Children's Hospital Colorado

Epilepsy Syndromes: Where does Dravet Syndrome fit in?

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Disclosures

Scott Demarest has consulted for Upsher-Smith on an unrelated subject matter.

No conflicts of interest

Objectives

- What is an Epilepsy Syndrome?
  - How do we define epilepsy syndromes?
  - Genetic vs Phenotype (Features)
  - So what? Why do we care about Epilepsy Syndromes?
- How do we organize and categorize Epilepsy Syndromes?
- What epilepsy syndromes are similar to Dravet Syndrome and what is different about them?

Good Resource

International League Against Epilepsy

Epilepsydiagnosis.org

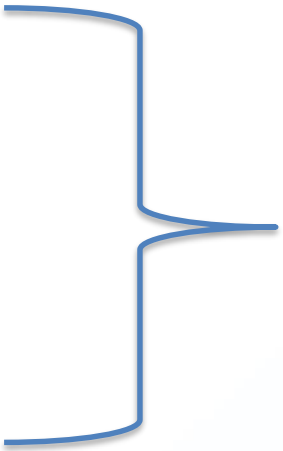
https://www.epilepsydiagnosis.org/syndrome/epilepsy-syndrome-groupoverview.html

What is an Epilepsy Syndrome?

A syndrome is a collection of common clinical traits.

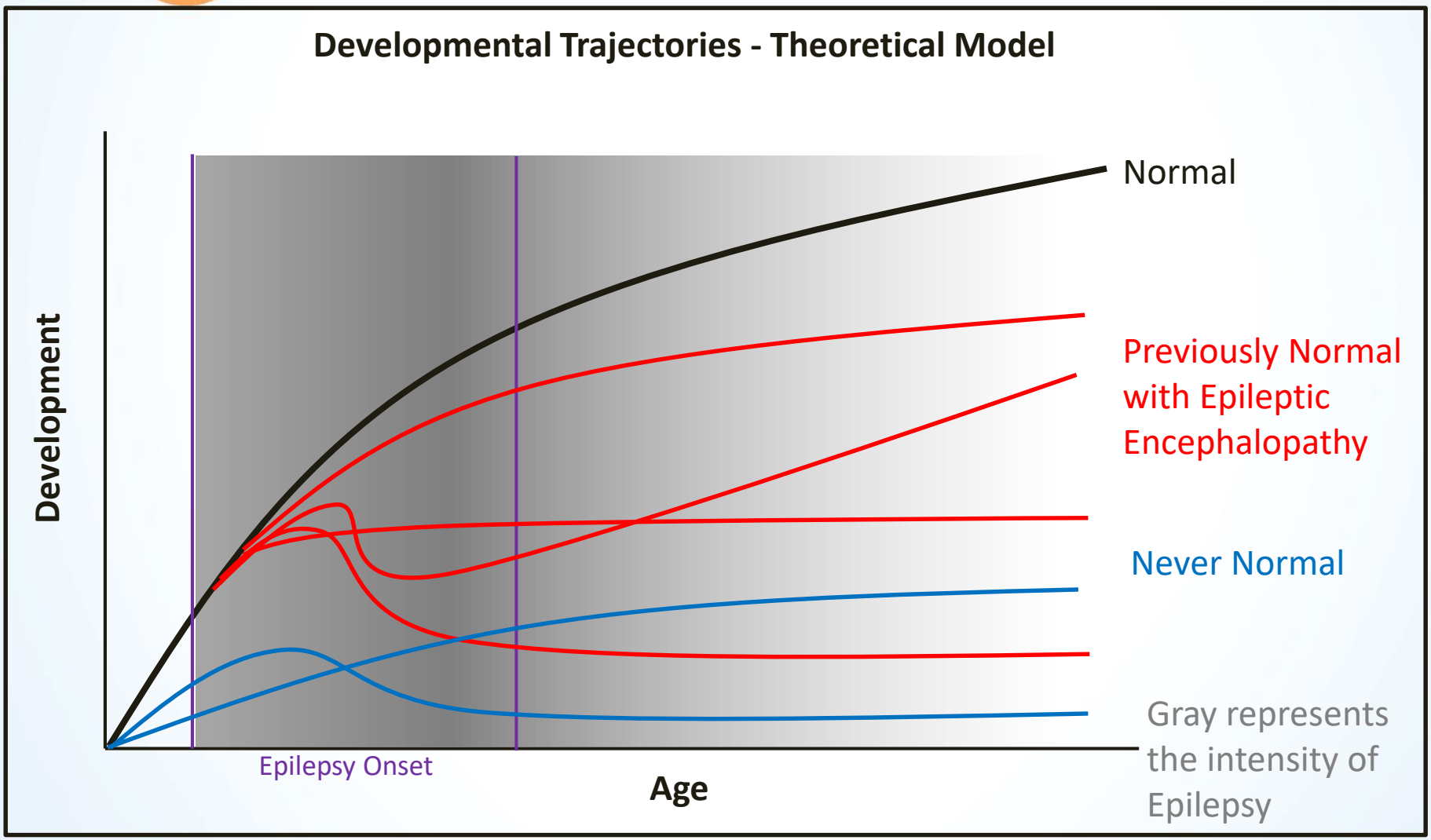
For Epilepsy this is usually about:

