High-Density Electrophysiology Recordings Reveal M-L/D-V Gradient of Neuronal Responses in the SNr

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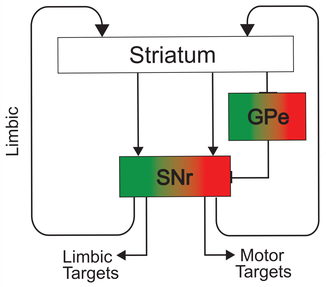
Background

The SNr may have functionally distinct projection targets / inputs

The basal ganglia (BG) is a collection of subcortical nuclei that are critical for gating voluntary movement. In rodents, the main output nucleus of the BG is the Substantia Nigra Pars Reticulata (SNr). The effects of cell type specific modulation is well characterized in the striatum, but very little attention has been paid to the heterogeneity of cellular identity and function of the SNr.



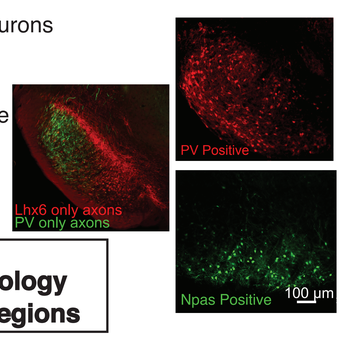
Most studies of the SNr have treated it as a homogeneous structure and have not considered anatomical differences when looking at its physiological output. However, new histology and anatomical data show that there are specific cell types in the SNr (PV, NPas) and that they occupy specific regions along a medial-lateral (ML) gradient.

Here, we supply evidence for different anatomical regions in the SNr and provide a framework for studying the physiology of these regions.

Npas and PV neurons are distributed along a M-L gradient and receive topographically restricted input from PV and Lhx6 GPe neurons

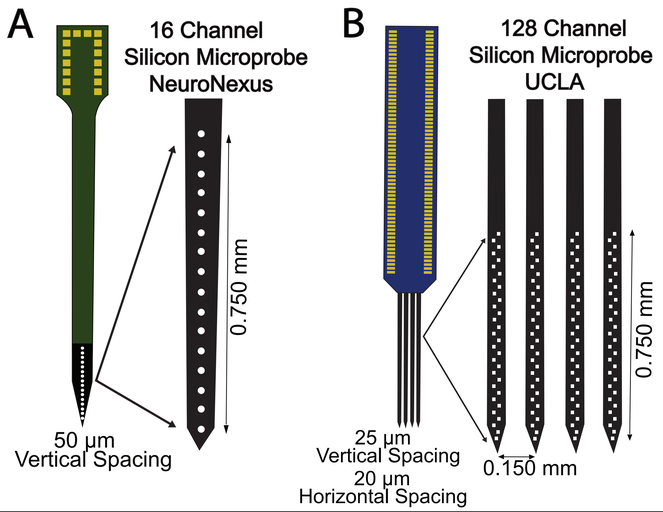
Functionally and genetically distinct GPe neurons innervate different regions of the SNr.
- PV→ Lateral - Lhx6 → Medial

Genetically distinct cell bodies of the SNr are distributed along a medial-lateral gradient.
PV neurons → Lateral SNr
Npas → Medial SNr



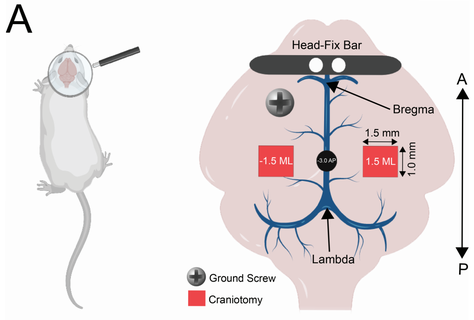
Goal:
Use new probes to study physiology of these anatomically defined regions

4 Shank Probe Enables Recording Across M-L Distance



New Probe = New Challenges

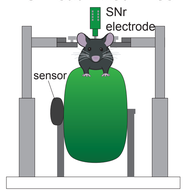
Surgery setup for implanting head-fix bar and ground screw



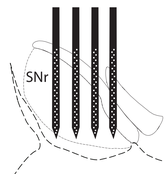
Problem: Size of probe necessitates a new method of grounding.
Solution: Skull screws
Problem: Probe is too big for normal sized craniotomy.
Solution: Wider craniotomy
Problem: Find optimal locations of implants for minimal interference.
Solution: Move head bar to more anterior position
Problem: New type of data requires new code to read/analyze.
Solution: Write new functions

Test: Record from SNr and isolate raw data / single units

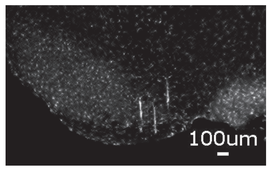
B In-vivo recording of head-fixed mice



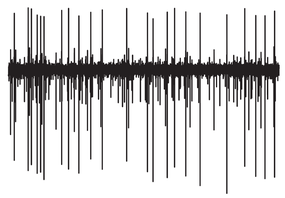
C Ideal recording location for high-density probes



