavior" approached "1–below average". Descriptively, most scores showed improvements at T2. Multivariate repeated measures ANOVA obtained a significant main effect of time (T1 versus T2; Wilk's lambda = 0.61, F = 2.47, p = 0.033); partial η^2 was 0.390 indicating a large effect [34]. Post hoc univariate testing by t-tests for paired samples obtained significant effects of time for "motor function", "figural memory", "language", "visuoconstruction", and "behavior" but not for "intelligence", "attention", and "verbal memory".

3.4. Cognitive outcome: individual level

Table 3 shows the number of significant declines and improvements of KOPKIJ ratings on the individual level at the 95% confidence limit (sorted by % declined).

A total of 33 patients (35%) experienced decline in at least one KOPKIJ domain; thereof, 18 (19%), 6 (6%), and 9 (9%) patients experienced declines in one, two, and three or more domains, respectively. Significant improvements of domain scores occurred more than twice as often as declines (156 vs. 62). Fifty-nine patients (62%) experienced improvement in at least one domain; thereof, 19 (20%), 11 (12%), and 29 (30%) patients improved in one, two, and three or more KOPKIJ domains, respectively. Ten patients (10%) showed declines and improvements while 23 patients (24%) showed only declines (and unchanged score) and 49 patients (51%) showed only improvements (and unchanged scores); 14 patients (15%) had stable KOPKIJ scores in all six scales. Thus, while the chance for improvement was about twice as large as the risk of decline, the cognitive outcome as seen by the parents was (partially) critical in about one-third of the patients.

Table 3 also shows the number of categorical declines and improvements of neuropsychological scores. A total of 56 patients (58%) experienced decline in at least one domain; thereof, 36 (38%), 11 (12%), and 9 (9%) patients experienced declines in one, two, and three or more domains, respectively. Improvements of domain scores occurred more than twice as often as declines (218 vs. 92). Eighty-two patients (85%) experienced improvement in at least one domain; thereof, 20 (21%), 20 (21%), and 42 (19%) patients improved in one, two, and three or more cognitive domains, respectively. As many as 49 (51%) patients showed declines and improvements while 7 patients (7%) showed only declines (and unchanged scores) and 33 patients (35%) showed only improvements (and unchanged scores); 7 patients (7%) had stable neuropsychological scores in all scales. Thus, while the chance for cognitive improvements clearly exceeded the risk for declines, the cognitive outcome as obtained from neuropsychological testing was (partially) critical in more than half of the patients.

While parental evaluations suggest that "executive" and "language" functions are at highest risk for individual decline, psychometric evaluation indicated verbal and figural memory as most critical functions.

Table 3
Individual postoperative performance changes (sorted by % declined).

	N	Declined n (%)	Improved n (%)
KOPKIJ[a]			
- Executive functions	96	16 (17)	43 (45)
- Language	96	15 (16)	25 (26)
- Memory	96	12 (13)	32 (33)
- School	72	7 (10)	22 (31)
- Visuospatial	96	6 (6)	9 (9)
- Attention	96	6 (6)	25 (26)
Neuropsychological rating scores[b]			
- Verbal memory	79	19 (24)	30 (38)
- Figural memory	75	16 (21)	33 (44)
- Attention	77	14 (19)	28 (36)
- Motor function	69	10 (15)	30 (43)
- Visuospatial abilities	75	11 (15)	29 (39)
- Intelligence	65	8 (12)	12 (18)
- Language	78	9 (12)	32 (41)
- Behavior	93	5 (5)	24 (26)

[a] Reliable changes at the 95% confidence limit.
[b] Categorical changes of neuropsychological scores.

