

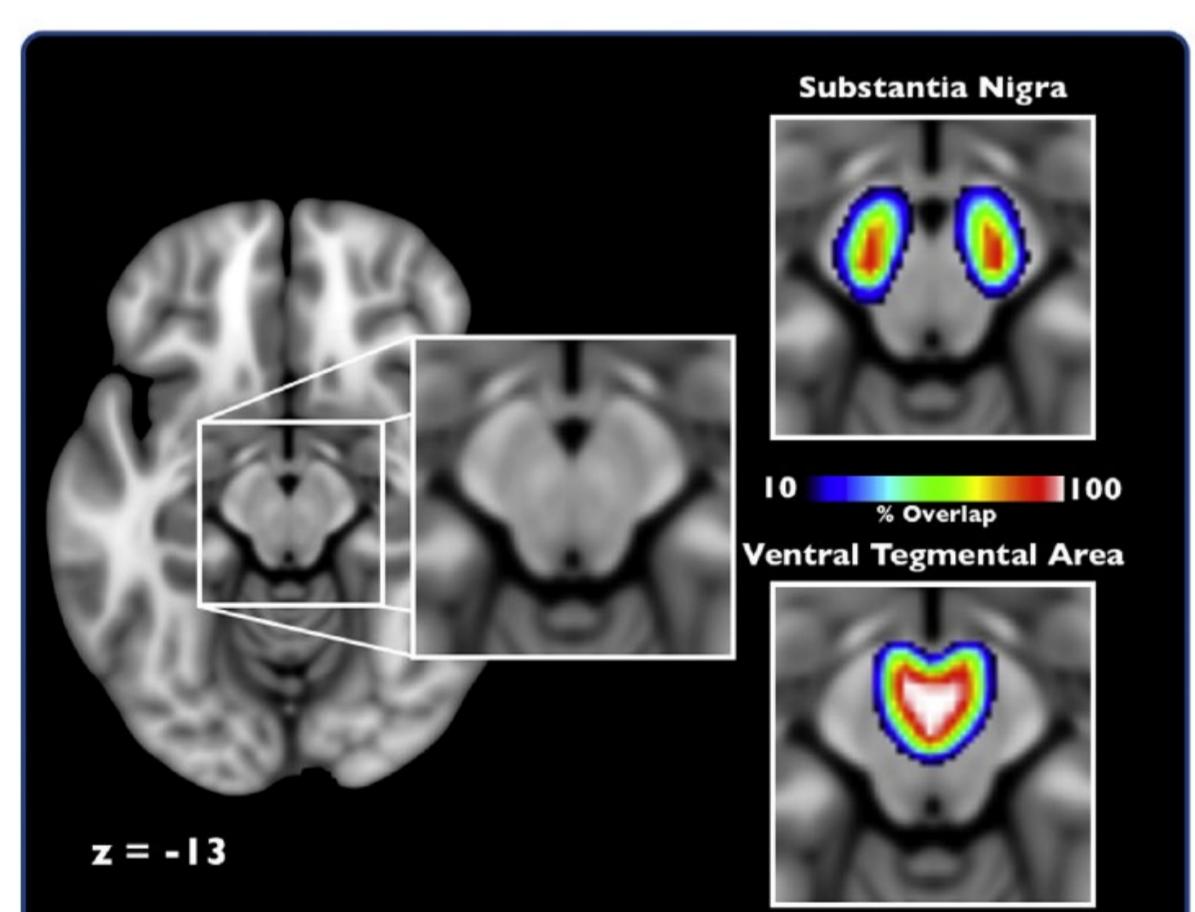
Introduction

- Functional MRI has shown dissociations between dopaminergic networks centered on the Substantia Nigra (SN) and the Ventral Tegmental Area (VTA)^{1,3,5}
- Connectivity of the dopaminergic midbrain is known to mediate the neurobehavioral deficits associated with Parkinson's disease (PD)
- In the early phases of the disease, PD is defined by the degradation of the SN while the VTA is spared²
- Prior fMRI studies have characterized SN connectivity in PD using resting-state fMRI, but with smaller sample sizes
- These studies did not characterize interactions across SN and VTA, which could be altered by sub-region specific changes in dopaminergic tone

