Comparison with histology of quantitative MR properties of the brain stem tissue in 3T and 7T

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Introduction The substantia nigra (SN) is important in motor control and is known to be affected in Parkinson's disease. Quantifying MR properties of this region of the brain stem and relating them to histology stains will assist in understanding tissue changes in disease and in image optimization. **Aim:** to measure the T2* and magnetization transfer ratio (MTR) of regions of interest (ROIs) in the brain stem at 3T and 7T and to correlate the resulting values with histopathology stains of post mortem (PM) brains.

Table Summary of the scanning parameters for patients at both field strengths.

	name	resolution	slices	TR/TE/ΔTE	FA additional	time
3T	T2*w	0.43x0.43mm	2D 8 x 1.5mm	300/50ms	42°NSA=5	9:57
	T2*w ME	0.7x0.7mm	2D 35 x 1.5mm	2122/7/10ms	80°5 echoes	5:16
	MT-FSE	0.6x0.6mm	2D 8 x 2.5mm	699/9ms	90°NSA=4, MTC=no/off	2x9.23
	PRESTO	1.0x1.0mm	3D 200 x 1.0mm	15/21ms	10°	4:34
7T	T2*w	0.35x0.35mm	2D 20 x 1.0mm	525/16ms	40°	12:00
	T2*w ME	1.0x1.0mm	3D 129 x 1.0mm	24/5/5ms	11°4 echoes	7:31
	MT-TFE	0.5x0.5mm	3D 40 x 1.0mm	12/6.2ms	8° MTC=no/off	11:18
	PRESTO	1.0x1.0mm	3D 200 x 1.0mm	13/18ms	10°	3:49

Methods *In vivo:* Eight healthy subjects (33±11y.o.) were scanned at 3T (one dataset excluded due to insufficient coverage) and two (29, 49y.o.) at 7T with the following scans: high resolution T2* weighted (hrT2*w), PRESTO, multi-echo gradient echo sequence for T2* quantification (meT2*w), MT with one off-resonance pulse using FSE at 3T and a multi-pulse saturation train with an FFE readout at 7T (details in Table 1). R2* maps were calculated from the meT2*w images and MTR maps were created from the MT images. Circular regions of interest (ROIs) were drawn on slices of hrT2*w images in which nigrosome 1 was clearly visible (2x1.5mm slices at 3T image and 3x1mm slices at 7T image) for the following structures: nigrosome 1 (N), substantia nigra (SN), ventral tegmental area (VTA), cerebral peduncle (CP), white matter (WM), grey matter (GM) of the medial-temporal lobe and periaqueductal tissue (PAT); ROIs for the red nucleus (RN) were placed on higher slices in the 7T data (the 3T scan did not have sufficient coverage). The diameter of the ROIs was 8 voxels for SN, RN, CP, WM, GM and PAT, and 4 voxels for N and VTA. ROIs masks, R2* and MTR maps were registered to PRESTO images (which had wide coverage) to allow the ROIs to be transferred to the maps. The mean R2* and MTR values of all the structures were calculated at both field strengths, averaged across all subjects and slices (Table 2). *Post Mortem:* Two sets of adjacent slices of PM midbrain from a subject with no known neurological conditions were stained with Perls' (for iron) and Solochrome cyanine (SC, for myelin). Circular ROIs were drawn on the digitized stains for: N, SN, VTA, CP and PAT, of equivalent size to those used on the MRI data. To compare MRI and histology measures related to iron and myelin, the 7T R2* values were correlated with Perls' stain intensity for corresponding ROIs averaged over both data sets and the MTR values were correlated against SC (Fig 3).

Results Example images and ROIs are given in Fig 1 (a,b,c)**.** Table 2 and Fig 2 present mean R2* and MTR values for each structure at both field strengths. 7T R2* values were larger than 3T values particularly in high iron areas. 3T MTR values were low compared to 7T values probably because of the low MT sensitivity of the 3T sequence used. 7T MTR values were highest in CP, PAT and RN and lowest in GM. R2* values were highest for SN and RN and lowest in GM; N had an intermediate value. Figure 3 shows that R2* values were correlated with Perls' stain and MTR values correlated with the SC stain.

