The Rest of the “Extrapyramidal Motor System”

• Recall the Other Descending Tracts: Extrapyramidal Motor Pathways
  • Rubrospinal pathway to regulate tone of flexors in limbs for locomotion & to organize repetitive movements that involve the flexors (e.g. walking, running, crawling)
  • Vestibulospinal pathway to stimulate extensors (antigravity) for standing, posture
  • Tectospinal pathway for reflexive motor reactions to visual stimuli
  • Reticulospinal pathway to regulate muscle tone by modulating the stretch reflex

• UMN Syndromes
  http://www.youtube.com/watch?v=yZUE2Dvf1Q4
  • UMN damage above red nucleus (rubrospinal still working) → “decorticate posture” with arms flexed, hands fisted (upper picture)
  • UMN damage between red nucleus and vestibulospinal & reticulospinal tracts (lower paths still working) → “decerebrate posture”

• Cortico – Forebrain
• Rubro and Tecto – Midbrain
• Reticulo and Vestibulo- Hindbrain

• Extrapyramidal Motor System
  • The descending extrapyramidal paths receive input from other parts of motor system:
    • From the basal ganglia or “corpus striatum”
    • From the cerebellum
    • (so these will be our next 2 chapters)

• Basal Ganglia or Corpus Striatum
  • Interconnected set of nuclei (gray matter) buried within the cerebral hemispheres that have primarily motor functions
  • Best known components:
    • Caudate nuclei (“tail shaped nuclei”)
    • Putamen (“seashell”)
    • Globus pallidus (“pale globe”)
- Basal Ganglia or “Striatum”

- Caudate & putamen get input from cortex, thalamus & substantia nigra, a midbrain motor area.
- They send commands to globus pallidus which sends them on to the motor portions of thalamus & brainstem.
- Very interconnected system with lots of feedback loops.
Functions

- The basal ganglia are important for:
  - Facilitating or initiating motor programs — often multiple programs at once (via what is known as its "direct pathway")
  - Inhibiting undesired movements; terminating voluntary movements (via what is known as its "indirect pathway")
  - We might think of the BG serving as both the gas pedal and the brake pedal for the activity of the motor cortex

Parkinson’s Disease
(paralysis agitans or shaking palsy)

- About 1% of those over 50 have PD (~ 1,000,000 total in US; 60,000 new cases/yr; 90% cases occur after age 60)
- Progressive deterioration of DA input to basal ganglia- the “nigrostriatal pathway” from substantia nigra in midbrain to the “striatum” in forebrain
- We lose about 4% of those DA neurons/decade, but those with PD have accelerated loss (70% or more gone)
- Results in difficulty initiating movements & tremor
The nigrostriatal path sends DA messages from the substantia nigra to the basal ganglia.

### Classic PD Symptoms
- Worsening bradykinesia (slowing of movement) & akinesia (loss of movement)
- Rigidity (too much muscle tone); clumsiness, decreased postural stability so tends to fall
- “Pill-rolling” tremor-at-rest
- Reduction in movement is also seen in lack of facial expression & blinking; shuffling walk without arm movements; soft, halting, monotone voice; slow blinks; small writing; feeling stuck or frozen

### Possible Causes
- Environmental toxin of some sort (industrial heavy metals, pesticides, “free radicals” currently under study)
- [YouTube Video](http://www.youtube.com/watch?v=oW3j8t3ySyS&context=C3c0a567ADOEgstoPDskL0gMaiaYEJ97F_lty3BqB8) (go to 9 min)
- Genetics (strong link in early-onset PD; weak link in regular PD)
- Brain trauma may increase your risk

### PD Concordance in Twins
- Late-Onset (161 pairs studied)
  - MZ 13%
  - DZ 16%
- Early Onset (16 pairs)
  - MZ 100% (4 pairs)
  - DZ 16%

### Treatments
- Increase DA production with l-dopa
  - Problems: l-dopa-induced dyskinesia side effects & loss of effectiveness over time: [YouTube Video](http://www.youtube.com/watch?v=27Uz50yd1T)
- Prevent DA breakdown or reuptake
  - E.g. Eldepryl (selegeline); Azilect (rasagiline)
- Stimulate DA receptors with DA agonist
  - Parldel (bromocriptine); Mirapex (pramipexole), Requip (ropinirole)

