Neuromelanin imaging in Parkinson's Disease at 7T

Dhairya A Lakhani, MD

Neuroradiology Fellow, PGY6

Johns Hopkins University

Research Mentor: **Erik H Middlebrooks, MD**; Mayo Clinic, FL

DISCLOSURES

Authors have no relevant disclosures

BACKGROUND

- Parkinson's disease can be a challenging clinical diagnosis
  - ❖ There is substantial heterogeneity in the presenting symptoms
  - ❖ It shares similar clinical features to several other conditions, particularly early in the disease course
- This makes it critically important to have a **sensitive** and **specific** biomarker for the diagnosis and management of PD

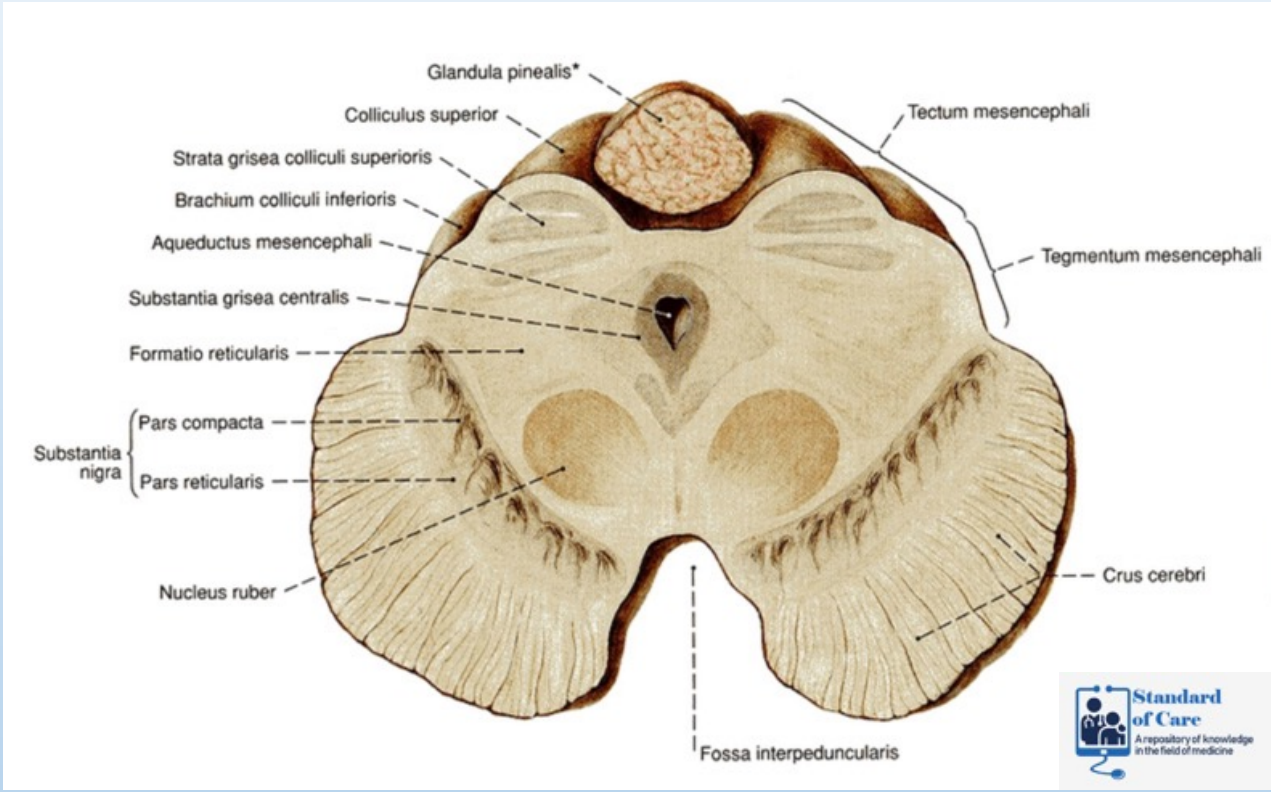
BACKGROUND

SUBSTANTIA NIGRA

- One of the brainstem nuclei
- Part of extrapyramidal system

- Consists of two parts:
  - **Inner:** SN Pars compacta
  - **Outer:** SN Pars reticularis

