Received: 10 January 2024 | Revised: 17 July 2024 | Accepted: 28 July 2024

DOI: 10.1002/epi4.13027

Epilepsia Open® Open Access

ORIGINAL ARTICLE

Epilepsy surgery below the age of 5 years: Are we still in time to preserve developmental and intellectual functions?

Simona Cappelletti[1] | **Cinzia Correale**[1] | **Mattia Mercier**[1] | **Giusy Carfi Pavia**[1] | **Chiara Falamesca**[1] | **Alessandro De Benedictis**[2] | **Carlo Efisio Marras**[2] | **Chiara Quintavalle**[1] | **Concetta Luisi**[1] | **Chiara Pepi**[1] | **Daniela Chiarello**[1] | **Federico Vigevano**[3] | **Luca De Palma**[1] | **Nicola Specchio**[1,4]

[1]Neurology, Epilepsy and Movement Disorders, Full Member of European Reference Network EpiCARE, Bambino Gesù Children's Hospital, IRCCS, Rome, Italy

[2]Neurosurgery Unit, Bambino Gesù Children's Hospital, IRCCS, Rome, Italy

[3]Department of Paediatric Neurorehabilitation, IRCCS San Raffaele, Rome, Italy

[4]Director of Research Unit on Neurological and Neurosurgical Diseases

Correspondence
Nicola Specchio, Director of Research Unit on Neurological and Neurosurgical Diseases, Neurology, Epilepsy and Movement Disorders, Bambino Gesù Children's Hospital, IRCCS, Piazza Sant' Onofrio, 4, Rome 00165, Italy.
Email: nicola.specchio@opbg.net

Funding information
Ministero della Salute

Abstract

Objective: The aim of this study is to describe the pre- and post-operative developmental and intellectual functions in a cohort of patients who underwent surgery for drug-resistant epilepsy (DRE) before the age of 5 years.

Method: We retrospectively reviewed the medical records and neurodevelopmental assessments of a cohort of 80 surgically treated pediatric patients with DRE. We included patients if they had at least one pre- and one post-surgical neuropsychological assessments; 27 met the inclusion criteria. We evaluated Developmental Quotient (DQ) and Intelligence Quotient (IQ) before and after surgery. We identified two groups based on psychological evaluation outcome: Group 1, with stable or improved developmental and intellectual functions, and Group 2, experiencing developmental and intellectual loss.

Results: The mean age at seizure onset was 1.2 ± 1.0 years, and the mean age at surgery was 2.9 ± 1.2 years. At the last follow-up (mean 4 years, SD ± 2), 19/27 (70%) patients were seizure- and drug-free; 18/27 patients (67%) fit in Group 1, and 9/27 (33%) fit in Group 2. The mean age at surgery was 2.6 years (SD ± 1.1; range 1.2–5.1) in Group 1 and 3.4 years in Group 2 (SD ± 1.1; range 1.6–5.0). Group 1 had a lower pre-operative DQ/IQ total score than Group 2 (median DQ/IQ respectively 82 vs 108, $p = 0.05$). Between pre- and post-assessments, we found that in Group 1, Performance scores improved (82.7 vs 102, $p = 0.001$), while in Group 2, the Total and Verbal scores worsened (respectively 108 vs 75, $p = 0.008$, and 100 vs 76, $p = 0.021$).

Significance: Our study's results emphasize the positive impact of surgery before the age of 5 years on developmental and intellectual outcomes. Despite limitations such as a small sample size, lack of a control group, and diverse etiologies,

Simona Cappelletti and Cinzia Correale have contributed equally to this work.

our findings support the crucial role of early intervention in preserving or enhancing developmental and intellectual functions in young patients with DRE.

Plain Language Summary: This retrospective study, conducted at the Bambino Gesù Children Hospital in Italy, reports neuropsychological and developmental and/or cognitive data for children undergoing early epilepsy surgery (before the age of 5). It found that children with lower developmental or cognitive profiles gained the highest scores on post-operative neuropsychological evaluations. This study provides information on the potential benefits of early surgery in shortening the duration of epilepsy, preventing or arresting deterioration, and enhancing plasticity and recovery.

KEYWORDS

developmental and intellectual outcomes, developmental quotient, drug-resistant epilepsy, intelligence quotient, pediatric epilepsy surgery

1 | INTRODUCTION

Epilepsy is a multifactorial disorder, and the etiologies of epilepsies can affect brain maturation and development.[1,2] Cognitive impairment is common in patients with early-onset epilepsy, especially in those with drug-resistant epilepsy associated with malformations of cortical development.[3] Younger age at seizure onset, the duration of epilepsy, and the extent of the cortical malformation predict worse cognitive outcome.[1–3]

Resective epilepsy surgery for a focal epileptogenic lesion is an effective treatment for both seizure control and cognitive improvement in patients with drug-resistant epilepsy.[4–6] Early intervention may benefit from the brain's maximum plasticity and from maturational and compensatory reorganization processes. It also helps preserve early neurological development from the interference of seizures and interictal epileptiform discharges.[7–9] It has been documented that the chances of improvement in Developmental Quotient/Intelligence Quotient (DQ/IQ) in pediatric patients undergoing surgery are higher than the risk of deterioration.[10] Freitag and Tuxhorn[11] reported that most pre-school patients who underwent surgery for drug-resistant epilepsy showed stability in cognitive development over the short-term follow-up and a positive trend over the longer period. In this regard, previous studies documented that pre-surgical DQ/IQ is an important predictor of post-operative developmental and intellectual outcomes.[3–7–10] While stagnation and slowing of post-surgical developmental and intellectual trends may be present in some cases, the level of evidence is still poor as most studies are characterized by small sample sizes and short follow-ups.