Study Goal

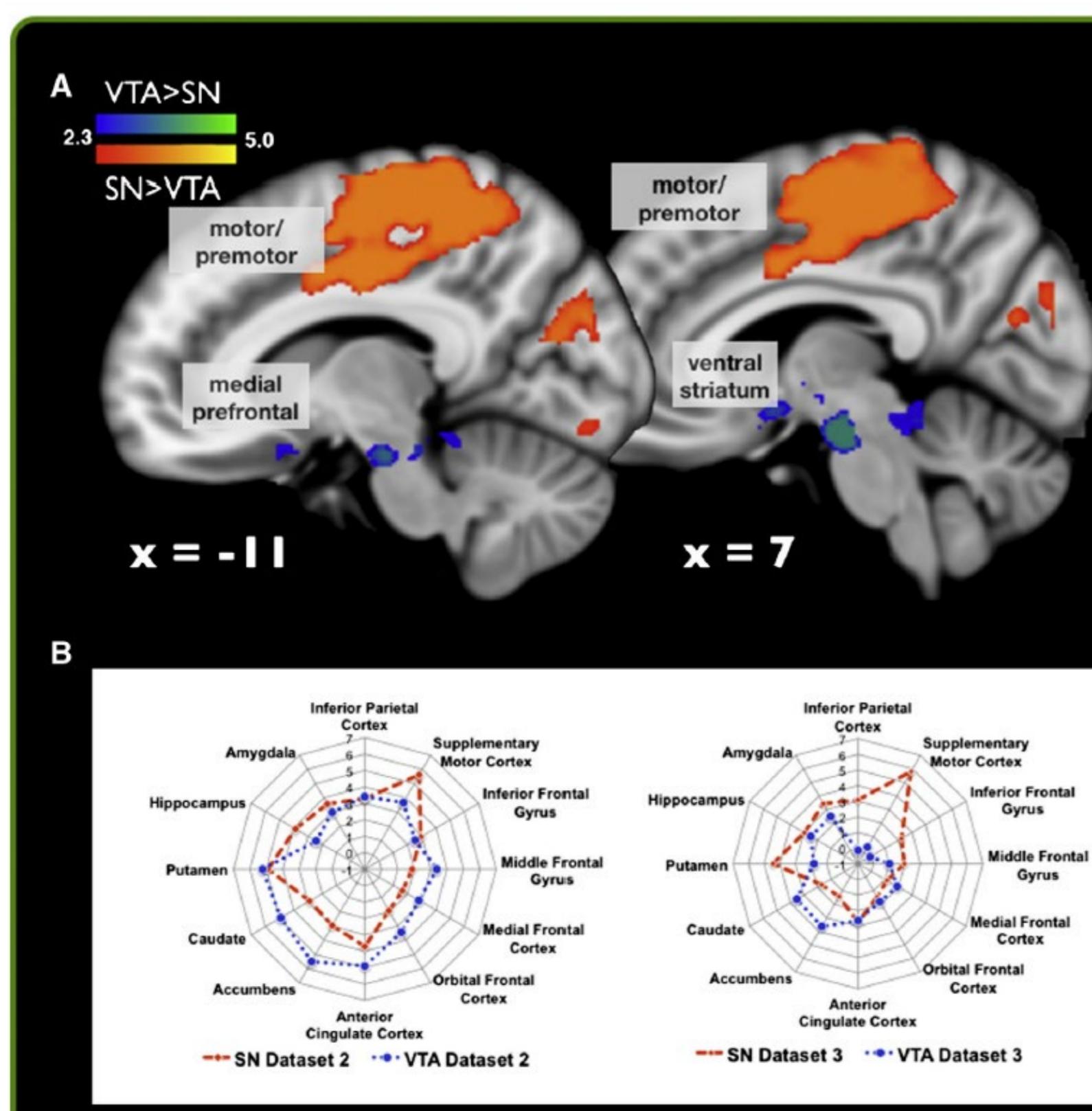
Characterize differences in connectivity from SN and VTA to cortical and sub-cortical regions between healthy controls and individuals with PD

Prior Results



Probabilistic midbrain atlas used to show differential connectivity between SN and VTA in healthy controls¹

Dual Regression analysis indicates differences in connectivity in cortical and sub-cortical target Regions of Interest¹ (ROI), which are used in the present study



Study Samples

This study combined three public datasets for a total of n = 111 participants

Tessa, C., et al. (2019). PloS one.

