The Role of Psychology in Deep Brain Stimulation and Neuro-restorative Surgeries

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Who and How Are We to Decide?

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AABS 2001

Studies of severely overweight persons conducted before their undergoing anti-obesity surgery have shown a) that there is no single personality type that characterizes the severely obese. b) that this population does not report greater levels of psychopathology than do average-weight control subjects; and c) that the complications specific to severe obesity include body image disparagement and binge eating. Studies conducted after surgical treatment and weight loss have shown 1) that self esteem and positive emotions increase; 2) that body image disparagement decreases; 3) that marital satisfaction increases, but only if a measure of satisfaction existed before surgery; and 4) that eating behavior is improved dramatically. In addition, numerous studies in the literature attempting to identify patient characteristics related to outcome have been reported, but no reliable psychological predictors of success have been identified.

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Right to determine medical outcome/surgery

Determination
Paternalism
Elective versus “non-elective”
Pregnancy
Right to make “bad decisions”
Cost of delaying intervention
Distress Associated with the Procedure
Time considerations/Hardship
Progression dementia/disease to disqualify
Insurance
Conflict of Interest

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Conflicts of interest

Referral Sources

Institutional Ties

Surgical Fees/Incomes

Administrative Agendas

Cherry Picking

Research/Outcome

Psychotherapy Requirements

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Validity of Determination

Objective

Subjective

Liability (withholding medical tx)

Teaching during evaluation

How Much Detail to Include in History?

If you assess do you need to include in the report?

- Spirit of HIPPA?
- (Sexual) Abuse (details in IV?)
- Breed of Dogs
- Education
- Work History
- Previous Medical interventions

Distribution of Report

Patient?

PCP?

Involve Therapist in Decision?

Mental Health Professional?

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Competing Treatments

Exhausted Options?

Quick Fix

Conflict of Interest

Loyalty to Referral Source

Pressure from Referral Source

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Bariatric Surgery

Relatively New Area in Health/Rehab Psych

Unclear Roles for Evaluation

Oversight Committee

NIH Criteria (BMI 35)

Lucrative ($46-65 Billion/yr US)

BMI >40 in 1/12 American Adults

Survey Says...

- To be healthier, be around for my family
- To live longer
- To take less medication
- Be more active
- To feel better
- To be more socially acceptable

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Bariatric Surgery Effectiveness

Effectiveness:

	Weight Loss Successful >2yrs	
Conservative	10%	5%
Surgery	34-45%	90%

Ten Years? Who Knows?

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Obesity: Fat Lies?

6/05 Scientific American

1988-2000 Flegal found even severe obesity was not significant mortality risk.

"Two to five years lost" not studied-off cuff

US High HTN & Chol declined ½ 1960-200
but obese still 2x as common

Declines due to better dx and tx.

CA risk (higher for some, lung CA reduced)

Does type II diabetes cause obesity?

2.5 hours exercise reduced D II 63 to 69%

1 in 710 children 6-18 Worst Obesity had DM " we never saw childhood obesity before"

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Bariatric Psychological Considerations

- Insulation From Distress
- Depression
- Coping Mechanism
- BED
- Impatience
- Unrealistic Expectations
- Marital Problems
- Friendship Conflicts
- Huge Risk Factors

Sex Abuse/Surgical Outcomes

The results suggest that females with a history of sexual abuse are as successful with weight loss following GBP as those without a history of abuse.

While females with a history of sexual abuse show significantly more depression 5 to 9 months after surgery, they are indistinguishable from those without a history of abuse 1 year following GBP.

Thus, sexual abuse does not appear to be a negative prognostic indicator for GBP.

[Psychological comorbidity and quality of life of patients with morbid obesity and requesting gastric banding]

79 consecutive applicants for laparoscopic gastric banding (60 females with a mean BMI of 47.4 kg/m2 and 19 males with a mean BMI of 48.9 kg/m2, mean age 39.6 years)

Most patients displayed multiple somatic symptoms and diseases,

The averages of all psychometric scales (General Symptomatic Index of Symptom Checklist [SCL-90-R], anxiety and depression states of the Hospital Anxiety and Depression Scale [HADS]) were higher than normal.

General life satisfaction and satisfaction with health (FLZM) were low.

Eating behavior in both sexes was characterized by marked irritability, disinhibition and ravenousness.

Binge eating was common, 27% reporting binges at least weekly and only 37% no binges at all. 46% were found to suffer from at least one psychiatric disorder, while half had an eating disorder with frequent bingeing and loss of control. 6.3% were diagnosed with atypical bulimia, 15.2% had an adaptational disorder and 10% a personality disorder.

(2000-Germany)

Obesity Psychological Complications

198 Abstacts, 17 papers 1980 to 2004.

RESULTS:

Severely Obese Patients have high incidence of:

- Depression,
- Negative body image
- Eating disorders
- Low QOL in severely obese patients.
- Rates of anxiety and depression are 3X to 4X higher among obese individuals.

Do psychosocial variables predict weight loss or mental health after obesity surgery? A systematic review.

Apart from serious psychiatric disorders including personality disorders, psychiatric comorbidity seems to be of more predictive value for mental and physical well-being as two essential aspects of quality of life than for weight loss postsurgery.

However, depressive and anxiety symptoms as correlates of psychological stress with regard to obesity seem to be positive predictors of weight loss postsurgery.

The severity of the symptoms of the disorder is more relevant for the outcome of obesity surgery than the specificity of the symptoms.

Not solely the consumption of distinct "forbidden" foods, such as sweets or soft drinks, but rather a general hypercaloric eating behavior, either as an expression of the patient's inadequate compliance or a dysregulation in energy balance, which is associated with a poor weight loss postsurgery.

MMPI-2 Predictors of Success

- Those who lost <50% excess weight scored significantly higher than those who lost >50% excess weight on the F,Hysteria, Paranoia, and Health Concerns scales of the MMPI-2, and significantly lower on the Masculinity-femininity scale.
- Stepwise regression analysis found that a combination of the Health Concerns and Masculinity-femininity scales was the most accurate predictor model for 1-year post-surgery weight loss.

Binge Eating predicting Success

Compared with the NBE group, the BE group had significantly higher levels of disinhibited eating, and hunger, and significantly lower levels of social functioning at pre-surgery and 6 months post-surgery.

The BE group had a significantly lower percentage of excess weight lost than the NBE group at 6 months post-surgery.

While there were more distinct differences between the BE and NBE groups before surgery, they were largely impossible to differentiate on psychosocial measures at post-surgery.

46% of participants reported recurrent loss of control over eating (objective or subjective bulimic episodes) on the EDE-Q. These patients constituted a distinctive subgroup with a less favorable outcome, including greater weight regain

What to do about the Marginal Bariatric Candidate?

Consult with Referral Source

Informed Consent

Sign Release

Second Opinion

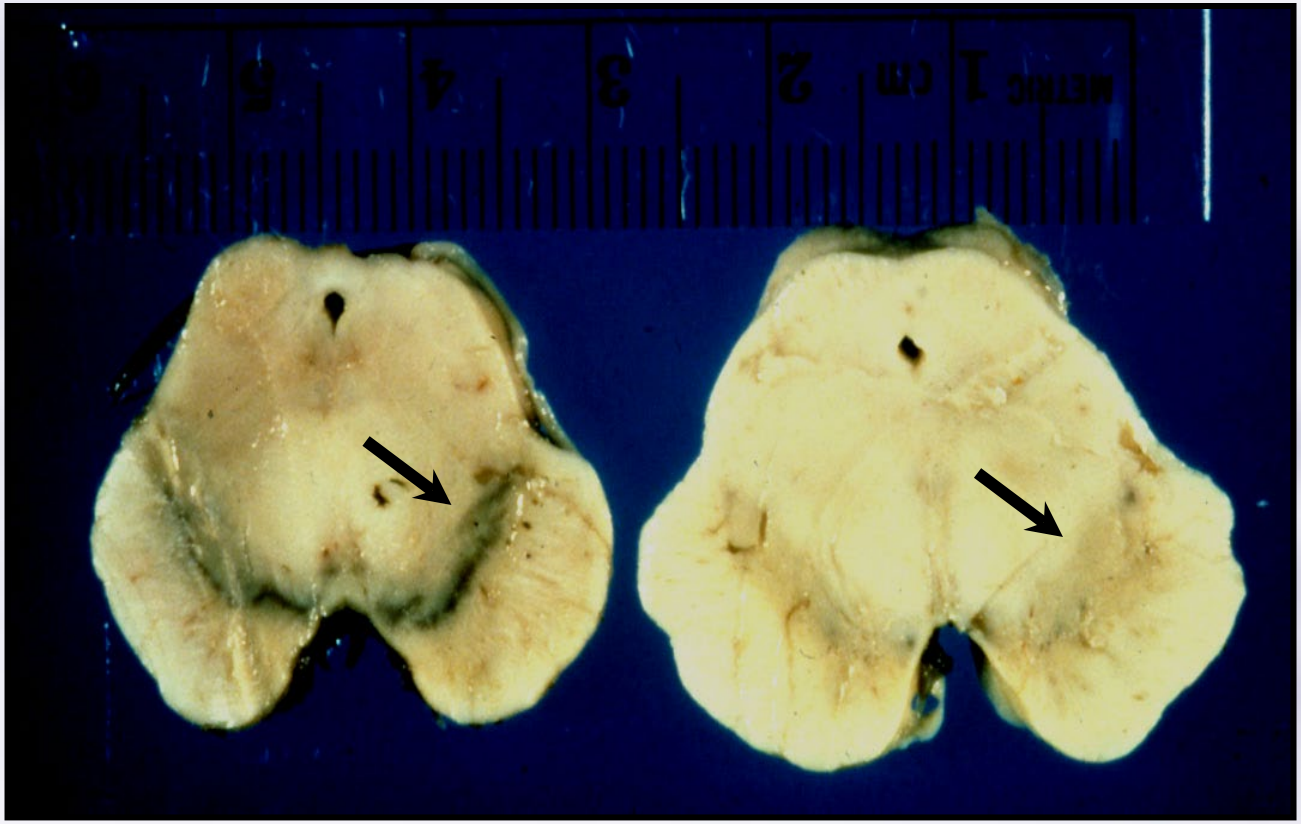
Counseling Referral/Requirements

Re-evaluation

Timing of Surgery

Set Weight Loss Criteria

Pathology in Parkinson's Disease



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Idiopathic PD

- Degeneration of pigmented nerve cells in the substantia nigra and locus ceruleus (two separate clusters of nerve cells in the brainstem).
- Within individual nerve cells in the midbrain, the degeneration is associated with Lewy bodies: large, relative to the cell, spherical inclusions within the cytoplasm.

PD Facts

PD incidence 31-187 per 100,000; Juvenile onset 4.5 per 100,000

Research estimates that about 1,500,000 Americans have Parkinson's disease, with approximately 50,000 new cases being diagnosed each year in this country.

Slightly more men than women are diagnosed each year, with similar incidence across the United States among all socioeconomical classes (the poor, mid-class and wealthy). Some studies have shown that Caucasians are more likely than African-Americans and Asians to develop Parkinson's disease, but no confirmed research has been established.

Age seems to be the most clear correlation with the disease, at least in the onset of symptoms. Parkinson's disease, in general, affects those over age 50, with the average onset at age 60. Recently, either due to early recognition of symptoms or earlier onset of the disease, physicians have reported more cases of Parkinson's under age 40. Some physicians estimate the incidence under age 40 to have risen to 5 to 10 percent over the past several years.

Estimates of dementia in PD range from 2-93%.

NINDS Diagnostic Criteria for Parkinson's Disease

Group A: Features Characteristic of PD:

Resting tremor

Bradykinesia (slowness and clumsiness of movement)

Rigidity (stiffness)

Asymmetric onset (one side had symptoms before, or more severely, than the other side)

NINDS Diagnostic Criteria for Parkinson's Disease (Contd.)

