Tremor diagnosis and Treatment

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Assessing a Tremor

- Can sometimes be a combination of disorders
- Other disorders can sometimes look similar to tremors
  - Chorea
    - Generally less rhythmic and more fluid
  - Tics
    - Can be repetitive, but usually brief and stereotyped
  - Myoclonus
    - Generally does not oscillate

Outline

- Tremor Assessment
- Types of Tremor
  - Physiologic,
  - **Essential,**
  - **Parkinson's,**
  - **Medication induced,**
  - Psychogenic,
  - Dystonic,
  - Cerebellar,
  - Metabolic
- Cases

Chorea

- http://www.youtube.com/watch?v=a9WB_PXjTBo

Assessing a Tremor

Tics

- http://www.youtube.com/watch?v=6DQk7L-V-XM&feature=related

Myoclonus

- http://www.youtube.com/watch?v=7z2FXVtxgaI

Assessing a Tremor

- Step 4 – Ask about tremor onset & progression
  - Present for many years but worse recently
  - Sudden onset
  - Came on over a few months

Assessing a Tremor

- It is a RHYTHMIC oscillation of a body part

Assessing a Tremor

- Step 5 – Aggravating and Alleviating factors
  - Alcohol
  - Medications
  - Stress
- Step 6 – Associated features
  - Slowness
  - Rigidity
  - Ataxia
  - Neuropathy

Assessing a Tremor

- Step 1 - Determine the location of the tremor
- Step 2 - Determine when the tremor is most active
  - Rest
  - Action
  - Certain actions
  - Certain positions
- Step 3 – Determine the rate of the tremor

Assessing a Tremor

- Step 7 – Ask about family history
  - Other people with tremors
  - Ataxia
  - Metabolic problems

Observational Description

- Where(upper/lower limbs, head, chin, voice…)
- When (rest, action, posture)
- Unilateral/bilateral/symmetric
- Frequency (very fast, medium, slow, variable)
- Amplitude (large, medium, small)

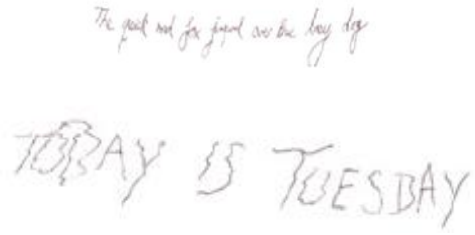
Cup Pour

- No tremor
- Tremor with holding cup, but pours well
- Spills some when pouring
- Spills before even attempting to pour

Further Examination

- Cognitive task to bring out tremor
- Draw Spirals
- Pour/drink from a cup
- Handwriting sample

Handwriting



Spiral

Common Tremor Disorders

- Physiological Tremor
- **Essential Tremor**
- **Parkinson's Disease**
- **Drug-induced Tremor**
- Psychogenic Tremor
- Dystonic Tremor
- Cerebellar Tremor
- Metabolic Tremor

Physiologic Tremor

- Prevalence – 100%
- All of us will have some tremor at some point in our lives
- This is often subtle and fast
- Usually present in the upper limbs
- Often brought out by caffeine and stress (i.e. giving lectures)

Essential Tremor

- When
  - Worst with action, but may be present at rest or with posture
- Rate
  - Fairly rapid (8-10Hz)
- Onset/Progression
  - Average age of onset is about 45yo
  - ET is more common and generally worsens with age
  - Generally present for **many, many** years before seeking medical attention

Physiologic Tremor

- Often times no treatment is necessary
- If very prominent called – enhanced physiologic tremor
- Might need to consider if a medication is exacerbating physiologic tremor
- Might focus on underlying anxiety that is exacerbating tremor

Essential Tremor

- Aggravating/Alleviating factors
  - Generally greatly diminished with small amounts of alcohol
  - Caffeine (especially on an empty stomach) can exacerbate
  - Medications that cause tremor can exacerbate an essential tremor

Essential Tremor

- Prevalence
  - 0.9% in all comers
  - 4.6% in persons over 65yo
- Location
  - **Upper limbs >94-95%**
  - Head 33-34%
  - Lower limbs 12-30%
  - Voice 12-16%
  - Tongue 7%
  - Face, trunk <5%

Essential Tremor

- Associated features
  - Should not really be any, may be some ataxia in longer standing, severe cases
- Family history
  - Can show an autosomal dominance inheritance, but there is reduced penetrance
  - Also can occur sporadically

Essential Tremor - Treatment

- Non-Pharmacological
  - Decrease ETOH intake
  - Decrease caffeine intake
  - Assistive devices
    - Weighted, shaped utensils
    - Weighted covered cups/ straws
    - Special pens
    - Signature stamps
    - Adjustment of computers (accessories/accessibility/accessibility wizard)



