UMN vs LMN

- UMN vs LMN
- UMN (Upper Motor Neuron) vs LMN (Lower Motor Neuron)
- UMN Damage vs LMN Damage
- Reflex Changes After UMN Damage
  - hyperactive stretch reflex, particularly in anti-gravity muscles
  - too much muscle tone (hypertonia or spasticity)
  - clonus (rapid repetitive response to stretch)
  - altered Babinski & weaker superficial reflexes after corticospinal damage

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
- Corticospinal path modulates activity of these tracts as well as spinal reflexes
- (don’t need to memorize exact route of these)
UMN Syndromes

- UMN damage above red nucleus (rubrospinal still working) → “darcortic peace posture” with arms flexed, hands fisted (upper picture)
- UMN damage between red nucleus and vestibulospinal & reticulospinal tracts (lower paths still working) → “decerebrate posture”

Amyotrophic Lateral Sclerosis (ALS)
or Lou Gehrig’s Disease

- Progressive loss of LMNs as well as corticospinal pathway (UMNs). Several genes involved.
- Onset most often in late 50’s-early 60’s; more men affected
- 70% will die within 5 years (eventually cannot swallow, breathe)

ALS – Symptoms

- First symptoms usually muscle cramping & twitching, with feelings of fatigue & weakness in a limb
- Loss of LMNs causes weakness, paralysis, loss of reflexes & atrophy in affected muscles. Loss of UMs causes spasticity (muscle stiffness, cramping from too much tonus).
- Combination of UMN + LMN symptoms at multiple levels is fairly diagnostic
- New treatments: riluzole (Rilutek) slows progression (on average extends life 2-3 months) and noninvasive ventilation & gastrostomy perhaps 6 months, but research on gene therapy or stem cell implants probably critical

New discovery (9/2011):

- Genetic mutation on chromosome 9 which seems to be linked to ALS as well as fronto-temporal dementia

Cross-Sections

- Cord does not look the same at all levels. Notice:
  1) the difference in the amount of white matter in the upper vs lower cord & whether or not the fasc. cuneatus is present
  2) Size of ventral horns (which reflects # of LMNs at each level
- You should be able to recognize the level of these sections
• Cervical 7

• Spinal Cord Injuries (SCI)
  • ~10,000/yr in US; 50% disabled
  • Today about 10% die (used to be 90%)
  • Estimated 500,000 survivors, 200,000 in wheelchairs
  • About 2/3 are under 30; 82% are males

• Causes of SCIs
  • Similar pattern to head injury data:
    • ~45% in motor vehicle accidents
    • ~22% in falls
    • ~16% due to violence
    • ~13% in sports
  • Must assume those with head injuries have spinal injury too until we know otherwise.

• What Damages Cord?
  • Can have SC concussion or contusion
  • Overstretching or twisting of cord (like a CHI)
  • Fracture or dislocation of vertebrae causing laceration or compression of cord
  • Penetrating injury (e.g. bullet)
  • Vascular problem causing infarct
  • SCIWORA - spinal cord injury without radiographic abnormality
• **Location of Damage**
  - Cervical vertebrae most fragile & likely to fracture
  - Most mobile parts of spine (C5-C6, T12-L1, C1-C2) most likely to dislocate or overstretch
  - Cervical injuries - quadriplegia
  - Lumbar injuries - paraplegia
  - Can also have incomplete injuries

• **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

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![PD vs normal SN](image1.png)

**Normal # of DA cells vs PD**

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• The nigrostriatal path sends DA messages from the substantia nigra to the basal ganglia.

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![Normal # of DA cells vs PD](image2.png)

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• **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

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![Normal # of DA cells vs PD](image3.png)

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  • If video at above link does not immediately appear, click on video # 31 in their list
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

**Possible Causes**

- Environmental toxin of some sort (industrial heavy metals, pesticides, “free radicals” currently under study)
  - [http://www.youtube.com/watch?v=oW33gBI3yys&context=C3c0a567AD0EpsToPDs&UqDpaMakaYEJ97F_lty23RoQ8](http://www.youtube.com/watch?v=oW33gBI3yys&context=C3c0a567AD0EpsToPDs&UqDpaMakaYEJ97F_lty23RoQ8) (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%

**Pallidotomy**

[http://www.youtube.com/watch?v=7bEKQGHrzrc](http://www.youtube.com/watch?v=7bEKQGHrzrc)
[http://www.youtube.com/watch#v=1DPw8NI5I&feature=related](http://www.youtube.com/watch#v=1DPw8NI5I&feature=related)
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=2TU2s3VxEI4
• Prevent DA breakdown or reuptake
  – E.g. Eldepryl (selegeline)
• Stimulate DA receptors with DA agonist
  – Parlodel (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
• When drug effectiveness declines, experimental options include:
  • Deep brain (thalamic) stimulation to block hyperactivity in this system
    http://www.youtube.com/watch?v=a1xdB1jNBu8
  • 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

When Drug Therapy Fails
• 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 (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
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

Tourette Syndrome
- Another 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, gesturing) plus:
  - Phonic or vocal tics - both simple (throat-clearing, coughing, hiccuping, 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
- Evidence suggests a single gene with sex-linked, varied forms of expression of disinhibition
- 50-73% concordance in identical twins vs 8-22% in fraternal twins

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
• Huntington’s Disease
  - Bad gene has excess “CAG repeats” (more than 36-250 instead of usual 28 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