Lecture XIII.
Brain Diseases I - Parkinsonism

Bio 3411

Wednesday

October 7, 2009

Brain Diseases I

NEUROSCIENCE
THE BRAIN ATLAS 3rd ed

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72		*Coronal Section including SN*
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200-201		*Direct Corticospinal tract*
212-213		*Basal Ganglia Pathways*

References

†Barker RA, Dunnett SB 1999 Functional integration of neural grafts in Parkinson's disease. Nature Neuroscience 2:1047-1048.

†Gulie S 2007 A shock to the system: to slow the progress of Parkinson's disease, doctors planted electrodes deep in my brain. Then they turned on the juice. [http://www.wired.com/wired/archive/15.03/brainsurgery.html?pg=2&topic=brainsurgery&topic_set=] (check out the video!!)

†Perlmutter JS 2006 [http:/www.Harrisonline.Com/audio/parkinsons.Mp3]

†Starr PA, Vitek JL, Bakay RAE 1998 Ablative surgery and deep brain stimulation for Parkinson's disease. Neurosurgery 43:989-1015.

†Wichmann T, DeLong MR 1998 Models of basal ganglia function and pathophysiology of movement disorders. Neurosurgery Clinics of North America 9:223-236.

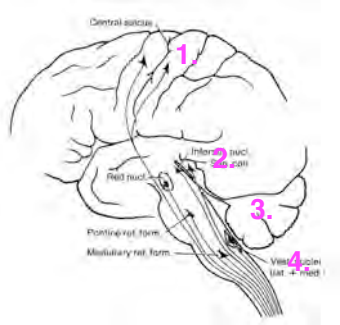
†Articles/Abstract/Audio posted on website.

What this lecture is about:

- Motor Systems - Reprise
- Pyramidal and Extrapyramidal (Basal ganglia)
- Parkinsonism a Movement Disorder
- Mechanisms and Treatment Strategies

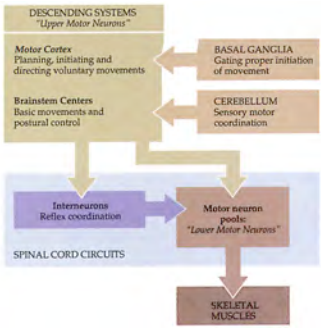
Sources of Descending Pathways for Movement Control

1. **Forebrain (Cortex)**
2. **Midbrain (Red Nucleus & Superior Colliculus)**
3. **Pons (Reticular Formation)**
4. **Medulla (Reticular Formation and Vestibular Nuclei)**



Neuroscience, Fig 16.1, p. 398

Descending systems from the brain influence cells in the spinal cord to create movements. The cerebellum and the basal ganglia indirectly influence movements as indicated schematically here.



Basal Ganglia (Extrapyramidal) Pathways.

The basal ganglia inhibit unwanted movement patterns and permit selected ones. They may also inhibit unwanted mental activities such as inappropriate utterances, and permit selected ones, such as proper speech.

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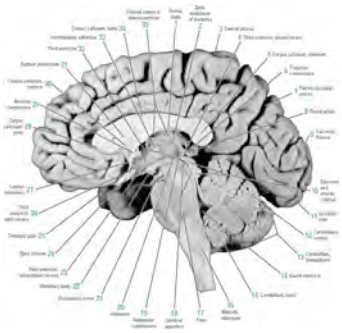
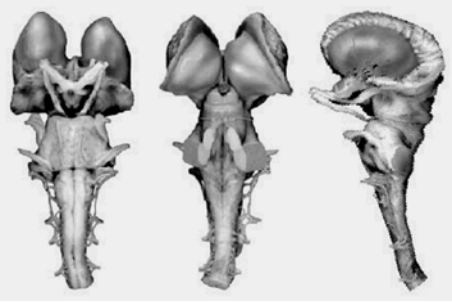