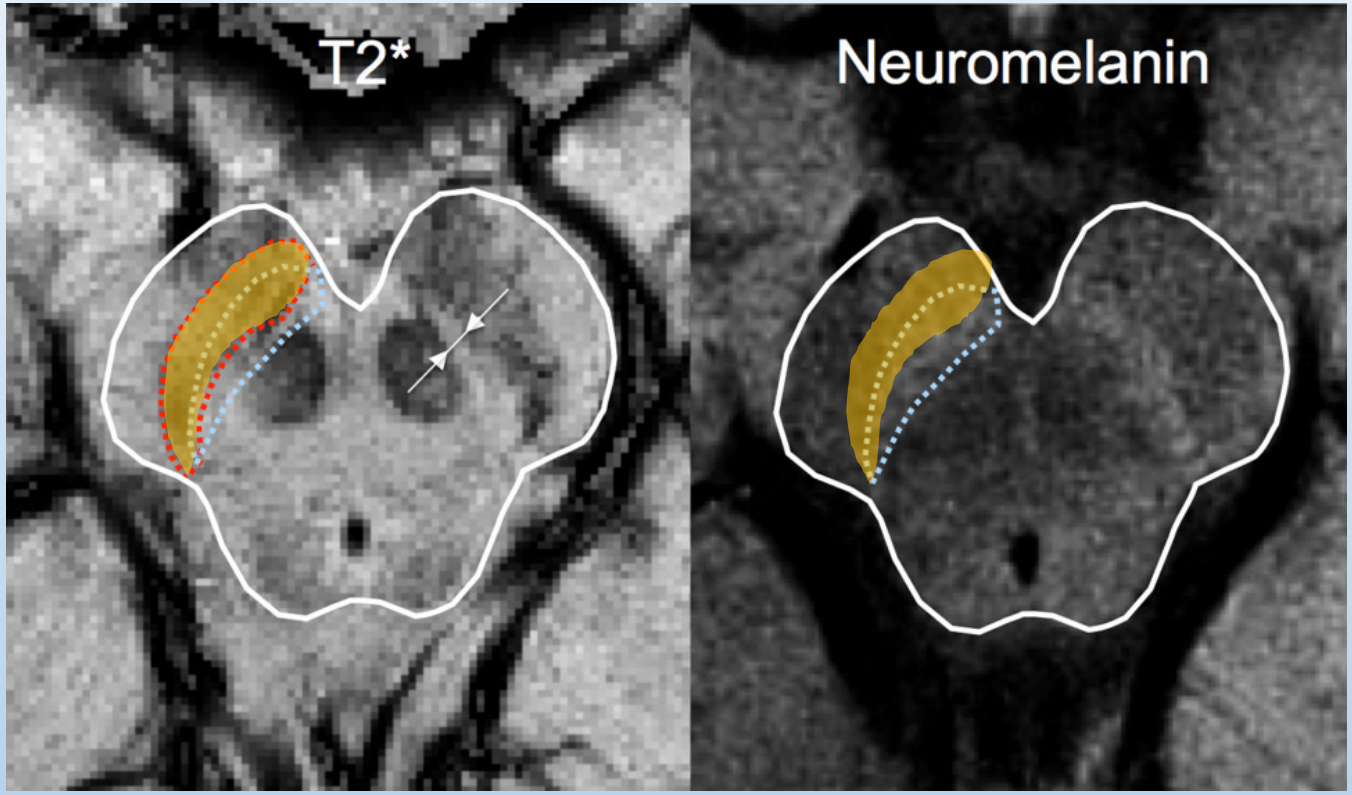
- Both have different functions and connections



BACKGROUND

(Outer) SN Pars Reticularis

- Rich in GABAergic neurons
- Has relatively higher Fe and lower NM concentration, compared to inner pars compacta