- What type of seizures occur?
- Age seizure start?
- Development?
- What does the EEG look like?
- Other Co-morbidities…

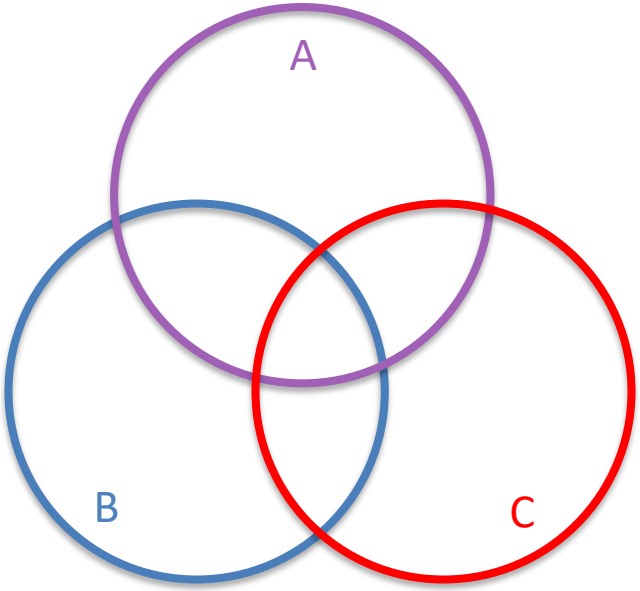


Electroclinical Features or Phenotype

Course of an Epilepsy Syndrome

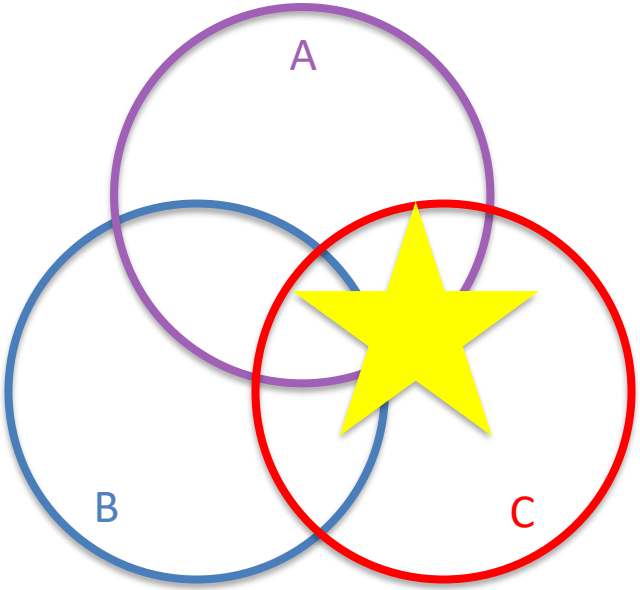


How distinct are Epilepsy Syndromes?



Many features might overlap, but the hope is that the cluster of symptoms are “specific” to that epilepsy syndrome…this is often better in theory than practice.

