Magnetic Resonance Imaging-Based Distribution and Reversibility of Lesions in Pediatric Vigabatrin-Related Neurotoxicity

Luis Octavio Tierradentro-Garcia, MD; Joseph Stern; Alireza Zandifar MD; Jorge Du Ub Kim, MD; Jean Henri Nel; Savvas Andronikou, MBBCh, PhD

Department of Radiology

Children's Hospital of Philadelphia

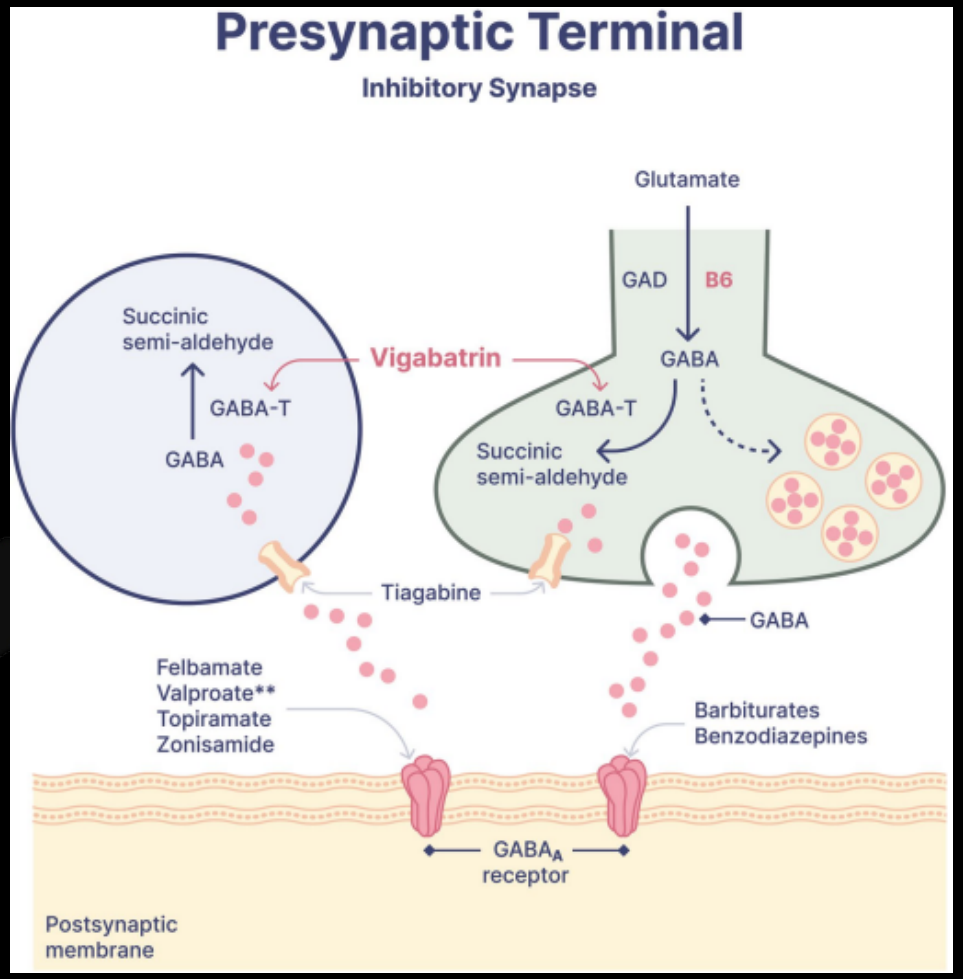
- No conflicts of interest to declare

Background

Vigabatrin is a first-line antiepileptic agent for infantile spasms and refractory epilepsy

It increases GABA at neuronal synapse and disrupts excitatory neurotransmission

Up **to 34%** of patients on vigabatrin treatment exhibit brain MRI changes:
- bilateral, symmetric, and reversible
- involve deep nuclei and brainstem.



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Purpose

- To systematically characterize the detailed anatomical locations of brain lesions in vigabatrin-related toxicity in children.

- To determine the reversibility of lesions based on follow-up images.

Methods

Retrospective, longitudinal, single-center study (2010-2021)

Inclusion:

- Children <5 years old + intractable /refractory seizures
- Available brain MRI.
- Vigabatrin therapy at time of brain MRI.