3.5. Correlation analyses

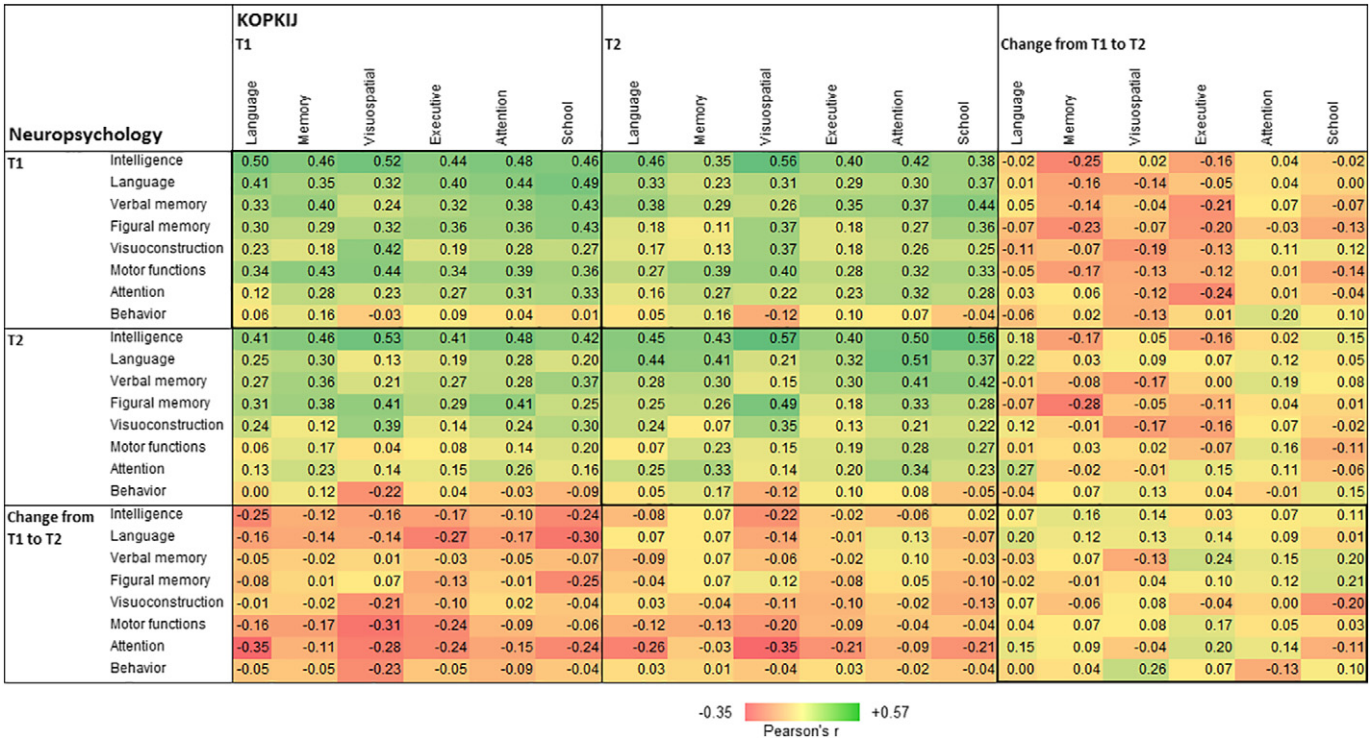
The KOPKIJ domain scores were strongly correlated to each other at both times (e.g., at T1, range of r: 0.49–0.74, p's < 0.001). Also most neuropsychological scores showed high correlations at both times (e.g., at T1, range of r: 0.25–0.74, p's < 0.001); however, "behavior" was uncorrelated to most other domains (negative correlation with "figural memory"). Fig. 1 shows the correlation matrix of parental rating scores and neuropsychological scores (for sample sizes and p-values see Supporting Table S3); correlation coefficients are color-coded. Overall, KOPKIJ versus neuropsychological performance scores showed highly significant correlations at T1 and T2 (p's < 0.001), partially with strong correlational effects (i.e., r > 0.50). However, the maximum percentage of variance explained was only about 30% and correlations were small when regarded as validity coefficients. Furthermore, correlations were unspecific with regard to the cognitive domains. As regards change over time, negative baseline-change correlations were obtained between both measures indicating higher risks of decline for well versus low performing subjects and better chances to improve for low versus well performing patients. Almost no correlations between the change scores for associated cognitive domains from both data sources were obtained.

3.6. Predicting the outcome

The KOPKIJ scores at T1 were strongly correlated with KOPKIJ scores at T2 (p's < 0.001; range of r: 0.64–0.77). Also the neuropsychological domain scores at T1 were strongly correlated with respective scores at T2 (p's < 0.001; range of r: 0.46–0.84). Thus, baseline scores were strong predictors of the cognitive outcome for subjective and objective measures.

Fig. 2 shows the correlation matrix between KOPKIJ scores at T2 (performance and change) and possible clinical outcome predictors (for sample sizes and p-values see Supporting Table S4); the correlation coefficients were color-coded. The baseline performance scores were excluded from the following analyses.

All correlations were weaker than those with the baseline KOPKIJ scores (see above). Higher age at seizure onset was positively correlated with the outcome at T2 but did not affect KOPKIJ change scores; consistently, epilepsy duration was negatively correlated with KOPKIJ performance at T2 with no effect on change. In contrast, seizure-free status had positive impact on KOPKIJ performance at T2 as well as change



