Quantitative EEG in pediatric epilepsies

Andreea Nissenkorn
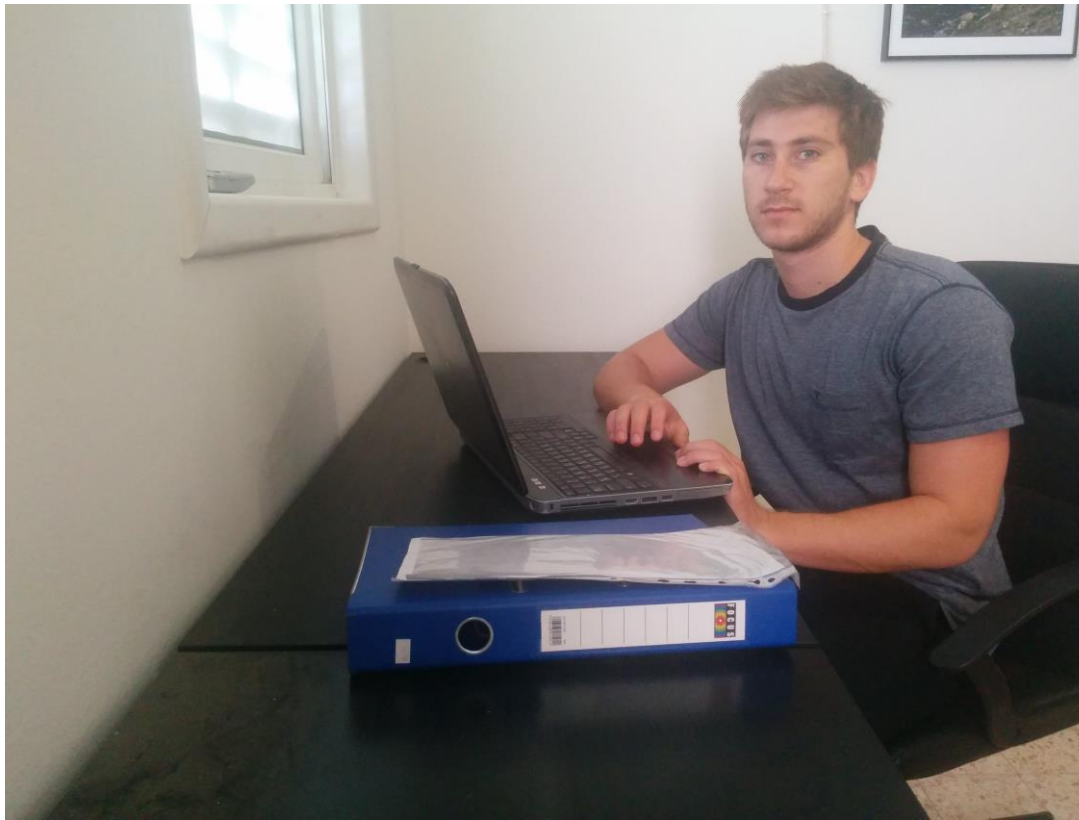
Head of Service for Rare Neurologic Disorders