As PD progresses ON's get shorter & upping dose increases side effects.
• When Drug Therapy Fails
  When drug effectiveness declines, experimental options include:
  • Deep brain stimulation to block hyperactivity in this system
    http://www.youtube.com/watch?v=abHuHFt_izI
    http://www.youtube.com/watch?v=xzxsspsgZG4
  • DBS has pretty much replaced earlier surgical treatments like pallidotomy; thalamotomy (Michael J. Fox
  • Experimental: Transplant of DA producing cells into brain

• Parkinson’s Disease Update
  • Although PD is thought of as a motor disorder, the decline in DA also produces cognitive and emotional changes in some
    • depression
    • “bradyphrenia” (cognitive slowing); decreased attention
    • “frontal lobe” symptoms (disinhibition of behavior, poor judgment and planning)
    • Full-blown dementia in ~40-50% (associated with neuropathological sign called Lewy bodies)
    • PD treatment, on the other hand, can produce hallucinations and other symptoms of psychosis

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• Tourette Syndrome
  • A usually hereditary BG disorder characterized by involuntary movements
  • Multiple motor tics - simple tics of face or limbs and/or more organized complex tics (touching, grimacing, pinching, poking, adjusting, hitting, jumping, kissing, throwing, gestures) plus:
    • Phonic or vocal tics - both simple (throat clearing, coughing, hiccupping, grunting, yelping) and/or complex tics (actual words, coprolalia, echolalia, palilalia, assuming different voices, talking to oneself in different voices)
    • Seems to affect frontal lobe-BG connection that is important for our ability to inhibit actions

• Link with Other Disorders
  • ~50-60% also suffer OCD (others estimate that up to 90% experience some involuntary touching compulsions, ritualistic behaviors, intrusive thoughts)
  • ~50-90% show evidence of ADHD as well; first signs of GTS are usually impulsive, hyperactive behaviors (before tics appear)
  • About 30% have learning disabilities, emotional lability, rage, aggressiveness; 40-50% depressed
  • Initially suspected a single gene with sex-linked, varied forms of expression of disinhibition, but now appears more genetically complicated
  • 50-73% concordance in identical twins vs 8-22% in fraternal twins

• Tourette Syndrome
  • 40% report “sensory tics” — uncomfortable sensations that may be a reason for some of the involuntary movements
  • Some degree of suppressibility, but individual experiences increased tenssion/ until tic is released
  • Pattern of tics changes & waxes & wanes with changes in stress, anxiety, fatigue.
  • Treated with DA blockers (Haldol, Orap). Milder tics may respond to NE agonist clonidine.
  • Majority experience decreased tics as adults.
  • In a small % of kids symptoms are aggravated or first appear after a strep infection (“PANDAS”)
  • https://www.youtube.com/watch?v=4vI2DmMPaI

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• Impairment of the Inhibitory Functions of the BG
  • Dyskinesias – involuntary movements
    • Chorea ("dance-like") – quicker irregular movements
    • Athetosis – slower writhing, twisting movements
    • Dystonias – abnormalities of excessive muscle tone; muscle spasms
    • Can also have much more complex involuntary movements

• Huntington’s Disease
  • Transmitted by a dominant gene on chromosome 4 (about 30,000 US cases with 150,000 at risk kids)
  • Deterioration of striatum produces involuntary chorea, athetosis & other motor difficulties
  • Cortical deterioration causes progressive & debilitating dementia, aggressiveness, mood swings, depression, psychosis
  • Death due to health complications in 15-20 yrs

Ventricles enlarged, caudate & other BG reduced in size

•CAG Repeats & Age of Symptom Onset

• Huntington’s Disease
  • Bad gene has excess “CAG repeats” (more than 36-250 instead of usual 29 or fewer) resulting in an abnormal form of protein known as huntingtin.
  • The more repeats, the earlier symptoms appear.
  • # of repeats can increase across generations, especially in kids inheriting gene from father
  • Brain damage may be due to decrease in normal protective huntingtin + adverse effects of abnormal protein on critical growth factors keeping cells alive.
  • HD may cause increased susceptibility to excitotoxic glutamate and/or abnormal programmed cell death.