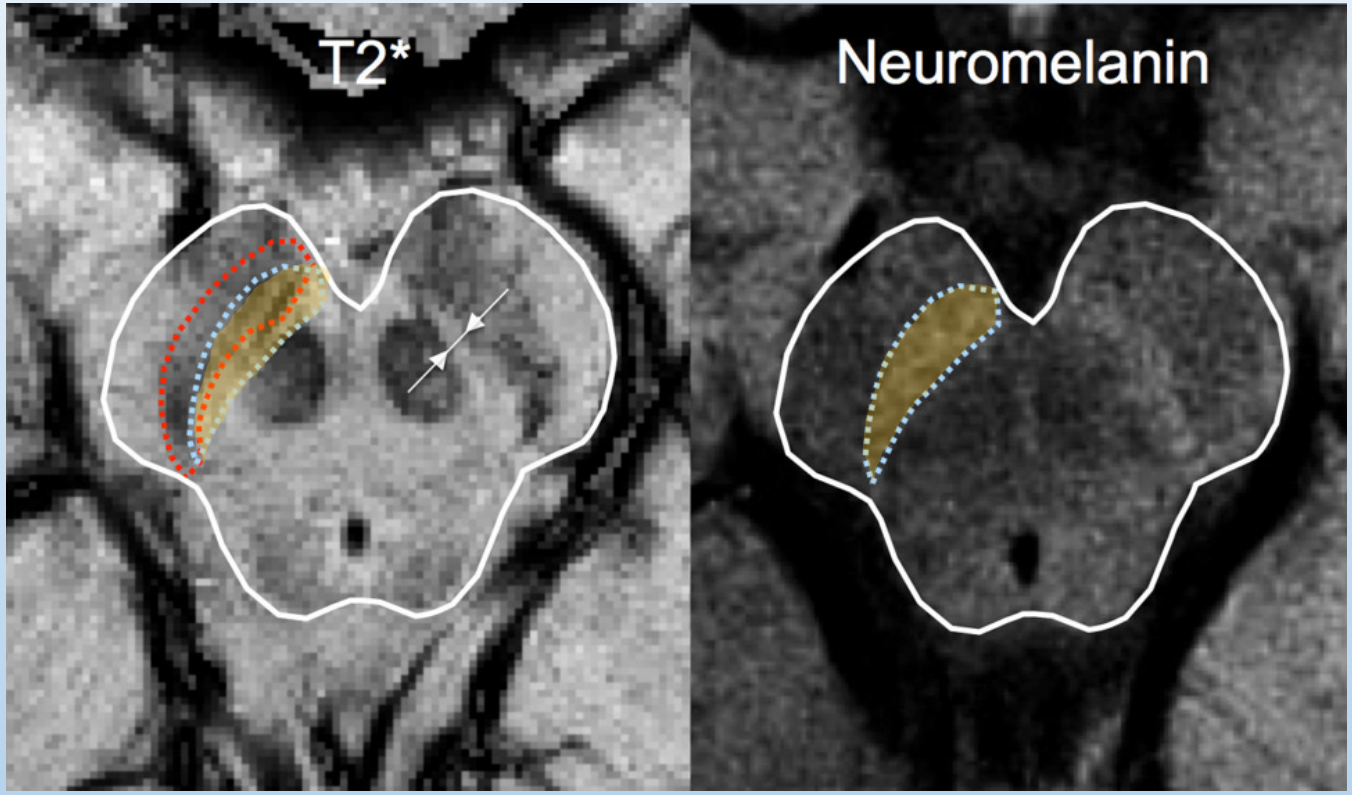


Lehéricy S, et al. 2014

BACKGROUND

(Inner) SN Pars Compacta

- Rich in dopaminergic cells
- Has lower Iron and higher Neuromelanin content relative to the outer Pars Reticularis



