Texture Response of Deep Gray Matter in Patients with Multiple Sclerosis Treated with Minocycline

Y. Zhang[1], L. M. Metz[1], H. Zhu[2], V. W. Yong[1], J. R. Mitchell[1]
[1]University of Calgary, Calgary, Alberta, Canada, [2]York University, Toronto, Ontario, Canada

Introduction

Diffuse deep gray matter (GM) pathology has been increasingly recognized in the pathogenesis of multiple sclerosis (MS).[1] Deep GM dysfunction may cause physical disability and cognitive deficits in patients with MS. However, deep GM abnormalities are difficult to detect on conventional MRI because of their small size and their low contrast with surrounding tissue.[1] MS treatment has advanced in recent years, but the therapeutic response of deep GM has not yet been addressed. We believe that as tissue becomes abnormal, its MRI texture will change. We are using the recently developed polar Stockwell Transform (PST) to study image texture.[2] The PST is a new local multiscale Fourier analysis that provides rotationally invariant Fourier spectral information around each pixel.[3] Therefore, it allows detection of subtle intensity changes in an image. Previous PST texture analysis of T2- weighted (T2w) MRI from MS patients showed that low frequency energies (coarse texture components) decreased in an area when it evolving from active to inactive lesion, then to normal appearing white matter.[4] In this study, we applied the PST on T2w MRI to analyze texture changes over time in the deep GM of MS patients treated with minocycline.

Subjects and Methods

Ten relapsing remitting MS patients (age 18 ~ 50 years, expanded disability status scale 1.5 to 5.5) were enrolled in a cross over trial of minocycline.[5] Eight completed 24 months study. Texture on 3T MRI was analyzed pretreatment (at baseline), at months 6 and then annually during treatment. T2w MRI was acquired using a fast spin-echo sequence with the following parameters: TR/TE = 2716/80 ms, FOV = 24 cm^2, matrix size = 512 x512, slice thickness = 3 mm, no gap. All MR images were corrected for non-uniformity utilizing N3,[6] then co-registered using 3D FLIRT[7] to align the sequential MRI for each patient. We identified 4 deep GM structures: thalamus, globus pallidus, putamen, and the head of caudate nucleus. Regions of interest (ROIs) were manually drawn along the margins of these structures on slices showing the greatest cross section on baseline MRI (Figure). The ROIs were then superimposed on the co-registered MRI at months 6, 12, and 24. The PST spectrum of each ROI (central 64 x 64 pixels) was computed to generate a local 2D Fourier spectrum for each pixel. Each local 2D spectrum was then reduced to a local 1D spectrum by integrating it along rings of constant width (0.33 cm^{-1}) in the Fourier domain. The local 1D spectra from the central 5x5 pixels were averaged for analysis. The low frequency energy (LFE) in each ROI was calculated by summing the area under the local frequency distribution below 3.3 cm^{-1}. Statistical analysis was performed using a one-way ANOVA for texture changes between time points, and a Student's *t*-test for texture differences between patients with active scans (active patients) and that without (inactive patients). A confidence level $\alpha = 0.05$ was deemed significant.

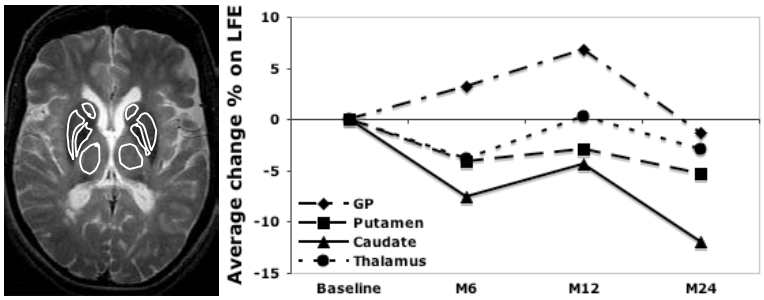

Fig. 1. Deep GM ROIs on T2w MRI (left). Plot shows mean texture (LFE) % change in each structure over time. The standard deviation ranged from 5% (globus pallidus, GP) to 6% (thalamus).

Results

Active scans were identified in 5/10 patients pretreatment.[5] No visible T2 lesions were detected in the deep GM of any patient. Each deep GM structure had similar local spectral distributions. There was variable magnitude change on LFE during treatment ($p > 0.05$). But at months 24, the LFE decreased in each deep GM structure compared to baseline (Figure). Furthermore, the LFE change in the head of caudate nucleus was the highest ($p = 0.01$) at each time point during treatment. Finally, deep GM structures showed larger LFE change in active patients than in inactive ones. Such differences displayed a trend to be significant at months 6 and 24 (Table).

Discussion and conclusions

The LFE decreased over 24 months of treatment, indicating a milder change tendency on deep GM abnormality compared to baseline. The larger texture change in active patients may be due to the rapid effect of minocycline attacking acute inflammation. Our small cohort limits broad conclusions. However, the texture improvement in the caudate nucleus after the commencement of treatment is important because this structure is known to suffer atrophy during MS progression.[8] The current, preliminary, study suggests that the PST-based texture analysis may be a new quantitative tool for monitoring deep GM pathology in MS. Future studies seek to compare deep GM texture in MS patients with healthy controls, and correlate texture features with the clinical indicators of disease status.

Table: Mean (standard deviation) LFE change % at each time point in active and inactive patients

	Months 6	Months 12	Months 24
Active pts	15.2 (5.4)	1.8 (7.2)	10.6 (5.6)
Inactive pts	4.3 (14.2)	0.26 (6.5)	3.6 (7.5)
P value	0.06	0.67	0.08

Active (inactive) pts = patients with (without) active scans.

References

[1] Inglese M, et al. *Neurology* 2004; 63: 170-172. [2] Zhu H, et al. #1200, *ISMRM* 2003. [3] Zhou Y. PhD Thesis, *Univ of Western Ontario* 2002. [4] Zhang Y, et al. # 1500, *ISMRM* 2004. [5] Metz LM, et al. *Ann Neurol* 2004; 55: 756. [6] Sled JG, et al. *IEEE TMI* 1998; 17:87-97. [7] Jenkinson M, et al. *NeuroImage* 2002; 17: 825-841. [8] Prinster A, et al. *Neuroimage* 2005; Sep 30. Epub.