Management of Complex Seizure Disorders

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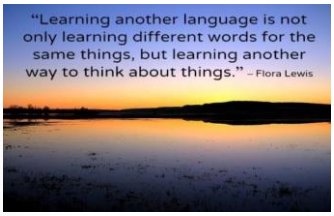
What's Changed in regards to Epilepsy & Seizures?



Seizure

Definition: **"A transient occurrence of signs &/or symptoms due to an abnormal excessive or synchronous activity in the brain"**

An **"electrical storm"** or surge of activity in the brain that affects how a person appears or acts for a short time.
Imbalance between brain cells sending messages in certain areas

- Seizure symptoms depends on many factors:
  Circuit(s) involved in the brain
  Individual's genes, brain injury
  Effectiveness of treatment regime

What ever the brain & body can do *"normally"* can also occur during a seizure.

Epilepsy

- Fourth most common Neurological Disorder / **"Disease"**.
- Tendency of the brain to have ***recurrent* unprovoked *seizures*. Seizures that are not the result of an electrolyte imbalance, drug detoxification, low BG.**
- Unpredictable seizures
- **Spectrum** with wide range of symptoms &/or control of the seizure activity.

Diagnosis of Epilepsy

Diagnostic criteria:

1) At least 2 unprovoked (reflex) seizures within 24 hours or
2) One unprovoked (reflex) seizure & the probability of further seizures or
3) Diagnosis of an Epilepsy Syndrome

Labeled as "**Disease**" & not Disorder now

- Considered to be a Serious Disease
- Considered to be **"Resolved"** when seizure free for 10 years, with the most recent 5 years off AEDs.
- A **Seizure Diagnosis** may be "**minor**" & may not require treatment

Seizure Classification Then & Now

First there was Petit Mal vs Grand Mal used loosely to refer to a "little" or "big" seizures.

Then Partial onset vs Generalized Seizures used to describe & divide seizures into those occurring in **one area or side of the brain** from those occurring on **both sides of the brain at the same time**.

New "Operational Classification"

Observation

Was / is the beginning of the seizure actually always observed or known?

Documentation

- Used to use "labels"
- Now use description of what is observed with some acknowledgement that Onset/ start has possibly been missed

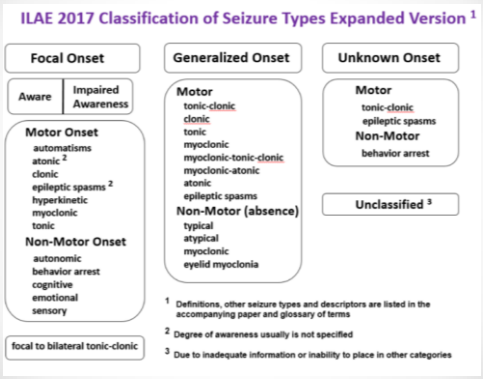
1981 Seizure Classifications

Partial Seizures (start in one place)
- **Simple (no loss of consciousness of memory)**
  - **Sensory**
  - **Motor**
  - **Sensory-Motor**
  - **Psychic (abnormal thoughts or perceptions)**
  - **Autonomic (heat, nausea, flushing, etc.)**
- **Complex (consciousness or memory impaired)**
  - **With or without aura (warning)**
  - **With or without automatisms**
- **Secondarily generalized**

Generalized Seizures (apparent start over wide areas of brain)
- **Absence (petit mal)**
- **Tonic-clonic (grand mal)**
- **Atonic (drop seizures)**
- **Myoclonic**
- **Other**

Unclassifiable seizures

New Operational Classification



New Operational Classification

Based upon 3 key features:

1) Where **the seizure begins**: Focal or General

2) The **level of awareness** during seizure

3) The **features or symptoms** of the seizure

Where the Seizure Begins

1) **Focal**
Previously known as "partial seizures", involves only one side of brain.

2) **Generalized**
Previously known as "primary generalized"; involve both sides of the brain at onset, but not necessarily "the whole brain"!

3) **Unknown Onset**
Start of seizure is unknown.

4) **Focal to Bilateral Seizure**
Previously known as a "secondary generalized seizure".

"Level of Awareness" During a Seizure

Focal Aware / AKA Simple Partial
Can have " intact awareness" / recall even if not able to respond!

Focal Impaired / AKA Complex Partial
If awareness / recall becomes affected at any point then the seizure is considered "Impaired'.

Awareness **Unknown**

Generalized Seizure
Affects awareness or consciousness during the seizure

"Level of awareness" has implications for driving, safety during the seizure, employment & interference with learning.

Seizure "Features or Symptoms"

- **Motor** = **movement** involved
  Automatisms: repeated movement, licking lips, walking, running ,rubbing hands.
  Clonic = jerk
  Tonic = stiff
  Atonic = loss of muscle tone (drop)
- Changes in **sensation**, **emotion**, **thinking** or **experiences**
- **Aura** = symptoms a person may feel at the onset of a seizure. These early symptoms are **usually the start of the seizure**.