Lehéricy S, et al. 2014

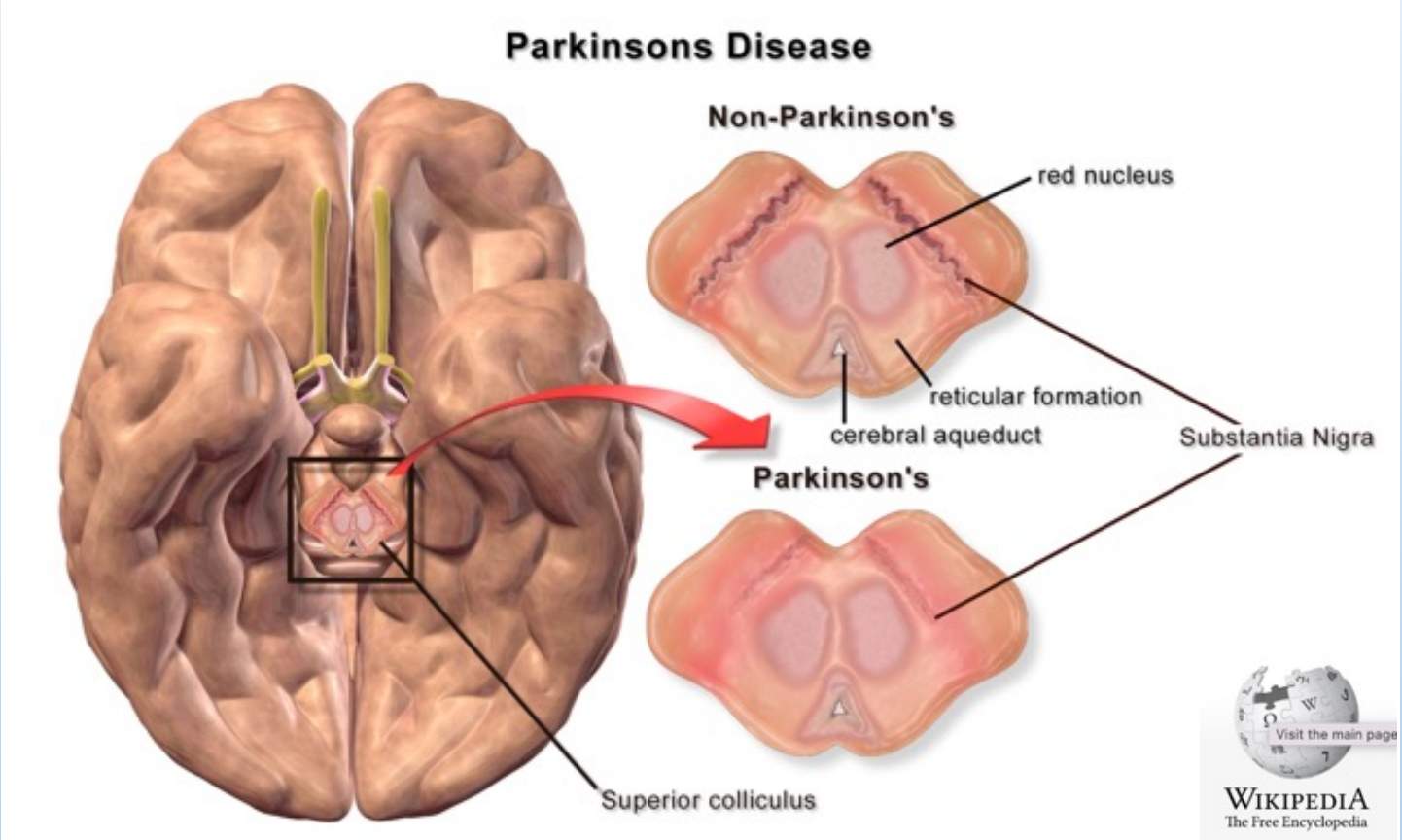
BACKGROUND

HALLMARK OF PD

- Loss of NM pigmented dopaminergic cells of SNpc

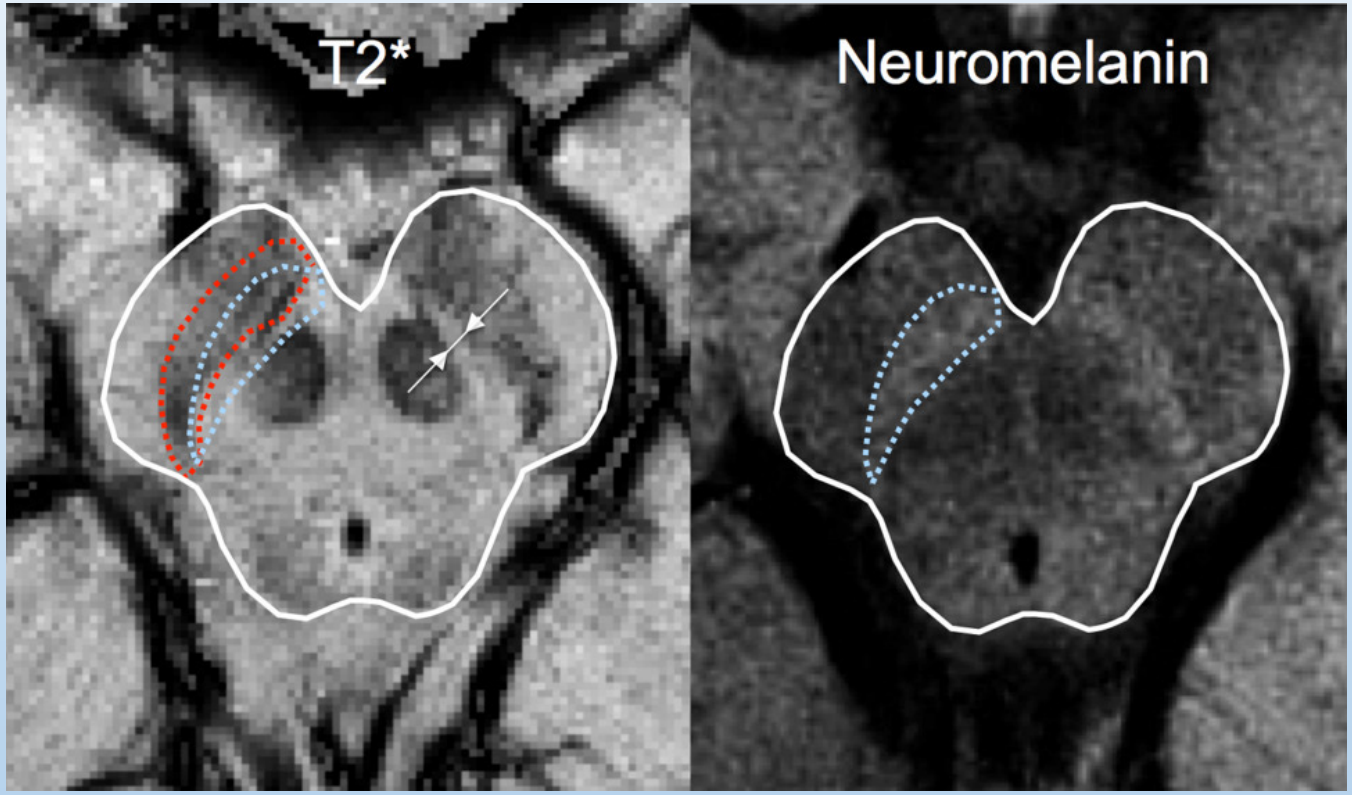
AND

- Loss of NM pigmented noradrenergic cells of locus coeruleus (LC)



BACKGROUND

- NM imaging have been exclusively studied at 3T
- There are several technical challenges and limitations to imaging NM at lower field strength
- These include: Poor SNR and higher Specific Absorption Rate (SAR)



Lehéricy S, et al. 2014

BACKGROUND

- To overcome these technical limitations we need longer acquisition time, and increased slice thickness

- Potentially resulting in volume averaging of small region of interest we intend to image, and variable test reliability

- Thereby preventing widespread implementation of NM imaging in clinical practice

BACKGROUND

- Ultra-high field MRI at 7T offers several benefits that addresses technical challenges of imaging NM at lower field strength

- These include: Higher SNR, tissue contrast, and spatial resolution in comparable or shorter scan time

BACKGROUND

- However, there are barriers to implementation of NM imaging at 7T
