Why does DBS do the same thing in the STN and GPi?

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Overview

DBS in Parikinson's

In the basal ganglia, deep brain stimulation (DBS) of the subthalamic nucleus (STN) or internal segment of the globus pallidus (GPi) is thought to alleviate the akinesia and rigidity of Parkinson's disease by removing the pathological inhibition of the thalamus by GPi.Disinhibiting the thalamus should restore thalamocortical activity.

Target inhibition vs. efferent activation

How electrical stimulation leads to inhibition is unclear, as is whether inhibition of nerve tissue near the electrode is the main therapeutic mechanism of DBS. Here we show a computational model demonstrating how DBS of the STN and GPi induce different patterns of brain activity. These differences may explain the increased incidence of adverse effects in STN stimulation, increased medication reductions with STN stimulation, and preference of GPi stimulation for dystonia.

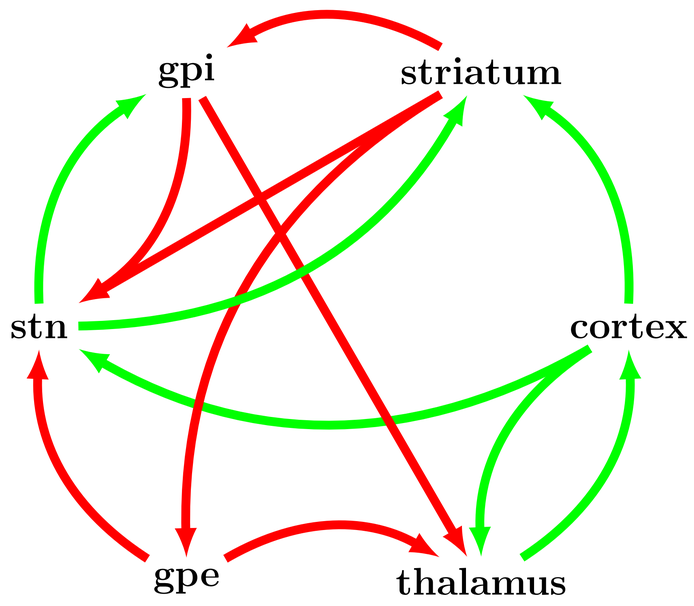
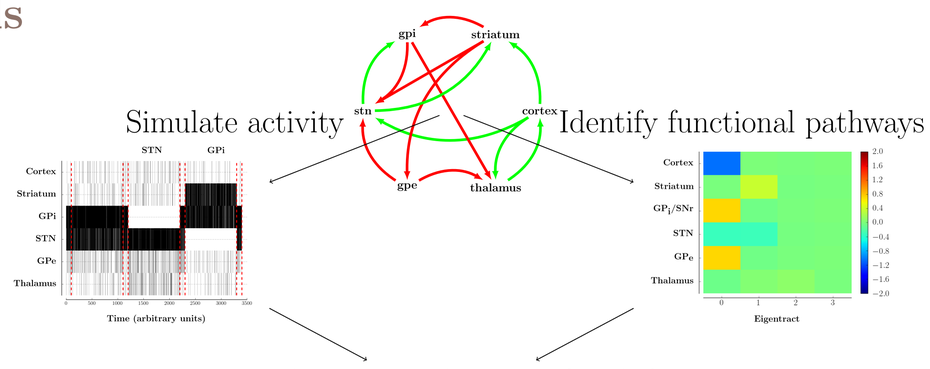


