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NON-INVASIVE NEUROMODULATION IN DRUG-RESISTANT PEDIATRIC EPILEPSY: A SCOPING REVIEW

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Abstract

Background: Drug-resistant epilepsy (DRE) in childhood is associated with a substantial seizure burden, neurodevelopmental morbidity, and limited treatment options, particularly when surgery is not feasible. Non-invasive neuromodulation has emerged as a potential adjunctive strategy; however, the pediatric evidence base remains fragmented across modalities and study designs.

Objectives: This study aimed to map the extent, characteristics, and reported outcomes of the published literature on non-invasive neuromodulation for pediatric DRE.

Methods: This scoping review was conducted according to a pre-registered OSF protocol (Registration DOI: 10.17605/OSF.IO/Q2D5Y) and aligned with JBI guidance and PRISMA-ScR reporting standards. The review focused on children and adolescents aged 0–18 years with DRE treated using non-invasive neuromodulation techniques, including transcranial direct current stimulation (tDCS), repetitive transcranial magnetic stimulation (rTMS), and transcutaneous vagus nerve stimulation (tVNS/taVNS). Primary studies with original clinical data were included. A total of 5,846 records were identified from PubMed, Scopus, and Web of Science; 1,560 duplicates were removed; 4,286 records were screened; 19 full texts were assessed; and 16 studies were included.

Results: The included studies (2008–2025) were predominantly small exploratory designs: four randomized sham-controlled trials, three prospective or pilot non-randomized studies, one case series, and eight case reports or brief reports. tDCS was the most frequently investigated modality, followed by rTMS and tVNS. The evidence encompassed a heterogeneous range of conditions, including focal DRE, Lennox–Gastaut syndrome, epileptic spasms, Rasmussen encephalitis, epilepsia partialis continua, early-onset epileptic encephalopathy, and epileptic encephalopathy with spike-wave activation in sleep. Most studies

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reported improvements in seizure-related and/or EEG outcomes, particularly in sham-controlled trials of tDCS and rTMS and in prospective tVNS cohorts. Safety outcomes were generally favorable, with transient scalp discomfort and headache being the most commonly reported adverse effects. However, the evidence is limited by small sample sizes, heterogeneous protocols, short follow-up periods, variable outcome definitions, and a reliance on uncontrolled designs.

Conclusions: Non-invasive neuromodulation in pediatric DRE represents a promising but still evolving field. The most encouraging findings are associated with cathodal tDCS for focal epilepsy and Lennox–Gastaut syndrome, low-frequency rTMS for focal pediatric DRE, and tVNS for selected refractory epileptic encephalopathy phenotypes. Larger, well-designed, syndrome-specific studies with standardized protocols and long-term outcome measures are required before definitive clinical recommendations can be established.

Keywords: Drug-resistant epilepsy; Pediatric epilepsy; Neuromodulation; Transcranial direct current stimulation; Repetitive transcranial magnetic stimulation; Transcutaneous vagus nerve stimulation; Scoping review.

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