Surgical Management of Movement Disorders

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Neurosurgery Teaching Rounds

In this session…

- Neurocircuitry
- Indications
- Surgical Targets
- Technical aspects of DBS
- Outcomes and Complications

NEURAL CIRCUITRY OF MOVEMENT DISORDERS

- animal models contributed significantly to understanding of underlying neurocircuitry of PD and other movement disorders.

- Provided data support the concept of cortico-striatal-pallidal-thalamic-cortical (CSPTC) circuits.

- Network of five parallel, segregated circuits exists that underlies a variety of functions.

CSPTC CIRCUITS

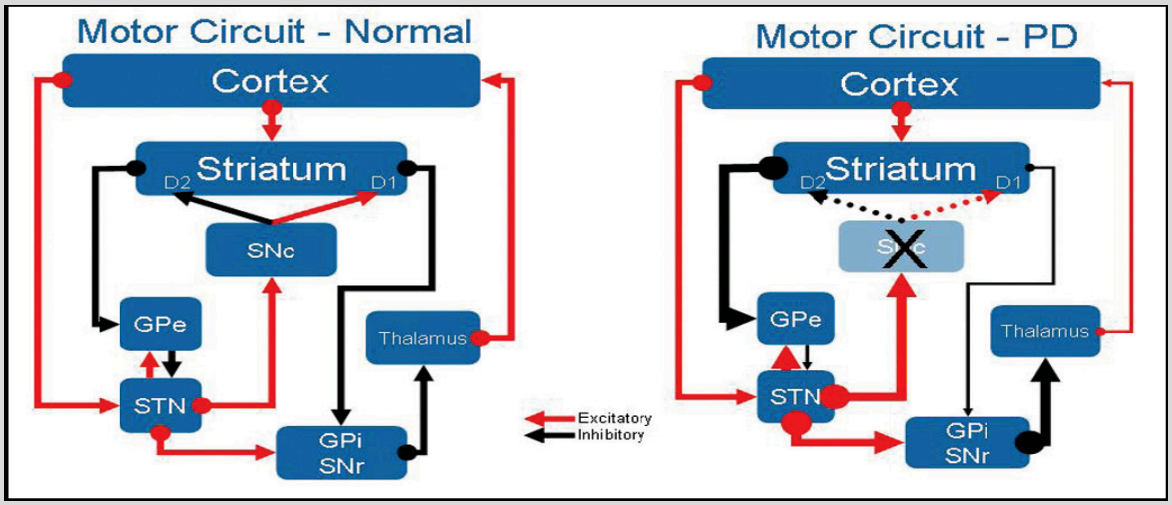
- Circuits originate in frontal lobes and then traverse through different nodes in the striatum, pallidum, and thalamus before returning to their cortical points of origin.

- Concept of CSPTC motor circuit or loop implies that **a number of the nodes involved in the circuit are potential targets for neuromodulation**

CSPTC CIRCUITS

- Circuit originates in the precentral motor regions.