Pediatric Neurology Unit

Edmond And Lilly Safra Children Hospital

Sheba Medical Center

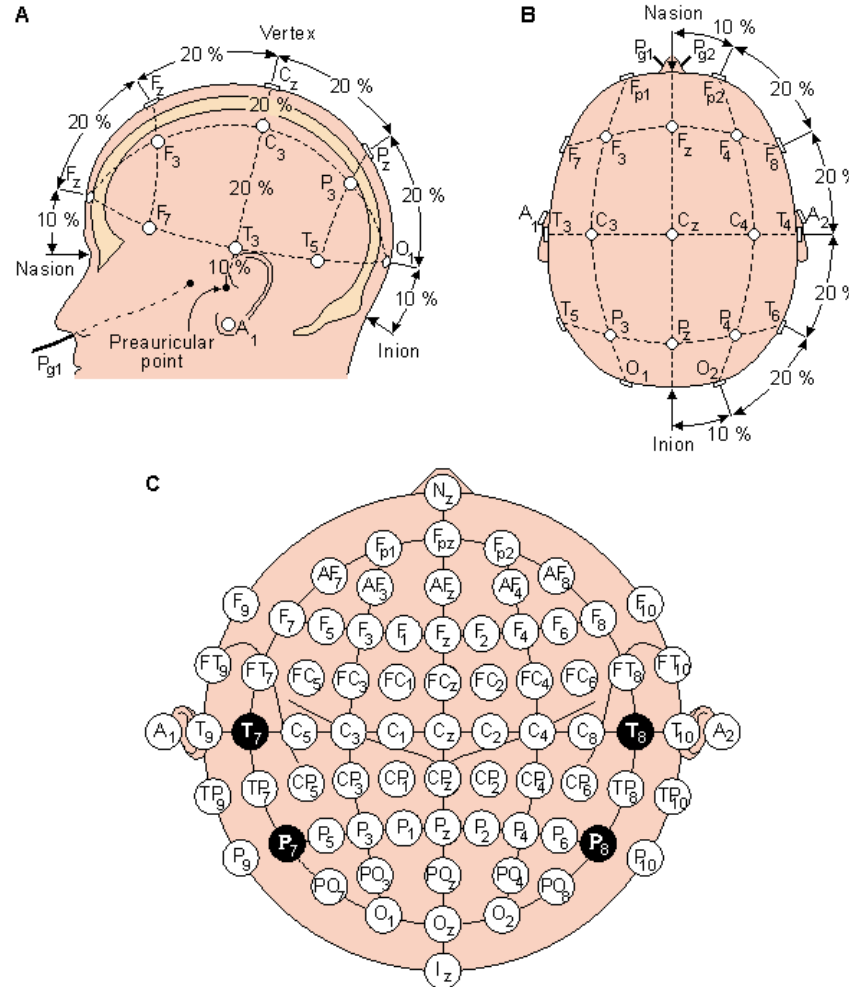# Shay-el Berkovich, Arrow project student

What is an EEG?

- ▶ Records brain oscillation from closed skull
- ▶ Brain oscillation change according to functional state
  - ▶ Sleep/awake
  - ▶ Eyes opened/eyes closed
  - ▶ Epileptic discharges
- ▶ Main diagnostic tool in epilepsy

10-20 System of Electrode Placement

- F = Frontal
- P = Parietal
- T = Temporal
- O = Occipital
- C = Central
- A = Auxiliary

