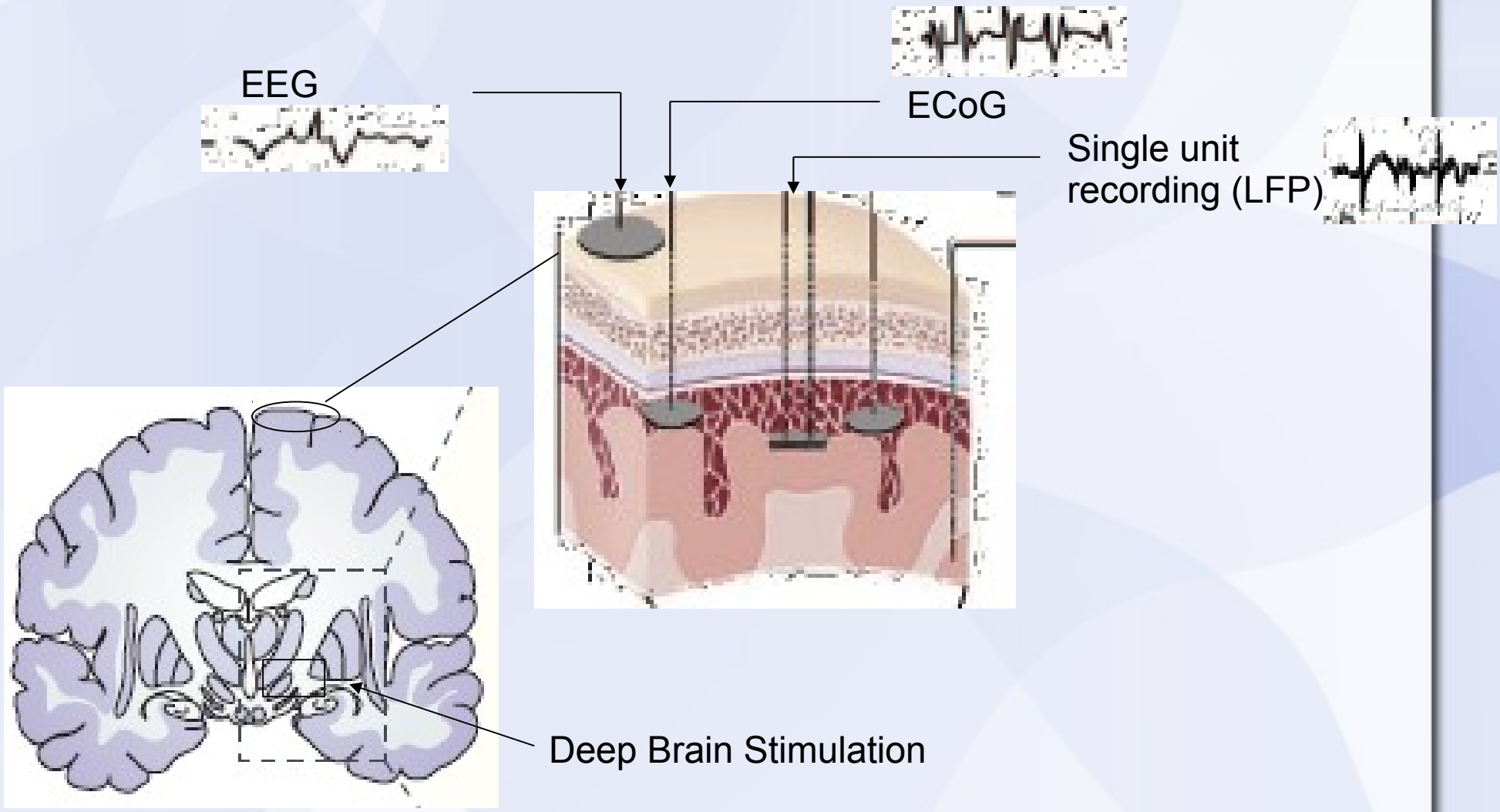
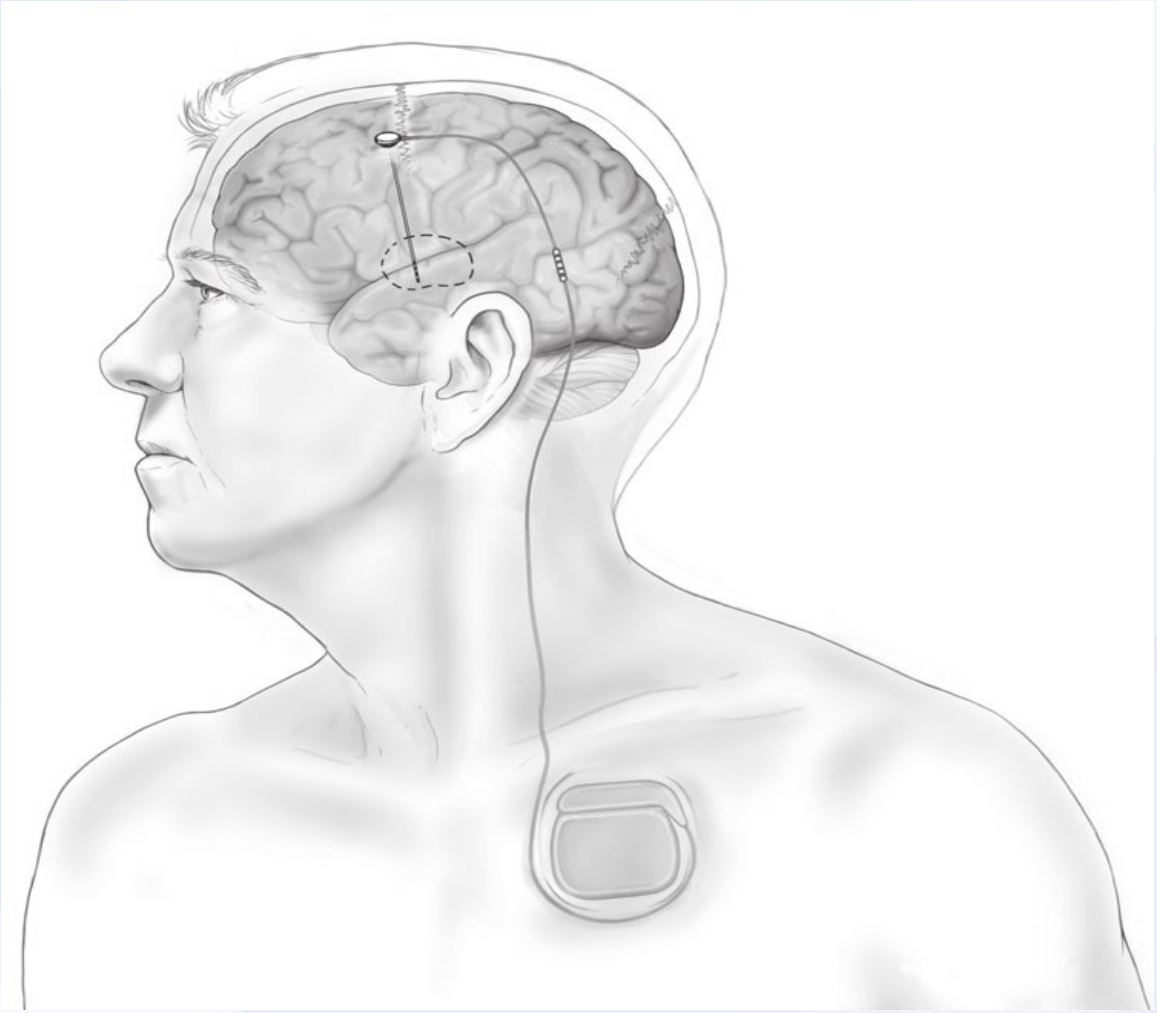
Translational Principles of Deep Brain Stimulation

by Ping Mamiya

Why do we study Deep Brain Stimulation (DBS) in BCI?



Deep Brain Stimulation System



What DBS is used for?