Discussion R2* and MTR have been measured in the brain stem. The nigrosome appears highly hyperintense on T2* weighted images at 3T and 7T, but these results suggest that that is only because of the contrast with the neighbouring SN. The good correlations found between R2* and Perls' stain, confirm that R2* is dominated by iron. The correlation between MTR and SC also indicates that the MTR stains are sensitive to myelin in this region. The MT in vivo correlation was relatively weak, but we have also correlated PM MTR against SC stains for the same PM samples and found good correlations (r=0.93 for R2*, r=0.97 for MTR) indicating that the weaker in vivo correlation is partly due to PM changes probably due to the fixing process. These results will be useful in setting up new sequences and in interpreting pathological changes. **Conclusion:** R2* and MTR values have been characterized for key regions in the brain stem, and PM correlations suggest that they are good indicators of iron and myelin content respectively in the brain stem.

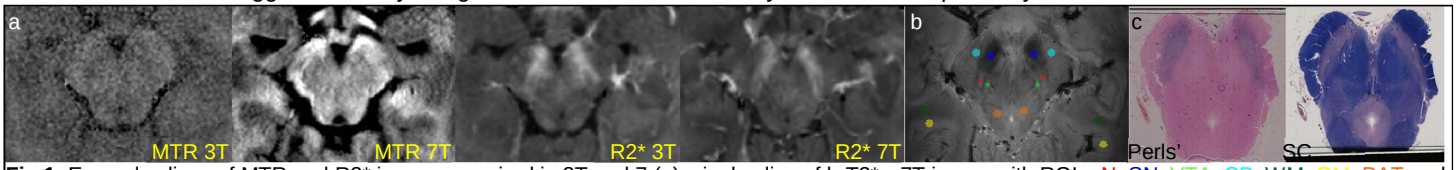

Fig 1. Example slices of MTR and R2* images acquired in 3T and 7 (a); single slice of hrT2*w 7T image with ROIs: N, SN, VTA, CP, WM, GM, PAT and RN (not in the picture) (b); two slices of the PM midbrain: MTR map, R2* map, Perls' (iron), SC (myelin) (c)

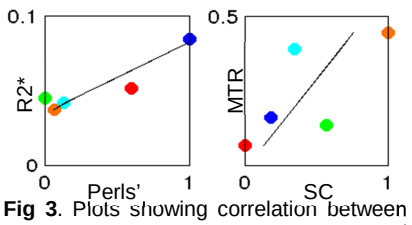

Fig 3. Plots showing correlation between 7T R2* and MTR values with Perl's and CS stains for corresponding ROIs: N, SN, VTA, CP, PAT; r=0.92 (p=0.03), r=0.72 (p=0.17).

	R2* (s)				MTR			
	3T		7T		3T		7T	
N	36.9	±3.6	51.0	±0.7	0.099	±0.10	0.330	±0.040
SN	53.4	±5.1	83.9	±7.4	0.095	±0.12	0.360	±0.020
CP	25.3	±1.3	37.4	±10.0	0.104	±0.12	0.480	±0.010
VTA	29.9	±1.4	44.6	±0.9	0.086	±0.10	0.354	±0.005
PAT	25.6	±3.3	41.3	±2.5	0.096	±0.12	0.455	±0.007
GM	22.6	±1.6	26.2	±0.2	0.081	±0.09	0.230	±0.020
WM	27.8	±2.2	34.0	±4.9	0.095	±0.10	0.340	±0.090
RN			77.5	±4.0			0.460	±0.005

Table 2. Mean values of R2* and MTR calculated for both field strengths across all the subjects using ROIs: N, SN, CP, VTA, PAT, GM, WM and RN.

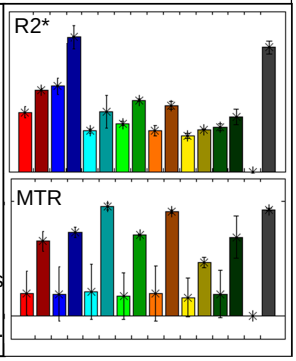

Fig 2. (right) Bar charts presenting values from the table.