How does the individual patient fit?



Is this patient at type A,B or C?

What about Syndromes Defined by Genes?

Is SCN1A the same as Dravet Syndrome?

…I don’t have a perfect answer for this… many diseases are being defined by the gene (CDKL5, SCN8A, CHD2).

But many patients with the same gene changes look different

We call this Genotype-Phenotype Correlation.

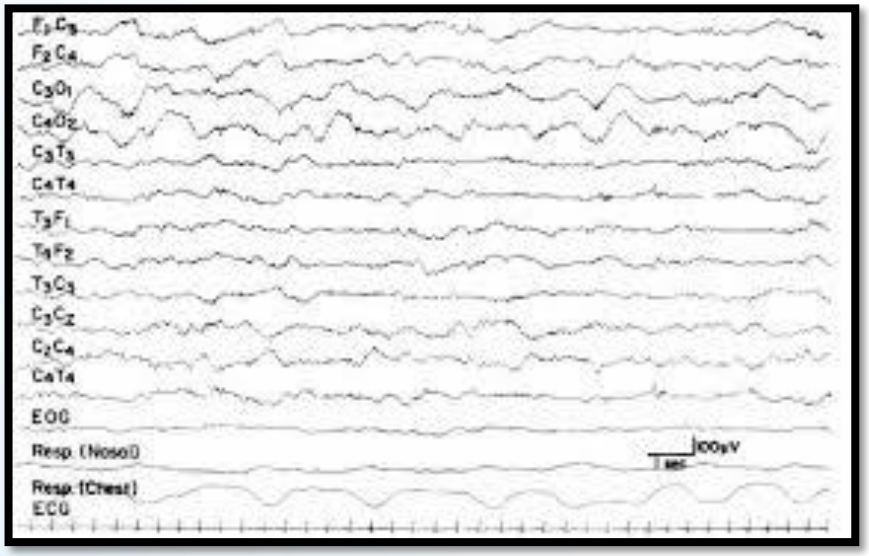
So why do we care about epilepsy syndromes?

When we can categorize correctly this tells us a lot of information:

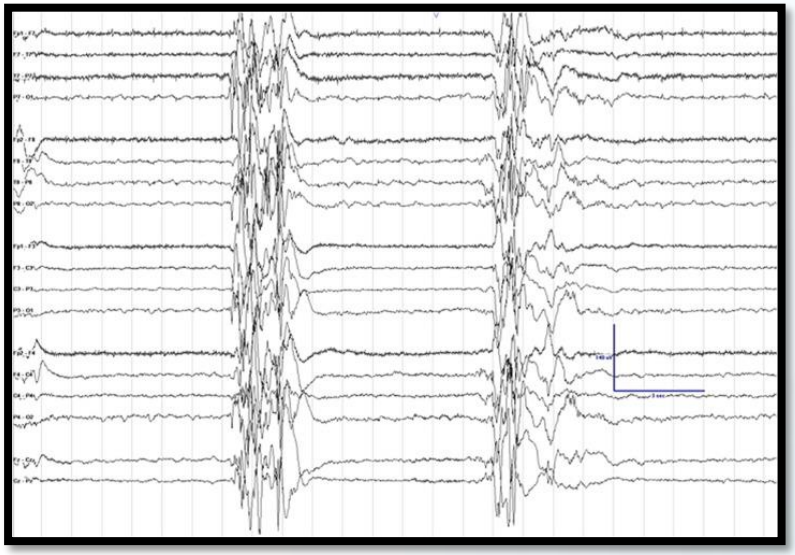
- What is the epilepsy or developmental prognosis?
- What treatment might be best?
- What treatment might be harmful?
- What are the potential etiologies (underlying cause)?