1. Movement disorders – in the advanced state of PD, and less responsive to dopamine medication.
   - Tremor, Dystonia, and Bradykinesia in Parkinson's disease (PD)
   - Huntington's chorea

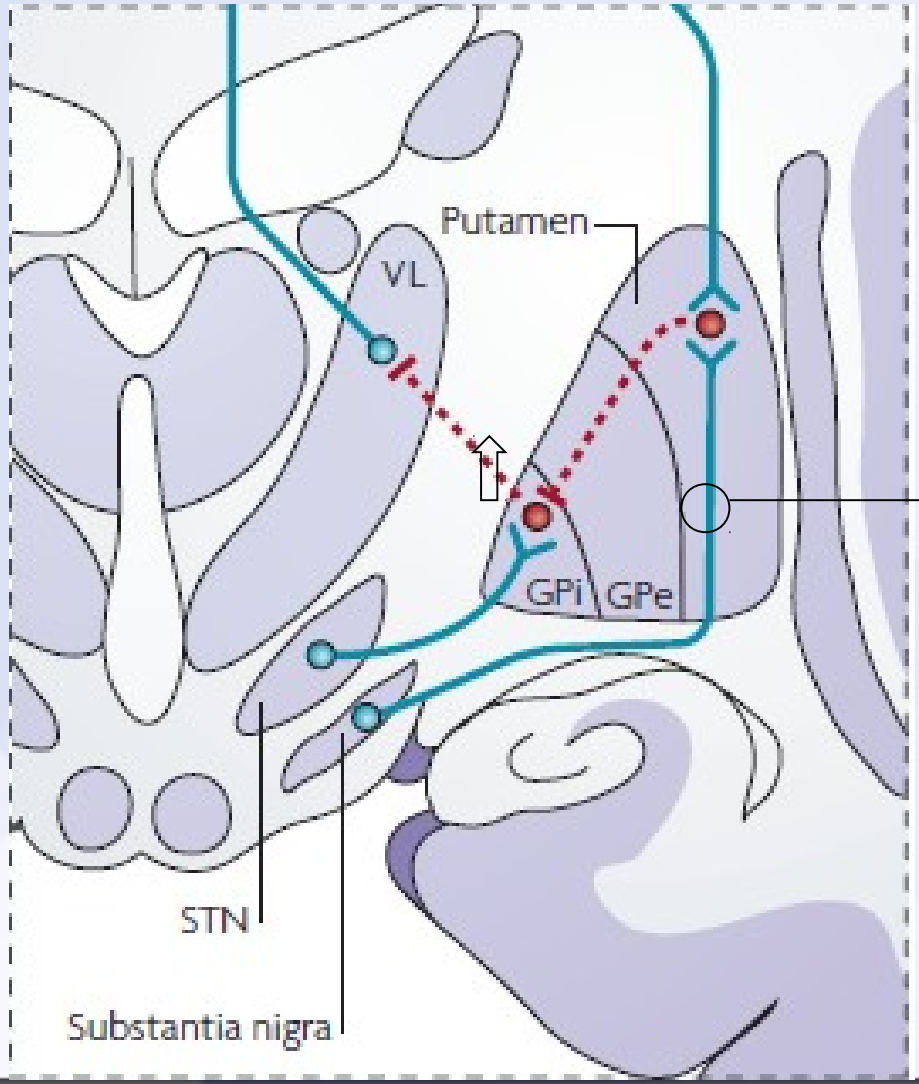
Dystonia: a movement disorder that leads to involuntary sustained muscle contractions, causing distorted posturing of the foot, leg or arm.

Bradykinesia: the slowing of, and difficulty in initiating, movement that is characteristic of Parkinson's disease.

Changes of DA in Basal Ganglia lead to the hypokinetic features in Parkinson Disease

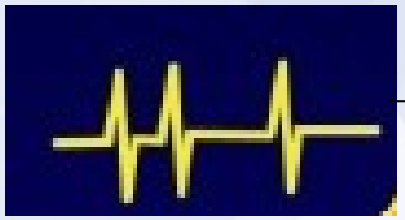
DA: dopamine

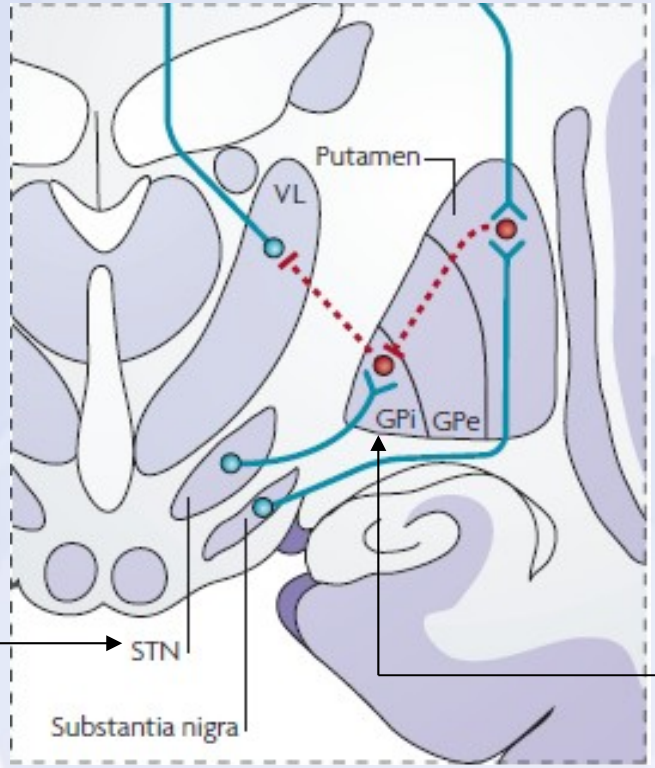
SNc: Substantia Nigra Pars Compacta



DBS in treating motor dysfunctions in PD

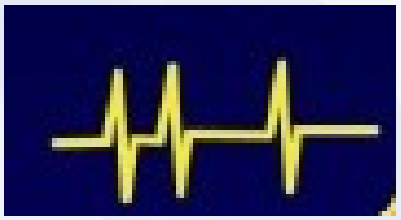
130-185 Hz





200-400 Hz

2.2-7 V



What DBS can and cannot do in treating advanced PD

Can:

1. Reducing the required dose of DA medication (thus reducing the side effects of medication)

2. Alleviating the PD symptoms as measured by motor and daily living scores while the medication is less effective in the advanced PD state

Cannot:

1. DBS effect does not exceed the therapeutic effect of DA medication

DBS in treating psychiatric disorders

- Obsessive-Compulsive disorder
- Treatment Resistant Depression

Animal model used in study of PD may be a possible model for studying the effect of DBS in severe depression (justification: PD and affective disorders share some parts of brain structure in their circuitry)

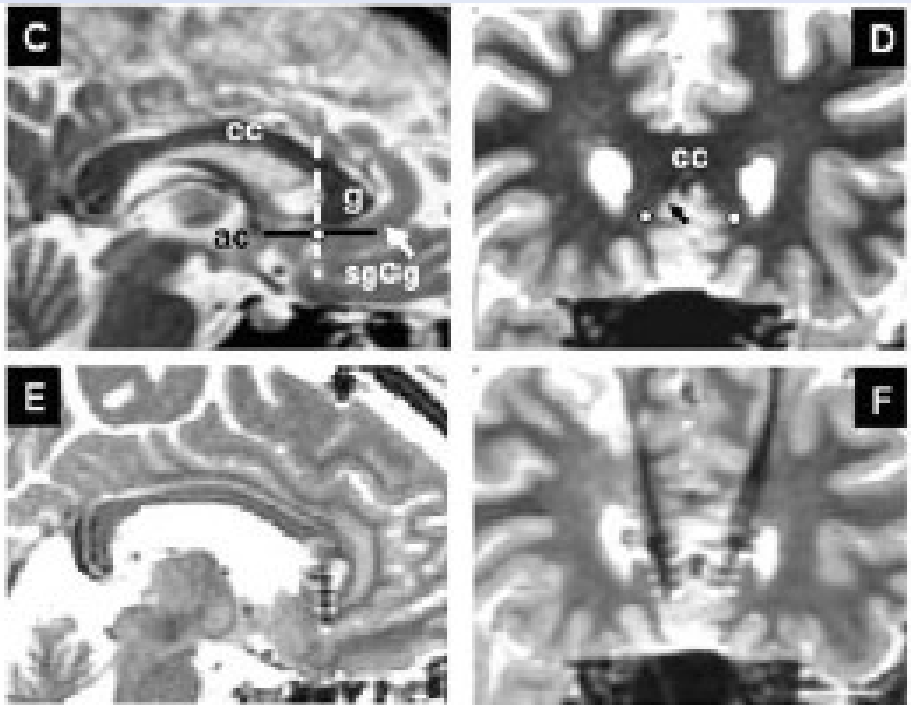
Little to moderate effects on symptoms

The termination of DBS in OCD treatment results in depression, but not OCD symptoms.

DBS in Treatment-Resistant Depression

Pre-op MRI Target Localization

Post-op MRI Electrode Location



Monopolar stimulation:

- 30-250 μs pulsewidth

-- 10-130 Hz

-- up to 9V @ each eight electrode

Pitfalls of DBS in Treatment-Resistant Depression

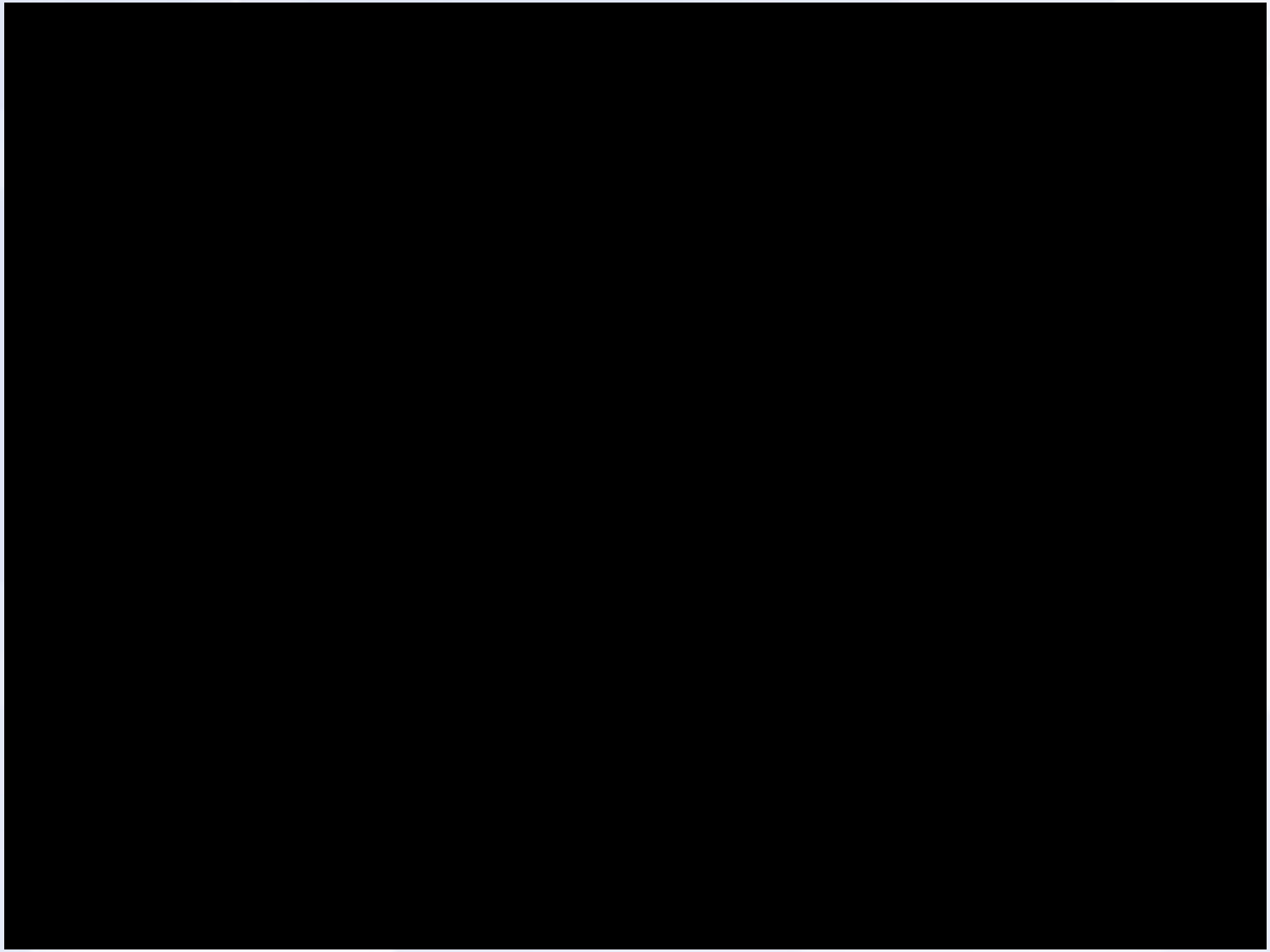
1. Local infection due to the connector cables on the chest
2. Skin erosion over the hardwire

DBS in treating pain after amputation and stroke

Targeting brain areas that are further deep down to nearly brain stem (PVG/PAG).

Device manufacturers did not pursue FDA approval for DBS in these brain region following the failed clinical trials.

video – phantom limb



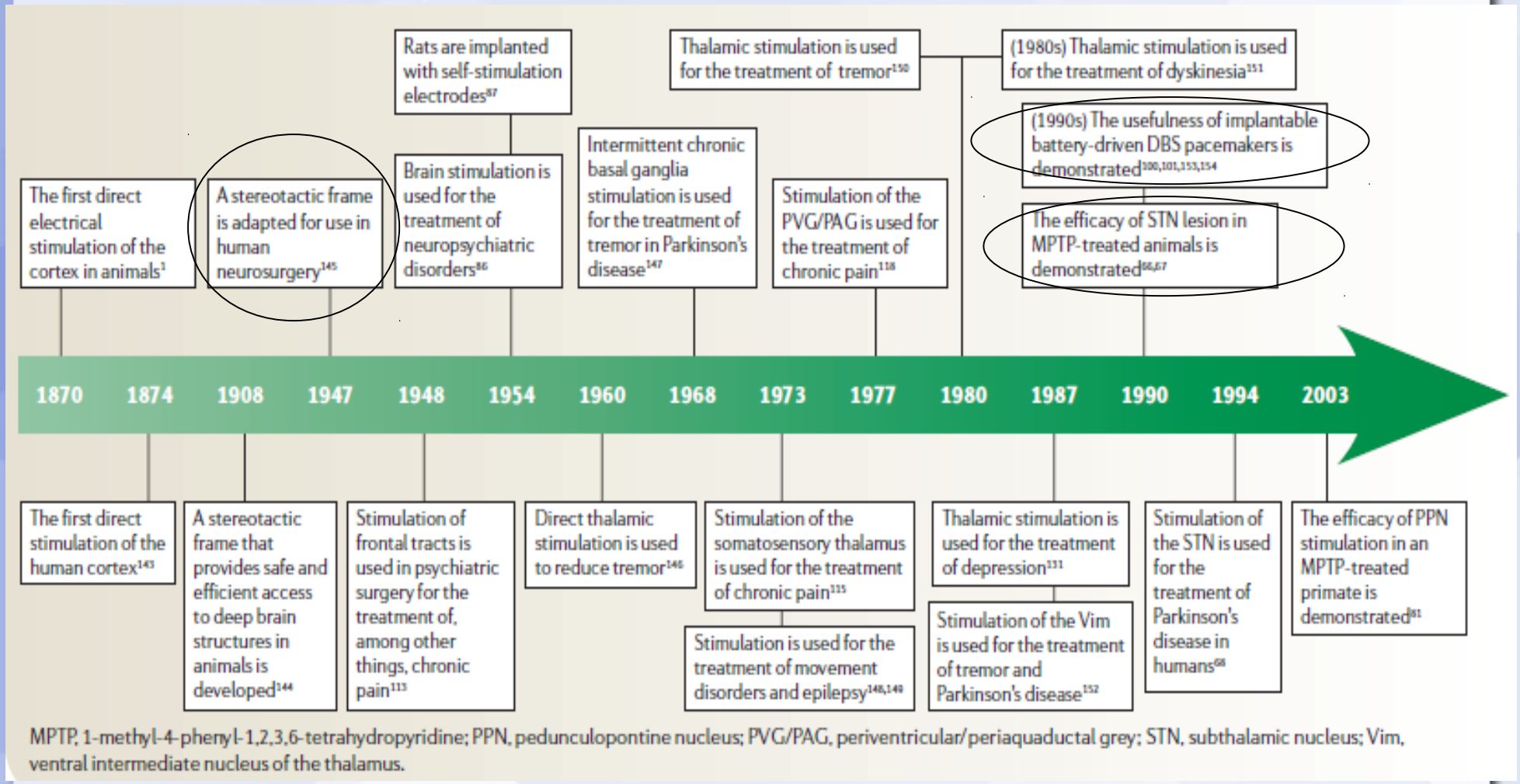
Benefits and risks associated with stereotactic procedures

A marked long-term improvement in motor function in advanced Parkinson's disease (PD)

Downsides:

- Intracranial hemorrhage
- Infection
- Complications associated with anesthesia
- Malfunction of DBS system
- Repeated minor surgery to replace the IPG

History of DBS

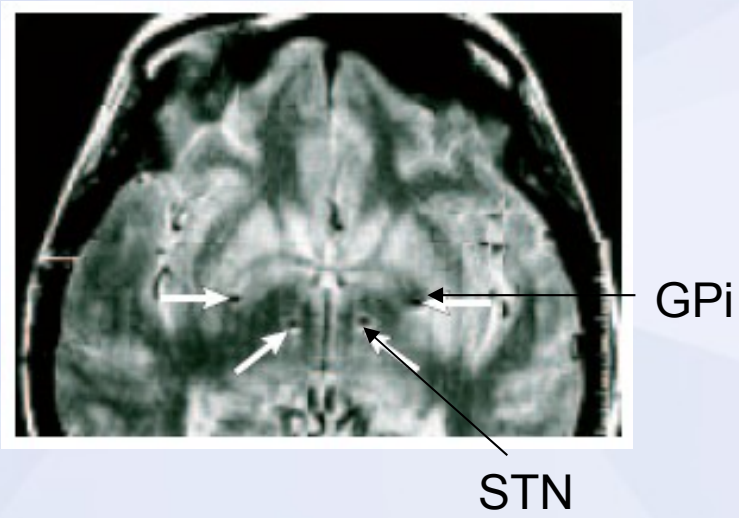


MPTP, 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine; PPN, pedunculopontine nucleus; PVG/PAG, periventricular/periaquaductal grey; STN, subthalamic nucleus; Vim, ventral intermediate nucleus of the thalamus.