The present study aims to describe the clinical features and developmental and intellectual trajectories of a group of pediatric patients who received resective surgery as a treatment for drug-resistant epilepsy before the age of 5 years.

Key points

- Cognitive impairment is common in patients with early-onset epilepsy.
- Resective surgery is an effective treatment for both seizure control and cognitive improvement.
- Most of our sample showed a cognitive improvement or stability after surgery.
- Performance scores improved in Group 1 and Total and Verbal scores worsened in Group 2.

2 | PARTICIPANTS AND METHODS

2.1 | Participants

We retrospectively reviewed the medical records and neurodevelopmental assessments of a cohort of 80 pediatric patients with drug-resistant epilepsy who were surgically treated before the age of 5 at the Neurology Epilepsy Unit at the Bambino Gesù Children's Hospital between 2009 and 2019. We included patients who (i) underwent surgery before the age of 5 years and (ii) had at least one pre- and one post-surgery neuropsychological evaluations using verbal and non-verbal standard scales (Griffiths Scales of Child Development or Wechsler Preschool and Primary

Scale of Intelligence). Patients with incomplete or missing neuropsychological data were excluded.

Patients were assessed according to a pre-surgical neuropsychological standard protocol following international recommendations.[12] Considering the retrospective nature of the analysis, the current study did not require approval from the local ethics committee according to current legislation, but a notification was sent. Data were retrospectively analyzed in line with personal data protection policies.

2.2 | Procedures

Developmental and/or intellectual domains ware evaluated both before and after surgery. For the analysis of results, we considered the last available neuropsychological evaluation, which was conducted after a mean period of 4.0 ± 2.0 years (range 1.1–8.4 years). The neuropsychological assessment was carried out using standardized scales, selected based on the child's chronological age: Griffiths Scales of Child Development (GMDS)[13] in patients below the age of 4 years, Wechsler Preschool and Primary Scale of Intelligence (WPPSI-III)[14] in patients between 4 and 6 years, and Wechsler Intelligence Scale for Children (WISC-IV)[15] in patients from 6 years old and above. If the patient was too delayed, we repeated the Griffiths Scales. As previously reported, we used a single psychometric global measure (IQ/DQ) as an outcome measure.[16] DQ was converted in IQ as follows: We converted Griffiths' scale C (Hearing and Speech) and scale F (Practical Reasoning, for patients with mental age > 24 months) into Verbal Function, and we converted scale D (Eye and Hand Coordination) and scale E (Performance) into Performance Function. DQ/IQ represented the average value between the verbal function and the performance function.[17,18] Significant pre- and post-operative DQ/IQ scores were defined as a ±10 score cut-off.[10,19]

Further clinical variables were gathered by continuous scalp video-EEG monitoring and high-resolution magnetic resonance imaging (MRI).

Patients were assigned to two groups based on the post-intervention developmental and intellectual outcomes: One group included patients with improved or stable functions (Group 1), and the second group included patients who lost scores between the pre- and post-assessment (Group 2).

2.3 | Demographics and statistical analysis

We performed a descriptive analysis for demographic features. We computed frequency and distributions for all the available categorical data. We described continuous data with a normal distribution using mean and standard deviation, whereas for data with other distributions, the median and range (min and max) were reported.

We examined differences in clinical, developmental, and intellectual features, and we also performed Wilcoxon and Mann–Whitney tests to observe whether there was a difference in clinical and surgical characteristics between pre- and post-intervention periods between the two groups of patients. The Sankey plot was constructed using MATLAB Software to visually represent the relationships and transitions between developmental and/or intellectual evaluation. Parameters, including node spacing, link curvature, and color representation, were adjusted to optimize the visualization for developmental and/or intellectual changes over the three follow-up periods.

3 | RESULTS

3.1 | Pre- and post-surgical clinical features

We enrolled 27 patients, of which 7 were with a mean age at seizure onset of 1.2 ± 1.0 years and a mean age at surgery of 2.9 ± 1.2 years. Table 1 shows detailed patient's clinical features.

At the last neuropsychological evaluation (mean 4.0 SD ± 1.9 years; range 1.8–8.4 years), 18 patients (67%) had improved or stabilized developmental and/or intellectual functions (Group 1), while 9 patients (33%) had developmental and/or intellectual decline (Group 2).