Neuropsychology		KOPKIJ T1 Language	Memory	Visuospatial	Executive	Attention	School	T2 Language	Memory	Visuospatial	Executive	Attention	School	Change from T1 to T2 Language	Memory	Visuospatial	Executive	Attention	School
T1	Intelligence	0.50	0.46	0.52	0.44	0.48	0.46	0.46	0.35	0.56	0.40	0.42	0.38	-0.02	-0.25	0.02	-0.16	0.04	-0.02
	Language	0.41	0.35	0.32	0.40	0.44	0.49	0.33	0.23	0.31	0.29	0.30	0.37	0.01	-0.16	-0.14	-0.05	0.04	0.00
	Verbal memory	0.33	0.40	0.24	0.32	0.38	0.43	0.38	0.29	0.26	0.35	0.37	0.44	0.05	-0.14	-0.04	-0.21	0.07	-0.07
	Figural memory	0.30	0.29	0.32	0.36	0.36	0.43	0.18	0.11	0.37	0.18	0.27	0.36	-0.07	-0.23	-0.07	-0.20	-0.03	-0.13
	Visuoconstruction	0.23	0.18	0.42	0.19	0.28	0.27	0.17	0.13	0.37	0.18	0.26	0.25	-0.11	-0.07	-0.19	-0.13	0.11	0.12
	Motor functions	0.34	0.43	0.44	0.34	0.39	0.36	0.27	0.39	0.40	0.28	0.32	0.33	-0.05	-0.17	-0.13	-0.12	0.01	-0.14
	Attention	0.12	0.28	0.23	0.27	0.31	0.33	0.16	0.27	0.22	0.23	0.32	0.28	0.03	0.06	-0.12	-0.24	0.01	-0.04
	Behavior	0.06	0.16	-0.03	0.09	0.04	0.01	0.05	0.16	-0.12	0.10	0.07	-0.04	-0.06	0.02	-0.13	0.01	0.20	0.10
T2	Intelligence	0.41	0.46	0.53	0.41	0.48	0.42	0.45	0.43	0.57	0.40	0.50	0.56	0.18	-0.17	0.05	-0.16	0.02	0.15
	Language	0.25	0.30	0.13	0.19	0.28	0.20	0.44	0.41	0.21	0.32	0.51	0.37	0.22	0.03	0.09	0.07	0.12	0.05
	Verbal memory	0.27	0.36	0.21	0.27	0.28	0.37	0.28	0.30	0.15	0.30	0.41	0.42	-0.01	-0.08	-0.17	0.00	0.19	0.08
	Figural memory	0.31	0.38	0.41	0.29	0.41	0.25	0.25	0.26	0.49	0.18	0.33	0.28	-0.07	-0.28	-0.05	-0.11	0.04	0.01
	Visuoconstruction	0.24	0.12	0.39	0.14	0.24	0.30	0.24	0.07	0.35	0.13	0.21	0.22	0.12	-0.01	-0.17	-0.16	0.07	-0.02
	Motor functions	0.06	0.17	0.04	0.08	0.14	0.20	0.07	0.23	0.15	0.19	0.28	0.27	0.01	0.03	0.02	-0.07	0.16	-0.11
	Attention	0.13	0.23	0.14	0.15	0.26	0.16	0.25	0.33	0.14	0.20	0.34	0.23	0.27	-0.02	-0.01	0.15	0.11	-0.06
	Behavior	0.00	0.12	-0.22	0.04	-0.03	-0.09	0.05	0.17	-0.12	0.10	0.08	-0.05	-0.04	0.07	0.13	0.04	-0.01	0.15
Change from T1 to T2	Intelligence	-0.25	-0.12	-0.16	-0.17	-0.10	-0.24	-0.08	0.07	-0.22	-0.02	-0.06	0.02	0.07	0.16	0.14	0.03	0.07	0.11
	Language	-0.16	-0.14	-0.14	-0.27	-0.17	-0.30	0.07	0.07	-0.14	-0.01	0.13	-0.07	0.20	0.12	0.13	0.14	0.09	0.01
	Verbal memory	-0.05	-0.02	0.01	-0.03	-0.05	-0.07	-0.09	0.07	-0.06	-0.02	0.10	-0.03	-0.03	0.07	-0.13	0.24	0.15	0.20
	Figural memory	-0.08	0.01	0.07	-0.13	-0.01	-0.25	-0.04	0.07	0.12	-0.08	0.05	-0.10	-0.02	-0.01	0.04	0.10	0.12	0.21
	Visuoconstruction	-0.01	-0.02	-0.21	-0.10	0.02	-0.04	0.03	-0.04	-0.11	-0.10	-0.02	-0.13	0.07	-0.06	0.08	-0.04	0.00	-0.20
	Motor functions	-0.16	-0.17	-0.31	-0.24	-0.09	-0.06	-0.12	-0.13	-0.20	-0.09	-0.04	-0.04	0.04	0.07	0.08	0.17	0.05	0.03
	Attention	-0.35	-0.11	-0.28	-0.24	-0.15	-0.24	-0.26	-0.03	-0.35	-0.21	-0.09	-0.21	0.15	0.09	-0.04	0.20	0.14	-0.11
	Behavior	-0.05	-0.05	-0.23	-0.05	-0.09	-0.04	0.03	0.01	-0.04	0.03	-0.02	-0.04	0.00	0.04	0.26	0.07	-0.13	0.10

Fig. 1. Correlation matrix of KOPKIJ and neuropsychological performance and change scores (Supporting Table S3 for details).

from T1 to T2. Also lower number of antiseizure drugs at T2 and stronger reduction of the drug load from T1 to T2 positively contributed to a better outcome and more improvement in KOPKIJ scores. Other clinical and sociodemographic factors (surgical side or site, chronological age, sex, handedness) showed only marginal or no correlations with KOPKIJ scores. As regards the neuropsychological rating scores, the number of improved and declined functions showed positive or negative correlations with KOPKIJ change scores, respectively, but these correlations did not reach statistical significance.

All correlating factors (i.e., intelligence, KOPKIJ baseline performance, age at seizure onset, epilepsy duration, seizure freedom, antiseizure drug load, reduction of antiseizure drug load) were considered for stepwise multiple linear regression modeling of the KOPKIJ total standard score at T2 as well as two KOPKIJ change scores (number of domains declined and number of domains improved from T1 to T2). As regards KOPKIJ performance at T2 (total score), only the factor "intelligence" was entered into the model if it was considered (adjusted $R^2 = 0.24$; $F = 23.09$; $p < 0.001$). However, if intelligence was excluded from consideration, the model included KOPKIJ baseline performance (total score), seizure-free status, and reduction of antiepileptic drugs as positive predictors (adjusted $R^2 = 0.57$; $F = 30.82$; $p < 0.001$). The same predictors were obtained for the number of improved KOPKIJ domains (adjusted $R^2 = 0.46$; $F = 20.72$; $p < 0.001$); however, KOPKIJ performance at T1 was a negative predictor in this case. No significant model was obtained for the number of declined KOPKIJ domains (irrespective of considering intelligence or not).

4. Discussion

In this retrospective monocentric treatment outcome study, we evaluated the parents' view of the surgical outcome in six cognitive domains in a large monocentric series of 96 children who underwent epilepsy surgery. On the group level, parent reports indicated not only cognitive safety and stability but cognitive improvements after surgery. Also individually, more than half of the patients experienced improvements in single cognitive domains. However, as one-third of all patients experienced decline in at least one cognitive domain according to parental evaluation, our findings also confirm the neuropsychological risks of epilepsy surgery and that cognitive decline may become relevant in the daily life of the patients. In the following, we discuss our findings on the background of the available literature.