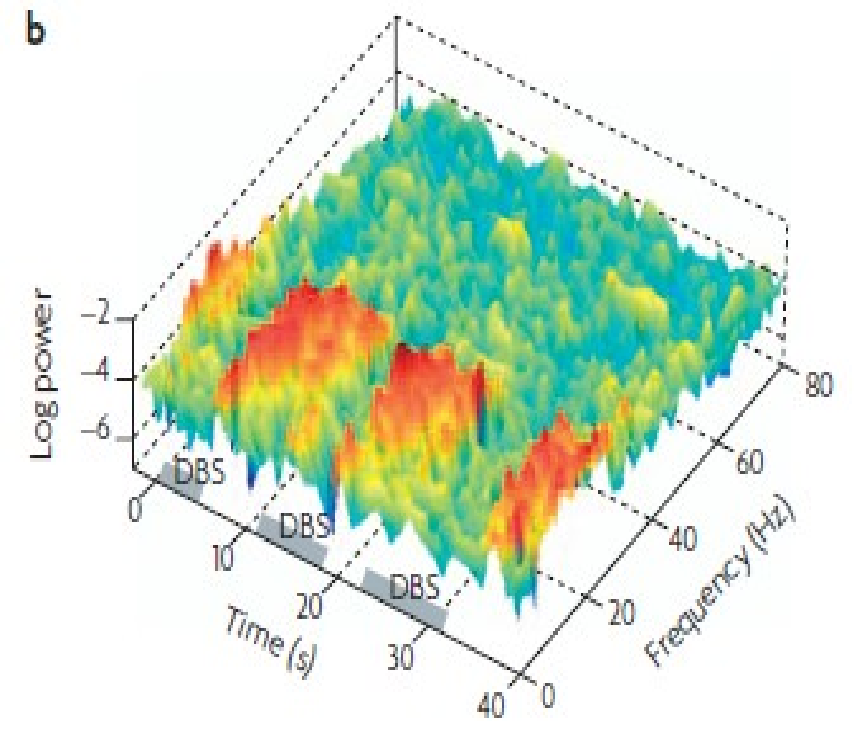
How does DBS work?

STN and GPi are prominent sites for DBS in Parkinson Disease

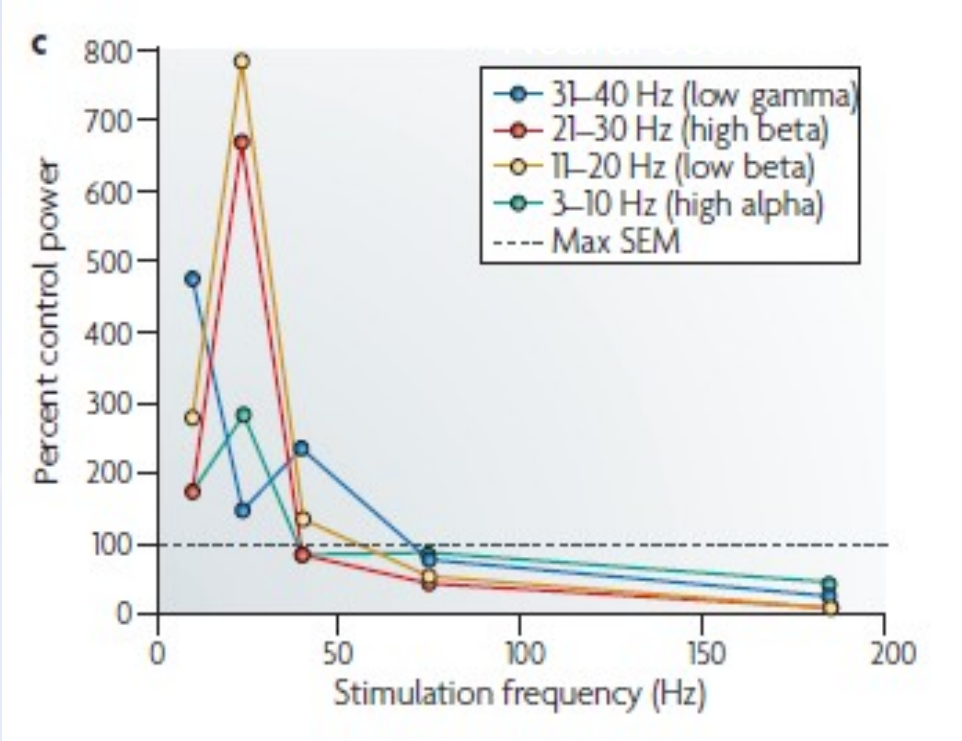
LFP (Local Field Potential): the extracellular voltage fluctuations that reflect the sum of events in the dendrites of a local neuronal population.



Stimulating GPi with low-frequency bands significantly decreases LFP

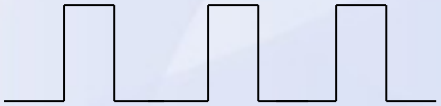


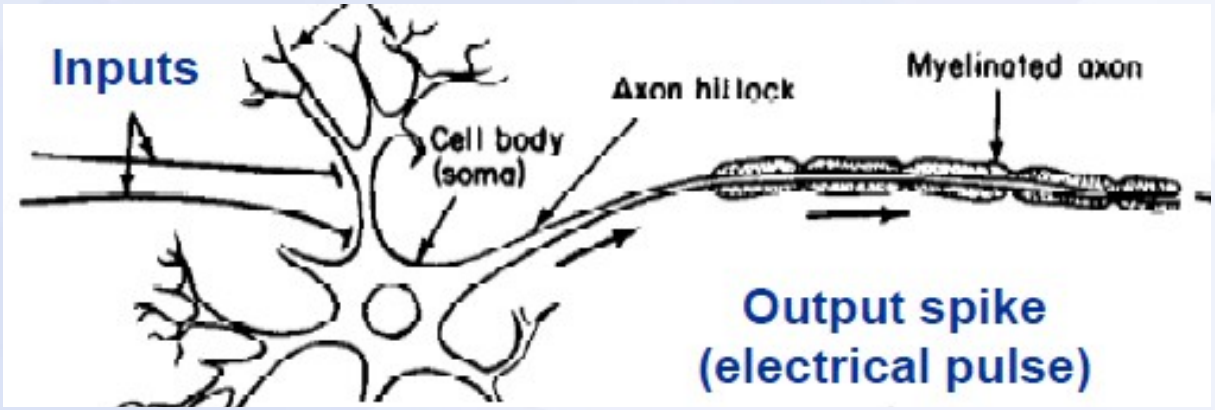
Neural oscillatory activities below 30Hz are maximally potentiated by low-frequency stimulation in STN

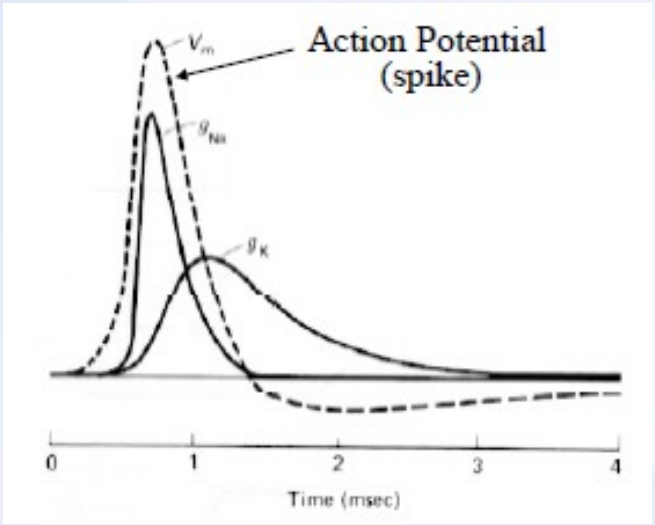


In clinical trial, DA medications decreases beta oscillation, but increases spontaneous synchronization in gamma band.

Neural Elements – cell body, axon, and glial

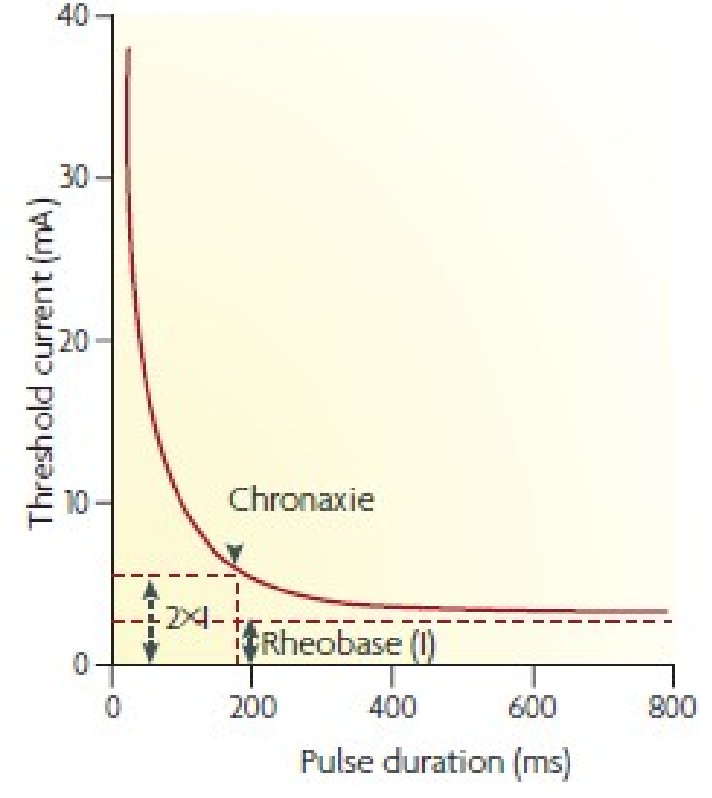






Electrical stimulation is more likely to induce action potential on axon (Node of Ranvier), than on cell body

