

Parkinson's Disease

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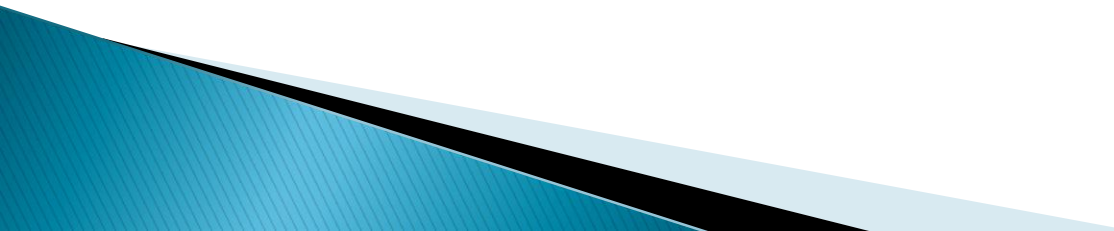
Parkinson Incidence

- 1.5 Million people affected worldwide
- 1% of Americans >50 years old
- About 40,000 cases diagnosed annually
- Male to female 3:2
- Despite promising research, no cure exists
- Direct health-related expenses, indirect disability expenses and lost productivity in the U.S. amount to 25 million annually*
- Anti-parkinsonian drugs cost insurers and patients \$1,000 to \$6,000 per year*

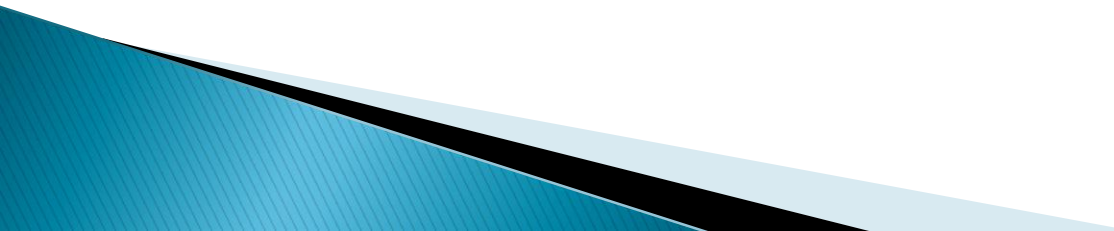
Parkinson's Disease Impact

- ▶ Direct cost: \$ 10,349 per patient per year
 - ▶ Indirect annual cost: \$25,326
 - ▶ Compared with controls
 - More neuropsychiatric complications
 - More falls
 - More autonomic dysfunction
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- 1. Huse DM, et al. *Mov disord.* 2005;20:1449–1454.
 - 2. Whetten–Goldstein K, et al. *J Am Geriatr Soc.* 1997;45: 844–849. Adjusted to 2002 price levels

Parkinson's Disease Defined

- Parkinson's Disease (PD) – a complex, progressive and degenerative neurological disorder that causes loss of control over body movements
 - Brain cell degeneration occurs in the pars compacta of the substantia nigra causing a decrease in the chemical messenger dopamine
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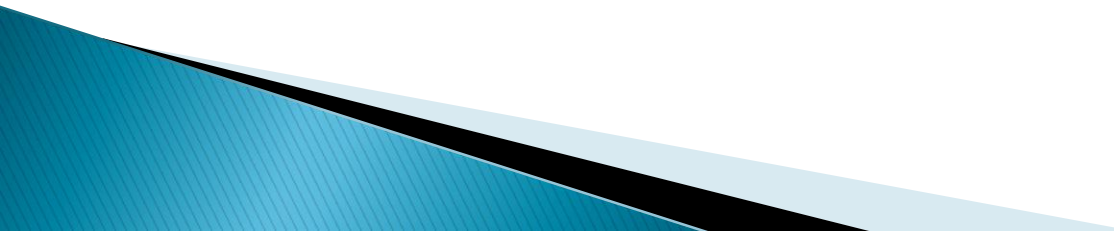
James Parkinson

- The major symptoms of the disease were originally described in 1817 by an English physician, Dr. James Parkinson, who called it "Shaking Palsy." Only in the 1960's, however, pathological and biochemical changes in the brain of patients were identified, opening the way to the first effective medication for the disease.
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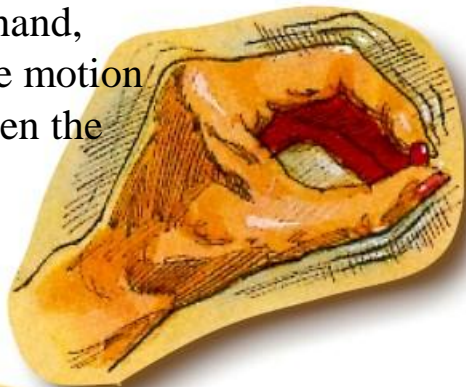
Symptoms which can predate diagnosis of PD

- Loss of sense of smell (anosmia)
- REM sleep behavior disorder
- Constipation

Parkinson's Disease Symptoms

- Rest tremor (4–7Hz)
 - Bradykinesia/akinesia
 - Rigidity
 - Postural instability
 - Decreased vocal tone
 - Cognitive dysfunction
- 

Rhythmic tremor often occurs at first in one hand, where it resembles the motion of rolling a pill between the thumb and forefinger



Leaning forward or backward when upright reflects impairment of balance and coordination.



Muscle rigidity shows itself in the cogwheel phenomenon: pushing on an arm causes it to move in jerky increments instead of smoothly.



Difficulty rising from a sitting position is a common sign of disordered control over movement. Some patients report feelings of weakness and of being constrained by ropes or other forces.

Risk factors for PD

- Age is strongest predictor of increased risk
- Genetic factors; family history of parkinsonism
 - ◉ 5% have genetic causes
 - ◉ Multiple genes have been identified
- Other risk factors include
 - ◉ Exposure to environmental toxins
 - Herbicides, pesticides and heavy metals

Risk Factors

- Increased risk
 - Age
 - Family history
 - Head injury
 - Exposure
 - Well water
 - Pesticides