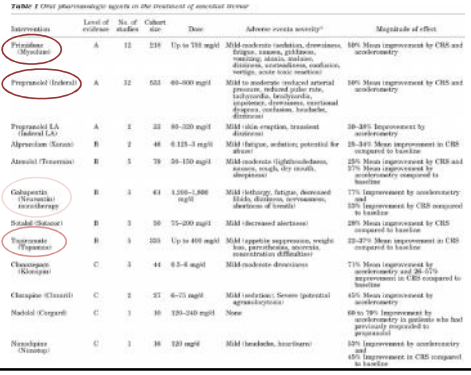

Essential Tremor-Treatment

Primidone (Mysoline) - antiepileptic

- 62.5- (500mg) 1,000mg
- Common side effects: sedation, drowsiness, fatigue, nausea, vomiting, ataxia, malaise, dizziness, confusion, vertigo
- Again about 50% reduction in amplitude

**Can use primidone and propranolol in combination

Essential Tremor - Treatment



Essential Tremor - Treatment

- There is also some data on botox for ET
- Less often used than other therapies

Essential Tremor-Treatment

Propranolol – beta-blocker

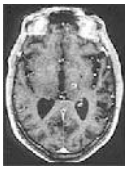
- 30-320 mg per day, can use long acting preparations
- One study found an average of approximately a 50% reduction in amplitude
- Most common side effects: lightheadedness, fatigue, impotence, bradycardia
- Caution in patients with heart failure, diabetes, pulmonary disorders
- Metoprolol has moderate CNS penetrance, atenolol very little

Essential Tremor - Surgical Therapy

- Thalamotomy or
- Deep Brain Stimulation

Thalamotomy

- Involves creating a lesion in the ventral intermediate nucleus (VIM) of thalamus
- Open label trials (n=181) showed:
  - 80-90% reduction in limb tremor(with most complete or almost complete reduction in tremor)
  - In general affects are much more dramatic then medications
  - Bilateral lesioning generally not done b/c of side effects
  - Advantage over DBS that no hardware, no programming

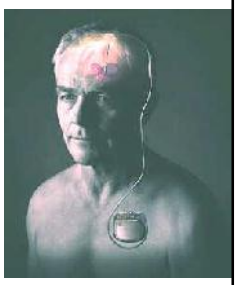


Parkinsonian(PD) Tremor

- Most often starts UNILATERALLY in an upper limb
- Unilateral leg tremor is less common, but almost always PD
- Head and neck tremor is uncommon, but chin tremor can be seen

Deep Brain Stimulation

- Involves implantation in the ventral intermediate nucleus (VIM) of thalamus
- 60-90% improvement in tremor on average
- Fewer side effects then thalamotomy
- May have benefit for bilateral implantation for voice and head tremor



Parkinsonian(PD) Tremor

- Tremor is most prominent at REST
- Tends to be about 3-4 Hz, so much slower than ET
- Often has a “pill rolling” quality
- PD most often presents in older age (1% of persons over age 65)

**1/3 to 1/4 of PD will not present with tremor

Video in OR DBS for ET

- http://www.youtube.com/watch?v=wk3wz4gQZ3Q

Parkinsonian(PD) Tremor

- Generally only present for a few months when seeking medical care, but can be longer at times.
- Often starts unilateral in a single limb then spreads into other unilateral limb and contralateral limb
- Stress makes worse (as will all tremors)

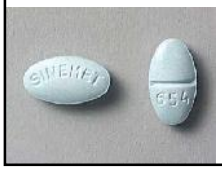
*** Just because someone has PD doesn’t mean they can’t have ET too

Parkinsonian(PD) Tremor

- Associated features are really the key with PD
- Four cardinal features of PD
  1. Bradykinesias (slowness)
  2. Rigidity (stiffness)
  3. Rest Tremor
  4. Postural instability (later feature)
- Sometimes these can be difficult to distinguish
  (i.e. made hand tremor can make finger tapping look slow)
- Sometimes these are very subtle

Carbidopa / Levodopa (Sinemet)

- Levodopa
  - Treats symptoms the best
  - Combination with dopa-decarboxylase inhibitor (carbidopa)
  - Starting dosage is 25/100 three times a day



25/100 – YELLOW
10/100 – DARK BLUE
25/250 – LIGHT BLUE

Parkinsonian(PD) Tremor

- Family history is not very common
- For young onset (<40yo) this is a little more common

