CELL SPECIFIC CONTROL OF THE PALLIDOSTRIATAL PATHWAY

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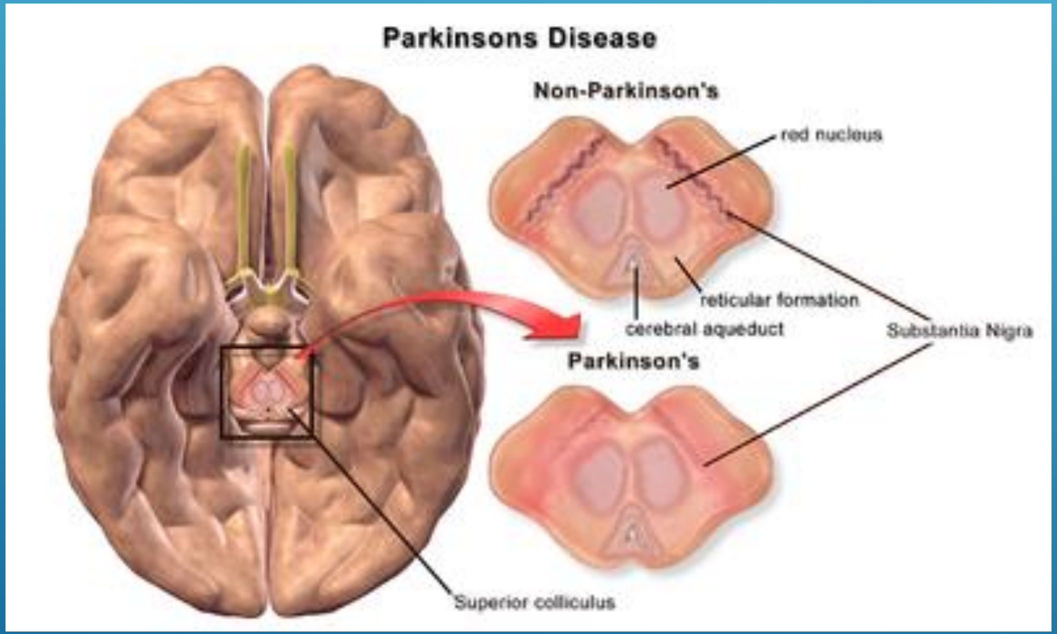
OUTLINE

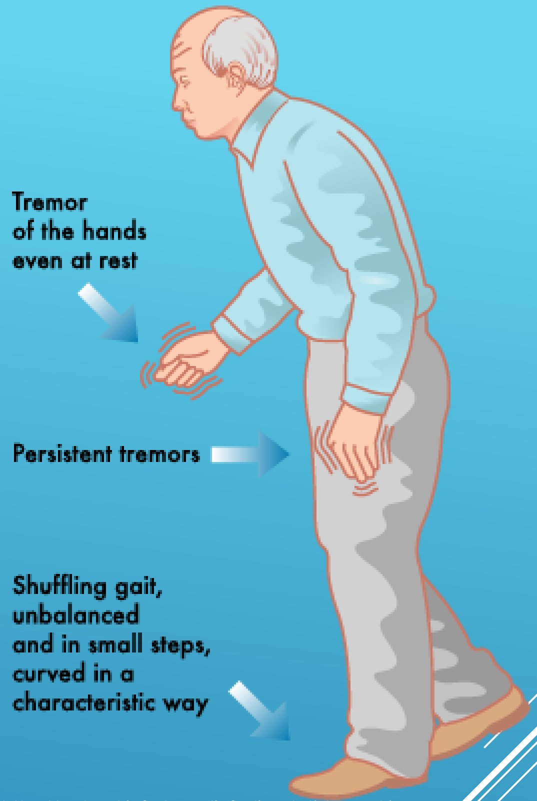
- Background
- Materials and Methods
- Data
- Analyses
- Discussion
- Acknowledgements

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



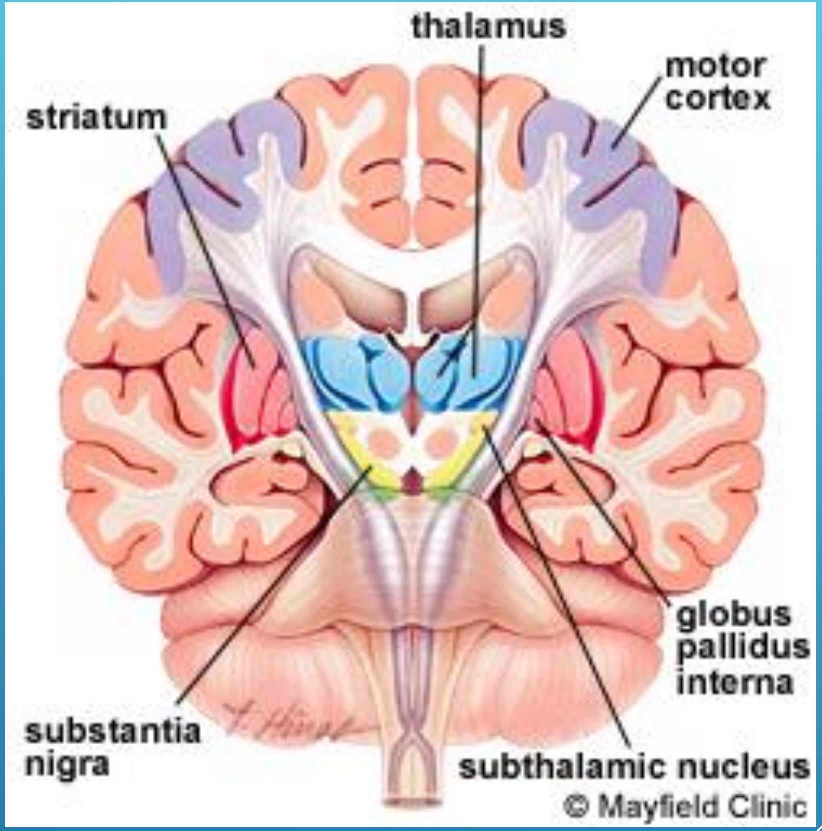
https://en.wikipedia.org/wiki/Pathophysiology_of_Parkinson%27s_disease



http://cuteurl.info/wwelinfo-liraglutide-parkinson-2018.html

THE BASAL GANGLIA

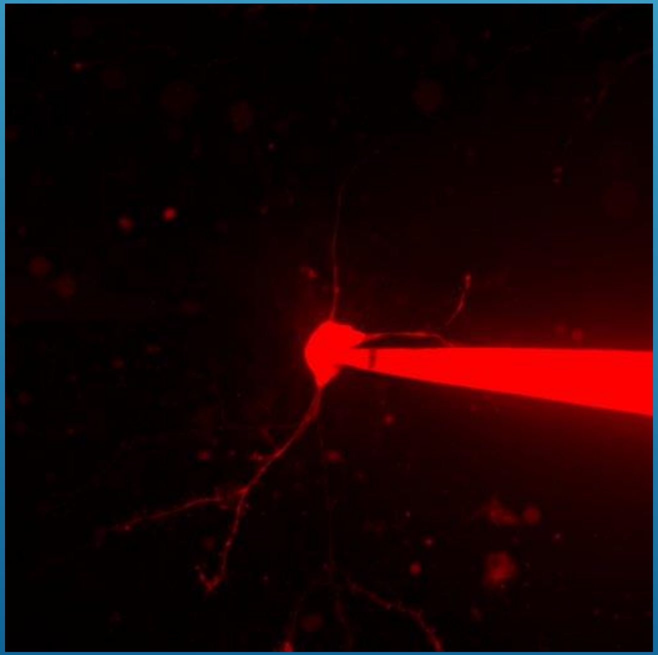
- Basal Ganglia
  - A collection of nuclei
    - Substantia Nigra
    - Subthalamic Nucleus
    - External Globus Pallidus
    - Striatum
- Areas of interest
  - Striatum
  - External Globus Pallidus