Parkinsonism

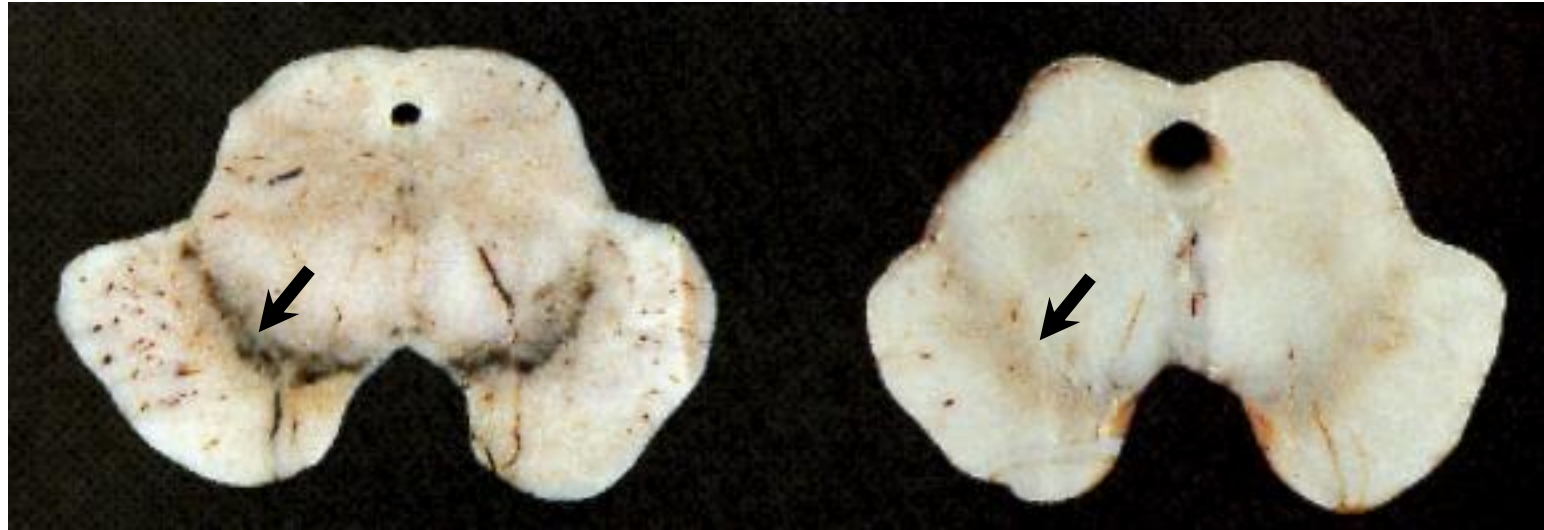
- Primary (idiopathic)–Parkinson's Disease
- “Parkinson's Plus”–Multisystem
 - Multisystem atrophy, progressive supranuclear palsy, corticobasal deg., etc
- Degenerative parkinsonism
 - Huntington's, Wilson's
- Secondary (acquired)
 - Infectious, drug, infarct, toxin, etc

Causes of Parkinson's Disease

- Degeneration of the brain's substantia nigra reduces dopamine
- Lack of dopamine hinders communication between brain cells involved in motor control, which leads to symptoms

Normal

Parkinson's

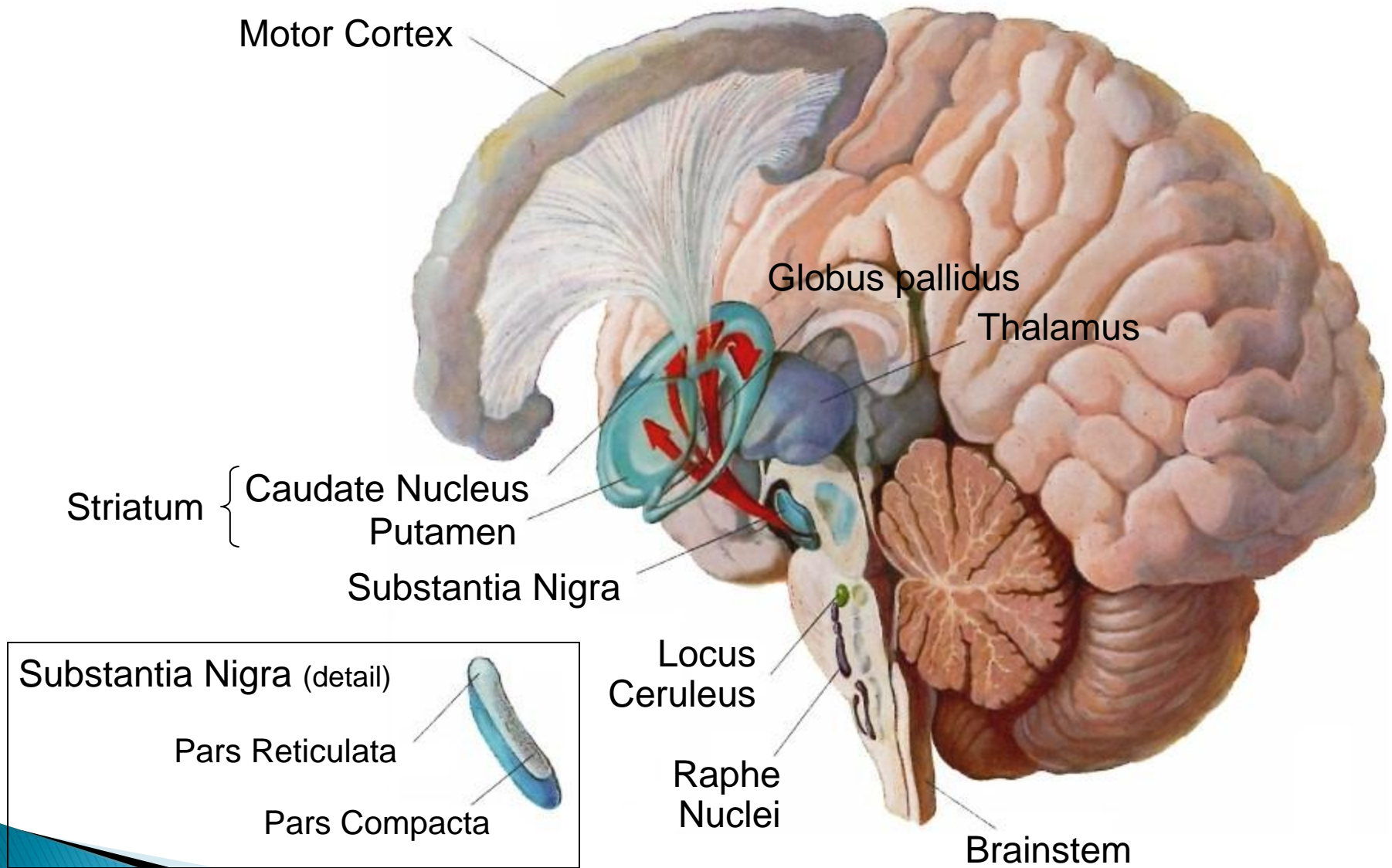


The pars compacta region of the substantia nigra in the normal brain appears dark because dopamine-producing neurons are highly pigmented; as neurons die from Parkinson's disease, the color fades.

