

Diagnosis and Management of CNS Disorders

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Case 1-Movement Disorders

- A 65 year old man presents with a tremor

Clinical Recognition of Movement Disorder

- Identification of individual signs & symptoms
(*e.g. tremor, chorea, myoclonus, bradykinesia, ...*)
- Syndrome recognition (*e.g. parkinsonism, ...*)
- Disease recognition (*e.g. Idiopathic Parkinson's Disease, Essential Tremor, ...*)

Movement Disorders-Categories

- Hyperkinetic
 - Chorea
 - Ballism
 - Tremor
 - Myoclonus
 - Tics
 - Dystonia
 - Other (stereotypies, akathisia, RLS, moving toes/fingers)
- Hypokinetic
 - Bradykinesia

Tremor

- Repetitive, rhythmic movement that is consistent in time and space

Classification of Tremor

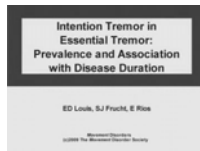
- Rest tremor
- Action tremor
 - Postural tremor
 - Kinetic tremor
 - Task- or position-specific tremor

Causes of Tremor

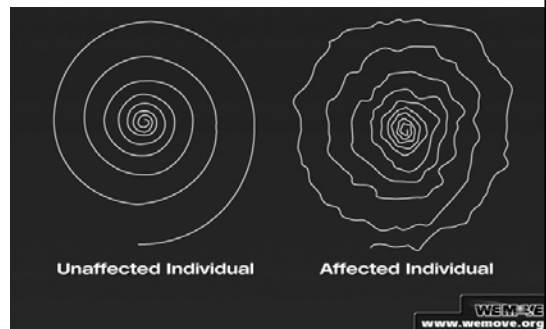
- Essential Tremor
- Parkinsonism
- Medication Induced
- Physiologic Tremor
- Psychogenic Tremor
- Trauma, Stroke, MS,...

Case 1-Movement Disorders

- A 65 year old man presents with a tremor
- Tremor involves both hands
- Present primarily with activity
- Father had similar tremor
- No associated symptoms
- Neurological examination notable for moderate frequency bilateral postural/intention tremor



Archimedes Spiral



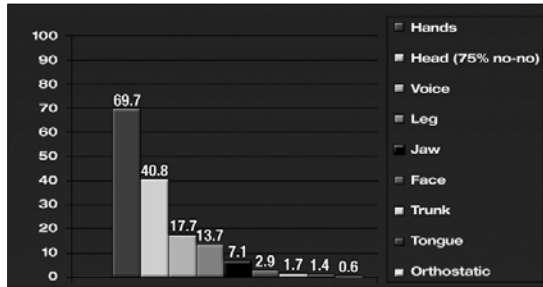
Classification of Tremor Based on Relative Frequency (Hz)

<u>Frequency in Hz</u>	<u>Typical Etiology</u>
2.4 - 4.0	Cerebellar
4.0 - 4.5	PD (rest), neuroleptic-induced
5.5 - 7.0	ET, drug (VPA)
7.0 - 12.0	Physiological, exaggerated physiologic, drug-induced (e.g., epinephrine)

Core Criteria for Identifying ET

1. Bilateral action (postural and intention) tremor of the hands and forearms
2. Absence of other neurologic signs, with the exception of the cogwheel phenomenon
3. May have isolated head tremor with no abnormal posture

ET Anatomic Distribution (n=350)



www.wemove.org

Secondary Criteria for Identifying ET

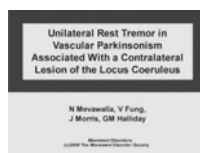
1. Long duration (>3 years)
2. Family history
3. Beneficial response to ethanol

Treatment of ET

- No treatment
- Weighted Utensils
- Propranolol (prn or scheduled)
- Topiramate
- Primidone
- Gabapentin
- Surgery (Thalamotomy, DBS)

Case 2-Movement Disorders

- A 68 year old man presents with a tremor
- Tremor involves primarily right hand
- Present primarily with at rest
- No family history of neurologic disease
- Patient also notes impaired gait and balance



Parkinsonism

- Resting Tremor
- Bradykinesia
- Rigidity
- *Masked face, hypophonic speech, swallowing difficulty, micrographia, flexed posture, shuffling gait, gait ignition failure and freezing*

Classification of Parkinson Syndromes in a Community

- Idiopathic PD 85%
- Neuroleptic-induced parkinsonism 8%
- Vascular parkinsonian syndrome 3%
- Multisystem atrophy 2.5%
- PSP 1.5%

