Epilepsy & Spells
Seizures & other causes of Transient Neurological Symptoms

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Overview

• Differential diagnosis of episodic neurologic symptoms

• Epilepsy
  – Syndrome definitions
  – Types of seizures
  – Diagnosis
  – Therapy
  – Special populations
Differential Diagnosis for Episodic neurologic symptoms

- Seizure
- Syncope
- Cerebral ischemia (TIA)
- Migraine
- Sleep disorders
- Transient Global Amnesia
- Conversion disorder
- Malingering

Syncope

- Loss of consciousness caused by cerebral hypoperfusion
  - Cardiac arrhythmia
  - Orthostasis
  - Dysautonomia
  - Cough, urination, defecation
- Much more common than epilepsy
- Convulsions may be present in up to 50%
New onset sudden loss of consciousness with loss of muscle tone in adulthood is syncope unless proven otherwise

TIA

- Usually negative symptoms
  – Exceptions, e.g. limb shaking TIA
- Last minutes to an hour
- Not as likely as seizures to be stereotyped or recurrent
Sleep Disorders

- Hypersomnolence
- Hypnagogic/Hypnapompic jerk
- REM behavior disorder
  - May be presenting sign of PD or LBD
- Cataplexy
- Periodic limb movements of sleep
- Night terrors

Migraine

- Transient, episodic, and stereotyped
- May involve neurologic symptoms (aura)
- Neurologic symptoms develop over minutes
  - seizures, usually over seconds
- Aura precedes headache
### TGA

- Sudden onset
- Duration typically 6 to 24 hours
- Memory impairment and confusion
  - May ask same question repetitively
- Usually able to carry on usual ADLs
- Resolves completely but no memory of events
- Up to 25% recurrence rate

### Psychogenic non-epileptic spells (PNES)

- Typical characteristics
  - Eyes closed
  - Side to side head movements
  - Bilateral motor involvement with preserved responsiveness
  - Pelvic thrusting
  - Back arching
  - Prolonged screaming or crying
Features favoring seizure

- Preceded by aura
- Occurring out of sleep
- Duration 30 to 120 seconds
- Eyes open
- Postictal confusion
- Amnesia
- Injury (lateral tongue and cheek biting)

EPILEPSY Definitions

- Generalized vs. Localization-related
- Symptomatic vs. Idiopathic
- Symptomatic vs. Cryptogenic
Types of Seizures

- Simple partial
- Complex partial
- Secondarily generalized
- Absence
- Tonic-clonic
- Myoclonic
- Atonic

Simple Partial

- Focal neurologic dysfunction
- Without impairment of consciousness
- Usually “positive” symptoms
  - i.e. jerking/stiffening as opposed to weakness or tingling as opposed to numbness
Simple partial seizures

• Motor – tonic / clonic
• Sensory – paresthesias / buzzing
• Special sensory - olfactory / oustatory / auditory / visual
• Psychic - Déjà vu, depersonalization, micropsia/macropsia
• Emotional – pleasure / fear / anger

Complex Partial

• Focal neurologic dysfunction
• With impairment of consciousness
• May have similar signs/symptoms as SPS
• May display automatic behaviors
  – Lip smacking
  – Repeated swallowing
  – Manual automatisms, i.e. fidgeting, rubbing, picking, scratching
Secondarily Generalized

- May occur with or without a recognized preceding SPS or CPS
- Head and eye deviation may indicate [contralateral] hemisphere of onset

Generalized from onset seizures

- Absence
- Tonic-clonic
- Myoclonic

- Tonic
- Atonic
Absence Seizures

- Most commonly appear in childhood and resolve in adolescence
- Rarely presents in adulthood
- May persist into adulthood as part of JME or JAE

Absence

- Sudden onset behavioral arrest, unresponsiveness
- Typically less than 10 – 15 seconds
- Little or no postictal confusion
- May occur dozens of times in a day
- Can be made worse by sodium channel modulators such as CBZ, PHT, OXC
Myoclonic Seizures

- Brief and shock-like
- Typically involve limbs but may involve torso or head
- Tendency to occur upon awakening
- May occur singly or in brief trains

Other uncommon seizure types

- Myoclonic
  - Generalized epilepsy phenomenon
  - Tend to occur close to sleep onset or upon awakening
- Tonic / Atonic (Drop attack)
  - Seen in Lennox-Gastaut and symptomatic generalized epilepsy syndromes
  - Very uncommon in adult-onset epilepsy
Seizure Therapy

Seizure Treatments

• Anticonvulsant medication
• Implantable devices
  – Vagal nerve stimulation
  – Responsive neurostimulation
  – Deep brain (thalamic) stimulation
• Epilepsy surgery
  – Resection
  – Radiosurgery
Older Anticonvulsants