Dataset 1

- n = 14 controls, 14 PD; aged 36-78
- Voxel size: 4x4x5 mm, Resting state: 8 min 10 sec

Badea, L., Et al. (2017). PloS one. – 2 datasets

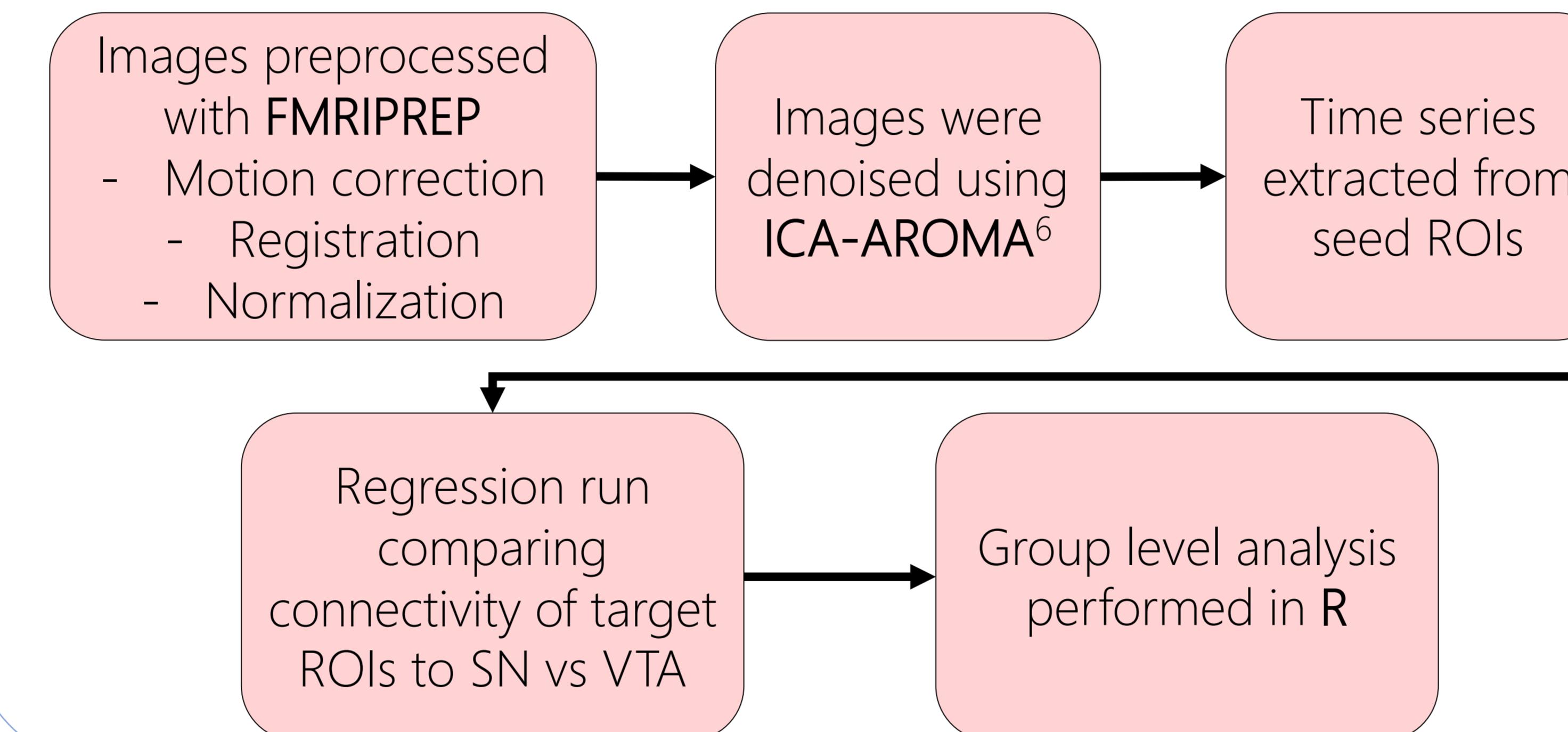
Dataset 2

- n = 16 controls, 27 PD; aged 45-86
- Voxel size: 3.8x3.8x5 mm, Resting state: 8 min 3 sec

