

**So, now that you've had  
DBS surgery....**

**Vicki Wheelock MD**  
Health Sciences Clinical Professor  
Department of Neurology  
UC Davis

# Learning objectives

- Understand the outcomes of DBS for Parkinson's disease, essential tremor and dystonia
- Appreciate DBS-associated side effects and complications
- Anticipate the timeline of clinical changes following DBS implantation
- Learn safety concerns about DBS in the medical environment

# Medtronic® DBS system

## 3 Neurostimulator



Lead and Electrodes

1

2 Extension



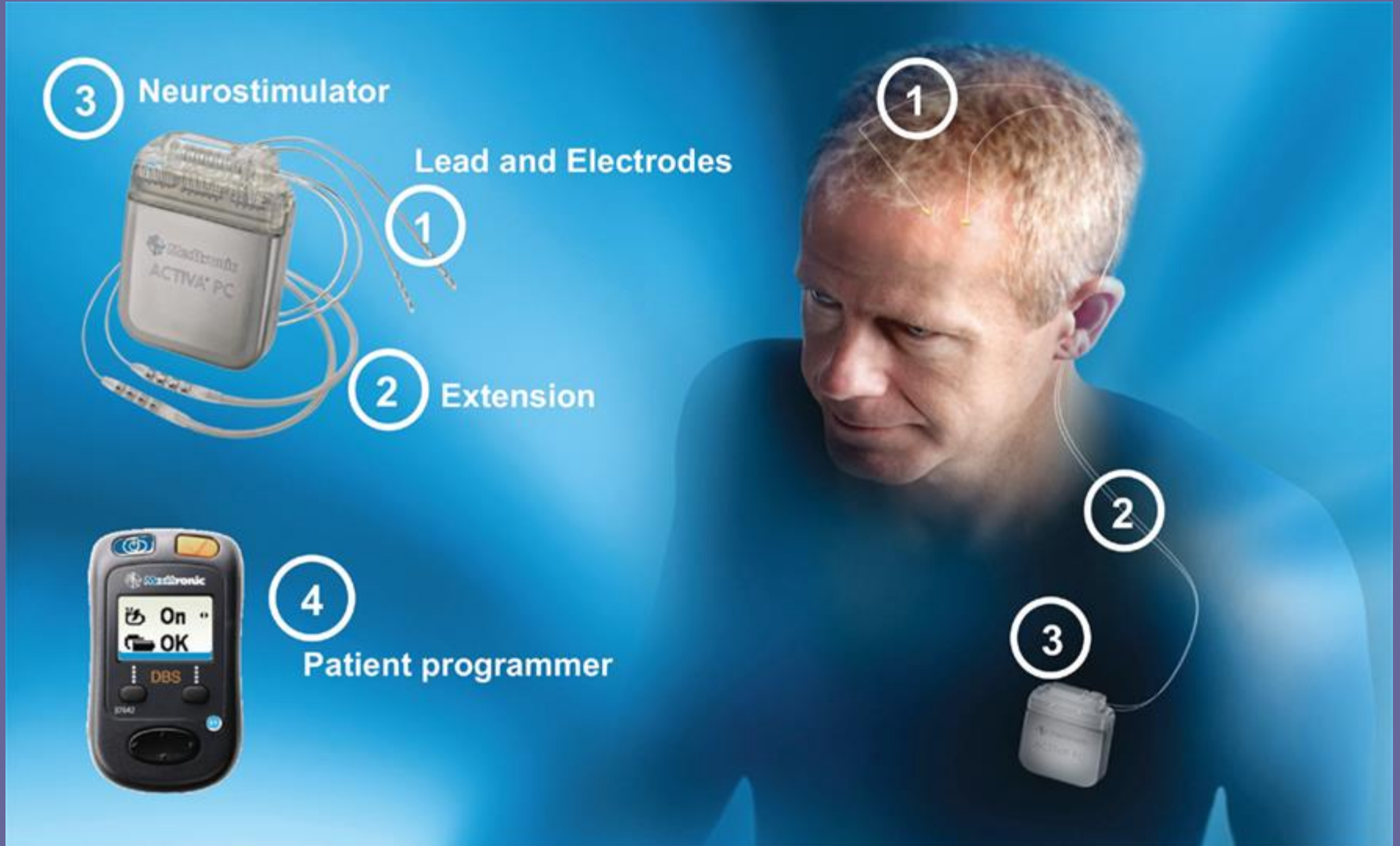
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Patient programmer