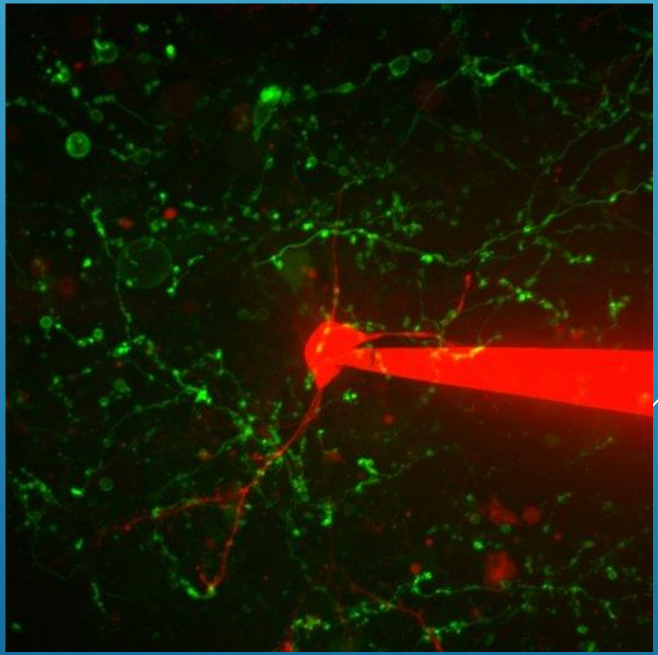


https://www.mayfieldclinic.com/PE-PD.htm

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)
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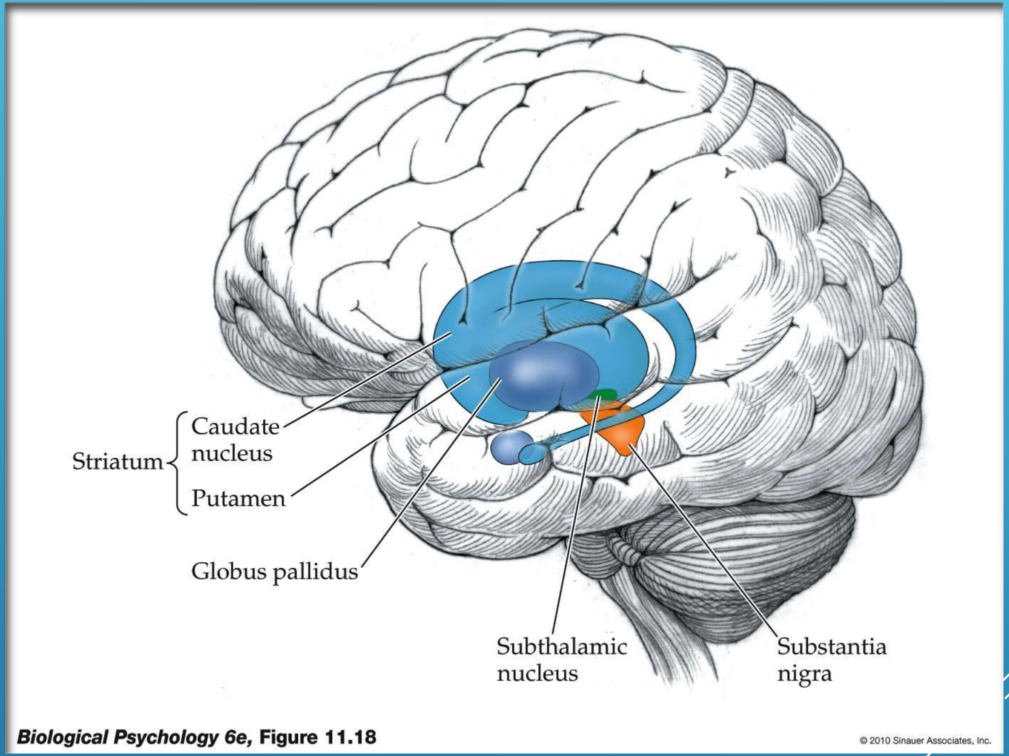
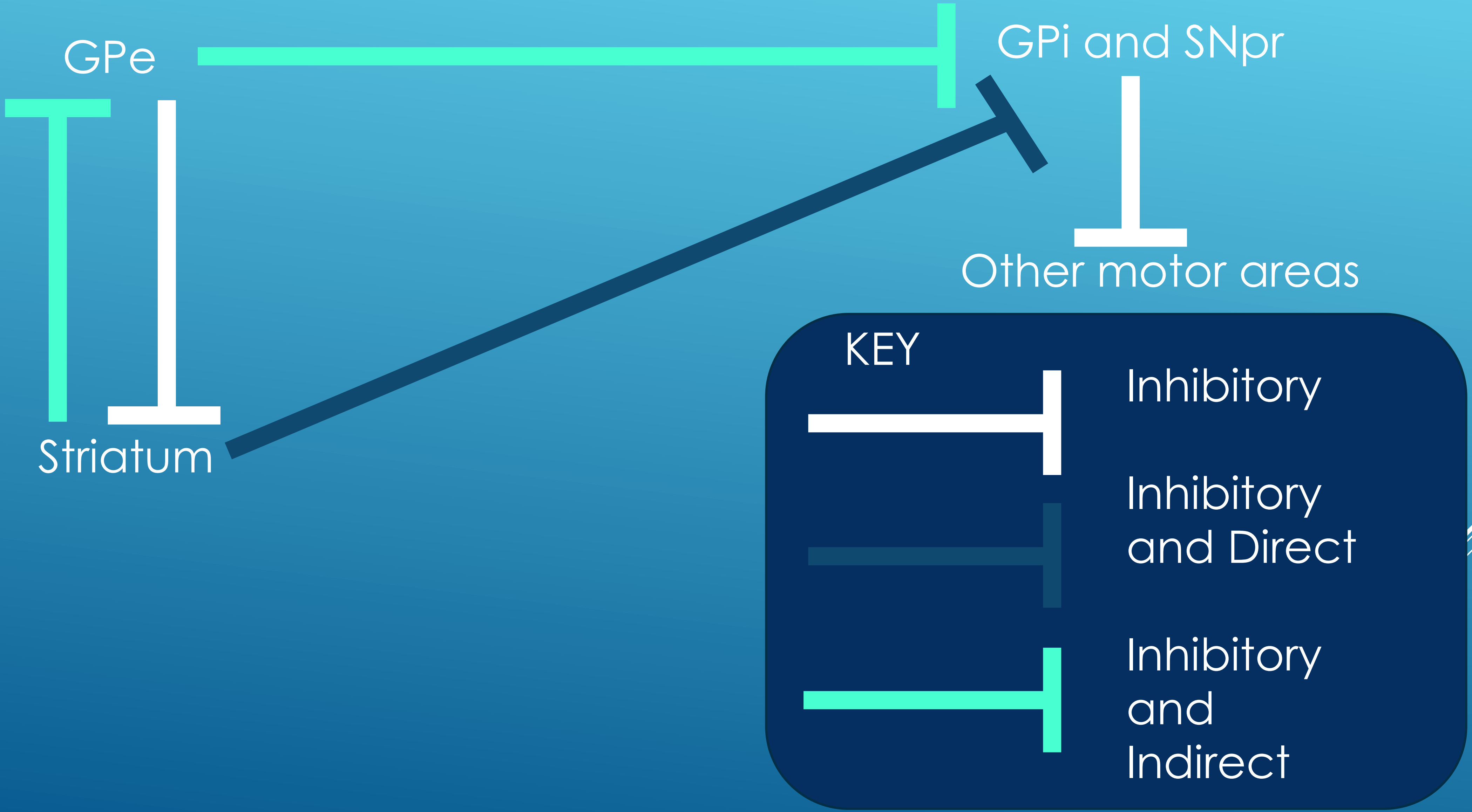
- Npas1+ GPe neurons project to the Str (Hernandez et al., 2016)