Group B: Features Suggestive of an Alternative Diagnosis:

Features unusual in early PD:

- prominent imbalance < 3 years after onset of first symptoms
- freezing phenomena < 3 years after onset of first symptoms
- hallucinations (excluding medication related) < 3 years after onset of first symptoms
- dementia before or < 1 year after onset of motor symptoms

Limitations of vertical eye movements (other than isolated limitation of upgaze)

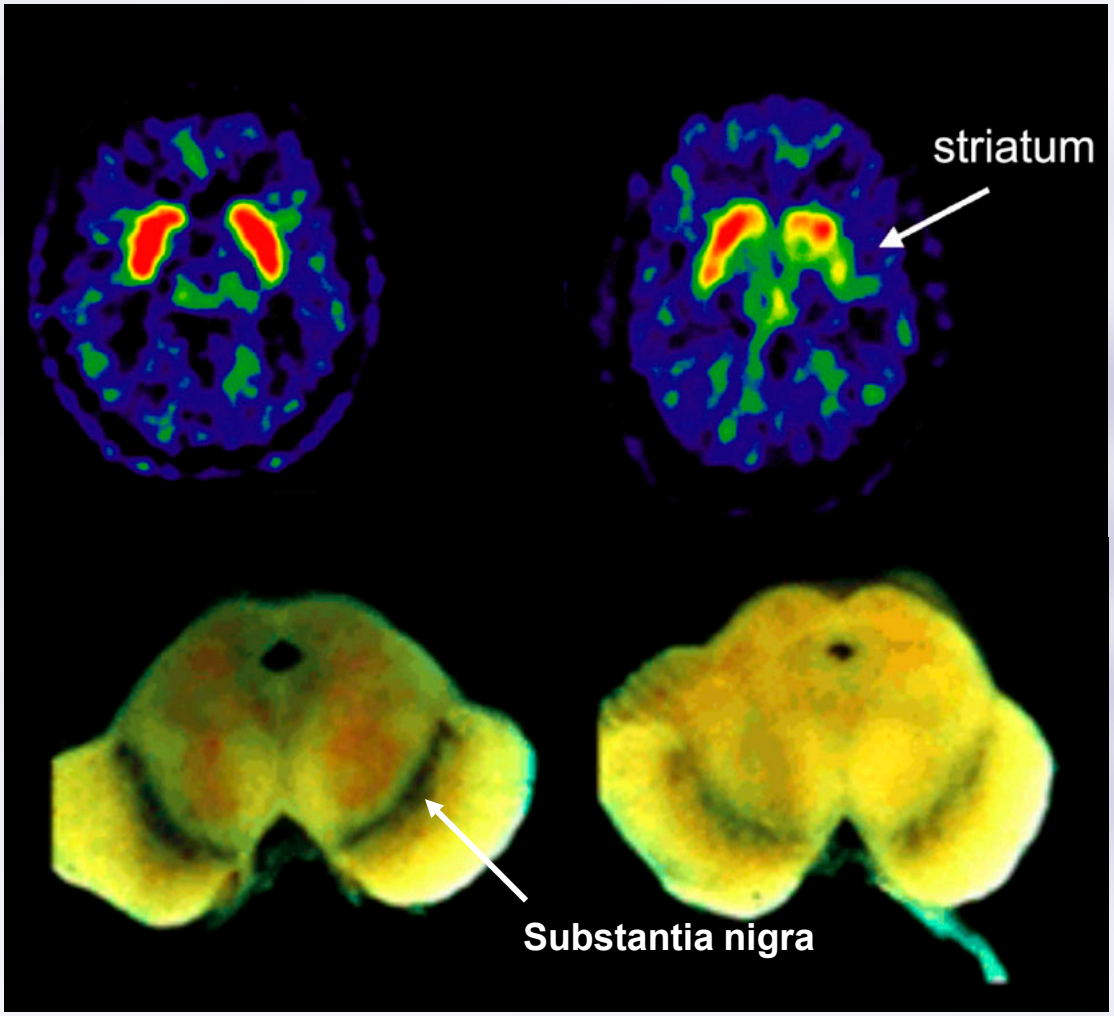
Severe or early orthostatic hypotension (lightheadedness upon standing due to a decreased ability to constrict the blood vessels to maintain proper blood pressure)

Documentation of a condition known to produce parkinsonism (e.g., suitably located brain lesion or neuroleptic use) that is plausibly connected to the patient's symptoms

Other Causes of Parkinsonism

- Drug-induced parkinsonism 7-9% (usually from either anti-psychotic or certain anti-nausea medications)
- Vascular (Stroke induced) Parkinsonism 3%
- Multiple System Atrophy (Shy-Drager syndrome, striatonigral degeneration, olivopontocerebellar degeneration) 2.5%
- Progressive Supranuclear Palsy 1.5%
- Rare causes: MPTP-induced parkinsonism, carbon monoxide poisoning, manganese poisoning, recurrent head trauma, etc.
- No new cases of postencephalitic parkinsonism since the 1960s.

Normal Parkinson's disease



PET scan showing striatal fluorodopa uptake of a normal brain versus PD

Gross pathology of the mid brain showing a normal brain versus PD

Brooks 1993
Lang & Lozano 1998
Marsden 1994

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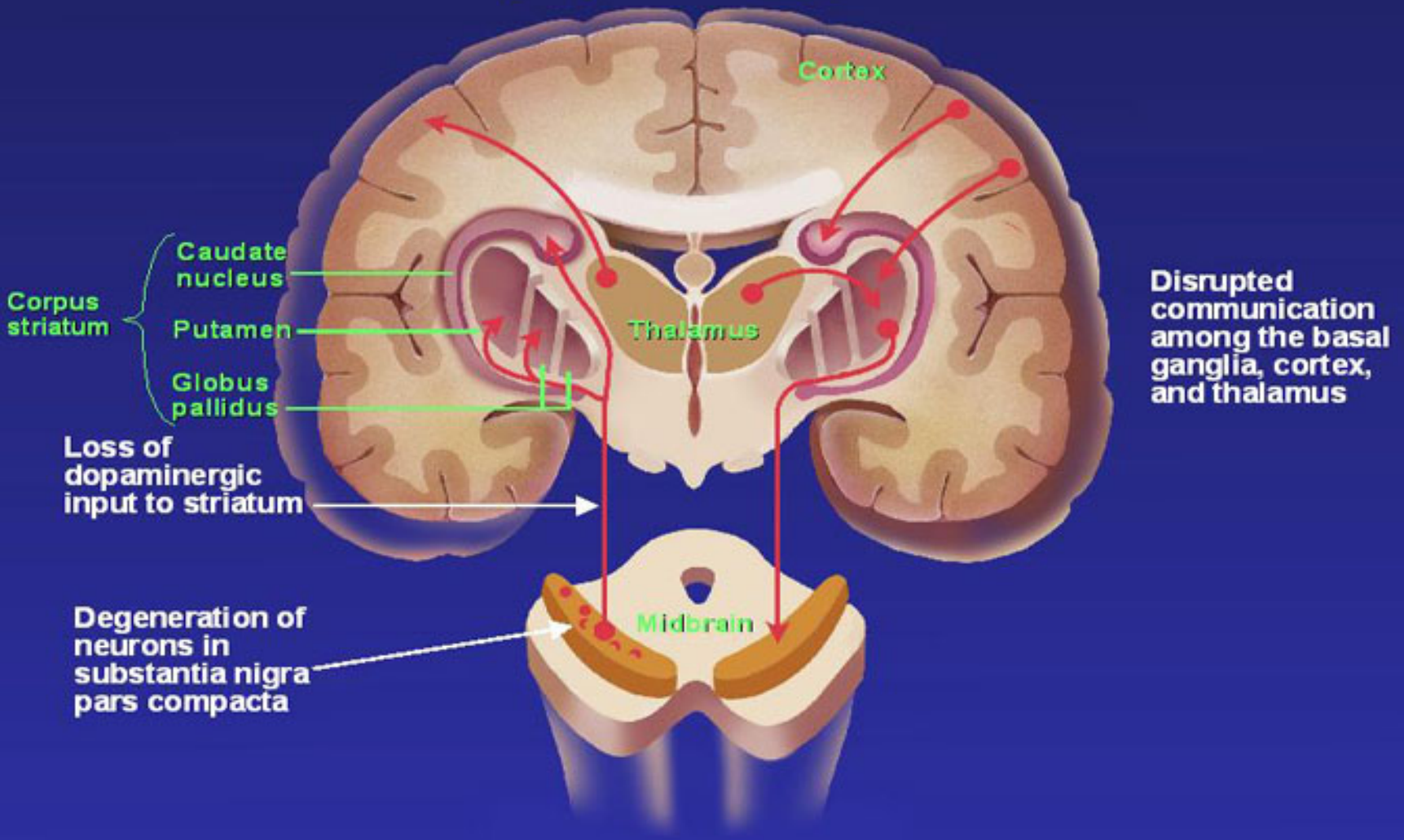
Pathophysiology of PD



Natural History of PD

Without treatment

- PD progresses over 5 to 10 years from mildly symptomatic state to rigid, akinetic state in which patients cannot care for themselves
- Death often occurs from complications of immobility (e.g., pneumonia, pulmonary embolism)

Adler & Ahlskog, eds. *Parkinson's Disease and Movement Disorders: Diagnosis and Treatment Guidelines for the Practicing Physician*. Totowa, NJ: Humana Press; 2000.

Hoehn and Yahr Stages

Stage 1
- Tremor, rigidity, or bradykinesia on one side; minimal functional impairment

Stage 2
- Features of Stage 1 become bilateral

Stage 3
- Bilateral symptoms progress but are still mild to moderate with a mild loss of balance
- Patient can still function independently

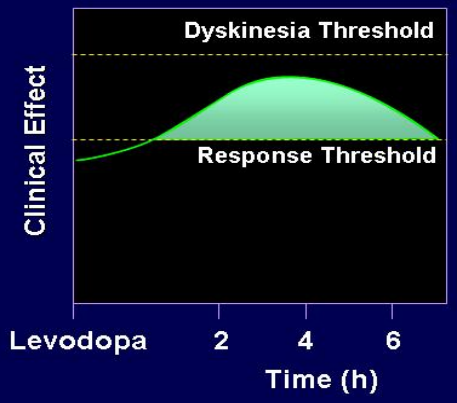
Stage 4
- Bilateral symptoms become more severe with significant loss of balance
- Patient requires substantial assistance

Stage 5
- Bilateral symptoms are severe
- Patient restricted to a bed or wheelchair

Hoehn & Yahr. *Neurology*. 1967;17:427-442.