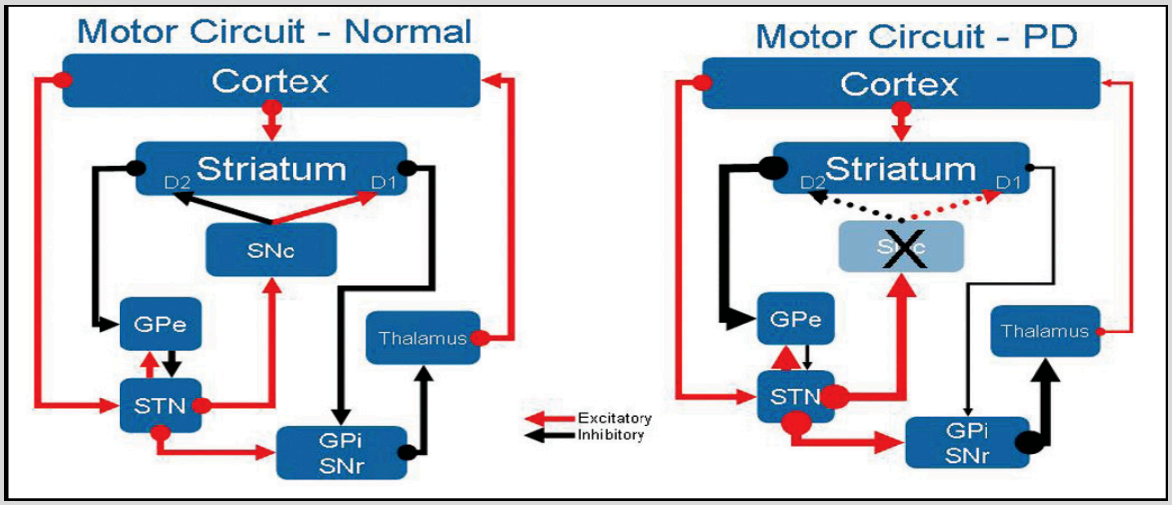
- Information in **direct pathway** passes monosynaptically from putamen to the output structures of the basal ganglia, the GPi, and the SNr.



CSPTC CIRCUITS

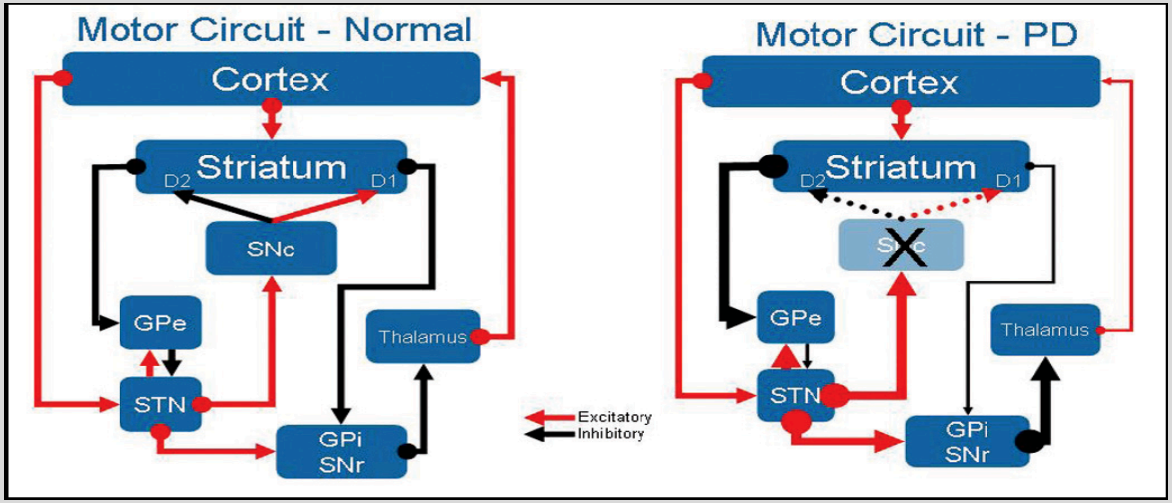
- Circuit originates in the precentral motor regions.

- Information from **indirect pathway** passes multisynaptically through globus pallidus externa (GPe) and the subthalamic nucleus (STN) before terminating on the GPi/SNr



CSPTC CIRCUITS

- Direct pathway is presumed to be responsible for initiation of action.
- Indirect pathway for braking of action or ability to switch from one action to another.