Non-linear relationship between pulse duration and threshold current necessary to stimulate a neural element



30-200 μs: myelinated axon

1-10 ms: cell body/dendrite

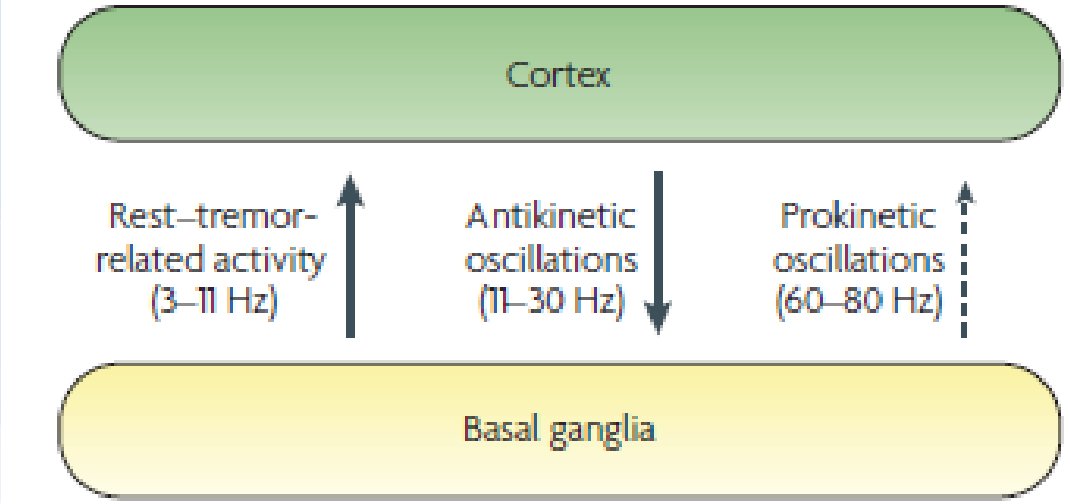
The goal of DBS is to increase prokinetic oscillations in basal ganglia

Stimulus amplitude

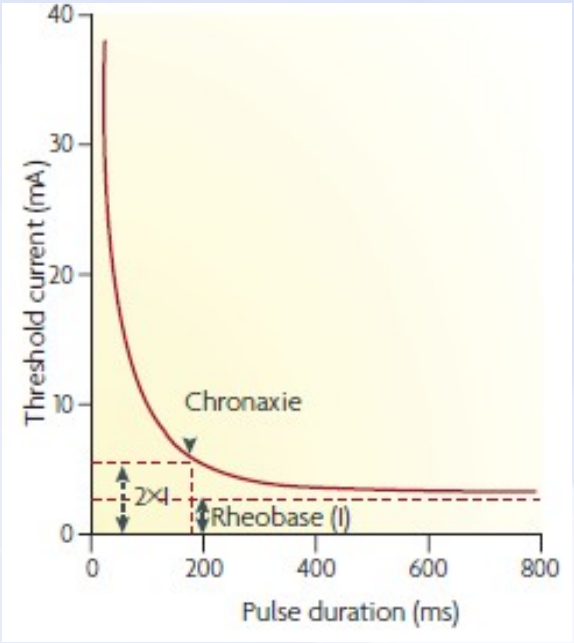
Duration

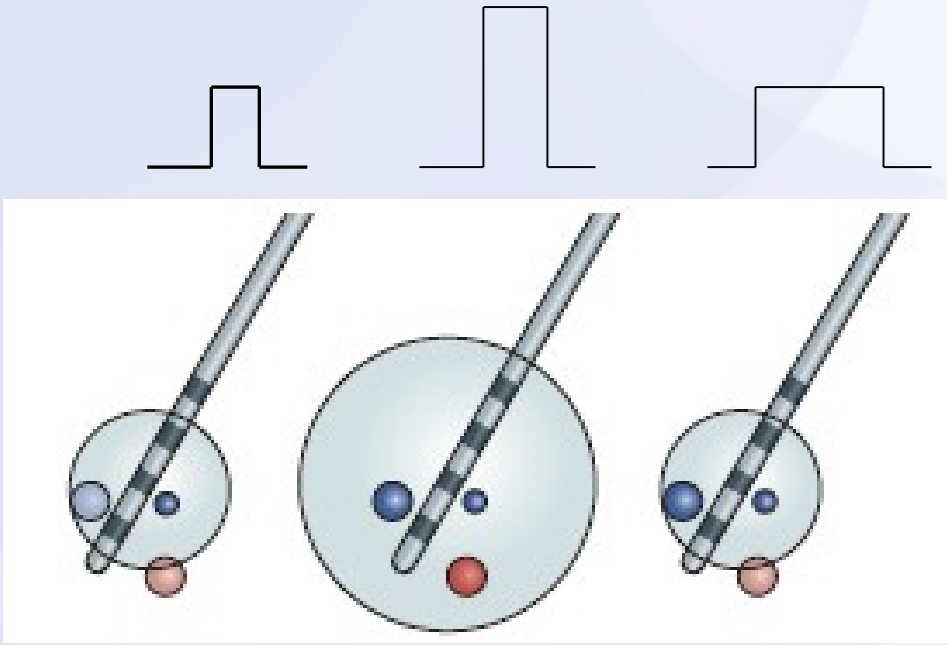
Frequency band

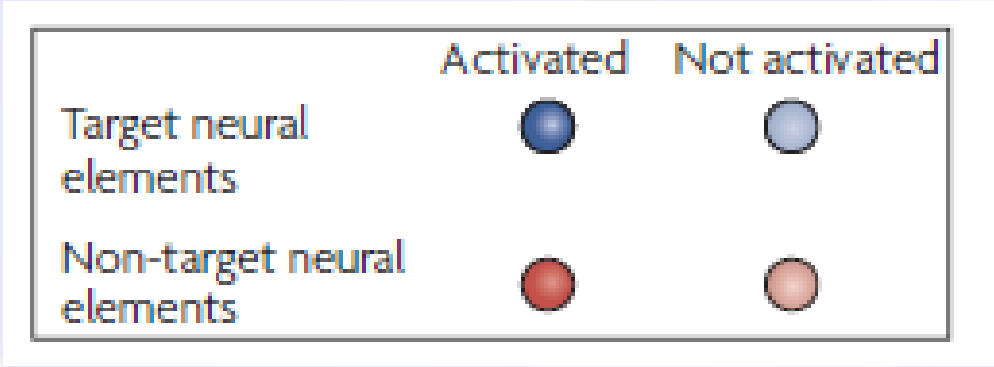
Vary depending on treatment, targeted brain region