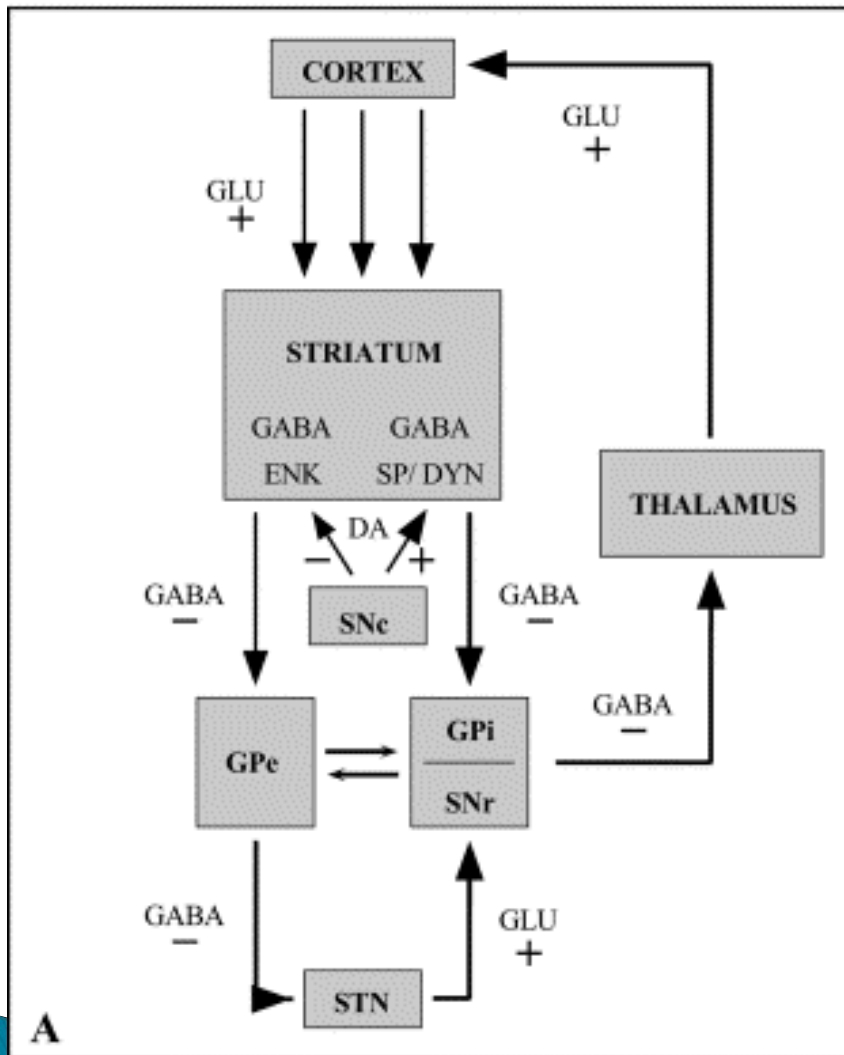
Diagnosis of PD

- Diagnosis of PD is based on
 - Clinical examination
 - Established diagnostic criteria (eg; United Kingdom Parkinson's disease Society Brain Bank criteria) UPDRS
 - Presence of premotor symptoms, such as olfactory impairment, constipation and REM sleep behavior disorder may raise the index of suspicion for PD
 - No definitive diagnostic imaging test is currently available for the diagnosis of PD
 - FDG PET Scan
 - DaTscan may help differentiate between presynaptic dopamine deficiency driven parkinsonism and non-parkinsonian syndromes, but does not confirm PD diagnosis

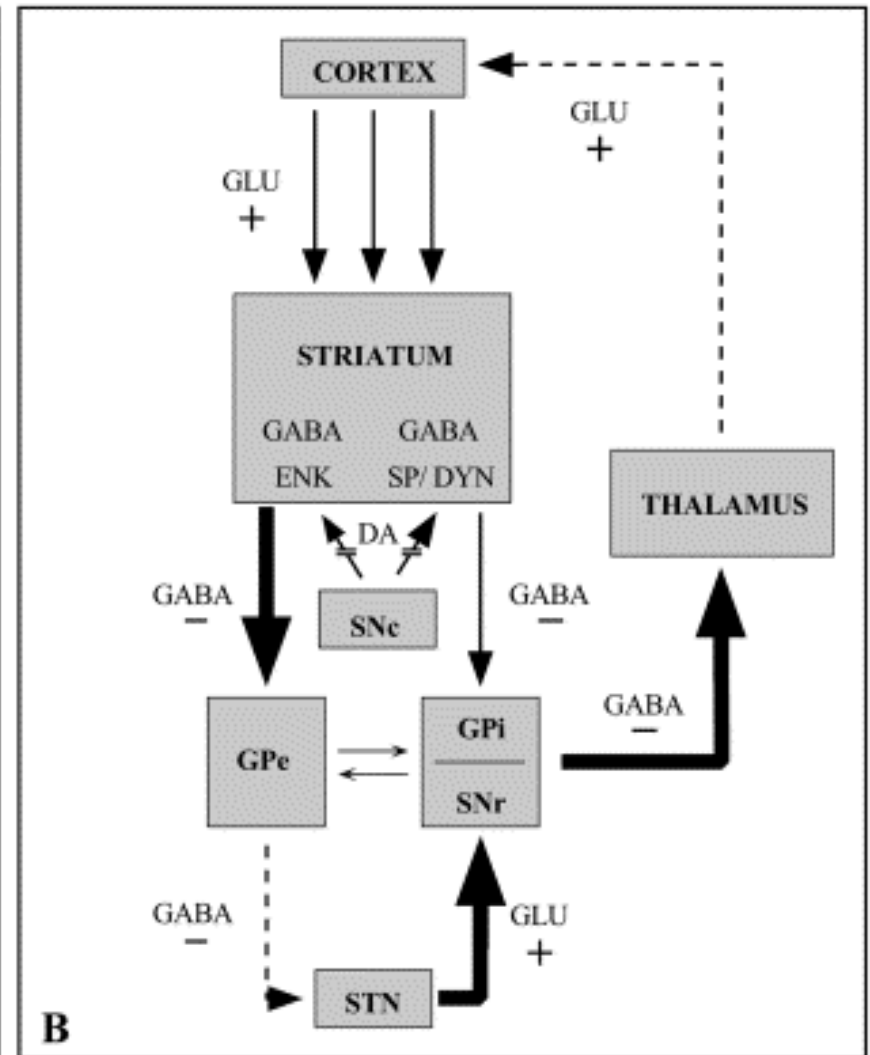
Brain Regions Affected by Parkinson's Disease



NORMAL



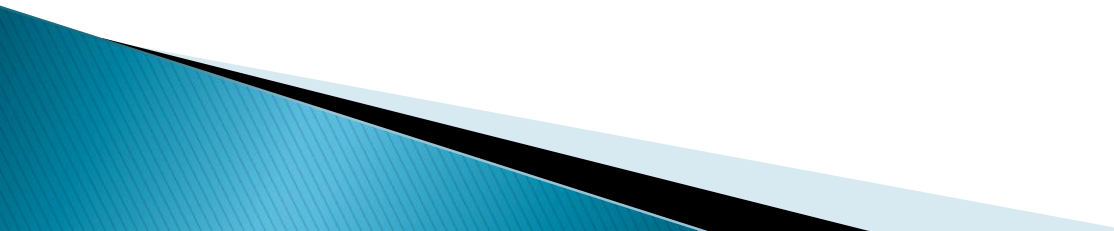
PARKINSON




Non-pharmacologic considerations

Physical Therapy	<ul style="list-style-type: none">• GOALS: Improve motor function Increase range of motion Build endurance• Techniques: counting steps, marching, visual fixation, balance training• Can be helpful for symptoms such as stooped posture, shuffling and other gait disturbances, difficulty rising from chairs
Occupational Therapy	<ul style="list-style-type: none">• Concentrate on fine finger and hand movements• Techniques: adaptive equipment, energy conservation, range of motion
Speech therapy	<ul style="list-style-type: none">• Concentrate on speech impairments and swallowing difficulties• Techniques: voice projection and vocal exercises
Diet	<ul style="list-style-type: none">• Patients should maintain a well-balanced diet• Meals rich in animal protein may reduce the absorption of levodopa

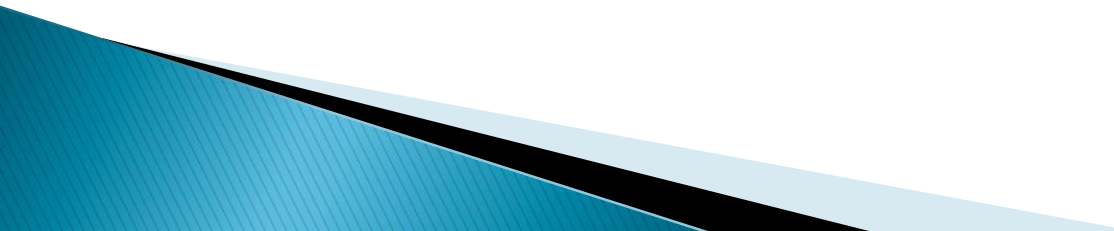
Pharmacotherapy

- Carbidopa/levodopa
 - Dopamine Agonists
 - COMT inhibitors
 - Monoamine oxidase B inhibitors
 - Anticholinergics
- 