Exclusion:

- Abnormal brain morphology in regions of interest
- Insufficient diagnostic quality (absence of axial/coronal T2-W, FLAIR, and/or DWI/ADC sequences)

Methods

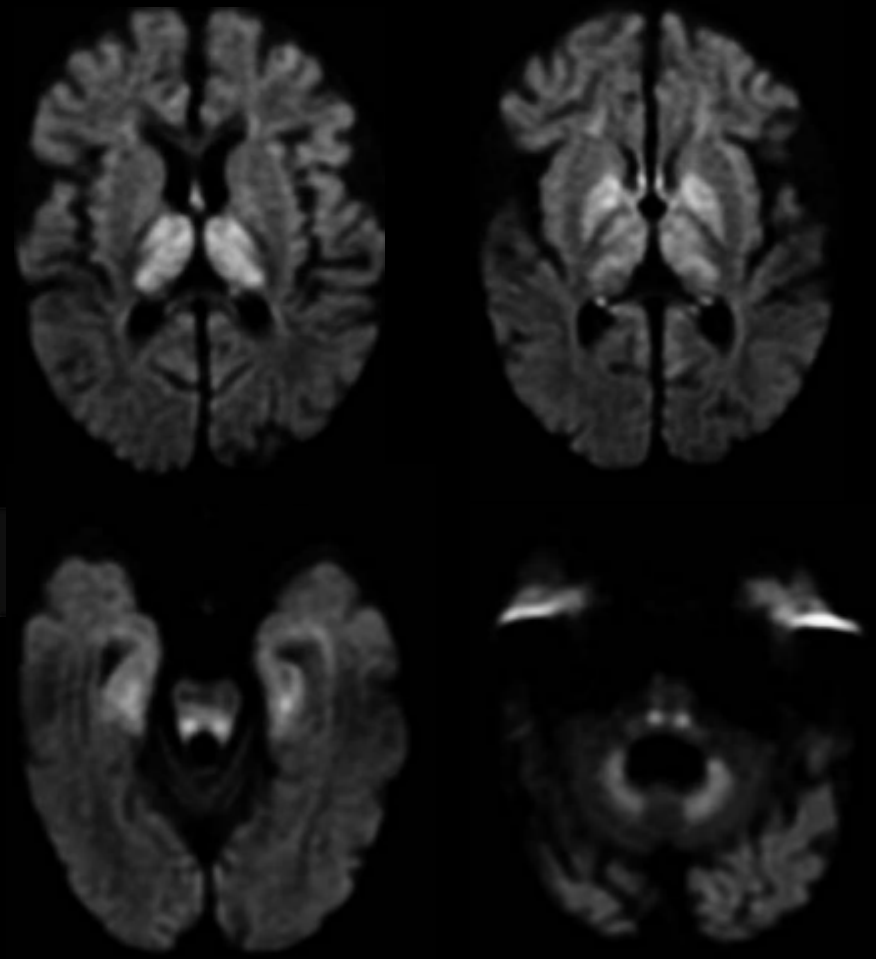
T2-W/FLAIR – hyperintense lesions

DWI/ADC – restricted diffusion

Pediatric neuroradiologist with > 20 years of experience

Brain MRI scans when available:
(a) Prior to vigabatrin initiation
(b) During vigabatrin treatment
(c) After vigabatrin discontinued

- **Frequency** of MRI abnormalities* before, during, and after recorded
- Documented **reversibility** after vigabatrin discontinued
- Concordance betweenT2/FLAIR and DWI restriction assessed



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Results

18 patients fulfilled the eligibility
50% were girls.
Tuberous sclerosis (33.3%);
Lennox-Gastaut syndrome (27.8%)

	Median (IQR) / count (%)
Age at exam (months)	18.5 (12-25.2)
Age at first dose of vigabatrin (months)	9.5 (5.7-15.2)
Length of vigabatrin therapy (days)	309 (93-683)
Peak dose of vigabatrin (mg/kg/day)	149 (120-150)

	Number (%)
MRI before	13 (72.2%)
MRI during	18 (100%)
MRI after	12 (66.6%)
Total	43

Median (IQR) days:

Between vigabatrin initiation and first MRI: **178 days** (80-423)