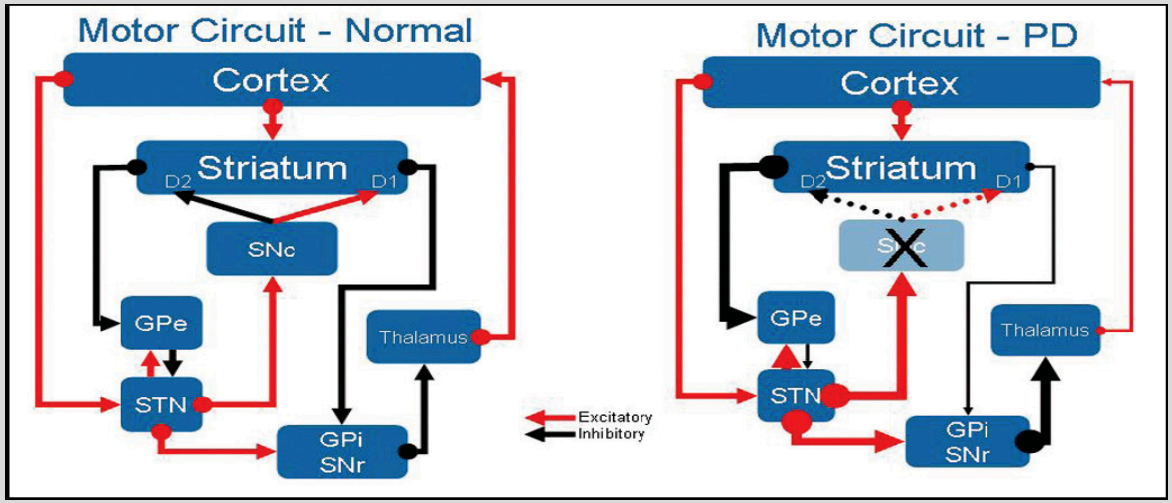


NEUROTRANSMITTORS

- **Dopamine** – one of the most powerful neurotransmitters influencing motor CSPTC circuit.
- Dopamine can have either excitatory or inhibitory role on striatal neurons, depending on dopamine receptor subtype:
  - D1 receptors are excitatory
  - D2 receptors are inhibitory.

CSPTC AND PARKINSON'S DISEASE

- PD – disorder characterized by dopamine loss in substantia nigra pars compacta, results in the classic motor symptoms of PD, including tremor, rigidity, bradykinesia, gait difficulties, and postural changes.



DYSTONIA

- Exact mechanisms are uncertain.
- No morphological changes involving specific components of CSPTC motor circuit have been consistently identified
- Motor GPi and ventral lateral (Voa/Vop) thalamus have been primary surgical targets for dystonia.

ESSENTIAL TREMOR

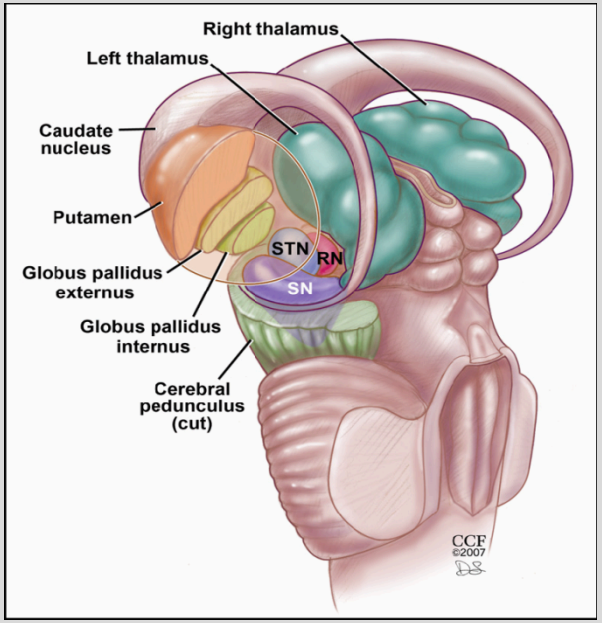
- Pathophysiology likely involves components of cerebellum, motor thalamus, and relevant frontal cortices, and, unlike PD and dystonia
- does not necessarily involve CSPTC circuit.
- Frontocerebellar circuits in which axons from cerebellum synapse on thalamic neurons that project to the cortex.
- Ablation of the cerebellar thalamus is highly effective in alleviating tremor.