Example of the power of Epilepsy Syndromes

New born baby having frequent seizures:



Normal EEG Background



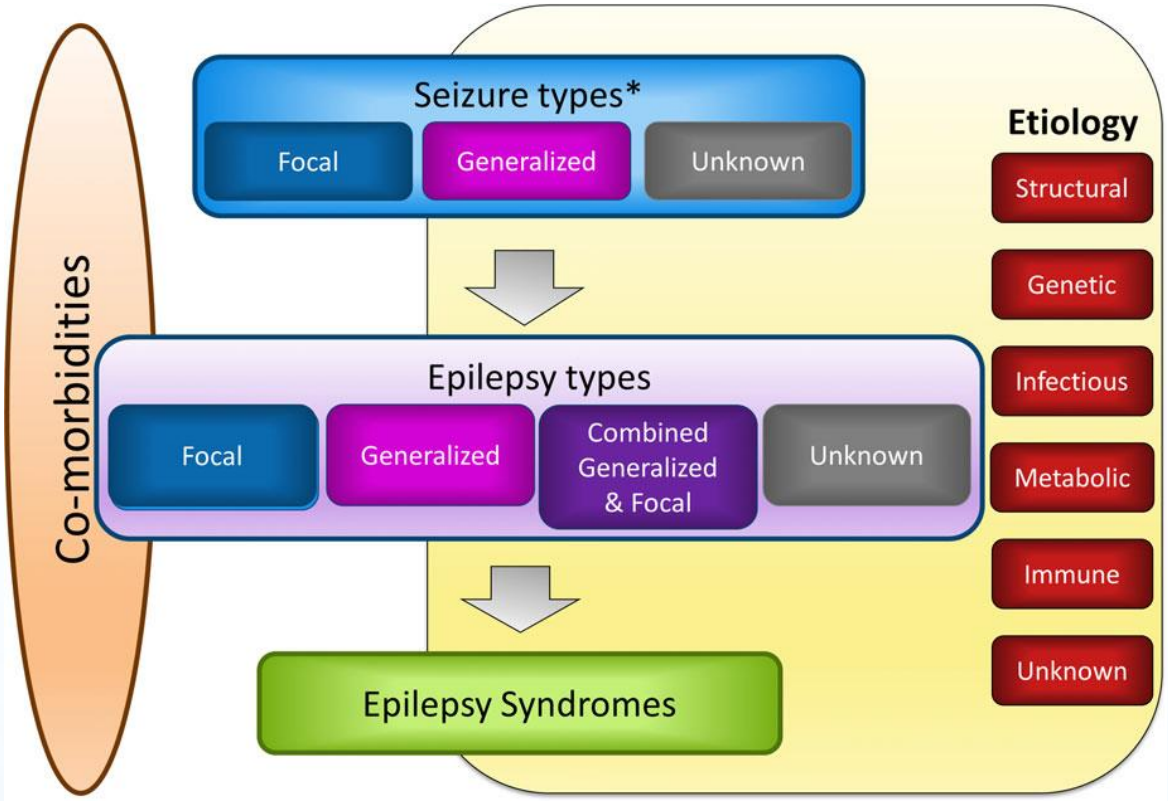
Burst- Suppression Pattern

How do we organize Epilepsy Syndromes?