Between MRI scan and vigabatrin discontinuation: **40 days** (14-142)

Between last dose of vigabatrin and subsequent scan: **75 days** (37-258)

Results: During vigabatrin treatment (n=18)

Anatomical structure	Hyperintensity on T2/FLAIR (n, %)	Restricted diffusion (n, %)
Globus pallidi	15 (83.3%)	14 (77.8%)
Thalami	15 (83.3%)	14 (77.8%)
Subthalamic nuclei	13 (72.2%)	14 (77.8%)
Midbrain	14 (77.8%)	12 (66.7%)
Central tegmental tracts	12 (66.7%)	12 (66.7%)
Pons	12 (66.7%)	11 (61.1%)
Hypothalamus	8 (44.4%)	6 (33.3%)
Medulla	11 (61.1%)	11 (61.1%)
Anterior commissure	8 (44.4)	13 (72.2%)
Dentate nuclei	6 (33.3%)	4 (22.2%)
Hippocampi	1 (5.6%)	2 (11.1%)

Lesion **symmetry** (left: right)
88%

Concordance T2/FLAIR DWI
33%

Anterior commissure***

Thalami

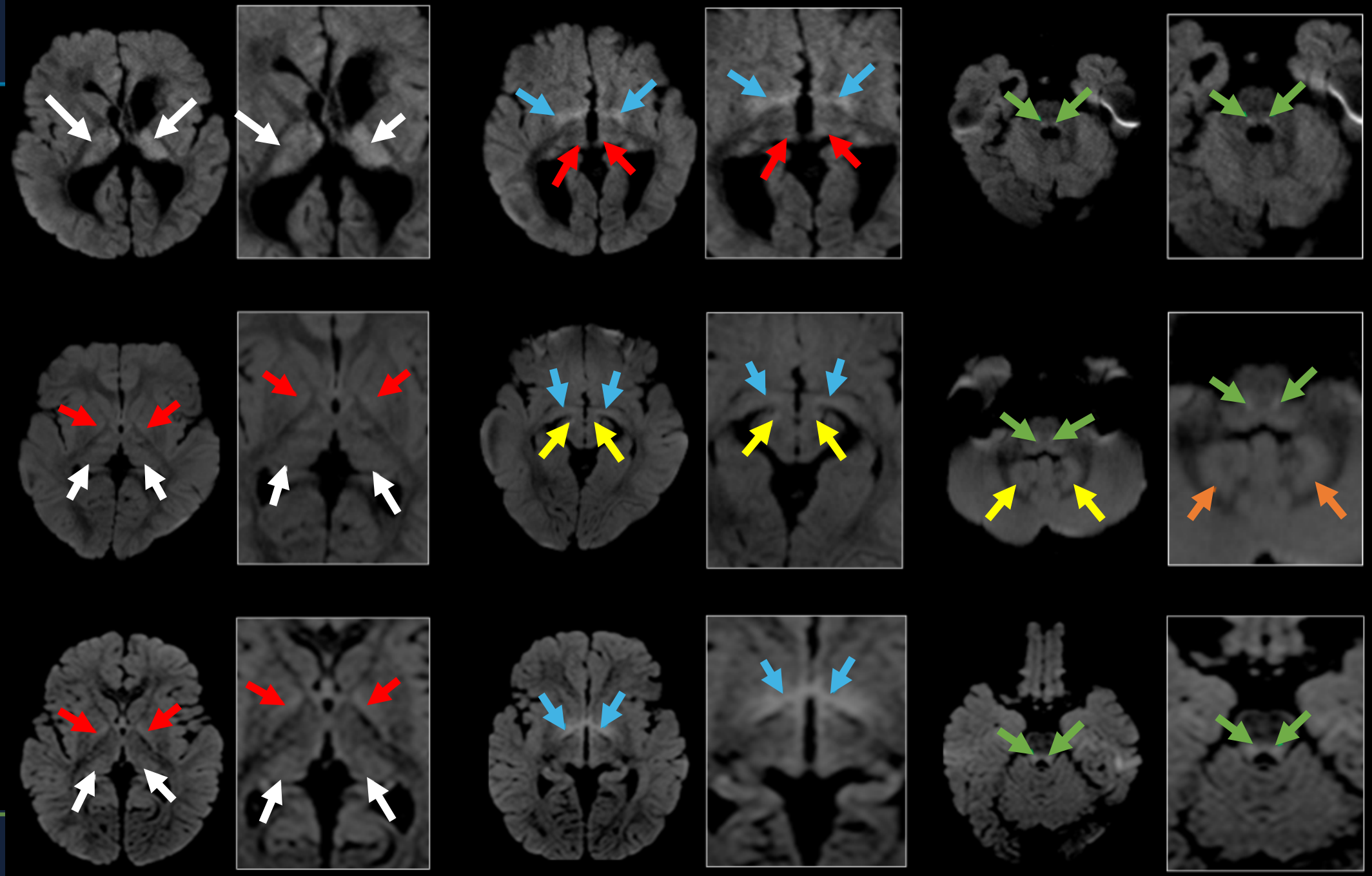
Globus pallidus

Anterior commissure

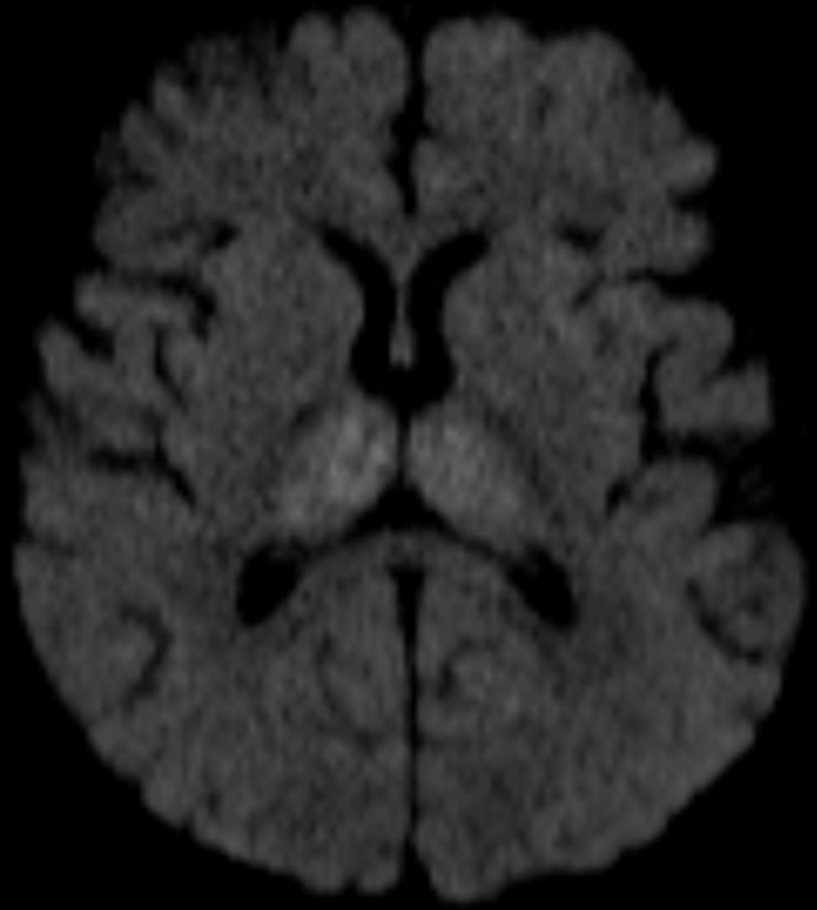