Dataset 3

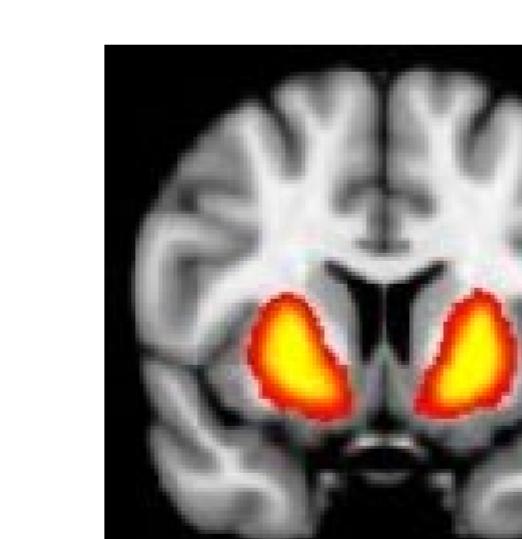
- n = 20 controls, 20 PD; aged 57-75
- Voxel size: 4x4x5 mm, Resting state: 8 min

Analysis Pipeline

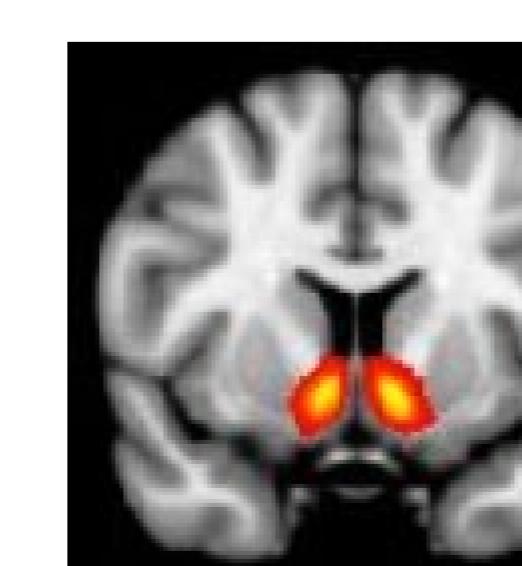


Sub-Cortical ROIs

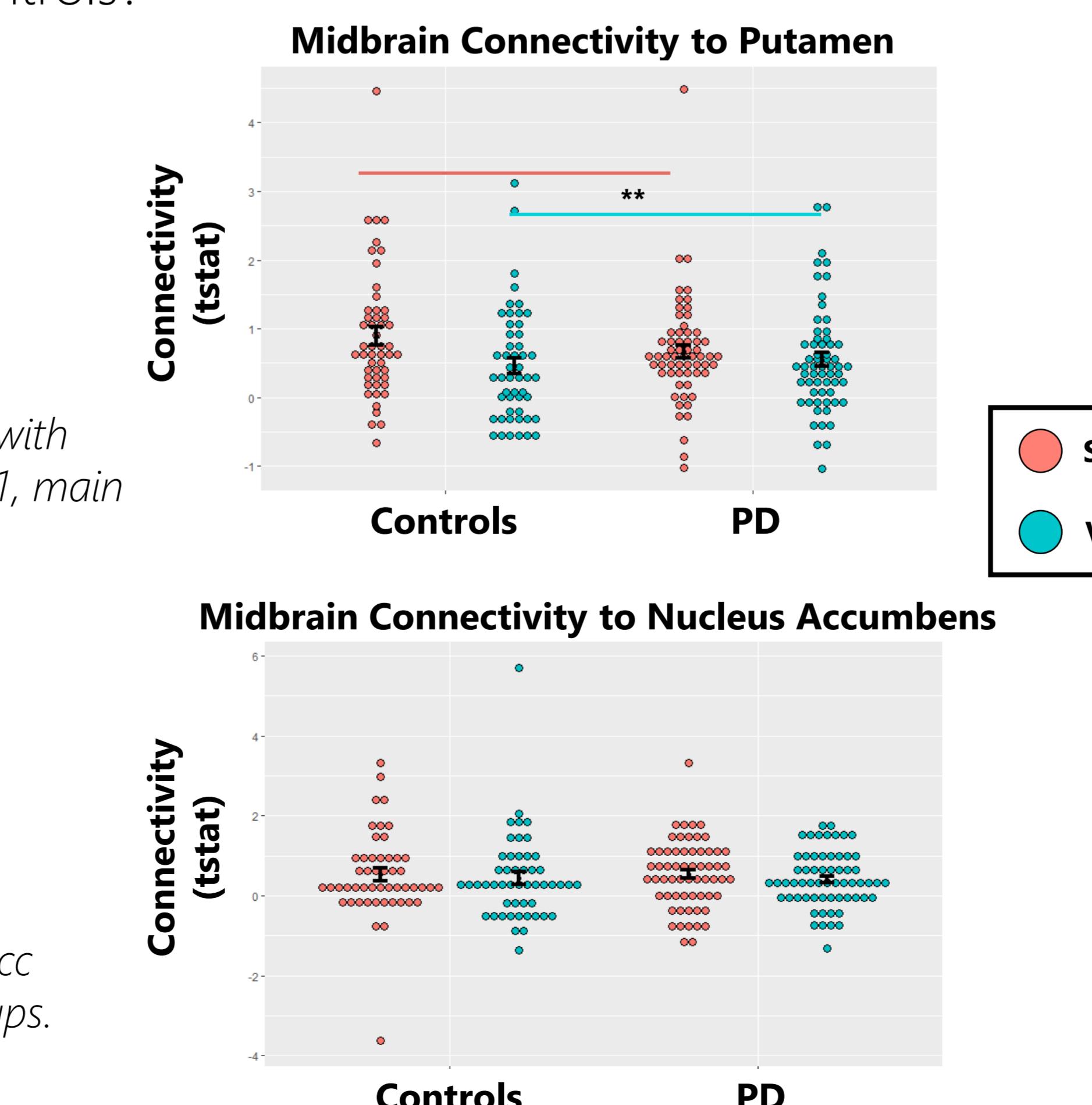
Do PD patients have different connectivity from midbrain to sub-cortical areas than healthy controls?



