DISCLOSURES

- I have no financial relationships with any for-profit corporations or entities.
- I received a training fellowship from the American Academy of Neurology.
- Today’s lecture does not involve any teaching materials or events/conferences produced by the AAN.
There are many types of abnormal movement:
- ataxic
- apraxic
- spastic
- paretic
- functional / conversion
- antalgic
- myopathic

In contrast to those types, movement disorders:
- Originate centrally (brain or spinal cord)
- Are more than just a failure of control or fine-tuning
- Result from abnormal motor control networks

Can be too much (hyperkinetic) or too little (hypokineti
Movement Disorders localize to a network

Movement Disorders connote a disruption in motor control networks

- More than just a “routing” problem – an emergent property
- Lesions at multiple sites within a network can produce abnormal

Abnormal Motor Control Networks in Dystonia

Carbon and Eidelberg, Neuroscience 164 (2009) 220–229
OVERVIEW

- Three steps to characterize a movement disorder
- Clues to recognizing each type of movement disorder
- Discussion of most common/important cause for each movement
- Brief discussion of treatment
STEP 1: DIAGNOSIS BEGINS WITH PHENOMENOLOGY

Describe the patient based on:
- How much movement? (Hyper- or Hypokinetlic)
- Type of movement
- Co-incidence with other Movement Disorders

If a picture is worth a thousand words, then a video is worth a million.
VIDEO EXAMPLE

CC: Difficulty eating, drinking

5yo RH girl with early motor delay, lifelong “twitchiness,” now with worsening difficulty when running, writing, eating, drinking.
EXAM — THINGS NOT SHOWN

- Writing: cramped and sloppy, progressive - a pattern consistent with hand dystonia
- Dystonic posturing of the L. foot while walking, R. hand while writing.

STEP ONE:
Myoclonus affecting trunk, neck and R > L arm
Dystonia affecting mostly L body, task specificity
HYPERKINETIC MOVEMENT DISORDERS

- Chorea - “Dance like”, continuous, irregular, often incorporating planned movements
- Tics
- Tremor
- Myoclonus
- Dystonia
HYPERKINETIC MOVEMENT DISORDERS

- **Chorea**

- **Tics**
  - Sudden, rapid, purposeless, repetitive, stereotyped non-rhythmic, suppressible.

- **Tremor**
  - Rules for tics: 1. Suppressible 2. Evolving

- **Myoclonus**
  - 3. Premonition 4. Associated factors (e.g., ADHD)

- **Dystonia**

Too broad a topic to consider today.
HYPERKINETIC MOVEMENT DISORDERS

- Chorea
- Tics
- **Tremor** - Oscillating, rhythmic about a fixed point, usually a single joint but can also be an axis
- Myoclonus
- Dystonia
HYPERKINETIC MOVEMENT DISORDERS

- Chorea
- Tics
- Tremor
- **Myoclonus** - Quick, shock-like movements. Key point: Not suppressable, no premonition.
- Dystonia
HYPERKINETIC MOVEMENT DISORDERS

- Chorea
- Tics
- Tremor
- Myoclonus
- Dystonia - Sustained muscle contraction, often leading to twisting movements or fixed postures. Co-contraction of agonist-antagonist muscles, overflow to surrounding muscles.
Also Included in Hyperkinetic Group...

- Paroxysmal Dyskinesias – multiple, often overlapping MovDis
- Motor Stereotypies
- Developmental (NORMAL) Movement Disorders
  - At least 12 distinct disorders for which the appropriate treatment is reassurance.

Often Forgotten:

- Functional Movement Disorders (Conversion Disorder)
  - Common, disabling, readily identified
  - More frequent than any other disorder discussed
Step 2: Distribution

What parts of the body are affected?