Dopamine Replacement

- Levodopa/Carbidopa (Sinemet)
 - Stalevo (combination of Sinemet and Comtan)
 - Mechanism: precursor to dopamine once converted, releases dopamine into synapse and attaches to dopamine receptors
 - 50% of PD patients develop motor fluctuations after 5–7 years of levodopa therapy
 - 70% after 15 years
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Dopamine Agonists (DA)

- Bromocriptine (Parlodel)
 - Pergolide (Permax)
 - Pramipexole (Mirapex)
 - Ropinirole (Requip)
 - Mechanism: mimic dopamine and act on dopamine receptors in the brain
 - Side effects drowsiness, nausea, vomiting, dry mouth, dizziness, orthostatic hypotension. At higher doses, DAs may cause confusion, hallucinations, or psychosis
- 

Catecholamine-O-Methyltransferase (COMT) Inhibitors

- Entacapone(Comtan)
- Tolcapone (Tasmar)–Risk of acute fulminant liver failure—monitor LFT's closely
- COMT inhibitors increase the availability of a dose of levodopa by inhibiting COMT (catechol O-methyltransferase), an enzyme that breaks down levodopa before it can be converted to dopamine in the brain

Dopaminergic Therapy: Impulse Control Disorders

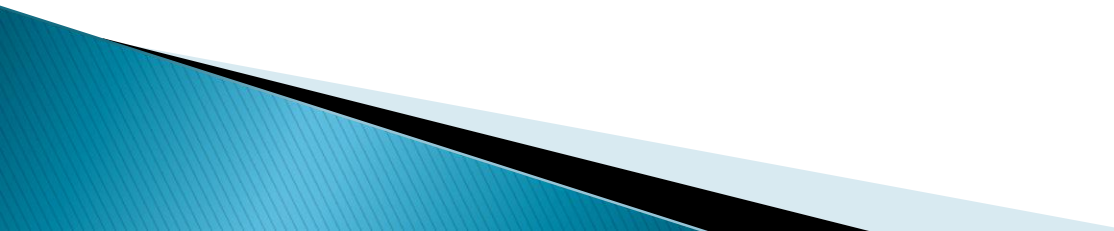
- ▶ Pathological, socially devastating symptoms^{1,2}
 - Compulsive buying (6%), compulsive gambling (55) binge eating (4%) hypersexuality (4%)

Prevalence of ICDs²

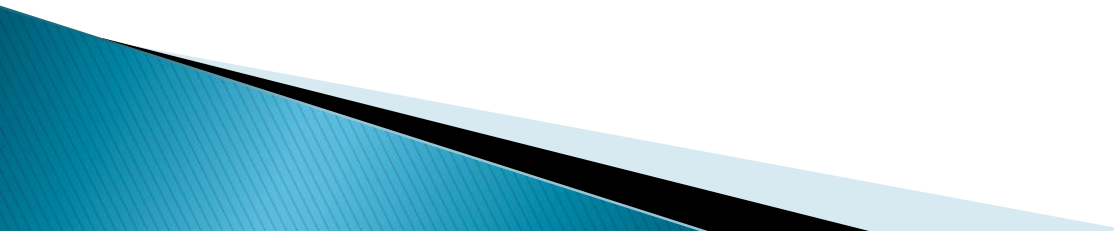
- Overall : 13.6%
- On dopamine agonist therapy : 17.1%
- Greater risk at upper end of therapeutic range
- Rare with levodopa(0.7%)³

- 1. Park A, Stacy M. Parkinson Dis 2011 Epub Apr 11
- 2. Weintraub D, et al Arch Neurol 2010; 67: 589–595
- 3. Voon V, et al. Neurology. 2006; 67 1254–1257

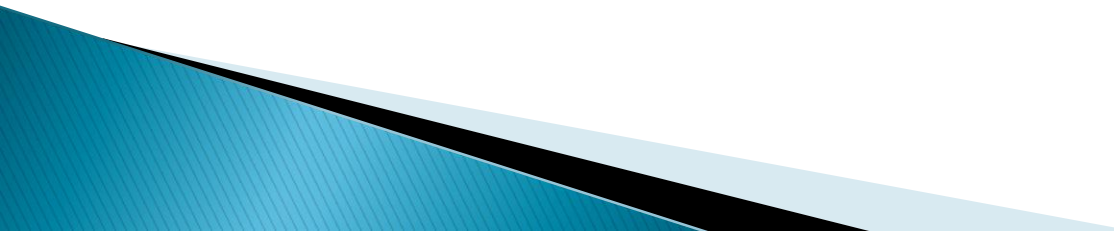
Antiglutamatergics

- Amantadine(Symmetrel)
 - Dextromethorphan(Delsym)
 - Mechanism: dopaminergic though possibly affecting other neurochemical pathways
 - Useful for lessening motor fluctuations and dyskinesias caused by long term use of Levodopa
 - Side effects: insomnia, daytime fatigue, anxiety, dizziness or hallucinations
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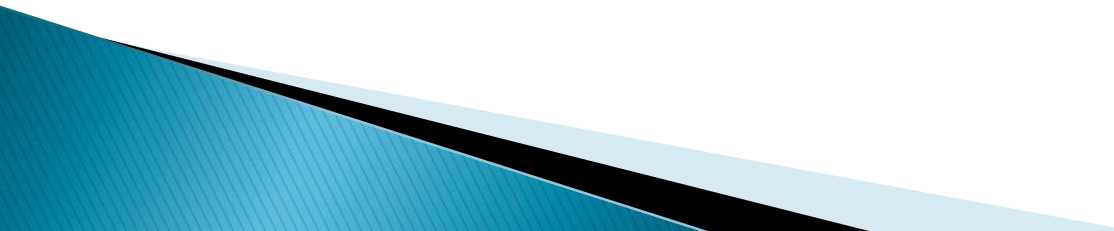
Monoamine oxidase B inhibitors

- Selegiline (Deprenyl or Eldepryl)
 - Mechanism: prevent the breakdown of levodopa
 - Caution: Increased risk of hypertensive crisis as well as a serotonergic crisis if given along with selective serotonin reuptake inhibitors or meperidine
 - Can cause agitation, insomnia, vivid dreams or hallucinations
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Rasagiline/Azilect

- selective irreversible MAO-B inhibitor
 - Neuroprotective
 - Stabilizing mitochondrial membrane potential is critical
 - Rasagiline inhibits activation of the apoptotic cascade triggered by dopamine neurotoxins and oxidative stress. Apoptosis is an active process of programmed cell-death induced by exposure to neurotoxins.
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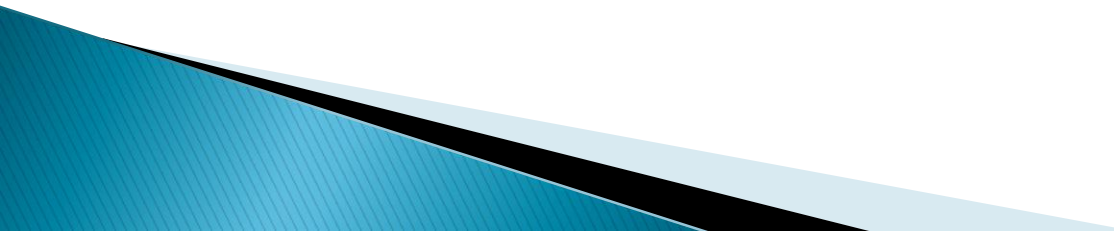
Anticholinergics