Treatment of PD

- No treatment
- Amantadine
- MAO-B inhibitors (e.g. selegiline, rasagiline)
- Dopaminergic agents
 - Levodopa
 - Dopamine agonists
- COMT inhibitors (e.g. tolcapone, entacapone)

Case 3-Spells

- 72 yowm presents with a 2 month history of spells
- Pt is unaware of spells
- Wife notes brief episodes when pt seems to be daydreaming and is slow to respond
- No associated si's or sx's
- Returns to baseline quickly

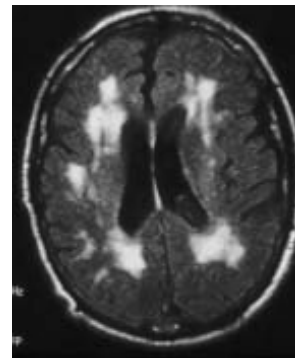
DDx of Spells in the Elderly

- Seizure
- Syncope
- TIA
- Transient Global Amnesia
- REM Behavior Disorder
- Periodic Limb Movements of Sleep
- Vertigo
- Movement Disorders
- Migraine
- Pseudoseizure

Case 3 (continued)

- Normal neurological examination
- Labs (CMP, Mg, Ca, CBC) are normal
- Holter is normal
- Carotid Dopplers show no significant stenosis
- MRI shows scattered white matter changes

MRI: White Matter Changes



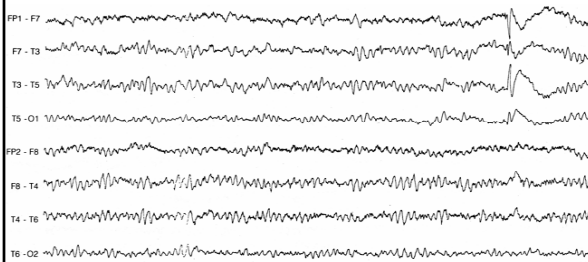
Neuroimaging

- MRI is the modality of choice in the non-emergent evaluation of seizure
 - Gadolinium contrast should be considered in the elderly to add sensitivity to tumor detection
- Abnormalities should be interpreted with caution
 - Non-specific changes (e.g. atrophy, periventricular white matter hyperintensities, prominent Virchow-Robin spaces) are common
 - 60% of elderly with non-epileptic spells have MRI abnormalities (with >1/3 being focal)

EEG

- Obtain shortly after the initial event
- A single EEG may be normal in many individuals with epilepsy
- Serial EEG's improve sensitivity
- Sleep deprivation may improve sensitivity
- Video-EEG is the gold standard for seizure diagnosis

Interictal Epileptiform Discharge



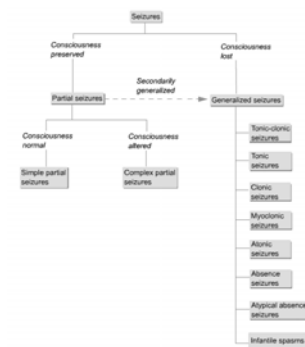


Definitions

- A **seizure** is a temporary disturbance of brain function caused by abnormal electrical activity in the brain
- **Clinically**, seizures tend to be **brief** (1-2 minutes), **stereotyped** when recurrent, with a wide array of potential manifestations
- **Epilepsy** is a chronic condition marked by recurrent seizures

Classification of Seizures

- Divided into partial vs generalized based on degree of brain involvement
- Partial seizures are further subdivided based on alteration in consciousness
(e.g. *simple and complex partial seizures*)
- Partial seizures may become secondarily generalized
- Seizures can also be further subdivided by symptomology (e.g. *GTCS, atonic,...*)



Flowchart of ILAE seizure classification

Importance of seizures in the elderly

- One of the most common neurological diseases in the elderly
- Morbidity and mortality associated with seizures are higher in the elderly
- Incidence of status epilepticus (SE), and resultant mortality, is higher in the elderly

Age-Related Incidence of Epilepsy



S. LaRoche, 2007

Treatment of Seizures

- Acute treatment may not be necessary (*unless pt is in status epilepticus*)
 - Only approximately 30% of patients with a normal neurological examination, normal EEG and normal MRI will go on to have recurrent seizures
- If long-term treatment is necessary:
 - Select a single agent and titrate gradually to maximum tolerated dose before switching medications
 - Strive for monotherapy
 - Seizure type, or epilepsy syndrome, might help direct medication choice