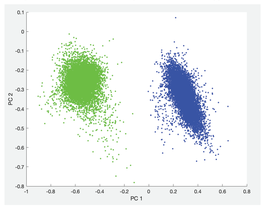
D Microglial stain of first high-density recording



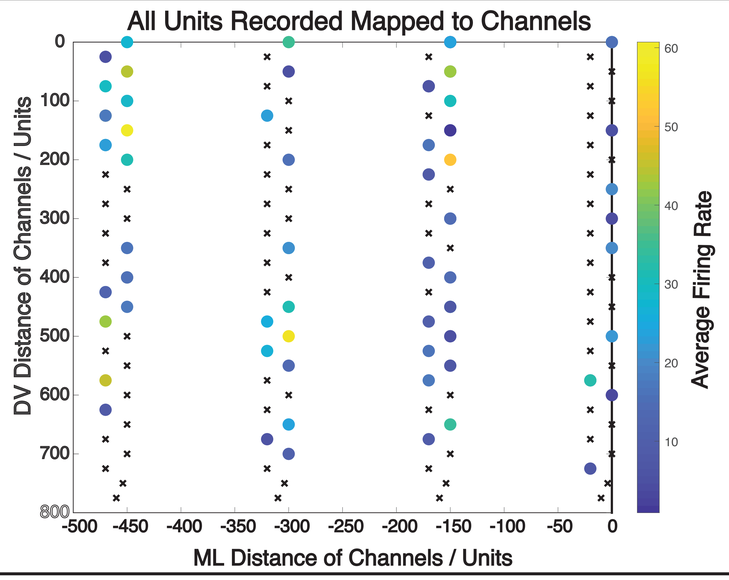
E Example raw-data trace from first recording



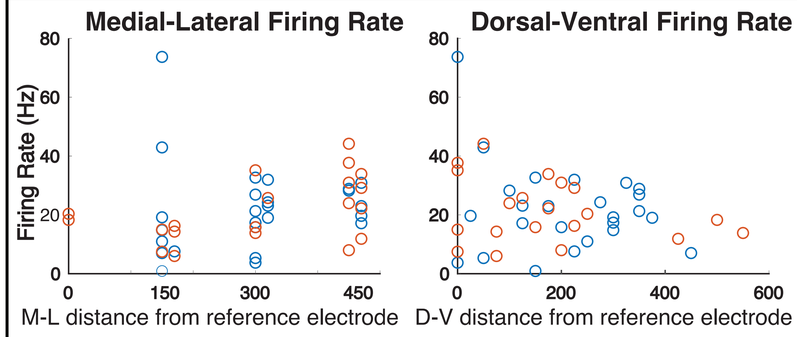
F Example PCA to seperate single unit activity



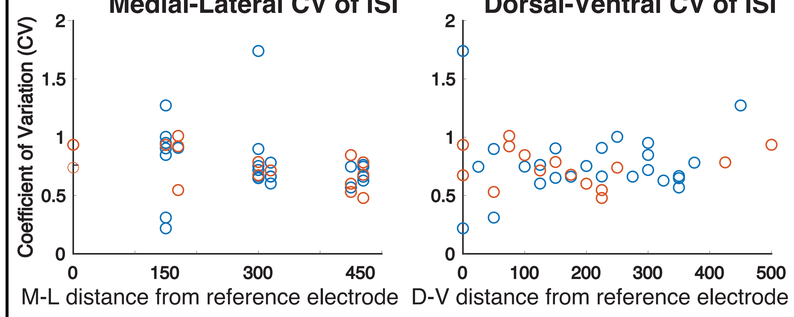
New Function Plots Recorded Units Along M-L/D-V Axis



Variability and Avg. FR as M-L/D-V Function



Conclusion: Firing rate shows upwards trend from medial to lateral

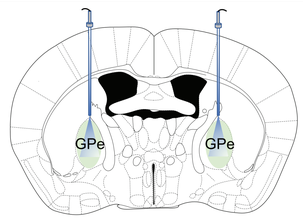


Conclusion: Variability shows downward trend from medial to lateral

Future Directions

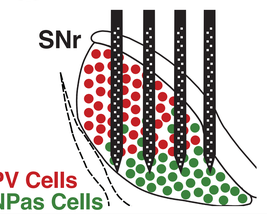
Next Steps

- Record in dopamine depleted mice
- Combine with optogenetics
  - optotag neurons in the SNr
- Record from SNr during a GPe stim
- Correlate recorded activity to movement on the wheel



Following dopamine depletion, optogenetic stimulation of PV cells in the GPe may:

- Have diminished capability to inhibit lateral PV SNr cells and even switch to an excitatory effect
- Be correlated with arrested or impaired locomotion on the running wheel



Acknowledgements

Thank you to the CNBC for organizing the uPNC, it has been an invaluable learning experience. The authors would like to thank Dr. Sotiris Masmanidis for his support and for providing a channel map for the new probes. Thank you to everyone in the Gittis Lab for answering my many questions and being so welcoming during my time here! Finally, thank you to Dr. David Moorman for his continued support as a mentor as I continue my career in science.