1

2

3



# Medtronic® DBS system



**PC  
Implantable  
Pulse  
Generator**

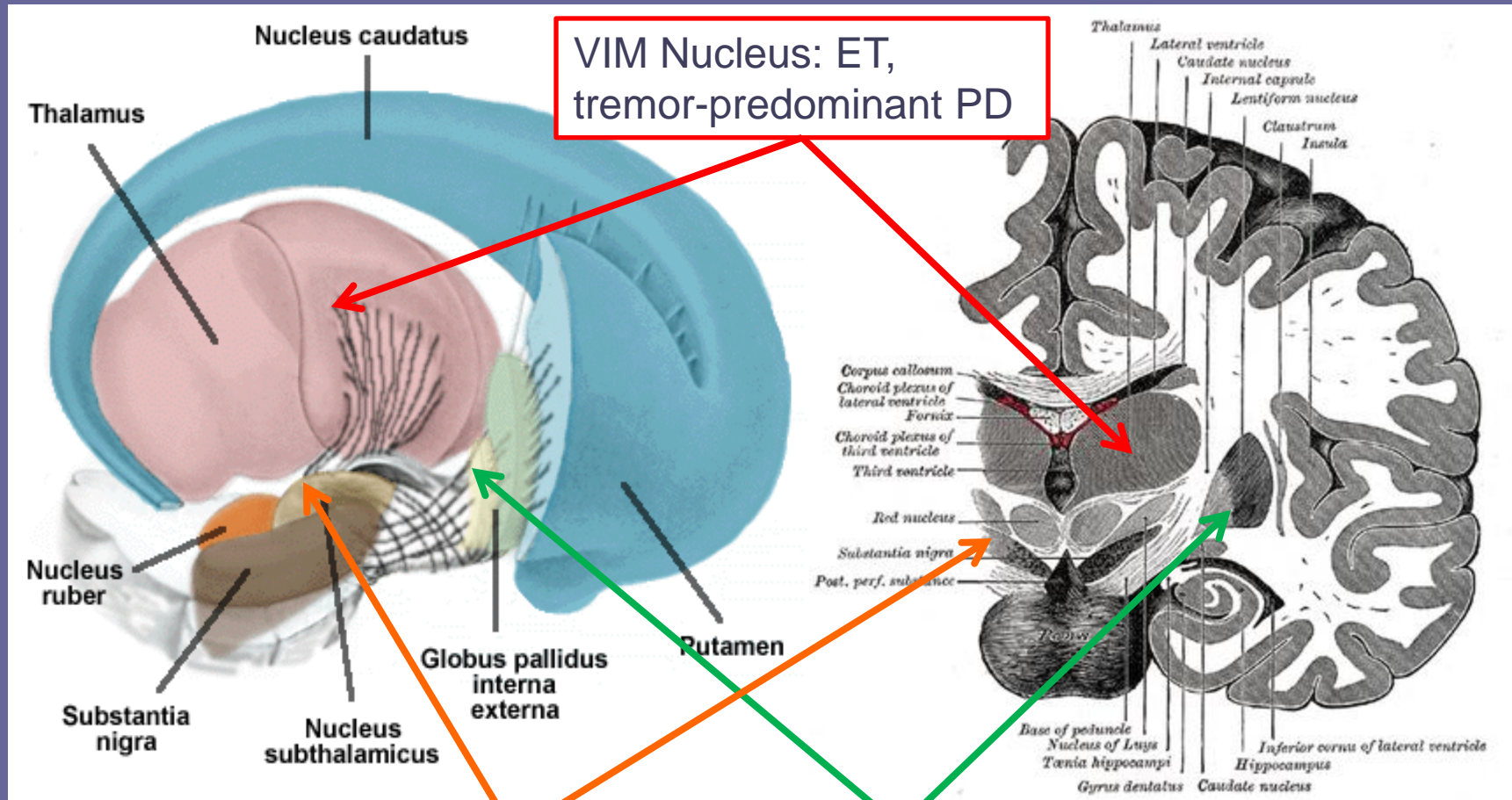


**RC IPG**



**Patient  
Programmer**

# Anatomic targets of DBS

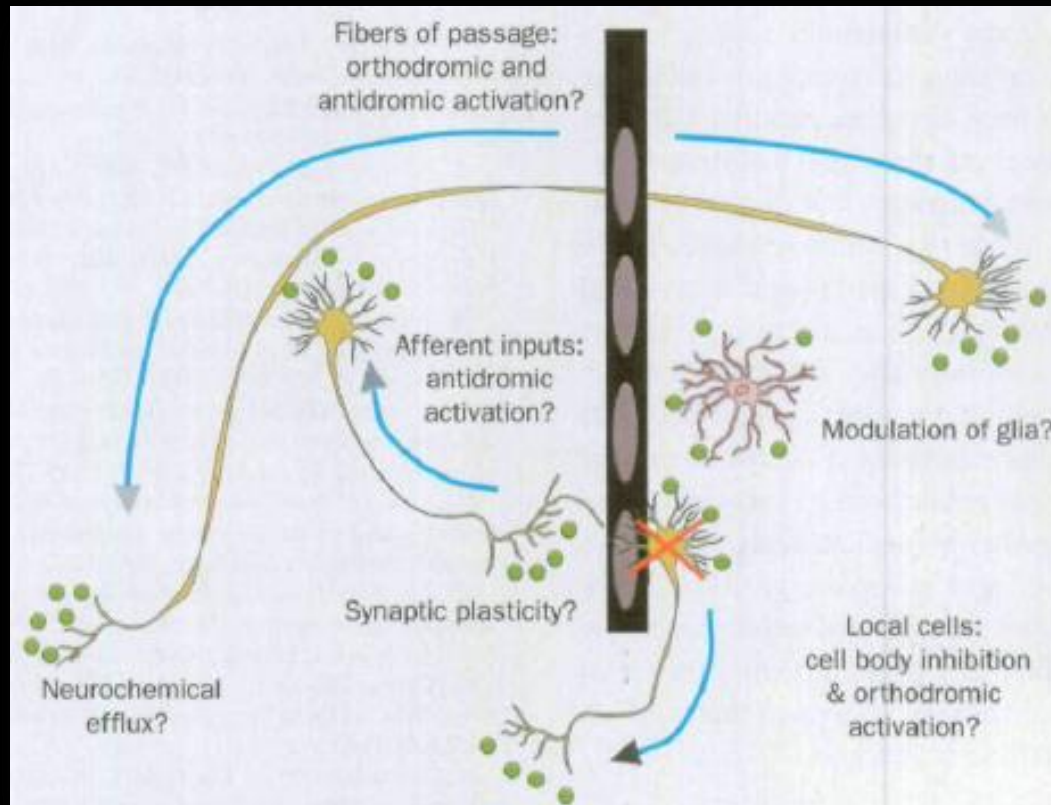


VIM Nucleus: ET,  
tremor-predominant PD

Subthalamic nucleus:  
PD, dystonia

Globus pallidus interna:  
PD, Dystonia

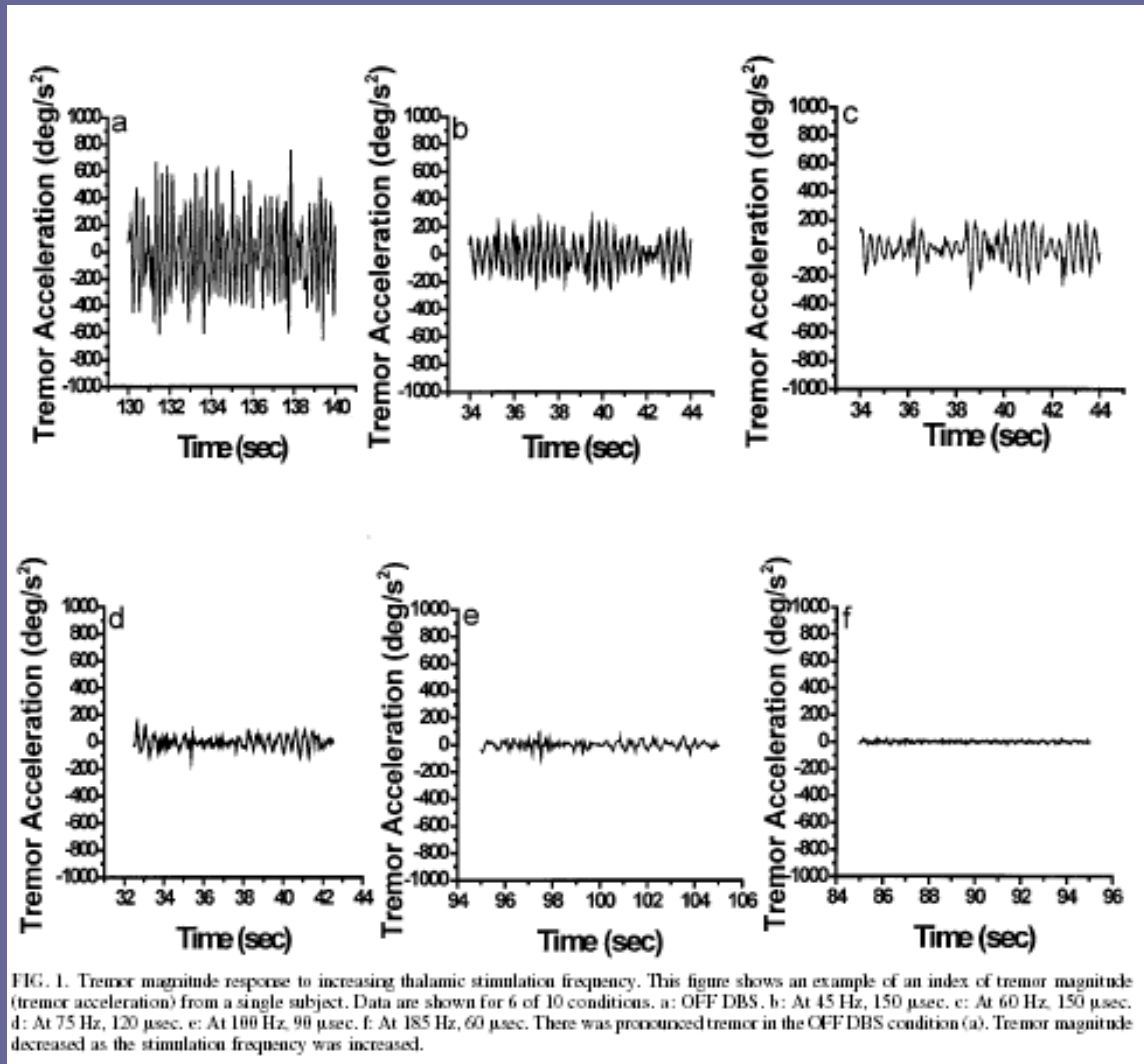