- Trihexypneidyl (Artane)
 - Biperiden (Akineton)
 - Benztropine (Cogentin)
 - Typically used for refractory tremors
 - Caution: increased confusion can be one of the significant side effects of anticholinergics. Other side effects may include dry mouth, sedation, delirium, hallucinations, constipation, and urinary retention
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Parcopa

- Sinemet in an orally dissolving tablet
- Faster onset of action often used for patients with significant freezing

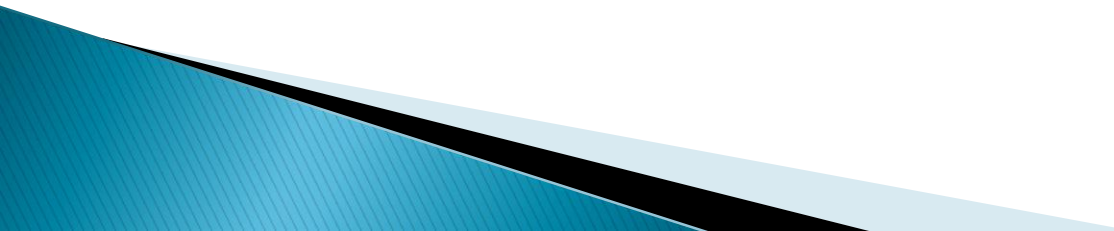
Apokyn(Apomorphine)

- Apomorphine works by mimicking the action of dopamine, a natural substance in the brain that is lacking in patients with PD.
 - Should not be used if taking a 5HT₃ (serotonin) blocker such as alosetron (Lotronex), dolasetron (Anzemet), granisetron (Kytril), ondansetron (Zofran), or palonosetron (Aloxi).
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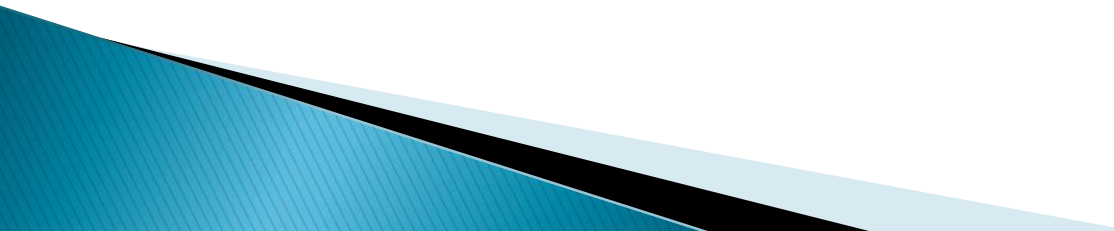
Medications Contraindicated in Parkinson's Disease

- Haloperidol (Haldol)
 - Chlorpromazine (thorazine)
 - Thioridazine (Mellaril)
 - Molindone (Moban)
 - Perphenazine/Amitriptyline (Triavil)
 - Metoclopramide (Reglan)
 - Prochlorperazine (Compazine)
- 

Movement Disorders with Surgical Treatment Options

- Parkinson's disease
 - Essential tremor
 - Dystonia
 - Spasticity
-
- **NOVEL STUDIES**
 - Alzheimer's
 - Cocaine addiction
 - Epilepsy
 - Refractory depression
- 

Goals of Surgery for PD

- Reduce motor fluctuations
 - Reduce total “off” time
 - Reduce side-effects of medication
 - Disabling dyskinesias, nightmares
 - Reduce/eliminate tremors
 - Primary function to reduce the motor symptoms of Parkinson's disease
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Pallidotomy

- destruction of part of the globus pallidus (GPi), Pallidotomy is most useful for the treatment of peak-dose dyskinesias and for dystonia that occurs at the end of a dose

Thalamotomy

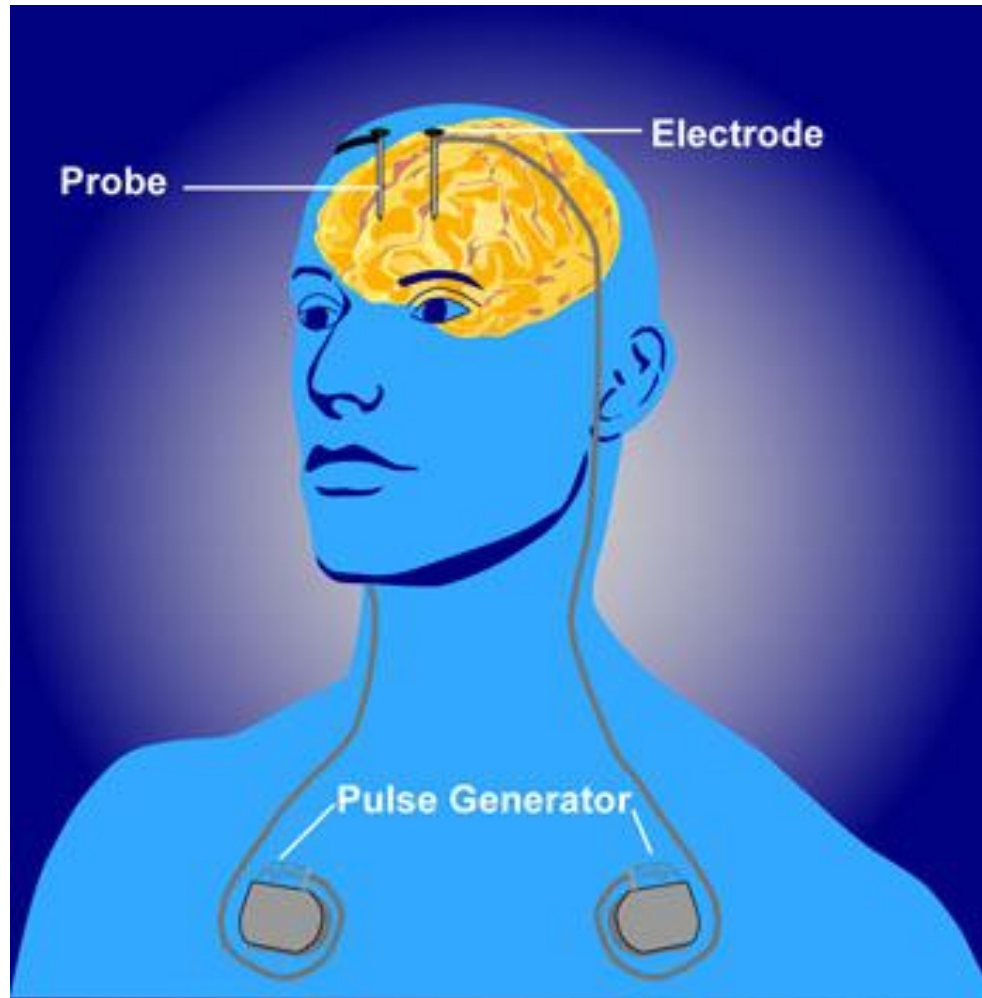
- **Thalamotomy** destroys part of the thalamus. Can be effective for the treatment of tremor, rigidity, and peak-dose dyskinesia. However, the risks of thalamotomy are increased structures and the potential for worsening some PD symptoms, including gait and speech difficulties. It can be an effective treatment, especially for tremor, in patients without pre-existing gait and speech problems.

