Quantitative 3.0 Tesla Perfusion MRI of Deep Gray Matter in Multiple Sclerosis Patients: Correlation with Disease Status

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Introduction

Mutiple sclerosis (MS) is an idiopathic inflammatory disorder of the central nervous system that predominantly affects white matter. However, increasing evidence for cortical and deep gray matter (GM) involvement based on neuroradiologic and histopathologic studies [1-4] raises the possibility that radiologic GM changes can be exploited to follow disease progression. In fact, deep GM hypointensities on T2-weighted images have been proposed as predictors of clinical course [5].

Although the exact pathogenesis of MS remains unknown, vascular inflammation as the critical event has been advocated [6-8]. If the observed changes in the deep GM indeed have a vascular etiology, then one might expect that altered perfusion characteristics of deep GM structures [9] would correlate with clinical progression. Significant association between such perfusion parameters and measures of disease status would provide clinicians with a quantitative means to monitor disease progression. Therefore, the goals of our study were: 1) to quantify hemodynamic variables derived from dynamic susceptibility contrast-enhanced perfusion MR imaging of deep GM structures in patients with MS using a 3.0 Tesla scanner, and 2) to determine whether such variables correlate with clinical indicators of disease progression.

Methods

Thirty-two patients with clinically definite MS [28 relapsing-remitting MS, 1 primary progressive MS, 3 secondary progressive MS, 12 men, 20 women, mean age 39.6±7.3 yrs (range 23.6-54.7 yrs), mean extended disability status score (EDSS) 2.2±1.5 (range 0.0-6.0), mean disease duration to scan time 7.8±5.4 yrs (range 0.4-18.4 yrs)] underwent MR examination after providing informed consent. Images were acquired on a 3T GE Signa Echospeed system with EXCITE platform, with an 8-channel phased-array coil. After conventional MR imaging which included T2-weighted and T1 SPGR images (Figure 1), a series of gradient-echo, echo planar images (EPI) using sensitivity encoding (SENSE) [10] with a reduction factor of 2 were obtained. The dynamic susceptibility-weighted perfusion imaging consisted of the injection of a bolus of 0.1 mmol/kg body weight of gadopentetate dimeglumine (Gd-DTPA) contrast agent at a rate of 5 mL/s. A series of 60-80 $T2^*$-weighted gradient-echo, echo-planar images were acquired during the first pass of the contrast agent bolus injection, with a TR/TE 1500/54 ms, 35^o flip angle, FOV of 26×26 cm^2, 128×128 reconstructed image matrix, and 3-6 mm slice thickness. Regions-of-interest (ROIs) were manually drawn along the margins of deep GM structures (thalamus, head of caudate, lentiform nucleus) on each axial SPGR image showing these structures. As these structures are more centrally located, the distortion was minimized. The T2* signal time curve, S(t), was converted to the change in relaxation rate for all voxels using the relationship $\Delta R2^* \sim -\ln(S(t)/S_0)$, where S_0 is the average pre-contrast signal intensity baseline. Peak height (PH) and percent recovery (REC) (Figure 2) of the post bolus signal from the maximum $\Delta R2^*$ curve were calculated for each voxel in each ROI. An automated routine to select/segment normal appearing brain voxels based on histogram analysis of the image intensities from the pre-contrast echo planar images was utilized to normalize peak height values. Maximum and mean peak height values, as well as minimum and mean recovery values, were calculated for each GM structure of interest for each patient. Statistical analyses were performed using the t-test (for lesion number) and Spearman's rank correlation coefficient (for disease duration and Expanded Disability Status Scale (EDSS)).

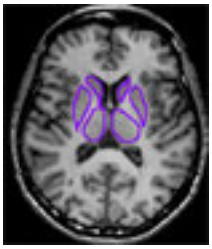

Figure 1. Deep GM ROIs on a SPGR image

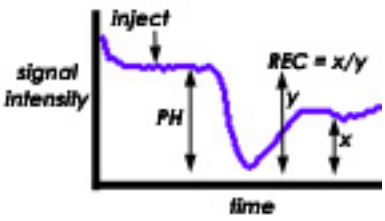

Figure 2. Peak height (PH) and percent recovery (REC)

Results

Four perfusion parameters were determined for each ROI based on images collected using SENSE: maximum peak height (Max PH), average peak height (Ave PH), minimum % recovery (Min REC), and average %recovery (Ave REC). The mean and SD for these parameters in the thalamus (T), head of caudate (C), and lentiform (L) nuclei in these clinically definite MS patients were: Max PH 3.1±0.8(T), 3.1±0.9 (C), 3.2±1.5(L); Ave PH 1.0±0.1(T), 1.2±0.2 (C), 1.3±0.3(L); Min REC 57.8±15.7(T), 59.9±17.6 (C), 53.0±17.5 (L); Ave REC 74.2±12.1(T), 73.3±12.6(C), 73.8±13.2(L). These four perfusion parameters were assessed for correlation with indicators of clinical status including EDSS, disease duration, and lesion number. All P values for Spearman rank correlations between deep GM perfusion parameters and EDSS or disease duration were greater than 0.05. There was no correlation between perfusion characteristics of the deep GM and lesion number (Table).

# of Lesions	Thalamus				Caudate				Lentiform			
	Max PH	Ave PH	Min REC	Ave REC	Max PH	Ave PH	Min REC	Ave REC	Max PH	Ave PH	Min REC	Ave REC
≤10 (n=13)	3.4±0.9	1.0±0.1	56.6±19.9	71.9±159	2.9±0.6	1.2±0.2	58.2±22.1	70.5±16.6	3.6±2.0	1.3±0.3	48.3±20.5	70.4±17.7
>10 (n=19)	2.9±0.6	1.0±0.2	58.6±12.7	75.7±8.8	3.2±1.0	1.2±0.3	61.1±14.4	75.2±8.9	3.0±0.8	1.2±0.3	56.3±14.8	76.1±8.8
P value	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05

Max PH=maximum peak height; Ave PH=average peak height; Min REC=minimum % recovery; Ave REC=average %recovery

Discussion

Peak height (PH) and percent recovery (REC) of the T2* relaxivity curve have previously been shown to be valuable in characterizing the vasculature of brain tumors. In this study, we assess the utility of these perfusion parameters in MS. The results of our study suggest that quantitative analyses of the T2* relaxivity curve do not yet provide a means to reliably monitor the clinical progression of MS. The lack of correlation between the measured perfusion parameters and EDSS could, in part, be due to the bias of EDSS towards ambulation and its limited utility in assessing cognitive deficits. Future studies will be directed toward comparing these perfusion parameters in MS patients versus healthy controls as well as correlating these and other imaging parameters with various indicators of clinical status.

References

[1] Peterson JM et al. *Ann Neurol* 50:389-400 (2001)
[2] Cifelli A et al. *Ann Neurol* 52:650-653 (2003)
[3] Inglese M, et al. *Neurol* 63:170-172 (2004)
[4] Audoin B et al. *JMRI* 20:765-771 (2004)
[5] Bakshi R, et al. *Arch Neurol* 59:62-68 (2002)
[6] Putnam TJ..*Arch Neurol Neuropsychol* 32:1298-1321 (1935)
[7] Wakefield A et al. *J Clin Pathol* 47:129-133 (1994)
[8] Lassmann H. *J Neurol Sci* 206:187-191 (2003)
[9] Ge Y et al. *ISMRM* Abstract 1356 (2004)
[10] Pruessmann KP, et al. *MRM* 42:952-962 (1999)

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