# Mechanism of DBS: neuromodulation



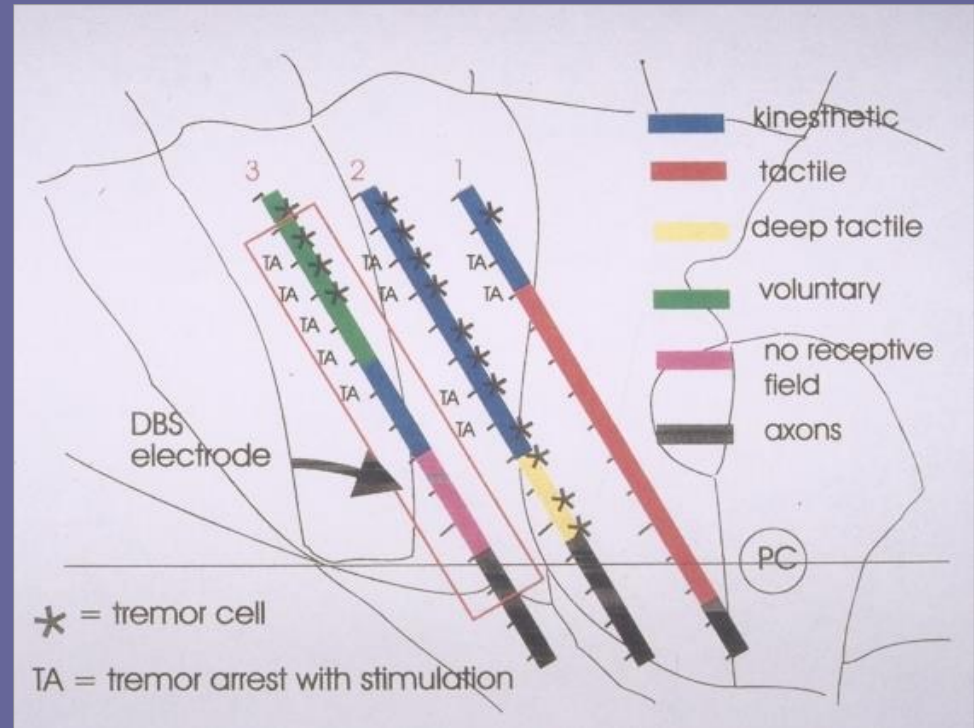
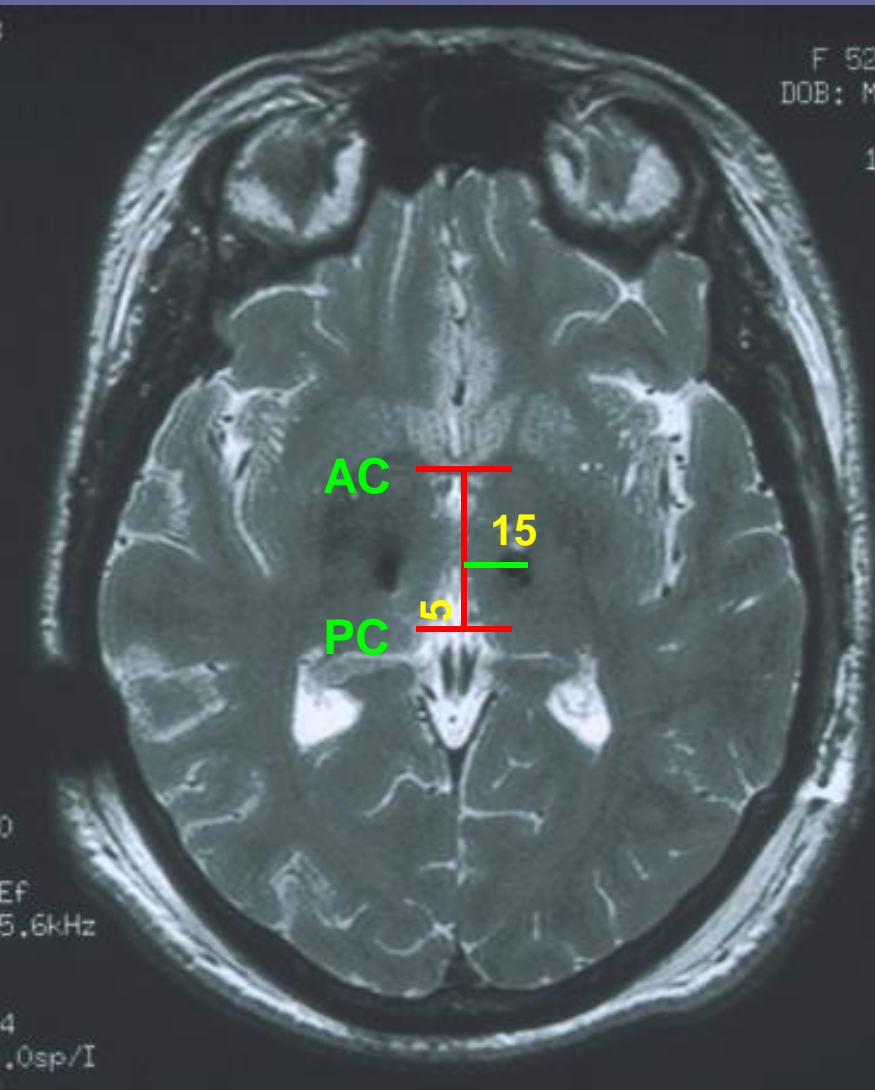
- **Inhibits** local neuronal activity
- Possibly **stimulates**
  - orthodromic action potentials
  - antidromically active afferent inputs
  - neurons near the electrode

Possibly **modulates** local glial activity, neurotransmitter release, plastic synaptic changes locally or distally.