THE BRAIN ATLAS, 3rd ed pp 43-44



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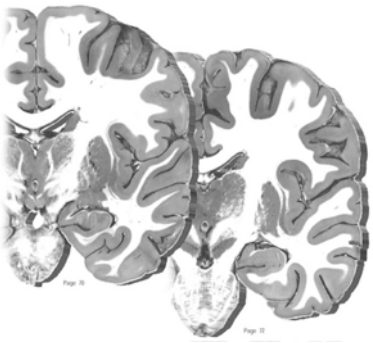
Sections



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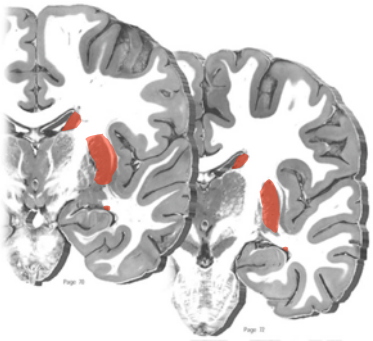
Caudate Nucleus & Putamen



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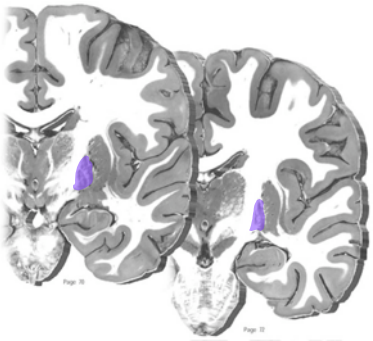
Globus Pallidus



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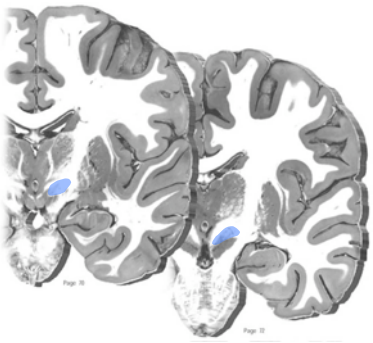
Subthalamic Nucleus



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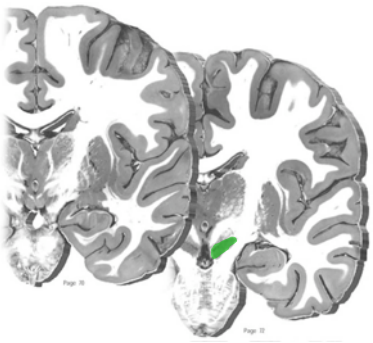
Substantia Nigra



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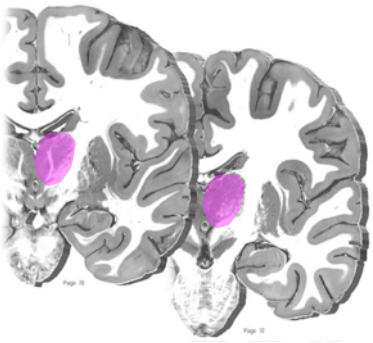
Thalamus



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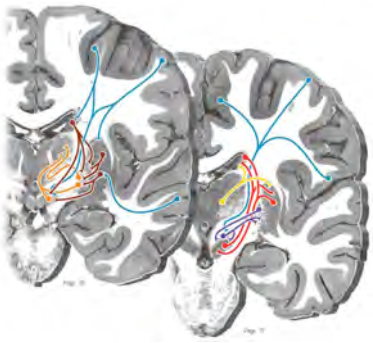

Patient(s) with tremor and paralysis

Movie Clip # 1

Parkinsonism

- Symptoms and Signs: akinesia (no movement or bradykinesia, poverty of movement); poor sequences of movement; rigidity; tremor at rest
- Prevalence: ≤ 1%
- Predisposition/cause: probably not genetic, occurs after encephalitis (brain inflammation), certain toxins, but largely unknown
- Prevention: none known
- Pathophysiology: loss of **dopamine** neurons in substantia nigra that project to caudate and putamen
- Diagnosis: physical examination