- Phenobarbital
- Primidone
- Phenytoin
- Valproic acid *
- Carbamazepine
- Clonazepam

2nd Generation Anticonvulsants

- Gabapentin
- Felbamate
- Lamotrigine *
- Topiramate *
- Levetiracetam *
- Zonisamide *
- Oxcarbazepine
- Pregabalin
- Lacosamide
- Clobazam*
- Tiagabine
Anticipated Anticonvulsants

• Brivaracetam
  – Chemically related to but more potent than levetiracetam

• Eslicarbazepine
  – Active metabolite of oxcarbazepine

Phenobarbital/Primidone

• M.o.A. - enhancement of GABA-A
• [+]  
  – Effective  
  – inexpensive  
  – can be taken QD

• [-]  
  – side effects – sedation, mood, bones, liver  
  – drug interactions
Phenytoin (Dilantin)

- **M.o.A.** – inhibition of VG Na channels
- [+]  
  - effective  
  - inexpensive  
  - can be taken QD (Dilantin)
- [-]  
  - non-linear kinetics  
  - side effects (ataxia, gingival hyperplasia, PN)  
  - drug interactions (p450 inducer)

Carbamazepine (Tegretol, Carbatrol)

- **M.o.A.** – mainly inhibits VG Na channel
- [+]  
  - Effective  
  - Inexpensive  
  - Well-tolerated
- [-]  
  - Rare bone marrow or hepatic toxicity  
  - 3\textsuperscript{rd} leading cause of Steven-Johnson  
    - HLA- B 1502 8\% of Han Chinese  
    - Drug interactions (p450 inducer)
Valproate (Depakote)

- M.o.A. – mainly GABA-A modulation, also affects Ca and K conduction
- [+] – Broad Spectrum
  - Non-sedating
  - Available in QD preparation
- [-] – Weight gain
  - Potential for hepatotoxicity
  - Hirsuitism, PCOS, teratogenicity

Gabapentin (Neurontin)

- M.o.A. - ? – VG Ca Channel modulation
- [+] – Favorable side effect profile, some beneficial
  - Renal clearance, no drug interactions
  - Little toxicity
- [-] – Low efficacy (except in elderly)
  - TID dosing
Lamotrigine (Lamictal)

- M.o.A. – VG Na Channel inhibit, N-type Ca Channel modulation
- [+]
  - Very favorable side effect profile, some beneficial
  - Broad spectrum
- [-]
  - Rash, potential for S.J. synd, slow titration
  - Tremor, headache, insomnia

Topiramate (Topamax)

- M.o.A. – VG Na, GABA, AMPA, Ca, etc.
- [+]
  - Highly effective
  - Weight loss
  - Mood stabilizing, migraine preventive
- [-]
  - *Cognitive side effects
  - May cause renal stones
  - Weight loss
Levetiracetam (Keppra)

• M.o.A. – binds SV2A synaptic vesicle protein
• [+]
  – Broad spectrum, effective
  – Renal clearance, no drug interactions
  – Safe
• [-]
  – Mood and behavioral changes

Treatment of epilepsy in women

• Must take into account additional factors
  – Menstrual cycle
  – Contraception
  – Potential for pregnancy/teratogenicity
  – Reduced drug levels during pregnancy
  – Cosmetic effects of anticonvulsants
  – Special attention to bone health
Menstrual cycle and seizures

- Estrogen – pro-convulsant
- Progesterone – anti-convulsant
- Treatment of catamenial epilepsy
  - Increase AED during at risk period
  - Add BZD during at risk period
  - OCP
  - Progesterone IM depot

Contraception

- Estrogen and progesterone metabolized by p450
- Several AEDs decrease effectiveness of OCP
- Higher dose OCPs may be more effective
- Depot progesterone or IUD recommended
- OCP may reduce LMT levels
Pregnancy - counseling

- Risk of birth defects increased 2x in WWE
- All AEDs potentially teratogenic
- Seizures during pregnancy also hazardous
- Planned better than unplanned
  - Seizure free 1 year before pregnant, high probability seizure free through pregnancy
  - Major organogenesis occurs early in 1st trimester (before she knows)
  - Selection of effective and preferable AEDs prior to pregnancy is critical

Pregnancy - AEDs

- Valproate – XXXXXXXXX
  - Neural tube defects
  - Lower IQ
- Phenytoin – XXXXX
- Phenobarbital – XXXX
Pregnancy – AEDs (cont)

- Carbamazepine – XX
- Topiramate – XXX
  - Low birth weight
- Lamotrigine – X
  - Cleft palate
- Levetiracetam - X

Pregnancy - recommendations

- If no seizures in past year, consider weaning AED
- If unable to wean AED, transition to lower risk AED (LMT, LEV)
- Avoid polytherapy if possible
- Check serum AED level
- Attempt to maintain therapeutic level through pregnancy