In Group 1, mean age at surgery was 2.6 years (SD ±1.1; range 1.2–5.1). The mean age at seizure onset was 1.1 years (SD ± 0.9; range 0.1–4.0), while the mean duration of epilepsy was 1.5 years (SD ±0.8; range 0.1–3.1). The mean duration of neuropsychological follow-up post-operatively was 3.8 years (SD ± 2.0; range 1.8–7.1). Eleven patients (61%) presented focal cortical dysplasia type I (3 patients) or II (8 patients), while 4 patients (22%) presented long-term epilepsy-associated tumors (LEAT). Fourteen patients (78%) were seizure-free. At last follow-up, seven patients had psychopathological comorbidity; two of them presented attention deficit disorder, four presented emotional and behavioral dysregulations, and one child presented both conditions.

In Group 2, the mean age at surgery was 3.4 years (SD ± 1.1; range 1.6–5.0). The mean age at seizure onset was 1.4 years (SD ± 1.1; range 0.2–3.0), while the mean duration of epilepsy was 2 years (SD ± 1.1; range 0.6–4.1). The mean duration of neuropsychological follow-up post-operatively was 4.5 years (SD ± 2.0; range 2.0–8.4). Six patients (67%) had a focal cortical dysplasia type I (1 patient) or type II (5 patients). Five patients (56%) were

TABLE 1 Clinical and demographic features of study sample of patients.

Patient characteristics	Total ($n=27$)	Group 1 ($n=18$)	Group 2 ($n=9$)
Sex	**F:7, M:20**		
	M (SD; range)	**M (SD; range)**	**M (SD; range)**
Age at first seizure (*in years*)	1.2 (0.9; 0.1–4)	1.1 (0.9; 0.1–4)	1.4 (1.06; 0.2–3)
Age at surgery (*in years*)	2.9 (1.2; 1.2–5.1)	2.6 (1.1; 1.2–5.1)	3.4 (1.10; 1.6–5)
Duration of epilepsy (*in years*)	1.7 (0.9; 0.1–4.1)	1.5 (0.8; 0.1–3.1)	2 (1.1; 0.6–4.1)
Time neuropsychological follow-up[a]	4.05 (2.0; 1.1–8.4)	3.8 (1.9; 1.8–7.1)	4.5 (2.02; 2–8.4)
Seizure outcome	***N* (%)**	***N* (%)**	***N* (%)**
IA	19 (70.4)	14 (77.8)	5 (55.5)
Other	8 (29.6)	4 (22.2)	4 (44.5)
Diagnosis/Etiology/Pathology			
Focal cortical dysplasia		11 (61.1)	6 (66.7)
LEAT		4 (22.2)	1 (11.1)
Hypothalamic hamartoma		2 (11.1)	1 (11.1)
Hippocampal sclerosis		0	1 (11.1)
Other		1 (5.6)	0
Type of surgery			
Lesionectomy	4 (14.9)	3 (16.7)	1 (11.1)
Lesionectomy + cortectomy	17 (62.8)	11 (61.1)	6 (66.7)
Hemispherectomy	2 (7.4)	2 (11.1)	0
Other	4 (14.9)	2 (11.1)	2 (22.2)
Drug resistance		**15 (83.3)**	**6 (66.7)**
Seizure outcome (Engel Scale)		***N***	***N***
IA		14 (77.8)	5
IC		1	2
ID		1	–
II		–	1
III		1	1
IV		1	–

Abbreviation: LEAT, long-term epilepsy-associated tumors.

[a]Time from date of surgery to last psychological follow-up.

seizure-free after surgery. At last follow-up, three patients had psychopathological comorbidity including attention deficit disorder and emotional and behavioral dysregulation. One child had been diagnosed with autistic spectrum disorder.

3.2 | Developmental and intellectual trajectories and seizure outcomes after surgery

Developmental and intellectual outcomes are summarized in Table 2.

We found that patients in Group 1 had a lower preoperative DQ/IQ total score than in Group 2 (median DQ/IQ respectively 82 vs 108, $p=0.05$). Within Group 1, Performance scores statistically improved between pre- and post-assessments (82.7 vs 102, $p=0.001$), while in Group 2, the Total and Verbal scores statistically worsened between pre- and post-assessments (respectively 108 vs 75, $p=0.008$, and 100 vs 76, $p=0.021$; Figure 1). Figure 2 represents the trajectories of developmental and intellectual performances before and after surgery for the entire sample of patients.

The post-surgical seizure outcome is presented in Table 1. Of the 27 patients, 19 (70.4%) were seizure- and drug-free (mean follow-up of 4 years, SD ± 2), while 8

TABLE 2 Cognitive abilities before and after the surgical procedure.