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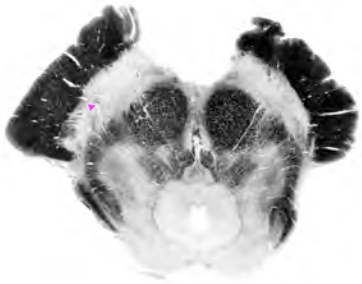
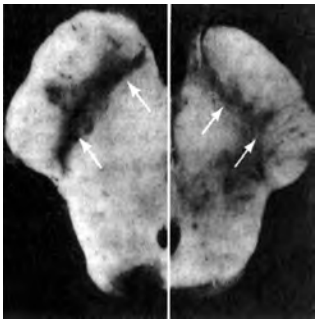
Substantia Nigra



NEUROSCIENCE, fig 18.10 A, p. 465

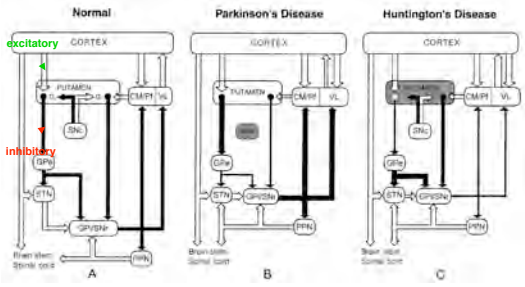
The dopaminergic cells of the substantia nigra (pars compacta - compact or cellular part) make a pigment (neuromelanin) as a by-product of dopamine synthesis which identifies them and the region to the naked eye. These cells are lost in persons with Parkinson's Disease (PD). Compare left (normal) to right (PD) in these sections through the midbrain.



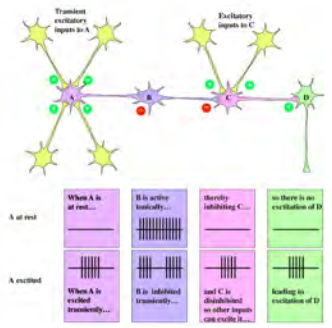
THE BRAIN ATLAS, 3rd ed p 235

Dopaminergic Pathways

(See NEUROSCIENCE, fig 18.11, p 467)



NEUROSCIENCE, Fig 18.6 p 460



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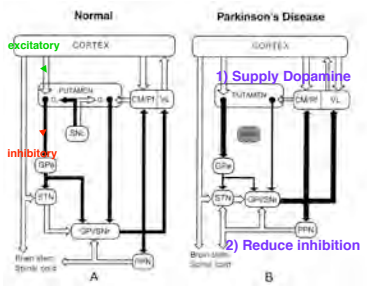
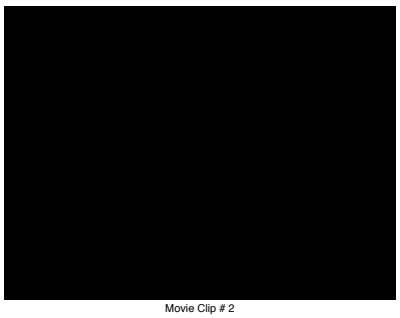
(See NEUROSCIENCE, fig 18.11, p 467)

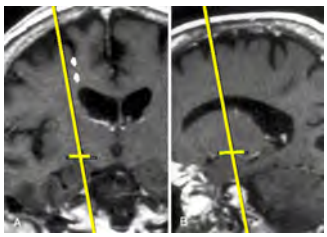


L-DOPA relieves the tremors and paralysis but can produce involuntary (choreiform) movements

