CELL SPECIFIC CONTROL OF THE PALLIDOSTRIATAL PATHWAY

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OUTLINE

• Background
• Materials and Methods
• Data
• Analyses
• Discussion
• Acknowledgements
PARKINSON’S DISEASE

• A neurodegenerative disease of the basal ganglia
• Caused by dopamine depletion (DeMaagd & Philip, 2015)
• 1-3% of people older than 80 years old (DeMaagd & Philip, 2015)
• Symptoms
  • Tremors
  • Muscular rigidity
  • Bradykinesia
  • Dementia

https://en.wikipedia.org/wiki/Pathophysiology_of_Parkinson%27s_disease
THE BASAL GANGLIA

- Basal Ganglia
  - A collection of nuclei
    - Substantia Nigra
    - Subthalamic Nucleus
    - External Globus Pallidus
    - Striatum
  - Areas of interest
    - Striatum
    - External Globus Pallidus

https://www.mayfieldclinic.com/PE-PD.htm
SPINY PROJECTION NEURONS

• Neurons of the Striatum (Surmeier et al., 2007)
• Sometimes referred to as Medium Spiny Neurons
• Two main classes of receptors: D1 and D2 receptors (Surmeier et al., 2007)
• Direct and Indirect SPNs
PALLIDOSTRIATAL PATHWAY

- Striatal input to GPe is inhibitory (Jaeger et al., 2011)
- GPe input to Striatum is inhibitory (Jaeger et al., 2011)
- Npas1+ GPe neurons project to the Str (Hernandez et al., 2016)

https://beyondthedish.wordpress.com/tag/striatum/
STRIATAL AND PALLIDAL PATHWAYS

**KEY**
- Inhibitory
- Inhibitory and Direct
- Inhibitory and Indirect

- GPe
- GPi and SNpr
- Other motor areas
- Striatum
MATERIALS AND METHODS

• Parkinsonian Mice
  • Symptoms produced using 6-hydroxydopamine (6-OHDA)
  • 6-OHDA injected into the brain
  • Destroys dopaminergic neurons of the substantia nigra
  • Induces symptoms of Parkinson’s Disease
MATERIALS AND METHODS

- Data Collection
  - Transgenic mice brain slices
    - Npas1-Cre;D2-GFP
  - Whole Cell Patch Clamping
    - Fluorescent Dye (Alexa 647 hydrazide)
  - Surrounding GPe axons
    - YFP+ (visualized in the 488 nm range)
  - Protein Fluoresce
  - Confocal Microscopy
MATERIALS AND METHODS

• Fiji ImageJ software

• Pallidostriatal contacts
  • Between SPN dendrites and axons of the GPe
  • Verified in the orthogonal plane

• Contacts measured via two methods
  • Euclidian distance calculated
  • Trace of dendrite to soma
GENERAL LOCATION OF SYNAPSES

Location on Dendrite

- Dendritic shaft: 73.9%
- Head of spine: 23.8%
- Neck of spine: 1.4%
- Soma: 1.0%
GENERAL BRANCH ORDER AND LOCATION OF SYNAPSES

Dendritic Branch Order

- 2' den: 41.2%
- 1' den: 6.0%
- 3' den: 36.9%
- 4' den: 13.2%
- 5' den: 1.4%
- soma: 1.0%

- 6' den: 0.0%
BRANCH ORDER FOR EACH GROUP OF SPNS

Count of Branch order for D1 Naive SPNs
- Branch order: 3 der, 4 der, 2 der, 1 der, 5 der
- Count of Branch order: 10, 5, 25, 40, 10

Count of Branch order for D2 Naive SPNs
- Branch order: 3 der, 4 der, 2 der, 1 der, 5 der
- Count of Branch order: 50, 40, 20, 10, 5

Count of Branch Order for D1 Lesioned SPNS
- Branch order: 3 der, 4 der, 2 der, 1 der
- Count of Branch order: 10, 25, 40, 10

Count of Branch Order for D2 Lesioned SPNS
- Branch order: 3 der, 4 der, 2 der, 1 der
- Count of Branch order: 50, 40, 20, 10
GENERAL BRANCH ORDER AND LOCATION OF SYNAPSES
## CONTACTS PER CELL

<table>
<thead>
<tr>
<th></th>
<th>D1 SPNs</th>
<th>D2 SPNs</th>
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<tbody>
<tr>
<td>Naive</td>
<td>6.9 contacts</td>
<td>7.1 contacts</td>
</tr>
<tr>
<td>Lesioned</td>
<td>6.3 contacts</td>
<td>7.1 contacts</td>
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NAÏVE GROUP PROJECTIONS

Naive D1 SPNs vs. Naive D2 SPNs

Percentage of Contacts

Distance from Soma
Lesioned group projections

Lesioned D1 SPNs vs. Lesioned D2 SPNs

- Lesioned D1 SPNs
- Lesioned D2 SPNs

Percentage of Contacts vs. Distance from Soma
WEAKENED PROJECTIONS OF D1 SPNS

![Graph showing Naive D1 SPNs vs. Lesioned D1 SPNs](image)

- **Naive D1 SPNs**
- **Lesioned D1 SPNs**

**Y-axis:** Percentage of Contacts

**X-axis:** Distance from Soma
STRONGER PROJECTIONS OF D2 SPNS
DIRECT STRIATAL AND PALLIDAL PATHWAYS

KEY
Inhibitory
Inhibitory and Direct
Inhibitory and Indirect

Striatum
GPe
GPi and SNpr
Other motor areas

Weakened
INDIRECT STRIATAL AND PALLIDAL PATHWAYS

**KEY**
- Inhibitory
- Inhibitory and Direct
- Inhibitory and Indirect

- Strengthened: Striatum to GPe
- Weakened: GPi and SNpr to Other motor areas
SUMMARY

• Most synapses occurred on 2’ and 3’ dendrites
  • Inhibits cortical excitatory input
• Most synapses occurred on the dendritic shaft
• The frequency of synapses was unaffected.
• The projections of the iSPNs are increased in the lesioned model.
  • Further inhibits cortical excitatory input
• The projections of the dSPNs are diminished in the lesioned model.
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LITERATURE CITED