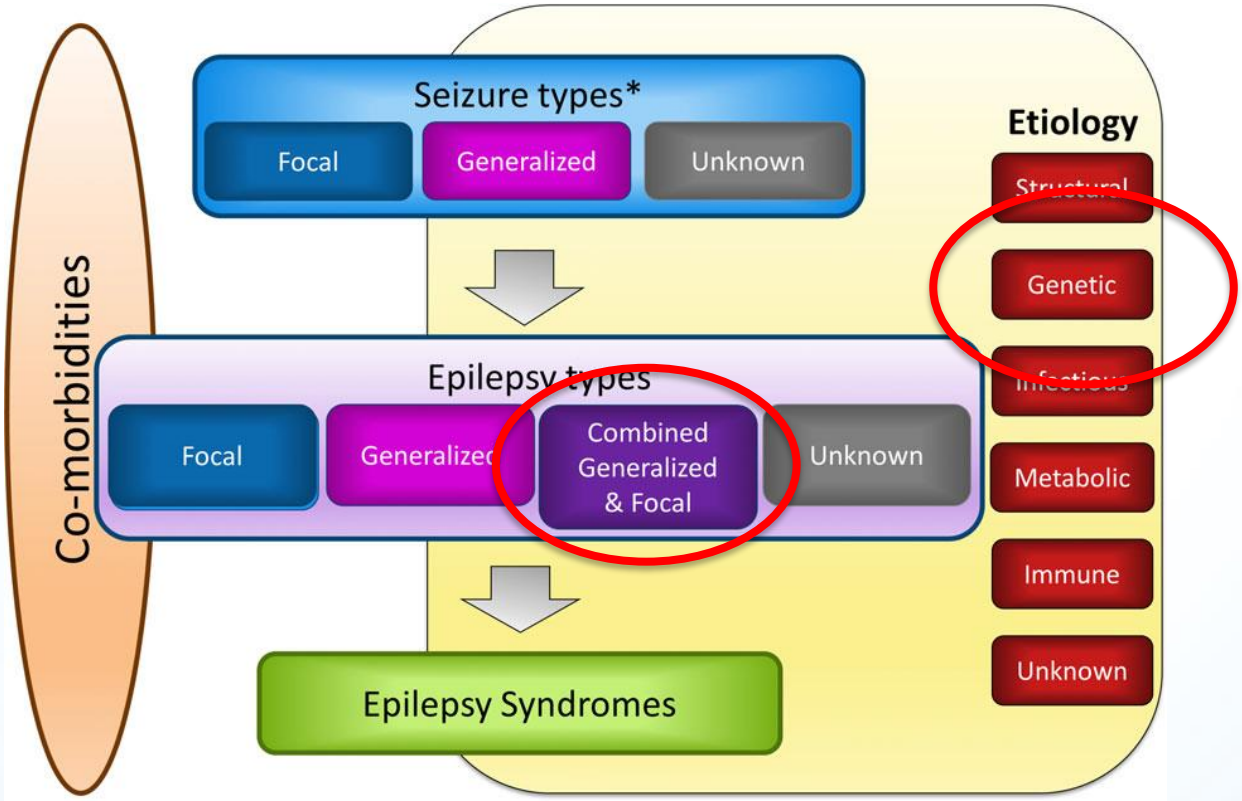
There is no one way but these are some ways we think about it:

- Age of onset
- Generalized or Focal, or both
- Etiology (Genetic, Structural, Metabolic, Immune, Infectious…)

