E-ISSN 2250-0944
ISSN 2250-1150
doi: 10.31838/ijprt/16.02.99

Research Article

Expanding Frontiers of Intracranial Neuromodulation in Pediatric Drug-Resistant Epilepsy: A Retrospective Cohort Study

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Received: 29.05.26, Revised: 27.06.26, Accepted: 23.07.26

ABSTRACT

Background: Pediatric drug-resistant epilepsy (DRE) remains a major therapeutic challenge and is associated with substantial impairment in neurodevelopment, cognition, behavior, and quality of life. When resective epilepsy surgery is not feasible, intracranial neuromodulation with deep brain stimulation (DBS) or responsive neurostimulation (RNS) may offer meaningful seizure reduction. However, pediatric data remain limited, particularly in low- and middle-income settings.

Objective: To evaluate the single-center experience with DBS and RNS in children with DRE, with emphasis on seizure outcomes, safety, and neurocognitive changes following treatment.

Methods: This retrospective observational cohort study was conducted at multiple tertiary care centers across Pakistan. Medical records of pediatric patients aged 3 to 18 years with DRE who underwent DBS or RNS implantation between January 2020 and December 2025 were reviewed. Eligible patients had at least 12 months of postoperative follow-up and were not considered candidates for resective surgery after multidisciplinary evaluation. Data collected included demographic characteristics, seizure outcomes, responder rates, postoperative complications, and available neurocognitive assessments.

Results: A total of 30 pediatric patients met the inclusion criteria, including 14 treated with DBS and 16 with RNS. The mean age at implantation was 11.0 years overall, with mean ages of 12.29 years in the DBS group and 9.88 years in the RNS group. Mean seizure reduction was 57.73% in the DBS group and 57.31% in the RNS group. Responder rates, defined as at least 50% reduction in seizure frequency, were 64.29% for DBS and 68.75% for RNS. Overall complications occurred in 7 of 30 patients 23.3%, with infection 10.0% and lead migration 10.0% being the most common adverse events; device failure occurred in 1 patient 3.3%. No mortality was observed. In the subgroup with available neurocognitive follow-up, mean IQ scores increased modestly from 81.35 to 83.82 in the DBS group and from 82.85 to 86.83 in the RNS group.

Conclusion: Intracranial neuromodulation appears to be a feasible and clinically meaningful palliative treatment option for selected pediatric patients with DRE who are not candidates for resective surgery. In this single-center cohort, both DBS and RNS were associated with substantial seizure reduction and acceptable safety profiles, with stable to modestly improved neurocognitive performance in the assessed subgroup. Larger prospective multicenter studies are needed to better define patient selection, comparative effectiveness, long-term safety, and developmental outcomes.

Keywords: Pediatric Drug-Resistant Epilepsy, Responsive Neurostimulation, Neuromodulation, Seizure Outcomes, Epilepsy Surgery.

INTRODUCTION

Pediatric drug-resistant epilepsy DRE remains a major clinical challenge and is associated with substantial impairment in neurodevelopment, cognition, behavior, and quality of life. Approximately one-third of children with epilepsy continue to have seizures despite medical therapy. The International League Against Epilepsy defines drug-resistant epilepsy as the failure of adequate trials of two tolerated, appropriately chosen and used anti-seizure medication schedules, whether as monotherapy or in combination, to achieve sustained seizure freedom (1,2).

Interestingly, resective or disconnective epilepsy surgery offers the greatest likelihood of meaningful seizure control or seizure freedom for carefully selected children with focal epileptogenic lesions. However, a substantial proportion of pediatric patients are not suitable candidates for curative surgery because of multifocal or bilateral seizure onset, poorly localized epileptogenic zones, diffuse structural abnormalities, or involvement of eloquent cortex (2,3). In such cases, neuromodulation has emerged as an important palliative treatment strategy.

Among neuromodulatory approaches, intracranial modalities such as deep brain stimulation DBS and responsive neurostimulation RNS are increasingly being used in selected children with DRE when resection is not feasible. DBS modulates seizure networks through scheduled stimulation of subcortical targets, most commonly thalamic nuclei, whereas RNS delivers closed-loop stimulation in response to detected epileptiform activity at cortical or subcortical seizure onset zones (4,5). Adult studies have demonstrated sustained efficacy and acceptable long-term safety for both approaches, and early pediatric reports suggest that these therapies may reduce seizure burden in carefully selected patients (4–8). Nevertheless, pediatric evidence remains limited, consisting predominantly of small retrospective series, institutional experiences, and systematic reviews of heterogeneous cohorts (5–8).