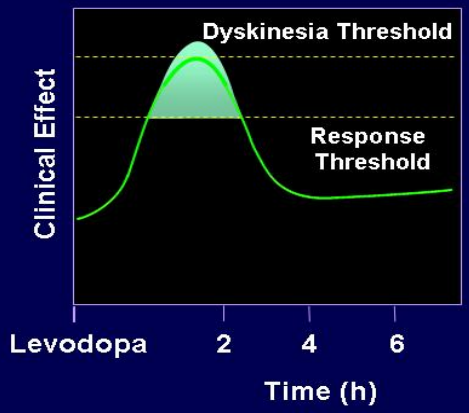
Response to Levodopa and Progression of Parkinson's Disease

Early PD



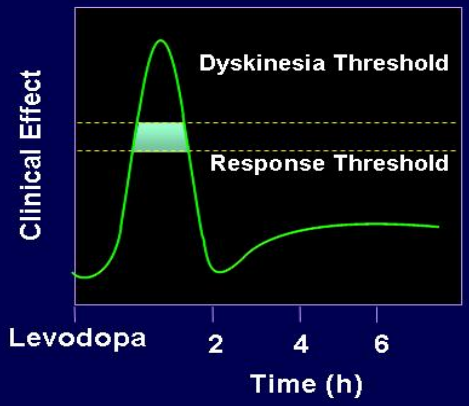
- Long duration motor response
- Low incidence of dyskinesias

Moderate PD



- Shorter duration motor response
- Increased incidence of dyskinesias

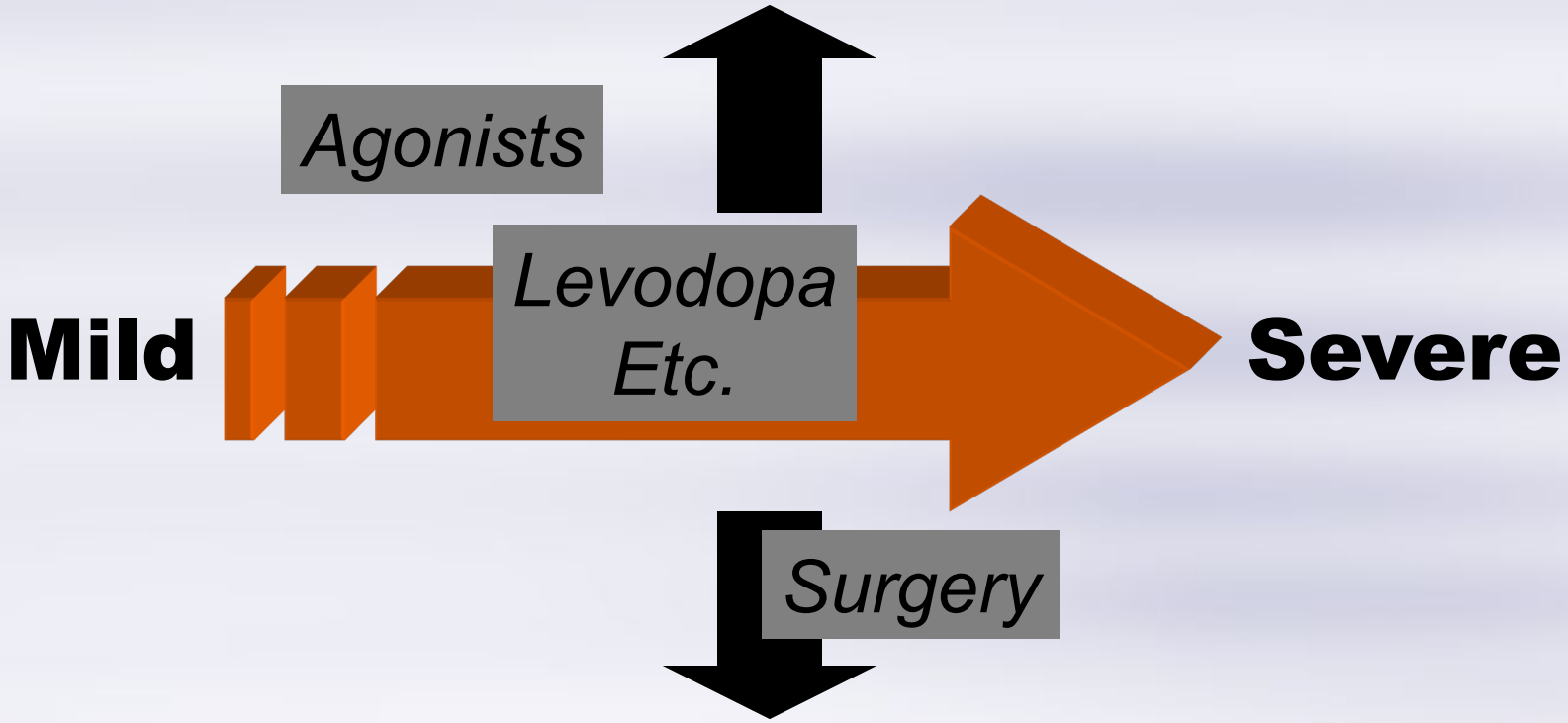
Advanced PD



- Short duration motor response
- "On" time consistently associated with dyskinesias

Olanow CW, Agid Y. http://www.medscape.com/viewprogrm/1847-pnt.

Parkinson's Disease Treatment: Continuum of Interventions



Impact of Motor Complications: Fluctuations and Dyskinesias

"The fluctuations in motor response often result in patients requiring more frequent dosing of medication that is less convenient, and they begin to lose control of their daily life. Their ability to work or to perform activities of daily living may fluctuate with response to medication, and the involuntary movements may interfere with activities."

CH Adler, 2002

Adler. *Neurology*. 2002;58(4 suppl 1):S51-S56.

What are motor fluctuations?

Types of Motor Complications

- Motor fluctuations (changes between akinetic and mobile phases; inability to control voluntary movement)
  - End-of-dose deterioration
  - Delayed onset of response
  - Drug-resistant "offs"
  - Random oscillation ("on-off" phenomenon)
  - Freezing (unpredictable inability to initiate or finish a movement)
- Dyskinesias (abnormal involuntary movements)
  - Peak-dose
  - Diphasic
  - Wearing-off

Adler & Ahlskog, eds. *Parkinson's Disease and Movement Disorders: Diagnosis and Treatment Guidelines for the Practicing Physician.* Totowa, NJ: Humana Press; 2000.

Risk Factors for L-Dopa–Associated Motor Complications

- **Disease**
  - Younger age of onset of Parkinson's disease (for motor fluctuations)
  - Longer duration of Parkinson's disease (for motor fluctuations)
- **Drug**
  - Longer duration of treatment with L-dopa (for dyskinesias and motor fluctuations)
  - Higher doses of L-dopa (for dyskinesias)

Schrag & Quinn. *Brain*. 2000;123:2297-2305.

Deep Brain Stimulation for the Treatment of Movement Disorders

•FDA approves thalamic DBS in 1997 for Parkinson's Disease (PD) and Essential Tremor.

•FDA approval January 2002 of DBS of globus pallidus and subthalamic nucleus for PD.

•Use of DBS being expanded to treat other movement disorders (e.g., dystonia).

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History of surgery for Parkinson's

Initial discovery was by accident

- Accidental lesion of area in the basal ganglia showed decreased symptoms relating to the patient's Parkinson's

Initial surgery was ablation of the area of the brain done by exerting a wire and heating it

- Complications were found when both sides were done such as problems with speech and ambulation

DBS ADVANTAGES

It doesn't destroy brain tissue and “won't” limit future treatment.

The device can be removed at any time.

It is adjustable.

It may be more effective in controlling tremors than thalamotomy.

Medication Reduction Likely

Research in Off mode

DBS: Disadvantages

- Risks of chronically implanted device: infection, movement over time, erosion through skin
- Finite battery life of generator
- Device malfunction
- Time/staff investment for programming
- Cost
- Cosmetic appearance

More DBS Factors

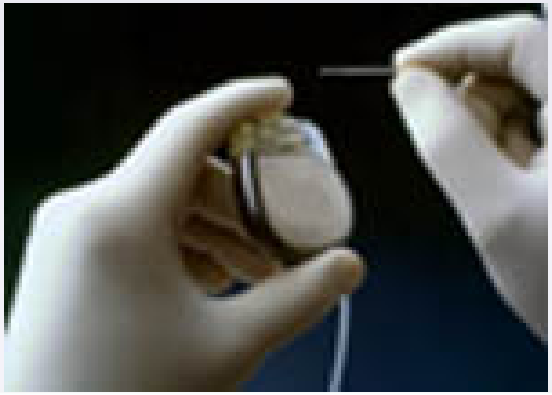
Some disadvantages of deep brain stimulation:

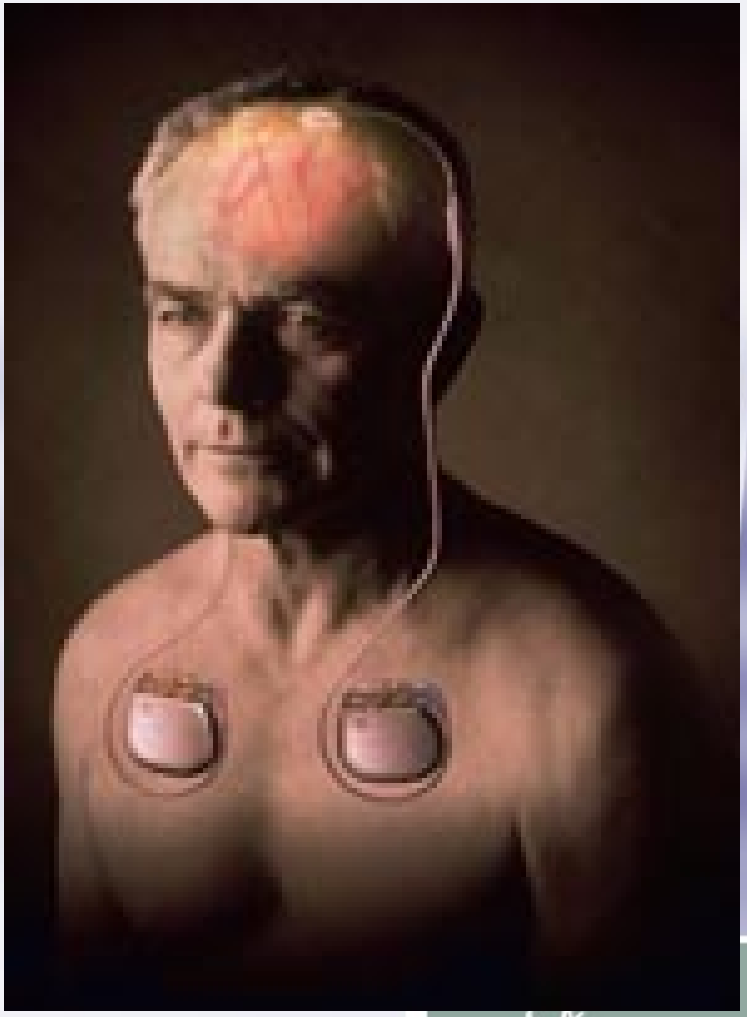
The presence of a foreign object in the body may increase the risk of infection.

Repeat surgery may be required every three to five years in order to replace the battery in the device.

Uncomfortable sensations may occur during stimulation.

