Baylor College of Medicine

DEPARTMENT OF PEDIATRICS

Texas Children's Hospital®

Division of Neurology and Developmental Neuroscience

Epilepsy in Xia-Gibbs Syndrome

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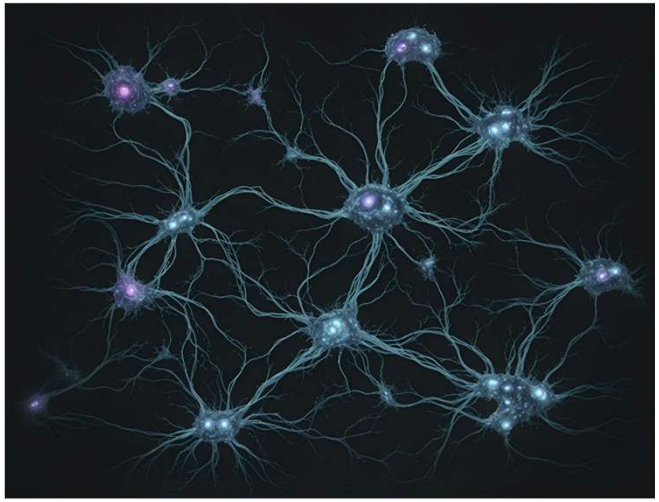
Epilepsy: Definitions and Epidemiology

- Seizure: sudden attack; sudden clinical event with an outward change in neurologic function



- Not all clinical events referred to as seizures are “epileptic” events
  - **non-epileptic paroxysmal events**
- Convulsion: episode of excessive, abnormal muscle contractions, usually bilateral, may be sustained or interrupted
- Frequency: 10% of population

ILAE 2017 Classification of Seizure Types

Focal Onset		Generalized Onset	Unknown Onset
Aware	**Impaired Awareness**	**Motor**	**Motor**
Motor Onset		tonic–clonic	tonic–clonic
automatisms		clonic	epileptic spasms
atonic		tonic	
clonic		myoclonic	**Nonmotor**
epileptic spasms		myoclonic–tonic–clonic	behavior arrest
hyperkinetic		myoclonic–atonic	
myoclonic		atonic	
tonic		epileptic spasms	
Nonmotor Onset		**Nonmotor (absence)**	
autonomic		typical	
behavior arrest		atypical	
cognitive		myoclonic	
emotional		eyelid myoclonia	
sensory			
focal to bilateral tonic–clonic			**Unclassified**