DBS Therapy for Parkinson's

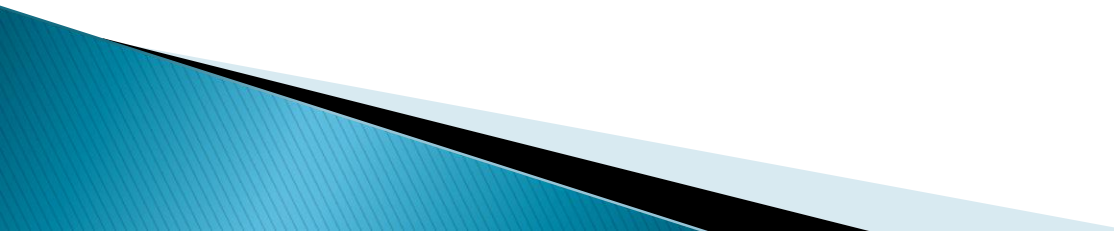
- Pacemaker-like technology delivers electrical pulses to targeted structures in the brain
- Electrical pulses may block brain signals that cause symptoms of Parkinson's disease
- Implanted device can be programmed non-invasively
- Therapy is reversible to preserve future therapy options



DBS System



Preoperative Evaluation

- Pet Scan
 - Neuropsychological testing
 - MRI
 - Videotaped on and OFF medications
 - Medical Clearance
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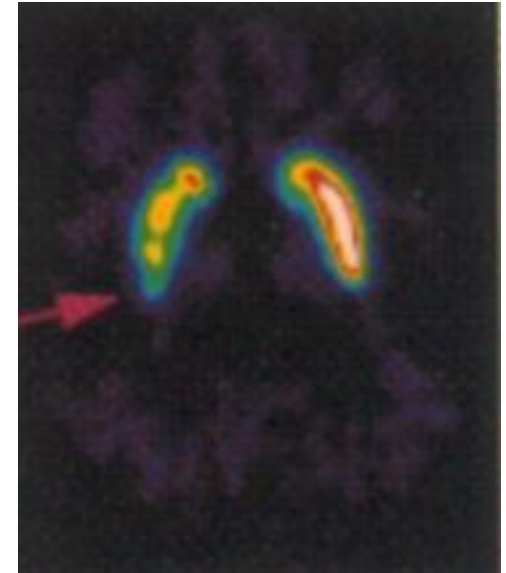
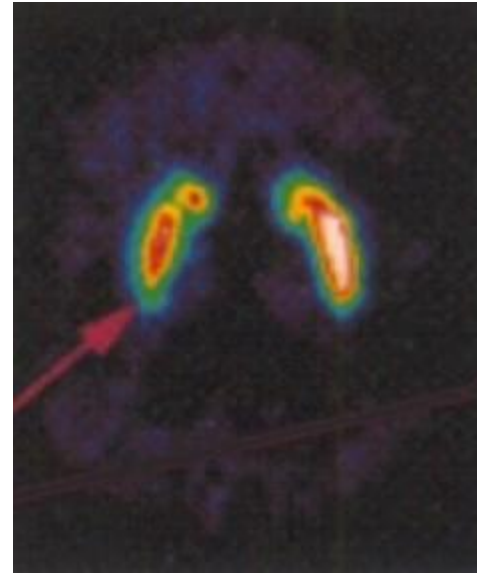
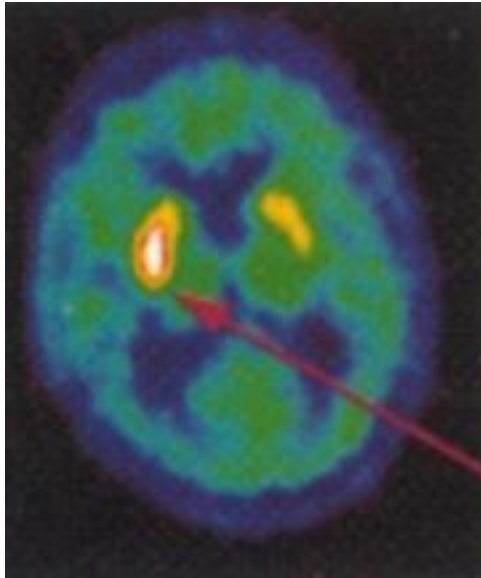
[¹⁴F]-Dopa

[¹⁴F]-Raclopride

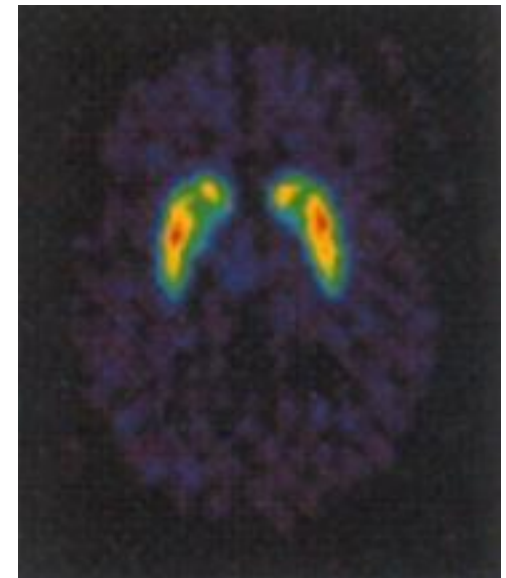
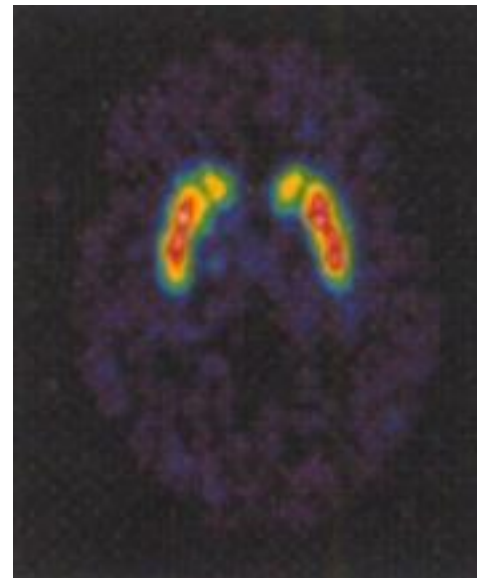
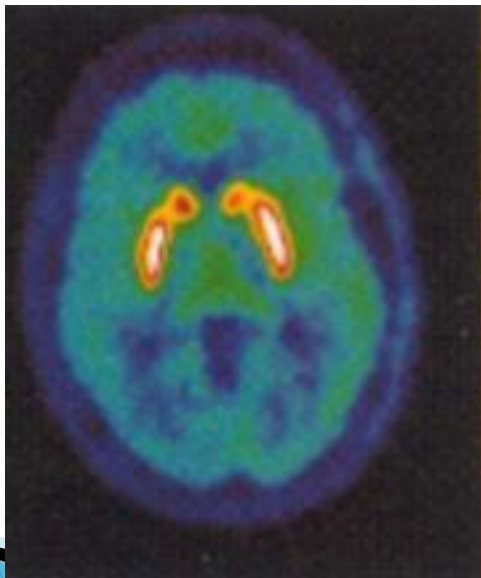
saline