Many people have more than one type of seizures

Some Features & Symptoms

Automatisms / automatic behaviors,
Emotions (laughing, crying)
Tonic / extension,
Aautonomic (flushing, sweating)
Myoclonus, jerking arrhythmically
Clonus, jerking rhythmically
Cognitive, language / thinking impairment (deja vu)
Eyelid Myoclonia, eyelid jerks
Atonic, limp / drop
Sensations: numb, tingling, sounds, smells, tastes, visions, vertigo
Behavior Arrest, pausing, freezing, activity arrest
Hyperkinetic, thrashing, pedaling
Spasm, trunk flexion

Generalized Seizures

- Seizures start on both side of the brain.
- Can be Motor or Non-motor.
- Can occur on brain surface / in deeper brain areas.
- Does not need to involve the "whole brain", but at least parts of both sides of the brain.
- Associated with impaired awareness

Classified by:

- Motor includes Tonic-Clonic, Clonic, Myoclonic, Atonic, Epileptic Spasms

- Non-motor includes Absence: Typical & Atypical

Tips for Observing & Recording

- Behavior just before the seizure began
- When (date & time)
- Possible "triggers" / factors that contribute
- What happens / observed / heard
- Describe part(s) of body involved
- What happens after? & for how long?

http://www.epilepsy.com/sites/core/files/atoms/files/tips_seizure_observation_recording.pdf

Same First Aid – Safety Focused

At least some familiar / good news!

Epilepsy Syndromes

Syndromes are defined by a **cluster of features or symptoms.**

Features or symptoms can include:

Types of seizures, the age seizures began, causes, whether an inherited "disease", genetic information, the part(s) of brain involved, certain common provoking / "trigger" factors, the severity & frequency of seizure activity, the patterns on an EEG, brain image findings (MRI / CT), comorbid disorders, the prospects for worsening or recovery.

Some "minor" Syndromes should / will "resolve".

Other Syndromes are quite difficult to control.

Epilepsy Syndromes

- **Lennox-Gastaut Syndrome** = multiple types of seizures, tonic, atonic, ID, classic EEG pattern, hard to control seizures, behavioral problems, will need rescue therapy to shorten or stop "**cluster seizures**".
- **Dravat Syndrome** = Genetic mutation, which causes malfunction of Sodium channels in the brain, begins 1st year of life with normal development until seizures begin, then loss of developmental milestones, seizures are refractory / do not respond to medication, many different seizure types, usually sensitive to **infections**, seizures **triggered** by **slight change in body temperature, lights, emotional stress, excitement**, can have other Neurological motor, behavioral, Autism problems.

Avoid the use of Sodium Channel AED medications in Dravat Syndrome due to Na+ channel dysfunction.

"Intractable" Epilepsy

"Refractory", "Uncontrolled", "Drug Resistant"

Epilepsy controlled quickly with medicine in only about 1/3 of cases.

- **"Refractory" =** Seizures that are **frequent & severe** enough or the **AED therapy is troublesome** enough to seriously **interfere with quality of life.**
  - **Person has failed to become & to stay seizure free with adequate trials of 2 AEDs.**
  - **The AED Rx chosen was correct for the person's seizure type, was tolerated & either tried alone or together with other AEDs.**

Goal is to improve seizure control with the least amount of side-effects

Reasons for Intractable Seizures

- Diagnosis of a seizure disease or the seizure type is wrong
- Treatment is wrong AED
- Despite best treatment, triggers & lifestyle factors affect seizure control
- Properly diagnosed seizures that are associated with some Syndromes do not respond to the best medical treatment.
- Find an Epilepsy Center

https://www.naec-epilepsy.org/about-epilepsy-centers/find-an-epilepsy-center/

Reasons for Suboptimal Control

- **Wrong Medication** - AEDs have several different mechanisms of action
- **Inadequate dose** of medication (persistence in AED trial)
- **Polypharmacy & Toxicity** (increased interactions & increased side effect risk) T
  To simplify Polypharmacy = increased seizures during withdrawal of AEDs
- **Poor compliance** (missed doses)
  PONS should include how to handle missed doses.
  Sometimes **"level of awareness"** is concern for admin.
- **Complicating factors**: illness, **stress**, sleep deprivation.
  Stress is associated with both loss & exciting positive events

Management of Triggers

Goal = **Limit exposure to "Triggers"**

Triggers can be:

- ***noises** (use ear phones)
- ***specific time** of day / night
- ***sleep deprivation** (practice sleep hygiene)
- ***fever / illness**
- ***flashing bright lights or patterns** (polarized glasses)
- *use of **alcohol** / drugs **(PONS)**
- ***stress** (staff loss?, get any regular exercise?)
- *menstrual cycle / **hormone changes** (OCP use)
- ***poor diet / low blood sugar** (eat regularly)
- *excess **caffeine**
- ***medications** (avoid if will lower seizure threshold)

Medication Management

The new **"operational" classification system**:

1) Recognizes that:
- Some seizure types / presentations / features observed can be either **Focal or Generalized seizure activity**.
- We often miss the "onset" or beginning of the seizure activity.
- We do not always know the "level of consciousness".