# Relationship between DBS frequency and tremor



# DBS for Essential Tremor

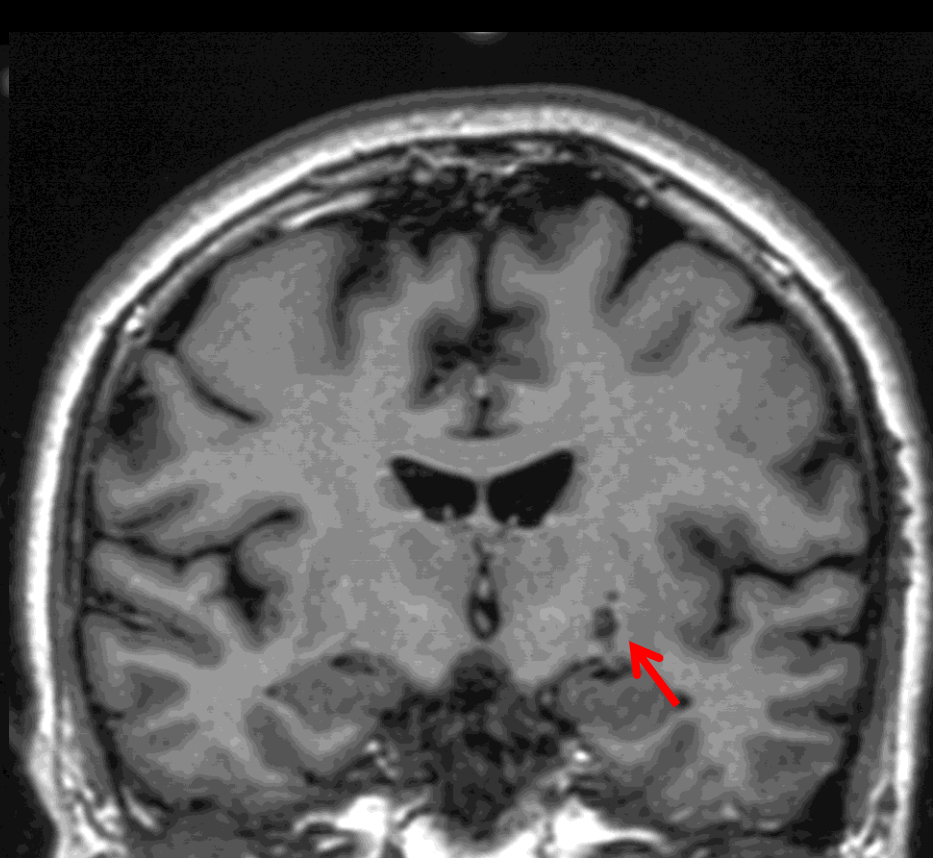
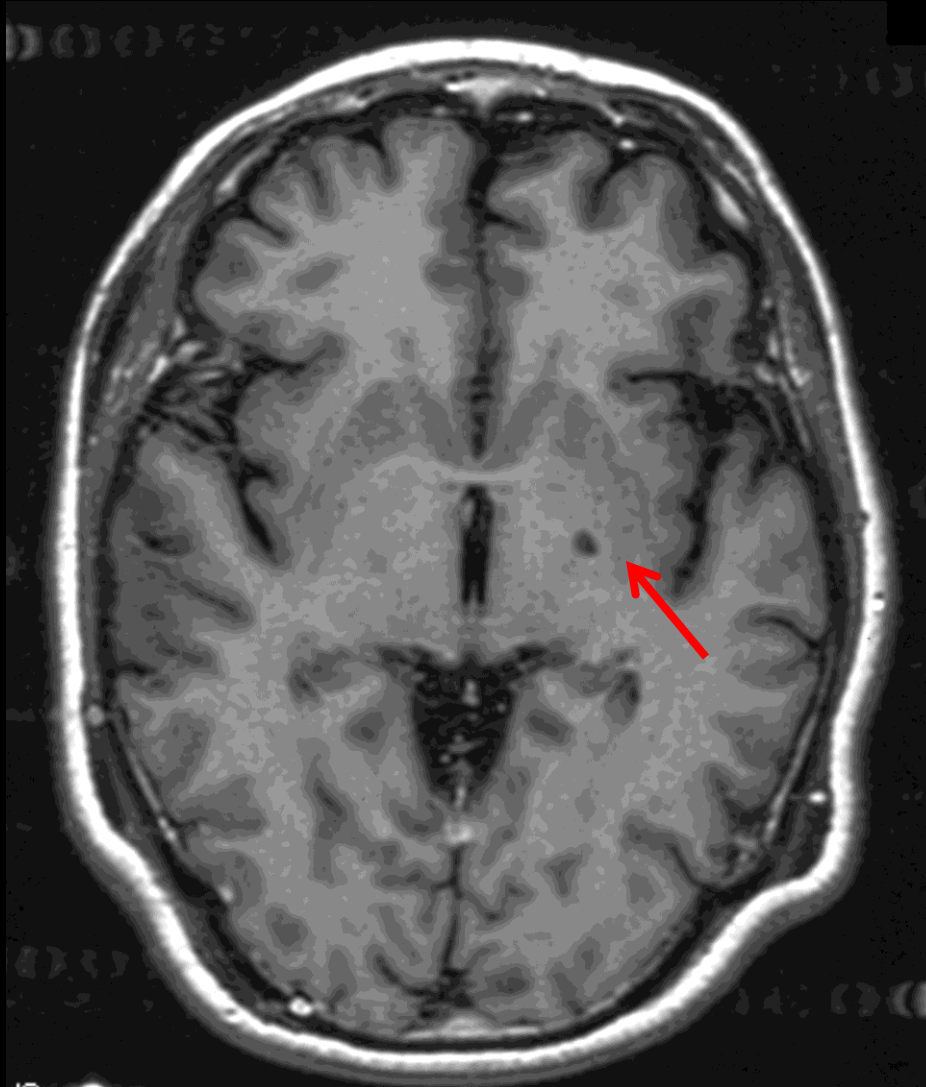


*From Lozano, University of Toronto*

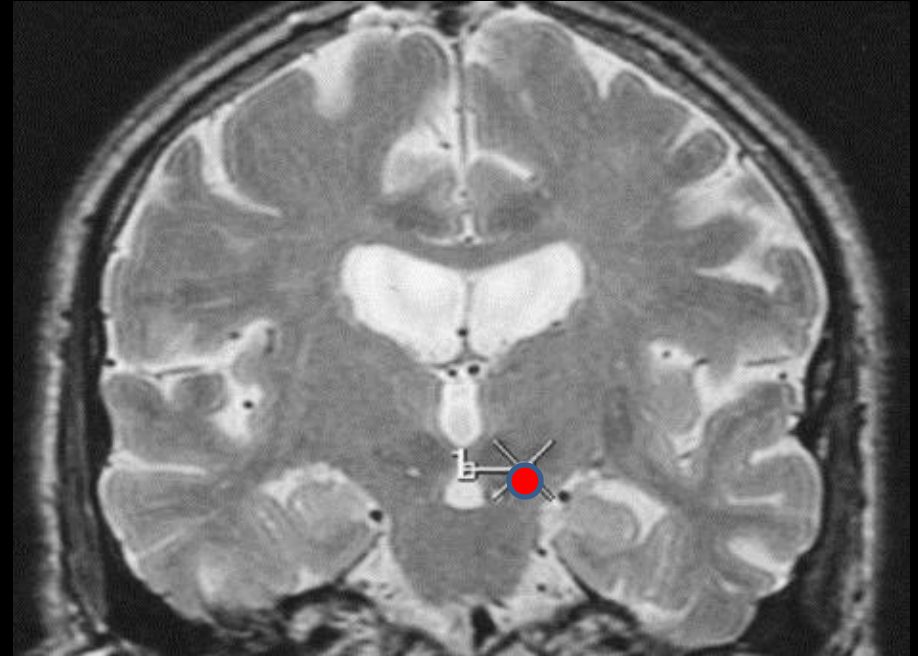
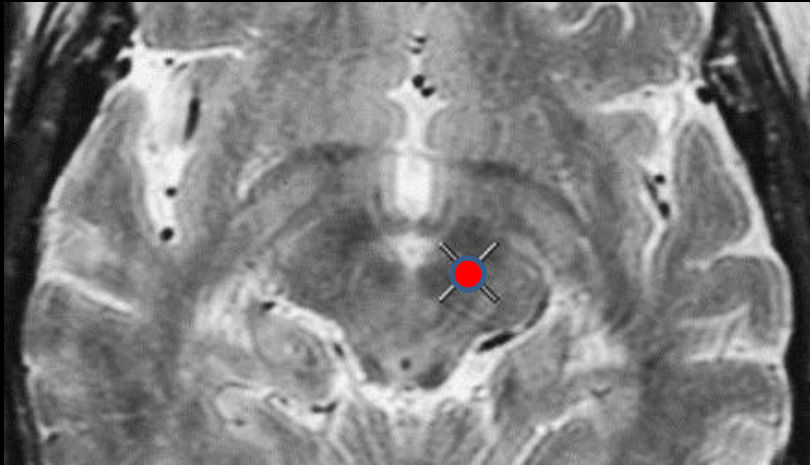
Target: Vim nucleus of the thalamus



# Globus pallidus interna target



# Subthalamic nucleus target



Planning coronal MRI showing anatomical targeting of left subthalamus (10 mm anterior to posterior commissure, 9-10 mm lateral from midline).

The target on the coronal images is lateral to the inferior border of the red nucleus and medial to substantia nigra.