SURGICAL TARGETS

Surgical Targets

- three important surgical targets include: GPi, STN and VIM

Parkinson's	STN and GPi
Dystonia	GPi
Tremor	VIM



PATIENT SELECTION CRITERIA

PREOPERATIVE CONSIDERATIONS

- Patients should be in stable overall health with respect to cardiac, pulmonary, and systemic conditions

- Neuropsychological assessment is recommended as a part of preoperative assessment to determine candidacy for neurosurgical intervention for treatment of movement disorder.

- Psychiatric conditions such as anxiety, depression, and mania must be identified and medically optimized by a specialist preoperatively.

PD: SELECTION CRITERIA

- Neurosurgery has been shown to consistently benefit only patients with idiopathic PD.
- Atypical parkinsonism (supranuclearpalsy, nigrostriatal degeneration, etc.) have not been shown to respond favorably to surgery.
- Surgery is most likely to benefit symptoms affecting the extremities rather than axial symptoms (posture, balance, gait, and speech).

PD: SELECTION CRITERIA

Symptoms in Surgical Candidates

- severe tremors
- off-medication-related rigidity
- freezing
- dystonia
- bradykinesia
- on-medication related dyskinesias
- significantly disabling on-off medication motor fluctuations.

- important predictors of neurosurgical treatment response is patient's response to L-dopa.
- Tremor is the only identified motor symptom that can improve with DBS regardless of response to off-on-medication testing.

Selection Criteria for Tremor

- once patients have failed medical management
- in general, patients with resting and distal tremor fare the best with surgery
- patients with intention or action tremor tend to have lesser benefits
- head, neck and tremors of lower extremity are more difficult to treat

Selection Criteria for Dystonia

- DBS most useful for patients with primary dystonia
- patients that are refractory to medical treatment (anticholinergics, baclofen, benzodiazepines) and botox are candidates
- patients with primary generalized dystonia as well as patients with idiopathic cervical dystonia can obtain the best motor benefits
- appendicular symptoms respond better than axial
- surgery for secondary dystonia less effective

DBS Surgery

MECHANISM OF DBS ACTION

- Placement of stereotactic lesions and DBS reflect two different methods of neuromodulation.