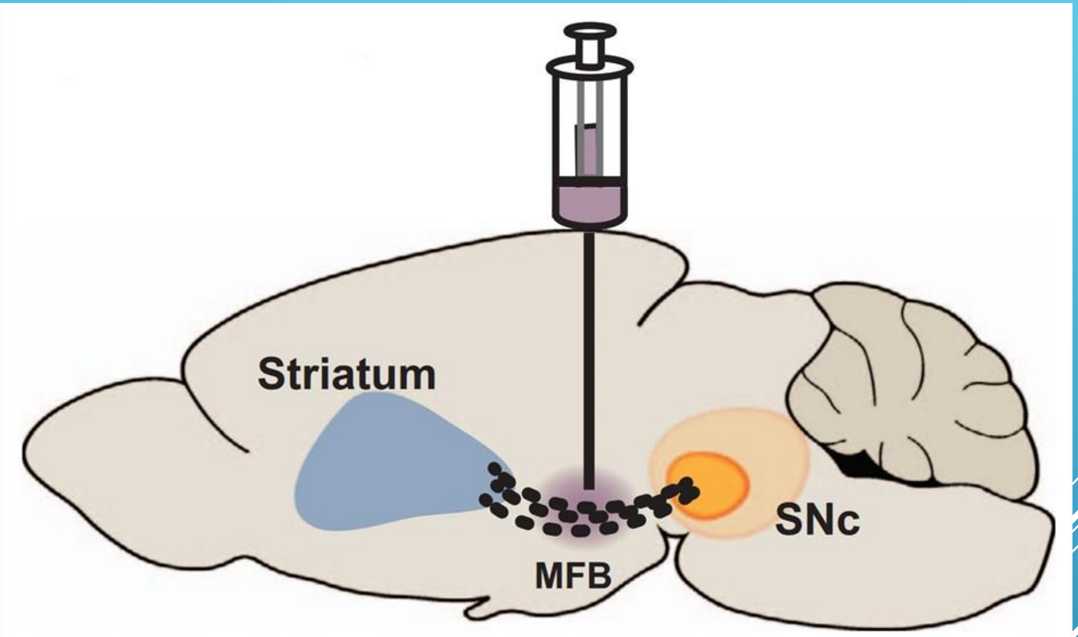
https://beyondthedish.wordpress.com/tag/striatum/

STRIATAL AND PALLIDAL PATHWAYS



MATERIALS AND METHODS

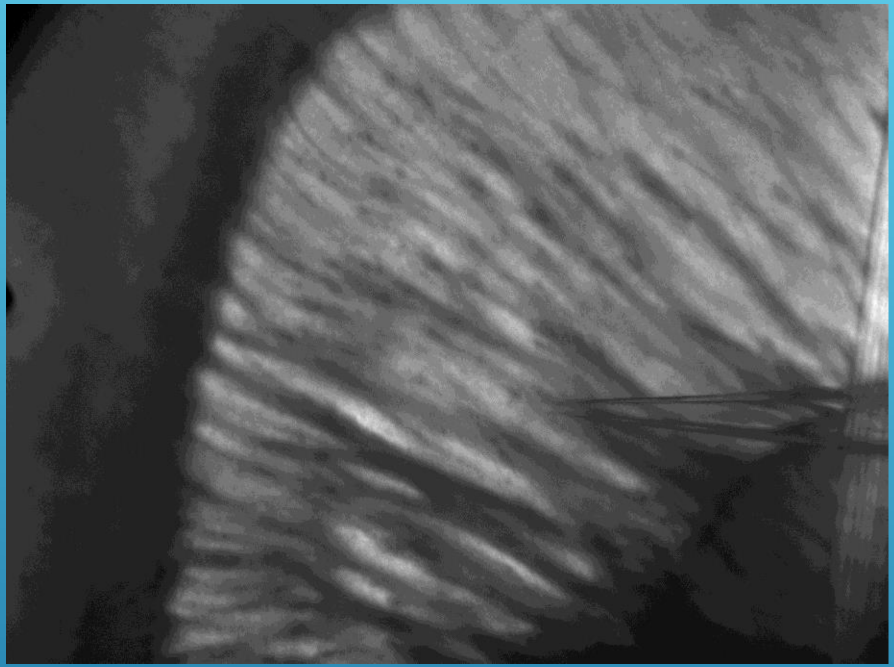
- Parkinsonian Mice
  - Symptoms produced using 6-hydroxydopamine (6-OHDA)
  - 6-OHDA injected into the brain
  - Destroys dopaminergic neurons of the substantia nigra
  - Induces symptoms of Parkinson's Disease



https://www.creative-biolabs.com/drug-discovery/therapeutics/6-ohda-unilateral-lesion-rat-model-of-parkinson-s-disease.htm