# Differences between GPi and STN targets

Effects on motor symptoms are equivalent

## GPi

- More challenging for NS targeting
- Benefits take days to weeks to appear
- No PD medication reduction
- Side effect profile simpler

## STN

- Somewhat easier for NS targeting
- Benefits are immediate
- About 50% reduction in PD meds
- Side effect profile more complex; cognitive, behavioral more common

# DBS patient post-op instructions

- Re-start PD meds, typically at pre-op dosage
- Review wound care instructions: *AVOID INFECTIONS!*
- Fall prevention
- Sleep with head elevated for first week
- Common post-op behavioral effects may include
  - Apathy
  - Hypomania
  - Depression
  - Impaired judgment
- Strongly recommend 24 hr caregiver for at least the first week
- No driving until cleared by medical team

# Initial DBS programming

Timing: Before leaving hospital, or 1-2 weeks later

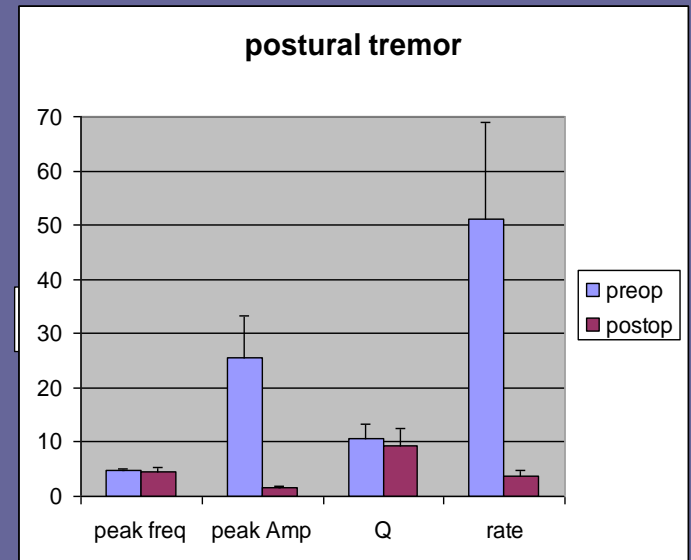
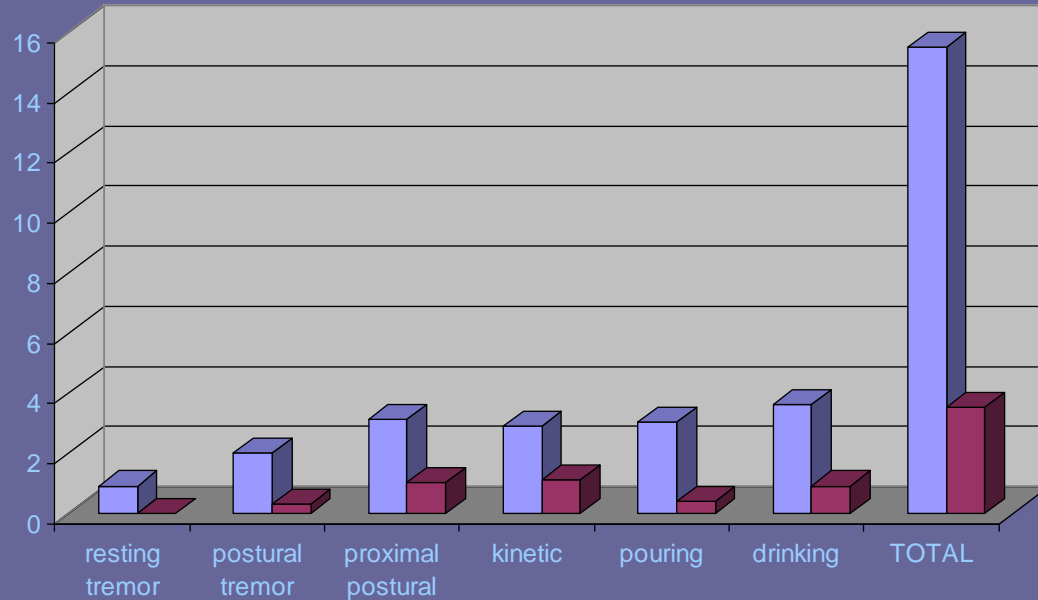
For PD: off meds

Each of the 4 contacts for both sides of the brain will be mapped for clinical benefits and side effect thresholds

Often only one contact on each side needs to be activated. Once the best contact is identified, it will be turned on at a low, initial setting.

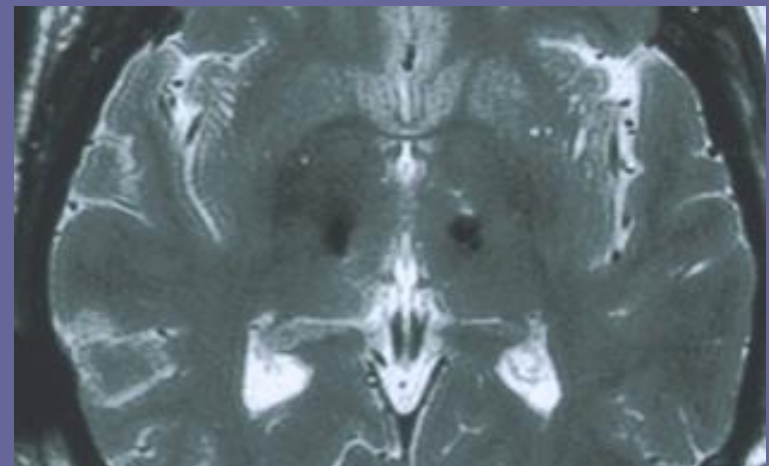


# Benefits and side effects for Essential Tremor

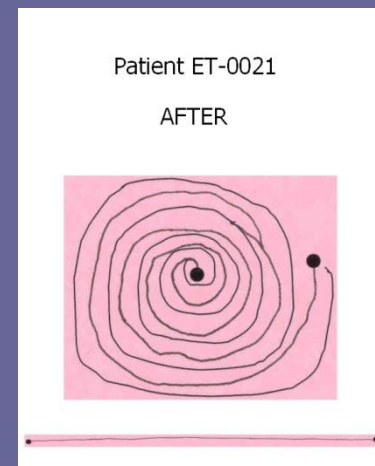
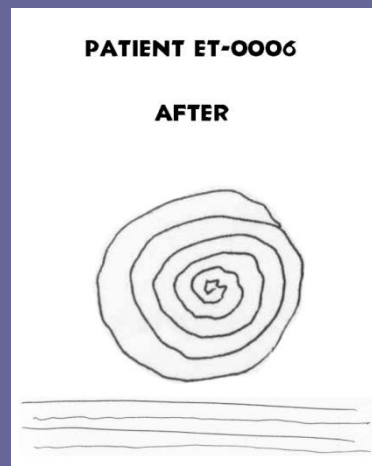
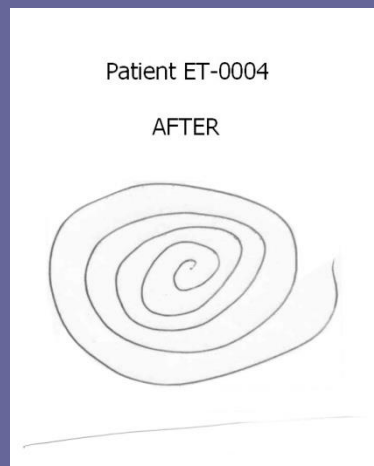
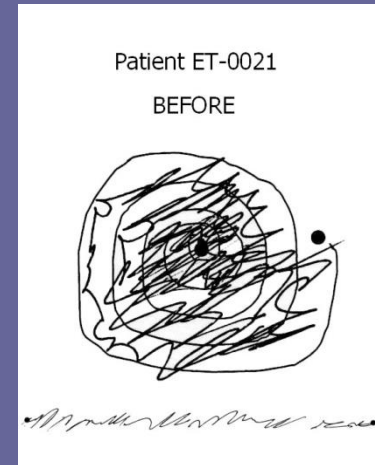
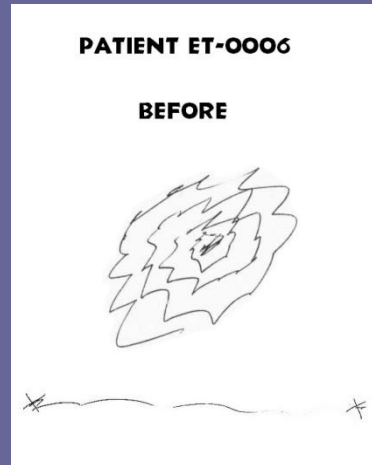