Hardware





Common Abbreviations

DBS= Deep Brain Stimulation

STN= Subthalamic Nucleus

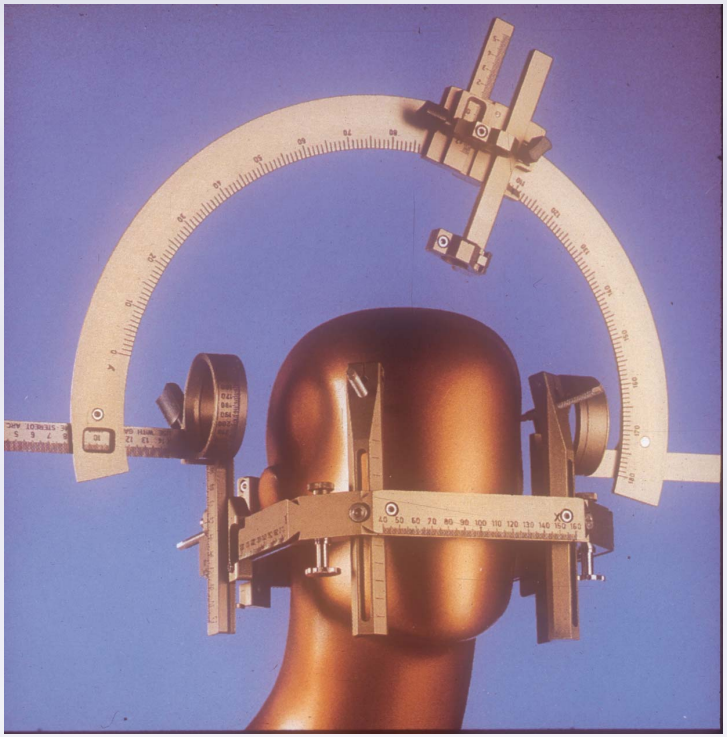
GPi= Globus Pallidus interna

IPG= Implanted Pulse Generator

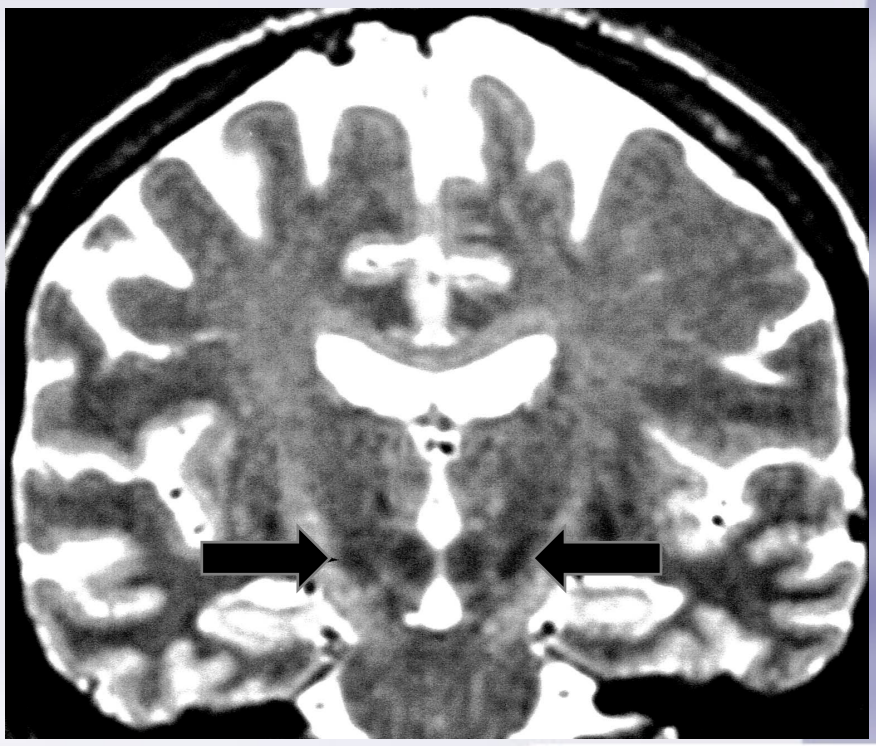
DBS for PD: Which Procedure?

- Target selection
  - **Vim (Thalamic)**—treats contralateral limb tremor only
  - **GPi (Pallidal)**—reduces tremor, rigidity, bradykinesia, dystonia, l-dopa-induced dyskinesias, gait dysfunction
  - **STN**—reduces tremor, rigidity, bradykinesia, gait dysfunction, levodopa requirement
- Unilateral vs. bilateral

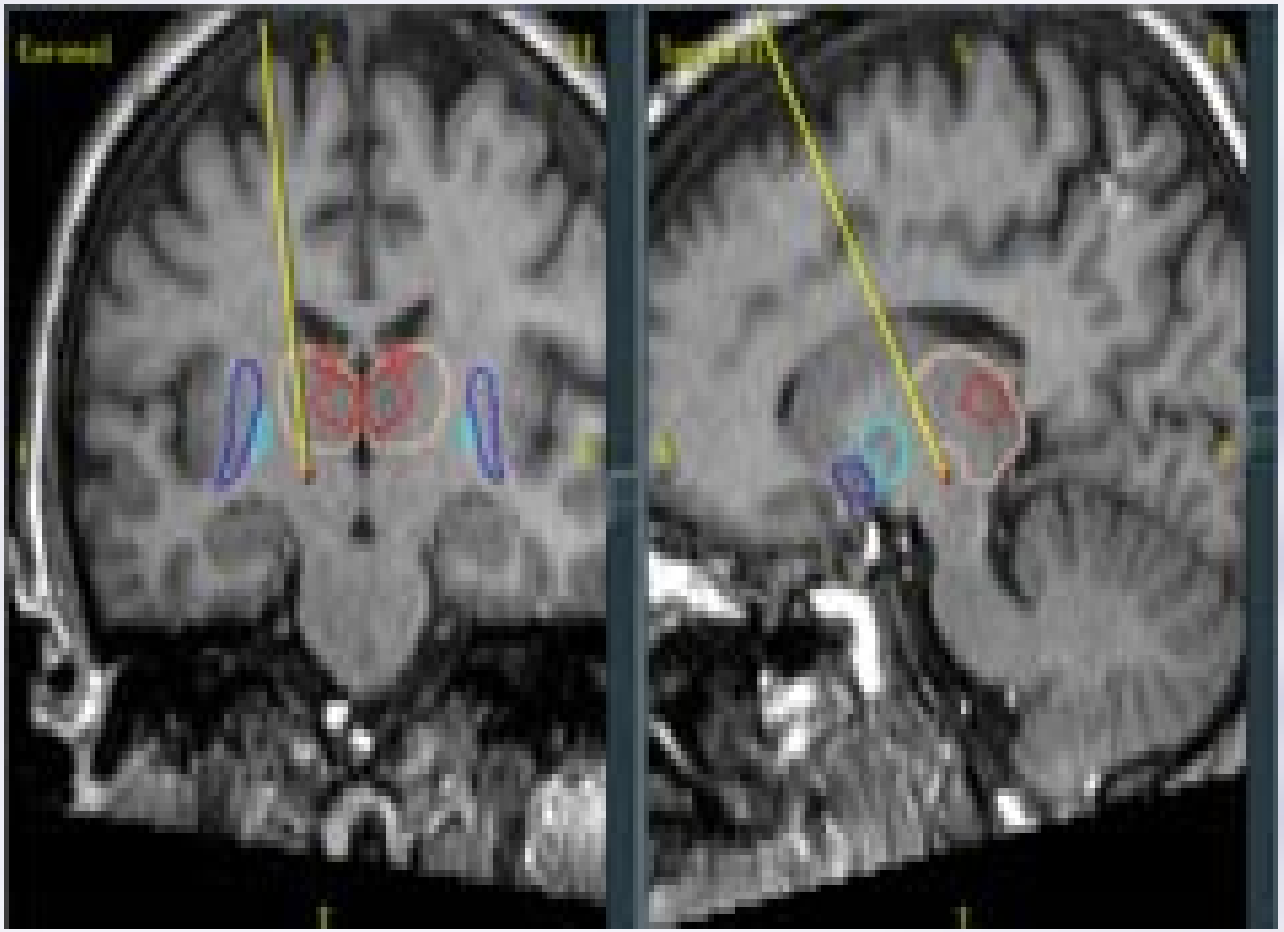
Stereotactic Headframe



MRI Targeting of STN



Location, Location, Location



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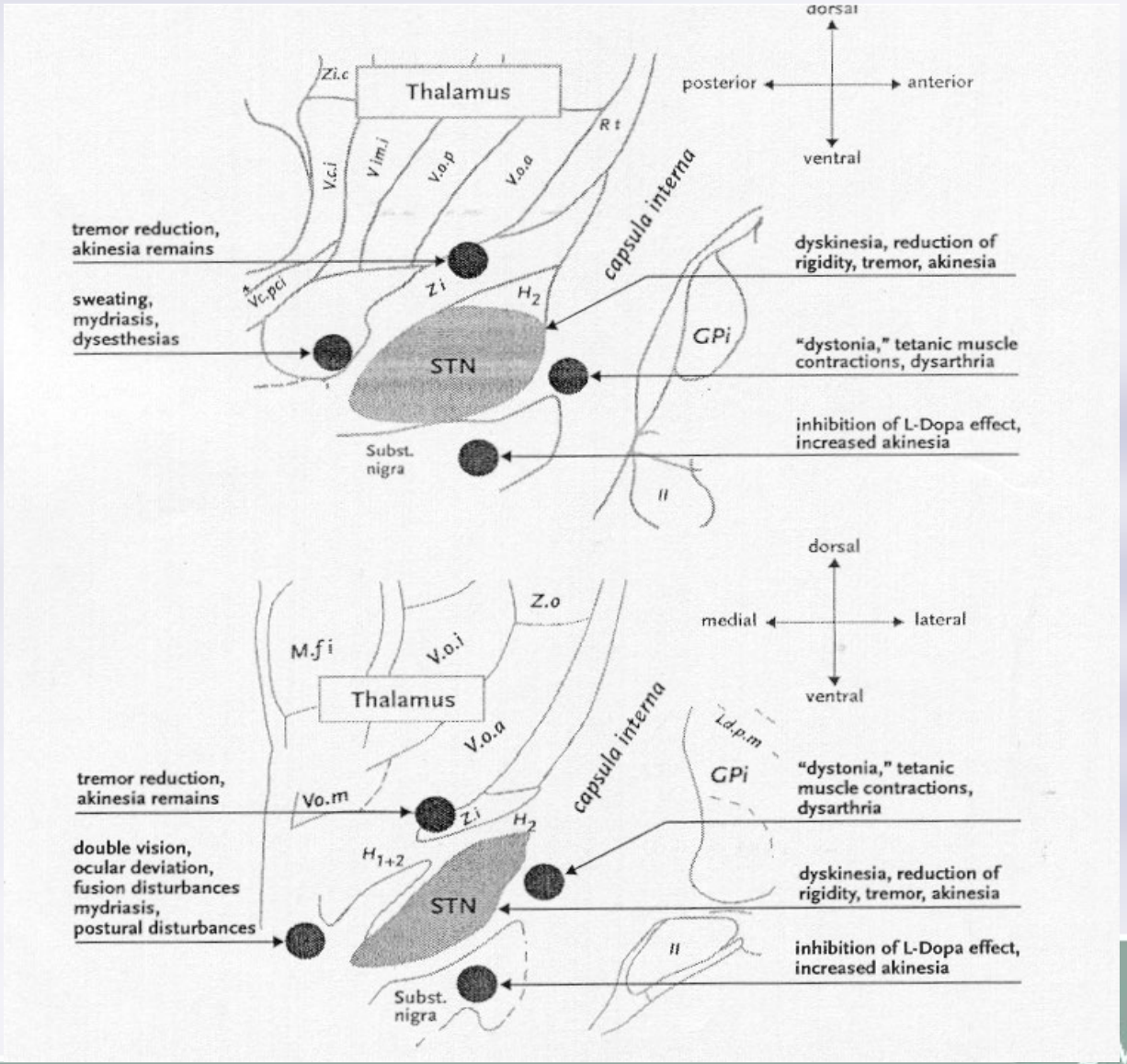
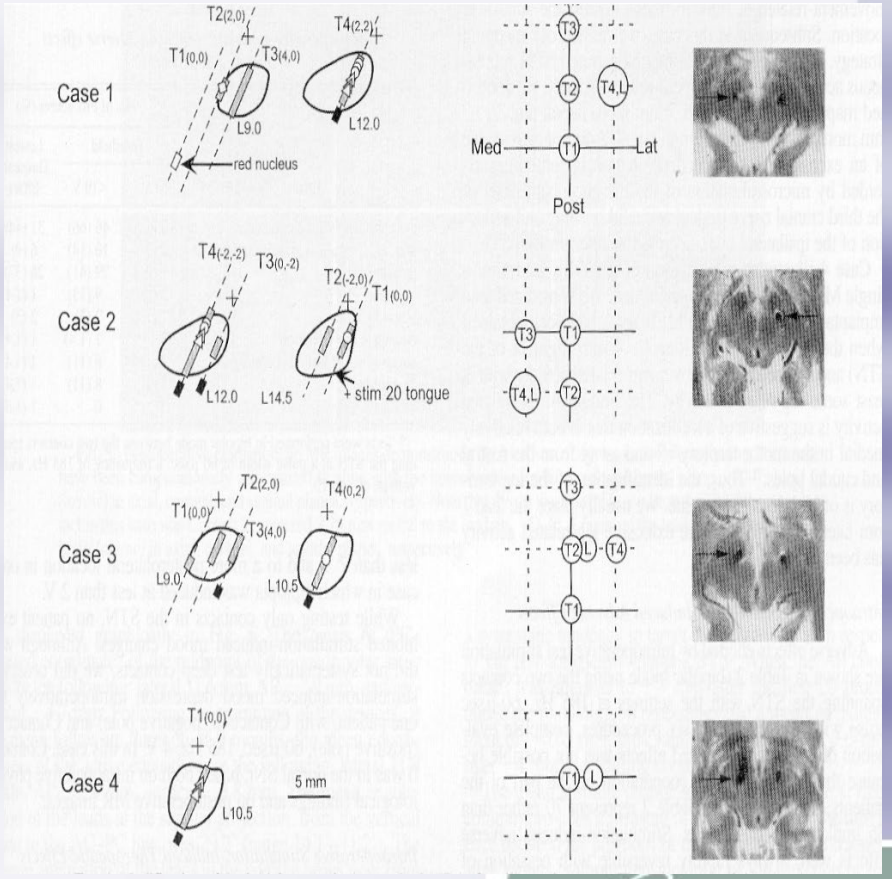
Side effects of stimulation are largely location dependent