Figure 1: **Simplified model of basal ganglia.**

Methods



Simulate activity

$$\mathbf{v} = \mathbf{M} \cdot \mathbf{v} + \mathbf{I} \qquad \text{Update rule}$$

$$P[I_i] = \frac{1}{1 + e^{-I_i}} \qquad \text{Stochastic update}$$

Identify functional pathways

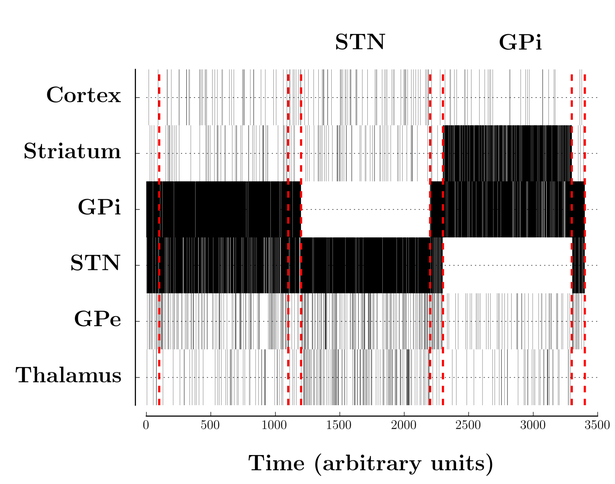
$\mathbf{M} \cdot \mathbf{e}_i = \lambda_i \mathbf{e}_i$ Each eigenvector is a functional pathway.

Represent relative contributions

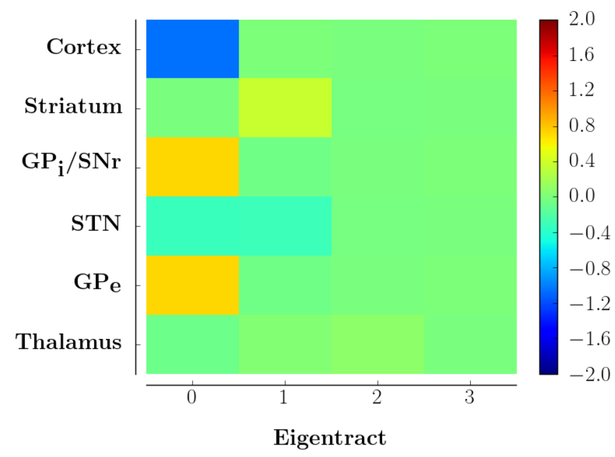
Compare $\mathbf{I}_{\text{STN}} \cdot \mathbf{e}_i$ and $\mathbf{I}_{\text{GPi}} \cdot \mathbf{e}_i$

Results

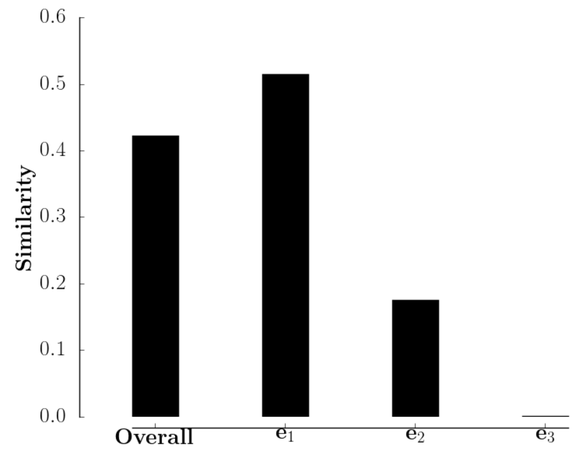
Stimulating STN and GPI induce different patterns of network activity



STN and GPI are part of the same eigenvector



Stimulation of STN and GPi activate the second eigenvector similarly



Next steps:

1. Include subdivisions of thalamus and cortex
2. Study multiple stimulation at different frequencies, currents

Conclusions

1. STN and GPi stimulation (i) activate the same functional pathway (eigenvector) similarly (ii) inhibit their immediate target and (iii) require activation of adjacent white matter afferents to alter thalamocortical activity.
2. STN stimulation increases activity throughout the basal ganglia more than GPi stimulation with the same pattern—may explain why STN stimulation reduces the amount of antiparkinsonian medication needed but also is associated with more adverse effects.
3. Stimulation of GPi but not STN decreases firing rates in GPe —may explain why GPi stimulation is more favored in dystonias.