**Motus quantification**

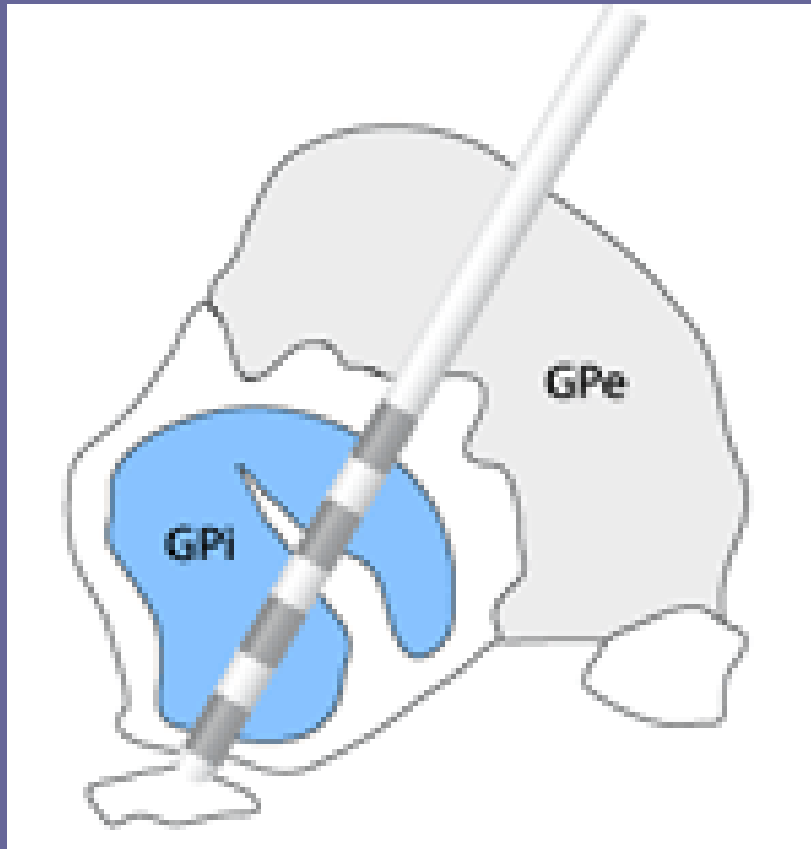
- Side effects:
  - Contralateral paresthesia or corticospinal tract activation
  - Dysarthria
  - Hemiataxia
  - Loss of benefit: 10-20% patients



# Pre- and post-op writing samples

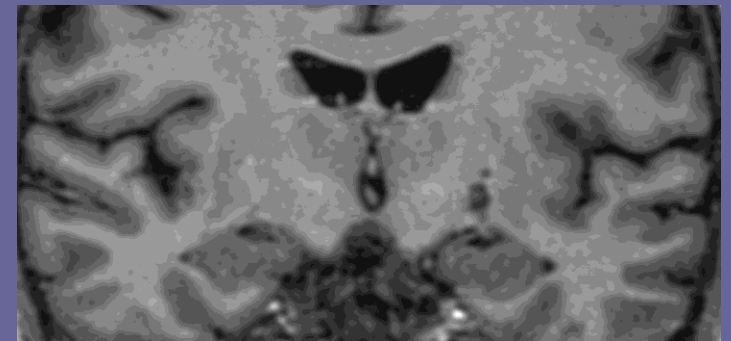


# GPI DBS



## Side effects:

Contralateral  
corticobulbar activation  
Visual phenomena



## Benefits:

Reduction in tremor,  
rigidity, dyskinesia,  
dystonia  
No reduction in PD  
meds



