

Diffusion Tensor Imaging and Cognition in patients with Neuropsychiatric Systemic Lupus Erythematosus

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Background: Systemic Lupus Erythematosus (SLE) is a chronic, inflammatory, immune-mediated disease. Symptoms can range from rashes, fatigue and joint pain to involvement of major organs such as the brain – this latter case is termed Neuropsychiatric SLE (NPSLE). NPSLE presents a diagnostic challenge as it is not clear to what extent the symptoms are a direct consequence of immune activity on brain tissue, particularly symptoms such as cognitive dysfunction, which is present in 20-60% of patients with NPSLE [1]. Diffusion Tensor Imaging (DTI) is a sensitive technique that has been used to identify subtle differences between healthy controls and a variety of patient groups, even in normal-appearing brain tissue [2]. Previous studies have shown changes in DTI parameters of patients with NPSLE that are consistent with subtle brain damage, [3-5] but have used acute NPSLE patients and have not correlated this with performance on cognitive tasks.

Aims: (1) To see if we can identify differences between patients with NPSLE, non-NPSLE (nSLE) and healthy controls using diffusion tensor imaging (2) To see whether there is a correlation between DTI parameters and performance cognitive performance.

Methods: Participants: We recruited 13 patients with NPSLE (mean age 46.31±10.67; all female), 21 patients with nSLE (mean age 44.81±12.77; 19 female) and 28 healthy controls (mean age 45.04±12.02; 26 female).

Imaging: Scanning was performed on a Siemens Avanto 1.5T MR imager. DTI was acquired using a diffusion-weighted 2D EPI sequence (TR/TE = 6400/110ms, flip angle= 90°, FOV = 220x220 mm, matrix size = 128x128, slices=34, thickness=5mm, 30 diffusion directions, $b=1000\text{s/mm}^2$, averages=2). Analysis of the images was performed using the on-board analysis software to produce apparent diffusion coefficient (ADC) and fractional anisotropy (FA) maps. Normalised ADC and FA Histograms were created and the mean value, peak height and peak position were analysed to identify group differences.

Cognitive assessment: Participants completed a broad cognitive test battery. Task performance was converted to z scores and averaged to produce domain scores based on factors obtained in a previous factor analysis. The domains were termed “memory”, “speed-of-processing”, “frontal”, “inhibition”, “sustained attention”, “compound RT” and “incidental capacity”.

Results: *White matter* Figure 1a and 1b show the ADC and FA white matter histograms. The patient groups show higher ADC and lower FA but these differences were not statistically significant. Figures 2a and 2b show the spread of values in mean ADC/FA. An outlier is evident in the control group (greater than 3 standard deviations from group mean). Removal of this participant reveals a significant effect of group on mean ADC $F(2,58)=4.297$, $p<.05$. Post hoc tests show that the NPSLE group differs from the controls, and the nSLE group fall between the two.

Grey matter No significant differences were found for any of the histogram parameters.

Whole brain Figure 1c and 1d show the whole brain (WB) ADC and FA histograms. A significant group difference was found in mean ADC $F(2,58)=3.498$, $p<.05$ and mean FA $F(2,58)=3.583$, $p<.05$. Post hoc tests revealed that the nSLE group differed significantly from controls whereas the NPSLE group did not. An ANCOVA was run adding age and relative brain volume as covariates and these removed the significant effect of group $F(2,55)=2.307$, $p>.05$ (ADC) and $F(2,55)=2.433$, $p>.05$ (FA).

Correlation with cognition Due to the small sample size, the only significant correlation in the NPSLE group was between “incidental capacity” and white matter FA $r = .61$, $n=12$, $p<.05$, though large effect sizes were found ($r > 0.37$) for the correlation between white matter FA and “inhibition” and “frontal”. Significant correlations were also found between WM FA and cognitive domains in the control group, whereas in the nSLE group cognitive domains “speed-of-processing”, “inhibition” and “compound RT” were related to whole brain ADC and FA. Adding age as a covariate increased the strength of the correlations in the NSPLE group ($r > .7$, $p<.01$) for white matter FA and “frontal” and “speed-of-processing”, but reduced the significance of the correlations in the nSLE group.

Discussion: White matter ADC revealed the most compelling group differences, where patients with NPSLE exhibited increased ADC, consistent with subtle brain damage. However, this parameter did not correlate with cognitive performance. Instead white matter FA correlated with cognitive performance in the NPSLE group, particularly when age was added as a covariate. Adding age as a covariate removed significant group differences between controls and the nSLE group and removed correlations with cognition suggesting that these effects were driven by age.

References: [1] Denburg, SD, Lupus, 2003. 12: 883-890 (2003). [2] Tofts, PS, “QMRI of the brain” Wiley (2003). [3] Bosma, GP, Am J Neuroradiol, 24: 850-854 (2003). [4] Hughes, M, Acta Radiol, 48:213-222 (2007). [5] Jung, RE, BMC Neurol. 10:65-73 (2010).

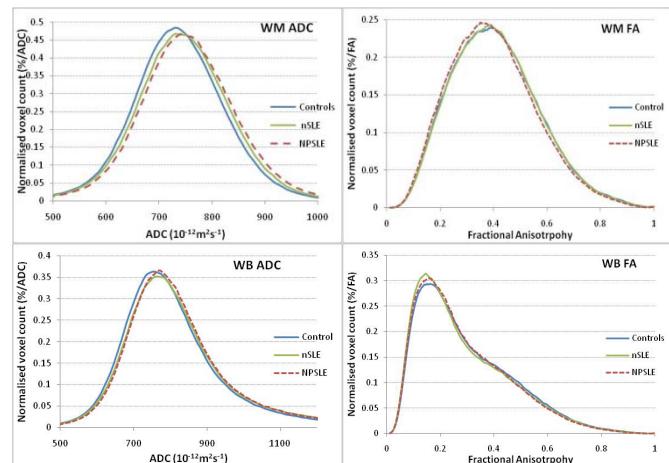


Figure 1a-d. White matter (WM) and whole brain (WB) ADC and FA histograms.

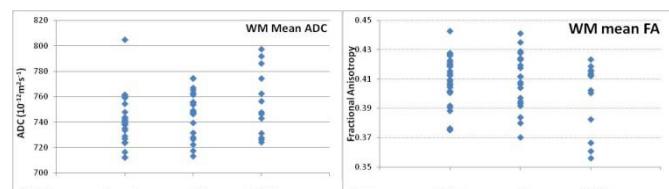


Figure 2a-b The spread of white matter (WM) mean ADC and FA