- Including higher SAR, & B0, B1+ inhomogeneity
- To date, the feasibility of NM imaging at 7T has not been reported

OBJECTIVES

- Assess the feasibility and accuracy of 7T NM imaging in patients with PD

Hypothesis:

- There is a significant decrease in SNpc volume in patients with PD compared to the controls

METHODS

- Retrospective case-control study
- Following IRB approval, a total of 21 patients with PD, 13 patients with Essential Tremor (ET) and 18 controls were enrolled
- Diagnosis of PD was determined by a movement disorder neurologist as meeting criteria for one of 4 PD subtypes and response to levodopa

Subtypes of PD

- ❖ Tremor dominant
- ❖ Postural instability / Gait Difficulty
- ❖ Akinetic rigid
- ❖ Mixed subtype

STUDY COHORT DEMOGRAPHICS

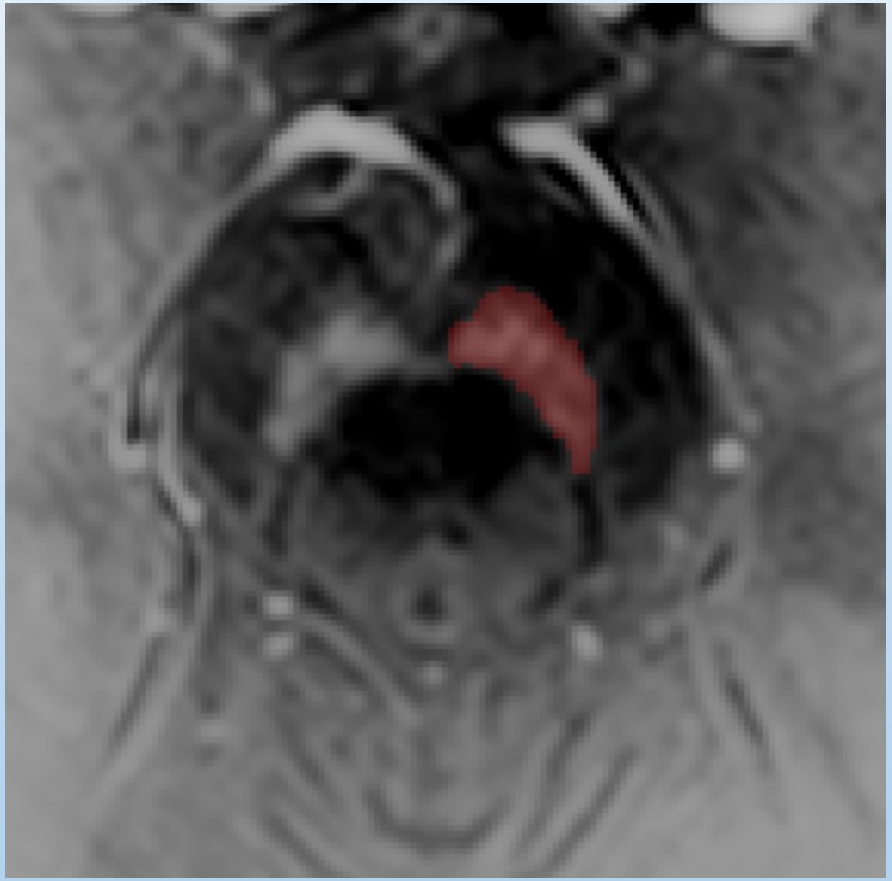
	Parkinson's Disease	Essential Tremor	Controls
Study Participants	21	13	18
Man	17 (80.95%)	8 (61.54%)	13 (72.22%)
Woman	4 (19.05%)	5 (38.46%)	5 (27.78%)
Age (Mean ± SD)	64.33 ± 10.86	61.08 ± 14.11	63.11 ± 13.34
Subtypes			
• Akinetic Rigid	7 (33.33%)		
• Tremor Dominant	12 (57.14%)		
• Postural Instability/ Gait Difficulty	2 (9.52%)		