Cognitive outcome				
	Pre-surgery (median)	**Post-surgery (median)**	**Raw score difference (pre-post)**	***p*-Value**
Group 1 (*n* = 18)				
Total score	82	93	11	0.114
Verbal score	75.5	94	18.5	0.053
Performance score	82.7	102	19.3	**0.001***
Group 2 (*n* = 9)				
Total score	108	75	−33	**0.008***
Verbal score	100	76	−24	**0.021***
Performance score	102.5	82	−20.5	0.314

*Statistically significant value, $p < 0.05$, CI = 95%.
Bold values indicates statistically significant values ($p < 0.05$)

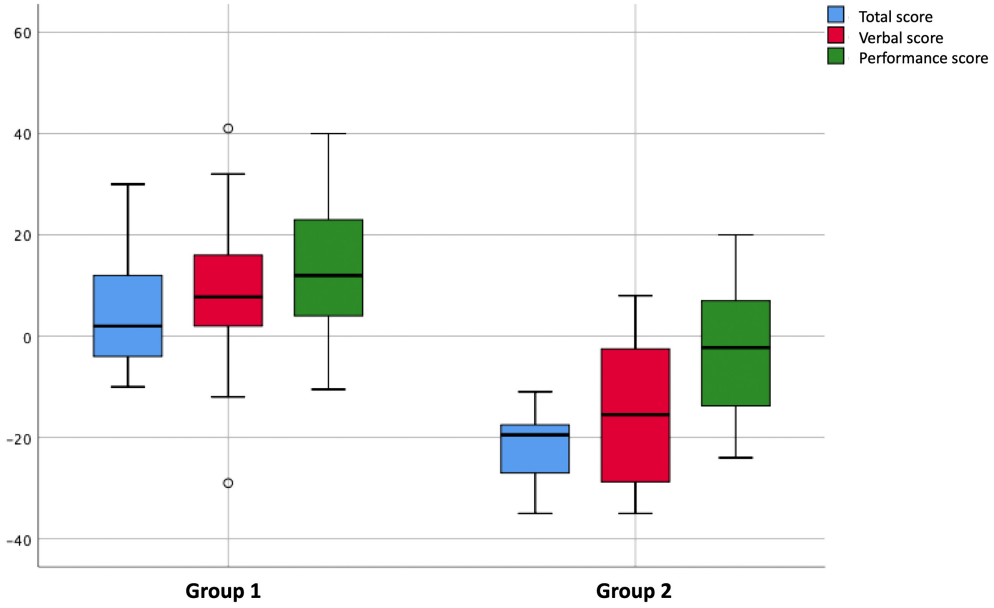

FIGURE 1 The box plot illustrates the distribution of differences in total, verbal, and performance scores evaluated before and after surgery among patients in Group 1 and Group 2. The boxes delineate the interquartile range (IQR), with the median depicted as the central black line. Whiskers extend to the minimum and maximum values, while individual data points beyond this range are considered outliers. The box plot provides a visual summary of the central tendency and variability across both patient groups.

(29.6%) continued to have seizures at the last follow-up. Among the seizure- and drug-free patients, 14 (73.6%) showed improved or stabilized developmental and/or intellectual functions. In contrast, among those who continued to have seizures, 4 (50%) showed a worsened developmental and/or intellectual trajectory.

We found no statistically significant correlation between seizure outcome and developmental and intellectual functions. Among seizure-free patients, we confirmed that performances were stable or slightly improved (Figure 3). We did not find any statistically significant correlation between post-surgical developmental and intellectual outcomes and seizure outcome ($p = 0.573$), age at seizure onset ($p = 0.426$), age at surgery ($p = 0.097$), or the duration of epilepsy ($p = 0.246$). These descriptive results are summarized in Table 1.

4 | DISCUSSION

Cognitive impairment is common in patients with epilepsy, especially in those with early-onset, drug-resistant seizures, and extensive malformations of cortical development.[1,2] Early resective surgery and shorter seizure