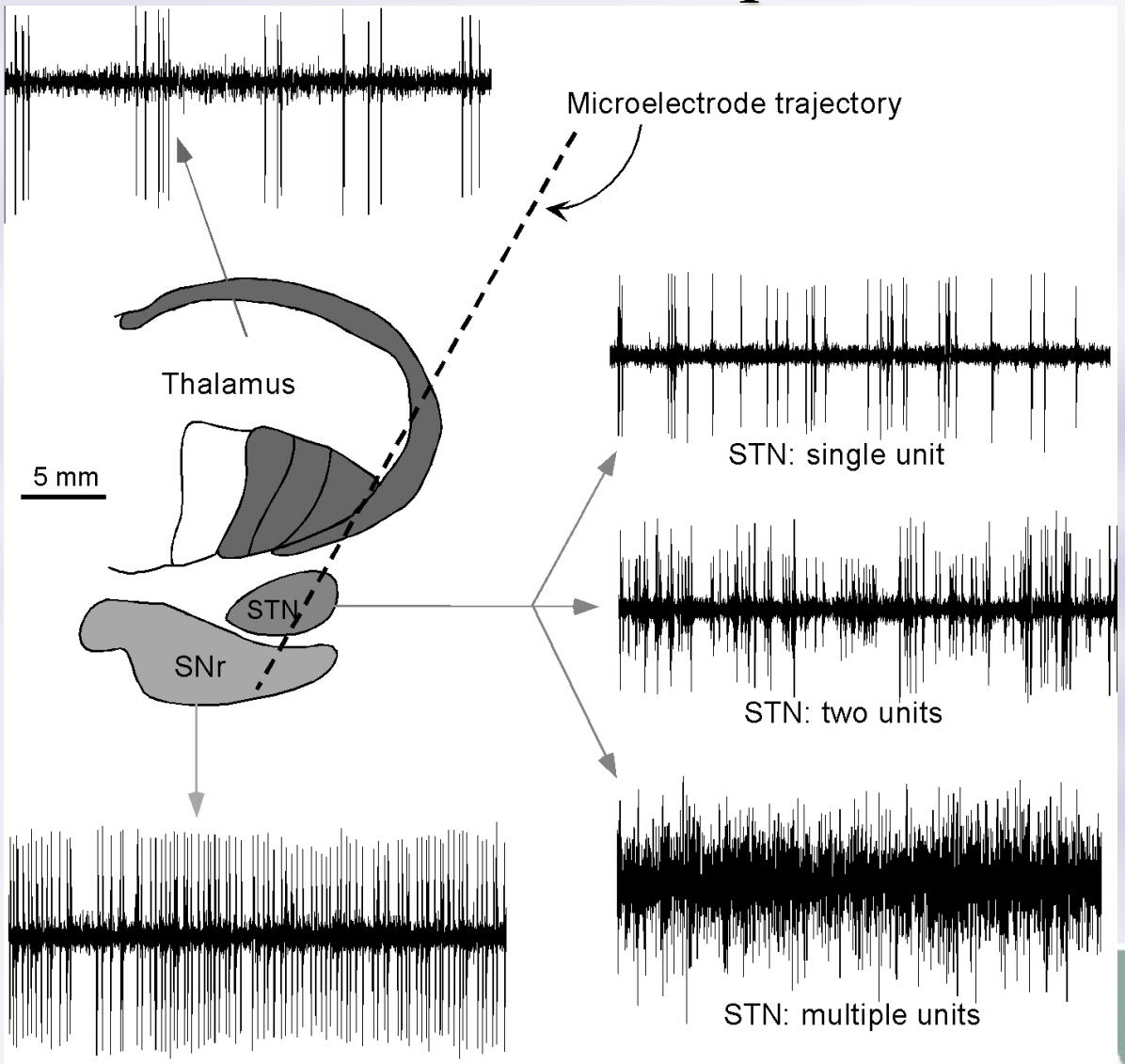


Mapping

- The first major part of the surgery involves finding the correct location to implant the leads (so called “mapping”).
- This is done while the patient is awake so that (s)he can respond to questions, follow commands, and report side effects.
- There are usually several mapping passes to determine the location for each lead; each lead usually takes a couple of hours or longer to map and place.



Microelectrode Recording for Target Localization: Example for STN



How does deep brain stimulation work?

High-frequency deep brain stimulation (DBS) of the thalamus or basal ganglia:

General hypotheses to explain the mechanisms:

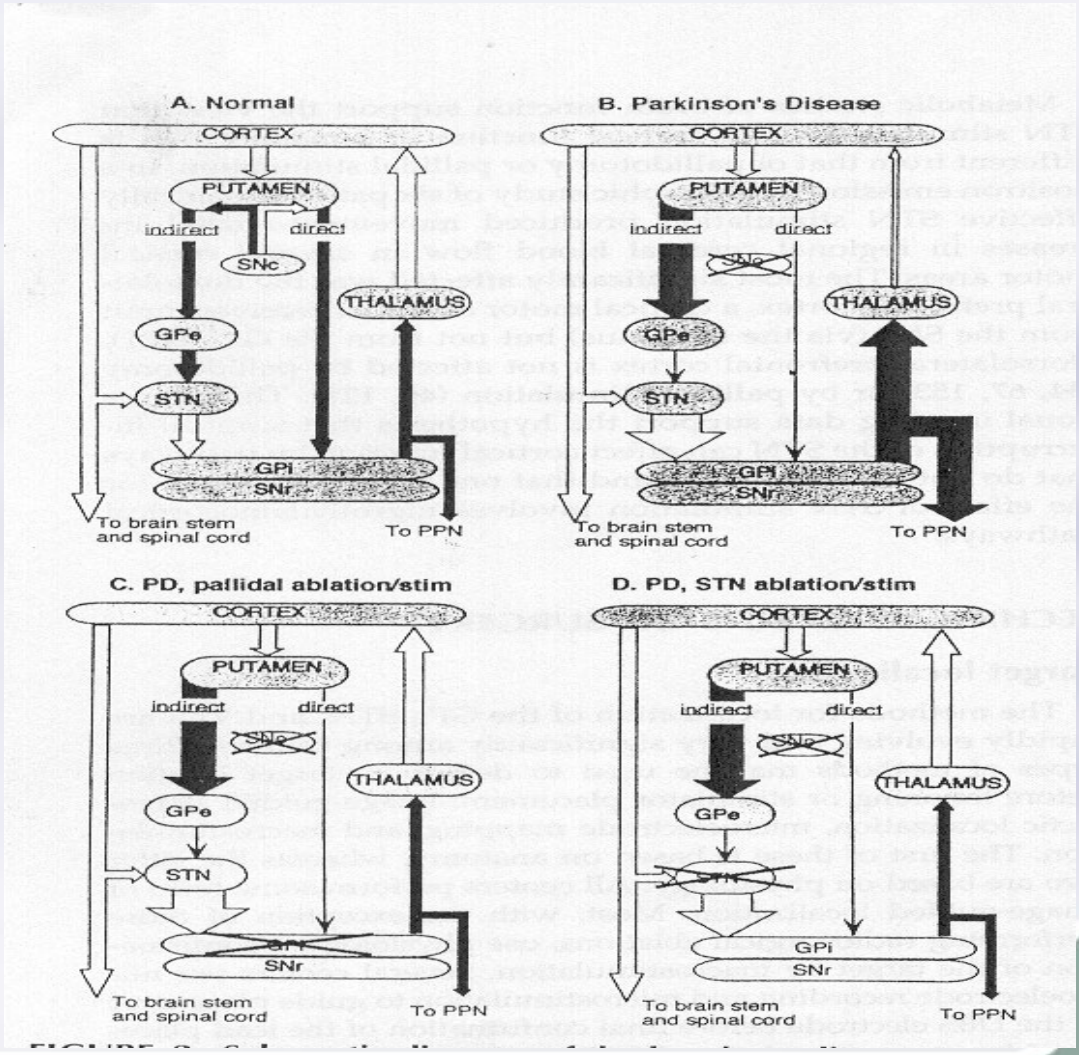
Depolarization blockade

Synaptic inhibition

Synaptic depression

Stimulation-Induced modulation of pathologic network activity.

Theoretical Foundation for Pallidotomy and DBS of the GPi or STN



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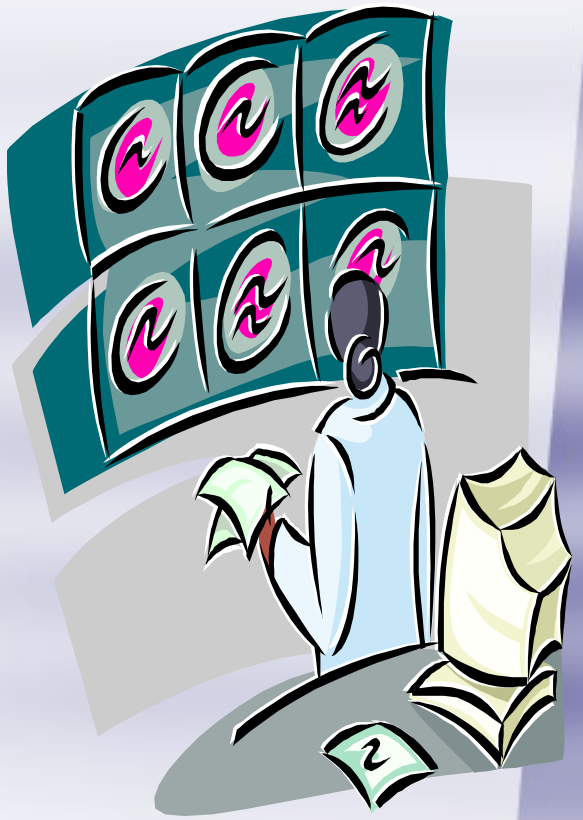
Who is a good surgical candidate?

- Idiopathic Parkinson's disease (atypical parkinsonism doesn't respond as well).
- Continued response to levodopa; being able to walk in the best "on" state.
- Disabling symptoms, despite attempts with frequent and multiple medications.
- Inability to tolerate medications (l-dopa motor complications and other side effects).
- Realistic patient expectations for the procedure.



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Neuropsychological assessment for management of patients with deep brain stimulation.

(1) selection of the best candidates for surgery,

(2) evaluation of the consequences of surgery,

(3) research of the best electrode implantation:

Aggravation of behavioral disorders possibly more related to (STN) stimulation and depends on electrode location;

STN (but not the GPi stimulation), improves psychomotor efficiency and working memory.