MRI PROTOCOL

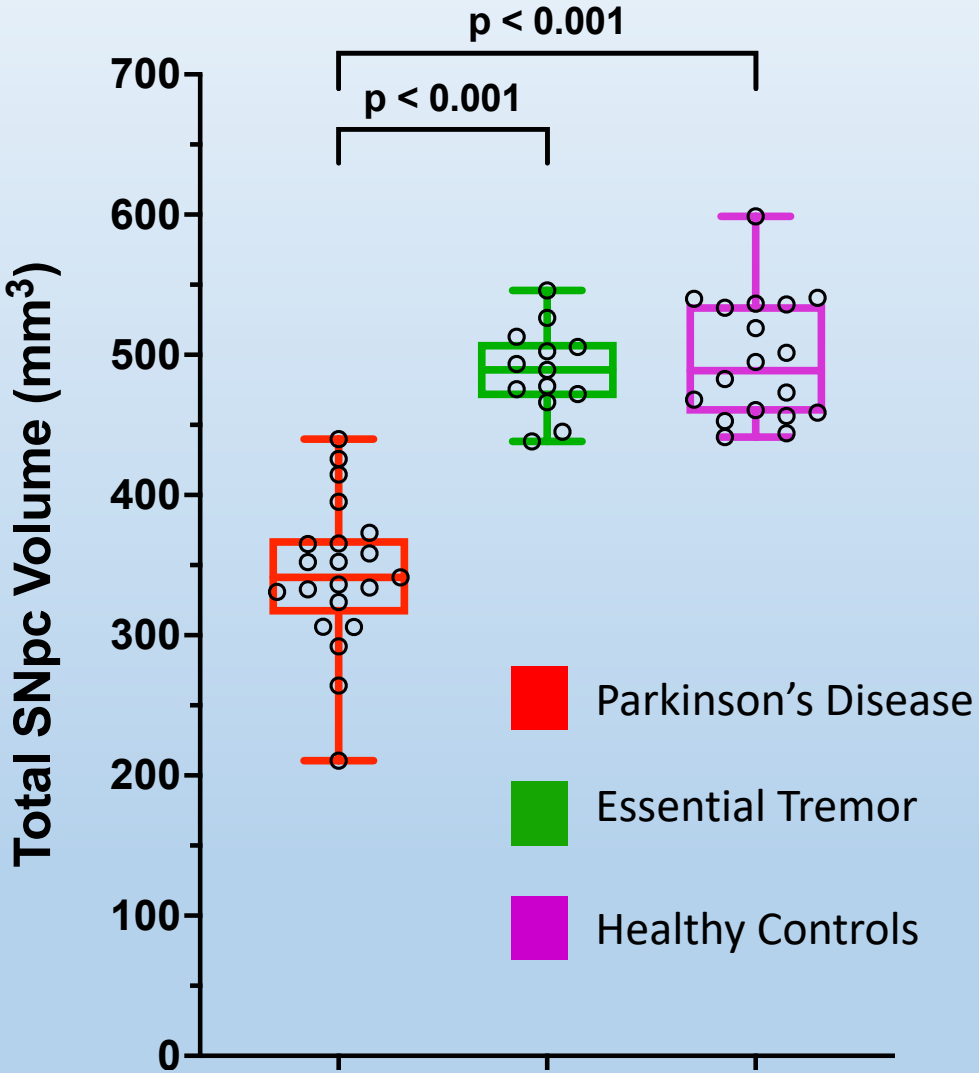
- Scanning was performed on 7T Siemens Terra scanner
- 3D multi-echo FLASH MRI with magnetization transfer pulse was used to image NM
- Technical parameters of the study protocol included: TR=52 ms, TE=2.18, 4.15, and 7.09 ms, slice thickness=1.5 mm, flip angle=16°, and interpolated voxel size=0.4 x 0.4 x 1.5 mm
- Acquisition time for the protocol was 10:19 minutes.