Importance of Classification

- Guides subsequent evaluation
  - EEG
  - Neuroimaging

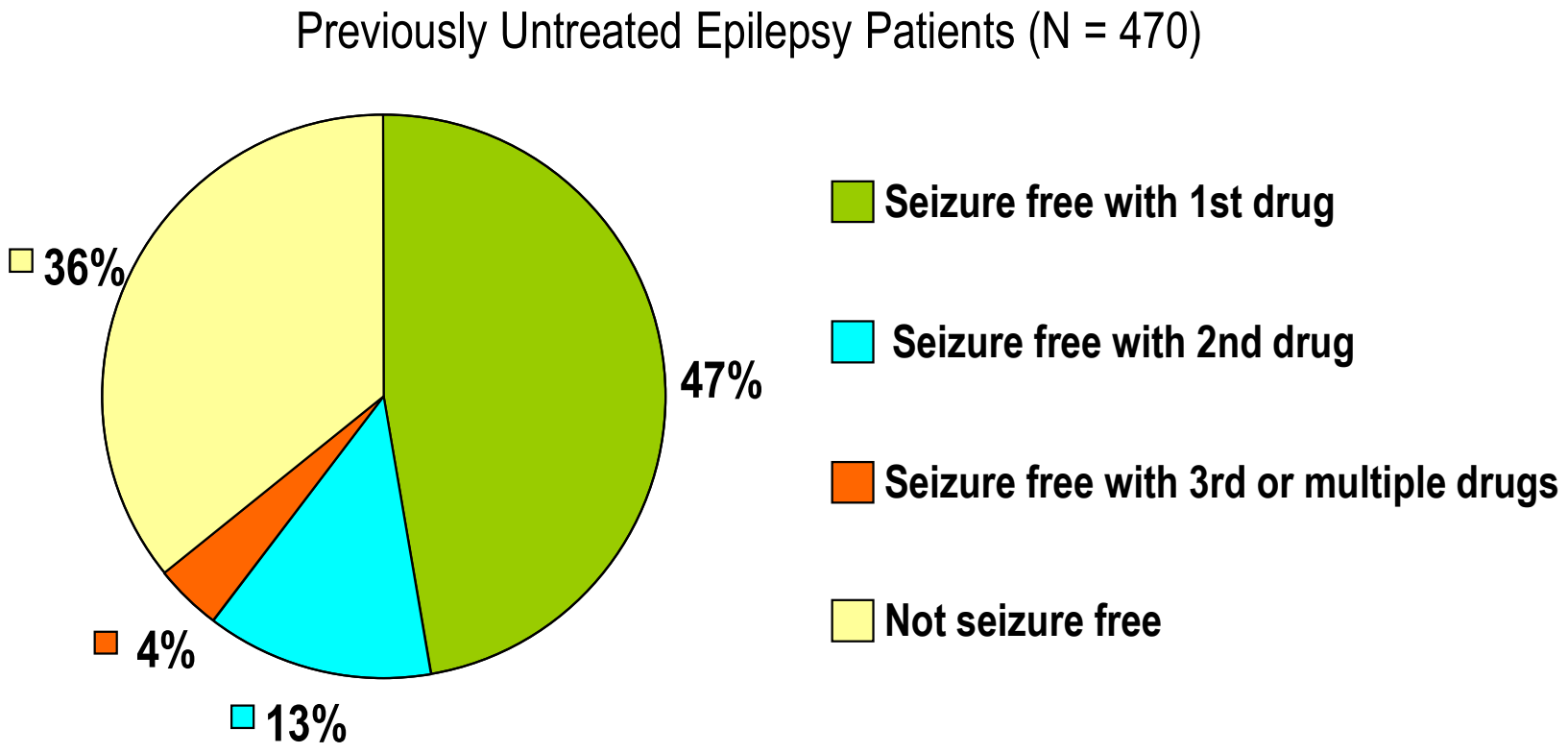
- Determine risk of recurrence: some seizure types always recur
  - absence, atypical absence, infantile spasms, myoclonic, atonic, and tonic seizures

- Guides selection of antiseizure medications: focal versus generalized dichotomy