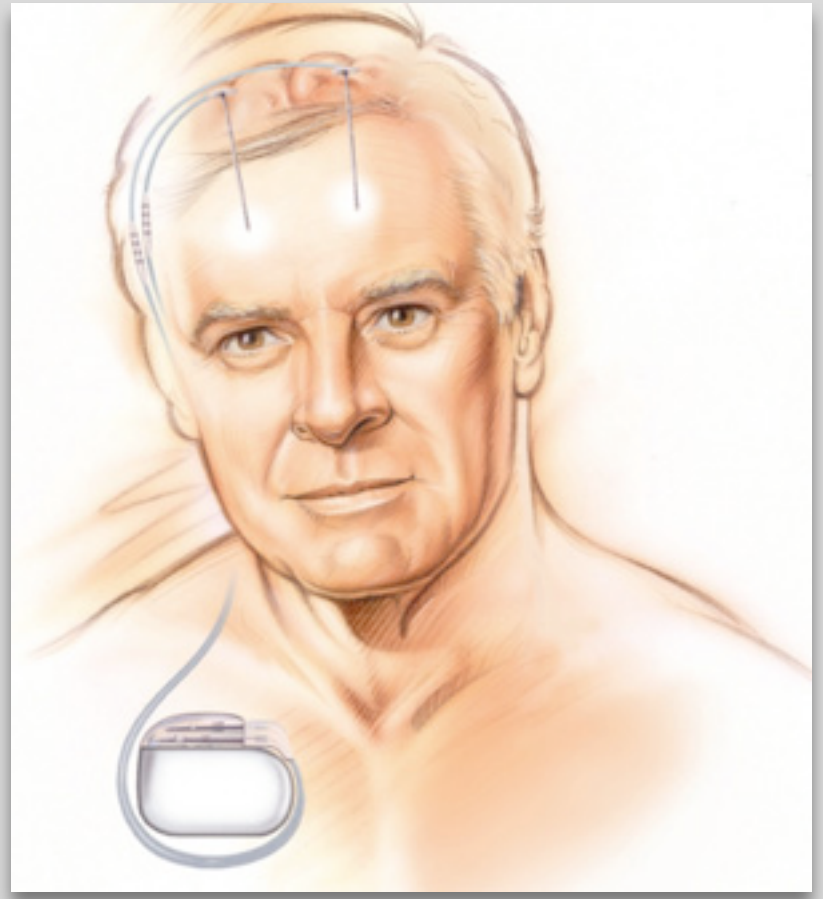
LESIONING VS. DBS

- Lesioning destroys a given volume of tissue
- DBS exerts a reversible electrical field on the surrounding nervous tissue elements.

DBS SURGERY

- Most common surgical treatment for movement disorders today.
- Surgical technique has its foundation in stereotactic principles.
- Evolved from strong reliance on stereotactic atlases and incorporates advances in imaging and neuro-physiological mapping techniques.

Components of DBS



STEREOTACTIC ANATOMIC TARGETING

PHYSIOLOGICAL TARGET VERIFICATION

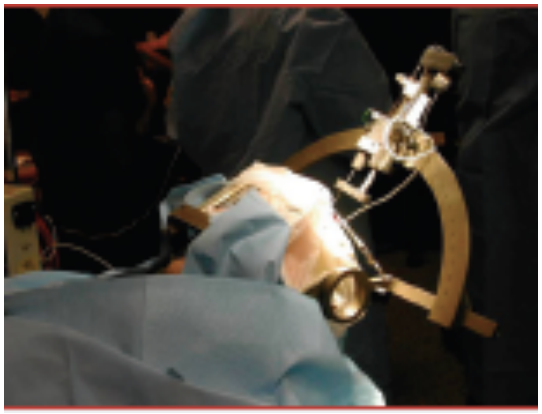
DBS LEAD IMPLANTATION

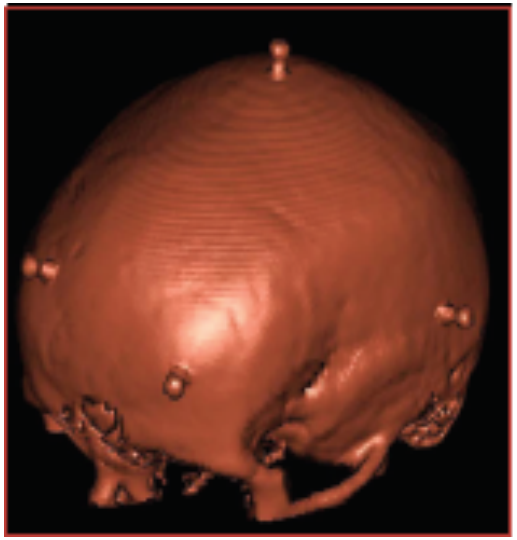
IMPLANTABLE PULSE GENERATOR

HEADFRAMES AND ACQUISITION OF STEREOTACTIC COORDINATES

- **Frame-based VS Frameless Systems**

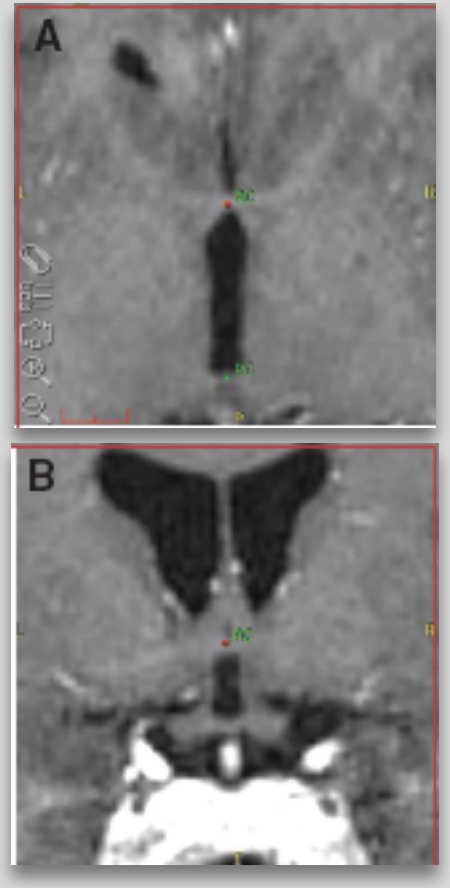
The frame-based approach is the “gold standard” that has been used for many years with proven precision and reliability.