methamphetamine

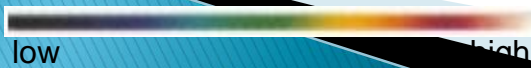
PD
patient



Normal
subject

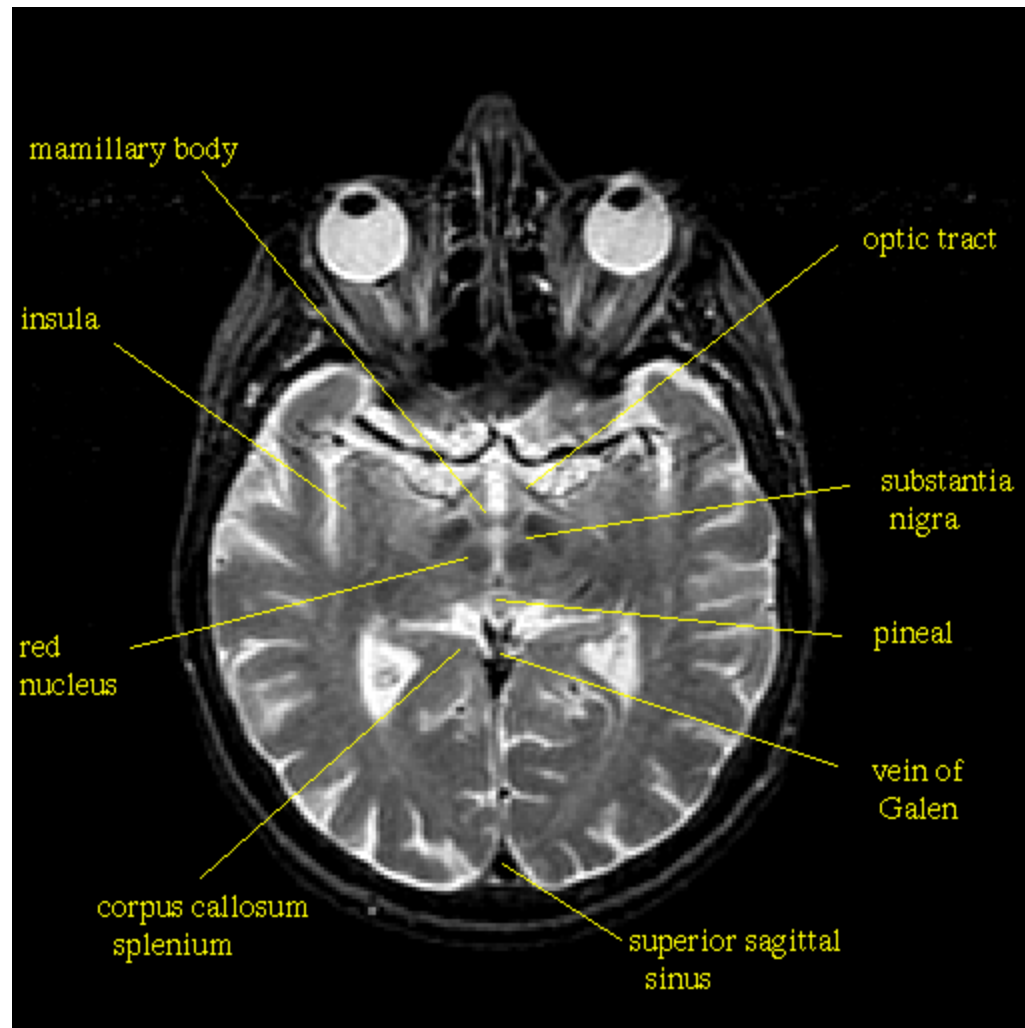


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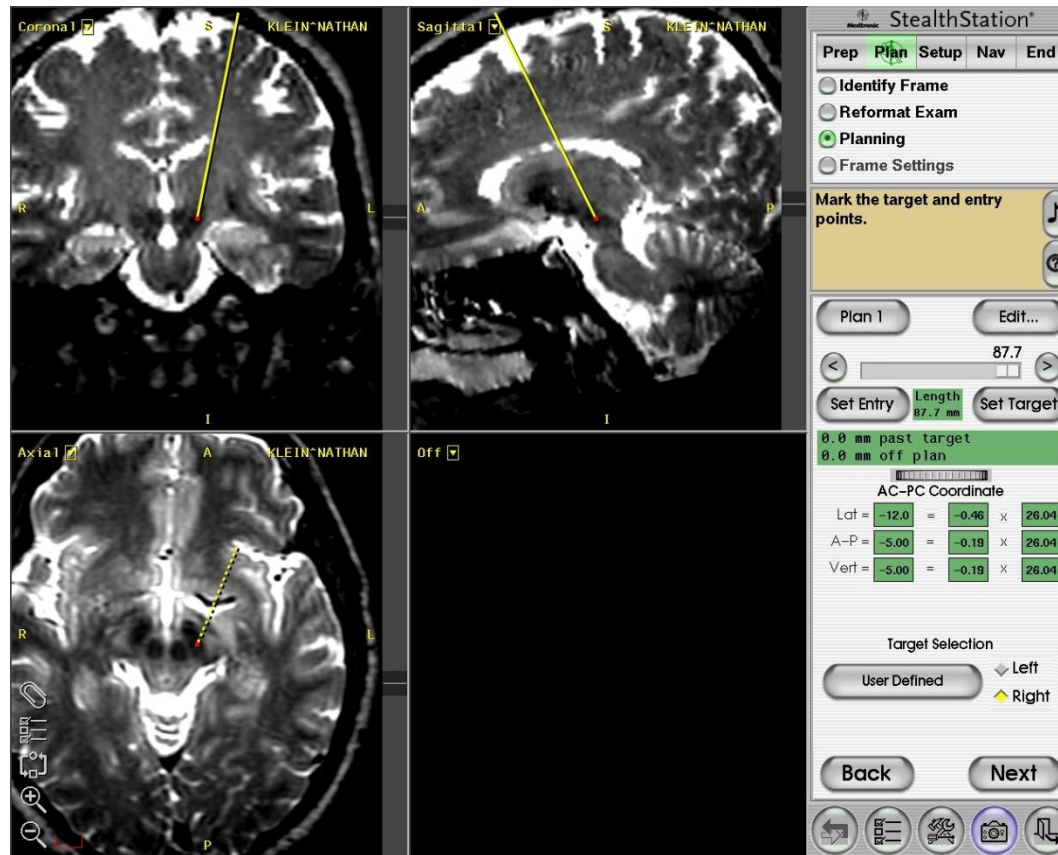