ILAE Epilepsy Classification System

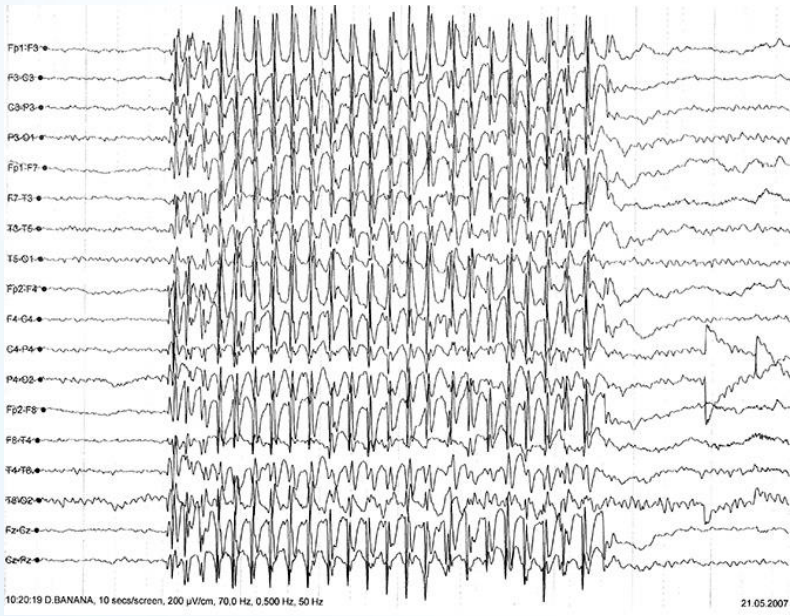


ILAE Epilepsy Classification System

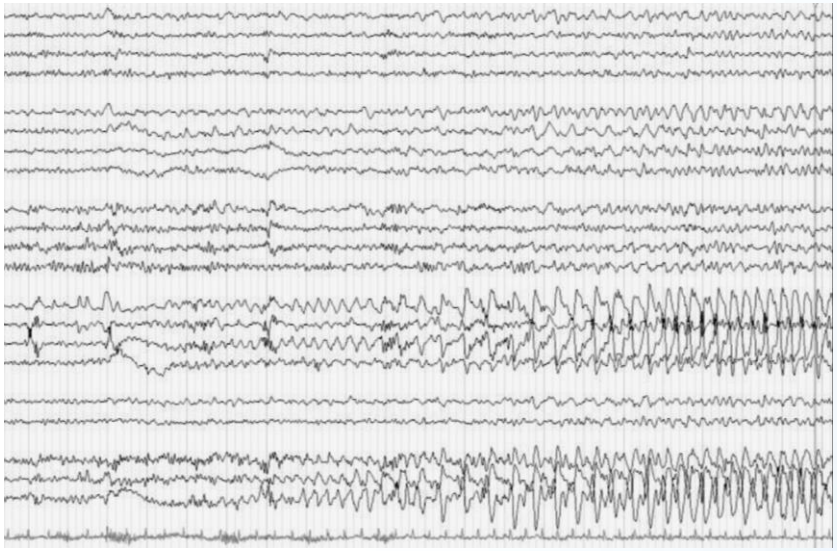


Seizure Type vs Epilepsy Type

Generalized



Focal (partial)



Seizure Type vs Epilepsy Type

Generalized

Myoclonic

Atonic

Absence

Tonic clonic

Focal (partial)

Focal

Impaired awareness

Generalized tonic clonic

(secondary generalized)

Co-morbidities

Everything related to the epilepsy that is not seizures.

- Intellectual disability
- Behavioral challenges
- Motor or language difficulties
- Abnormal Sleep

What Epilepsy Syndromes are Confused for DS?

Lennox-Gastaut Syndrome

Doose Syndrome

Progressive Myoclonus Epilepsy

Benign Myoclonic Epilepsy of Infancy

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What Epilepsy Syndromes are Confused for DS?

Lennox-Gastaut Syndrome
Doose Syndrome
Progressive Myoclonus Epilepsy
Benign Myoclonic Epilepsy of Infancy

All of these often have:

- Onset of epilepsy <3 years
- Myoclonic seizures
- Drop seizures
- Generalized tonic clonic seizures
- Febrile seizures

So how are these really different?

LGS and Doose – typically start a little later, have some unique EEG findings, and often less focal seizures

Benign Myoclonic Epilepsy of infancy – typically don't have developmental delays and seizures stop

Progressive Myoclonus epilepsy - associated with a persistent developmental decline that does not stop – eventually this is fatal

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None of these patients should have SCN1A mutations