Recommended AED's for New Onset Epilepsy

- Older AED's
 - Phenytoin (Dilantin)
 - Valproate (Depakote)
 - Carbamazepine (Tegretol)
- Newer AED's
 - Gabapentin (Neurontin)
 - Lamotrigine (Lamictal)
 - Oxcarbazepine (Trileptal)
 - Topiramate (Topamax)
 - Levetiracetam (Keppra)

Recommended AED's for Adjunctive Therapy in Refractory Partial Epilepsy

- Older AED's
 - Phenytoin (Dilantin)
 - Valproate (Depakote)
 - Carbamazepine (Tegretol)
- Newer AED's
 - Gabapentin (Neurontin)
 - Lamotrigine (Lamictal)
 - Oxcarbazepine (Trileptal)
 - Topiramate (Topamax)*
 - Levetiracetam (Keppra)
 - Tiagabine (Gabatril)
 - Zonisamide (Zonegran)

*Topiramate can also be recommended for refractory generalized epilepsy

Case 4-Sleep

- 29 year old man with an 8 year h/o excessive daytime somnolence
- Multiple brief, unexplained awakenings during night-time sleep period
- Sleep is non-refreshing
- No other significant PMH
- No medications

Hypersomnia in the U.S.

- 75% of adults report frequent sleep related problems (with EDS among the most common)
- 60% of adults admit to driving while drowsy
- 4% have had a MVA or near accident related to drowsiness

National Sleep Foundation

Importance of Hypersomnia

- >100,000 MVA's annually in US are caused by driving while drowsy
- Major disasters including Three Mile Island, Exxon Valdez, Bhopal and Challenger were all officially attributed to sleepiness-related impaired judgment in the workplace

Report of the National Commission on Sleep Disorders Research, 1992

DDx of Hypersomnia

- Volitional sleep deprivation (we get 20% less sleep than previous generations)
- Sleep Disordered Breathing (e.g. OSA)
- Narcolepsy
- Idiopathic CNS hypersomnia
- PLMS
- Circadian Rhythm Disorders
- Other (Medications, etc.)

Evaluation of Hypersomnia

- History
- Sleep Diary
- Actigraphy
- Overnight Polysomnography (PSG)
- MSLT and/or MWT

Elements of the History

- Presence/degree of sleepiness (ESS)
- Sleep patterns (onset, continuity, ...)
- Amount of sleep per 24 hours
- Naps (refreshing or not?)
- Snoring, witnessed apneas
- Environment during sleep
- Associated sx's (sleep paralysis, ...)

Epworth Sleepiness Scale (ESS)

EPWORTH SLEEPINESS SCALE

How likely are you to doze off or fall asleep in the following situations? Even if you have not done some of these things recently try to estimate the effect it might have on your level of drowsiness. Use the following scale to choose the most appropriate number for each situation.

- 0 = would NEVER dozing
- 1 = SLIGHT chance of dozing
- 2 = MODERATE chance of dozing
- 3 = HIGH chance of dozing

Situation	Chance of Dozing			
	0	1	2	3
Sitting and reading	0	1	2	3
Watching T.V.	0	1	2	3
Sitting, inactive in a public place (in a meeting or watching a movie)	0	1	2	3
As a passenger in a car for an hour without a break	0	1	2	3
Lying down to rest in the afternoon when circumstances permit	0	1	2	3
Sitting and talking to someone	0	1	2	3
Sitting quietly after lunch without alcohol	0	1	2	3
In a car, while stopped for a few minutes in the traffic	0	1	2	3

Total: _____

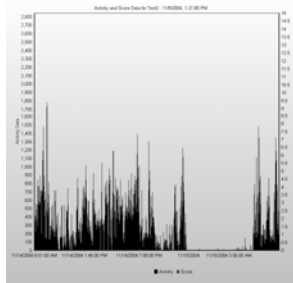
Sleep Diary

National Sleep Foundation Sleep Diary											
COMPLETE RESPONSES						COMPLETE ANSWERS					
WSP last sleep is a full night sleep? (1 or 2)	WSP last sleep is a full night sleep? (1 or 2)	WSP last sleep is a full night sleep? (1 or 2)	WSP last sleep is a full night sleep? (1 or 2)	WSP last sleep is a full night sleep? (1 or 2)	WSP last sleep is a full night sleep? (1 or 2)	WSP last sleep is a full night sleep? (1 or 2)	WSP last sleep is a full night sleep? (1 or 2)	WSP last sleep is a full night sleep? (1 or 2)	WSP last sleep is a full night sleep? (1 or 2)	WSP last sleep is a full night sleep? (1 or 2)	WSP last sleep is a full night sleep? (1 or 2)
DAY 1	WSP	WSP	WSP	WSP	WSP	WSP	WSP	WSP	WSP	WSP	WSP
DAY 2	WSP	WSP	WSP	WSP	WSP	WSP	WSP	WSP	WSP	WSP	WSP
DAY 3	WSP	WSP	WSP	WSP	WSP	WSP	WSP	WSP	WSP	WSP	WSP
DAY 4	WSP	WSP	WSP	WSP	WSP	WSP	WSP	WSP	WSP	WSP	WSP