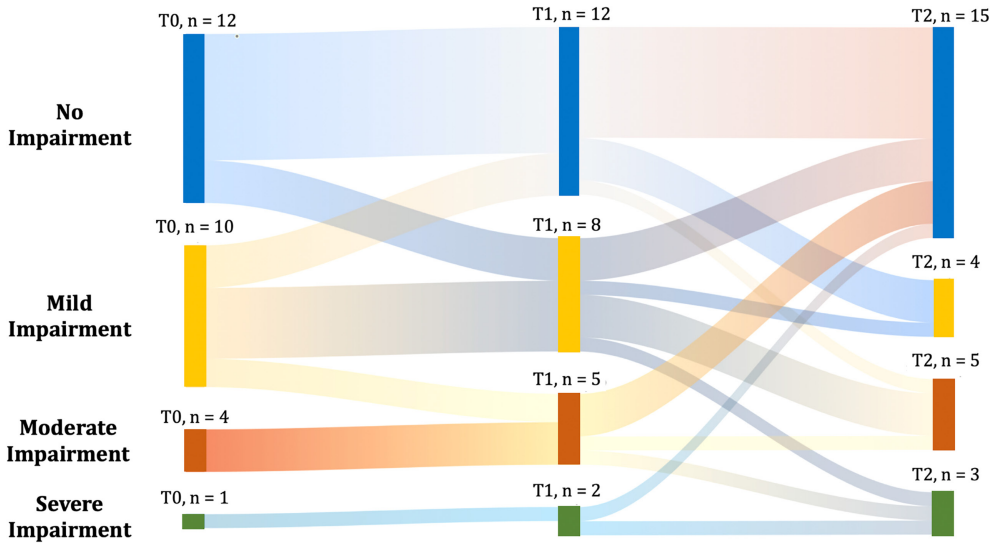

FIGURE 2 Example of a Sankey flow diagram with components labeled, defined, and explained. The x-axis represents three time points regarding follow-up evaluation. T0 represents the pre-surgical evaluation, T1 represents the evaluation done 2 years after surgery, and T2 represents the evaluation done 4 years after surgery. The total of the y-axis represents the full sample (100%). This Sankey diagram depicts the flow among four different cognitive functions represented by colors. The connections between nodes are referred to as flows and represent the proportion of the sample transitioning from one node to the next, indicating cognitive outcome during the assessment. These flows highlight changes in cognitive outcomes over time. On the right side of the diagram, the colors of the vertical bars align with the cognitive functions represented on the left side. This alignment allows for straightforward tracking of cognitive function changes over the evaluated periods. Each vertical bar signifies the distribution of cognitive functions at each time point.

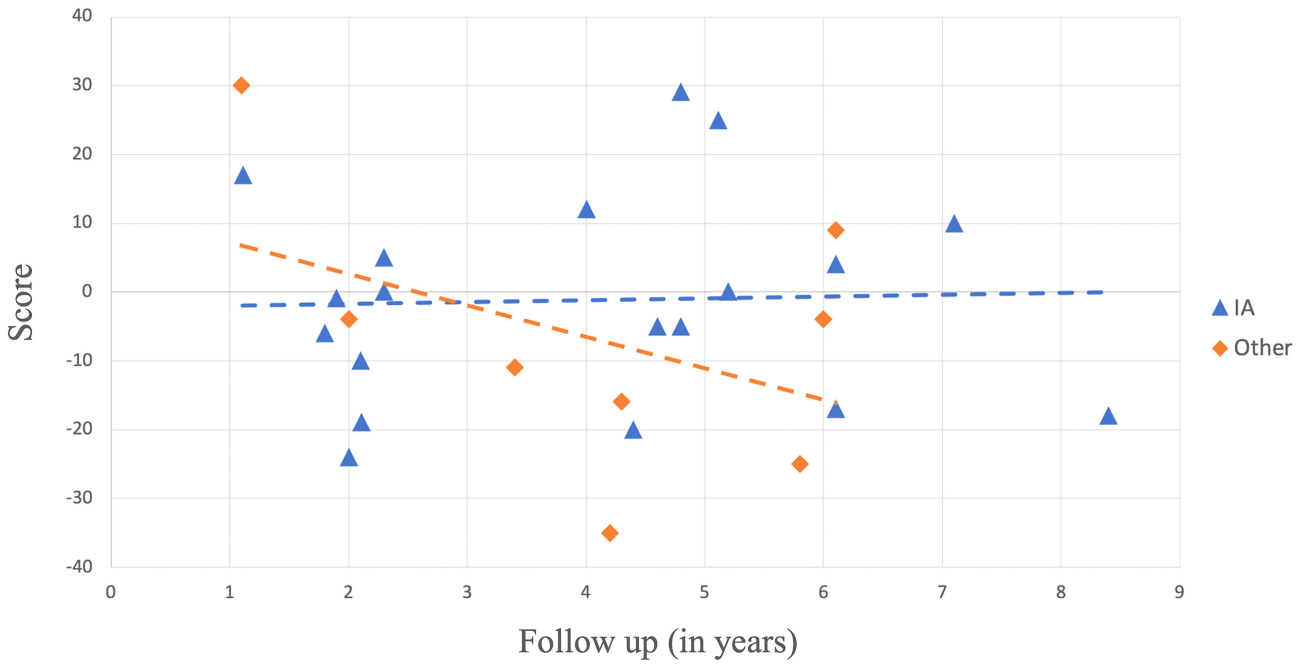

FIGURE 3 Correlation between cognitive function (DQ/IQ) and the time of neuropsychological post-surgery follow-up for both seizure outcome groups (IA vs. other). *IA: completely seizure-free since surgery, others: no seizure-free according to Engel Surgical Outcome Scale. The y-axis represents the change in cognitive function scores (DQ/IQ) over the specified follow-up periods, represented by the x-axis. Patients who worsened were all reported to have a pre-surgical higher median DQ/IQ score than patients who improved or were found stable on cognitive trajectory. The correlation coefficients are Pearson = 0.036 for the duration of follow-up and DQ-IQ outcome for the for "IA Group", and Pearson = 0.114 for the duration of follow-up and DQ-IQ outcome for the "Others" group.

duration before surgery may result in stable or improved post-operative developmental and intellectual outcomes.[4–6] In this study, we included patients who were operated before the age of 5 years, and our findings show that most of them (67%) improved or maintained stable their developmental and intellectual trajectories after surgery.