Carbidopa / Levodopa

- Levodopa
  - Most patients end up on levodopa
  - Ideally give about 30 minutes before meals
  - Side Effects:
    - Fatigue
    - Confusion
    - Hallucinations
    - Leg edema
    - Dyskinesia

Sámi A, Nutt J, et al. *Lancet*. 363. 178-93. 2004

PD Treatment

- If suspected probably best to refer to a neurologist or other specialist before starting treatment
- Medication options
  - Sinement (carbidopa/levodopa)
  - Dopamine Agonists (ropinirole, pramipexole)
  - MAO inhibitors (selegiline, rasagiline)
  - Amantidine
  - Anticholinergic (trihexyphenidyl/Artane)

Carbidopa / Levodopa

- Controlled Release
  - Irregular absorption
  - Unpredictable effects
  - Recommended mostly in evening to improve rigidity interfering with normal sleep
  - Can improve early AM symptoms

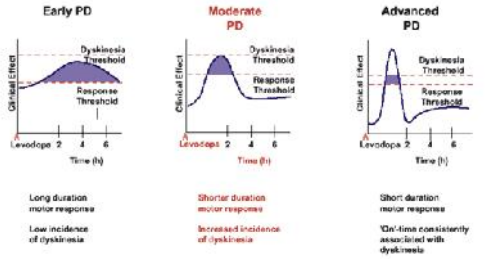
Carbidopa/Levodopa

- Motor fluctuations
  - Effects wear off
  - Slowness and tremor worsens
  - Unpredictable ON/OFF
  - 25-50% develop within 5 yrs
  - 90% of young onset pts within 5 yrs

Dopamine Agonists

- Often first medication used in younger patients (< 60)
- Rarely used in persons over 70 yo because of concern for worsening confusion


Changes in Levodopa Response Associated With Progression of PD



Dopamine Agonists

- Used in younger people because
  - Delay onset of dyskinesias
- Used less often in older people because
  - Cause more confusion and give less benefit than levodopa


Dopamine Agonists

- 2 available:
  - Ropinirole (Requip)
  - Pramipexole (Mirapex)
  - Doses are not equivalent
- Usually given three times a day
- There are also once a day (XL) formulations


Dopamine Agonists

- Side effects include:
  - Fatigue
  - Nausea
  - Confusion
  - Postural hypotension
  - Leg edema
  - Hallucinations
  - Obsessive behaviors
    - Gambling, cleaning, Increased sex drive, eating

Mao-Inhibitors

- Rasagaline (Azilect) &
- Selegiline (Eldepryl)
- These may slow progression of disease
- They have only modest symptomatic benefit
- Dietary restrictions are often over exaggerated

Medications to **Avoid** in PD

- Neuroleptics: Haldol, Thorazine, Abilify…
- Anti- nausea: Promethazine, prochlorperazine, metoclopramide

Sámi A, Nutt J, et al. *Lancet*. 363. 1783-93. 2004

Anticholinergics

- Trihexyphenidyl (Artane)
  - Best treatment for tremor
  - Significant confusion and urinary retention
    - Do not give to those with cognitive complaints or > 65 yrs old

Watts R, Koller W. Movement Disorders. 2004

Surgical Treatments

- Lesional surgeries
  - Thalamotomy (could be appropriate for tremor)
  - Pallidotomy
- **Deep brain stimulation**
  - Gpi
  - STN
  - VIM

Amantidine

- Only medication that decreases dyskinesias
- But also does improve other symptoms
- Side effects
  - Urinary hesitancy
  - Leg edema
  - Livedo
  - Insomnia
  - Confusion

Crosby N. *Cochrane Review*. 2002

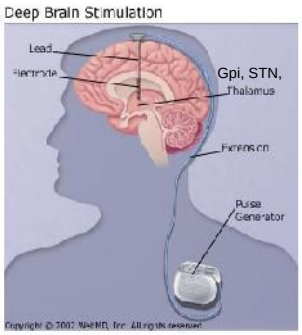
Deep Brain Stimulation

Inclusion criteria
1. Clinically definite Parkinson's disease
2. Hoehn and Yahr stage 2–4 (moderate to severe bilateral disease, but still ambulatory when on)
3. L-dopa responsive with clearly defined off and on periods
4. Persistent disabling motor fluctuations despite best drug treatment with some combination of
   - At least 3 h of off period daily
   - Unpredictable off periods
   - Disabling dyskinesia
5. Intact cognition as measured by neuropsychological testing and no active psychiatric disturbances
6. Strong social support system and commitment from patient and family members to keep follow-up appointments