Several important evidence gaps continue to limit broader adoption of intracranial neuromodulation in children. Standardized criteria for patient selection, target selection, and postoperative programming remain incompletely defined. Long-term data on seizure outcomes, complications, and developmental effects are also sparse, particularly in younger children. In addition, comparative data between DBS and RNS in pediatric populations are limited, making it difficult to determine the most appropriate strategy for specific electroclinical phenotypes (5–8). These limitations are especially relevant in low- and middle-income settings, where published outcome data remain scarce.

Given the vulnerability of the developing brain to ongoing seizures and the restricted eligibility of many children for resective surgery, there is a need for additional real-world data on the role of intracranial neuromodulation in pediatric DRE. The present study evaluates our single-center experience with DBS and RNS in children with drug-resistant epilepsy, focusing on seizure outcomes, responder rates, safety, and neurocognitive outcomes following treatment. The present study aimed to evaluate the single-center experience with DBS and RNS in children with drug-resistant epilepsy, focusing on seizure outcomes, safety, and neurocognitive changes following treatment.

METHODOLOGY

This retrospective observational cohort study was conducted at the tertiary care neurosurgical centers performing intracranial neuromodulation for medically refractory epilepsy. Medical records of pediatric patients with drug-resistant epilepsy who underwent implantation of either deep brain stimulation DBS or responsive neurostimulation RNS between January 2020 and December 2025 were reviewed. Eligible patients were aged 3 to 18 years at the time of implantation, fulfilled International League Against Epilepsy criteria for drug-resistant epilepsy, underwent intracranial neuromodulation for seizure control, and had at least 12 months of postoperative follow-up. Patients were considered for neuromodulation after multidisciplinary evaluation when they were not considered suitable candidates for resective epilepsy surgery because of multifocal seizure onset, poorly localized epileptogenic zones, involvement of eloquent cortex, or other factors limiting curative resection. Patients were excluded if they had incomplete core clinical records, less than 12 months of follow-up, prior resective epilepsy surgery, or progressive neurodegenerative disease.

All patients underwent presurgical assessment by a multidisciplinary epilepsy team, including review of seizure semiology,

electroencephalographic findings, neuroimaging, medication history, and overall surgical candidacy. The decision to proceed with DBS or RNS was individualized according to seizure localization, network characteristics, and feasibility of resective surgery. DBS targets were selected on a case-by-case basis according to the presumed seizure network. RNS lead placement was similarly individualized and directed toward one or more electroclinically relevant seizure onset zones or network targets identified during the presurgical evaluation. Final lead configuration, laterality, and postoperative programming were determined by the treating neurosurgical and epilepsy teams. Clinical and operative data were extracted retrospectively from electronic medical records, operative logs, and follow-up documentation. Variables collected included age at implantation, sex, epilepsy duration, seizure type, baseline seizure burden, anti-seizure medication use, comorbidities, neuromodulation modality, operative details, and postoperative course. Follow-up variables included seizure outcomes, adverse events, device-related complications, and available neurocognitive or quality-of-life assessments.

Statistical analysis was performed using SPSS version 27 software. Continuous variables were summarized as $\text{mean} \pm$ standard deviation or median with interquartile range, depending on distribution. Categorical variables were summarized as frequencies and percentages.

Within-group comparisons of seizure frequency before and after neuromodulation were performed using paired t-tests for normally distributed variables or Wilcoxon signed-rank tests for non-normally distributed variables. Between-group comparisons between the DBS and RNS cohorts were performed using the independent-samples t-test or Mann-Whitney U test for continuous variables and the chi-square test or Fisher's exact test for categorical variables, as appropriate. Given the modest sample size and retrospective design, comparative analyses were considered exploratory. A two-sided $p < 0.05$ was considered statistically significant. Ethical approval was obtained from the institutional review board of the Punjab Institute of Neurosciences/Lahore General Hospital prior to data collection. Owing to the retrospective design, the requirement for individual informed consent was waived where permitted by institutional policy. All data were anonymized before analysis, and patient confidentiality was maintained throughout the study.