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

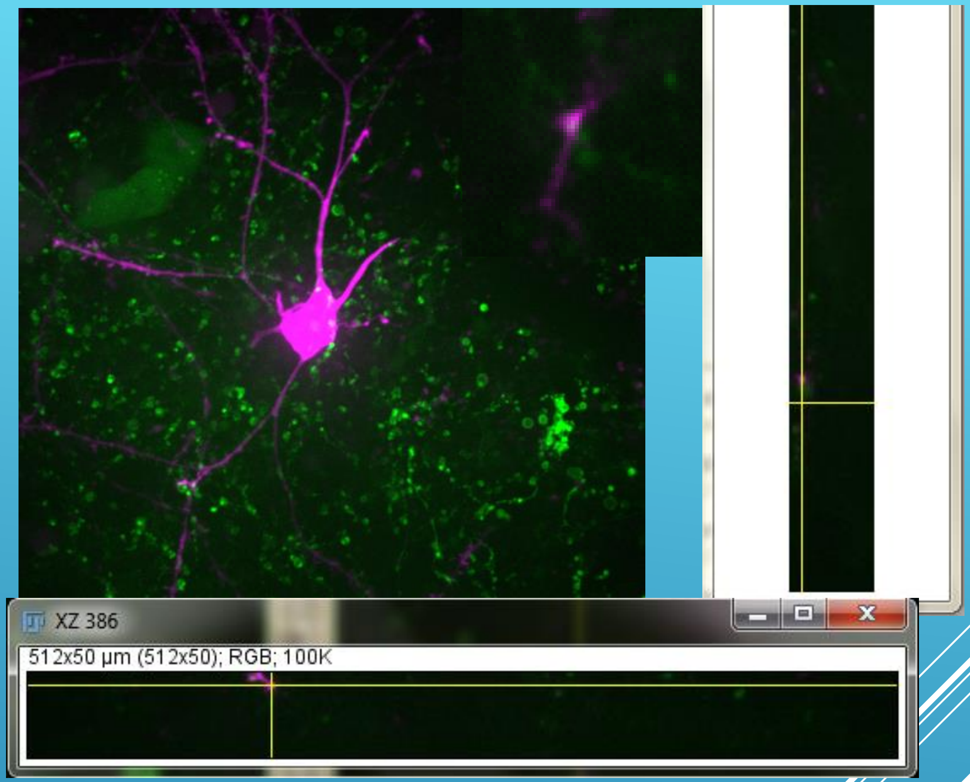


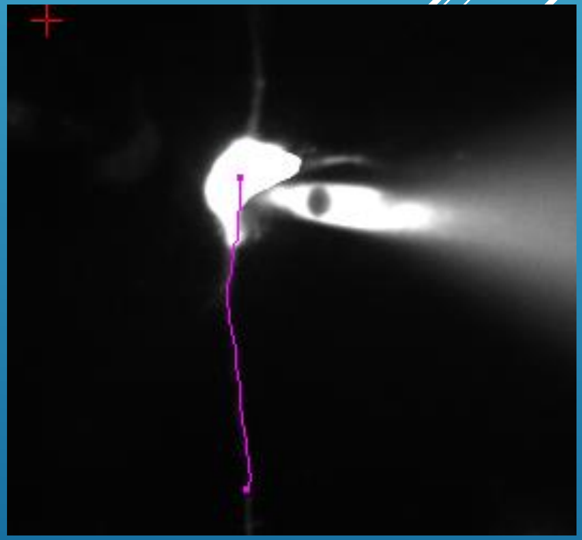
MATERIALS AND METHODS

- Fiji ImageJ software

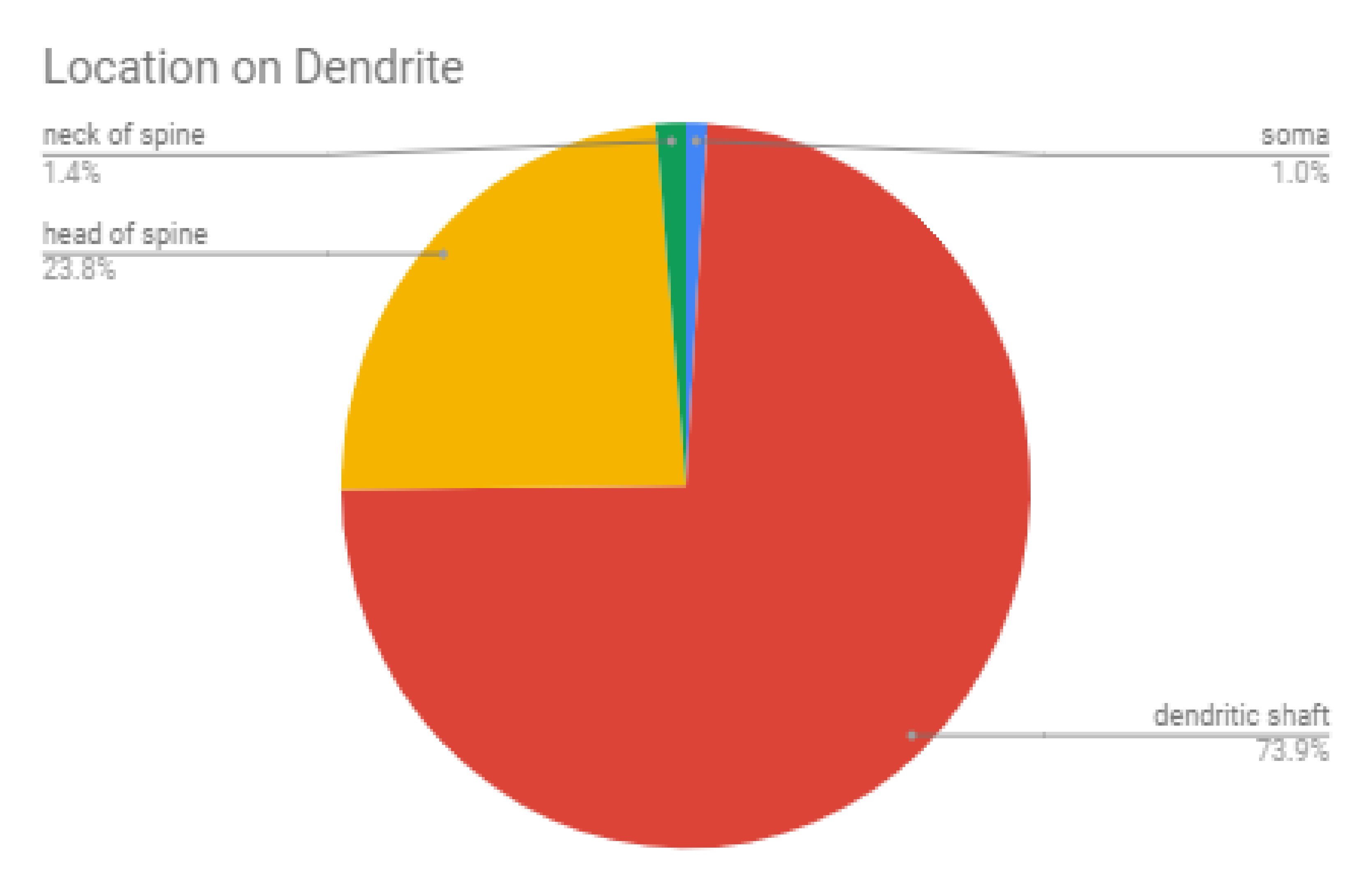
- Pallidostriatal contacts
  - Between SPN dendrites and axons of the GPe
  - Verified in the orthogonal plane

- Contacts measured via two methods
  - Euclidian distance calculated
  - Trace of dendrite to soma