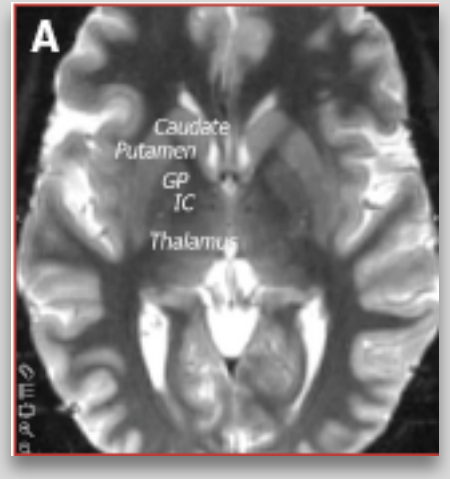


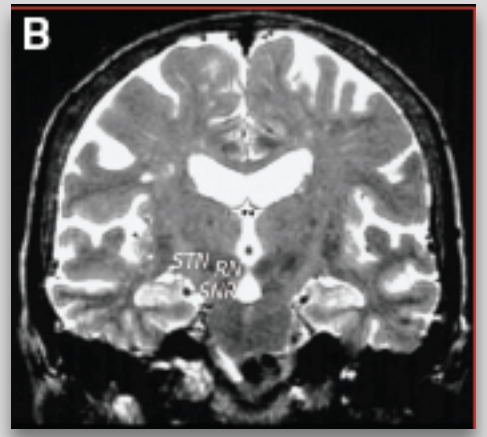


Direct Anatomic Targeting

- target localization can be done based on high resolution MRI imaging.







Indirect Targeting Formulas and Brain Atlas Approaches

- Indirect targeting techniques use the stereotactic coordinates of the AC and the PC as determined by imaging
- The locations of the STN, GPi, and VIM can be subsequently determined based on their average anatomic distances with respect to the AC, PC, and midcommissural point (MCP).

Indirect Targeting Formulas and Brain Atlas Approaches

STN	11-13mm lateral to midline, 4-5mm ventral to AC-PC plane and 3-4 mm posterior to the MCP
GPi	19-21m lateral to the midline, 2-3mm anterior to the MCP and 4-5mm ventral to the AC-PC plane
VIM (upper extremity)	11-12mm lateral to wall of third ventricle at the level of the AC-PC plane and anteroposterior location between two and three twelfths of the AC-PC distance anterior to the PC

Trajectory Planning

- Imaging is necessary for accurate targeting as well as for planning of the surgical trajectory to the target.
- The strategy is to avoid surface and sub cortical vessels and to have an angle of approach that passes through a large segment of the structure of interest.
- The precise entry point may be refined on the planning console, such that the trajectory passes through the crown of a gyrus rather than into a sulcus
- as well as away from the vessels associated with the wall of the ventricle, thereby helping to avoid hemorrhagic complications