Increased connectivity of SN with Putamen in both groups ($p < 0.01$, main effect of seed).

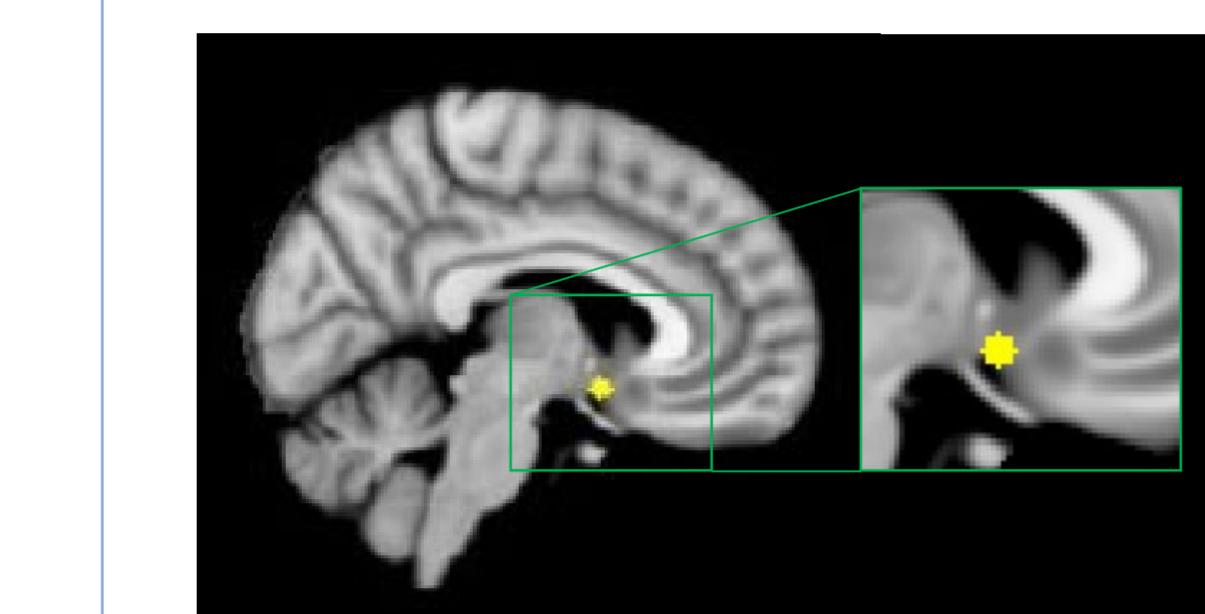


No significant differences in NAcc connectivity across seeds or groups.