Subthalamic nuclei

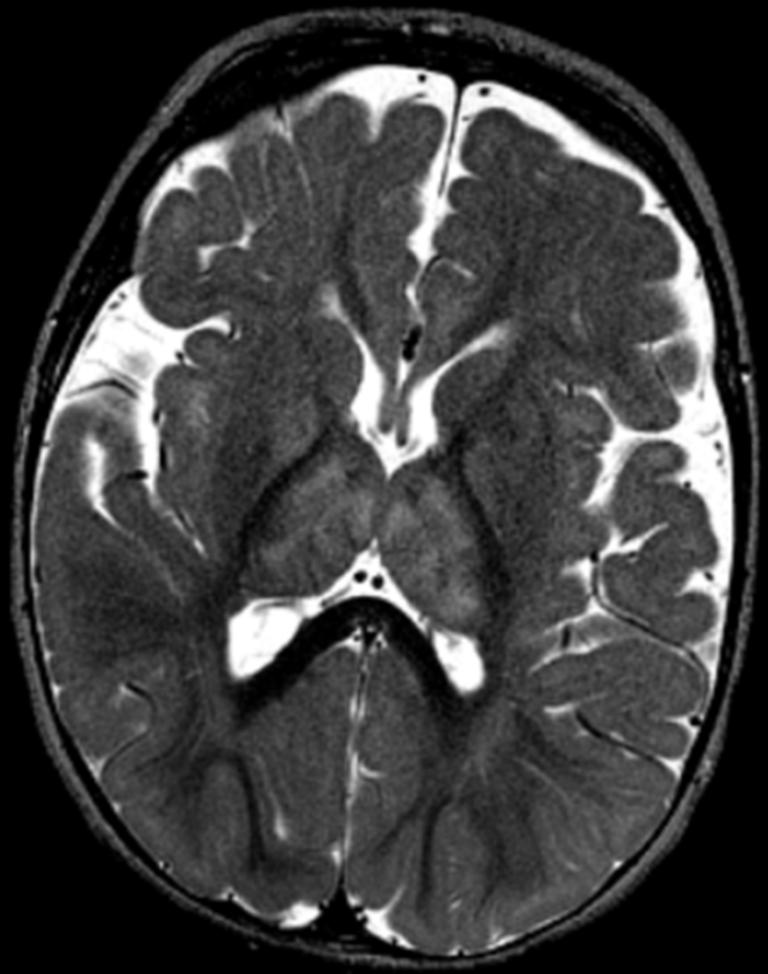
CTT

Dentate nuclei



Speckled Egg Pattern: distinctive signal abnormality of thalami





Results: after vigabatrin discontinued (n=12)

Anatomical structure	Hyperintensity in T2/FLAIR (n, %)	Restricted diffusion (n, %)
Globus pallidi	2* (16.7%)	0 (0%)
Thalami	1* (8.3%)	1* (8.3%)
Subthalamic nuclei	0 (0%)	0 (0%)
Midbrain	0 (0%)	0 (0%)
Central tegmental tracts	2* (16.7%)	1* (8.3%)
Pons	2* (16.7%)	1* (8.3%)
Hypothalamus	0 (0%)	0 (0%)
Medulla	1* (8.3%)	1* (8.3%)
Anterior commissure	2* (16.7%)	0 (0%)
Dentate nuclei	0 (0%)	0 (0%)
Hippocampi	1 (8.3%)	0 (0%)

All patients had at least **partial** resolution

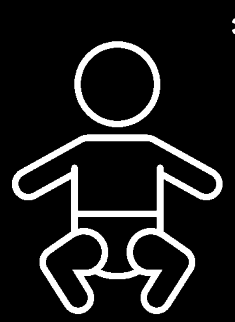
Two-thirds **complete** resolution T2/FLAIR

Four locations recovery to normal:

- **midbrain**
- **dentate nuclei**
- **subthalamic nuclei**
- **hypothalami**

Results

Preterm patients
(n=3)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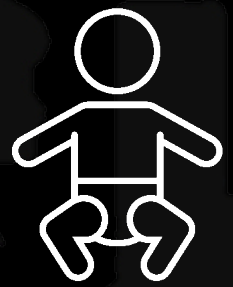
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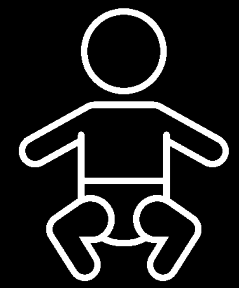
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* Continued to demonstrate signal hyperintensity in T2/FLAIR after discontinuation of vigabatrin.
# Ongoing restricted diffusion on MRI.
& This patient did not have a follow-up MRI because he died shortly after vigabatrin was discontinued.

Conclusions

- Globus pallidi and thalami are most commonly involved in vigabatrin-related toxicity

- Most vigabatrin-related neuroimaging findings are reversible.

- Diffusion restriction did not add value except in demonstrating anterior commissure

- Premature patients had persistent signal abnormalities on follow-up MRI

Thank you!

tierradenl@chop.edu