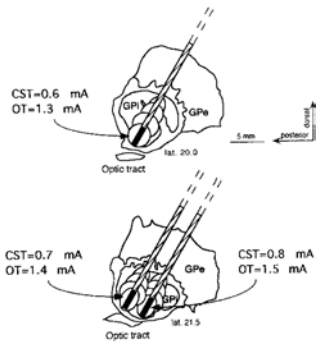


Movie Clip # 2

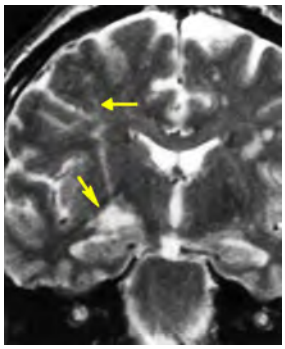
This is a perioperative MRI of a patient whose PD was relieved by lesions of the internal part of the globus pallidus in the coronal (left) and parasagittal (right) planes.



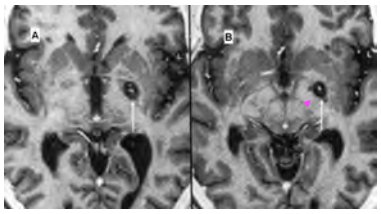
To release inhibition of the thalamus, the source of fibers to the thalamus in the globus pallidus is lesioned. This mimics (under control) a stroke that "cured" a patient of PD. These drawings of images in the coronal plane show the planned trajectory to target electrodes and the resulting electrolytic lesions (circles). The procedure is done in awake patients and accuracy of the targeting of the electrodes is determined by imaging and stimulating the brain. Currents necessary to activate nearby structures the optic tract (OT) and the cortical spinal tract (CST) are indicated.



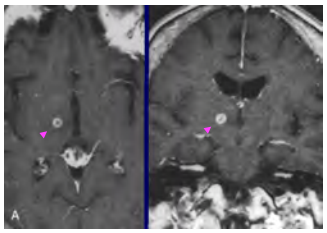
This is a post operative MRI in the coronal plane of a patient whose PD was relieved by lesions of the internal part of the globus pallidus. The upper arrow shows the reaction along the electrode tract; the lower arrow changes in the globus pallidus (compare to the opposite side.)



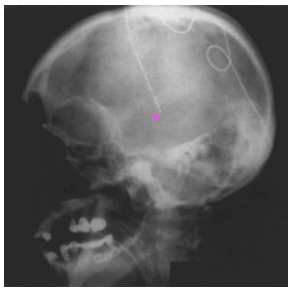
This is a post operative MRI of a patient whose PD was relieved by lesions of the internal part of the globus pallidus. The images in the axial plane show that the globus pallidus is missing (arrows). (Compare to intact GP on the opposite side.) In this plane the proximity of the GP to the posterior limb of the internal capsule in which axons of the corticospinal tract travel is apparent (arrow).



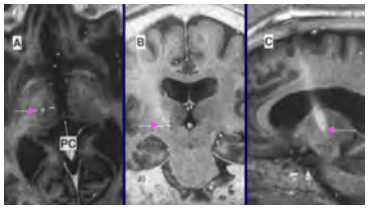
This is a post operative MRI of a patient whose PD was relieved by lesions of the thalamus. The images in the axial plane show (left) and in the coronal plane (right) show the lesion site (arrows). (Compare to intact thalamus the opposite side.)



This is a post-operative X-ray of a patient whose PD was relieved by electrical stimulation of the globus pallidus. Film in the lateral (side) projection shows the electrode site (arrow). The wires connect to a controllable stimulator usually implanted under the skin of the chest.



These are post-operative MRIs of a patient whose PD was relieved by electrical stimulation of the subtalamic nucleus. The axial, coronal and sagittal planes (left to right) show the position of the stimulating electrode in the target.



When the electrode is targeted the tremors cease

Movie Clip # 3

Parkinsonism

- Treatment:
  - a) replace missing DA - levodopa; transplant
  - b) counter tonic imbalances - make lesions; stimulate
- Long Term Changes: improvement with drugs and others above
- Brain Science: DA, pathways, model of treatment for other brain diseases
- Prevention – if there are contributions from the environment.

