Investigation of brain iron content in patients with Parkinson's disease using phase and R_2^* obtained with multi echo susceptibility weighted imaging

C. Denk[1], S. Palmer[2], M. J. McKeown[3], and A. Rauscher[1]
[1]UBC MRI Research Centre, University of British Columbia, Vancouver, BC, Canada, [2]Brain Research Centre, Vancouver, BC, Canada, [3]Pacific Parkinson's Research Centre, Vancouver, BC, Canada

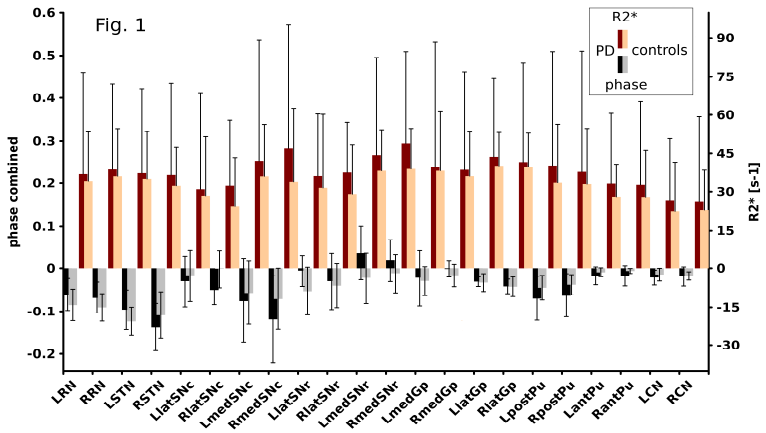
Introduction: The main pathologic feature of Parkinson's disease (PD) is the loss of dopaminergic neurons in the substantia nigra pars compacta (SNc) [1]. There is increasing evidence that iron-mediated oxidative stress via the Fenton reaction is responsible for this loss of neurons [2]. Iron's paramagnetism leads to changes in the relaxation rates R1, R2 and R2* [3] and the phase of susceptibility weighted images (SWI) [3,4]. While R2* has been previously used to assess iron deposition in the SNc in PD [5], the advantage of phase is that it is independent of relaxation mechanisms and has a higher signal to noise ratio (SNR). The aim of this study was therefore to use multi echo SWI for the investigation of both phase and R2* relaxation in deep brain structures of patients with PD.

Material & Methods: Multi echo SWI data of 16 patients with PD (age range 46 to 76 years; United Parkinson Disease Rating Scale (UPDRS) score ranging from 7 to 34 (mean = 21)) and, so far, 11 age-matched controls were acquired on a Philips Achieva 3T system equipped with an 8 channel head coil using a 3D gradient echo sequence. Scan parameters were: TE = 13-41 ms; ΔTE = 7 ms; TR = 45 ms; flip angle = 17°; readout bandwidth = 157Hz/pixel; acquisition voxel size = 0.5 x 0.75 x 1.5 mm^3; reconstruction matrix = 512 x 512 x 80. The phase images were corrected with an adaptive homodyne filter with a width of 0.2 of k-space data size at TE =13 and increments of 0.05 for each later echo. Maps of R2* relaxation rates were computed from the five magnitude images using a Levenberg-Marquardt least squares method for non-linear equations using a correction for signal decay due background field inhomogeneities [6, 7] estimated from a field map computed from the first two echoes. Regions of interest (ROI) were drawn on both hemispheres (labelled as L and R) on the medial (med) and lateral (lat) part of the pars compacta (c) and reticulata (r) of the substantia nigra, the subthalamic nucleus (STN), the red nucleus (RN), lat and med of the globus pallidus (Gp), the posterior (pos) and anterior (ant) part of the putamen (Pu), and the caudate nucleus (CN). A least-square linear regression and the Pearson correlation coefficient were calculated for all ROI's in R2* and the average phase of the five echoes.

Pearson Correlation

	*R2**	*phase*
Substantia Nigra pars compacta		
LmedSNc	0.2	−0.4
RmedSNc	0.2	−0.5
LlatSNc	0.1	−0.3
RlatSNc	0.15	−0.5
Red Nucleus		
LRN	0.15	−0.5
RRN	0.4	−0.5

Results: Fig 1. shows the phase and R2* averaged over 11 patients and 11 controls (bright) in all ROI's. The largest phase differences were found in the SNc (Fig. 1), the medial SNr and in the putamen. The strongest correlation with the UPDRS score was found in the medial SN pars compacta (-0.5 in the RmedSNc, as shown in Fig.2; -0.4 in the LmedSNc) and in the red nuclei. R2* showed a much smaller correlation in these regions (see table).



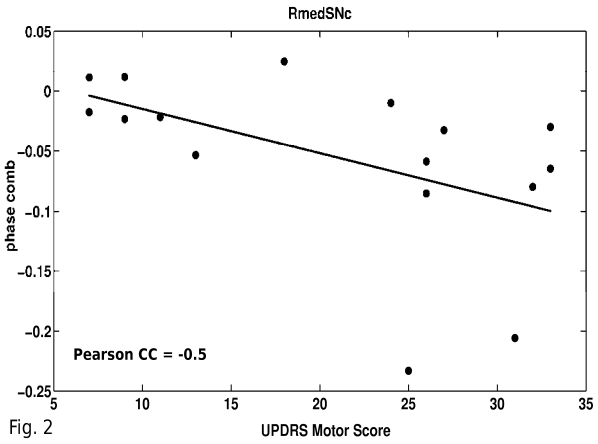


Fig. 2

Discussion: Our findings agree with histopathological studies, that demonstrate increased iron levels in the SNc of patients with PD [8]. The correlation between R2* and UPDRS is also similar to values reported by Martin et al. (Pearson correlation of 0.27 in Snc) [5]. However, in all relevant regions the correlation was much higher with the phase than with R2*. An explanation for this finding, apart from the phase's higher SNR compared to magnitude, may be that an increase in iron content can lead to both local field inhomogeneities and local offsets of the magnetic field. The former lead to accelerated R2* relaxation, whereas offsets lead to a constant change in phase, which does not change R2*. A further advantage of SWI is that its high spatial resolution allows the subdivision of SNr and SNc into medial and lateral parts.

References: **[1]** Lees et al. Lancet. 2009 13;373(9680):2055-66 **[2]** Zecca et al. Nat Rev Neurosci. 2004 Nov;5(11):863-73. **[3]** Haacke et al. Magn Reson Imaging. 200523(1):1-25 **[4]** Reichenbach et al. NMR Biomed 2001 14(7-8):453-67 **[5]** Martin et al. Neurology. 2008 Apr 15;70(16 Pt 2):1411-7. **[6]** Fernández-Seara et al. Magn Reson Med 2000;44:358-366. **[7]** Dahnke et al. Magn Reson Med 2005;53:1202-1206. **[8]** Götz et al. Ann N Y Acad Sci. 2004 1012:193-208.