Diffusion Tensor Metrics Changes in the White Matter of Systemic Lupus Erythematosus Patients

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BACKGROUND AND PURPOSE: Systemic Lupus Erythematosus (SLE) is a multi-system autoimmune disorder that also affects the central nervous system(CNS). The involvement of the nervous system is characterized by a broad spectrum of clinical presentations and often occurs in the subcortical white matter. Early detection of subcortical white matter damage can aid in the detection of CNS involvement related to SLE disease processes. Diffusion Magnetic Resonance Imaging is the imaging tool of choice to detect subcortical white matter damage. The purpose of this study is to investigate whether Mean Diffusivity (MD), Fractional Anisotropy (FA), and eigenvalues in the white matter of the brain of SLE patients differ from those of healthy controls.

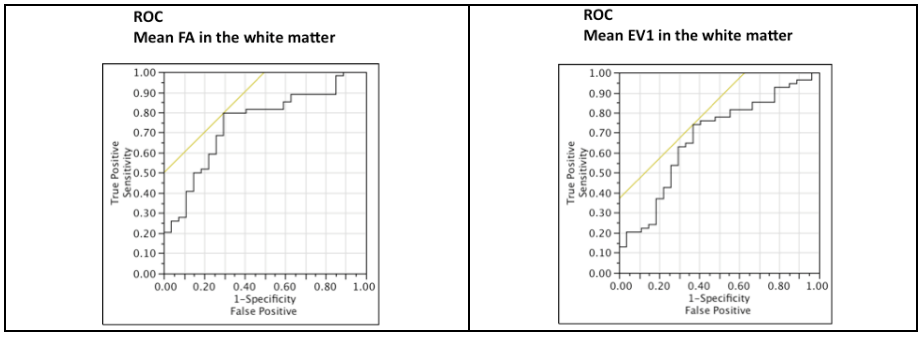
METHODS: We used High Angular Resolution Diffusion Imaging (HARDI) to assess white matter diffusion tensor metric changes in 55 SLE patients without overt neurological syndromes (e.g., stroke, seizure) (mean age 46±12 years), and 27 healthy controls (40±12 years). All subjects were diagnosed with SLE American College of Rheumatology Criteria for , and the mean disease duration was 14±7 years.
Data Acquisition and Data Analysis: the Diffusion Tensor Metrics maps were derived from HARDI data on a 3T scanner with 55 directions (2.2 mm slice thickness, TR/TE 6200/74, b=2000s/mm² and one b=0s/mm² reference image). We calculated the mean of Mean Diffusivity (MD), Fractional Anisotropy (FA), Axial Diffusivity (λ_1) and Radial Diffusivity (λ_2+ λ_3)/2 in the white matter of the brain of each subject. Focal T2 hyperintense lesions in the white matter of the SLE patients have been manually outlined by an expert neuroradiologist and the total lesion volume has been calculated. To estimate the difference between SLE patients versus controls we performed a general linear model using age, total intracranial volume and lesion volume as covariates. The significant measures were compared with regard to their sensitivity to detect white matter changes in the SLE patients using the receiver operating characteristic (ROC). To assess possible cognitive impairment two cognitive indices were derived, including 1) a dichotomous cognitive impairment versus intact index and 2) a continuous variable referring to the proportion of measures impaired (of 12 indices).

RESULTS: SLE patients showed a significant decrease on FA (P=0.010) and on Axial Diffusivity (λ_1) (P=0.017) measures compared to control subjects in the normal appearing white matter (Table 1). No differences were found between the normal appearing white matter (NAWM) and the global white matter in the SLE patients. ROC analysis revealed a threshold > 0.409 (sensitivity 80%, specificity 68%) for the mean FA and a threshold > 0.917 (sensitivity 74% and specificity 60%) for the λ_1 measure (Figure 1). The white matter changes did not correlate with broad-based cognitive impairment indices. The mean FA in the lesions was decreased and the axial diffusivity increased compared to control white matter.

Table 1. The table shows the results from GLM analysis in SLE patients versus controls.
MD=Mean Diffusivity; FA= Fractional Anisotropy.

	MD [× 10^{-6} mm^2/s]	FA	Axial Diffusivity	Radial Diffusivity
Controls	618 ±17.2	0.415 ±0.02	0.923±0.029	0.466±0.017
SLE patients	617±17.2	0.394±0.02	0.905±0.029	0.474±0.018
P value	n.s.	0.010	0.017	n.s.

Figure 1 ROC analysis curve of FA and Axial Diffusivity in the white matter



DISCUSSION: SLE is generally considered a subcortical white matter disease. Our results showed that there are significant changes on FA and Axial Diffusivity (λ_1) measures in the white matter of SLE patients versus control subjects. The T2 hyperintense lesion volume in these patients was very small and had no impact on the diffusion metrics in the normal appearing white matter. Furthermore the axial diffusion was increased in the lesions but decreased in the NAWM, suggesting that the lesions did not contribute significantly to the observed decrease of FA and Axial Diffusivity. Our results suggest that the diffusion tensor changes may become a strong independent predictor of subcortical white matter involvement even in absence of NPSLE manifestations.