• Treatments for HD
  • Genetic testing to identify presence of the gene
  • Involuntary movements may be decreased by DA blockers (antipsychotics)
  • New drugs being tried to delay progression:
    • Rilutek (riluzole), Neurontin (gabapentin) decrease glutamate transmission
    • Rapamycin (transplant drug) speeds elimination of abnormal protein
    • Growth factor supplementation being studied
  • Experimentation with brain cell transplants/surgeries is underway
• Anatomy of the Cerebellum
  • 2 hemispheres with vermis in between
  • Very folded cerebellar cortex
  • Underlying white matter & deep nuclei
  • Deep nuclei are the output pathway
  • Massive cerebellar peduncles (axon bundles to and from cerebellum) connecting to brainstem
• Evolution of Cerebellum
  • Oldest part is the flocculonodular lobe - it gets input from the vestibular system (Vestibulocerebellar path)
  • Next: the region around the vermis gets proprioceptive & cutaneous input via spinal cord (spinocerebellar tr.)
  • Most recent region – the hemispheres - get input from cortex via the pons (corticopontocerebellar path)
  • All input goes to cerebellar cortex; all output is from the deep cerebellar nuclei
  • Loop-like feedback to each of those sources of input

• Primitive Frog  Cerebellum in Blue

• Mode of Functioning
  • Totally unconscious
  • Computer-like feedback loops
  • Moment-to-moment adjustments
  • Ipsilateral in its control (right side of cerebellum related to movements of right side of body)

• Cerebellum Is Needed For:
  • Fluid coordination of movements
  • Synergy/cooperation between muscles
  • Precise timing & targeting of movements
  • Appropriate force & muscle tone
  • Refining & storing these details during motor learning
  • Automatic adjustments to changing conditions & to maintain balance
Symptoms of Cerebellar Damage

- **Gait ataxia** – wide-based, staggering walk, may shuffle, veer to side, may fall. [Video](http://www.youtube.com/watch?v=5Dj827uCP3g)
- Disturbed balance (can’t balance on 1 foot; walk heel-to-toe)
- Poor muscle tone (hypotonia)
- Adiadochokinesia/Dysdiadochokinesia - can’t rapidly alternate movements. [Link](http://www.neuroexam.com/36.htm)
- Nystagmus – jerky, oscillating eye movements [Video](http://www.youtube.com/watch?v=oUlUVWQx7zI)
- Midline lesion most likely to cause gait, posture, balance problems - Romberg test [Link](http://www.neuroexam.com/neuroexam/content.php?p=37)

Symptoms

- **Dysmetria** - poor targeting of movement; over or under-reach
- Can’t do finger to nose test
- Intention tremor while targeting movements
- **Aynergia** - loss of fluid coordination & cooperation between muscles; movements jerky & disjointed
- **Dysarthria/Dysphonia** - slurred, uncoordinated speech & speech volume
- Lateral lesion - affects ipsilateral limbs [Video](http://www.youtube.com/watch?v=5eBwn22Bnio)
- **Asynergia**

Causes of Cerebellar Damage

- Strokes or tumors affecting cerebellum
- Demyelination due to MS
- Genetically based degenerative disorders (e.g., Friedrich’s ataxia caused by degeneration of spinocerebellar tracts)
- Alcoholic cerebellar atrophy. Cerebellum can also be damaged by some anticonvulsants or chemotherapy.
- Tumor
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- **Genetically based degenerative disorders**
- **Alcoholic cerebellar atrophy**
- **Tumor**

Test for Dysdiadochokinesia

- 3 year old with cerebellar symptoms
  - [Video](http://www.youtube.com/watch?v=399E6J9g9s)

Medulloblastoma

- A cerebellar tumor usually originating in the vermis, which then presses down on the brainstem
- Accounts for ~1 in 20 brain tumors (1 in 5 in kids).
- 2/3 cases occur before age of 15 (median age = 5-6)
- Symptoms: Falling, nausea & vomiting, double vision, headache, eventually trouble moving. If its located on midline child will tend to fall forward or backward

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