4.1. Parental view of cognitive surgical outcome

As mentioned in the Introduction, several working groups evaluated the surgical cognitive and/or behavioral outcome in pediatric patients from the parents' perspective during the last years (e.g., [22–26]), and our findings largely corroborate the reported outcomes. In fact, the literature clearly converges into the consensus that the cognitive and behavioral outcome of pediatric epilepsy surgery as perceived by the parents is not only stable and safe but, on the group level, rather shows a tendency towards improvement. Controlled studies reported cognitive improvements in surgical patients in contrast to no or even negative developments in nonsurgical controls [29,35,36]; only single studies reported no improvement (but stable courses) [37–41].

Of interest, the parent-perceived surgical cognitive outcome pattern largely mirrors the findings from neuropsychological test-based outcome studies [8–13,32,42–44]. These indicate (i) a cumulated risk for experiencing decline in at least one domain in about one out of three patients; (ii) a risk for significant decline in a single domain in about one out of six patients; and (iii) the chance for reliable improvement in a single domain as well as the cumulated chance for improvement in at least one domain as being twice as large as the risk for decline [23,41,45–47]. However, in our study, parents and tests indicated other critical functions. While the parents experienced declines most often in executive and language functions, neuropsychological testing obtained the most frequent negative effects on verbal and figural memory.

In sum, studies on parental evaluations of the surgical outcome including the present paper provided no evidence of risks for

KOPKIJ		Clinical predictors	Age at seizure onset	Seizure free	N of AEDSs at Follow-up	delta N AEDs (12 mo-BL)	Epilepsy duration	Side of surgery (1-r 2-l)	N of AEDs at Baseline	Site of surgery (1-FL 2-TL)	Age at baseline test	Sex (1-m 2-f)	Handedness (1-RH 2-LH)	n of improved nps domains	n of declined nps domains
- T2	Language		0.188	0.264	-0.191	-0.188	-0.189	-0.151	-0.057	-0.201	0.025	0.091	0.020	0.031	0.124
	Memory		0.168	0.301	-0.214	-0.139	-0.186	-0.117	-0.127	-0.055	0.004	0.043	-0.054	0.060	-0.029
	Visuospatial		0.358	-0.114	0.062	0.079	-0.251	-0.032	-0.153	-0.013	0.162	-0.026	0.008	-0.034	0.238
	Executive		0.210	0.276	-0.243	-0.143	-0.202	-0.113	-0.148	-0.031	0.037	0.034	0.011	-0.039	0.072
	Attention		0.110	0.245	-0.309	-0.224	-0.194	-0.128	-0.069	0.034	-0.074	0.107	-0.022	0.051	-0.031
	School		0.274	0.078	-0.122	-0.021	-0.146	-0.217	-0.091	-0.174	0.199	-0.067	-0.153	-0.075	0.051
- change	Language		-0.007	0.245	-0.150	-0.212	0.025	-0.068	0.118	-0.010	0.019	0.059	0.018	0.178	-0.268
	Memory		-0.100	0.039	-0.076	-0.225	0.117	0.030	0.212	-0.056	0.004	0.116	0.037	0.158	-0.173
	Visuospatial		0.075	-0.027	-0.047	-0.003	-0.074	0.064	-0.032	0.083	0.012	0.023	-0.045	0.036	-0.020
	Executive		-0.028	0.298	-0.341	-0.282	-0.037	0.020	0.025	0.173	-0.073	0.084	0.024	0.149	-0.061
	Attention		-0.135	0.234	-0.230	-0.270	0.051	-0.179	0.127	0.033	-0.107	-0.113	-0.011	0.146	-0.245
	School		-0.131	0.136	-0.115	-0.228	0.004	0.008	0.173	-0.006	-0.196	0.028	0.010	0.002	-0.157
	n declined		-0.006	-0.181	0.147	0.190	0.026	0.087	-0.094	-0.072	0.020	-0.099	0.053	-0.093	0.177
	n improved		-0.093	0.206	-0.233	-0.293	0.060	0.009	0.148	0.020	-0.048	0.009	0.050	0.197	-0.190

Fig. 2. Correlation matrix of KOPKIJ scores at T2 and potential clinical predictors (Supporting Table S4 for details).

everyday cognition that was overseen so far but largely confirmed the overall positive findings as obtained from neuropsychological assessments.

4.2. Predicting the cognitive outcome?

As expected scores on tests of intelligence were correlated with KOPKIJ total performance at T1 and these two measures were both strong predictors of KOPKIJ performance at T2; i.e., the baseline status most likely represents the best guess of what can be expected after surgery, which is perfectly consistent with the notion of "safety". In addition, lower intelligence and lower KOPKIJ performance predicted a higher number of improved cognitive domains. As the KOPKIJ asks for problems only ("Cognitive Problems in Children and Adolescents"), but not for higher degrees of performance (no above-average category exists), this finding might have resulted from a ceiling effect in relative high-performers. No predictors were obtained for cognitive declines. A similar pattern of negative baseline-change correlations (i.e., high performers have more to lose but less to win) was reported by many psychometric surgical outcome studies [8–13,32,42–44].

Apart from the presurgical performance level, seizure freedom and low antiseizure drug load at T2 as well as reduction of the antiseizure drug load from T1 to T2 were the only clinical factors that showed significant positive correlations with both postsurgical KOPKIJ performance and pre- to postsurgical KOPKIJ changes. This implies that the postoperative cognitive outcome as perceived by the parents could not be predicted by clinical factors etc. As regards the role of postoperative seizure freedom, findings in the literature on cognitive and behavioral surgical outcomes are mixed. Conway et al. [39] recently reported more behavioral improvement in seizure-free patients – thus confirming previous findings from our group [48] and other researchers [47,49] – but no changes in cognition, irrespective of the seizure outcome. Of interest, behavioral improvements were shown to partially mediate the well-established relationship between seizure freedom and improved parent-reported health-related quality of life in children with epilepsy [41]. Methodologically, seizure-free status comes close to confound the surgical condition as such if the seizure freedom rate approaches 80%; low variance in one factor of course yields low covariance with other factors.