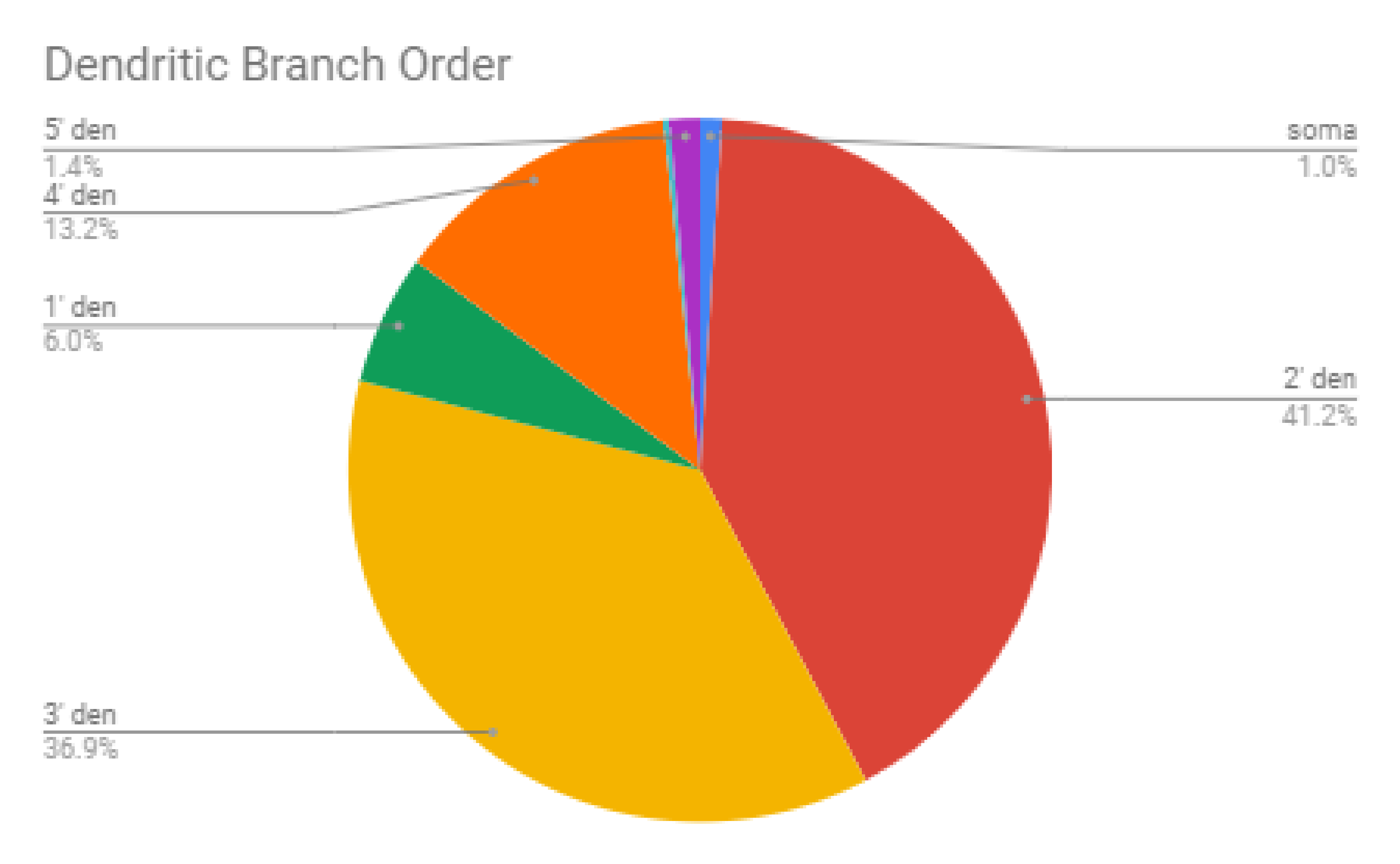




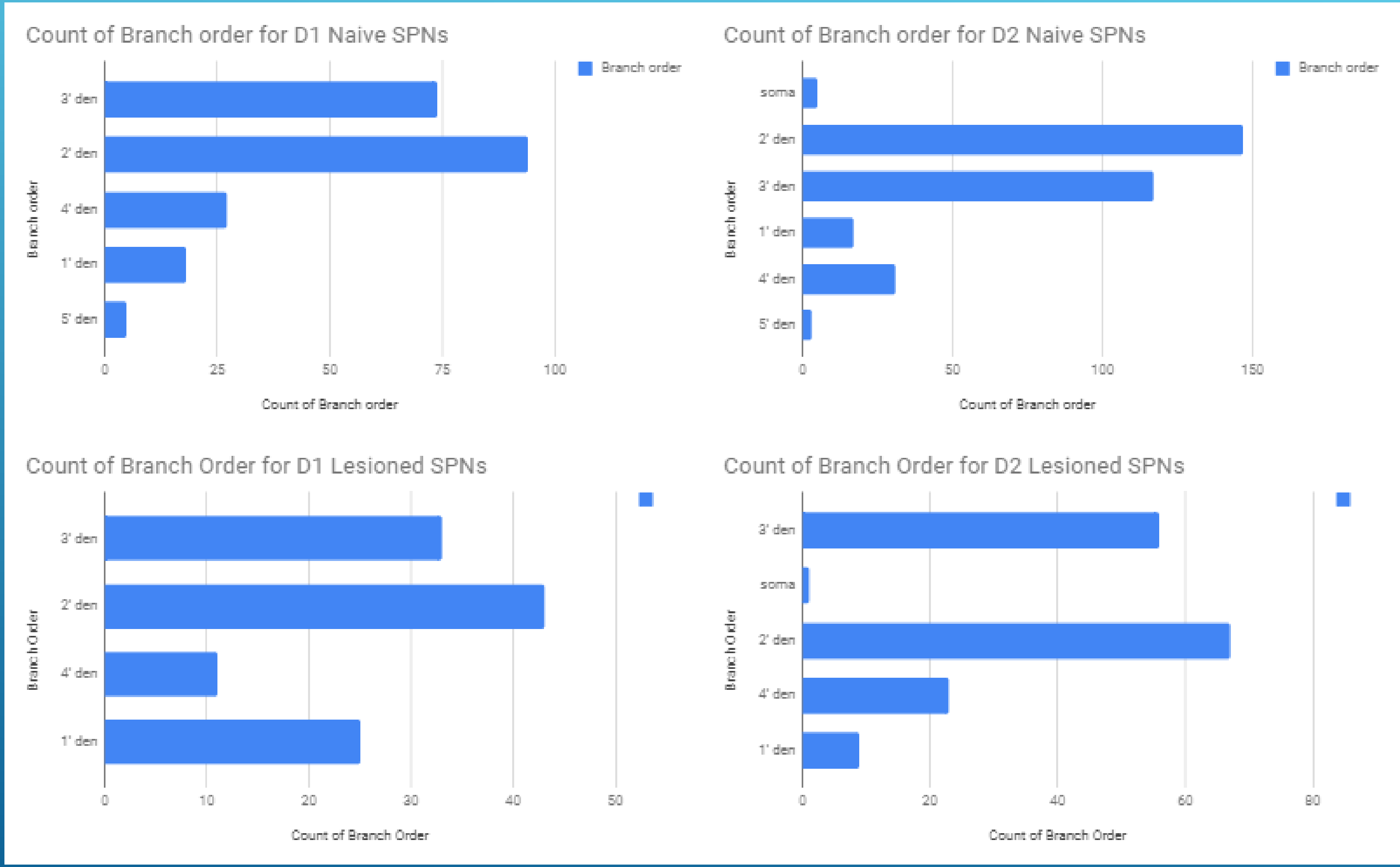
GENERAL LOCATION OF SYNAPSES



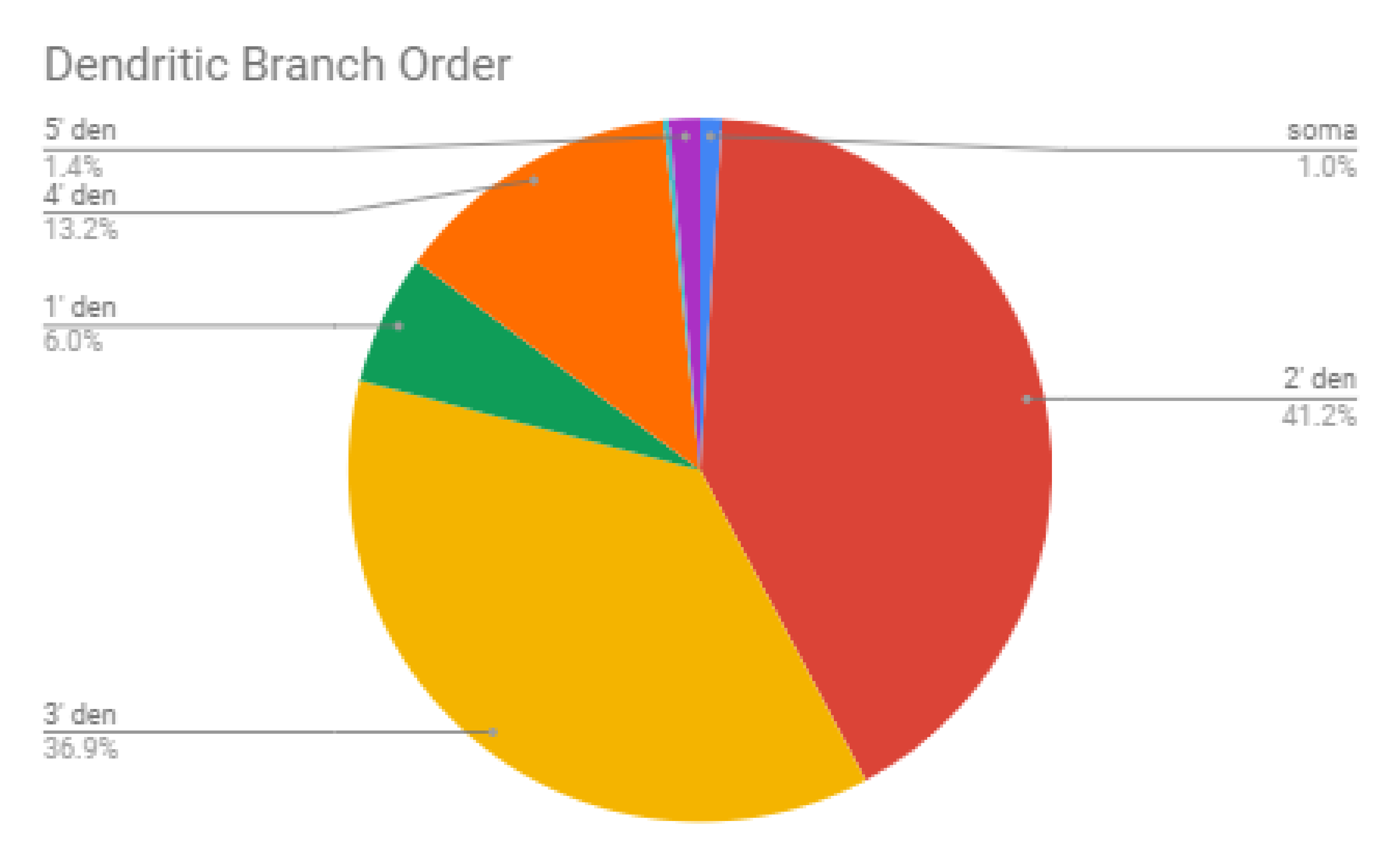
GENERAL BRANCH ORDER AND LOCATION OF SYNAPSES



BRANCH ORDER FOR EACH GROUP OF SPNS