- Focal - Segmental - Multifocal - Generalized
- Often will start with one area and later spread
- Pattern of presentation and later spread aids diagnosis

Timing

- Early morning?
- Late in the day?
- Induced by action? After exercise?
Bilateral and trunk involvement, upper and lower: Generalized

No clear progression, though with age sx impacted her more

Stimulus-induced myoclonus

Multi-focal task-specific dystonia
STEP 3: APPROXIMATE THE ETIOLOGY

- Presence of cognitive decline or epilepsy
  - a broader encephalopathy?
- Primary movement disorder (symptom in isolation)
  vs.
  Secondary to injury or degeneration.
  - Will often require MRI
- Incorporate family history, response to prior med trials,
  results of imaging / EEG / etc.
**CHOREA**

- “dance like,” continuous, irregular, often incorporating planned movements
- Random movements of chorea rarely repeat, are not suppressible. Watch in 10s bins – can you predict movement in next 10s bin?
- Important to distinguish from akathisia – inner restlessness
- Most important clues on exam are motor impersistence: the inability maintain a fixed posture
  - Jack-in-the-box tongue
  - Milk maid’s grip
  - Touchdown sign
- Hypotonia
EXAM FINDINGS IN CHOREA: MOTOR IMPERSISTENCE

Jack-in-the-box tongue

Milk maid’s grip

Touchdown sign
IDIOPATHIC CHOREA

11yo F, progressive chorea over 5 years, now with cognitive decline and mood lability
HANDWRITING IN CHOREA

11yo F with idiopathic chorea
8yo normally-developing F
The most common cause of acute chorea in children

Symptoms develop over a few hours or days

Historical note (1969, SK Wilson): The child with SC is thrice cursed: “once for general fidgetiness, once for breaking crockery, and once for making faces at his grandmother”

Chorea plus… akathisia; diffuse, mild hypotonia; changes in personality; emotional lability; moderate behavioral regression; dysarthria; moderate gait disturbance with few falls

Largely confined to ages 5y-prepubertal years, F > M

Strep-related anti-basal ganglia antibodies present
SYDENHAM CHOREA – PROGNOSIS

- Chorea resolves <6mo in ~half, can take 2y. Rarely, permanent.
- Up to 20% of children with SC develop ADHD or OCD-like symptoms
- 2/3 are left with bradykinesia, many have executive function deficits
- One third have recurrence with subsequent strep infection.
**CHOREA IN LUPUS**

- Uncommon among all lupus sufferers, but...

- When chorea is the first symptom of lupus, it is commonly seen in isolation

- Lupus should be in the differential for all acute-onset choreas, especially in teens or with any signs of systemic inflammation
TREMOR

- Oscillating, rhythmic about a fixed point, usually a single joint but can also be an axis (neck, trunk)
- Varies with position (rest, kinetic, postural, etc.)
- Uncommon in kids, but makes up 10-20% of MvDis clinic visits
- Most common in systemically-ill child – more frequently, an inpatient consult, rarely contributes to diagnosis
WHEN IS TREMOR... NOT TREMOR?
ESSENTIAL TREMOR

- The most common movement disorder in adults
- In 30-50% of adult ET cases, symptoms begin in childhood – mean: 6-7 years. M > F
- Dominantly inherited with variable severity within a family, but penetrance is 100% by the age of 60.
- Very slowly progressive (years to decades), exacerbated by stress.
- Two peaks of referral: school-age children, late adolescence
- In children ET is typically a mixed postural and action tremor which affects the hands much more than the legs, neck, or voice. Tremor
MYOCLOONUS

- A brief, involuntary muscle jerk that is non-suppressible and generally has no premonitory features.
- May be an isolated finding (primary myoclonus) or can be a symptom of many diseases.
- Physiologic myoclonus occurs episodically throughout life: hiccups, hypnic jerks, fatigue-related benign myoclonus.
- Developmental conditions (e.g., benign neonatal sleep myolonus, benign myoclonus of infancy)
- May come as a referral for ataxia!
CLASSIFYING MYOCLONUS

1. Epileptic vs. Non-Epileptic
2. Co-incidence with other Movement Disorders
3. Primary vs. secondary to injury or degeneration
4. Focal - Segmental - Multifocal - Generalized
5. Spontaneous - Stimulus sensitive/Reflex - Action induced
6. Anatomical origin: Cortical, Subcortical, Spinal cord, Periphery
SEIZURE TYPES WITH MYOCLONUS AS A PROMINENT FEATURE