Who is NOT considered for surgery?

- Unclear diagnosis of Idiopathic Parkinson's disease or lack of response to Levodopa medication (atypical parkinsonism doesn't respond reliably to surgery)
- Presence of Dementia
- Presence of other CNS disease or brain atrophy
- Unobtainable expectations for outcome
- Unstable co-morbid medical disease
- Severe depression

Neuropschological Evaluation

For DBS

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Informed Consent

- Medical Risks
  - Limits of Benefits
  - Re-injury
  - Death
  - Dis-implantation
  - Cost
  - Psychiatric
  - Ability to understand consent forms and discussions

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Psychological Preparation

Endurance of Surgery
Halo
Sights and Sounds
Off Medications
Anxiety Management
Relaxation Techniques
Psychological Exacerbation
Post-Christmas Depression
Injury Risk
Personality Changes-Disinhibition (ex)
Commitment to Follow Up

Expectations

Personal

Family (hoping to relieve burden)

Day After Christmas

Fixing the Muffler but…

Parkinson's Confounds

- Parkinson's Related Cognitive Changes
- Dementia Due To Parkinson's
- Mild Cognitive Impairment
- Diffuse Lewy Body Dementia
  - Medication Effects
  - Hallucinations
  - ACHEI confounds
  - Anticholinergic Medications
  - Depression

Confounds on Cognitive Retesting

- Retesting Effects (Practice-Learning)
- Motivation-No Carrot
- Medication Cycling
  - Anxiety
  - Depression
  - Insurance

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What is the DBS surgery like?

Off meds
Halo Attachment
Imaging
Drilling the hole
Sounds, Sights and Smells
Hours of Probing
Recovery
Hospitalization
Lesion Effect
Programming

Parkinson's Testing Factors

Intrusion of Medications/Off Effects

Dyskinesia-Distraction (towel ex)

Head Movements-Visual Tracking

Rigidity

Tremor

Staying in Chair

Sleeping

Hallucinations/Illusions

Mental and Physical Fatigue

Common Neuropsychological Measures

- WASI
- Trails
- WMS Faces
- WMS Logical Memory
- Word List Rey/CVLT-2
- Verbal Fluency
- PDQ
- Dementia Rating Scale
- BDI
- BAI
- FrSBE
- Stroop

Neuropsychology: Making Surgical Decision

- 10-80-10 %
- Informed Consent
- Dementia
- Disease Course: Future Physical and Cognitive Projections
- Expectations Realistic
- Current Level of Disability
- Support in Place
- Other Options
- Buying a Computer Analogy

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Adversity

Stress Tolerance

Pain Tolerance

Fatigue

Investment

Anxiety management

Longer Evaluation

Tools Common to Pre DBS Assessment

Advantage of Alternate Forms
- WASI
- DKEFS*
- DRS-2
- WMS Log Memory and Faces
- CVLT-2
- BDI
- BAI*
- Verbal Fluency
- Trails
- WTAR
- FrSBE Self/Family
- POMS

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Common Parkinson's Cognitive Weaknesses

Memory Loss with Benefit From Prompts

Limited Divided Attention

Limited Visual Attention

Visual Spatial Deficits

Declined Executive Functions

Declined Verbal Fluency

Expectations

Personal

Family (hoping to relieve burden)

Day After Christmas Depression

Fixing the Muffler but…

Psychological

- Depression
  - Anxiety
  - Specific Phobia
  - Psychosis
  - Realistic Expectations
  - Impulsivity (roof, mower, falls)
  - Mania
  - Hedonistic Homeostasis Syndrome

Severity of Depression

Correlates more with degree of disability versus disease stage/neurological stability

Degree of disability self-determined to a degree

Clients often resistant to medication use

…..Expense

Concerns/Fears regarding expense, medication complexity, side effects…

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Depression Confounds

- Level of Disability
- Fatigue
- Sleep Disruption
- Psychomotor Retardation
- Hopelessness: progressive incurable
- Activity more difficult less pleasure-(Anhedonia)
- Communication difficulties
- Social Discomfort
- Fears of Being a Burden-Guilt
- Sexual Dysfunction

Must Treat the Depression

- Numerous studies showing accelerated decline with depressed versus non-depressed patients, when level of disability is factored out

- Placebo effects of sham surgery and placebo dopamine supplementation

Management of surgical anxiety

- Psychotherapy
- Pharmacology
- AD-AA
- In Vivo-Imaginal Exposure
- PMR
- Mental Activities
- Music
- Coach
- Massage

Informed Consent For Family

Living Will-Advanced Directives
Power of Attorney
Life Insurance
Long Care Insurance
Stress On Relationship
Personality Changes
Divorce
Independence
Financial Cost of Complications
Disability: Driving, Home Care, Etc

Post Surgical Factors

Medication List (20 copies)

Typed Medical History

Airline Travel

Supervision Needs

Driving

Injury Prevention

Increased Falls/Increased Activity

Physical Therapy

May Need Other Surgeries Now (knee)

Will I have to limit my activity following DBS?

You should not engage in light activities for two weeks after surgery. (housework/sexual activity).

You should not engage in heavy activities for four to six weeks after surgery. This includes jogging, swimming or any physical education classes. Anything strenuous should be avoided to allow your surgical wound to heal properly.

You should not lift more than five pounds for at least two weeks.

Depending on the type of work you do, you may return to work within four to six weeks.

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Programming

It is common for the IPG's to be turned on a day or two after surgery, but aggressive programming should be delayed for a week or two.

An initial programming session will usually take at least 2 hours (including breaks).

It typically takes several programming sessions (each one to four weeks apart) to get to optimized parameters, hence it usually takes at least a couple of months.

Programming is best done in a practical "off" state (holding PD meds overnight prior to the programming session)

Can I use electrical devices?

While you should be able to use most electronic devices, you should be aware that:

- Some devices, such as theft detectors and screening devices, like those found in airports, department stores, and public libraries, can cause your neurotransmitter to switch on or off.
- You will be able to use home appliances, computers and cellular phones.
- You will be provided with a device to activate and deactivate your stimulator.
- Ask your doctor before you undergo MRI or surgical procedures for any other reasons

What About the Marginal PD Candidate?

- Tweak Medications
- Anxiety Management for Testing
- Address Depression
- Cognition Preserving Medication Trail
- Stimulant Medication
- Retest Against Baseline for Stability
- Education Regarding Options
- Informed Consent
- Family Conference

Billing Considerations

Medical Procedure

Medicare Factors

Wording the Appropriate Referral Reason

Retesting-Medical Necessity?

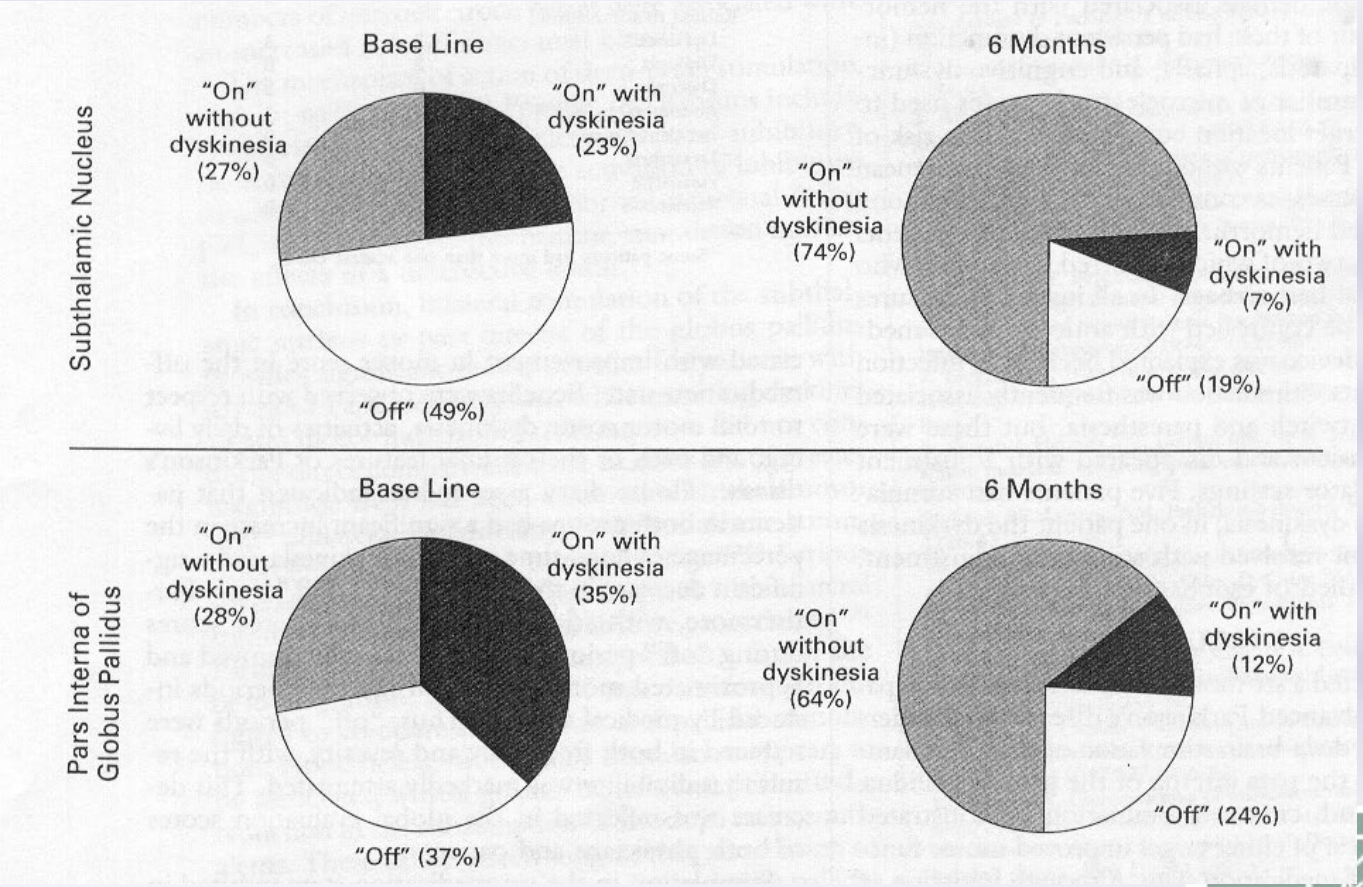
Does DBS Work?

At what expense?

Expected Outcomes

- Tremor
- Dyskinesia and/or Dystonia
- Rigidity
- Bradykinesia
- Imbalance
- Medication reductions
- Extension of the patients best ON state

Published double-blind evaluation of GPi versus STN DBS



Neuropsychological functioning following bilateral subthalamic nucleus stimulation in Parkinson's disease.

Does the performance of the Patients vary more than that that variability of the assessment measures?

To examine this issue, 17 PD patients were tested before and after bilateral STN stimulator implantation, both on and off stimulation.

11 Matched PD controls were administered the same repeatable neuropsychological test battery twice.

Relative to changes seen in the controls, the surgery for electrode placement mildly adversely affected attention and language functions.

STN stimulation, per se, had little effect on cognition.

The STN DBS procedure as a whole resulted in a mild decline in delayed verbal recall and language functions.

One DBS patient demonstrated significant cognitive decline following surgery.

Cognitive outcomes after deep brain stimulation for Parkinson's disease: Troster 2000

Nonetheless, recent studies indicate that neurobehavioral functions commonly compromised in Parkinson's disease (PD) (e.g., executive functions, verbal fluency, and memory) are negatively impacted in some patients by lesion placement.

These studies suggest that DBS is relatively safe from a cognitive standpoint and that the benefits of motor improvements probably outweigh the cost of minimal cognitive morbidity.