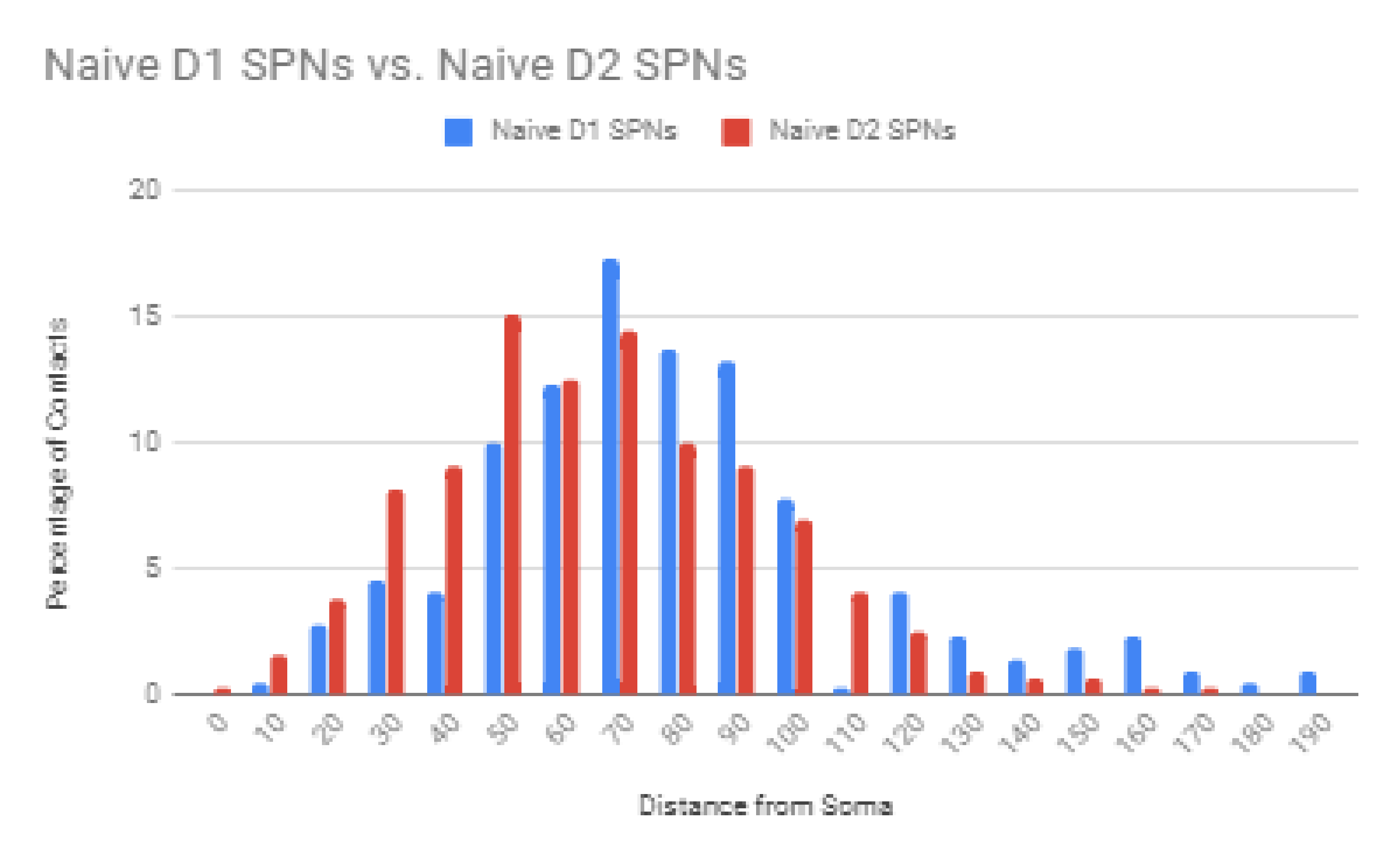
GENERAL BRANCH ORDER AND LOCATION OF SYNAPSES



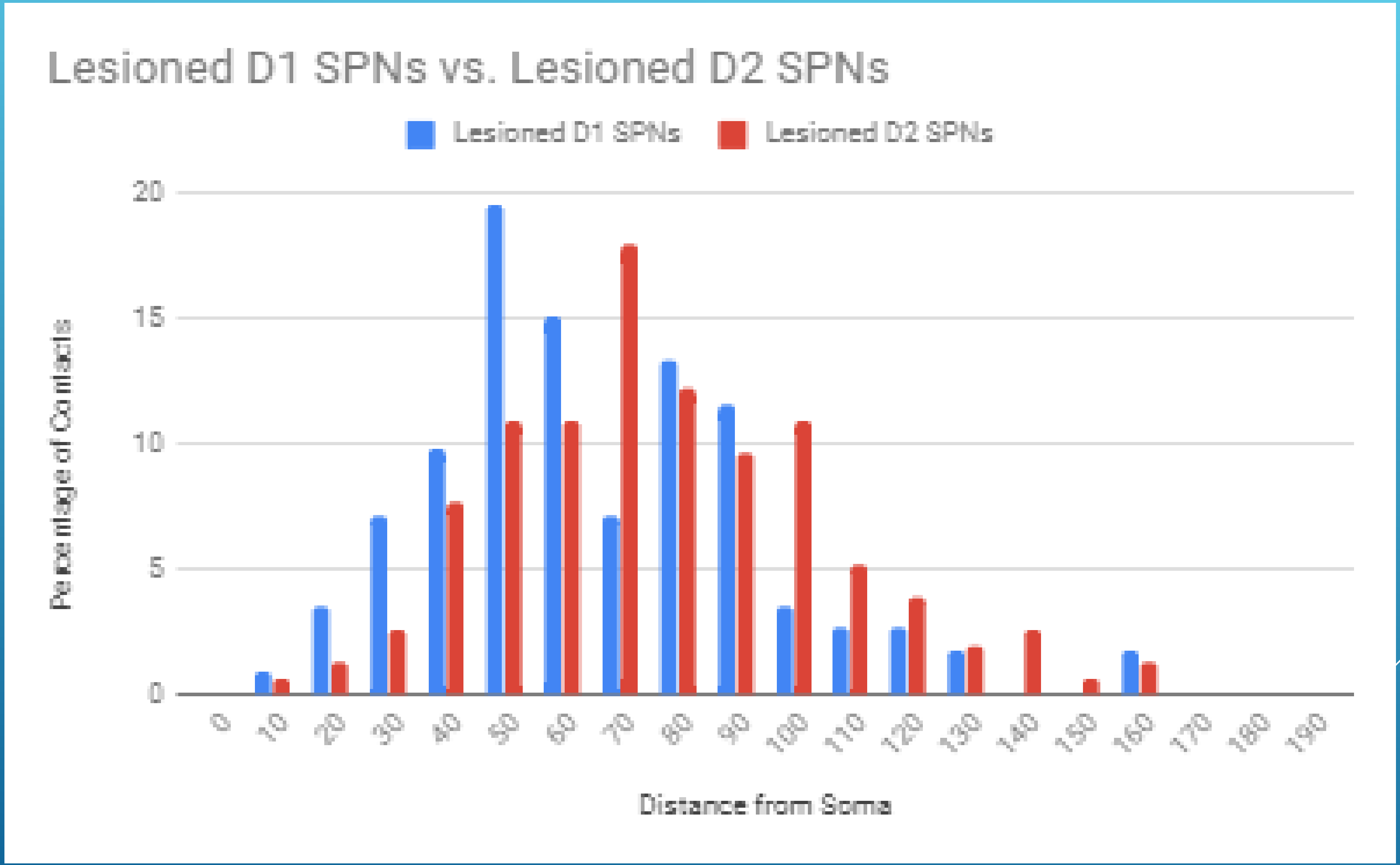
CONTACTS PER CELL

	D1 SPNs	D2 SPNs
Naive	6.9 contacts	7.1 contacts
Lesioned	6.3 contacts	7.1 contacts