2) Looks for:
Signs & Symptoms of an event (see slides 10 & 11)
Familiar **patterns** in those signs & symptoms

3) Uses other **data** (EEG, Video-monitor, MRI, Labs & genetic testing) to identify seizure type.

AED Medication Management

Goal(s) of treatment *realistically* may be the reduction in the intensity & frequency of seizure activity with some *tolerable* side-effects??

- Different AED medications have different chemical activities In the Brain
- The use of different AEDs for Focal vs Focal to General vs Generalized
- What is realistic?
- AED side-effects & Interactions

AED Mechanisms of Action

Multiple different chemical mechanisms of action to interrupt seizures & many AEDs have more then one action.

Seizure control / chemical activity = achieving balance between factors that influence **(EPSP) excitatory postsynaptic potential** & those that influence **(IPSP) inhibitory postsynaptic potential**.

***Simplified version*: the sending & receiving messages between neurons in different areas of the brain aimed at stopping abnormal electrical activity.**

- Sodium Channel Blocker Action(s)
- Calcium Current Inhibitor Action(s)
- GABA inhancer Action(s) (GABA =Gamma-aminobuteric)
- Glutamate Blockers
- Carbonic Anhydrase Inhibitors
- Hormones
- Unknown actions

- http://emedicine.medscape.com/article/1187334-overview#showall

AED vs Intractable Seizure effects

- Cognitive Adverse Effects (CAE)
- Improved or worsened mood
- Decreased concentration
- Increased irritability
- Hyperactivity
- Depression

Studies are limited, so the jury is still out around fully determining what are the brain effects of poorly controlled seizures &/or the AED side-effects.

Many Identified AED Side-effects

- GI Disturbances, weight gain or loss
- Depression / suicidal thoughts / behavior changes
- Rash (Stephens-Johnson Syndrome), Dermatitis
- Bone marrow (Aplastic Anemia, Thrombocytopenia)
- Loss of bone density
- Tremors
- Tolerance & dependence
- Drowsiness, dizziness
- Double vision, loss of actual visual fields
- Headache
- Liver failure
- Sleep disturbances
- Hyperactivity
- Hair growth on face
- Dental problems

Drug specific Information sheets should include the significant serious with the common "side-effects".

Epidiolex

GW Pharmaceuticals in UK has developed **Epidiolex** (Cannabidiol or CBD).

Pharmacy grade CBD, so this means the CBD is now available in a **clinically consistent (drug) effective manufactured format**.

Current clinical trials "indicated" in the treatment of both **Lennox-Gastault & Dravat's Syndomes** are showing some promising results.

Also in clinical trials for **Multiple Sclerosis** Therapy.

GW applied December 2016 to the FDA for approval in clinical trials in US for the above Epilepsy Syndromes.

Note: For any non-FDA approved drug, we cannot use Medicaid $ for purchase.

And then there are OPWDD regulations….

Cluster & Status Rescue Rx

Cluster vs Status

Status = Medical Emergency

Defined as "**a continuous seizure lasting more than 30 minutes** or **2 or more seizures without full recovery of consciousness between the seizures**.

Status can occur in different seizure presentations.

Cluster / Acute Repetitive Seizures = seizures of any type that occur in groups / clusters over hours or days. Often present a risk for Status if seizures last longer, they occur close together, the person does not recover well between the seizures or the rescue medications fail to stop the clusters.

Complications of Status / Clusters

Cognitive impact of the actual seizure activity

Brain insult / further damage after repeated seizures

Death during a Status episode

A higher intensity &/or frequency of seizure activity has been associated with SUDEP (Sudden Unexplained Death in Epilepsy)

Cluster & Status Rx

It is wise in both **Status & Cluster** seizure situations to have **Protocols** for Treatment indicating:

*When to treat

*What to treat with

* Monitoring post treatment

*Default Plan - 911 if treatment is not able to be administered for some reason &/or the individual does not respond to treatment.

Diastat (rectal valium / diazepam) is indicated for the Treatment of Cluster Seizures & for Status Epilepticus.

Diastat does require rectal administration(training), very quick absorbtion / action, also consider monitor respiration, BP & P.

Sublingual Ativan liquid is another treatment option.

VNS

What is it?