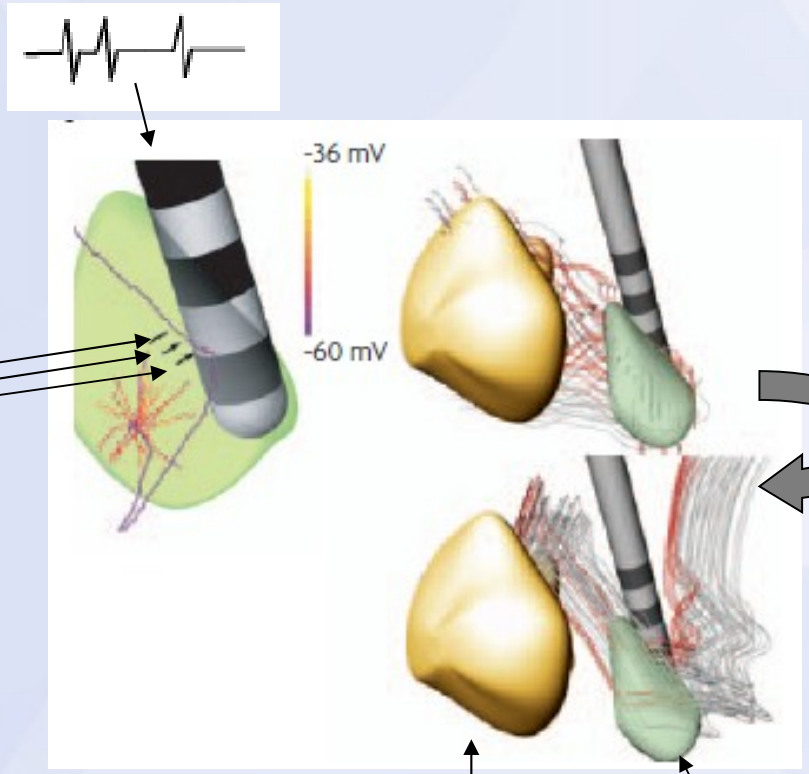


High voltage stimulation activates target and non-target neural elements







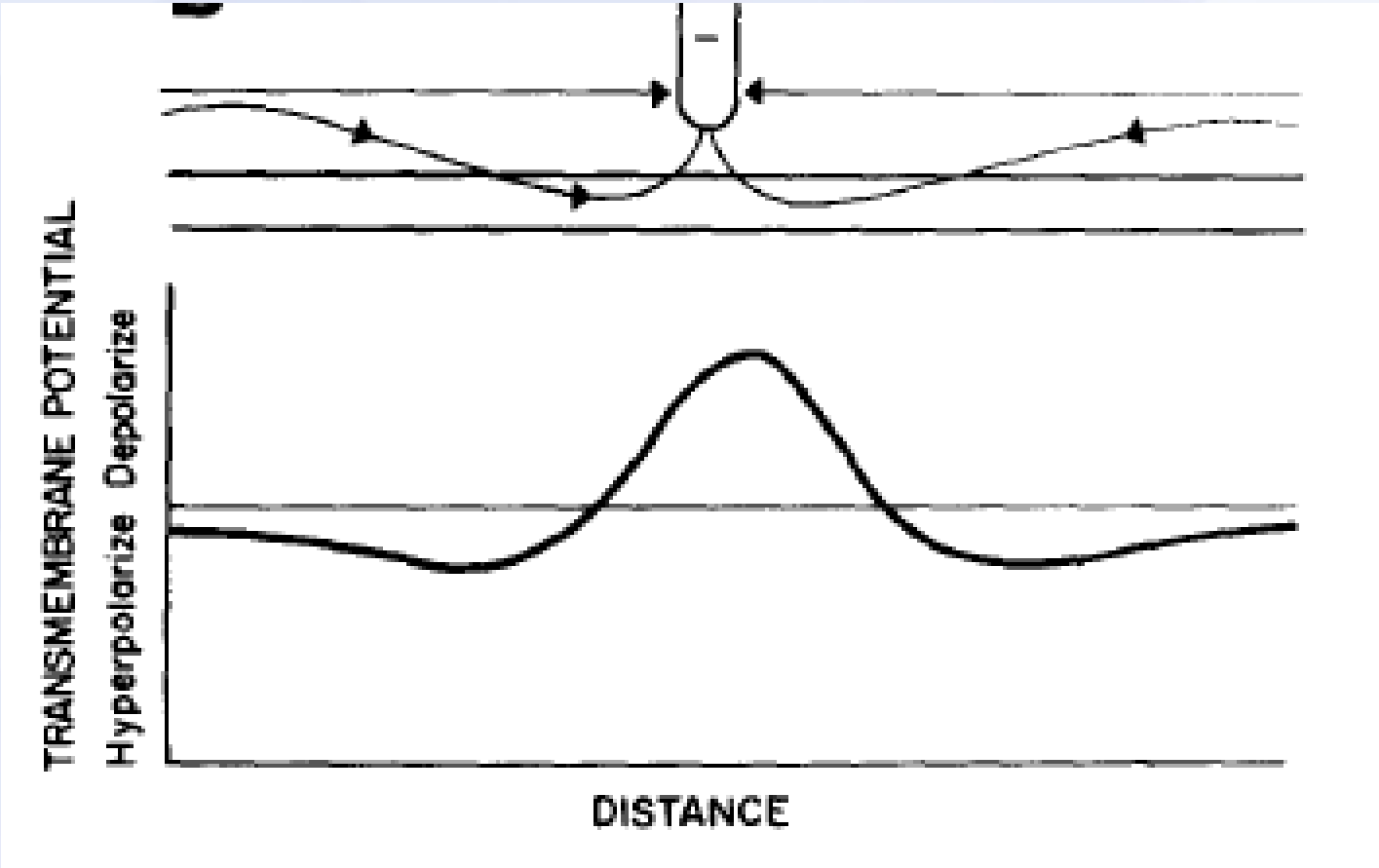


Node of Ranvier

Transmembrane polarization

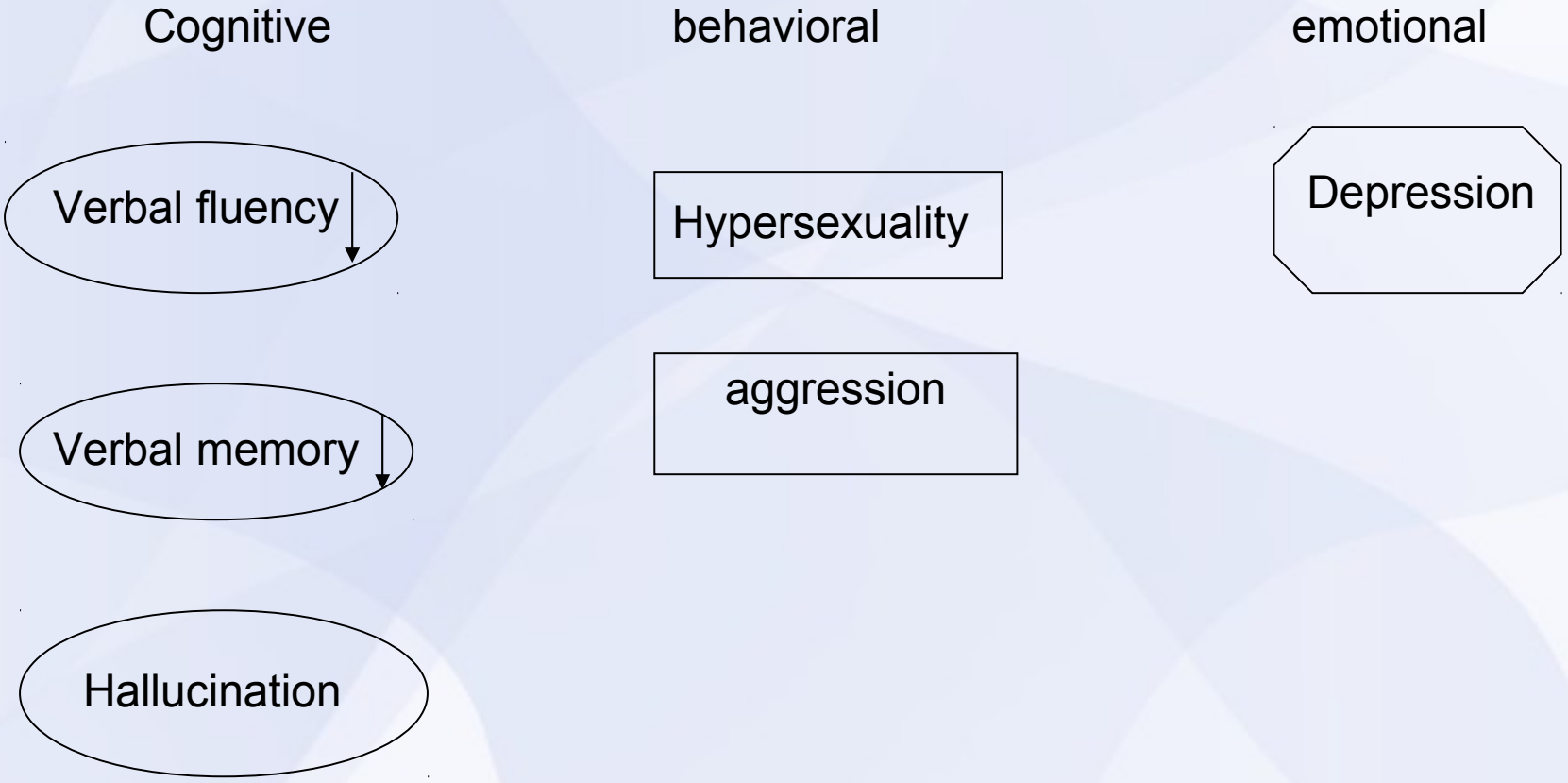
Changes in oscillatory neural activity between cortex and basal ganglia