According to the 2006 ILAE Pediatric Epilepsy Surgery Task Force recommendations, early surgery—meaning at the earliest stages of development—should be considered to improve seizure frequency and to prevent the detrimental effects of severe and frequent seizures on neurodevelopmental progress.[7–9] Following these recommendations, if DQ/IQ regression is observed, a surgical approach should be considered urgent.[20] Epilepsy duration is considered a predictive variable for post-operative cognitive abilities: Children with shorter intervals between epilepsy onset and surgery have greater gains in DQ/IQ.[11] In fact, pre-school patients who were operated within 6 months of seizure onset were reported to have a better outcome than patients whose seizures lasted longer before surgery, although the difference was not statistically significant.[4]

In our study, patients with lower pre-surgical median DQ/IQ get the better scores gain, supporting the assumption that pre-surgical DQ/IQ is inversely correlated with post-surgical DQ/IQ.[21] We believe that earlier surgery may have protected patients with lower DQ/IQ from worsening and enhanced neuroplasticity and recovery.

A recent study on neuroconnectivity showed that children undergoing temporal lobe surgery with greater pre-operative impairments in neurocognitive functions had wider bilateral intrinsic connectivity networks, which seemed to be related to a greater propensity for post-operative improvements.[22] This has been demonstrated only in children operated for temporal lobe epilepsy, while in children with heterogenous resections sites, improvements in IQ were slighter and only observed in longer post-surgical follow-up (average 7 years after surgery).[23]

Differently from what we found in our study, in 48 pediatric patients it has previously found that patients with higher pre-operative DQ scores after surgery gained more scores if compared with patients with lower pre-operative DQ scores. Authors hypothesized that patients with higher pre-operative DQ scores may have greater reserve capacities and superior resources.[24]

A meta-analysis on cognitive outcomes after pediatric epilepsy surgery indicates that, on average, children who undergo epilepsy surgery experience a stabilization in intellectual and developmental functioning, with no further decline.[25] This study revealed that the greatest cognitive loss was seen in the youngest, and authors hypothesize that this finding may be reflect the fact that early-onset epilepsies are typically severe and can lead to developmental and epileptic encephalopathies or developmental encephalopathies.

From a neuropsychological perspective, data from our study revealed that in the group of patients who lost scores, the verbal domain was the most affected subdomain. Previous findings are controversial: In a cohort of 20 patients,[26] no changes in verbal fluency after surgery were documented, while other studies have shown a loss of scores in verbal tasks after temporal lobe resection.[20,21,26,27] It is worth mentioning that these previous findings are only related to temporal lobe surgery and not to other heterogenous site resections.

We found that the group of patients who improved or stabilized their developmental or intellectual abilities after surgery had a statistically significant improvement in the Performance domain of WPPSI. Performance abilities—being the result of a group of functions—are more susceptible to reorganization and therefore may have a better compensational capacity.

None of the clinical variables taken into consideration, such as age at seizure onset, age at surgery, epilepsy duration, and follow-up duration, were statistically correlated with the DQ/IQ changes. However, epilepsy duration was shorter in patients with stable or improved post-surgical DQ/IQ, underlining the importance of early surgery.[3–4–7]

It is worth noting that even though most of our patients had stable or improved global developmental and intellectual functions at the last neuropsychological post-surgery follow-up, not all of them achieved satisfactory developmental profiles, and this is consistent with previous findings.[3,7,28–30]

5 | LIMITATIONS

This study is limited by the small sample size, the open-label design, the lack of a control group, the heterogeneity of etiologies and histopathologic findings, and the combination of developmental and cognitive scores from the GMDS and the Wechsler scales. Specifically, the latter may have introduced some bias in the evaluation of the results; therefore, we should consider that some of our conclusions should be confirmed with future studies using a single evaluation tool. These limitations may impact our data, so the results should be interpreted carefully.

Despite several limitations, our study's strengths lie in selecting patients at a very sensitive developmental age (younger than 5 years), the duration of the follow-up, and the overall good developmental and intellectual outcome observed after surgery.

6 | CONCLUSIONS

This study showed that most patients with drug-resistant epilepsy operated before the age of 5 years

had stability or improvement in developmental and intellectual domains. Short epilepsy duration and surgery at an early age—which is now indicated as good clinical practice in the international scientific community—may positively influence developmental and intellectual trajectory and allow for a better long-term quality of life. We suggest that future studies with larger and more homogenous sample sizes and more consistent follow-up intervals should be planned using age-specific neuropsychological tools.