What does DBS really cost ?

fine print

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Subthalamic stimulation differentially modulates declarative and nondeclarative memory.

Declarative memory has been reported to rely on the medial temporal lobe system, whereas non-declarative memory depends on basal ganglia structures.

(DBS) we manipulated neural activity of the STN in humans. We found that DBS-STN differentially modulated memory performance: declarative memory was impaired,

Non-declarative memory was improved in the presence of STN-DBS indicating a specific role of the STN in the activation of memory systems.

What Causes the Cognitive Decline with DBS?

- “Reversible Procedure”
- “Dis-Implantable”
- Number of Passes
- Single Pass Possible?
- Does “On Stimulation” Help/Hurt
- What About Medication Reduction?
- Reduction of Attention to Movement Dysfunction
- Reduced Anxiety?
- Decreased Speech AND Decreased Language

Efficacy of deep brain stimulation of the subthalamic nucleus in Parkinson's disease 4 years after surgery:

Double blind crossover evaluation of the efficacy of DBS of the STN in the "off" medication condition in 10 patients with Parkinson's disease.

(UPDRS) part III (motor) and two timed tests (arm tapping and walking).

The mean amount of levodopa daily dose at base line, 1 year, and 4 years after surgery was compared.

A significant ($p<0.04$) effect of stimulation was observed in the overall group regarding both the UPDRS motor and the timed tests.

Open evaluation also showed a significant benefit of STN DBS with respect to preoperative assessment in both the motor and activities of daily living scales, dyskinesia scale, and in global assessment.

Levodopa daily dose was reduced by 48% and 50% at 1 and 4 years, respectively.

There was no difference between the 1 and 4 years evaluations in any of the parameters evaluated.

DBS and Depression

23 Articles reported the effect of STN DBS on mood state in Parkinson's disease (PD):

Antidepressant, 16.7 to 76%

Depressant: 2 to 33.3%

Mania Induced Effects: 4.2 to 8.1%

Most articles reported larger subgroups showing antidepressant effects than those showing depressant effects.

The average depression scale score of all subjects was improved or unchanged after STN DBS.

However, the studies reporting severe depressant symptoms, such as suicidal attempts, after STN DBS indicated the importance of careful attention to mood state as well as to motor symptoms after STN DBS.

Long term effects of bilateral subthalamic nucleus stimulation on cognitive function, mood, and behaviour in Parkinson's disease.

3 Year Follow Up

Consecutive series of 77 PD patients Seven patients died or were lost for follow up.

Before, One, and Three years after surgery.

Mean age at surgery was 55 (8 SD). Only two cognitive variables worsened (category fluency, total score of fluency).

Age was a predictor of decline in executive functions.

Depression improved whereas apathy and thought disorders worsened.

Major behavioral changes were 2 transient aggressive impulsive episodes, 1 suicide, 4 suicide attempts, 1 permanent apathy, 1 transient severe depression, 4 psychoses (1permanent), and 5 hypomania (one permanent).

Apathy scores mildly increased. Depression scores mildly improved. Behavioural changes were comparatively rare and mostly transient. Single case reports show the major synergistic effects of both medication and stimulation on mood and behavior, illustrating the importance of a correct postoperative management.

Hedonistic Homeostatic Dysregulation in patients with Parkinson's disease on dopamine replacement therapies

These patients take increasing quantities of their DRT, despite increasingly severe drug induced dyskinesias.

May develop a cyclical mood disorder with hypomania or manic psychosis.

There is impairment of social and occupational functioning.

Tolerance develops to mood elevating effects of DRT and a negative affective withdrawal state occurs if the drugs are withdrawn or doses decreased.

Gambling and DBS

Apathy and reward sensitivity (Apathy Scale, Stimulus-Reward Learning, Reversal, Extinction, and Gambling tasks) were assessed in 18 PD patients treated by bilateral STN stimulation ("on" and "off" conditions) compared with 23 matched patients undergoing long term treatment with levodopa ("on" and "off" conditions).

Apathy decreased under both STN stimulation and levodopa treatment, whereas explicit and implicit stimulus reward learning was unchanged.

Pseudobulbar crying induced by stimulation in the region of the subthalamic nucleus

The patient exhibited pseudobulbar crying when on monopolar stimulation at all four lead contacts. The pseudobulbar crying resolved off stimulation.

Speech and DBS

22 PD (Matched with 25 Non-PD) participants with PD.

Neurosurgical intervention did not significantly change the surgical participants' perceptual speech dimensions or oromotor function despite significant postoperative improvements in ratings of general motor function and disease severity.

Delayed DBS Complications

Follow-up

2.5% had infections requiring system removal,
3.7% had infections requiring implantable pulse generator (IPG) removal,
12.5% had misplaced leads,

26.2% had hardware complications including lead migration, lead fracture, extension erosion, extension fracture, and IPG malfunction.

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Parkinson's disease patients with bilateral subthalamic deep brain stimulation gain weight.

19 Parkinson's disease (PD) patients after subthalamic deep brain stimulation (STN-DBS) versus 14 nonoperated ones.

Operated patients had a significant weight gain (WG, + 9.7 +/- 7 kg) and BMI increase (+ 4.7 kg/m2).

The fat mass was higher after STN-DBS.

A significant correlation was found among WG, BMI increase, and pre-operative levodopa-equivalent daily dose and their reduction after STN-DBS.

Post Surgical Risks that Therapy can Anticipate and Treat

- High fall risk from newly found mobility
- High risk for progressive musculoskeletal pathology to emerge
  - Spine Alignment changes and/or changes in longstanding tone that affects joint alignment
- High risk for weight gain
  - Dyskinesia associated with increased BMR
  - Tremor associated with decrease food intake
- High risk for worsening OA pain due to increased joint mobility

Complications

Hemorrhage

- 1-2% (higher in certain patients)
- May be symptomatic or silent
- Risk for both ablative & DBS surgery

Infection

- 3-5% for DBS

Hardware breakage/malfunction

- 1%/year for DBS

Possible Complications

TABLE 5. ADVERSE EVENTS ASSOCIATED WITH SUBTHALAMIC AND PALLIDAL STIMULATION.*

TYPE OF ADVERSE EVENT	SUBTHALAMIC NUCLEUS (N=102)	PARS INTERNA OF THE GLOBUS PALLIDUS (N=41)
	number	
Related to procedure		
Intracranial hemorrhage	3	4
Hemiparesis secondary to hemorrhage	3	3
Seizures	3	1
Infection	4	0
Improper lead placement	2	0
Brachial plexus injury	1	0
Confusion	1	0
Dysarthria	0	1
Paralysis (nonhemorrhagic)	1	0
Pulmonary embolus	1	0
Related to device		
Migration	3	2
Infection	3	1
Lead break	1	1
Seroma	1	1
Erosion	1	0
Abnormal healing	1	0
Intermittent function	1	0
Related to stimulation		
Dyskinesia	2	3
Diplopia	2	0
Dystonia	0	2
Abdominal pain	0	1
Accidental injury	1	0
Dysarthria	1	0
Headache	1	0
Paresthesia	1	0

*Some patients had more than one adverse effect.

Brief Communications

Expedited Publication

DBS and diathermy interaction induces severe CNS damage

Article abstract—Pulse-modulated radiofrequency diathermy treatment to the maxilla produced permanent diencephalic and brainstem lesions and a vegetative state in a patient with PD with implanted subthalamic electrodes for deep brain stimulation.

NEUROLOGY 2001;56:1384–1386

J.G. Nutt, MD; V.C. Anderson, PhD; J.H. Peacock, MD, PhD; J.P. Hammerstad, MD; and K.J. Burchiel, MD

What else is out there, besides DBS?

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Treatment options for Parkinson's disease.

(1) the incidence of levodopa-related dyskinesias decreases as a result of initial use of dopamine agonists;

(2) surgery, primarily in the form of the bilateral, high-frequency stimulation of the subthalamic nucleus, is highly effective in patients who are responsive to levodopa but experience marked motor fluctuation or other complications;

(3) while neuroprotection has not yet been demonstrated with any currently used therapeutic agent, improved understanding of mechanisms of cell death will undoubtedly result in the discovery of new drugs with potential disease-modifying effects; and

(4) implantation of fetal mesencephalon tissue and other grafts may be effective in younger patients with Parkinson's disease, but is associated with significant complications and remains experimental.

Surgical Outcome Considerations

- Outcome Studies/Findings
  - DBS
  - Sham Surgeries
  - Placebo Scientific American 2002
  - Basleline Functioning (CP/DD/LD/TBI)?

Comparative cognitive effects of bilateral subthalamic stimulation and subcutaneous continuous infusion of apomorphine in Parkinson's disease (2004 Spain)

Bilateral subthalamic deep brain stimulation (STN-DBS) and continuous subcutaneous infusion of apomorphine (APM-csi) can provide a comparable improvement on motor function in patients with advanced Parkinson's disease (PD).

We studied 9 patients treated with STN-DBS and 7 patients with APM-csi.

Neuropsychological: Rey's Auditory-Verbal Learning, Stroop, Trail Making, phonetic verbal fluency, and Judgment of Line Orientation tests.

In the APM-csi group, significant changes were not observed in the neuropsychological tests performance.

By contrast, in the STN-DBS group, moderate worsening was found in phonetic verbal fluency and Stroop Naming scores that was partially reversible at long-term follow-up and did not have consequences on regular activities.

Parkinson's Surgery

- DBS
- Ablative Surgeries
- Gamma Knife
- Fetal Cell
- Retinal Cell Implantation
- Stem Cell Implantation

Thalamotomy

Primarily effective for tremor, and is therefore used mainly in patients for whom tremor is the only disabling symptom. During a thalamotomy, a selected portion of the thalamus is surgically destroyed (ablated)

Bilateral (both sides of the brain) procedures are poorly tolerated because of increased complication risks, including vision and speech problems

Pallidotomy

Until the late 1990s, pallidotomy was the most common type of PD surgery; deep brain stimulation or DBS is now being performed more often. A pallidotomy involves destruction of part of the globus pallidus (GPi)

Improvements from pallidotomy range from 70% to 90% reduction of dyskinesias and dystonia, and 25% to 50% for tremor, rigidity, bradykinesia, and gait disturbance.

GAMMA KNIFE

What is gamma knife?

Not actually a "knife" at all, the gamma knife is a machine that emits hundreds of powerful, highly focused gamma radiation beams. The gamma knife allows for a more precise and concentrated treatment than do other radiation treatment options. This helps the doctors target the diseased area of the brain while sparing the healthy areas surrounding it.

The frame is positioned in a special helmet so the radiation will be directed at the targeted area. The patient lies on a bed that slides into the gamma knife machine. Radiation is delivered through 201 ports inside the helmet, with the beams intersecting at the target.

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When is gamma knife treatment used for PD?

Gamma knife treatment is considered only when a person is not able to get relief from medication and when deep brain stimulation, which is a more effective therapy, is not appropriate.

Gamma Knife Information

- Established effectiveness after 25 years of world wide experience with no reported mortality and few complications
- Common Complications
  - Local Pain/Swelling
  - Headache
- Rare Complications
  - Seizure
  - Nausea
  - Irritation
- Delayed Complications
  - Uncommon
    - Local Loss of Hair
    - Brain Swelling in treatment site
    - Necrosis in treatment site
  - Rare
    - Visual Loss Depends on (Treatment Site)
    - Hearing Loss Depends on (Treatment Site)

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Neuropsychological change following gamma knife surgery in patients with left temporal lobe epilepsy: a review of three cases.

- Results revealed a significantly long delayed verbal memory decline on one measure following GKS.
- No patient declined on measures of IQ, visual memory, or language.
- Radiation-induced edema was present at the time of testing in all three patients, which may have affected verbal memory performance.

Short-term neuropsychological outcome following Gamma Knife radiosurgery for arteriovenous malformations: a preliminary report.