i > 8X threshold blocks action potential in axons

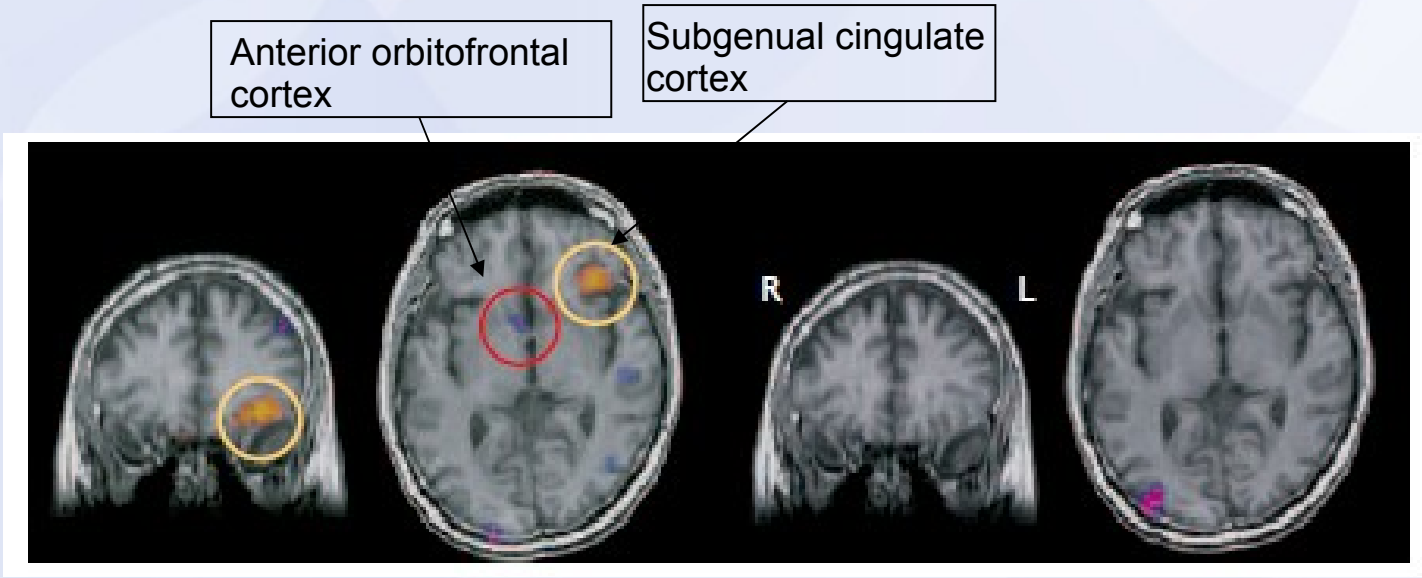


James Ranck Jr. *Brain Research* 1975

Pitfalls of electrical stimulation of STN in DBS



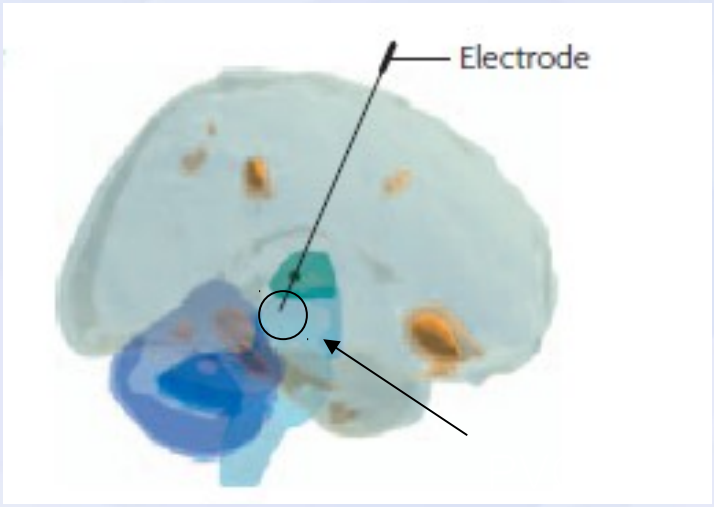
Pain sensation resumed when DBS was turned off