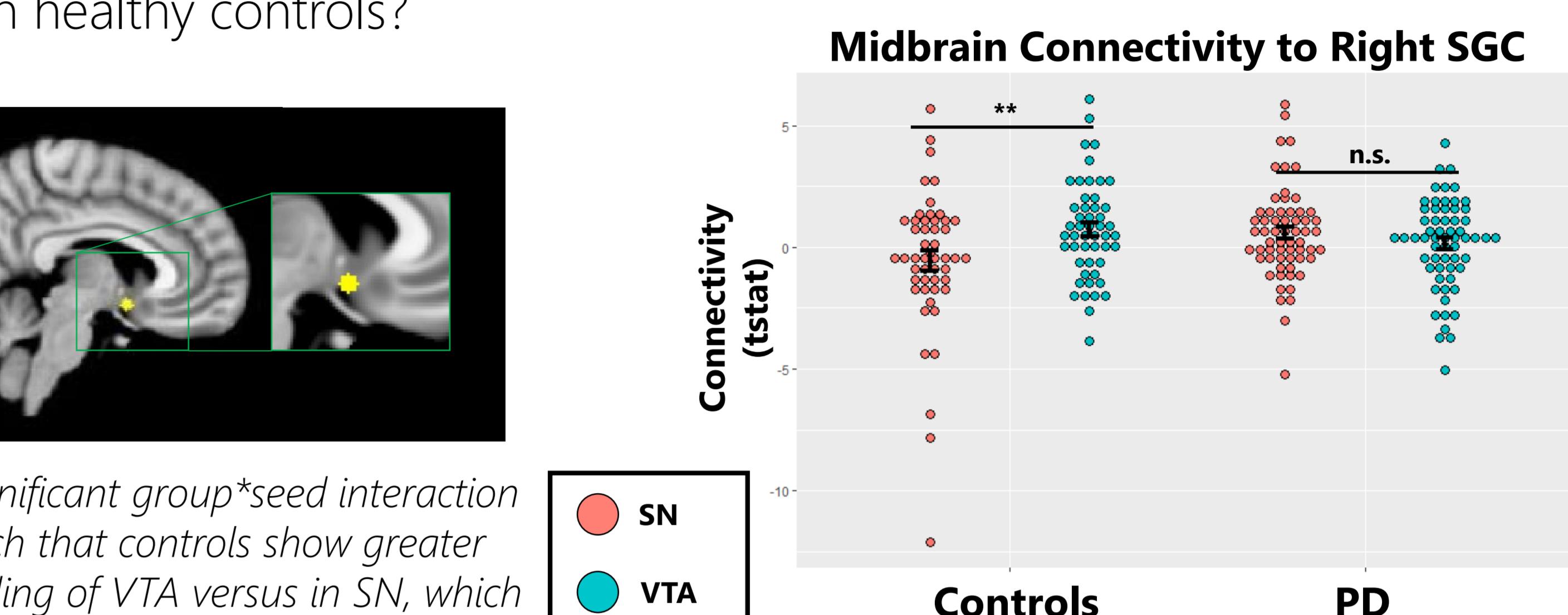


Cortical ROIs

Do PD patients have different connectivity from midbrain to cortical areas than healthy controls?



A significant group*seed interaction such that controls show greater coupling of VTA versus in SN, which is not apparent in PD ($p < 0.005$).



No significant differences in connectivity by seed or group in our other cortical ROIs.

Discussion

- VTA has higher connectivity to the right SGC than the SN in controls, but not in patients with PD
- SN has significantly higher connectivity to Putamen in both groups
- Given the role of VTA-SGC interactions in guiding motivated behavior, functional coupling in this circuit may be associated with aberrant goal-directed behavior in PD populations.
- This differential connectivity in the midbrain could provide a novel target for understanding the pathophysiology and neurobehavioral deficits in PD

Future Directions

- Independent component analysis (ICA) and dual regression (DR) may further elucidate these connectivity differences⁴
- These analyses can map out ROIs based on fMRI data, rather than using probabilistic atlases
- This data may corroborate the data from the first analysis and/or introduce new region-specific difference not originally captured

References

1. Murty, V. P., et al., (2014). *NeuroImage*; 2. Fearnley, J. M., & Lees, A. J. (1991). *Brain*;
3. Dagher, A. & Robbins, T.W., (2009) *Neuron*; 4. Leech, R., et al., (2012). *Journal of Neuroscience*; 5. Damier, P., et al., (1999). *Brain J. Neurol*; 6. Pruij et al., 2015, *NeuroImage*