Actigraphy



Actigraphy



Case 4-continued

- 8-9 hours of uninterrupted sleep per night (approx. 10pm-6:30am)
- Mild-moderate snoring, but no witnessed apneas
- Occasional leg jerks during sleep
- 1-2 episodes of possible sleep paralysis in the past
- No problems noted in the environment
- ESS=21

Case 4-continued

- PSG
 - Sleep Efficiency = 91%
 - Onset to sleep = 8 minutes
 - Onset to REM sleep = 45 minutes
 - AHI = 4.5
 - PLM-arousal index = 6.6
 - Mild snoring noted

Case 4-continued

- MSLT
 - Mean Sleep Latency = 1.5 minutes
 - 4/4 SOREM's
- Toxicology Screen-negative

Classification of Narcolepsy (ICSD Criteria)

- Classified by presence or absence of cataplexy
- EDS almost daily for at least 3 months
- MSLT testing (following sufficient nocturnal sleep)
 - Mean sleep latency \leq 8 minutes
 - \geq 2 SOREMP's
 - MSLT recommended in all cases, and required in the absence of definite cataplexy
- Hypersomnia not better explained by another sleep d/o, medical d/o, etc.

Clinical Manifestations of Narcolepsy

- Onset most often in teens/early 20's
- Chronic sleepiness
- Hypnagogic hallucinations
- Sleep Paralysis
- Cataplexy
- Automatic Behavior

Cataplexy

- Sudden muscle weakness brought on by strong emotions
- May be partial (e.g. affecting only the face)
- Usually brief (seconds to two minutes)
- Occurs almost exclusively in narcolepsy
- 60% of narcoleptics develop cataplexy (usually within 3-5 years of sx onset)

Cataplexy



Cataplexy



Narcolepsy-Treatment

- Treat other associated sleep d/o's
- Scheduled naps
- Medications
 - EDS (stimulants, modafinil)
 - Cataplexy (SSRI's, TCA's, γ -hydroxybutyrate)
 - Disrupted nighttime sleep (zolpidem, γ -hydroxybutyrate)

Treatment of EDS

- Modafinil
 - 100-400 mg per day (daily or bid dosing)
 - HA, nausea, insomnia
- Methylphenidate
 - Up to 60 mg per day (bid or tid)
 - Anxiety, insomnia
- Dextroamphetamine
 - Up to 60 mg per day (bid or tid)
 - Insomnia, psychosis
- Pemoline
 - Up to 112.5 mg per day (daily or bid)
 - Hepatic toxicity

Treatment of Cataplexy

- TCA's
 - Protriptyline (5-30 mg per day)
 - Imipramine (50-250 mg per day)
 - Nortriptyline (50-200 mg per day)
- SSRI's
 - Fluoxetine (20-60 mg per day)
 - Citalopram (20-40 mg per day)
- Gamma-hydroxybutyrate (Xyrem)
 - 4.5-9.0 grams/night in two doses separated by 2.5-4 hours
 - May also help with EDS

Case 5-Sleep

- 60 year old man dreamed he was working on a loading dock and saw a man running; someone yelled “stop him” and the patient jumped after the man.
- The patient’s wife reports he jumped off the end of the bed and awoke on the floor with a “bloody lip, head, and knee.”
- Initial evaluation revealed facial abrasions and a subdural hematoma.

Parasomnia

- Parasomnias are undesirable movements and behaviors occurring during sleep
- Parasomnias are disorders of arousal, partial arousal, and sleep stage transition

Parasomnias-Evaluation

- History
 - Description of Events
 - Including report of bedpartner
 - Can patient recall events?
 - Timing
- Past Medical History/Medication History
- Physical Exam
 - Obesity
 - Parkinsonism
 - Dementia

Parasomnias-Evaluation (cont.)