We obtained positive effects of lower antiseizure drug loads and antiseizure drug reduction on the postoperative cognitive performance as perceived by the parents. This finding is in line with results from a large multicenter study (to which we contributed) that reported improved intelligence after postoperative withdrawal of antiseizure drugs [50]. A recent psychometric study from our group showed that negative effects of antiseizure drugs on intelligence in children with epilepsy are most likely mediated via their impact on executive functions [51]. The KOPKIJ data from the present study underline that drug effects impact everyday performance, and consistent to our previous findings, parents most often reported improvement in "executive functions" (45%) after drug reduction. More research on the effects of antiseizure drugs on the neurocognitive development of children with epilepsy who need to use these drugs is needed. Similar effects of antiseizure drug reduction on parent-perceived cognition were reported by one study [52] but not obtained in another [53].

Like other studies, we found no effects of the lateralization or localization of the surgical site on the outcome variables. Most psychometric studies in pediatric patients also failed to establish strong correlations between side or site of the morphological lesion (presurgical) or resection (postsurgical) and the obtained patterns of functional deficits; this also applies to our own recent neuropsychological outcome study [32]. We presume that the lack of such structure–function correlations in children indicates a generally lower degree of regional and hemispheric specialization for cognitive functions in younger age [54]. In children

with structural epilepsy, the relatively diffuse brain structure–function relationships might also result from the complex compensatory processes that are initiated during neurocognitive development in an attempt to cope with early brain damage (e.g., intra- and interhemispheric shift of functions). Also, the development of executive functions, which is still ongoing during childhood and youth, may play an important role for the low levels of lateralization and localization of higher cognitive functions in children. In particular, we did not find the classical pattern of memory deficits in the case of temporal lobe epilepsy and executive deficits in the case of frontal lobe epilepsy that was reported by Martin et al. [29]. Even the parent-perceived deficits in language functions could not be lateralized to the speech-dominant hemisphere.

Consistent with the notion that epilepsy starts early in the case of severe prenatal brain malformation or insults, earlier onset and longer epilepsy duration were associated with worse KOPKIJ performance at T1 and T2 (but had no effect on change). Stepwise multiple linear regression analyses indicated that these correlations were even stronger for daily life performance as measured by the KOPKIJ than for psychometric intelligence (which is usually used as a summary measure of neurocognitive integrity). Thus, neuropsychological profiles of cognitive performance in children with structural epilepsy rather reflect the extent and time period of the pathological impact on the neurocognitive development than its side or site [54].

4.3. Parental ratings versus neuropsychological tests

As mentioned above, we recently reported low correlations between the KOPKIJ domain scores and the scores from psychometric performance tests associated with the respective cognitive domains [31], and in fact, such discrepancies were already noted by the KOPKIJ's test authors [30]. Of interest, also, other groups found only low correlations between psychometric tests scores and parental ratings [22,55–58]. Evidently, both types of measures imply behavioral sampling, but they do so in entirely different settings. Psychometric test scores are obtained in a highly standardized and therefore artificial situation, especially for children; they rely on an objectively defined scoring algorithm; and, most importantly, the observed scores are referred to a well-defined and standardized scale (namely, the distribution of normative data) for individual diagnostic evaluation. In contrast, when asked to fill-in surveys, parents are implicitly encouraged to apply their own individual reference frame; thus, the obtained rating data are essentially subjective. For example, while some parents tend to compare the performance of their challenged child with healthy siblings or peers (like standardized tests do), other parents may want to account for the given challenge and compare their child with his/her classmates (e.g., in the special-needs school). Obviously, different "normative" standards result in different judgments of objectively similar conditions. However, KOPKIJ change scores are controlled for different underlying subjective standards (as T1 performance scores are subtracted from T2 performance scores) but nevertheless showed almost no correlation with neuropsychological change scores.

Therefore, the question is whether the evident lack of correlation queries the clinical validity of parental ratings; or conversely, threatens the ecological validity of established psychometric tests; or rather indicates that both types of measures contribute complementary clinically valuable diagnostic information. We favor the latter interpretation because similar performance profiles and patterns of change as well as similar clinical predictors (i.e., seizure-free status, antiseizure drug load) indicate that the KOPKIJ survey and the neuropsychological assessment finally refer to the same latent psychological factors. Furthermore, daily life demands in a specific cognitive domain are essentially different from respective psychometric task demands (e.g., due to different time frames in the case of memory) constituting an insurmountable gap between scientific and everyday psychological concepts. Finally, scores from different KOPKIJ domains were highly correlated at both times suggesting that parents rather form a "general impression" [31]. High correlation (i.e., redundancy) of subjective data that apparently address specific domains was often reported, for instance, in studies on subjective memory complaints and depressive mood [59]. In our recent publication, the KOPKIJ data could actually be reduced to two factors, "basic cognition" and "school achievement" [31]. Parental ratings necessarily refer to salient behavioral properties and, thus, may not be expected to provide highly differential information. Both approaches have their own merit to provide clinically valuable information. Mutual replacement of the one by the other seems impossible.

