Learning Objectives

At the end of this presentation the participant will be able to:
1. Understand that there are a large number of disorders characterized by abnormal movements
2. Understand how to describe abnormal movements
3. Be able to name some examples of Pediatric Movement Disorders

Baby P-G

- Term neonate. Born via c/s for NRFHT
- T of 38.4 at birth, taken to NICU
- On attempt to do LP, baby went "stiff as a board", could not be bent into LP position
- Transfer here for concern for neonatal meningitis

Case 1
Baby P-G

Hospital course

- Baby had several events concerning for seizures
- All were elicited by stimulic touch, loud noise
- When stimulated, baby would go stiff and all 4 limbs would extend out
- EEG did not show seizures, labs did not show sepsis
- Mom arrived on d1 3 and stated that she, her son, and several members of her family had the same problem
**AKA Hereditary Startle Disease**

**Hyperekplexia**

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**Characteristics**
- Infants have exaggerated startle with noise, sound, touch
- When startled, the whole body becomes rigid
- Infants can stop breathing with attacks (can be fatal)
- Are hypertonic between attacks
- May also have seizures

**Prognosis/Treatment**
- Symptoms improve over the 2nd year of life
- Milder symptoms can recur throughout the life
- Can lead to falls once ambulatory

- Treated with scheduled benzodiazepines
- Vigevano Maneuver: Flexing of the limbs and head toward the trunk can stop and attack

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**Historical perspective:**

**The Jumping Frenchmen of Maine**
- Occurred in late 19th century, in Canada
- Genetically isolated group of French lumberjacks
- Symptoms began in teens, then lessened

**Symptoms:**
- Startle would induce jumping, screaming, yelling, throwing things
- Following this, there was echolalia and coprolalia
- Neuropsychiatric phenomenon or genetic neurological condition?
- Link to hyperekplexia?

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**George Beard and the Lumberjacks**
- Dr. Beard was a Neurologist who traveled to Maine and described the disorder in 1878
- His work would peak the interest of Gilles de la Tourette
- Initially was thought to be a cultural phenomenon, but discovery of hyperekplexia led some to doubt that...
Hyperekplexia

- The first unambiguous description of an affected family was in 1958 by Drs. Kisteine and Silverskiold
- They described a family as having heritable “drop seizures”
- Many years later, a large Dutch family cohort was studied, and the first mutation was found in the GLRA1 gene

Cause: Defective Glycine Receptor Function

- Ligand-gated chloride ion channel
- Facilitate fast-response inhibitory neurotransmission
- Location: brainstem and spinal cord
- #1 mutation: Gly-R α-1 subunit
- Most are Autosomal Dominant

Update

- Baby P+G has stopped having attacks
- Clonazepam is being weaned
- Brother had Mother have undergone PT to teach them “how to fall” without injuring themselves
- Genetic testing revealed an AD mutation in the alpha subunit of the Glycine Receptor (GLRA1 gene). Mutation previously described in 3 other families

Case 2

CA

CA

- CA is a 6 yr old female who had onset of abnormal movements this year
- First was finger tapping
- Then came head jerking and shoulder shrugging
- Recently, they noted she was clearing her throat a lot
- She can stop it for a few minutes if she thinks about it
- Trying to stop makes her feel anxious
- The behavior stops in sleep

CA

- Family notes issues with focus, sitting in seat
- She states she can’t focus on things because she is distracted by her movements
- Kids in school are making fun of her
* Not CA

Tourette Syndrome Historical Perspective
- French physician and hypnotist
- Described "La Maladie des Tics" in 1889
- Condition renamed Tourette Syndrome by Dr. Jean Martin Charcot, his mentor
- Died in a psychiatric hospital several years after being shot by a female patient
- He had hypnotized her against her will

Gilles De La Tourette

Tourette’s Syndrome vs Motor/Vocal Tic Disorder vs Provisional Tic Disorder

Credit: CDC Website
http://www.cdc.gov/nchbddd/tourette/diagnosis.html

Tourette’s Syndrome
- For a person to be diagnosed with TS, he or she must:
  - have two or more motor tics and at least one vocal tic
  - have had tics for at least a year.
  - have tics that begin before he or she is 18 years of age.

Persistent Vocal or Motor Tic
- For a person to be diagnosed with a persistent tic disorder, he or she must:
  - have one or more motor tics or vocal tics but not both.
  - have tics that occur many times a day nearly every day or on and off throughout a period of more than a year.
  - have tics that start before he or she is 18 years of age.
  - not have been diagnosed with TS.

Provisional Tic Disorder
- For a person to be diagnosed with this disorder, he or she must:
  - have one or more motor tics
  - have been present for no longer than 12 months in a row.
  - have tics that start before he or she is 18 years of age.
  - not have been diagnosed with TS or persistent motor or vocal tic disorder.
Pathophysiology of Tourette Syndrome

- Many NT systems implicated
  - The primary driver seems to be dysregulation of the dopamine systems:
    - Nigrostriatal pathway: movement selection and execution
    - Mesolimbic system: motivation and reward
    - Mesocortical system: Prefrontal cortex: attention and working memory

Time Course of Tics/Comorbidities

Credit: American Family Physician website
Credit: Brittany Fichter website

Treatment

Optimal treatment may depend on comorbidities present:
- 1st line for TS + ADHD: Clonidine and Guanfacine
- 1st line for pure TS: Risperidone
  - Typical antipsychotics are also effective, but SE profile is worse
- 1st line for TS + OCD: Risperidone +/- SSRIs

- Tics can be exacerbated by stimulants used for ADHD!
  - Some with severe tics and ADHD need Risperidone +/- low dose stimulants