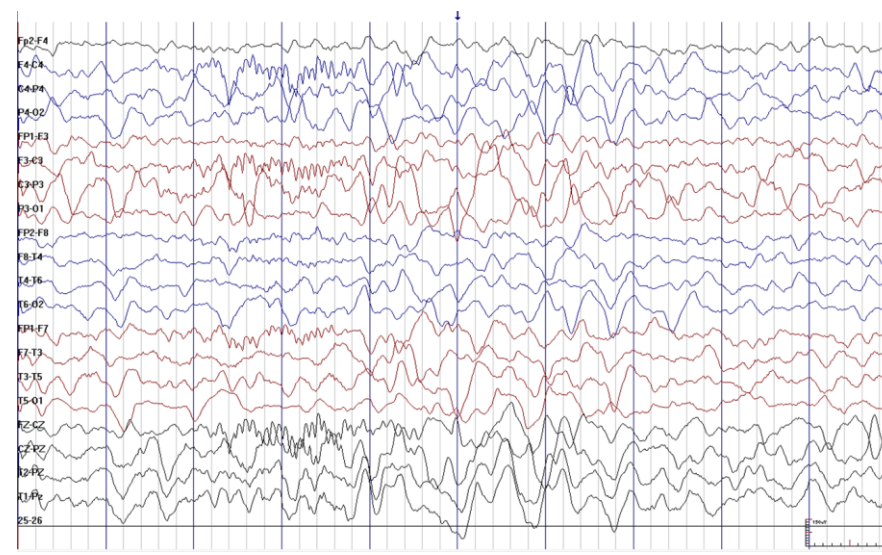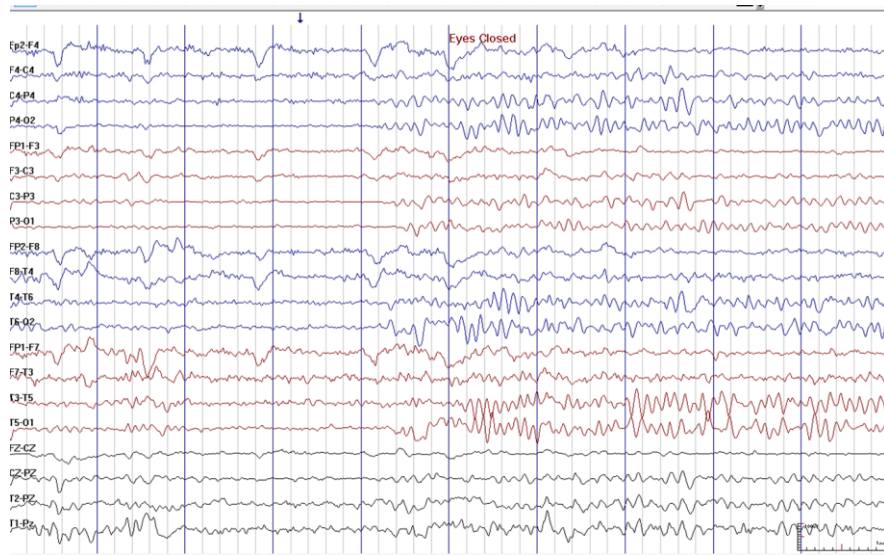- Odd # = Left
- Even # = Right

EEG language

Frequency
Ranges

Beta: 14 – 30 Hz

Alpha: 8 – 13 Hz

Theta: 5 – 7 Hz

Delta: 1 – 4 Hz
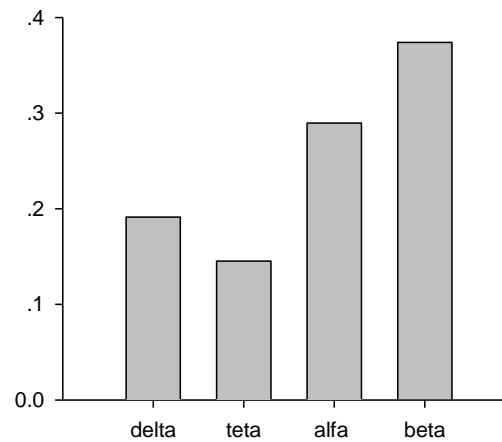
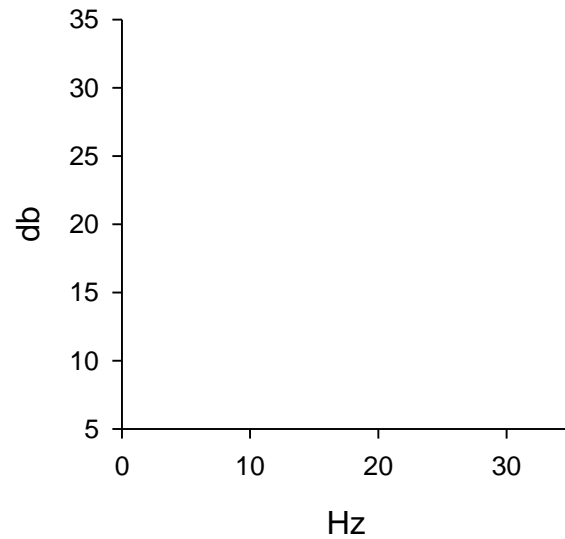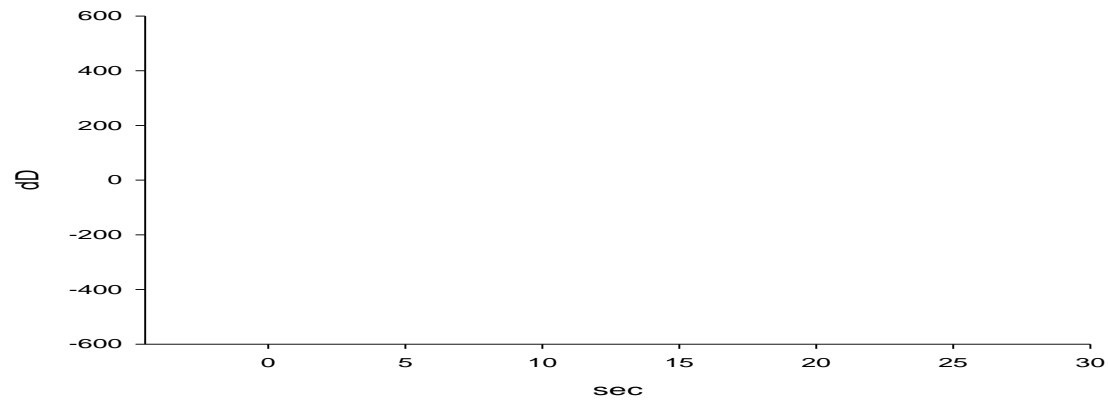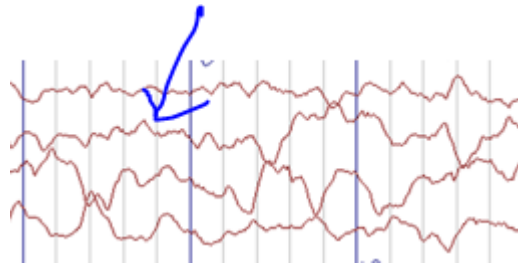# Background activity