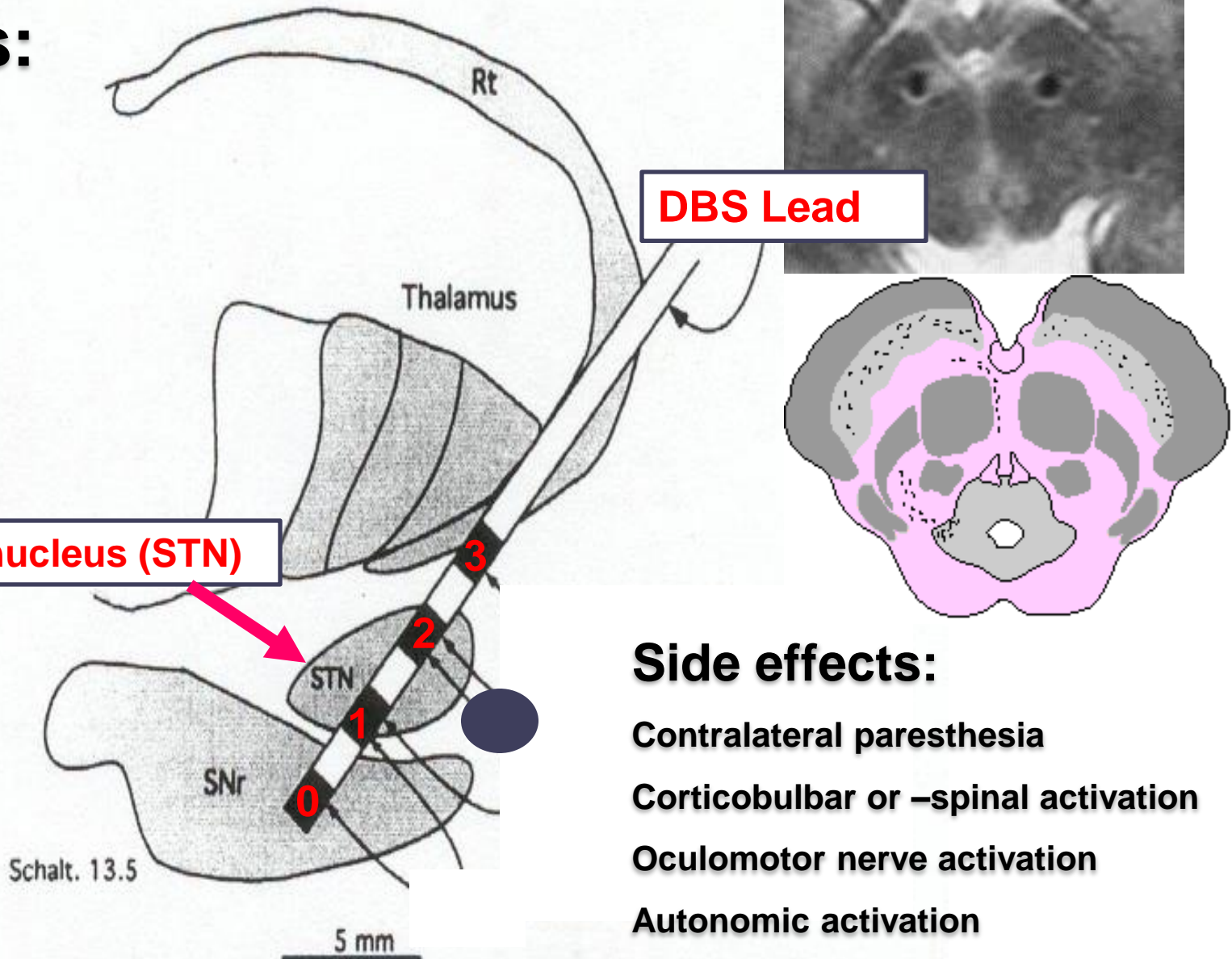
# STN DBS

## Benefits:

Tremor

Rigidity

Slowness



**DBS Lead**



## Side effects:

Contralateral paresthesia

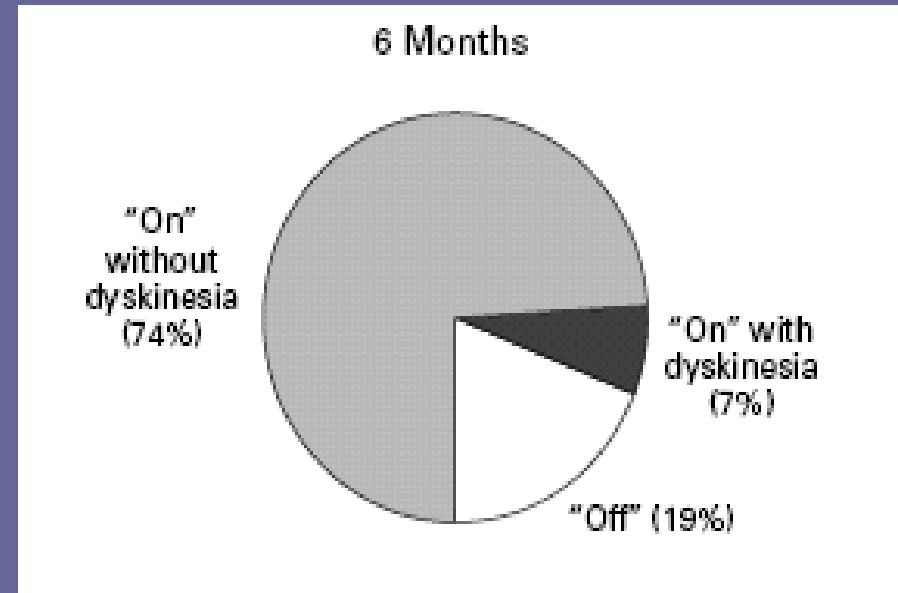
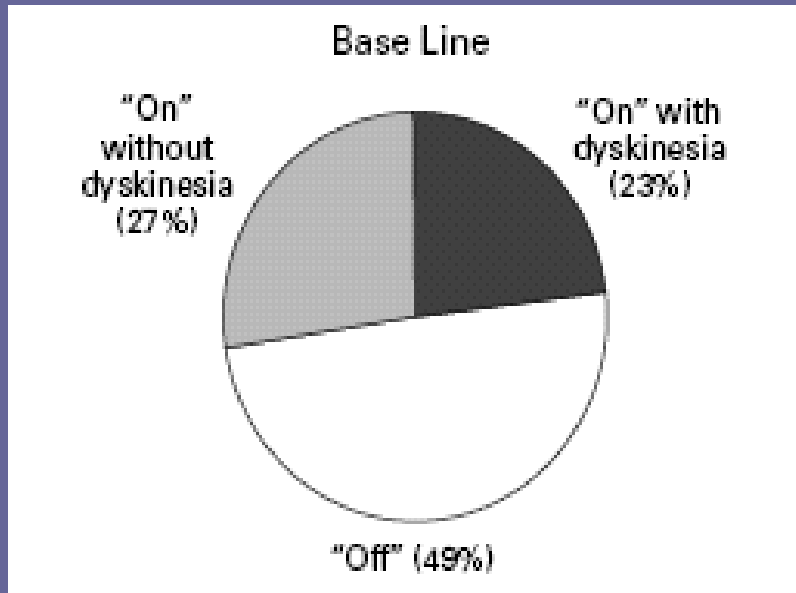
Corticobulbar or –spinal activation

Oculomotor nerve activation

Autonomic activation

Limbic changes

# Benefits of DBS for PD



More "on" time: 6 hours/day

Less "off" time, less severe "off" symptoms

Less dyskinesia

Source: DBS Study Group, NEJM 345:2001

# Randomized trial of STN DBS for PD

Deuschl et al, NEJM 2006;355:896-908

- N = 156 PD patients
- Patients randomized to DBS within 6 weeks vs. best medical therapy
- Outcome measures: PD QOL, UPDRS motor scores
- Results:
  - DBS group
    - QOL improved 25%,
    - Motor scores improved by 41%,
    - dyskinesia reduced by 54%
  - Medical therapy group: no improvement
  - AEs common in both groups (> 50%), but SAE from surgery rare.

## RCT of DBS vs best medical therapy in advanced PD

Weaver et al, JAMA 2009

- 255 patients enrolled; 134 assigned to BMT, 121 to DBS (60=STN, 61 =GPi)
  - 82% male, 25% age over 70, mean 12 yrs after onset of PD
- Outcome measures:
  - 1<sup>o</sup>: time spent in “on” state by motor diary
  - 2<sup>o</sup> : UPDRS motor, QOL, cognition, adverse events
- Results: Surgical group avg 4.6 hr/d more “on” time than BMT, better motor function, improved QOL, but more adverse events.
  - No difference in effect for age
  - SAE 49 DBS (2 deaths), 15 of BMT patients
  - 99% resolved by 6 months

# Reported complications of STN DBS surgery

- 222 patients from 15 sites, 2001-4
  - Brain hemorrhage: 0-5.2%
  - Seizure: 0-8.2%
  - Post-op confusion: 0-32%
  - Infection: 0-11.4%
  - New psychiatric: 0-25%
  - Eyelid apraxia: 0-36%
  - Speech problems: 0-28%

# Effects of STN DBS on cognition

- Morrison et al. *Arch of Neuropsych* 2003;612;1-17.
  - 17 patients with 11 non-operated PD controls, evaluated pre-op and 8 weeks post-op, with DBS on/DBS off.
  - Results: mild decline in attention and language. No effect of DBS.
- Higginson et al, *J Clin Exp Neuropsychol*. 2008 May 19:1-8.
  - N= 23 subjects, baseline vs 6 months post-op
  - Methods: Reliable Change Index (establish confidence interval surrounding each test score)
  - Results: 20% of pts. ↓ verbal memory, letter fluency, auditory attention.

# Adverse events from DBS, prospective RCT

Weaver et al, JAMA 2009

Symptom	0-3 months			4-6 months		
	BMT	DBS	p value	BMT	DBS	p value
Headache	1	20	.001	0	1	n.s.
Confusional state	1	13	.001	3	3	n.s.
Falls	6	16	.02	5	14	0.3
Pain	3	10	.04	3	8	n.s.
Bradykinesia	4	12	.04	3	4	n.s.
Speech	2	12	.004	3	7	n.s.
Phonemic fluency				-1.1	-4.6	.001
Working memory				-1	-2.6	.005
Processing speed				-0.7	-2.9	.005
Delayed recall				-2.2	-3.2	.03
Beck dep. index				-1	-1.5	n.s.
Wound Infection	n.a	12 pts had 16 infections				
Death	n.a.	2 ( 1 surgical), 1 lung CA				

# Differential effects on PD symptoms

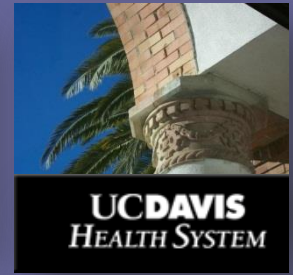
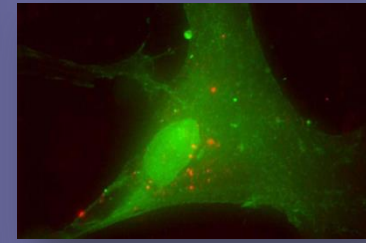
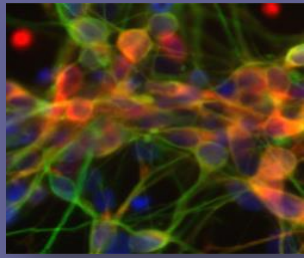
- The symptoms that respond best to PD meds are also the symptoms that respond to DBS.
- Tremor is usually better controlled with DBS than with meds.
- Dyskinesia is significantly improved
- With PC and RC IPGs, **group settings** can be programmed
  - Up to 4 different groups can be programmed by clinician to allow multiple types of adjustments
  - For instance, group can target specific symptoms or side effects
  - Use of groups limited by patient/caregiver factors



# DBS for dystonia

Pallidal DBS for dystonia, Dystonia Study Group, NEJM 2006;355:1978-90.