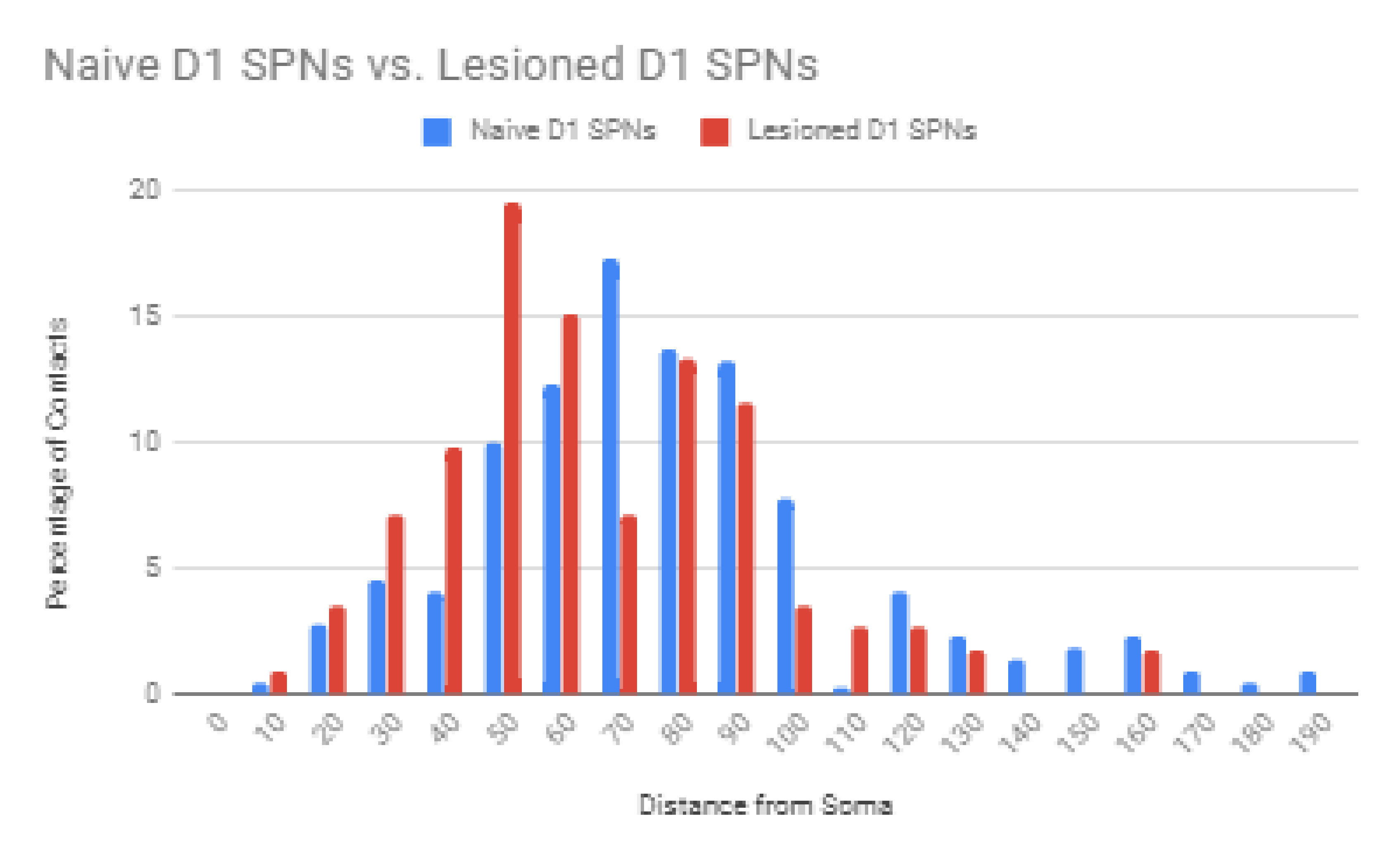
NAÏVE GROUP PROJECTIONS



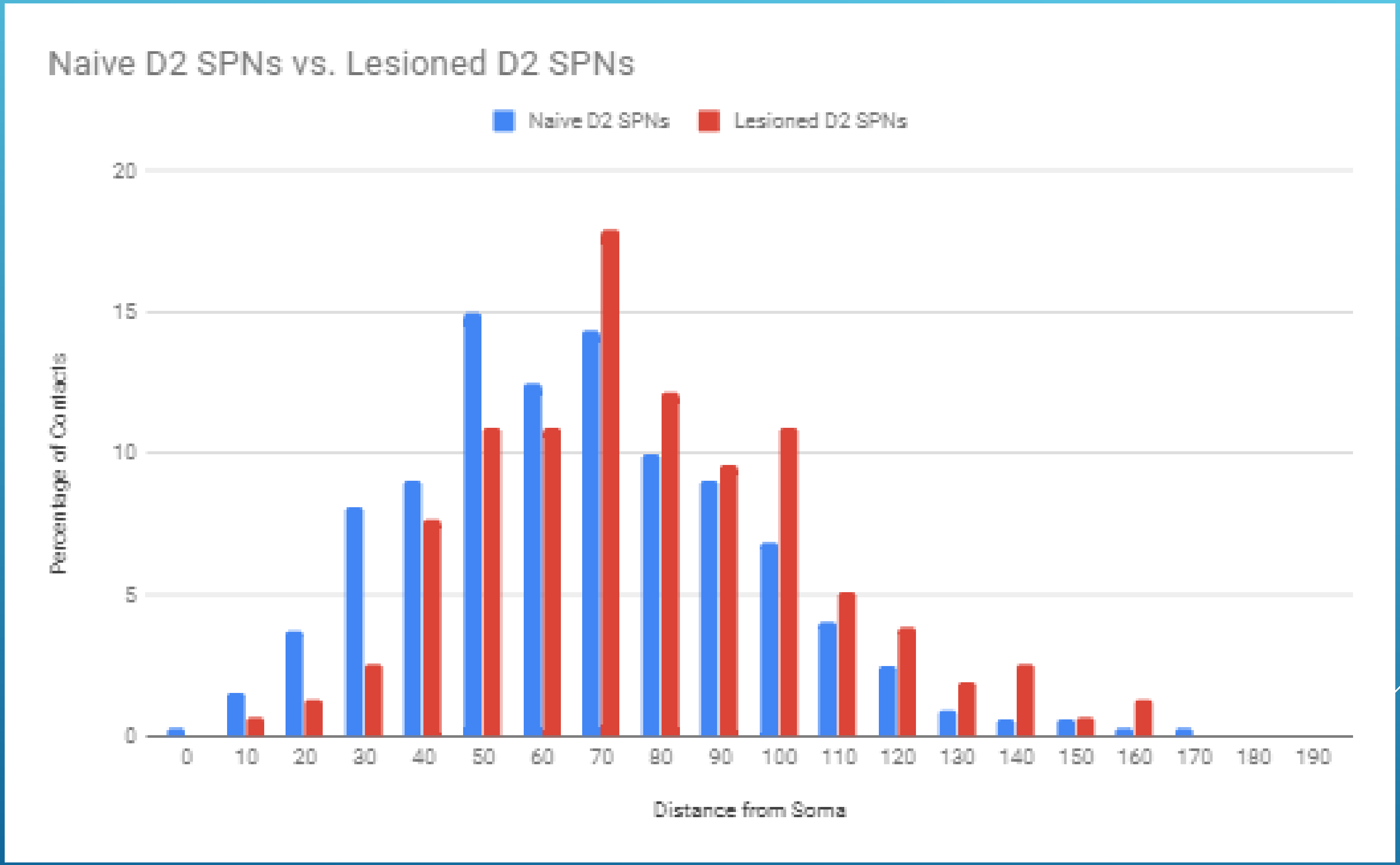
LESIONED GROUP PROJECTIONS



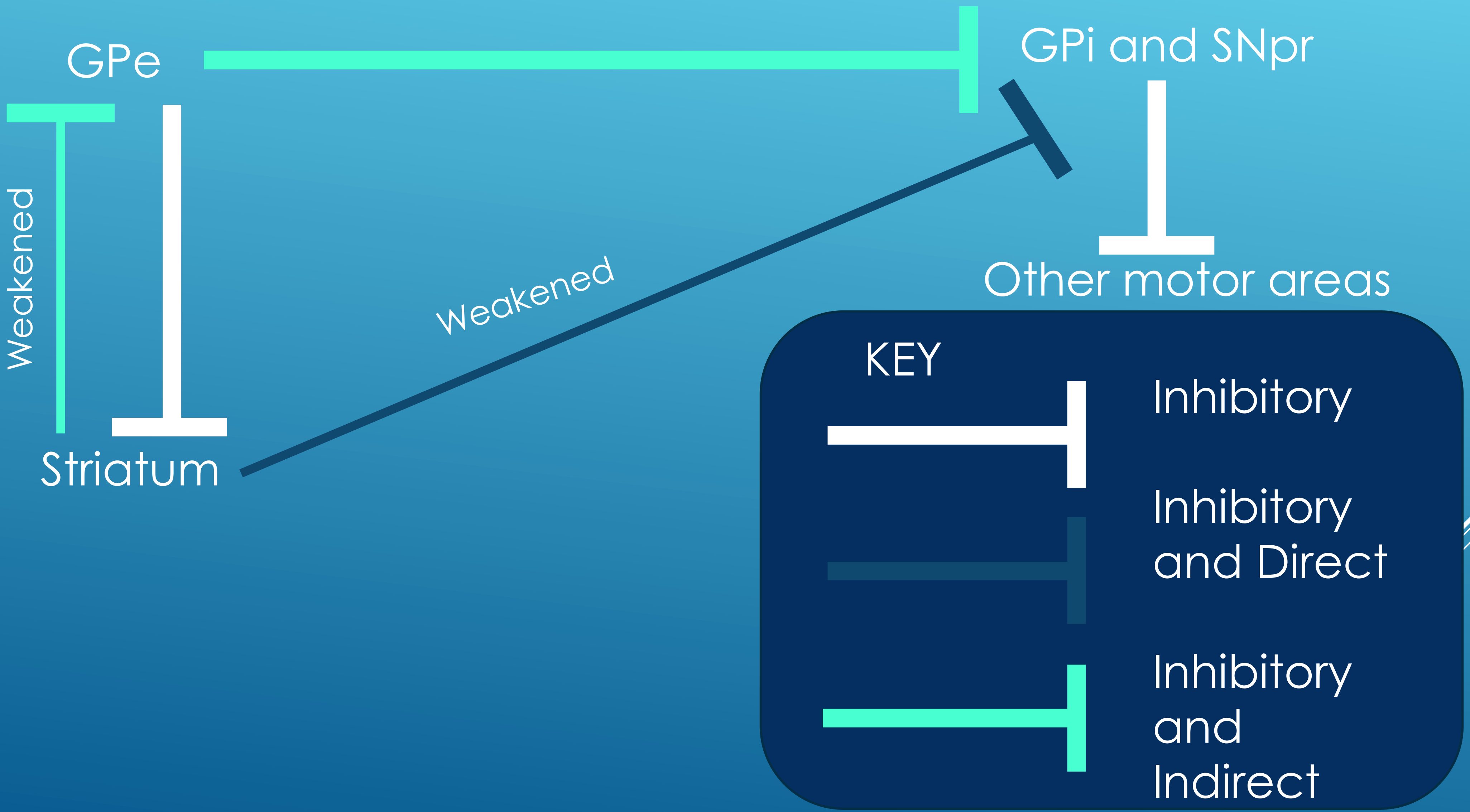
WEAKENED PROJECTIONS OF D1 SPNS



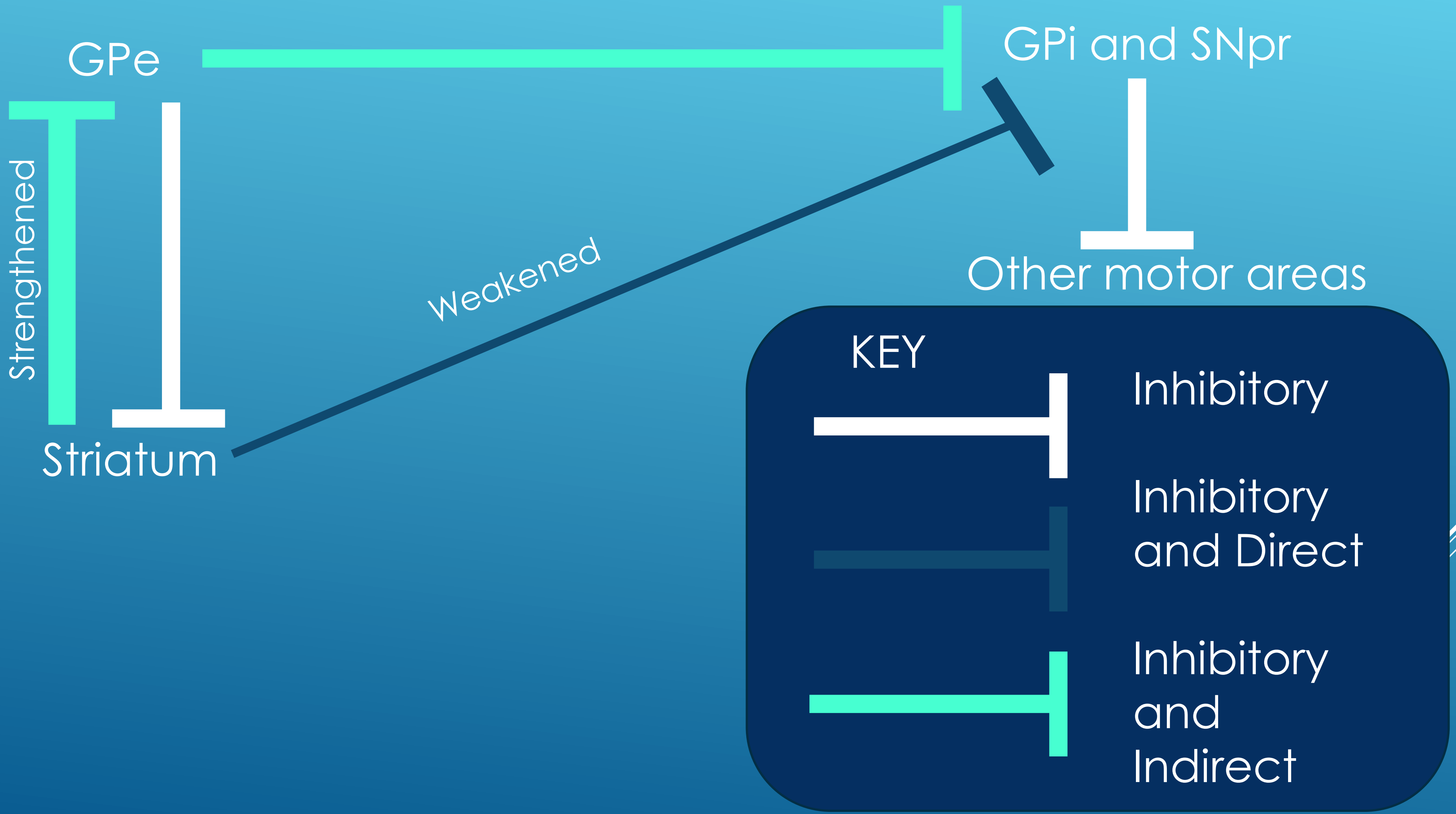
STRONGER PROJECTIONS OF D2 SPNS



DIRECT STRIATAL AND PALLIDAL PATHWAYS



INDIRECT STRIATAL AND PALLIDAL PATHWAYS



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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