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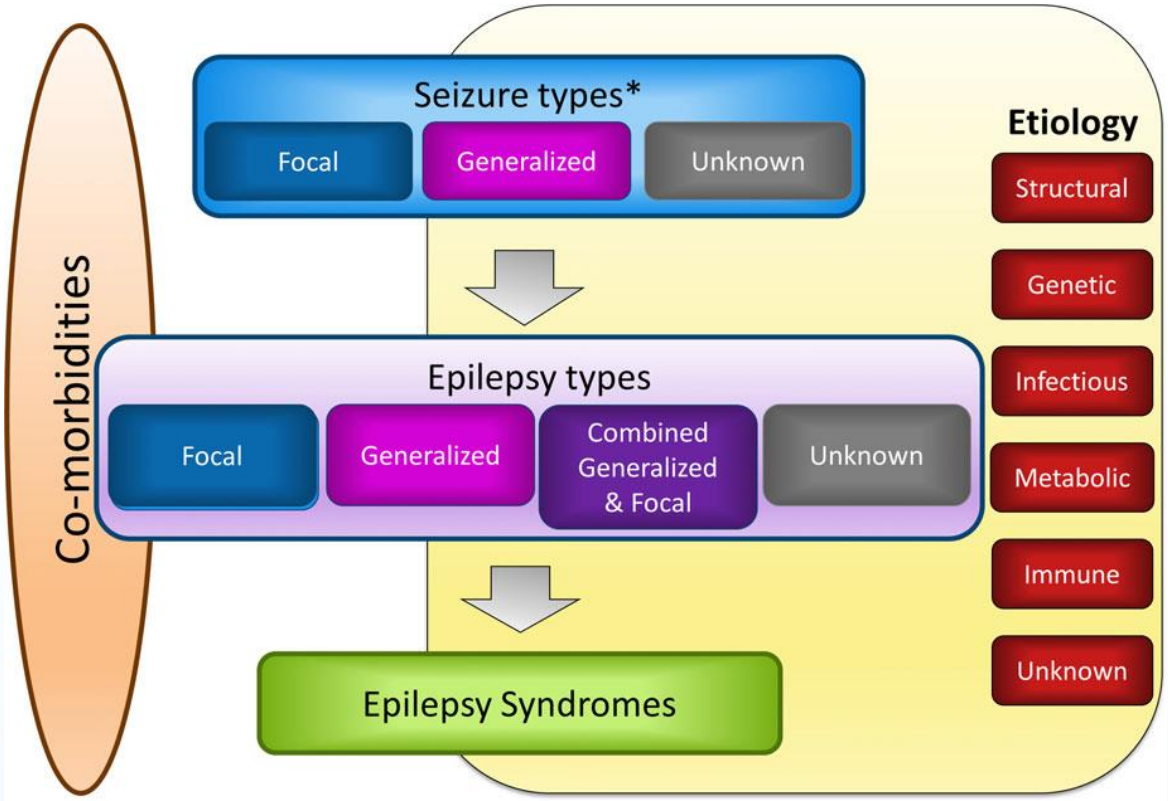

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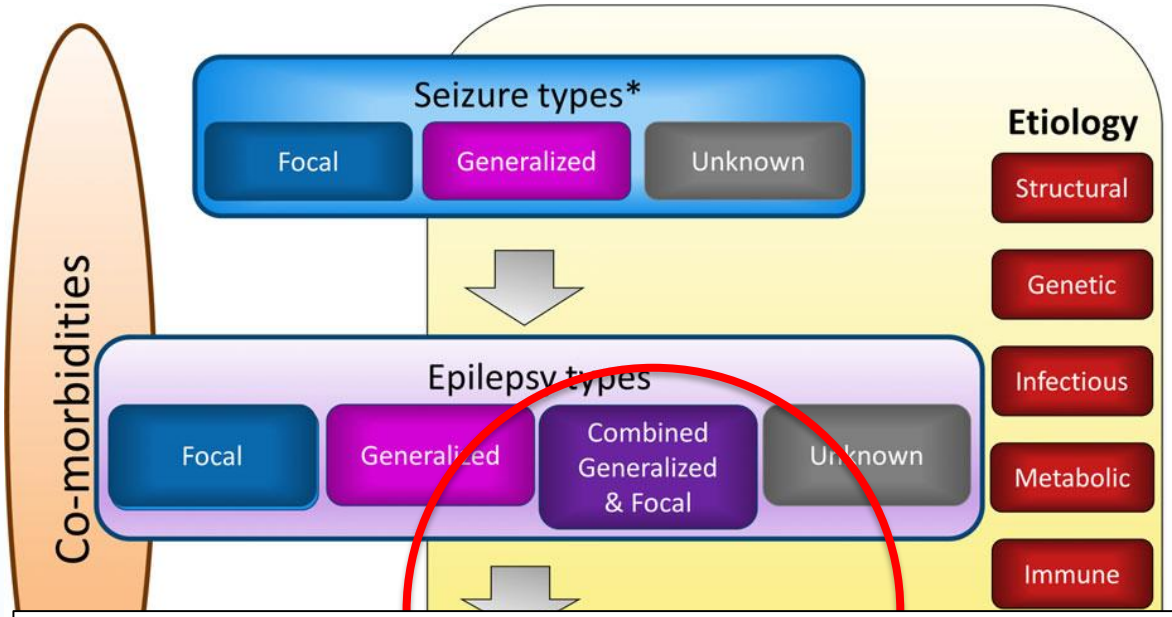