Epileptic activity

Quantitative EEG-Spectral Analysis

▶ Every wave is a mixture of different frequencies

▶ Fourier Transform analysis

$$f(\xi) = \int_{-\infty}^{\infty} f(x)e^{-2\pi i x \xi}\, dx$$

Where ξ = frequency
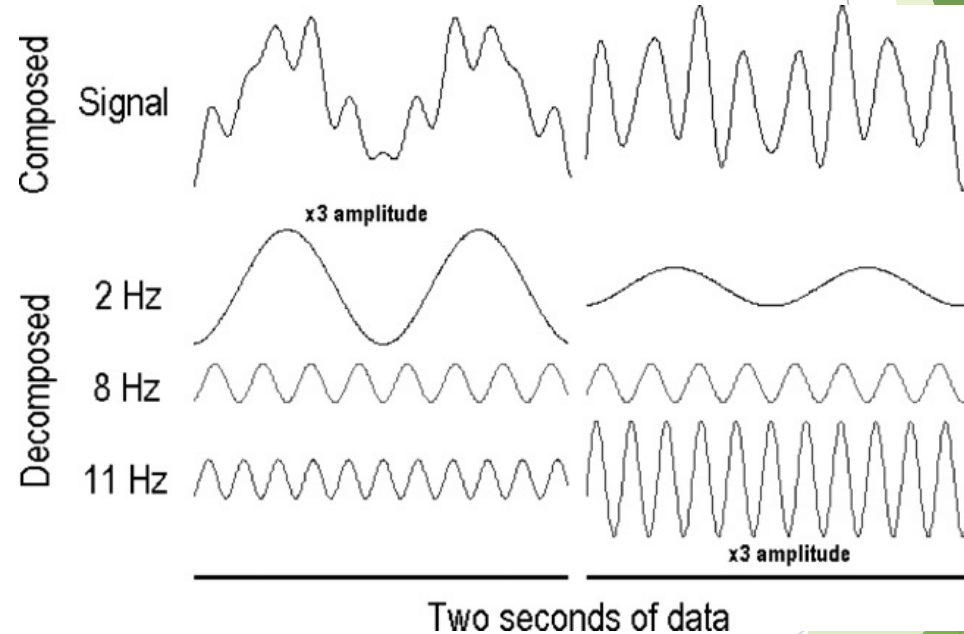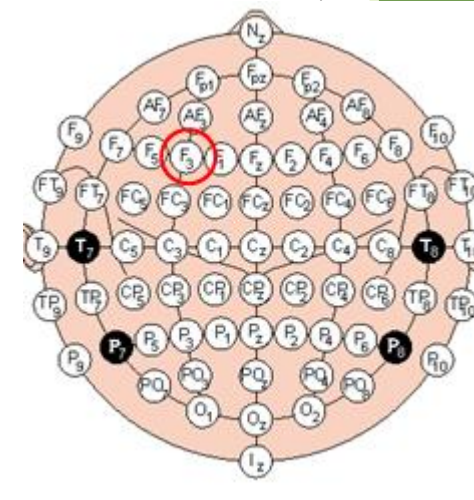
delta	teta	alfa	beta
19.1 %	14.5 %	28.9 %	37.4 %

