CAN MRI OF THE NIGROSOMES PROVIDE A BIOMARKER FOR PROGRESSION OF PARKINSON'S DISEASE?

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TARGET: People interested in biomarkers of Parkinson's disease.

INTRODUCTION: It has recently been shown that nigrosomes can be detected within the substantia nigra (SN) on 7T scans and that nigrosome-1 (N1) is lost in patients affected by Parkinson's disease (PD) [1,2,3]. It has subsequently been shown that nigrosome 1 can also be detected at 3T and is also absent in PD at 3T [4]. Despite the high sensitivity and specificity of nigrosome imaging to distinguish PD from controls, it is unclear whether alterations in the nigrosome MRI signal correspond to disease severity and progression. This study investigates the appearance of the nigrosomes on high resolution 7T scans on patients at various stages of Parkinson's disease, and compares the results to the current diagnostic gold standard of single photon emission tomography scan technique (FP-CIT SPECT, "DaTScan")

Aim: To determine whether MR features of the nigrosomes vary with disease severity.

METHODS: 13 patients with established Parkinson's disease (age 42-78y) and 3 controls (age 62, 66 and 69y) were scanned with ethics committee approval on a 7T Achieva Philips scanner, with a high resolution 2D FFE scan (TE=16ms, TR=412 ms, FA=40deg, NSL=16, 0.35x0.35x1.0mm voxels, no sense, Taq=9.5mins). 12 patients also underwent DaTScan. The UPDRS, disease duration, and symptom laterality were recorded. A neuroradiologist (SS) blinded to subject information scored the detectability of nigrosomes 1-5 on a 6 point *nigrosome visibility score* (5= normally bright and present; 0= darker than surrounding SN), and drew ROIs around the nigrosomes. The T2*w signal in the nigrosome ROIs was normalized by signal from a local white matter (WM) region. T2*w of the SN matrix was derived by averaging signal from a threshold-based segmentation of the SN with nigrosome ROIs removed, and was normalised to local WM.

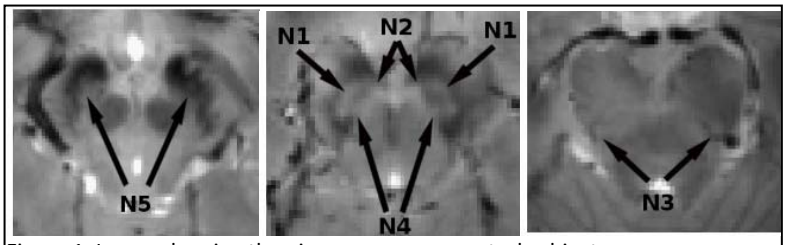

Figure 1: Image showing the nigrosomes on a control subject.

Table 1: Nigrosome visibility score

	Controls (N=3)	Patients (N=13)	p value (1 tailed t test)
N1	5,5,5	1.1 ± 1.2	$1\ 10^{-8}$
N2	5,5,4	2.9 ± 1.6	0.007
N3	4.5,5,3	1.9 ± 1.3	0.0002
N4	5,5,4	3.9 ± 1.3	(0.09)
N5	5,5,4	3.6 ± 1.7	(0.07)

RESULTS: Nigrosome visibility: In this group (dominated by patients) N1 was most reliably seen. N2, N3 and N5 were less reliably found than N1 or N4 and identifying N3 was most challenging as it was usually not surrounded by adjacent low SN signal. N1 was scored bilaterally as 5 in all 3 controls.

Laterality: For DaTScan: In 7/12 patients the loss of uptake in the basal ganglia correlated correctly to the clinically more affected side (by tremor or rigidity) or if symptoms were symmetrical. For MRI N1: 6/13 correlated correctly to more affected side. When adding the scores of all rated nigrosomes to assess which side was affected most severely 10 out of 13 correlated to the clinically more effected side or if symptoms were symmetrical.

Variation in visibility with UPDRS: Figure 2 shows that the Nigrosome 1 visibility score correlated against log(UPDRS) (assigning log(UPDRS) =0 to controls). Similar trends were seen if other nigrosomes were included.

Variation in T2*w signal from Nigrosomes with UPDRS: Figure 3 shows that this signal decreases with log (UPDRS) consistent with increased darkening of the nigrosomes.

Variation in T2*w signal of SN matrix (excluding nigrosomes): Figure 4 shows that there was a trend for T2*w signal of the SN excluding nigrosomes to decrease with log(UPDRS).

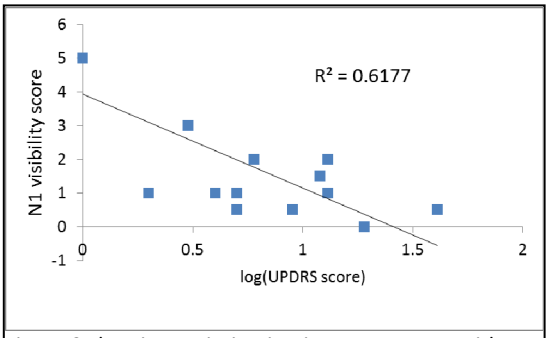

Figure 2 showing variation in nigrosome score with UPDRS

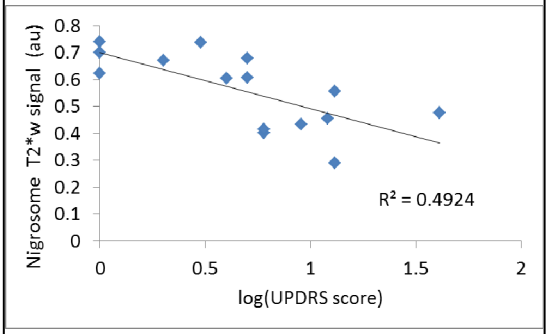

Figure 3 showing Variation in average T2*w signal in all nigrosomes with UPDRS

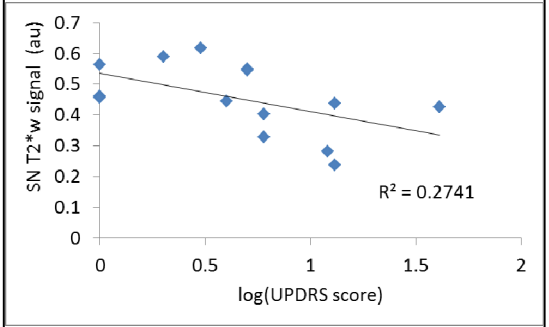

Figure 4 showing some variation in T2* of SN excluding nigrosomes with UPDRS

DISCUSSION: Nigrosomes 1-5 can be detected at 7T and are all less visible in PD patients than in controls. The laterality of loss of the nigrosomes correlates better with disease laterality than DaTscan results for this group. The variation in nigrosome visibility and nigrosome T2*w signal with UPDRS suggests that these measures may provide a quantitative biomarker of PD progression. Many previous MR studies have suggested that there is a decrease in R2* in the Substantia Nigra in Parkinson's disease, and these results suggest that this affect is not simply due to iron accumulation in the nigrosomes.

CONCLUSION: High resolution T2* weighted imaging has the potential to provide a quantitative biomarker of progression of Parkinson's pathology.

REFERENCES: [1] Kwon et al, Ann Neurol 71:267-277, 2012. [2] Blazejewska et al, Neurology 81:534-540, 2013. [3] Lehericy et al Movement Disorders, 1574, 29(13), 2014. [4] Schwarz et al, PLoS One 2014;9:e93814. **Acknowledgements**: This work was funded by the Medical Research Council.