Neurophysiological Monitoring

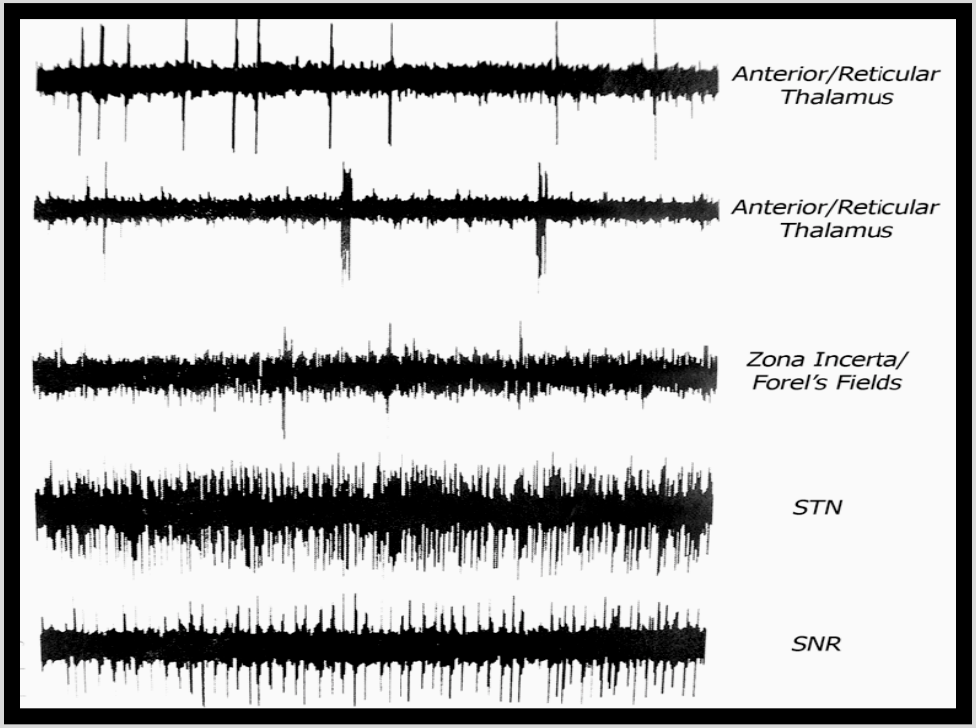
- physiological confirmation of surgical targets is necessary following anatomical localization
- crucial as there may be image distortion, brain shift, CSF loss...all factors which can alter location of target at time of surgery
- optimizes clinical outcome
- techniques include:
  - microelectrode recording
  - semi-MER
  - macrostimulation
  - DBS lead stimulation

MICROELECTRODE RECORDING

- microelectrodes are made of tungsten or platinum/ iridium.
- microelectrodes have high impedances with a tip diameter in the range of 2 to 4 μm
- These microelectrodes are capable of recording single units as well as delivering stimulation in the micro amp range (typically 100 mA).
- A hydraulic or electrical micro drive is used to advance a microelectrode
- can use single or multiple microelectrodes

MICROELECTRODE RECORDING

- recorded information allows one to determine location of electrode tip relative to target



sample recording with STN as the target of interest

MICROELECTRODE RECORDING

- when targeting the GPi, general strategy includes:
  - map long segment of sensorimotor GPi
  - determine border between GPe and GPi
  - identify the optic tract at the bottom of the trajectory by VEP
  - distinguish the internal capsule

DBS Lead Implantation

- once target has been identified, trajectory has been planned and target location has been confirmed with physiological localization, may implant DBS lead
- perform DBS intraoperative test to look for response
  - monitor tremor, rigidity and bradykinesia
- larger the difference between clinical threshold and side effects threshold, the better the therapeutic window
- once in place, lead is secured to cranium and tunneled through scalp in preparation for connection with the IPG

Implantation of Pulse Generator

- steps include placement of the pulse generator and extension lead connection DBS to IPG
- can be done same day or in delayed fashion
- IPG usually placed in a infraclavicular subcutaneous pocket

Outcomes and Complications

OUTCOMES OF DBS FOR MOVEMENT DISORDERS

- More than 1000 published articles pertaining to DBS for movement disorders.
- Reversibility feature (turning DBS on and off) on-demand allows for controlled, blinded assessments, making it one of the better-studied neuro surgical interventions.
- Validated rating scales for movement disorders have been established and are used in most surgical trials.
- These standardized , disease-specific rating scales allow for outcomes to be expressed in a more objective fashion that is specific to the disease of interest.

STN and GPi DBS for PD

- Outcomes from DBS are expressed more frequently as absolute or as percent score reductions in the Unified Parkinson's Disease Rating Scale (UPDRS) Part III during the medication-off state.
- Prospective studies have reported on the outcomes of Gpi and STN DBS for the cardinal symptoms of PD.
- targeting of GPi and STN has been shown to be beneficial
    - STN stimulation may be more effective.