4.4. Limitations

The significance of our study is particularly limited by the monocentric study design and the lack of an adequate control condition (besides the normative sample of healthy children). As regards the monocentric setting of our study, cohort effects concerning the distribution of etiologies and types of surgeries as well as the available pediatric neurosurgical expertise limit the generalizability of the reported medical and cognitive outcomes. The use of the KOPKIJ by other groups and independent replication studies would be highly appreciated. The lack of a control condition is probably one of the most serious issues for treatment effect studies in pediatric surgical patients and, to our opinion, no simple solution exists (as randomization cannot be justified ethically and medically). In the present study, the KOPKIJ standard values as well as the critical differences were derived from an indirect comparison with the normative sample of healthy children. However, especially for reliability, it remains unclear whether the estimates derived from this population do really apply to the clinical sample. As mentioned in the Methods section, the test authors also reported preliminary retest reliabilities which they obtained from a sample of nonsurgical pediatric patients with epilepsy (follow-up about 12 months) [30]. However, upon closer examination, these patients showed important differences in their clinical characteristics as compared with the surgical sample of the present study. Most importantly, a substantial rate of the nonsurgical patients (40%) did not suffer from therapy-refractory epilepsy at the baseline as they were seizure-free at the retest (unpublished data). For this reason, we changed our initial plans, revised the manuscript and decided to not include these children as controls. Of note, as we used the highest available reliability estimates, the reported percentages for both risks and chances represent the upper boundaries.

5. Conclusions

Our study provides further evidence for the medical success and the cognitive safety of pediatric epilepsy surgery with regard to the children's daily life. Even more, parents reported postoperative improvement on the group level. Individually, cognitive improvement was twice as likely as decline. However, one-third of the patients experienced decline in at least one cognitive domain reminding of cognitive risks of epilepsy surgery and their relevancy for daily life performance. The KOPKIJ provides complementary diagnostic information for clinical and scientific use in epilepsy and, probably, other pediatric conditions. Our findings are suggestive for using third party evaluation surveys also in adult therapy outcome research.

Ethical publication statement

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.

Funding

No funding.

Declaration of competing interest

The authors reported no conflicts of interests.

Acknowledgments

No funding was received for this study.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.yebeh.2019.106552.