Other treatments for Tics

- Botulinum for those with only a few focal motor tics
- Behavioral therapy
- Education of family and peers

Update on CA

- Clonidine trial was unsuccessful
- Doing well on low-dose risperidone
- No more motor tics; only some persistent throat clearing
- She is reluctant to go see a counselor regarding her issues with school bullying

Case 3

LR
LR
- 9 yr old male with a history of autism and global developmental delay
- At baseline, can perform ADLs such as dressing himself, using the toilet
- 1 mo pta, he developed a URI
- 3 weeks pta, he developed chronic abnormal movements in all 4 limbs
- Could not put on clothes, could not walk in a straight line
- Unable to sit still, constantly moving in his seat

Hospital course
- Movements observed, diagnosed with chorea
- Treated with steroids and risperidone, had rapid improvement in symptoms
- ECHO normal
- ASO and DNAase titers normal
- Group A strep negative
- No other respiratory virus testing done

*Not LR

Post-infectious choreas

St. Vitus
- A Italian Catholic martyr from the 3rd century
- Miraculous works centered on the curing of neurological ailments
- Following his death, his relics were reported to heal movement disorders
- In Europe in the 1400s, there was an outbreak of “dancing manias”, this came to be known as St. Vitus’ Dance

Dance at Molenbeek by Pieter Bruegel the younger
Sydenham's Chorea, historical perspective

- Described in 1686 by Thomas Sydenham
- "There is a kind of convulsion, which attacks boys and girls from the tenth year to the time of puberty. It first shows itself by trembling or unsteadiness in one of the legs. The hand cannot be steady for a moment. It passes from one position to another by a convulsive movement, however much the patient may strive to the contrary."

Historical Perspective, continued

- Sydenham also described manifestations of rheumatic fever, but did not link it to chorea
- Richard Bright made the link in 1831
- It is unclear how Sydenham's chorea and St. Vitus' dance came to be associated

Worldwide prevalence

- Treatment of GAS infections in the developed world led to an initial decline in incidence
- Incidence has risen again in some countries
- Remains a major cause of morbidity and mortality in the developing world

Sydenham's chorea

- Chorea that begins following a childhood infection with Group A Strept
- #1 cause of acute chorea in children
- Usually children, F>M

Sydenham's Chorea and Acute Rheumatic Fever

- Modified Jones Criteria (1944):
  - 2 major or
  - 1 major + 2 minor
  - + evidence of recent GAS infection
  - Exceptions: presence of chorea or indolent Carditis
  - ~40% will develop ARF

Pathophysiology

- Antibodies arise in response to GAS infection
- These cross-react with:
  - Basal ganglia
  - Frontal cortex
- Result: impaired DA transmission > Poor control of complex movements
Symptoms

- Chorea of all 4 limbs
- Kids classically attempt to incorporate chorea into a normal movement
- Movements interfere with gross and fine motor skills
- Movements stop in sleep

“Milk sign”

Behavioral manifestations

- OCD symptoms
- Emotional lability
- Regression
- Cognitive slowing

Other infectious causes of chorea

- It is recognized that there are other infectious and post-infectious causes of acute chorea in children:
  - EBV
  - Parovirus B19
  - HSV
  - Coxsackie virus
  - Varicella
  - Cytomegalovirus
  - Mycoplasma

Overview of treatment of chorea: Sydenham’s specific

- Eradication of GAS, penicillin remains treatment of choice
- Chronic penicillin treatment?
  - Does not seem to affect recurrence chance of chorea
  - Done to prevent chance of ARF developing

Fun Fact Friday!

- Things used to treat Chorea over the years:
  - Bleeding
  - Purging
  - Hyperthermia
  - Chloral hydrate
  - Barbiturate drips
Symptomatic management of chorea: Pitfalls

"Despite three centuries of experience there is still no globally accepted protocol to treat SC." - Walker and Wilmhurst, 2010.

- No reviews
- Few RTC with only small numbers of patients
- Most data comes from case series
- Countries with highest prevalence of SC are most resource poor, which often drives the treatment decision
- Most common agents all have the potential to cause their own movement disorders

Overview of treatment of chorea: treating the movements

- Dopamine agents: Risperidone > Haloperidol
- Antagonizes dopamine receptors
- GABA agents: Valproic acid > benzodiazepines
- Inhibits Dopaminergic hyperactivity by influencing GABA transmission

Treating the Immune system hyperactivity

- Steroids
  - Decrease immune response
  - Decrease inflammation in the vessels of the basal ganglia
- IVlg
- Plasmapharesis

- Goal is to shorten the course of the illness
- Recurrence rate does not seem to change
- IVlg and Plasmapharesis seem more effective in limited RTC

Describing movement disorders

- Sometimes a movement is hard to categorize. Focus on determining:
  - What body parts are affected?
  - Distal or proximal or both?
  - Stereotypical or not? Rhythmic? Writing? Dancing?
  - Impairment of consciousness?
  - Comorbidities?
  - Recent illnesses?
  - What happens in sleep?
  - Triggers?
  - Family history?

Summary

- We have talked about 3 different movement disorders
- Etiology and pathophysiology of all are different
  - 2 involve Dopamine neurotransmitter system and basal ganglia connections
    - 1 involves inhibitory spinal cord neurotransmission
  - All 3 were misunderstood in their time
    - 2 were thought to be primarily psychiatric phenomenon
    - 1 was thought to be a seizure disorder
  - All can be successfully treated once the diagnosis has been made

Time for a joke

What did the neuron say to the glia?
- Thanks for the support!
References