Non-Epileptic Paroxysmal Events

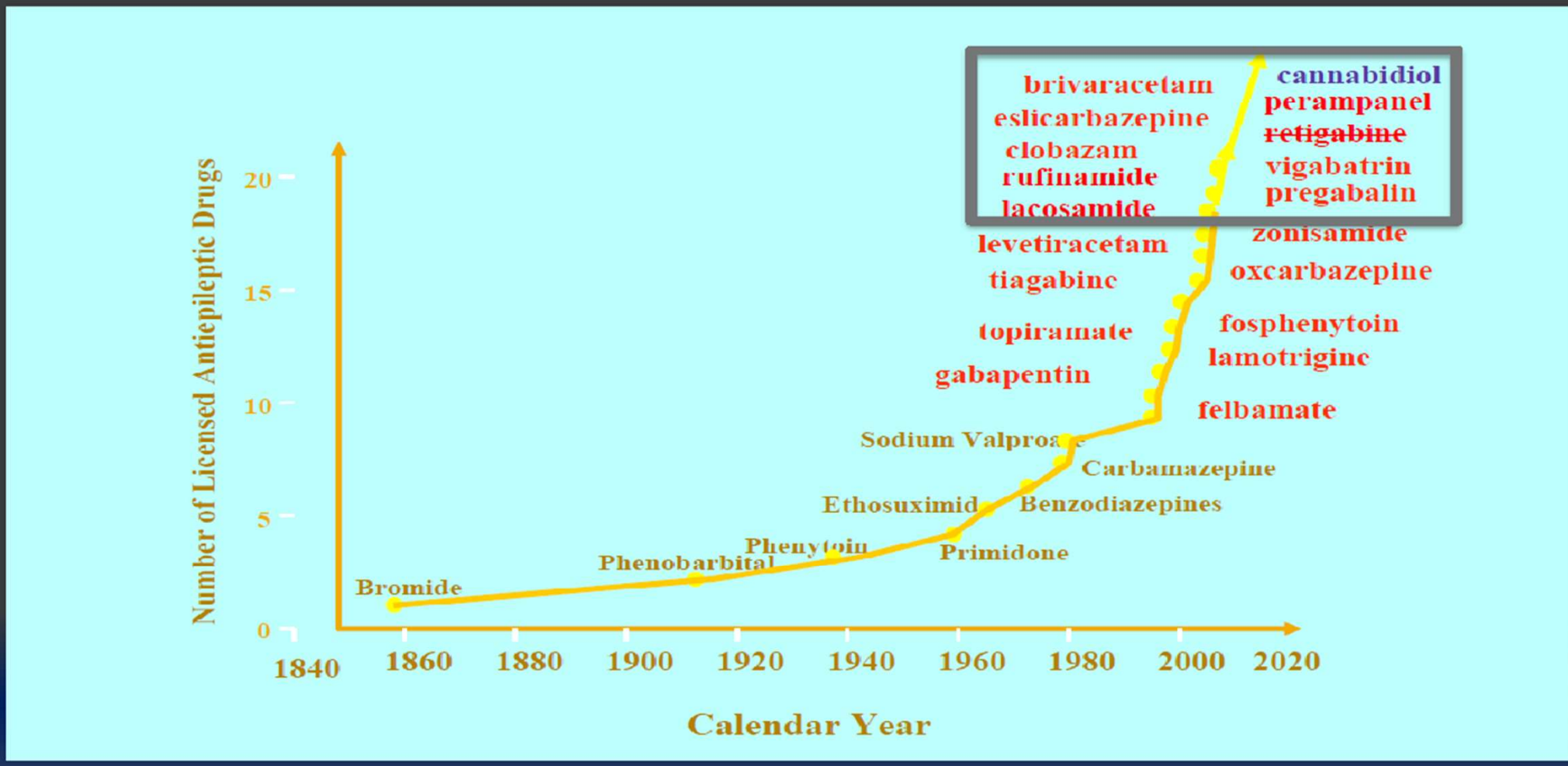
- Pseudoseizures
- Munchausen Syndrome
- Rage attacks, episodic dyscontrol, panic attacks
- Breath-holding spells, pallid infantile syncope
- Syncope, convulsive syncope: reflex anoxic seizure
- Cardiac arrhythmias
- Night terrors, somnambulism, parasomnias
- Migraine Syndromes
- Narcolepsy, cataplexy, hypersomnia
- Movement disorders
- Hyperexplexia
- Sandifer Syndrome, reflux, esophageal spasms
- Infantile gratification
- Spasmus Nutans
- Ocular Movements (tics, spasms, nystagmus)
- TIAs

Success with Antiseizure Medication (ASM)



Kwan P, Brodie MJ. *N Engl J Med*. 2000;342(5):314-319.

Antiepileptic drug development



Alternative Treatment Approaches

- Ketogenic Diet

- Surgical Options
  - Focal resections (lesion removal, hemispherectomy)
  - Non-resective strategies
    - Corpus Callosotomy
    - Subpial transections
    - Vagal Nerve Stimulation

- Newer neurostimulations
  - Deep Brain Stimulation (DBS)
  - Responsive Neurostimulation (RNS)
  - Transcranial Magnetic Stimulation (TMS)

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Limited literature knowledge

ORIGINAL ARTICLE

The phenotypic spectrum of Xia-Gibbs syndrome

Yunyun Jiang[1,2] | Michael F. Wangler[2,3] | Amy L. McGuire[4] | James R. Lupski[1,2,3,5] | Jennifer E. Posey[2] | Michael M. Khayat[1,2] | David R. Murdock[1,2] | Luis Sanchez-Pulido[6] | Chris P. Ponting[6] | Fan Xia[2] | Jill V. Hunter[3] | Qingchang Meng[1,2] | Mullai Murugan[1,2] | Richard A. Gibbs[1,2]