AUTHOR CONTRIBUTIONS

Simona Cappelletti: Conceptualization, Data curation, Investigation, Project Administration, Writing original draft, Writing—review and editing. Cinzia Correale: Data curation, Formal analysis, Investigation; Methodology, Writing—review and editing. Mattia Mercier: Data curation, Formal analysis, Methodology, Writing—review and editing. Giusy Carfì Pavia: Data curation Writing—review and editing. Chiara Falamesca: Data curation, Investigation, Writing—review and editing. Alessandro De Benedictis: Data curation, Investigation, Writing—review and editing. Carlo Efisio Marras: Data curation, Investigation, Writing—review and editing. Chiara Quintavalle: Data Curation, Investigation, Writing—original draft. Concetta Luisi: Data Curation, Investigation, Writing—review and editing. Chiara Pepi: Data Curation, Investigation, Writing—review and editing. Daniela Chiarello: Data Curation, Investigation, Writing—review and editing. Federico Vigevano: Writing—review and editing. Luca De Palma: Data Curation, Formal analysis, Investigation, Writing original draft, Writing—review and editing. Nicola Specchio: Formal analysis; Funding acquisition, Investigation; Methodology; Project administration, Supervision, Validation, Writing—review and editing.

FUNDING INFORMATION

This work was supported by the Italian Ministry of Health ("Current Research Funds").

CONFLICT OF INTEREST STATEMENT

None of the authors has any conflict of interest to disclose. 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.

ETHICS STATEMENT

Considering the retrospective nature of the analysis, the current study did not require the approval of the local ethics committee according to current legislation, but a notification was sent. Data were retrospectively analyzed in line with personal data protection policies.

ORCID

Simona Cappelletti https://orcid.org/0000-0003-0738-1240
Cinzia Correale https://orcid.org/0000-0002-9302-5412
Mattia Mercier https://orcid.org/0000-0003-4239-8267
Giusy Carfi Pavia https://orcid.org/0000-0001-5383-113X
Chiara Falamesca https://orcid.org/0000-0001-8323-044X
Alessandro De Benedictis https://orcid.org/0000-0002-5414-198X
Carlo Efisio Marras https://orcid.org/0000-0003-0790-8903
Chiara Quintavalle https://orcid.org/0000-0001-8937-7805
Concetta Luisi https://orcid.org/0000-0003-2310-9992
Chiara Pepi https://orcid.org/0000-0003-0880-6140
Daniela Chiarello https://orcid.org/0000-0002-0150-9453
Federico Vigevano https://orcid.org/0000-0001-7513-0051
Luca De Palma https://orcid.org/0000-0002-0714-8230
Nicola Specchio https://orcid.org/0000-0002-8120-0287

REFERENCES

1. Holmes GL. Effects of seizures on brain development: lessons from the laboratory. Pediatr Neurol. 2005;33:1–11. https://doi.org/10.1016/j.pediatrneurol.2004.12.003
2. Ibrahim GM, Cassel D, Morgan BR, Lou SM, Otsubo H, Ochi A, et al. Resilience of developing brain networks to interictal epileptiform discharges is associated with cognitive outcome. Brain. 2014;137:2690–702. https://doi.org/10.1093/brain/awu214
3. Ramantani G, Kadish NE, Strobl K, Brandt A, Stathi A, Mayer H, et al. Seizure and cognitive outcomes of epilepsy surgery in infancy and early childhood. Eur J Paediatr Neurol. 2013;17:498–506. https://doi.org/10.1016/j.ejpn.2013.03.009
4. Shurtleff HA, Barry D, Firman T, Warner MH, Aguilar-Estrada RL, Saneto RP, et al. Impact of epilepsy surgery on development of preschool children: identification of a cohort likely to benefit from early intervention. J Neurosurg Pediatr. 2015;16:383–92. https://doi.org/10.3171/2015.3.PEDS14359
5. Baba H, Toda K, Ono T, Honda R, Baba S. Surgical and developmental outcomes of corpus callosotomy for West syndrome in patients without MRI lesions. Epilepsia. 2018;59:2231–9. https://doi.org/10.1111/epi.14594
6. Braun KPJ. Influence of epilepsy surgery on developmental outcomes in children. Eur J Paediatr Neurol. 2020;24:40–2. https://doi.org/10.1016/j.ejpn.2019.12.014
7. 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
8. Braun KPJ. Preventing cognitive impairment in children with epilepsy. Curr Opin Neurol. 2017;30:140–7. https://doi.org/10.1097/WCO.0000000000000424
9. Moosa ANV, Wyllie E. Cognitive outcome after epilepsy surgery in children. Semin Pediatr Neurol. 2017;24:331–9. https://doi.org/10.1016/j.spen.2017.10.010