- Take home point: for any grade-school to high-school aged child with isolated myoclonus, you must evaluate for epilepsy.
Onset from early childhood to late adolescence
Myoclonus in all; dystonia in half
Myoclonus is action-induced and predominantly affects the head, neck and shoulders
EtOH reduces symptoms for many
Dominant with variable penetrance – maternal inheritance is relatively protective (~10% penetrance)
Epsilon-sarcoglycan. No gene mutation? Then called DYT15
ESSENTIAL MYOCLONUS ≈ MYOCLONUS-DYSTONIA

Before Alcohol

After Alcohol
Dystonia

- Sustained muscle contraction, often leading to twisting movements or fixed postures. Often painful.
- Co-contraction of agonist-antagonist muscles; overflow to surrounding muscles not typically involved in that action.
- Predilection for over-learned actions – writing, typing, walking, speech, musical instruments
- Normal motor function in between triggering-tasks, normal in other body parts

3rd-most common movement disorder
DYSTONIA OFTEN LEADS TO BIZARRE MOVEMENTS
WRITING: DYSTONIA VS. CHOREA

1. Wafffe

2. Wafffe

3. Wafffe

Dystonia: Progressive loss of control, Tightening of script

Chorea: No Progression, but irregular intrusions into text
DYSTONIA CAN BE FOCAL...

14yo with segmental dystonia of hand, arm, and shoulder
Patients in dystonic storm can suffer fractures, severe muscle breakdown, dehydration, hyperthermia…

Typically requires barbiturate or benzodiazepine coma to break dystonic status
EXAMPLES OF FOCAL DYSTONIA
# Genetic Causes of Primary Dystonia

<table>
<thead>
<tr>
<th>Site of Onset</th>
<th>Age at Onset, Likelihood of Generalization</th>
<th>Inheritance</th>
<th>Gene or Locus</th>
<th>Penetrance</th>
<th>Clinical Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>DYT1</td>
<td></td>
<td>Autosomal Dominant</td>
<td>TorsinA</td>
<td>30 - 40%</td>
<td>Rapidly generalizes, abnormal gait is norm &gt;50% are Ashkenazi</td>
</tr>
<tr>
<td>DYT2</td>
<td></td>
<td>Autosomal Recessive</td>
<td>Unknown, likely multiple</td>
<td>100%</td>
<td>Rapid generalization, stability, exacerbation at puberty</td>
</tr>
<tr>
<td>DYT3</td>
<td></td>
<td>X-Linked Recessive, rare females reported</td>
<td>Possibly TAF1, other genes in locus not excluded</td>
<td>100%</td>
<td>Only in Filipino ancestry 50% develop parkinsonism, after ~5 years</td>
</tr>
<tr>
<td>DYT5a</td>
<td></td>
<td>Autosomal Dominant</td>
<td>GTP cyclohydrolase</td>
<td>Low, 2-3x F&gt;M</td>
<td>Normal development, mood d/o, OCD</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Sx worsen during day, improve with rest; gait disorder</td>
</tr>
<tr>
<td>TH deficiency</td>
<td></td>
<td>Autosomal Recessive</td>
<td>Tyrosine Hydroxylase</td>
<td>100%, variable severity</td>
<td>Mild: Normal devel. Severe: infantile onset, motor + cognitive delay</td>
</tr>
<tr>
<td>DYT6</td>
<td></td>
<td>Autosomal Dominant</td>
<td>THAP1</td>
<td>60%</td>
<td>All ethnicities, often involves speech Late upper &gt; lower limb involvement</td>
</tr>
</tbody>
</table>

To read more about the primary dystonias: Waugh and Sharma, “Dystonia: From genotype to phenotype” Neurology Clinics, Nov 2013
Spasticity vs. Dystonia

Very common consult question. How to distinguish?