RESEARCH ARTICLE

Phenotypic and protein localization heterogeneity associated with *AHDC1* pathogenic protein-truncating alleles in Xia–Gibbs syndrome

Michael M. Khayat[1,2] | He Li[1] | Varuna Chander[1,2] | Jianhong Hu[1] | Adam W. Hansen[1,2] | Shoudong Li[1] | Josh Traynelis[1] | Hua Shen[1] | George Weissenberger[1] | Fabio Stossi[3,4] | Hannah L. Johnson[3] | James R. Lupski[1,2,5,6] | Jennifer E. Posey[2] | Aniko Sabo[1] | Qingchang Meng[1] | David R. Murdock[1,2] | Michael Wangler[2,5] | Richard A. Gibbs[1,2]

CASE REPORT

Genotype–phenotype spectrum and correlations in Xia-Gibbs syndrome: Report of five novel cases and literature review

Ferruccio Romano[1,2] | Mariateresa Falco[3] | Gerarda Cappuccio[4,5] | Nicola Brunetti-Pierri[4,5] | Fortunato Lonardo[3] | Annalaura Torella[5,6] | Maria Cristina Digilio[7] | Maria Lisa Dentici[7] | Paolo Alfieri[8] | Emanuele Agolini[9] | Antonio Novelli[9] | Livia Garavelli[10] | Andrea Accogli[11,12] | TUDP[13] | Pasquale Striano[2,14] | Gioacchino Scarano[3] | Vincenzo Nigro[5,6] | Marcello Scala[2,14] | Valeria Capra[1]

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Contents lists available at ScienceDirect

Seizure: European Journal of Epilepsy

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

Short communication

Different epilepsy course of a novel *AHDC1* mutation in a female monozygotic twin pair

Andrea Salvati [a,1], Tommaso Biagioni [a,1], Anna Rita Ferrari [b], Diego Lopergolo [c], Paola Brovedani [b], Emanuele Bartolini [b,*]

[a] Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy
[b] IRCCS Stella Maris Foundation, Department of Developmental Neuroscience, Pisa, Italy
[c] IRCCS Stella Maris Foundation, Molecular Medicine for Neurodegenerative and Neuromuscular Disease Unit, Pisa, Italy

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Frequency of Seizures and Abnormal EEG/MRI

- Three relatively large cohort studies
  - Jiang et al.: 30% (6/20)
  - Khayat et al.: 44% (15/34)
  - Romano et al.: 42% (24/57)

- Abnormal EEG
  - Jiang et al.: 20% (4/20)
  - Khayat et al.: 40% (11/27)

- Abnormal MRI
  - Jiang et al.: 60% (12/20)
  - Khayat et al.: 54% (17/31)

Epilepsy in XIGIS

- Age of onset mean: 5.3 and 6.3 years, median: 4 and 6 years

  Jiang *et al*. Am J Med Genet. *2018*;176A
  Khayat *et al*. Human Mutation. *2021*;42

- Types of seizures: GTC, focal, gelastic seizure

  Danda *et al*. Am J Med Genet. *2021*;188A

- There is no specific seizure medication that works better

- Varies from non-refractory to refractory seizures even in monozygotic twins

  Salvati *et al*. Seizure. *2022*;99

- Mutations closer to C-terminus are less likely to have seizure

  Khayat *et al*. Human Mutation. *2021*;42

Summary of XIGIS and Epilepsy

- Seizures occur in one third to half of XIGIS individuals
- Age of onset 5-6 years (9 months to 16 years old)
- Seizure types are broad
- No correlation with age
- Abnormal EEG and brain MRI are common (i.e., >50% of individuals)

Things to be done for epilepsy in XIGIS

- Is there any age-dependent pattern?
- Are certain mutations correlate with seizure and severity
- Any specific medications more efficient for seizures in XIGIS

Thank You

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