Deep Brain Stimulation
How does it work?

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Deep Brain Stimulation

Parkinson’s disease  Dystonia
How does it work?
Why do we care?

• Help to improve current applications
  – Have we perfected this technique?
• Aid the development of new applications
• Provide the rationale for design of new technology
  – Different disease states may require different targets
  – Different targets require different lead shapes
  – This is not a “one size fits all” technology
Electrode Designs

Current Design

Split Band Directional Electrode

3D Directional Electrode
Define the problem!

- What is the underlying pathophysiology?
- If you don’t know the problem, it is hard to find a solution!
- Lesion and Look
- Poke and Hope
Parkinson’s disease  Dystonia
Basal Ganglia

Model for Parkinson’s disease

Pathologic outflow
- ↑ rate
- bursty
- oscillatory
- synchronized

Symptoms
- akinesia
- bradykinesia
- rigidity
- ...

Diagram showing the model with brain regions such as Striatum, GPi, Thalamus, and CORTEX, and pathways between these regions.
Mean Discharge Rates - Dystonia

Mean Frequency GPe
Mean Frequency GPi

Mean Frequency (Hz)

JB | RB | CS | JY | WE | CG | DH | DW
---|----|----|----|----|----|----|----
60 ± 5 | 55 ± 4 | 50 ± 3 | 45 ± 2 | 40 ± 1 | 35 ± 0 | 30 ± 1 | 25 ± 2
Dystonia

![Graph](image)

- **Fx**: Force in the X direction
- **Fy**: Force in the Y direction
- **Fz**: Force in the Z direction
- **Neural**: Neural activity

**Force (N)** vs **Time (sec)** with overlaying **Fliring Rate (Imp/sec)**

- X-axis: Time (sec) from 0 to 20
- Y-axis for Force (N): -4 to 12
- Y-axis for Fliring Rate (Imp/sec): 0 to 70

The graph illustrates the fluctuation of forces and firing rates over time, highlighting the dynamics of dystonia.
# Neuronal Activity in GPi

<table>
<thead>
<tr>
<th></th>
<th>PD</th>
<th>HB</th>
<th>Dystonia</th>
<th>Dyskinesia</th>
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<td><strong>RATES</strong></td>
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<td>Altered</td>
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<tr>
<td><strong>SYNCH.</strong></td>
<td>Uncontrolled</td>
<td>Uncontrolled</td>
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<td>Uncontrolled</td>
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</table>
Pathophysiology of PD

A  Normal

B  Parkinson’s Disease
A Neuronal Model for Dystonia
Early Hypothesis for DBS Mechanism

• Based on “Rate” hypothesis of Parkinson’s disease, i.e. motor symptoms occur as a result of excessive activity in the STN and GPi

• Deep brain stimulation simulates a lesion
  – Behavioral effects of lesion same as stimulation
  – Early studies in anesthetized rats demonstrated decrease activity in the entopeduncular nucleus (GPi analogue in monkeys) after STN stimulation \((\text{Benazzouz and Hallett 2000})\)
  – Studies in humans undergoing implantation demonstrated a reduction of neuronal activity at the site of stimulation \((\text{Benazzouz and Hallett 2000; Dostrovsky et al.2000})\)

• Deep Brain stimulation improves clinical symptoms by suppressing output from the stimulated structure
“Because of the continuous interaction of all involved structures during STN-DBS, a precise allocation of effects in specific primary pathways may prove daunting” Li et al JNP 2007
Experimental approach
Effective STN DBS (135 Hz)

GPi (n = 38)  

VA/VLo (n = 21)
# Effect of GPi-DBS on VLo neuron

<table>
<thead>
<tr>
<th>Time after stimulus pulse (ms)</th>
<th>Before DBS</th>
<th>During DBS</th>
<th>After DBS</th>
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</tbody>
</table>

*VLo Neuron Ne55-280*
Effect of GPi-DBS on VPLo neuron

Before DBS

During DBS

After DBS

VPLo Neuron Ne39-319

Time after stimulus pulse (ms)

Spikes/s
Effect of GPi-DBS on PPN Neuron

Before DBS

During DBS

After DBS

PPN Neuron Ne53-368

Time after stimulus pulse (ms)

1 sec/sweep
Effective GPe DBS (135 Hz)
GPe DBS – 135 Hz
Effective GPe DBS (135 Hz)

- **GPi**
  - Pattern change (P <= 0.05): 86%
  - No pattern change: 14%

- **STN**
  - Pattern change (P <= 0.05): 66%
  - No pattern change: 34%

- **VA/VLo**
  - Pattern change (P <= 0.05): 50%
  - No pattern change: 50%

- **VPLo**
  - Pattern change (P <= 0.05): 19%
  - No pattern change: 81%
GPe Stimulation
Pattern Changes in Motor Cortex Activity during DBS

Very Therapeutic for Rigidity

Rest

Passive Movement
Motor Cortex Responses to DBS during Passive Limb Manipulation
Motor Cortex Responses to DBS during a Reaching Task

Motor Cortex Cell

Movement Velocity

Movement Position

DBS off (n=11)

DBS on (n=9)
Conclusion

• Net effect at effective stimulation parameters is **activation** of output from the stimulated structure.

• Pattern is changed from irregular bursty to one that is more **regular and time locked** to the stimulus.

• Shift in oscillatory activity to higher frequencies.

• Informational content of the signal is altered, removing interference from subcortical structures allowing cortical areas to function more normally.
Conclusion

• Re-evaluation of models of movement disorders and incorporation of changes in pattern of neuronal activity
  – Pattern/regularity
  – Oscillatory activity
  – Synchronization
  – Changes in network dynamics
    » Informational content of the network is altered
    » Distribution of changes across populations of neurons
Future Studies

- Multiunit recording across structures to assess population and network dynamics
- Determine the relationship of changes in network dynamic to the development motor symptoms
- Determine the effect of changing stimulation parameters on neuronal and network function
- Define the relationship of these changes to changes in clinical symptomatology
- Translate our understanding of DBS for movement disorders to other nervous system disorders
Deep Brain Stimulation

Applications

- Parkinson’s disease
- Dystonia
- Tremor
- OCD
- Depression
- Tourette syndrome
- Chronic Brain Injury
- Cluster Headache
- Pain
- Epilepsy
- Stroke
- Addiction
- Other
  - Autism
  - Obesity
  - Schizophrenia
  - Alzheimer’s disease
  - Huntington’s chorea
Proceed with caution

“When you have a hammer, everything looks like a nail”
“Whoa! That was a good one! Try it, Hobbs—just poke his brain right where my finger is.”
Scientific Method
WE ARE LIMITED ONLY BY OUR OWN CREATIVITY

Understanding of the circuitry