| Mean frequency |
|----------------|
| 13.69171 |

Dravet syndrome

- Severe epileptic encephalopathy of childhood with poor prognosis
- Early severe febrile seizures by six month of age
- Severe intractable seizures by one year of age
- Developmental delay by 2 years of age
- Drug resistant
- Lamotrigine aggravates seizures
- Some positive effect for valproate/topiramate+clobazame+stiripentol

SCN1a gene mutations

- Nav1.1. voltage gated sodium channels
- Initial depolarization of neurons
- Missense vs. nonsense mutations
- Loss of function of channel

Mapping the SCN1A Mutations
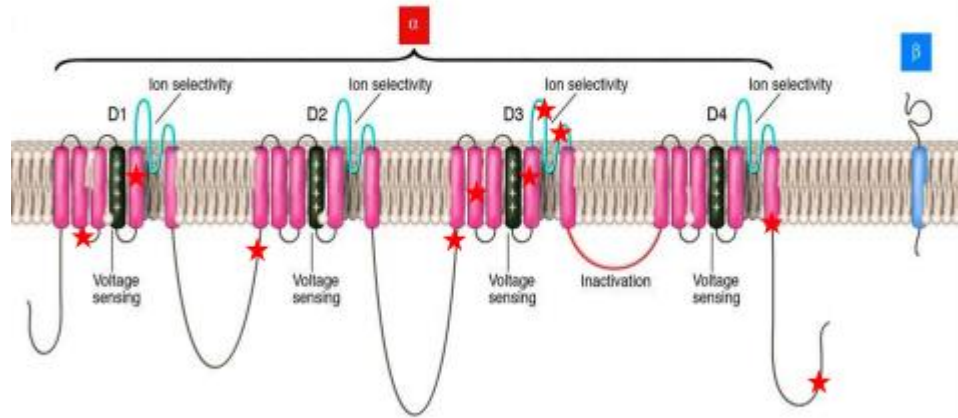
Loss of inhibition