Spasticity
- Severity increases with RATE of movement
- Typically large body-area involved: hemibody or at least most of limb
- Always referable to known/suspected injury or slowly-progressive process

Dystonia
- Increases with TYPE of movement
  e.g., may resolve when walking backward in foot dystonia, may resolve with drumming of fingers in dystonic writers cramp
- Often very specific for particular muscles. May generalize to other body areas, but even then is muscle-specific
- Usually on a background of stable function X years

End of the day: they just look different. Try to see lots of cases!
DYSKINESIAS

- “Dyskinesias” simply means abnormal movements – nonspecific term, but useful in that these conditions are recognized by the shifting combination of movement disorders.
- Intermittent, involuntary, often of a “strange/bizarre” character

PAROXYSMAL DYSKINESIAS

- 3 subtypes, all autosomal dominant with high penetrance
- Key ?’s: How often? How long? Just before?
3 README-DISTINGUISHABLE DYSKINESIAS

- Paroxysmal Kinesigenic Dyskineisa - PKD
- Paroxysmal Nonkinesigenic Dyskinesia - PNKD
- Paroxysmal Exertional Dyskinesia – PED

- 100’s per day, but short? PKD
- A few per year, but lasting hours/days? PNKD
- With exercise lasting longer than 10-20min? PED
3 READILY-DISTINGUISHABLE DYSKINESIAS

- Paroxysmal Kinesigenic Dyskinesia - PKD
- Paroxysmal Nonkinesigenic Dyskinesia - PNKD
- Paroxysmal Exertional Dyskinesia – PED

- Unilateral or highly asymmetric? PKD or PED (if unilat. exercise)
- Triggers?
  - Movement or plan to move? PKD
  - Foods, fatigue, alcohol? PNKD
  - Exercise? PED
HYPOKINETIC MOVEMENT DISORDERS

Parkinsonism

- Any two of the Parkinsonian quartet:
  - Bradykinesia
  - Tremor at rest
  - Rigidity (velocity *IN*-dependent resistance)
  - Postural instability

- Idiopathic Parkinson disease is exceedingly rare in kids
- Most commonly due to medications
- Post-infectious, stroke
- Many inherited causes
ACUTE ONSET MOVEMENT DISORDERS

40mo in a busy tertiary pediatric hospital – all inpatient or ER movement disorder consults
- Chorea – 38%
- Dystonia – 33%
- Tremor – 23%
- Myoclonus – 19%
- Parkinsonism – 19%

Most common cause: Inflammatory / Infectious – 42%
23% later proved to be functional/conversion

RC Dale et al., Dev Med Child Neuro. Aug 2010
IN SUMMARY:

- Capture a video whenever possible
- Organize the patient in a hierarchical fashion:
  - Phenomenology
  - Distribution and timing
  - Preliminary guess at etiology, inheritance pattern
- Test the most-likely 2-4 genes. If results normal...
- Treat symptomatically, assess for evidence for evolving encephalopathy or systemic disease
THANK YOU

Jeff.Waugh@Childrens.Harvard.edu
Childhood-onset Wilson disease often presents with both chorea and dystonia

Juvenile Huntington disease (late teens) rare but important to keep in mind

Onset of HD in childhood rarely has chorea in first few years. Instead, presents with parkinsonism +/- dystonia – the Westphal variant.
SEIZURE TYPES WITH MYOCLONUS AS A PROMINENT FEATURE

- 20% of neonatal seizures (all types) are myoclonic (Volpe)
- Severe Myoclonic Epilepsy of Infancy – Dravet syndrome
- Myoclonic-astatic epilepsy of childhood – Doose syndrome
- Juvenile Myoclonic Epilepsy – <5% have only myoclonus, but myoclonus often begins before other recognized seizure types
OTHER RELATIVELY-COMMON TYPES OF MYOCLONUS

- Opsoclonus-Myoclonus-Ataxia (all 3, or any 1 in isolation)
- Myoclonus-Ataxia – often the initial presentation of ataxia telangiectasia
- Post-anoxic myoclonus – both immediate post-injury (hours-day) and later (the Lance-Adams syndrome)
- Co-occurrence of myoclonus and tics

Key distinction: presence of progressive encephalopathy vs. isolated disorders of movement