Exclusion criteria
1. Parkinson-plus syndromes
2. Atypical parkinsonism—eg, vascular parkinsonism
3. Drug-induced parkinsonism
4. Medical contraindications to surgery or stimulation (serious comorbid medical disorders, chronic anticoagulation with warfarin, cardiac pacemakers, etc)
5. Dementia or psychiatric issues (untreated depression, psychosis, etc)
6. Intracranial abnormalities that would contraindicate surgery—eg, stroke, tumour, vascular abnormality affecting the target area
7. Severe brain atrophy on imaging (makes target localisation difficult)
8. Serious doubt about patient's commitment to return for follow-up visits (several no-shows in the past, poor compliance record, etc)

Sámi A, Nutt J, et al. *Lancet*. 363. 1783-93. 2004

DBS



Medication Induced Tremor

Action/Postural /Intention Tremor

Class	Drugs
Antiarrhythmics	Amiodarone, mexiletine, procainamide
Antiviral	Vidarabine
Antidepressants	Amitriptyline, SSRI's
Mood Stabilizers	**Lithium, valproic acid**
Antiepileptics	**Valproic acid**
Bronchobilators (β agonists)	**Albuterol, salmeterol**
Chemotherapeutics	Tamoxifen, cytarabine, ifosfamide
Drugs of abuse	Cocaine, ethanol, ecstacy, nicotine
Hormones	Thyroxine, calcitonin, medroxyprogesterone, epinephrine
Immunosuppressants	Tacrolimus, ciclosporin, interferon-alfa
Methlxanthines	Theoplylline, caffeine
Neuroleptics and dopamine depleters	Haloperidol, risperidone, reserpine, tetrabenazine, metoclopramide, cimetidine

PD Tremor

- http://www.youtube.com/watch?v=D4FD_rccz8E

Medication Induced Tremor

Rest Tremor

Class	Drugs
Antibiotics, antimycotics	Co-trimoxazole, amphotericine B
Antidepressants	SSRI's
Mood Stabilizers	Lithium, valproic acid
Antiepileptics	Valproic acid
Chemotherapeutics	Thalidomine
Drugs of abuse	Cocaine, ethanol, ecstacy, MPTP
Hormones	medroxyprogesterone
Neuroleptics	**Haloperidol, thioridazine, risperidol**
Dopamine depletors	**reserpine, tetrabenazine**
Gastrointestinal drugs	**Metoclopramide, proclorperazine**
Other	**hydroxyzine**

Drug Induced Tremor

- Most often involved upper limbs
- Most often postural, but can be more of a parkinsonian tremor depending on medication
- Often times it is fine and very fast
- Onset tends to coincide with exacerbating medication being started or increased
- Depending on drug there may be associated features

Medication Induced Tremor - ?'s to ask

- Was the tremor pre-existing?
  - Enhanced physiologic tremor is the most common drug induced tremor (often unnoticed prior)
- Have other medical causes of tremor been ruled out?
- Is there a temporal relationship to the start or increase of the drug?
- Is the tremor worsening over time?
  - Generally drug induced tremors are not progressive

Medication Induced Tremor - Treatment

- Is the tremor bothersome?
- Can the medication be switched to an alternative or be decreased?
- Can another drug mask the symptoms?
- Can other adaptive equipment be used?

Psychogenic Tremor – Treatment

- Key is to try to treat the underlying psychological disorder
- Try to not expose patient to unnecessary medications or procedures

Psychogenic Tremor

- Can be any location
- Can be most active in variable situations
- Rate can be variable
- Often comes on suddenly, sometimes goes away suddenly
- Often exacerbated by stress, psychological issues
- Associated features will vary based on case

Dystonic Tremor

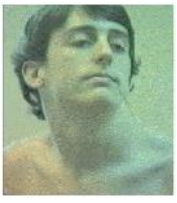
- Most often seen in the neck, but not uncommon in an upper limb
- Generally most prominent with posture but this is variable
- Rate is variable and tremor if often irregular
- Onset is usually fairly subacute
- There is often a null point, a position where the tremor will go away

Psychogenic Tremor – Special Testing

- See if tremor is distractible, i.e. ask to spell WORLD backwards
  - In PD generally tremor will get worse, psychogenic generally better
- Load the tremor by pushing down on it with your hand
  - Psychogenic often gets worse, organic often get better
- See is tremor frequently entrains to other activity such as finger tapping

Dystonic Tremor

- The key is really the associated dystonia
- Dystonia is an abnormal muscular contraction resulting in an abnormal posture or abnormal muscle movements
- Often have a sensory trick



Dystonic Tremor - Treatment

- Botulinum toxin is the treatment of choice for most people
- Some medications but not generally very helpful
  - Trihexyphenidyl
  - Tetrabenezine
- For generalized dystonias DBS can be extremely successful