References

[1] Kellermann TS, Wagner JL, Smith G, Karia S, Eskandari R. Surgical management of pediatric epilepsy: decision-making and outcomes. Pediatr Neurol 2016;64:21–31. https://doi.org/10.1016/j.pediatrneurol.2016.06.008.
[2] Ryvlin P, Cross JH, Rheims S. Epilepsy surgery in children and adults. Lancet Neurol 2014;13. https://doi.org/10.1016/S1474-4422(14)70156-5.
[3] Wiebe S. A randomized, controlled trial of surgery. 2001;345:311–8.
[4] Dwivedi R, Ramanujam B, Chandra PS, Sapra S, Gulati S, Kalaivani M, et al. Surgery for drug-resistant epilepsy in children. N Engl J Med 2017;377:1639–47. https://doi.org/10.1056/NEJMoa1615335.
[5] West S, Nolan SJ, Cotton J, Gandhi S, Weston J, Sudan A, et al. Surgery for epilepsy. Cochrane Database Syst Rev 2015:CD010541. https://doi.org/10.1002/14651858.CD010541.pub2.
[6] tao Liu J, Liu B, Zhang H. Surgical versus medical treatment of drug-resistant epilepsy: a systematic review and meta-analysis. Epilepsy Behav 2018;82:179–88. https://doi.org/10.1016/j.yebeh.2017.11.012.
[7] Rolston JD, Englot DJ, Knowlton RC, Chang EF. Rate and complications of adult epilepsy surgery in North America: analysis of multiple databases. Epilepsy Res 2016. https://doi.org/10.1016/j.eplepsyres.2016.05.001.
[8] Ormond DR, Clusmann H, Sassen R, Hoppe C, Helmstaedter C, Schramm J, et al. Pediatric temporal lobe epilepsy surgery in Bonn and review of the literature. Neurosurgery 2018;0:1–13. https://doi.org/10.1093/neuros/nyy125.
[9] Flint AE, Waterman M, Bowmer G, Vadlamani G, Chumas P, Morrall MCHJ. Neuropsychological outcomes following paediatric temporal lobe surgery for epilepsies: evidence from a systematic review. Seizure 2017;52. https://doi.org/10.1016/j.seizure.2017.09.011.
[10] Hosoyama H, Matsuda K, Mihara T, Usui N, Baba K, Inoue Y, et al. Long-term outcomes of epilepsy surgery in 85 pediatric patients followed up for over 10 years: a retrospective survey. J Neurosurg Pediatr 2017;19. https://doi.org/10.3171/2016.12.PEDS16197.
[11] Sibilia V, Barba C, Metitieri T, Michelini G, Giordano F, Genitori L, et al. Cognitive outcome after epilepsy surgery in children: a controlled longitudinal study. Epilepsy Behav 2017;73:23–30. https://doi.org/10.1016/j.yebeh.2017.03.001.
[12] Van Schooneveld MMJJ, Braun KPJJ. Cognitive outcome after epilepsy surgery in children. Brain Dev 2013;35:721–9. https://doi.org/10.1016/j.braindev.2013.01.011.
[13] Reinholdson J, Olsson I, Edelvik A, Hallböök T, Lundgren J, Rydenhag B, et al. Long-term follow-up after epilepsy surgery in infancy and early childhood — a prospective population-based observational study. Seizure 2015;30:83–9. https://doi.org/10.1016/j.seizure.2015.05.019.
[14] Gröppel G, Dorfer C, Mühlebner-Fahrngruber A, Dressler A, Porsche B, Czech T, et al. Improvement of language development after successful hemispherotomy. Seizure 2015;30:70–5. https://doi.org/10.1016/j.seizure.2015.05.018.
[15] Roulet-Perez E, Davidoff V, Mayor-Dubois C, Maeder-Ingvar M, Seeck M, Ruffieux C, et al. Impact of severe epilepsy on development: recovery potential after successful early epilepsy surgery. Epilepsia 2010;51:1266–76. https://doi.org/10.1111/j.1528-1167.2009.02487.x.
[16] Gleissner U, Sassen R, Schramm J, Elger CE, Helmstaedter C. Greater functional recovery after temporal lobe epilepsy surgery in children. Brain 2005;128:2822–9. https://doi.org/10.1093/brain/awh597.
[17] Vogt VL, Äikiä M, del Barrio A, Boon P, Borbély C, Bran E, et al. Current standards of neuropsychological assessment in epilepsy surgery centers across Europe. Epilepsia 2017;58:343–55. https://doi.org/10.1111/epi.13646.
[18] Dewey D, Crawford SG, Kaplan BJ. Clinical importance of parent ratings of everyday cognitive abilities in children with learning and attention problems. J Learn Disabil 2003;36:87–95. https://doi.org/10.1177/00222194030360011001.
[19] Diamond KE, Squires J. The role of parental report in the screening and assessment of young children. J Early Interv 1993;17:107–15. https://doi.org/10.1177/105381519301700203.
[20] Glascoe FP, Dworkin PH. The role of parents in the detection of developmental and behavioral problems. Pediatrics 1995;95:829–36.
[21] Kavanaugh BC, Scarborough VR, Salorio CF. Parent-rated emotional–behavioral and executive functioning in childhood epilepsy. Epilepsy Behav 2015;42. https://doi.org/10.1016/j.yebeh.2014.11.006.
[22] Conway L, Widjaja E, Smith M Lou. Impact of resective epilepsy surgery on health-related quality of life in children with and without low intellectual ability. Epilepsy Behav 2018;83:131–6. https://doi.org/10.1016/j.yebeh.2018.03.036.
[23] Law N, Kerr E, Smith M Lou. Evaluation of behavioral outcomes in children 1 year after epilepsy surgery. Epilepsia 2015;56:1605–14. https://doi.org/10.1111/epi.13126.
[24] Graham D, Tisdall MM, Gill D. Corpus callosotomy outcomes in pediatric patients: a systematic review. Epilepsia 2016;57:1053–68. https://doi.org/10.1111/epi.13408.
[25] Tavares TP, Puka K, Smith M Lou. Emotional functioning: long-term outcomes after pediatric epilepsy surgery. Epilepsia 2015;56. https://doi.org/10.1111/epi.12956.
[26] Puka K, Smith M Lou. Long-term outcomes of behavior problems after epilepsy surgery in childhood. J Neurol 2016;263:991–1000. https://doi.org/10.1007/s00415-016-8089-0.
[27] Reilly C, Baldeweg T, Stewart N, Wadhwani S, Jones C, Helen Cross J, et al. Do behavior and emotions improve after pediatric epilepsy surgery? A systematic review. Epilepsia 2019;60. https://doi.org/10.1111/epi.14737.
[28] Oitment C, Vriezen E, Smith M Lou. Everyday memory in children after resective epilepsy surgery. Epilepsy Behav 2013;28:141–6. https://doi.org/10.1016/j.yebeh.2013.04.013.
[29] Martin R, Cirino P, Hiscock M, Schultz R, Collins R, Chapieski L. Risks and benefits of epilepsy surgery in a pediatric population: consequences for memory and academic skills. Epilepsy Behav 2016;62:189–96. https://doi.org/10.1016/j.yebeh.2016.06.028.
[30] Gleissner U, Lendt M, Mayer S, Elger CE, Helmstaedter C. Kognitive Probleme bei Kindern und Jugendlichen. Vorstellung eines Fragebogens. A new questionnaire for recognizing cognitive problems in children and adolescents Nervenarzt 2006;77:449–65. https://doi.org/10.1007/s00115-005-2050-2.
[31] Helmstaedter C, Pandolfo RV, Hoppe C, Witt J-A. Cognitive-behavioral correlates of proxy reports on cognitive capabilities in pediatric patients with epilepsy. Seizure 2017;51. https://doi.org/10.1016/j.seizure.2017.08.016.
[32] Helmstaedter C, Beeres K, Elger CE, Kuczaty S, Schramm J, Hoppe C. Cognitive outcome of pediatric epilepsy surgery across ages and different types of surgeries: a monocentric 1-year follow-up study in 306 patients of school age. Seizure-European J Epilepsy 2019 pii: S1059-1311(18)30743-X. https://doi.org/10.1016/j.seizure.2019.07.021. [Epub ahead of print].
[33] Achenbach TM, Edelbrock C. Manual for the Child Behavior Checklist: 5–18 and 1991 profile. University of Vermont: Burlington/Vermont; 1991.
[34] Cohen J. Statistical power analysis for the behavioral sciences. . 2nd ed.Hillsdale/NJ: Erlbaum; 1988.
[35] Elliott IM, Lach L, Kadis DS, Smith M Lou. Psychosocial outcomes in children two years after epilepsy surgery: has anything changed? Epilepsia 2008;49:634–41. https://doi.org/10.1111/j.1528-1167.2007.01498.x.
[36] Law N, Kerr E, Smith M Lou. Evaluation of behavioral outcomes in children 1 year after epilepsy surgery. Epilepsia 2015;56:1605–14. https://doi.org/10.1111/epi.13126.
[37] Larysz D, Larysz P, Mandera M. Evaluation of quality of life and clinical status of children operated on for intractable epilepsy. Childs Nerv Syst 2007;23:91–7. https://doi.org/10.1007/s00381-006-0200-x.
[38] Oitment C, Vriezen E, Smith M Lou. Everyday memory in children after resective epilepsy surgery. Epilepsy Behav 2013;28:141–6. https://doi.org/10.1016/j.yebeh.2013.04.013.
[39] Conway L, Widjaja E, Smith M Lou. Impact of resective epilepsy surgery on health-related quality of life in children with and without low intellectual ability. Epilepsy Behav 2018;83:131–6. https://doi.org/10.1016/J.YEBEH.2018.03.036.
[40] Law N, Kerr E, Smith M Lou. Evaluation of behavioral outcomes in children 1 year after epilepsy surgery. Epilepsia 2015;56:1605–14. https://doi.org/10.1111/epi.13126.
[41] Puka K, Smith M Lou. Predictors of long-term quality of life after pediatric epilepsy surgery. Epilepsia 2015;56:873–81. https://doi.org/10.1111/epi.13004.
[42] Martin R, Cirino P, Hiscock M, Schultz R, Collins R, Chapieski L. Risks and benefits of epilepsy surgery in a pediatric population: consequences for memory and academic skills. Epilepsy Behav 2016;62:189–96. https://doi.org/10.1016/j.yebeh.2016.06.028.
[43] Lah S, Smith M Lou. Verbal memory and literacy outcomes one year after pediatric temporal lobectomy: a retrospective cohort study. Epilepsy Behav 2015;44:225–33. https://doi.org/10.1016/j.yebeh.2014.12.040.
[44] Viggedal G, Olsson I, Carlsson G, Rydenhag B, Uvebrant P. Intelligence two years after epilepsy surgery in children. Epilepsy Behav 2013;29:565–70. https://doi.org/10.1016/j.yebeh.2013.10.012.
[45] Aaberg KM, Eriksson A-SS, Ramm-Pettersen J, Nakken KO. Long-term outcome of resective epilepsy surgery in Norwegian children. Acta Paediatr 2012;101:e557–60. https://doi.org/10.1111/j.1651-2227.2012.02834.x.
[46] Pati S, Deep A, Troester MM, Kossoff EH, Ng YT. Lennox–Gastaut syndrome symptomatic to hypothalamic hamartoma: evolution and long-term outcome following surgery. Pediatr Neurol 2013;49:25–30. https://doi.org/10.1016/j.pediatrneurol.2013.03.016.
[47] Puka K, Smith M Lou. Long-term outcomes of behavior problems after epilepsy surgery in childhood. J Neurol 2016;263:991–1000. https://doi.org/10.1007/s00415-016-8089-0.
[48] Lendt M, Helmstaedter C, Kuczaty S, Schramm J, Elger CE. Behavioural disorders in children with epilepsy: early improvement after surgery. J Neurol Neurosurg Psychiatry 2000;69:739–44.
[49] Moseley BD, Nickels K, Wirrell EC. Surgical outcomes for intractable epilepsy in children with epileptic spasms. 2012;27. https://doi.org/10.1177/0883073811424463.
[50] Boshuisen K, van Schooneveld MM, Uiterwaal CS, Cross JH, Harrison S, Polster T, et al. Intelligence quotient improves after antiepileptic drug withdrawal following pediatric epilepsy surgery. Ann Neurol 2015;78:104–14. https://doi.org/10.1002/ana.24427.