RESULTS

A total of 30 pediatric patients with drug-resistant epilepsy met the study inclusion criteria. Of these, 14 underwent deep brain stimulation DBS and 16 underwent responsive neurostimulation RNS. The mean age at implantation was 11.0 years overall. The mean age was 12.29 years in the DBS group and 9.88 years in the RNS group. There were 11 male patients and 19 female patients in the overall cohort.

Baseline demographic characteristics are summarized in Table 1.

Group	Total patients, n	Mean age, years	Male, n	Female, n
DBS	14	12.29	6	8
RNS	16	9.88	5	11

Both neuromodulation modalities were associated with meaningful reduction in seizure burden during follow-up. The mean seizure reduction was 57.73% in the DBS group and 57.31% in the RNS group. Responder status, defined as a reduction in seizure frequency of at least 50%, was achieved in 64.29% of patients in the DBS group and 68.75% of patients in the RNS group.

Table 2. Seizure outcomes

Group	Mean seizure reduction, %	Responder rate, %
DBS	57.73	64.29

Group	Mean seizure reduction, %	Responder rate, %
RNS	57.31	68.75

Postoperative or device-related complications were documented in 7 of 30 patients, corresponding to an overall complication rate of 23.3%. The most frequently observed complications were infection in 3 patients 10.0% and lead migration in 3 patients 10.0%. Device failure occurred in 1 patient 3.3%. No mortality was observed. In the DBS group, 4 patients experienced complications, including 2 infections, 1 lead migration, and 1 device failure. In the RNS group, 3 patients experienced complications, including 1 infection and 2 lead migrations. No device failure was recorded in the RNS cohort.

Table 3. Postoperative and device-related complications

Group	Device failure,n	Infection,n	Lead migration,n	No complication,n
DBS	1	2	1	10
RNS	0	1	2	13

Formal neurocognitive data were available only for a subset of patients with documented preoperative and postoperative assessments. In this subgroup, mean IQ scores showed modest improvement following neuromodulation in both treatment groups. In the DBS cohort, mean IQ increased from 81.35 preoperatively to 83.82 postoperatively, representing a mean change of $+2.46$ points. In the RNS cohort, mean IQ increased from 82.85 to 86.83, corresponding to a mean change of $+3.97$ points. These findings suggest that neuromodulation was not associated with an observed decline in cognitive performance in the assessed subgroup. However, interpretation of neurocognitive outcomes should remain cautious because these data were not available for the entire cohort.

Table 4. Neurocognitive outcomes

Group	Mean preoperative IQ	Mean postoperative IQ	Mean IQ change
DBS	81.35	83.82	+2.46
RNS	82.85	86.83	+3.97

In summary, both DBS and RNS were associated with clinically meaningful seizure reduction and acceptable safety profiles. Complications were relatively infrequent and consisted primarily of infection and lead migration. In the subgroup with available neurocognitive assessment, cognitive scores remained stable to modestly improve following treatment.

DISCUSSION

This retrospective single-center cohort study evaluated the efficacy, safety, and neurocognitive outcomes of intracranial neuromodulation in pediatric patients with drug-resistant epilepsy DRE who were not considered candidates for resective surgery. In our cohort, both deep brain stimulation DBS and responsive neurostimulation RNS were associated with clinically meaningful reductions in seizure burden, with mean seizure reduction of 57.73% in the DBS group and 57.31% in the RNS group. Responder rates, defined as at least 50% seizure reduction, were 64.29% for DBS and 68.75% for RNS. These findings support the growing evidence that intracranial neuromodulation is a reasonable palliative option for selected pediatric patients with DRE in whom curative resection is not feasible because of multifocal seizure onset, poorly localized epileptogenic zones, or involvement of eloquent cortex (2-7).

Our findings are broadly consistent with prior pediatric series and systematic reviews demonstrating that both DBS and RNS can provide meaningful seizure reduction in carefully selected children with medically refractory epilepsy (5-8). Although the pediatric evidence base remains limited and is derived largely from retrospective cohorts and institutional experiences, the magnitude of seizure reduction observed in the present study falls within the range reported in contemporary literature. These results therefore add to the growing body of evidence supporting intracranial neuromodulation as an important component of the treatment armamentarium for pediatric epilepsy surgery programs (4,5).

