A 3T MRI study of brain iron deposition in Parkinson's Disease and MSA Patients using PRIME

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INTRODUCTION: Parkinson's Disease (PD) is a movement disorder in which increased iron is thought to accumulate in structures within the basal ganglia (1). This study was designed to measure transverse relaxation times in the brains of one hundred PD patients who had different disease durations and a sub-group with Parkinson's plus disease multiple system atrophy (MSA) using a 3T scanner.

METHODS: Patients were referred from a movement disorders clinic and gave written, informed consent prior to scanning. 100 patients were recruited and from these 70 scans using the PRIME sequence have been obtained. Patients' disease durations ranged from 1-33 years and their age at scan ranged from 41- 87 years. Movement symptom severity for each side of the body was assessed using the United Parkinson's Disease rating scale (UPDRS) following overnight withdrawal from medication. The MSA group comprised seven patients with an age range of 46-73 years and disease duration range of 3-12 years. A PRIME sequence (1) with 5 spin echoes and 8 interleaved gradient echoes per spin echo was implemented on a 3T Intera system (Philips, BEST, NL) for simultaneous measurement of R2 and R2* (and hence R2′). The imaging parameters were TR = 3000ms, Spin Echo TE = 30, 60, 90, 120, 150 ms, Gradient Echo TE = n x 3.3 ms (n=1-8) following each Spin Echo. FOV = 230 mm, SLT = 2.5mm, NEX = 1, Matrix = 128x256. Both raw data and images in Dicom format were stored for further processing using a least squares fitting routine written in-house using MATLAB. Region of interest analysis of known sites of neuropathology in the basal ganglia were conducted and yielded R2′ values that were analysed statistically using Pearson correlation, analysis of variance (ANOVA) and non-parametric Spearman correlation and Mann-Whitney U tests for the comparisons with the smaller MSA group.

RESULTS: Patients tolerated the scan session well with minimal artefacts due to involuntary movement. Figure 1 shows all 45 echoes from a single slice using the PRIME sequence. Figure 2 shows a typical R2′ map calculated from an R2 map from the five spin echoes and an R2* map from the first spin echo and subsequent gradient echoes in a coronal section of a PD patient. Increased R2′ relaxation rate is seen in the basal ganglia compared to white and grey matter as expected.

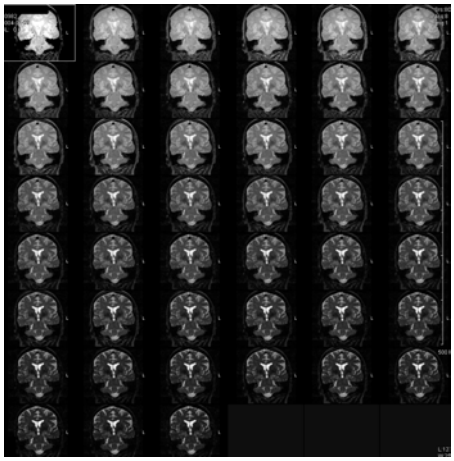

Figure 1

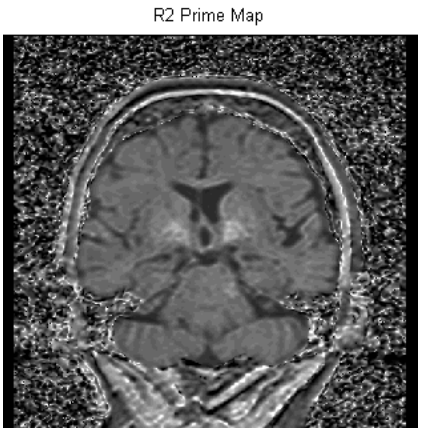

Figure 2

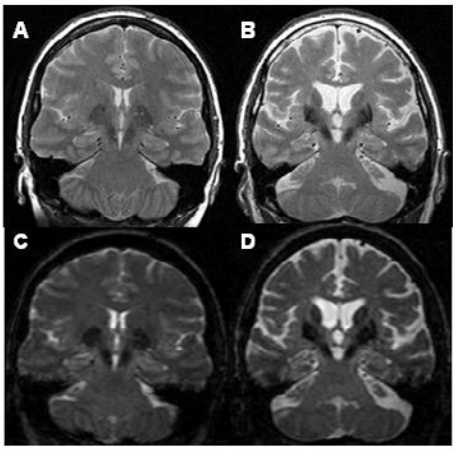

Figure 3

Examination of UPDRS symptom severity and substantia nigra R2′ revealed a significant positive correlation (r = 0.276, p = 0.037). No significant relationship was seen between substantia nigra R2′ and disease duration. Comparison with neurological rating of the putamen revealed an anterior to posterior gradient of hypo intense signal, and this was reflected in a significantly higher R2′ mean for both right (p=0.033) and left (0.021) posterior compared to medial putamen R2′ measures. Measures from the PD putamen did not reveal any significant correlations with UPDRS scores, but the posterior putamen R2′ measures showed a significant positive correlation with disease duration (r = 0.303, p = 0.020). Comparison of the PD and MSA groups revealed significantly higher medial putamen R2′ in the MSA group relative to those with PD (U = 49.0, P = 0.001). No significant differences were seen between the two groups for R2′ measures in the substantia nigra. Figure 3 highlights the medial putamen iron deposition differences between the patient groups for standard T2-weighted images (PD: A, MSA: B) and those generated from the PRIME sequence for ROI placement within MATLAB (PD: C, MSA: D). These images have been windowed for optimum contrast. The MSA patients revealed a trend towards a positive correlation between left posterior putamen iron R2′ and right UPDRS (r=0.741, p=0.057).

DISCUSSION AND CONCLUSION: R2′ is though to be the optimum relaxation parameter for investigating iron deposition in the brain (2). The finding of varying iron levels across the body of the putamen in PD patients may account for contradictory findings in the published literature (1). Measures of R2′ in the posterior putamen show a positive correlation with disease duration in PD. The results also link iron deposition in the substantia nigra to the severity of the movement disorder experienced by PD patients and a possible relationship between iron deposition in the posterior putamen and movement severity in MSA. These findings suggest that iron deposition relates to disease pathology and progression in PD and MSA, with the putamen and substantia nigra are differentially affected across the two patent groups. Such information may assist in giving the diagnosis of MSA, rather than PD, which can be difficult in the early stages of the disease.

REFERENCES: 1.Graham et al., Brain, 2000;123:2423. 2. Haake et al., Magn Reson Imaging, 2005;23:1.

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