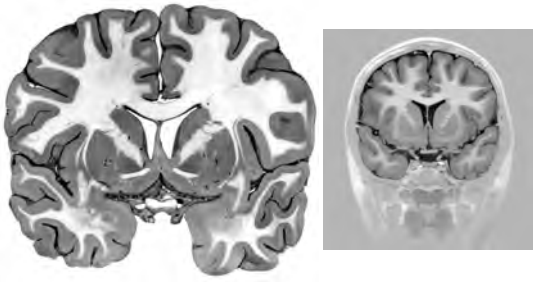
Parkinsonism

Shows prominent deficits with loss of neurons making dopamine. The disease has been mimicked by a toxin and can be treated by increasing the levels of dopa (levodopa), possibly by transplanting or engineering dopa producing cells (particularly stem cells) in the vicinity of the basal ganglia, or by restoring balance to the "extrapyramidal" circuit by lesions (mimics "cures" by stroke) or by stimulation (may work as a reversible or intermittent lesion).

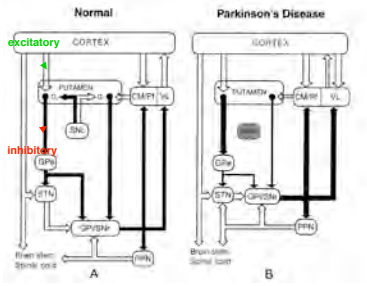
Two weeks later with the stimulator off the tremor returns; with the stimulator on it ceases

Movie Clip # 4

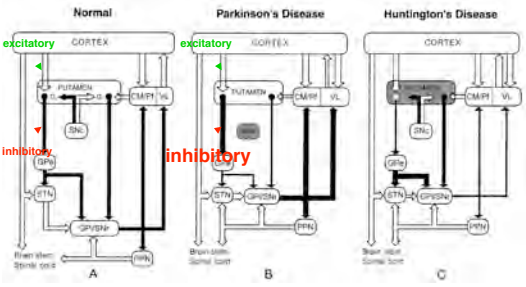
THE BRAIN ATLAS, 3rd ed pp 59, 60



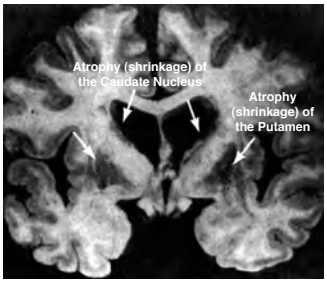
(See NEUROSCIENCE, fig 18.11, p 467)



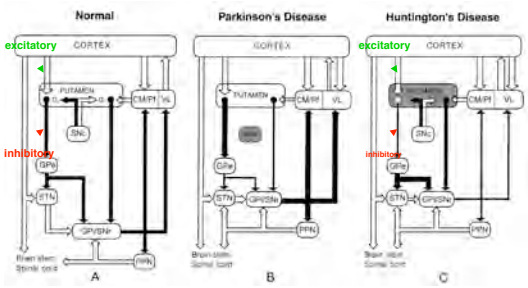
(See NEUROSCIENCE, fig 18.11, p 467)



Huntington's disease is an autosomal dominate condition (the gene is called Huntingtin) in which affected individuals have movement disorders characterized by writhing sinuous involuntary movements called chorea (as in choreography for dancing). Cells of the **caudate nucleus** and **putamen** degenerate and these nuclei atrophy (shrink).



See NEUROSCIENCE, fig 18.11, p 467



L-DOPA relieves the tremors and paralysis but can produce involuntary (choreiform) movements

Movie Clip # 2

Stimulators allow modulation of Rx in real time. Here the patient walks out of the hospital on her way home.

Movie Clip # 5

Science, medicine ≠ ignorance, politics

What this lecture was about:

- Motor Systems a Reprise
- Pyramidal and Extrapyramidal (Basal ganglia)
- Parkinsonism a Movement Disorder
- Mechanisms and Treatment Strategies

END