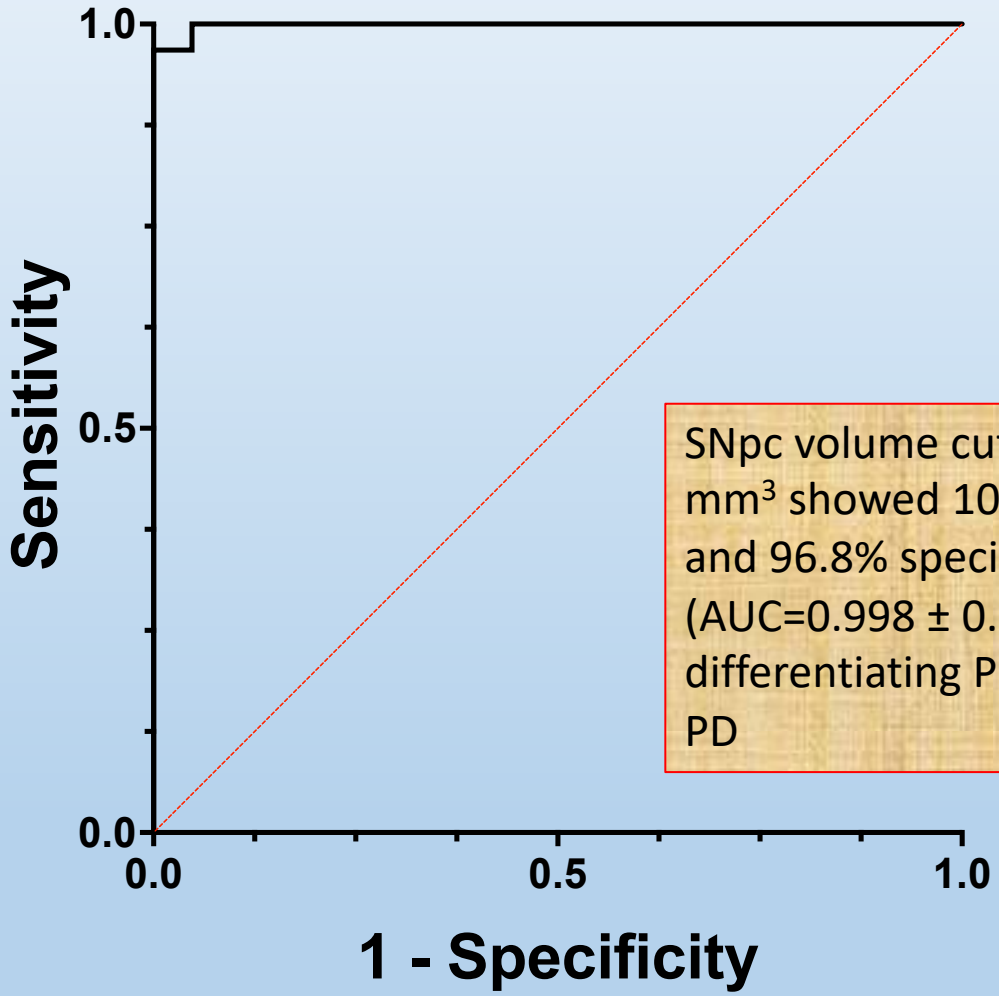
IMAGE ANALYSIS

- Following NM sensitive image acquisition, ROIs were manually segmented
    - ❖ SN pc
- SN pc was defined as region of hyperintensity on NM-sensitive images



