• Extrapyramidal Motor System
  
  • Descending extrapyramidal paths receive input from other parts of motor system:
    • From the cerebellum
    • From the basal ganglia or “corpus striatum”

• 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.

http://www.learner.org/vod/vod_window.html?pid=1599
• If video at above link does not immediately appear, click on video # 31 in their list

• 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 assoc. arm movements; soft, halting, monotone voice; slow blinks; small writing; feeling stuck or frozen

Parkinson’s Disease
  • About 1/100 of those over 50 have PD (about 1,000,000 total in US)
  • Progressive loss of DA cells in substantia nigra which normally send messages to basal ganglia
  • We all gradually lose neurons but those with PD may have accelerated loss (70% or more gone)
  • Symptoms: Difficulty initiating movements, slow movements, muscle rigidity & tremors-at-rest
  • http://www.rxlist.com/parkinsons_disease_slideshow_pictures/article.htm
• **Possible Causes**
  - Environmental toxin of some sort (industrial heavy metals, pesticides, “free radicals” currently under study)
  - [http://www.youtube.com/watch?v=oW33gBl3yvs&context=C3c0a567ADOfg7ToPDskLqMaiaYEpJ97F_Itv38QqR](http://www.youtube.com/watch?v=oW33gBl3yvs&context=C3c0a567ADOfg7ToPDskLqMaiaYEpJ97F_Itv38QqR) (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 side effects (dyskinesia, dystonia) & loss of effectiveness over time
    - [http://www.youtube.com/watch?v=2TU3H2fD4](http://www.youtube.com/watch?v=2TU3H2fD4)
  - Prevent DA breakdown or reuptake
    - E.g. Eldepryl (selegeline)
  - Stimulate DA receptors with DA agonist
    - Parlodol (bromocriptine); Mirapex (pramipexole)
  - Counteract the effects of the “opposing” neurotransmitter Ach to decrease motor symptoms (Artane, Cogentin (benztropine))

- **Balance Between DA and Ach in Basal Ganglia**
  - Increase availability of dopamine
  - Reduce acetylcholine output
  - Slow the loss of DA neurons

• **When Drug Therapy Fails**
  - When drug effectiveness declines, experimental options include:
    - Deep brain (thalamic) stimulation to block hyperactivity in this system
      - [http://www.youtube.com/watch?v=aSldB1JNBu8](http://www.youtube.com/watch?v=aSldB1JNBu8)
    - Lesion (damage) other parts of the system
      - Pallidotomy; thalamotomy (Michael J. Fox)
    - Transplant of DA producing cells into brain (but the results we saw were, sadly, not replicated)
• Alternative Surgery – Thalamotomy
  - Damages motor portion of thalamus
  - Michael J. Fox had this surgery done

• 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
    - Major depression
    - “bradyphrenia” (cognitive slowing): decreased attention
    - “frontal lobe” symptoms (dissynchronization 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

• 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

Pallidotomy

http://www.youtube.com/watch?v=7bEKQGYHzrc
http://www.youtube.com/watch#v=1DPw8NViI5I&feature=related