Metabolic Tremor

- Hypothyroidism can produce a very high frequency, fine amplitude, postural tremor in the upper limbs
- Often will have proptosis, sweating, weight loss…
- Always good to rule out
- Also consider renal failure, hypoglycemia, liver disease

Dystonic Tremor - Treatment

- https://www.youtube.com/watch?v=zW7aleG29kE

Cases 1

- 65 yo RH man with about 6-8 months of worsening right handed tremor. Notices it most when he is resting watching suspenseful TV in the evening. He has also noticed that he has trouble keeping up with his wife on their morning walks and she keep telling him to speak up. He does not feel like the tremor effects his ability to eat or write, but has trouble getting his wallet out of his back pocket and notices his writing is smaller.

Cerebellar Tremor

- Tremor gets worst with end point of a goal directed movement
- Usually low frequency, high amplitude, and irregular
- Depending on etiology could come on suddenly (stroke), over days (multiple sclerosis) or very gradually (spinocerebellar ataxia)
- Generally other cerebellar finding present – ataxia, nystagmus, dysarthria

Cases 1

- 65 yo RH man with about 6-8 months of worsening **right handed tremor**. Notices it most when he is **resting** watching suspenseful TV in the evening. He has also noticed that he has **trouble keeping up** with his wife on their morning walks and she keep telling him to **speak up**. He does not feel like the tremor effects his ability to eat or write, but has **trouble getting his wallet** out of his back pocket and notices his **writing is smaller.**

Diagnosis?

- Parkinson's
  - Unilateral
  - Rest tremor
  - Present a few months
  - Progressing
  - Small handwriting
  - Slowed walking
  - Soft voice
  - Trouble with dexterity

Case 2

- 55yo RH man with severe COPD. Ever since a **COPD** exacerbation **in May** he has noticed tremors in **both hands**. It is not really too bothersome to him. On exam you see a **fine, fast tremor** most prominent with **posture**. You see **albuterol** on his medication list which he says he has been using more frequently since the hospitalization.

What to do

- Probably best to refer to a neurologist

Diagnosis?

- Medication induced tremor
- Acute onset in response to a medication
- Fine, fast with posture
- Albuterol (a beta agonist) commonly causes tremor

Case 2

- 55yo RH man with severe COPD. Ever since a COPD exacerbation in May he has noticed tremors in both hands. It is not really too bothersome to him. On exam you see a fine, fast tremor most prominent with posture. You see albuterol on his medication list which he says he has been using more frequently since the hospitalization.

What do you do?

- If he is not bothered by it maybe nothing
- If able try to decrease the albuterol
- Consider OT consult if interferes with particular activities
- Could consider starting primidone if still bothered after the above (propranolol contraindicated in COPD)

Case 3

- 65yo RH man complaining of trouble dropping his food when he eats, especially peas and soup. He has had some bilateral hand tremor for about 20 years that caused him to stop model building 10 year ago. He remembers his Dad had a tremor in his 60's. When he goes out to eat he'll have a glass of wine right away which seems to help. His voice is also a bit shaky – "like Katherine Hepburn."

What do you do?

- Consider medications if bothered enough by it (primidone, propranolol)
- Consider OT referral specifically for utensils to help with eating
- Counsel on caution with ETOH
- If severe and not response after trial of 2-3 medication consider referral to neurology for DBS evaluation

Case 3

- 65yo RH man complaining of trouble **dropping his food** when he eats, especially peas and soup. He has had some **bilateral hand tremor** for about **20 years** that caused him to stop model building 10 year ago. He remembers his Dad had a tremor in his 60's. When he goes out to eat he'll have a **glass of wine** right away which seems to help. His **voice** is also a bit shaky – "like Katherine Hepburn."

Match spirals and tremor

Parkinson's disease

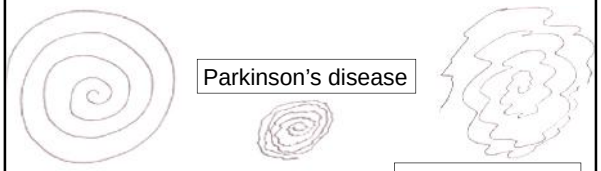
Essential Tremor

Normal

Diagnosis?

- Essential tremor
  - Bilateral hands and voice involved
  - Worst with action
  - Present for many years
  - Gradual worsening
  - Better with Etoh
  - Positive family history

Match spirals and tremor



Parkinson's disease

Normal

Essential Tremor

Match handwriting and tremor

Parkinson's disease

Normal

Essential Tremor

Match handwriting and tremor

Parkinson's disease

Essential Tremor

THE END