- 10 patients before and after radiosurgical treatment with Gamma Knife.
- Neuropsychological testing within 1 week before Gamma Knife radiosurgery.
- Testing was repeated an average of 11.4 months after treatment.
- There were no statistically significant differences between pre- and postradiosurgical neuropsychological test scores on any measure.

Gamma knife radiosurgery as a lesioning technique in movement disorder surgery.

Fifty-five patients underwent radiosurgical placement of lesions either in the thalamus (27 patients) or globus pallidus (28 patients) for treatment of movement disorders. Clinical follow-up evaluation indicated that 88% of patients who underwent thalamotomy became tremor free or nearly tremor free. Statistically significant improvements in performance were noted in the independent assessments of Unified Parkinson's Disease Rating Scale (UPDRS) scores in the patients undergoing thalamotomy.

Of patients undergoing pallidotomy who had exhibited levodopainduced dyskinesias, 85.7% had total or near-total relief of that symptom. Clinical assessment indicated improvements in bradykinesia and rigidity in 64.3% of patients who underwent pallidotomy.

No other complications of any kind were seen. Neuropsychological test scores that were obtained for the combined pallidotomy and thalamotomy treatment groups preoperatively and at 6 months postoperatively demonstrated an absence of cognitive morbidity.

How successful is gamma knife treatment?

The benefits of gamma knife treatment occur over time, usually several months to several years, depending on the person's medical condition.

Gamma knife treatment has up to a 70%-90% success rate, which depends on the patient and the disorder he or she is being treated for.

Cell Implantation

Reversibility?

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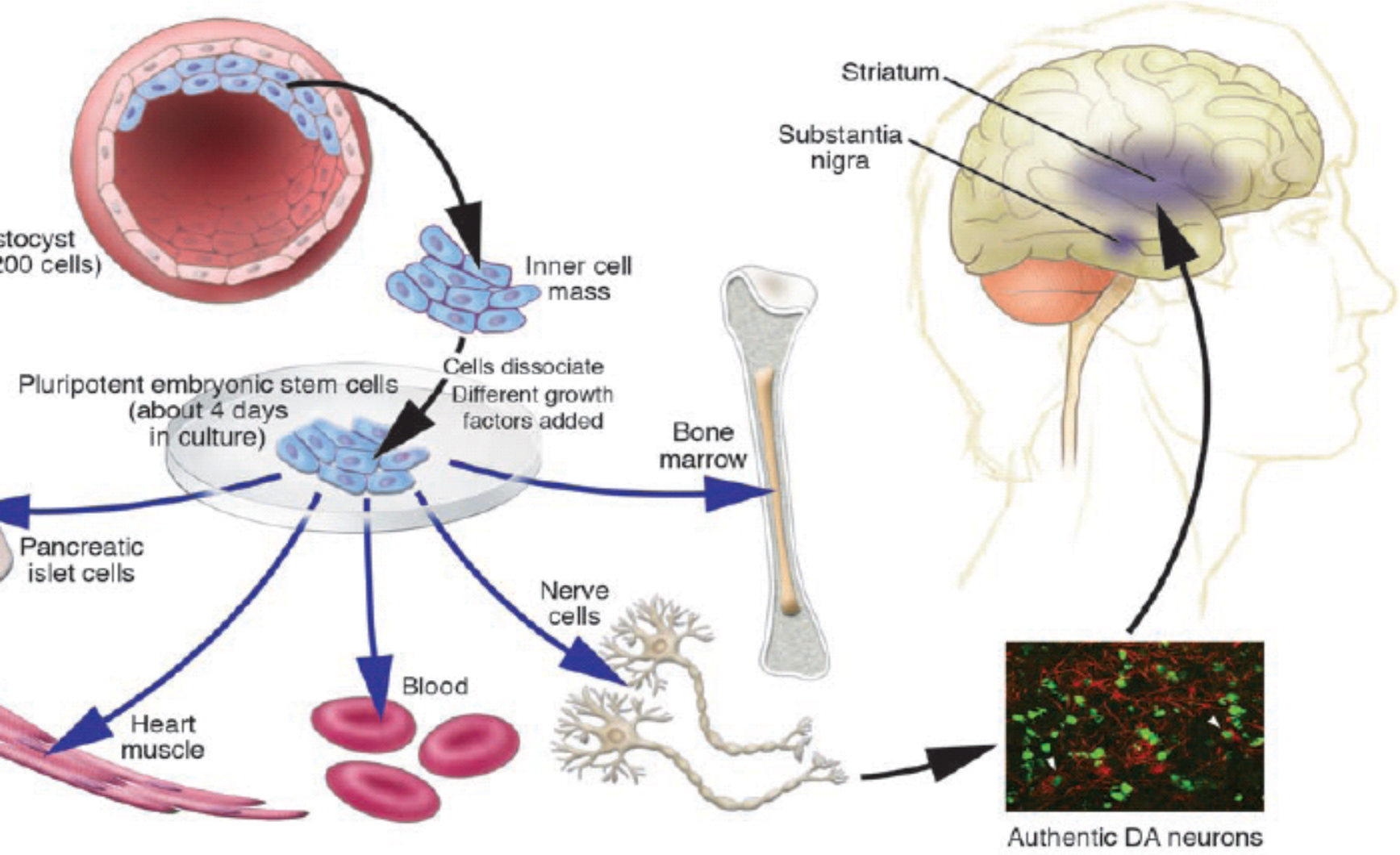

yonic stem cells are obtained from the inner cell mass of the blastocyst stage of development. These cells have the potential to tissue type. A variety of different treatments or "cocktails" have been devised to coax these cells into developing into a neuronal into authentic DA neurons. Green, BrdU; red, tyrosine hydroxylase–positive (TH-positive) DA neurons (8). These are then used ent therapy by transplantation into the area of the brain where DA nigrostriatal neurons have degenerated. To date, almost all nts have involved putting these cells into the striatum (which lies deep in the brain, below the shaded area in the figure) as have al studies. However, it is still not clear that this is the best target area; it is also possible that it will be necessary to transplant the sites, including the substantia nigra. The major challenge at the current time appears to be getting transplanted DA embryonic ntain their DA phenotype in large numbers and over a prolonged period of time.

Promise of Stem Cells

Thus, replenishing missing neurons in a limited area of the brain should in theory reverse parkinsonism, making this an attractive approach. But the challenge of actually replacing injured and/or lost neurons in the adult human nervous system has proven to be a daunting task with far more bumps in the road, both political and scientific, than anyone would have anticipated.

The promise of stem cells in Parkinson disease

J. William Langston The Journal of Clinical Investigation Volume 115 Number Jan 2005

Do patients with Parkinson's disease benefit from embryonic dopamine cell transplantation?

- Embryonic dopamine cell transplants survive in nearly all patients regardless of age and without immunosuppression. Transplants can improve Parkinson "off" symptoms up to the best effects of L-dopa observed preoperatively. They cannot improve the "best on" state.
- Transplants appear to survive indefinitely.
- In 10 to 15% of patients, transplants can reproduce the dyskinetic effects of L-dopa even after discontinuing all L-dopa.
- Neurotransplantation should be tried earlier in the clinical course of Parkinson's.

Dyskinesia after fetal cell transplantation for parkinsonism: a PET study.

(18)F]fluorodopa (FDOPA) and positron emission tomography to determine whether this complication resulted from specific alterations in dopamine function after transplantation.

Unbalanced increases in dopaminergic function can complicate the outcome of neuronal transplantation for parkinsonism.

Reaction time and movement time after embryonic cell implantation in Parkinson disease.

Double-blind, placebo-controlled trial. Patients Forty patients with levodopa-responsive, Hoehn and Yahr stage III or greater PD.

Random assignment to embryonic tissue implants or placebo (sham) operation.

Combined RT + MT scores measured preoperatively and at 4 and 12 months postoperatively in the "off" state.

RESULTS: The difference in mean RT + MT scores between the sham and implant groups was statistically significant (P =.005) and was greatest in those 60 years or older (P =.003). Changes correlated with Unified Parkinson's Disease Rating Scale off scores at 4 (r = 0.87, P =.001) and 12 (r = 0.75, P =.01) months in those younger than 60 years.

There was a significant deterioration in the sham surgery group at 12 months (P =.03) that was thought to be due to worsening in subjects 60 years and older (P<.001)..

Retinal Cell Implantation

Another cell transplant technique that shows some promise is the use of retinal pigment epithelial cells. These cells are derived from tissue at the back of the eye, and they produce and release dopamine. An open-label trial in six advanced PD patients has shown promise, and as of mid-2004, a double-blind trial is underway.

Implantation of Spheramine in advanced Parkinson's disease (PD).

Evaluation of the safety and efficacy of unilateral stereotactic implantation of cultured human retinal pigment epithelial (hRPE) cells attached to microcarriers (Spheramine) in patients with advanced PD in an open label pilot study. (3 males; 3 females; mean age 52.2 years; mean duration of PD 10.2 years; mean Hoehn and Yahr stage "off" 3.75) were assessed at baseline and post-operatively using the modified CAPIT.

The UPDRS Motor (UPDR-M) score in the practically defined "off" state was the primary outcome measure.

At 6 months post-op, the mean UPDRS-M (off) score improved to 35 (34%) from a pre-op baseline mean of 52 ($p < .001$).

Secondary outcome measures improved including the total UPDRS (33%), Timed Motor Tests (on, 14%; off, 23%),

PDQ39 QOL (30%), and Schwab and England score (on, 11%; off, 30%). Bilateral improvements have been observed in motor symptoms, with the greatest effect seen contralateral to the implants.

Three of six patients currently have lower Dyskinesia Rating Scale scores than at baseline, while the scores of the other three are unchanged from baseline values. No "off-state" dyskinesias have been observed.

Growth Factor Delivery

- Glial cell-derived neurotrophic factor (GDNF) stimulates sprouting of dopamine neurons in animal models.
- Direct delivery of GDNF to the brain has produced promising results in an open-label trial in a small number of patients, but by mid-2004 a larger, double-blind trial failed to show efficacy.

Gene Therapy

As of 2004, gene therapy has been tried in only a few PD patients, and is still highly experimental. While experiments in animal models of PD have shown promise, further research is needed. The only publicized trial is of delivery of the gene for glutamic acid decarboxylase (GAD) to the subthalamic nucleus or STN. GAD is a key enzyme in the production of the inhibitory neurotransmitter GABA. Gene therapy with GAD is meant to increase GABA production, reducing STN activity in the manner of STN DBS. Monitoring is still in progress.

Longer Term Maintenance

Therapies (don't forget psychological)

Long Term Therapy Intervention

- Motivation will continue to be your biggest barrier for successful therapy. Imagine being stuck in your body unable to move for years, forced habits are very hard to overcome.
- Surgery cannot cure or resolve all the complex symptoms of a chronic progressive neurological disease.

Physical Therapy

Physical therapy

Goals of physical therapy include maintaining or increasing activity levels, decreasing rigidity and bradykinesia, optimizing gait, and improving balance and motor coordination. Features of the PT program may include:

Regular exercise.

Stretching and strengthening

Exaggerated or patterned movements, such as high stepping and weight shifting

Mobility aids, orthotics (such as braces or splints)

Training in transfer techniques

Training in techniques to improve posture and walking

Occupational Therapy

Goals of occupational therapy include maximizing fine motor coordination, especially of the upper extremities, reducing energy expenditure, increasing safety and independence, and improved efficiency of activities of daily living. Features of the OT program may include:

Use of orthoses and adaptive equipment

Home and workplace modification, improving accessibility, and removing obstructions

Adaptation and simplification of utensils, toileting articles, beds, etc

Resources

Obesityhelp.org (provider ratings)

Cleveland Clinic Website

Medtronics.com

Wemove.org

Mac2. innanen.com (patient's personal website)

waparkinson's.org DVD