- STN DBS tends to allow for a greater reduction in the postoperative medication burden with consequent reduction in dyskinesias.
- STN stimulation may lead to cognitive and behavioral complications.
- meta-analysis suggests he mean reduction in UPDRS Part III scores was 52% (comparing the DBS-on, medication-off state to the medication-off, DBS-off state).
- The correlation between L-dopa response and positive outcomes after STN DBS was confirmed by this meta-analysis.

THALAMIC (VIM) DBS FOR TREMOR

- Tremor Rating Scale
- tremor from PD or essential tremor can be treated with stereotactic thalamotomies targeted at the VIM nucleus.
- Thalamotomies alleviate tremors without significantly affecting the other cardinal symptoms of PD.
- over time, focus shifted to chronic stimulation of VIM for treatment of tremor due to high rate of complication with thalamotomies

- The vast majority of thalamic DBS procedures have been targeted at treating tremors of the upper extremities
- Bilateral stimulation may be more effective than unilateral stimulation in alleviating axial tremors.
- Rate of neurological complications higher in patients who undergo bilateral stimulation (similar to patients undergoing bilateral thalamotomies)
- Dysarthria was observed in 27% of patients with bilateral stimulation.

GPi DBS FOR DYSTONIA

- Treatment outcomes for generalized dystonia are measured using the Burke-Fahn-Marsden Dystonia Rating Scale (BFMDRS).
- Stereotactic ablative surgery of the GPi (pallidotomy) has been attempted in the past in patients with generalized dystonia.
- effects of treatment appear over several weeks to months
- higher risk of neurological morbidity, including lethargy and hemiparesis with pallidotomy

GPi DBS FOR DYSTONIA

- over time, pallidal stimulation has been shown to be effective for primary generalized dystonia
    - 40% reduction in dystonia-movement scores one year post-operatively
- Patients who are positive for the DYT-1 mutation and those with disease of early onset may experience greater benefits.

COMPLICATIONS OF DBS SURGERY

- Include intracranial hemorrhages, infections, hardware-related issues,and stimulation-related complications.

Intracranial Hemorrhage

- Most important complications of movement-disorder surgery.
- Intraoperative hemorrhages are reported to occur in 0.2 to 12.5% of all STN DBS cases .
- Size are generally small . Little agreement on the predictors of intra operative hemorrhages in patients who undergo DBS.

COMMON FACTORS FOR INTRACRANIAL HEMORRHAGE

- **High blood pressure**
- **MER**: an increased incidence of bleeding in hypertensive patients who underwent MER was observed by Gorgulho et al.
  - Reports strongly implicate MER as a risk factor for hemorrhage.
- **Target:** Studies have documented GPi is more prone to hemorrhagic complication compared with the STN or the thalamus.
- **Trajectory Planning:** Use of image fusion of CT and MRI scans helps in performing accurate targeting.
- Images that help most in avoiding hemorrhagic

INFECTIONS

- Reported infection rates for DBS surgery vary widely, formless than 1% to as high as 15%.
- Infections of the IPG tend to present soon after surgery, as do infections at the burr hole.
- Infections at the connector may be related to erosions.

HARDWARE-RELATED COMPLICATIONS

- Hardware-related complications are the most common, with varying incidence that ranges from 2.7 to 50%
- These include DBS electrode fracture, extension wire failure, lead migration, skin erosion, IPG malfunction, and pain over the pulse generator
- Brain lead can malfunction or get damaged due to lead fracture, lead erosion, and lead malfunction.

STIMULATION-RELATED COMPLICATIONS

- Mainly associated with programming of the DBS system after surgery.
- Most common stimulation-induced complications are dyskinesias, worsening of axial symptoms, speech dysfunction , capsular stimulation, and ocular symptoms.
- Stimulation induced dyskinesias can be a good sign of accurate placement and are generally self-limiting