In the blink of an eye:
Seizures in newborns

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Importance of Accurately Recognizing and Appropriately Treating Seizures

- To evaluate possible underlying etiologies which may need specific treatments
- Uncontrolled/Untreated seizures may worsen long term outcome
- Antiepileptic medications can have side effects and/or long term detrimental effects

Disclosures

I have nothing to disclose

Seizures in neonates

- Seizures occur most frequent in the neonatal period than in any other time in life
- The neonatal brain presents with seizures in response to many different acute insults such as hypoxia-ischemia, infections, metabolic disorders, electrolyte disorders, stroke.
In the immature brain, excitation is required for brain development. One of the key factors in the human brain’s ability to change via neuroplasticity is that neurons form interconnections based on simultaneous firing over a period of time.

"Neurons that fire together wire together"

Baby girl 1

- 40 5/7 weeks, ROM x36 hours, GBS + adequately treated, terminal meconium, APGAR - 2, 9
- Admitted to ICN at 24 hours of life after 3 episodes of left arm and leg jerking noticed by parents.
- On admission witnessed left arm and leg rhythmic activity, EEG was started.

Neonatal seizures

Neonatal seizures differ from those of older children and adults. The most frequent neonatal seizures are described as subtle because the clinical manifestations are frequently overlooked. These in-
Classic presentation of stroke in a term infant
- Focal clonic seizures
- Seen clinically, and on EEG
- EEG helped reassure this was a limited insult
- Clinical, EEG and MRI findings were all consistent

Baby girl 2
- 35 weeks girl transferred for apnea
- C-section for known vasa previa.
- Fetal monitoring reassuring
- Required CPAP at birth with resolution of respiratory distress after 4 min. Cord and baby gasses normal.

Baby girl 2
- Within 6 hrs had multiple episodes of apnea with desaturation, some with spontaneous resolution but most required vigorous stimulation. No bradycardia. No abnormal movements.
- Rule out sepsis initiated; HUS normal; episodes continued so transport to UCSF
- Labs - metabolic panel, CBC, LP normal
- Neuro exam - appropriate for GA, no asymmetry
STROKE

- The most common clinical presentation of stroke in children is acute hemiparesis
- The most common clinical presentation of stroke in newborn are focal seizures
- The FIRST cause of congenital hemiplegia
- 1/4000 newborn at term
- Most are delayed diagnosis
Current clinical practice

- Neonates at risk are visually monitored for clinical manifestations of seizures
- Clinical suspicion of seizures → routine EEG or empiric treatment
- This approach presumes that most seizures give rise to visually observable clinical manifestations

EEG OR NOT EEG?
- Infants with severe diffuse encephalopathies
- Infants who had received AEDs
- Iatrogenically paralyzed infants
Seizures were diagnosed with EEG in 34% (14/41).
6/14 infants (43%) never had clinical correlate.
51 of 76 EEG seizures (67%) without clinical correlate.
3 of 4 infants with status epilepticus never had a clinical correlate.
Status epilepticus was only seen in newborns with moderate/severe MRI injury (p=0.01).
Nash et al, Neurology 2011

- The majority of seizures in the neonate are occasional seizures, occurring as reactive events to acute insults.
- A significant percentage are the first symptoms of epilepsies or epilepsy syndromes that can be already diagnosed in the neonatal period.

Neonatal seizures and epilepsies

- Social and economic benefit in making a definitive diagnosis in children with epilepsy.
- Neurologists continue to perform investigations looking for an etiology in children with cryptogenic epilepsies.
- Families are very grateful for a specific diagnosis especially with the treatment and genetic counseling implications that some of them carry.

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EARLY MYOCLONIC ENCEPHALOPATHY

- Onset in the neonatal period, sometimes within the first hours of life
- Hypotonic and poorly responsive
- Burst-suppression EEG pattern
- Segmental and erratic myoclonus, sometimes massive, affecting the face and limbs
- Absence of neurological development
- AEDs, steroids, ACTH, ketogenic diet are not effective

Fp2-T4
T4-O2
Fp2-C4
C4-O2
Fp1-C3
C3-O1
Fp1-T3
T3-O1
T4-C4
C4-Cz
Cz-C3
C3-T3
Fz-Cz
Cz-Pz
Chest Resp
Nasal Resp
Right Hand
Left Hand

Familial recurrence
Nonketotic hyperglycinemia
Methylmalonic or propionic acidemia
Pyridoxine deficiency
MRI is usually normal
MRS
For some cases no etiology can be found
OHTAHARA SYNDROME

- Onset often within the first 10 days of life
- Main seizure pattern: tonic spasms
- Burst-suppression EEG pattern
- Severe psychomotor retardation
- Poor prognosis
- Vigabatrin may improve the condition
- Progression to West syndrome

OHTAHARA SYNDROME

- Hemimegalencephaly
- Focal cortical dysgenesis
- Genetics:
  - STXBP1 gene mutations (Synaptin binding protein 1)
  - ARX gene mutations
Neonatal Epileptic Encephalopathies with Suppression–Bursts

Ohtahara syndrome       Early Myoclonic Encephalopathy

More important is the type of seizures (myoclonic versus tonic spasm) because this will influence the work-up and treatment.

Double trouble seizures in twins

• Twin girls born at 37 weeks GA by IVF, delivered vaginally, weighted 4 lb 9 oz, Apgar 7/8 and 8/9 respectively
• Normal neurological examination
• On day 2 twin A began having episodes of abrupt apnea and desaturation
• On day 5 twin B began having identical episodes
• Interictal EEG: normal

Double trouble seizures in twins

• Seizures were stereotyped and quite similar in each twin.
• The twins were having more than 20 episodes per day.
• MRI scan, CSF examination, organic acids, electrolytes, CBC, NH₃, and liver function tests: normal
• Review of the mother's history revealed that she had had seizures as a newborn.
### Benign Familial Neonatal Seizures

- Age-dependent genetic epilepsy of the newborn
- Autosomal dominant, penetrance 85%
- Two genes: KCNQ2 and KCNQ3
- Healthy neonates
- Seizure onset on day 2 or 3
- Brief frequent seizures lasting 1 to 2 minutes often progressing into status epilepticus
- Mean duration of clusters is about 20 hours, varying from 2 hours to 3 days
- Favorable outcome in regard to seizures and neurological development


### KCNQ2 Encephalopathy

- Tonic seizures accompanied by motor and autonomic features
- Mutations in KCNQ2 gene
- Normal interictal EEG
- Favorable seizure outcome
- Normal developmental outcome

In patients with KCNQ2 mutations the EEG pattern correlates better with prognosis than did the molecular genetic findings

### Key points

- Seizure recognition and characterization in babies remains the foremost challenge to overcome
- Continuous Video-EEG monitoring helps to detect seizures in high-risk infants
- Correct interpretation of the clinical manifestation is the first step toward the right diagnosis and appropriate treatment
- When seizures are diagnosed, they should be considered in their overall context: put the right piece of the puzzle in the right place
EEG

Diagnosis

Neonatal seizures

Genes

- Same pattern EEG but different seizure type
- Same seizure type but different pattern EEG
- Mutations in one gene may be linked to severe and benign epilepsies

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