- N= 40 patients with primary segmental or generalized dystonia randomized to either blinded active or sham DBS for 3 months, Primary outcome measure: change in Burke–Fahn–Marsden Dystonia Rating Scale at 3 months.
- Results: Significant reduction in the BFM DRS score ,  $p < 0.0001$
- Complications: Infection in 4, lead dislodgement 1, dysarthria 6, worsening dystonia in 2.
- Humanitarian Device approval FDA
- Indications:
  - Generalized dystonias
  - Focal or segmental dystonias, hemidystonias, cervical dystonia with 1<sup>o</sup> or 2<sup>o</sup> resistance to botulinum toxin therapy
  - Good responders: difficult to predict. DYT-1 gene + usually respond well. Possible responders: tardive dystonias.
  - Will not help fixed contractures
  - No dementia, serious medical/psychiatric illness



# After initial programming

- There should be improvement in tremor, rigidity or dyskinesia, “off” time
  - For ET, PD with STN target, changes are immediate
  - For dystonia and PD with GPi target, benefits appear more slowly
- Initial benefits may be transient
- DBS parameters need to be increased as instructed.
- Often clinical changes are asymmetric or incongruent

# Patient Programmer



Simple Mode



Advanced Mode

# What should patients watch for?

- Track primary symptoms: tremor, on/off time and dyskinesia, dystonia.
- Track benefits and side effects, including sidedness
- Practice using patient programmer.
- Watch for mood/behavior changes and report to neurologist.
- Report any signs of redness, drainage or new soreness/swelling around surgical sites **IMMEDIATELY**.
  - Both immediate AND late infections

# 2 weeks to 5 months after surgery

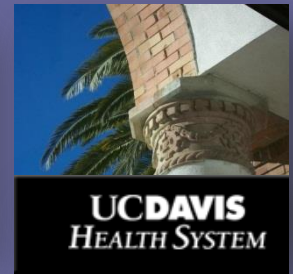
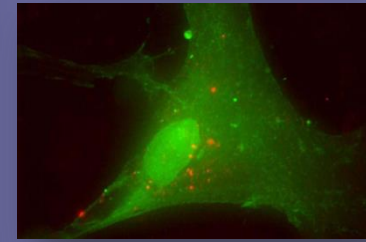
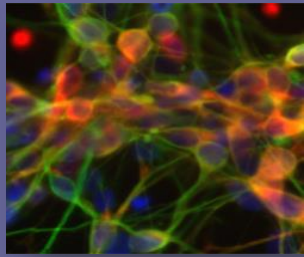
- Improvement in motor symptoms will continue. As the settings are adjusted, PD medications will be slowly reduced (STN only)
  - Most patients tolerate 50% reduction in PD meds after DBS is optimized
- On average, it takes 3-5 months of adjusting DBS settings and medications before optimal results are reached.
- Once optimal settings are reached, follow-up every 6-12 months
- DBS settings may need slight adjustments from year to year.

# Common adverse effects of DBS

- Parkinson's disease
  - Speech articulation and volume change in most patients; stimulation-related
  - Falls
  - Cognitive decline
  - Mood and behavioral changes
  - Eyelid opening apraxia
- Essential tremor: Paresthesia
  - Less common: loss of effectiveness
- Dystonia: Worsening of dystonia

# How long will IPG last?

- 3-5 years. The exact time is dependent on how much current is needed from each IPG.
- It's important to check IPG battery charge at least annually; more often as battery charge begins to drop off.
- Always avoid end-of-life for IPG if possible.



## MRI safety issues and DBS

- MRI fields can induce tissue damage
- Contraindications include using a full body radio-frequency (RF) coil, a receive-only head coil, or a head transmit coil that extends over the chest area
- **NO MRI of low back, hip, knee etc.**
- Only specific MRI protocols on specific MRI units are safe – the radiologist should be closely involved
- Before MRI, IPG should be re-programmed to factory settings before MRI by neurologist or nurse practitioner

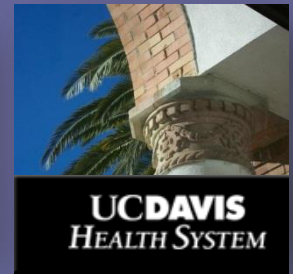
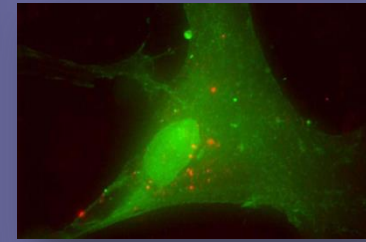
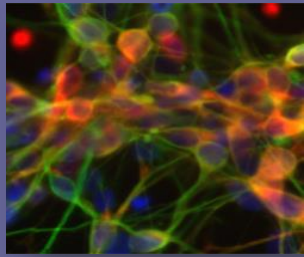


# SAFETY concerns for DBS

## Avoid:

- Diathermy, ultrasonic treatments in PT
- Electrocautery
- Electromagnetic fields, including metal detectors, security screening
- Welding
- Electrical work
- Some work places (metal detectors)
- Cardioversion ?
- Allowed, no restrictions:
  - CT, diagnostic ultrasound, X-rays
- Medic Alert Bracelet recommended

What about airline travel? OK, but ask for hand search and pack your Access Review in carry-on



# What about long-term results?

- For **ET**, benefits are long-lasting but may be less robust over time (Rehncrona S et al. *Movement Disorders* 18;2003:163–170)
- For **dystonia**, benefits are long-lasting
- For **PD**:
  - DBS remains very effective for relief of tremor, rigidity, dyskinesia
  - Speech and axial symptoms worsen
  - Cognition worsens
  - PD medications may need to be increased from year-to-year
  - DBS settings may also need to be slightly increased

# Long-term effects of STN DBS

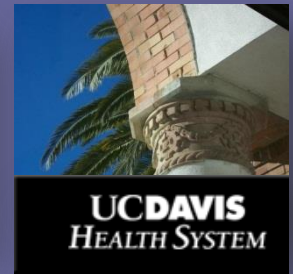
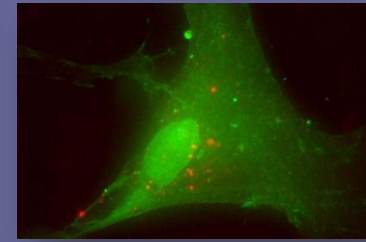
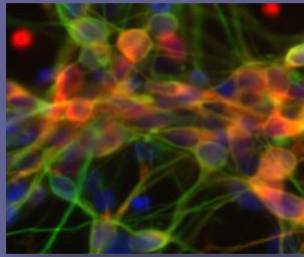
Kleiner-Fisman et al. J Neurosurg 2003; 99:489-495

- 2 year follow-up in 25 patients, mean age 57, PD duration 13.4 y
- PD symptoms were still 50% better than before DBS
- Axial scores: standing, gait, turning over in bed not sig. improved
- Dyskinesia decreased by 46%
- Patients needed 36% less PD medication
- About 1/3 were having side effects of speech change, thinking or mood changes

# Long-term effects of STN DBS

Krack et al NEJM 2003: 249:1925-34

- 5 year follow-up in 49 consecutive patients (mean age 55y, PD duration 14.6y)
- PD symptoms *overall* still improved 54%,
  - No improvement in speech
- Speech difficulties, balance, walking declined
- Cognition declined
- Continued side effects: 1/3 had eyelid opening difficulties; another 1/3 had mood changes



## Summary

- DBS is a highly effective treatment for disabling essential tremor, medication-resistant on/off symptoms and dyskinesia in PD, and dystonia.
- The full effects of DBS take time to develop and require close cooperation between patient and clinicians.
- DBS may produce adverse effects, but therapy is adjustable, reversible and safe
- Always consider medical and environmental safety concerns with DBS