Pacemaker like device implanted under the left armpit or left chest wall with electrodes attached & leading to the left vagal nerve.

Electrodes are never removed if VNS fails, as they become scarred to the Vagal Nerve (MRI consideration)

Initially requires 2 surgical incisions:

Left side of neck in fold

Left armpit / chest wall area

Replacement of this device is needed when the battery becomes low / starts to fail. Aim for before battery dies.

- A single incision under armpit or chest wall & depends on cycle settings & use of Magnet.

All usually done as Same Day Surgery

VNS Continued

Non Medication Treatment for Epilepsy (also Depression).

The VNS is programmed by a Neurologist to "cycle" "off" & "on" & includes the use of a "Magnet"

The VNS sends electrical stimulation to the Vagal Nerve to interrupt / stop seizure activity.

Indication(s):
- initially only indicated for Partial Onset (Focal to Generalized)
- Intended to stop the "spread" of seizure activity
- Recently approved for use in 4yr olds with "refractory Focal Onset Seizures
- * Now indicated for many "Epilepsy Diseases" that are either not well controlled with AEDs &/or as adjunct therapy to decrease the side-effects & dose of the AEDs.

VNS "Cycle" Settings

The VNS is programmed to "cycle" "on" & "off"

Three components to the Programmed "Cycle" plus Magnet setting

1) Off time or rest period between pulses
2) Intensity of pulse or stimulation to Vagal Nerve
3) Length of the time of stimulation of the Vagal Nerve

Everyone's VNS is individually programmed within certain parameters to interrupt their seizure activity.

Some individuals are "rapid cyclers" meaning there is a very short rest period between the "on cycles".

VNS Magnet

Purpose of Magnet swipe is to interrupt or stop a seizure &/or Focal to Generalized seizure activity.

Magnet swipe turns the VNS "off" as it comes within 6 inches of VNS pacemaker in left chest area.

Swiping with the Magnet early on during a seizure always turns the VNS "off".
The VNS can also be programmed by the Neurologist to a different "on cycle" than than usual after a Magnet swipe.

The VNS is often programmed to respond to a Magnet swipe to first turn "off", then "on cycle" at an increased intensity &/or for a longer period of time than the usual cycle.

Use of the Magnet

Side effects of the VNS could include:
- voice hoarseness, cough, discomfort (swallowing).

* if the Magnet is taped to the chest wall (within 6 inches of VNS) it will keep the VNS turned "off" & therefore the individual has no side-effects.

The VNS Magnet can be worn on necklace or wrist band by an individual or a staff, so it always readily available to use at the start of a seizure.

Once into a full blown Generalized Seizure, the Magnet has little benefit & its use will wear out the VNS battery unnecessarily.

The Magnet will demagnetize credit cards or ID badges, so be careful about how it is stored & carried.

Brain Surgery Interventions

Indications:

Surgery can have a **curative** (stop seizures) / **palliative** (reduce seizure intensity & frequency) **goal**.

Work up is required & candidate must meet certain criteria for a potentially successful **cure or a reduction in their seizure severity & frequency plus minimal further Neurological damage**.

Usually requires multiple days of stay in the hospital & may have some long term Neurological effects.

Responsive Neurostimulation

Newer approach to treat **medically uncontrolled Focal (Partial) Onset seizures**.

- Surgeon places device under scalp & within the scull, so a serious surgery with hospitalization.
- Device detects & records specific patterns the lead to seizures.
- Intended to disrupt a seizure before it starts.
- Also programmed by the Neurologist.
- Requires 1-2 day hospital stay.

Monitors electrical events & automatically responds as needed / **PRN**.

*** Only indicated when there is a Focal Onset of seizures in no more than 2 areas of the brain.**

Surgical Removal of Focal Point(s)

Removal / excision of focal point(s)

Work up includes identifying whether the removal of the "focal point(s)' would likely cause significant further Neurological impairment.

The excision of Focal Point can be seizure curative for some individuals.

- Serious surgery
- Potential for brain swelling post op.
- Several days of hospitalization

Corpus Callostomy Surgery

- **Surgical split of the Brain** within the front 2/3 of the Corpus Callosum.
- Usually only indicated for palliation of Atonic seizures in Lennox-Gastault Syndrome. Not a cure.
- Serious surgery
- Potential for brain swelling post op
- Several days of hospitalization
- May or may not decrease the overall seizure frequency
- Both sides of brain no longer integrate / communicate with each other very well, so this surgery **often impacts overall function**.

Non-compliance Intervention: Consider changing the approach to tasks toward the other side of the body if there is poor response, since the seizure activity will often vary from side to side & will often impact only the one side of brain.

Questions?

"This is your time & it feels normal to you, but really, there is no normal.
There is only change & resistance to it & more change"

Meryl Streep @ Barnard commencement speech 2010

Feel free to contact me:

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