BP





Preoperative Planning

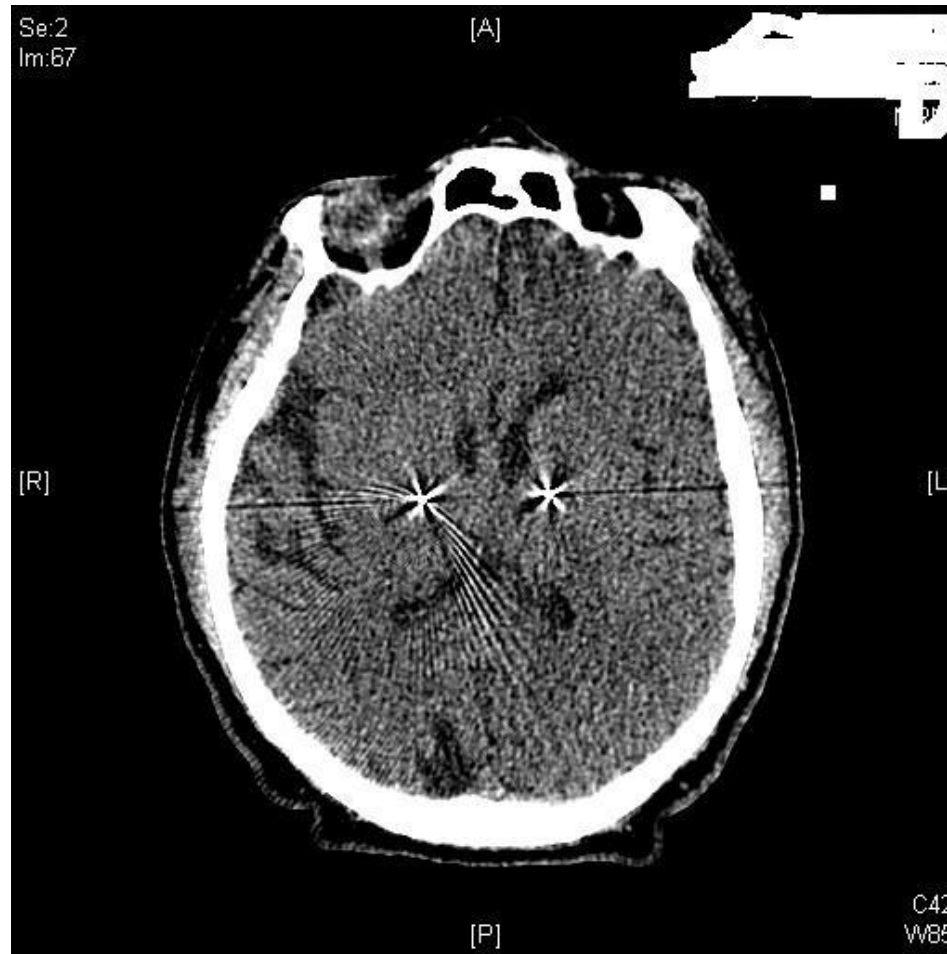


Complications of DBS

- Hemorrhage (1–2%)
- Infection (5–10%)
- Lead fracture (3–15%)
- Skin erosion
- Oddities

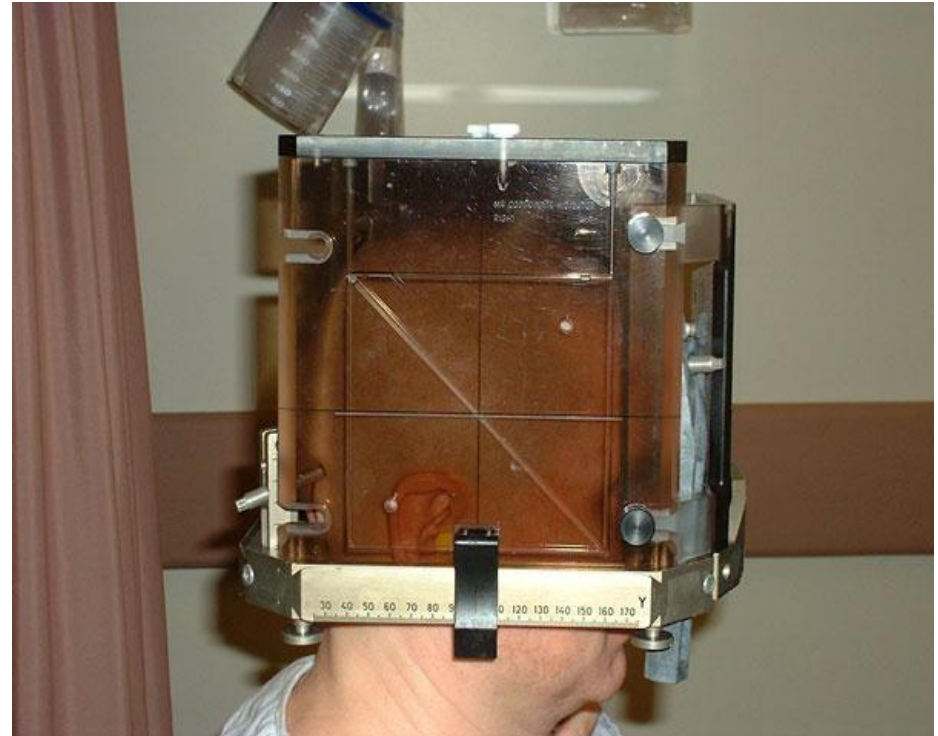


Post op CT with leads

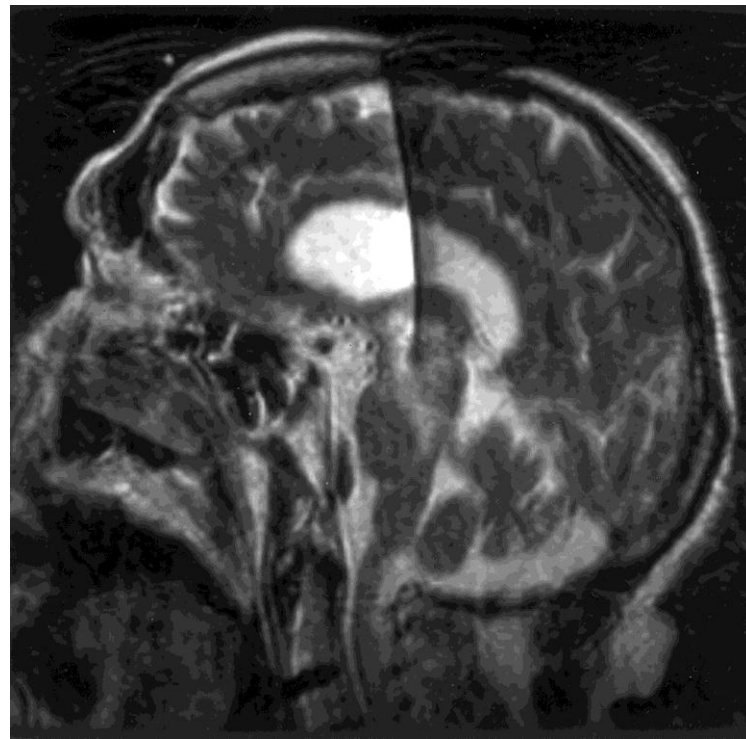


Sources of Error: Frame placement

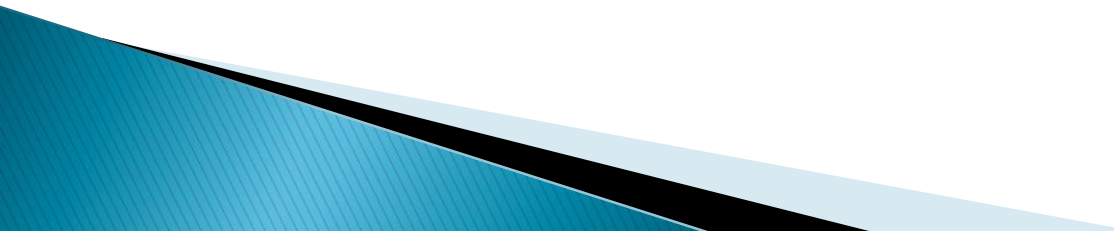
- **Frame placement**
 - Yaw (axial rotation)
 - Roll (coronal rotation)
 - Both can be minimized with ear bars
 - Pitch (sagittal rotation)
 - Optimal frame placement parallel to orbitomeatal plane (if no image software available)



Brainstem Lesion from Diathermy in DBS Patient



Nursing Considerations

- Restart Parkinson's Medications ASAP
 - Fall Risk
 - Cognitive Changes–Orientation
 - Aspiration Risk
 - Mobilize rapidly
 - Urinary Issues
 - No MRI with DBS unless special parameters met, post op CT is standard
 - DBS does NOT cure PD
- 

Thank you for your attention

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