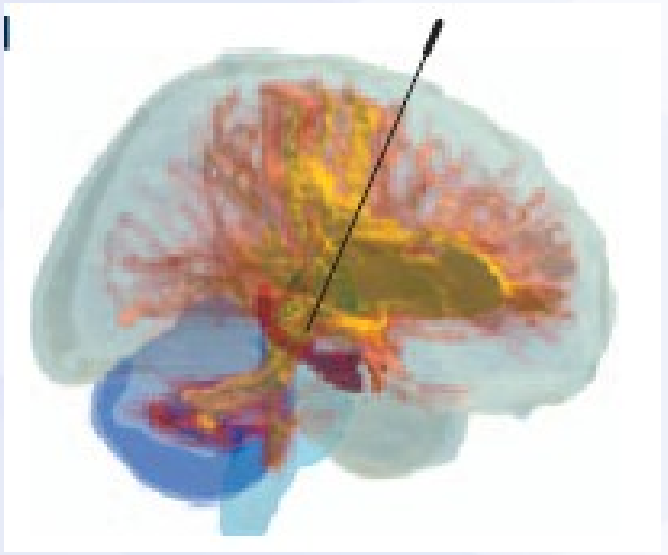


Synchronous power in frequency bands

Asynchronous power in frequency bands

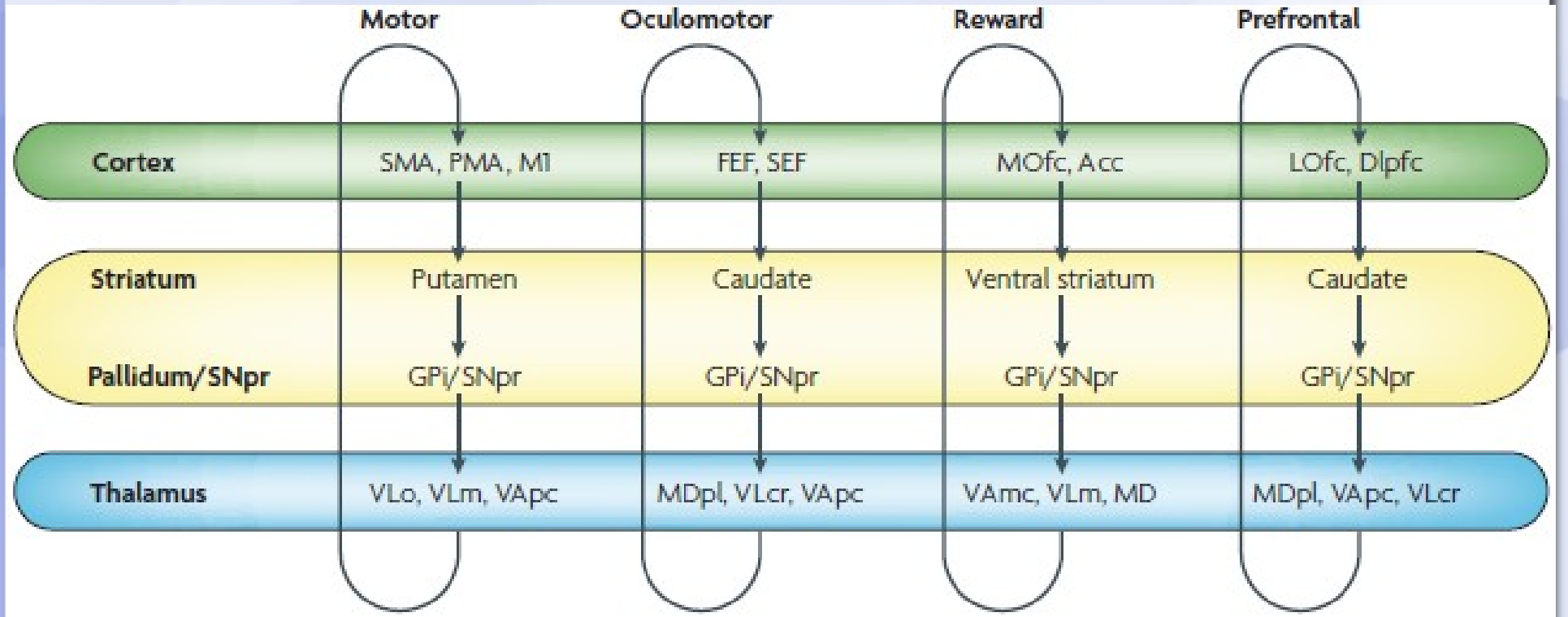
DBS in treating chronic pain



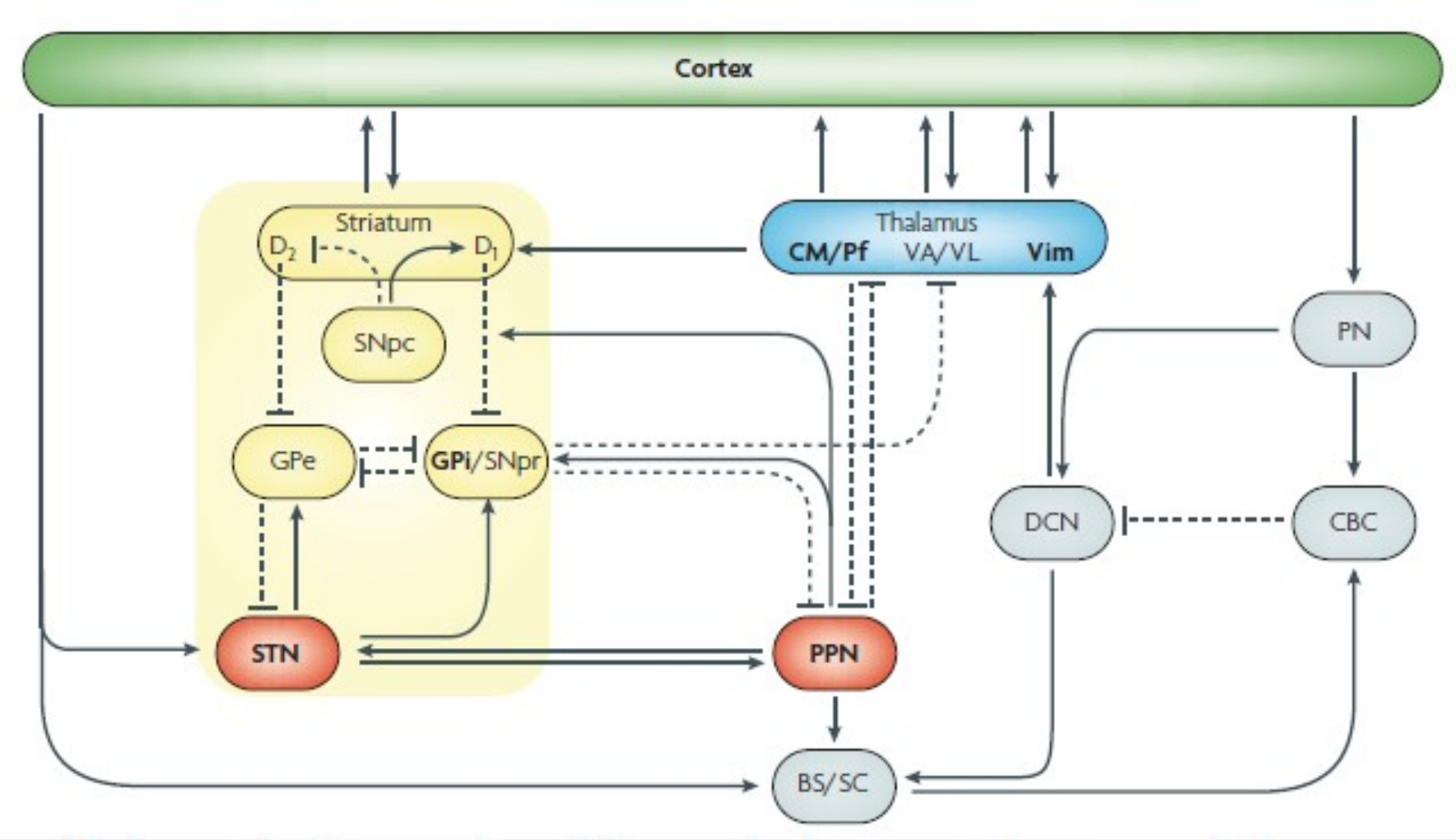


increased blood flow in thalamus, midbrain, but reduced blood flow in parietal and temporal cortices.

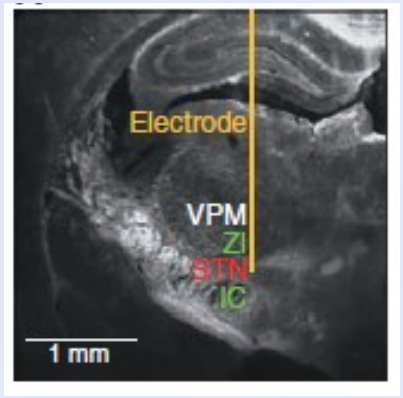
New Targets in DBS

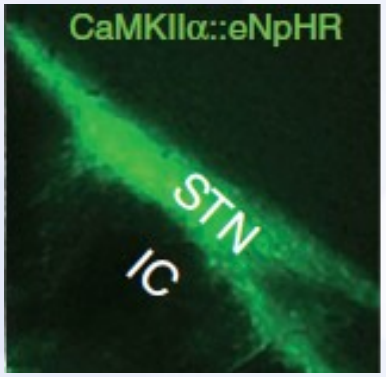


Going deeper….



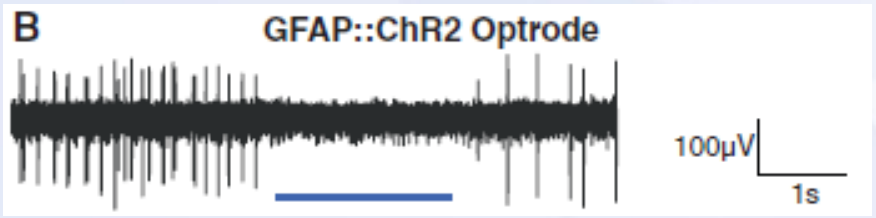
But wait……





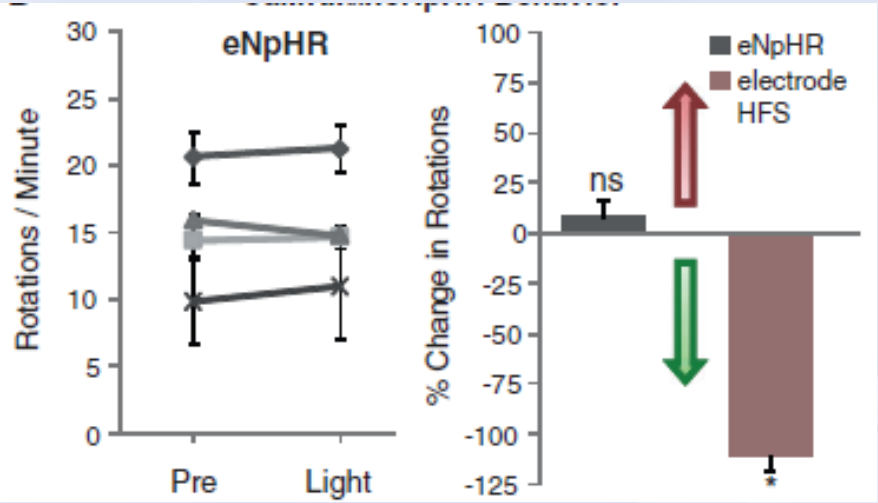
Inhibiting STN

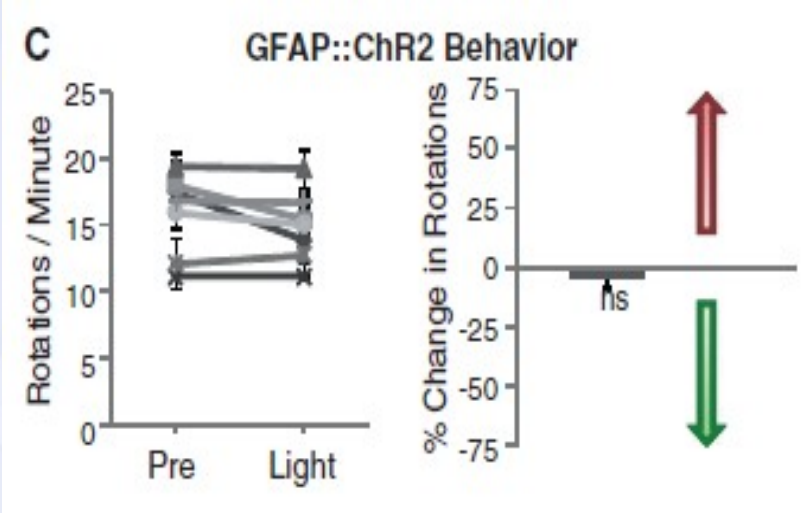
Exciting STN

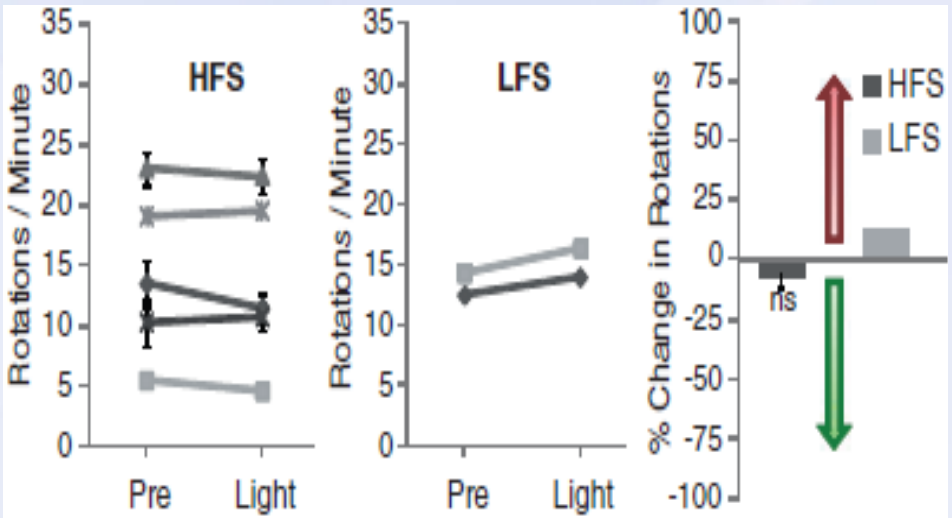


From Gradinaru et al., *Science* 2009

in rodents



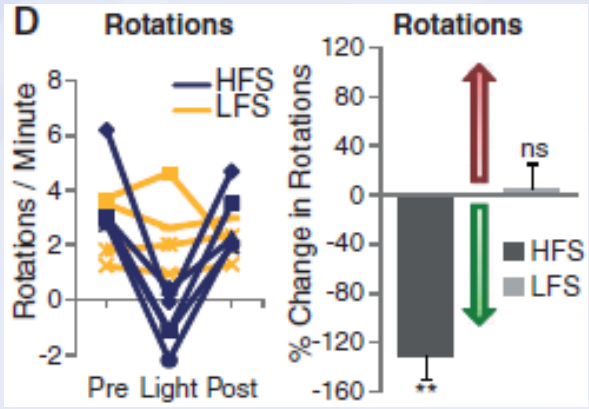




Stimulating STN has no effect on rotational behaviors in animal model of PD. It suggests that the stimulations of STN projects are not responsible for the therapeutic effect of DBS in PD.

How about the input from M1 cortex to STN?

Driving layer V projection neurons in M1 (primary motor cortex) with different optical stimulation….



Only high frequency Stimulation(HFS) is sufficient to ameliorate rotational behaviors in animals

Layer V Motor Cortex could be the potential site for BCI

Future directions

Externally rechargable battery -> reducing the risks associated with surgical replacement every few years.

Developing closed-loop variable DBS that is customized to anatomy and morphology of DBS target