- Epilepsy- imbalance between inhibitory and excitatory neurons
- SCN1a- inhibitory GABA ergic neurons in hypoccampus
- Dravet- loss of inhibition
- Most AED – block Na channels
- NA channel blockers should be avoided in Dravet
- GABA enhancing drugs should be used
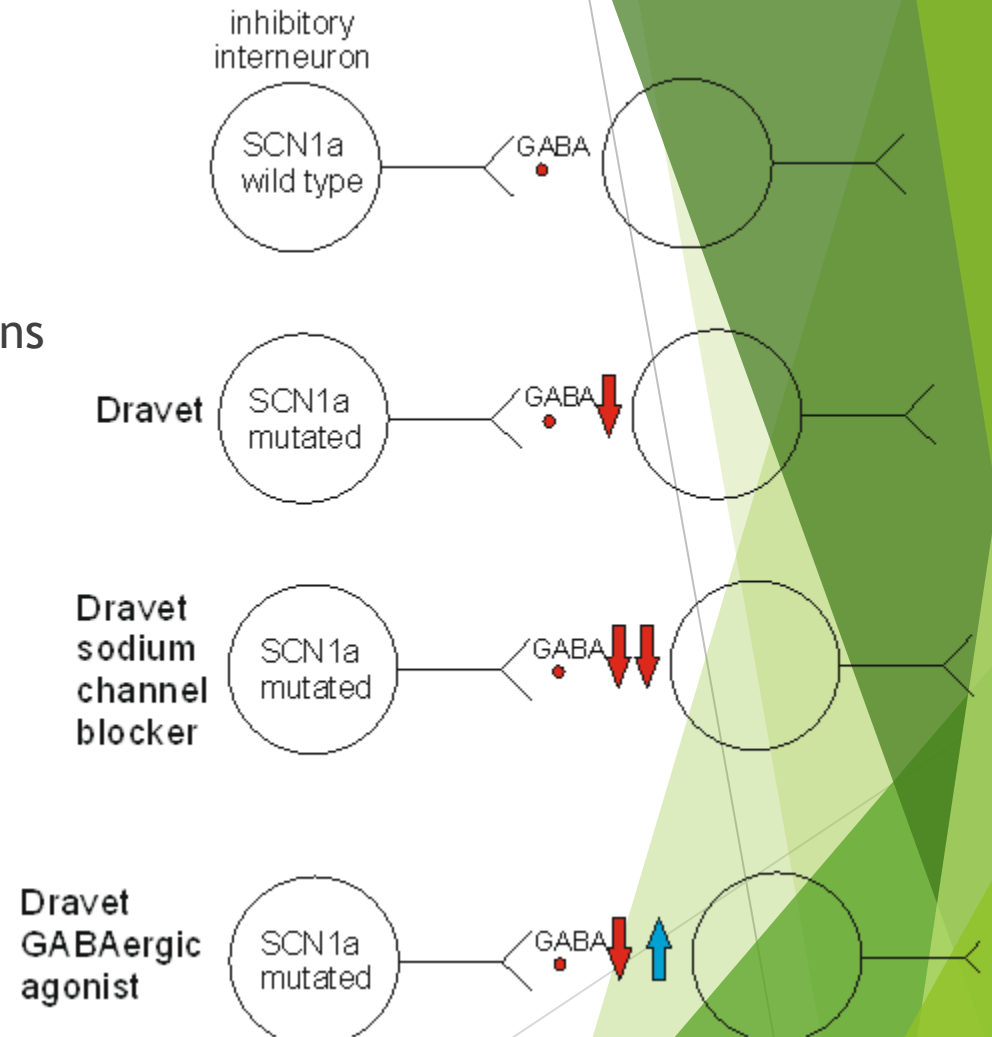
Power spectral analysis of background in Dravet/SCN1a- hypothesis

- ▶ Dravet patients have slower backgrounds than controls
- ▶ Missense vs nonsense mutation effect on background
- ▶ Effect of drug treatment on background EEG
  - ▶ Na channel blockers
  - ▶ GABA enhancing drugs

Results

- 10 patients, 5 missense , 5 truncating mutations
- Age: 7.91667 ±4.23102 (3-16)
- AED:2.34 (2.23 vs. 2.57, NS)
- 52 EEG recordings: Eyes open, awake: 20 , Eyes closed, awake: 7 ,Sleep: 25
- Eyes open_ F3 (frontal) –slower background activity for truncating mutations vs missense mutations
- Mean frequency 12.3 vs. 13.6 Hz ($p<0.01$, t test)
- Delta band power 25% vs. 21% ($p<0.01$, t test).
- Eyes open_T3(temporal) no difference
- Mean frequency 11.7 vs 13.2 Hz (NS)
- Delta power 26% vs 22.9 (NS)

QEEG as outcome measure in epilepsy

- Power spectral analysis before and after treatment
- The usual outcome measure-(number of seizures- 50% reduction- responders)
- Drug resistant epilepsy
  - Vagal nerve stimulator VNS
  - Ketogenic diet
- Secondary cognitive benefit

Plan for next year

- Controls for Dravet
- Spectral analysis for VNS treatment

- FUTURE
- Quantification of epileptiform activity on EEG
- Kinetic models of mutant neurons in DRAVET

Daniel Yakubovich, MD, PhD