SNpc Volume in mm^3





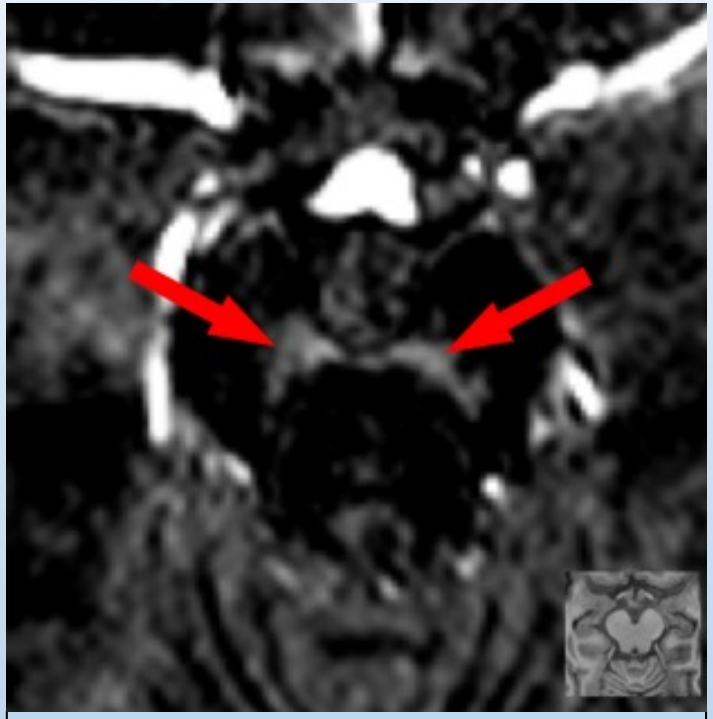
SNpc volume cutoff of < 440 mm^3 showed 100% sensitivity and 96.8% specificity (AUC=0.998 ± 0.005) for differentiating PD from non-PD

RESULTS

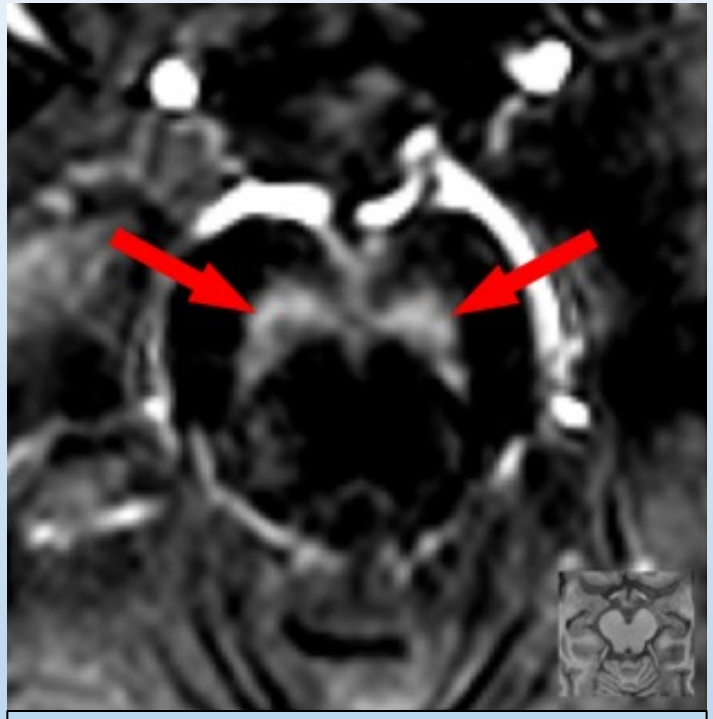
- SNpc volume was significantly lower in the PD versus non-PD
- SNpc volume cutoff of < 440 mm^3 showed 100% sensitivity and 96.8% specificity (AUC= 0.998 ± 0.005) for differentiating PD from non-PD
- SNpc volume was significantly lower in PD versus ET
- SNpc volume cutoff of < 432 mm^3 showed 100% sensitivity and 95.2% specificity (AUC= 0.996 ± 0.012) in differentiating PD from ET

RESULTS

Even on subjective assessment we can appreciate lower volume and signal intensity of SNpc in patient with PKD as compared to essential tremor patient



Right-Side Predominant PD



Essential Tremor

CONCLUSION

- 7T NM imaging is a promising biomarker in the diagnosis of PD, but currently with limited clinical adoption
- Higher SNR, contrast, and spatial resolution at 7T may be advantageous in increasing diagnostic performance
- Future studies are needed to further optimize NM imaging sequences at 7T, as well as show its performance across a wide range of parkinsonian syndromes and mimics

MAYO CLINIC

THANK YOU!