Different patients have different features and not all fit a classic epilepsy syndrome. Genes are proving a useful way to classify but this is also not perfect…

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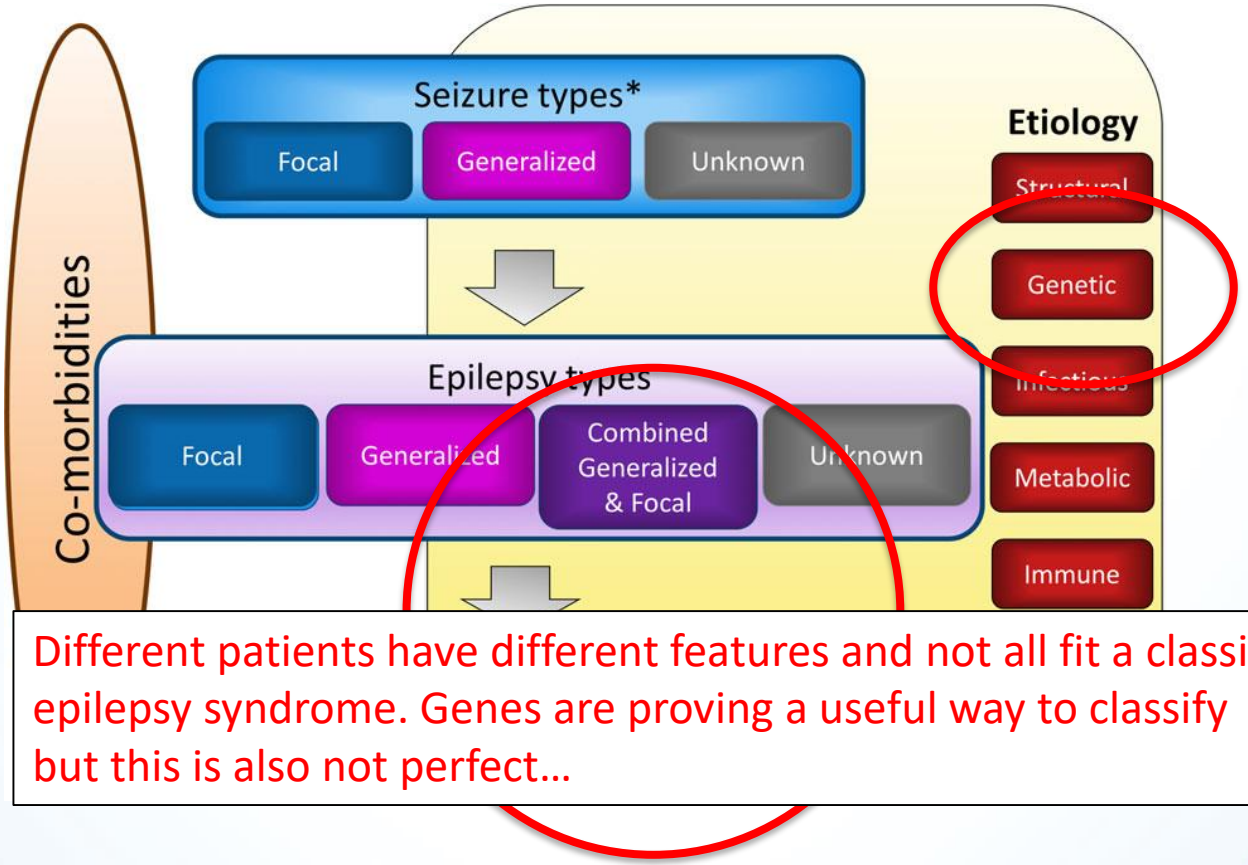

SCN1A

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Recap

Epilepsy syndromes are clusters of certain traits

Genes are starting to define this

This is not perfect and there is overlap between syndromes no matter how you classify.

Better than nothing because it does help guide treatment and prognosis

Thank You

Questions?