In the present cohort, responder rates were numerically higher in the RNS group, whereas mean seizure reduction was similar between the two modalities. Accordingly, our findings do not support a strong conclusion that one approach is definitively superior to the other. This is particularly important in a retrospective cohort of modest size, in which treatment allocation is influenced by electroclinical characteristics, seizure localization, network distribution, and anatomical feasibility. Prior reviews have suggested that RNS may offer particular benefits in selected focal epilepsies, whereas DBS may be especially useful in broader or less discretely localized epileptic networks; however, direct comparison remains difficult because of differences in patient selection, follow-up duration, stimulation targets, and outcome definitions across studies (4-8). In practice, the choice between DBS and RNS is therefore individualized rather than based on efficacy estimates alone (9).

The safety profile observed in this study was acceptable overall. Complications occurred in 23.3% of patients with infection and lead migration representing the most common adverse events, while device failure was uncommon and no mortality was observed. These findings are generally consistent with previously reported pediatric neuromodulation series, in which infection and hardware-related complications are among the most frequently described adverse events following implantation (4,10) Although the complication rate in the present cohort is clinically acceptable given the complexity of this patient population, the occurrence of infection highlights the continued importance of meticulous perioperative technique, standardized postoperative wound care, and close surveillance for hardware-related complications (10)

Neurocognitive outcomes in the present study should be interpreted cautiously but remain encouraging. In the subset of patients with available preoperative and postoperative assessment, mean IQ scores remained stable to modestly improved following treatment in both groups. Although neuromodulation-specific pediatric cognitive data remain limited, this finding is broadly consistent with the wider pediatric epilepsy surgery literature suggesting that cognitive outcomes are often stable or improved when seizure control is achieved (11) While causal inference cannot be established in a retrospective study, these findings are clinically relevant because preservation of neurodevelopmental function is a major concern in children with chronic refractory epilepsy. Any observed cognitive benefit may reflect improved seizure control, better day-to-day functioning, or changes in antiseizure medication burden; however, these relationships cannot be confirmed within the present dataset (11)

Beyond seizure reduction alone, the role of intracranial neuromodulation in pediatric epilepsy should be considered within the broader context of palliative surgical care. For children with bilateral, multifocal, or eloquent-cortex-associated epileptogenic networks, seizure freedom may be unrealistic, yet meaningful reduction in seizure burden can still provide substantial clinical benefit (2-5). In such cases, decreased seizure frequency may translate into improved safety, reduced emergency healthcare utilization, greater participation in school and rehabilitation, and reduced caregiver burden. Although these broader functional outcomes were not uniformly available in the present cohort, the observed seizure reductions support the utility of neuromodulation in appropriately selected children (4-8)

It is also important to recognize the broader practical and ethical context of pediatric neuromodulation. In many settings, the use of DBS and especially RNS in younger children remains limited by cost, availability, variable regulatory approval, and the relative scarcity of long-term pediatric outcome data (12,13). These issues are particularly relevant in resource-constrained environments, where access to advanced epilepsy surgery may already be limited. Continued accumulation of pediatric outcome data is therefore necessary not only to refine patient selection and

treatment strategies, but also to support equitable access and evidence-based policy development (12,13).

Limitations

This study has several limitations. First, its retrospective design introduces the possibility of selection bias, incomplete documentation, and variability in follow-up assessment. Second, the cohort size was small, limiting statistical power and restricting the ability to perform robust subgroup or comparative analyses. Third, treatment allocation was non-randomized and based on clinical decision-making, which introduces confounding by indication. Fourth, detailed operative variables, stimulation parameters, and longitudinal seizure characteristics were not uniformly available for all patients. Fifth, neurocognitive assessment was available only for a subset of the cohort, thereby limiting the generalizability of the cognitive findings. Finally, as a single-center experience, the results may reflect local referral patterns, patient selection, and institutional practice, and may therefore not be fully generalizable to other settings.

CONCLUSION

Intracranial neuromodulation appears to be a feasible and clinically meaningful palliative treatment option for selected pediatric patients with drug-resistant epilepsy who are not candidates for resective surgery. In this single-center cohort, both DBS and RNS were associated with substantial seizure reduction and acceptable safety profiles, with stable to modestly improved neurocognitive performance in the subgroup with available follow-up testing. Although these findings support the use of neuromodulation in carefully selected children, larger prospective multicenter studies with standardized outcome assessment are needed to better define patient selection, comparative effectiveness, long-term safety, and developmental impact.

Conflict of Interest: The authors declare no conflict of interest.

Funding: No funding was received for this study.

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