- Sleep Diary
- EEG
- PSG
 - Expanded EEG montage
 - Expanded EMG monitoring
 - Video monitoring

Differential Diagnosis

- Sleepwalking
- Sleep Terrors
- REM-Sleep Behavior Disorder
- Nocturnal Seizures
- Hypnogenic Paroxysmal Dystonia
- Obstructive Sleep Apnea
- Rhythmic Movement Disorders
- Nocturnal Psychogenic Dissociative Disorders
- Malingering

Case 5-Sleep

- *60 year old man dreamed he was working on a loading dock and saw a man running; someone yelled “stop him” and the patient jumped after the man.*
- *The patient’s wife reports he jumped off the end of the bed and awoke on the floor with a “bloody lip, head, and knee.”*
- *Initial evaluation revealed facial abrasions and a subdural hematoma.*
- **PSG demonstrated elevated EMG activity during REM sleep**

REM Behavior Disorder (ICSD-2)

- REM sleep without atonia
- At least one of the following
 - Sleep related injurious or disruptive behavior
 - Abnormal REM sleep behavior during PSG
 - Awakening short of breath
- Absence of associated epileptiform activity
- Not better explained by another disorder

REM Sleep Behavior Disorder

- A multifaceted parasomnia involving REM sleep and the motor system in which there is problematic behavioral release that is usually experienced by the individual as enactment of distinctly altered, unpleasant, and combative dreams

(Schenck and Mahowald)

RBD-Potential Causes

- Withdrawal
 - Alcohol
 - Meprobamate
 - Pentazocine
 - Nitrazepam
- Medications
 - Venlafaxine
 - SSRI's
 - Mirtazepine

RBD-Epidemiology

- Male predominance (87%)
- Mean age of onset 52-62 years
- Sleep related injuries common (up to 96%)
- Altered dream process and content (more vivid, intense, action-filled and violent)
- Preserved sleep architecture (REM/NREM cycling)
- Often associated with parkinsonism (current or future)

REM Sleep (Paradoxical Sleep)

- Defining features
 - REM atonia
 - Rapid Eye Movements (REM's)
 - Activated EEG
 - High level of brain activity
- "Paradoxical Sleep"
 - Paradoxical suppression of skeletal muscle tone despite a highly activated brain state

RBD-Paradox Lost

- Loss of the paradoxical atonia in REM sleep
- Dreams are subsequently acted out in reality

RBD-treatment

- Initial trials of REM suppressing TCA's were unsuccessful
- Clonazepam was tried next based on its beneficial effect on nocturnal myoclonus, another parasomnia
 - Clonazepam was found to be immediately effective in approximately 90% of cases

RBD-treatment

- Clonazepam
 - Suppresses excessive phasic motor activity
- Melatonin
 - Restores REM-atonnia
- Sinemet
- Anecdotal reports of response to
 - L-tryptophan
 - Clonidine
 - Carbamazepine
 - Gabapentin
 - MAOI's

Case 6-Head Injury

- 16 yowm brought to office after having "bell rung" at football practice
- Needs doctor's permission to return to practice

- Helmet to helmet contact
- No loss of consciousness, but was dazed for a few minutes
- Headache for a few hours

Concussion in Sports

- Concussion is a trauma-induced alteration in mental status that may or may not involve loss of consciousness
- Confusion and amnesia are hallmarks

Concussion in Sports

- Grade 1
 - Transient confusion
 - No LOC
 - Si's and Sx's resolve in less than 15 minutes
- Grade 2
 - Transient confusion
 - No LOC
 - Si's or Sx's last longer than 15 minutes
- Grade 3
 - Any LOC

Concussion in Sports-Evaluation

- Orientation
- Concentration
 - Digits backwards
 - Months of year in reverse order
- Memory
 - 3 words
 - Details of game,...
- Provocative tests (40 yard sprint, push-ups, sit-ups,...)
- Neurologic exam (pupils, coordination, sensation)

Concussion in Sports- Recommendations for Return to Play

- Grade 1
 - May return if si's and sx's clear in 15 minutes
 - A second concussion eliminates player from competition for at least one week
- Grade 2
 - May return if asymptomatic at rest and with exertion for one week, with a normal neurologic exam
 - CT or MRI recommended if sx's persist
 - Return deferred for at least 2 weeks after a second Grade 2 concussion

Concussion in Sports- Recommendations for Return to Play

- Grade 3
 - Consider transport to ER (especially for prolonged LOC)
 - Assess neurologic status daily
 - After a brief (seconds) LOC, may return after asymptomatic at rest and with exertion for 1 week
 - After a prolonged (minutes) LOC, may return after asymptomatic at rest and with exertion for 2 weeks
 - Return is deferred for at least one asymptomatic month after a second Grade 3 concussion