10. Cloppenborg T, van Schooneveld M, Hagemann A, Hopf JL, Kalbhenn T, Otte WM, et al. Development and validation of prediction models for developmental and intellectual outcome following pediatric epilepsy surgery. Neurology. 2022;98:E225–E235. https://doi.org/10.1212/WNL.0000000000013065
11. Freitag H, Tuxhorn I. Cognitive function in preschool children after epilepsy surgery: rationale for early intervention. Epilepsia. 2005;46:561–7.
12. Baxendale S, Wilson SJ, Baker GA, Barr W, Helmstaedter C, Hermann BP, et al. Indications and expectations for neuropsychological assessment in epilepsy surgery in children and adults: report of the ILAE neuropsychology task force diagnostic methods commission: 2017–2021 neuropsychological assessment in epilepsy surgery. Epileptic Disord. 2019;21:221–34.
13. Huntley M. The Griffiths mental developmental scales manual from birth to two years. Oxford, UK: Test Agency; 1996.
14. Wechsler D. Wppsi-III: technical manual. San Antonio: Pearson; 2002.
15. Wechsler D. Wechsler intelligence scale for children. fourth ed. IT: Firenze; ENG: Florence. Giunti OS; 2013.
16. 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
17. Engman ML, Adolfsson I, Lewensohn-Fuchs I, Forsgren M, Mosskin M, Malm G. Neuropsychologic outcomes in children with neonatal herpes encephalitis. Pediatr Neurol. 2008;38:398–405. https://doi.org/10.1016/j.pediatrneurol.2008.02.005
18. Hedvall Å, Fernell E, Holm A, Åsberg Johnels J, Gillberg C, Billstedt E. Autism, processing speed, and adaptive functioning in preschool children. Sci World J. 2013;2013:158263. https://doi.org/10.1155/2013/158263
19. Van Schooneveld MMJ, Braun KPJ. Cognitive outcome after epilepsy surgery in children. Brain Dev. 2013;35:721–9. https://doi.org/10.1016/j.braindev.2013.01.011
20. Matsuzaka T, Baba H, Matsuo A, Tsuru A, Moriuchi H, Tanaka S, et al. Developmental assessment-based surgical intervention for intractable epilepsies in infants and young children. Epilepsia. 2001;42:9–12. https://doi.org/10.1046/j.1528-1157.2001.05403.x
21. Skirrow C, Cross JH, Owens R, Weiss-Croft L, Martin-Sanfilippo P, Banks T, et al. Determinants of IQ outcome after focal epilepsy surgery in childhood: a longitudinal case-control neuroimaging study. Epilepsia. 2019;60:872–84. https://doi.org/10.1111/epi.14707
22. Arski ON, Martire DJ, Young JM, Wong SM, Suresh H, Kerr EN, et al. Connectomic profiles and cognitive trajectories after epilepsy surgery in children. Neurology. 2022;98(22):e2233–e2244.
23. Puka K, Tavares TP, Smith ML. Development of intelligence 4 to 11 years after paediatric epilepsy surgery. J Neuropsychol. 2017;11:161–73.
24. Kadish NE, Bast T, Reuner G, Wagner K, Mayer H, Schubert-Bast S, et al. Epilepsy surgery in the first 3 years of life: predictors of seizure freedom and cognitive development. Neurosurgery. 2019;84(6):E368–E377.
25. Stefanos-Yakoub I, Wingeier K, Held U, Latal B, Wirrell E, Smith ML, et al. Long-term intellectual and developmental outcomes after pediatric epilepsy surgery: a systematic review and meta-analysis. Epilepsia. 2023;65:251–65. https://doi.org/10.1111/epi.17834
26. Lendt M, Helmstaedter C, Elger CE. Pre- and postoperative neuropsychological profiles in children and adolescents with temporal lobe epilepsy. Epilepsia. 1999;40:1543–50. https://doi.org/10.1111/j.1528-1157.1999.tb02038.x
27. Vega C, Brenner LA, Madsen J, Bourgeois B, Waber DP, Boyer K. Lexical retrieval pre- and post-temporal lobe epilepsy surgery in a pediatric sample. Epilepsy Behav. 2015;42:61–5. https://doi.org/10.1016/j.yebeh.2014.10.003
28. Lettori D, Battaglia D, Sacco A, Veredice C, Chieffo D, Massimi L, et al. Early hemispherectomy in catastrophic epilepsy. A neuro-cognitive and epileptic long-term follow-up. Seizure. 2008;17:49–63. https://doi.org/10.1016/j.seizure.2007.06.006
29. Sherman EMS, Wiebe S, Fay-Mcclymont TB, Tellez-Zenteno J, Metcalfe A, Hernandez-Ronquillo L, et al. Neuropsychological outcomes after epilepsy surgery: systematic review and pooled estimates. Epilepsia. 2011;52:857–69. https://doi.org/10.1111/j.1528-1167.2011.03022.x
30. Dunkley C, Kung J, Scott RC, Nicolaides P, Neville B, Aylett SE, et al. Epilepsy surgery in children under 3 years. Epilepsy Res. 2011;93:96–106. https://doi.org/10.1016/j.eplepsyres.2010.11.002

How to cite this article: Cappelletti S, Correale C, Mercier M, Pavia GC, Falamesca C, De Benedictis A, et al. Epilepsy surgery below the age of 5 years: Are we still in time to preserve developmental and intellectual functions? Epilepsia Open. 2024;9:1901–1909. https://doi.org/10.1002/epi4.13027