[51] Helmstaedter C, Witt J-A, Hoppe C. Evaluating the mediating role of executive functions for antiepileptic drugs' effects on IQ in children and adolescents with epilepsy. Epilepsy Behav 2019;96:98–103. https://doi.org/10.1016/j.yebeh.2019.04.003.
[52] Elliott IM, Lach L, Kadis DS, Smith M Lou. Psychosocial outcomes in children two years after epilepsy surgery: has anything changed? Epilepsia 2008;49:634–41. https://doi.org/10.1111/j.1528-1167.2007.01498.x.
[53] Law N, Kerr E, Smith M Lou. Evaluation of behavioral outcomes in children 1 year after epilepsy surgery. Epilepsia 2015;56:1605–14. https://doi.org/10.1111/epi.13126.
[54] Gleissner U, Helmstaedter C. Presurgical neuropsychological workup in children and mentally retarded adults with epilepsy. In: Lüders HO, editor. Textb. Epilepsy Surg. Oxfordshire: Taylor & Francis Books; 2008.
[55] Vriezen ER, Pigott SE. The relationship between parental report on the BRIEF and performance-based measures of executive function in children with moderate to severe traumatic brain injury. Child Neuropsychol 2002;8:296–303. https://doi.org/10.1076/chin.8.4.296.13505.
[56] Samarasekera SR, Helmstaedter C, Reuber M. Cognitive impairment in adults with epilepsy: the relationship between subjective and objective assessments of cognition. Epilepsy Behav 2015;52:9–13. https://doi.org/10.1016/j.yebeh.2015.08.013.
[57] Titus JB, Lee A, Kasasbeh A, Thio LL, Stephenson J, Steger-May K, et al. Health-related quality of life before and after pediatric epilepsy surgery: the influence of seizure outcome on changes in physical functioning and social functioning. Epilepsy Behav 2013;27:477–83. https://doi.org/10.1016/j.yebeh.2013.03.003.
[58] Yang TF, Wong TT, Kwan SY, Chang KP, Lee YC, Hsu TC. Quality of life and life satisfaction in families after a child has undergone corpus callostomy. Epilepsia 1996;37:76–80.
[59] Grewe P, Nikstat A, Koch O, Koch-Stoecker S, Bien CG. Subjective memory complaints in patients with epilepsy: the role of depression, psychological distress, and attentional functions. Epilepsy Res 2016;127:78–86. https://doi.org/10.1016/j.eplepsyres.2016.08.022.