Tract Based Spatial Statistics of Diffusion Tensor Imaging in Neuropsychiatric Systemic Lupus Erythematodus Reveals Diffuse Involvement of White Matter Tracts.

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Introduction

Systemic lupus erythematodus (SLE) is an autoimmune disease caused by autoantibodies. Up to 75% of the SLE patients develop neuropsychiatric symptoms. However, the exact origin of these symptoms is still unknown. Studies using a mouse model of the disease reported damage in specific limbic brain structures, i.e. the hippocampus and the amygdala. This damage was associated with poor performance on stress-response and memory tests (1, 2). So far, these structures have not been found to be specifically involved in humans. On the other hand, diffuse microscopic damage has been reported in human studies (3). The aim of this study is to determine whether there are differences between SLE patients and healthy controls in the connecting fibers, using tract based spatial statistics (TBSS) on diffusion tensor imaging (DTI) data (4). Whether possible differences in the connecting fibers are focally located in the limbic system or are, in contrast, more widespread is of specific interest.

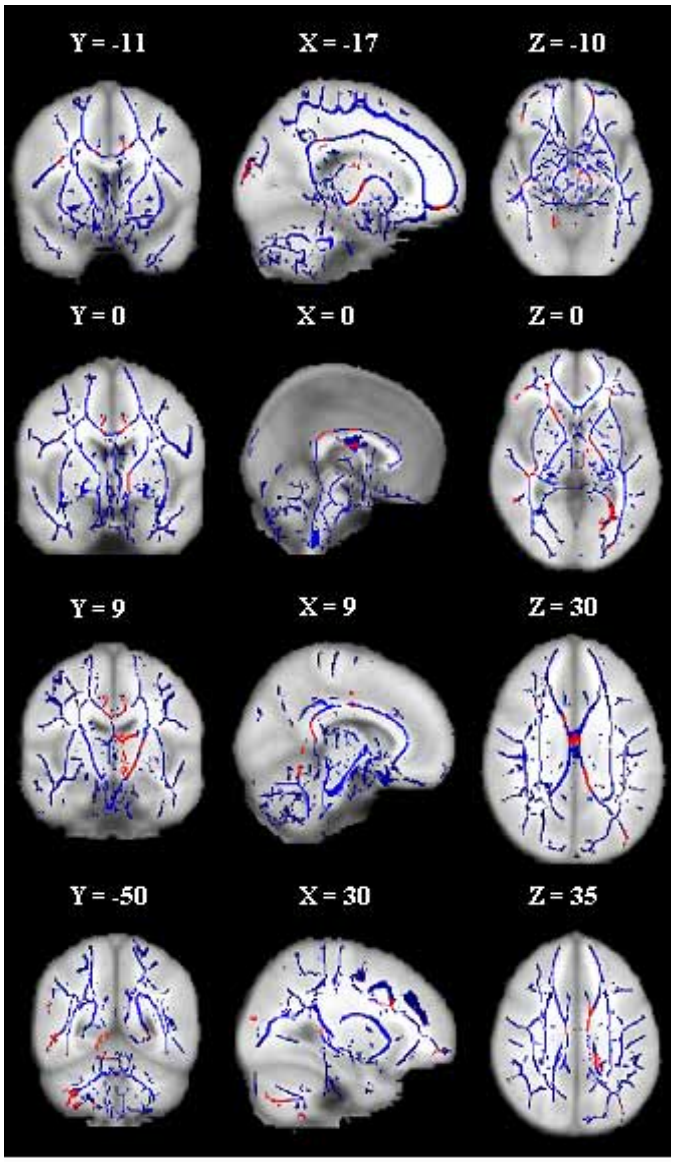

Figure 1 *TBSS results*

Materials and methods

DTI was acquired on a 3T MRI scanner using the following parameters: single shot EPI = 47; max b factor = 800; total scan duration was 1 minute an 54 seconds; Flip angle = 90°; Echo time 48 ms; repetition time 6269 ms; voxel size =2.00 mm/ 2.04 mm/ 3.60 mm; number of directions = 6. 15 SLE patients (all female), diagnosed according to the ACR criteria for SLE, with neuropsychiatric symptoms or complaints were included in the study. In addition 20 healthy controls (10 male, 10 female) were included. The average age of the patients was 46 (range 29-61) and 44 years (range 21-61) for controls. Patients with obvious infarction or other macroscopic damage on conventional MRI were excluded from the analysis. For all subjects FA maps were calculated using the Diffusion Toolbox from FSL (FMRIB Software Library, FMRIB Centre, Oxford). Next, FA data was preprocessed for statistics. Non-linear registration was applied between FA maps, which were subsequently registered to the standard MNI-152 brain. FA maps were then skeletonised and merged, resulting in an alignment-invariant tract representation, i.e. the mean FA skeleton, which was thresholded at an FA-value of 0.3.Voxelwise statistics using TBSS was carried out on the mean FA skeleton, applying a control-patient unpaired *t* test. Cluster-size thresholding was used for inference with clusters initially defined by $t > 3$. The null distribution of the cluster-sized statistic was built up over 5000 permutations of group membership, with the maximum size (across space) recorded at each permutation. The clusters were thresholded at a level of $P < 0.05$, which is fully corrected for multiple comparisons across space (4).

Results

The TBSS results are shown in Figure 1. Blue is the mean FA skeleton and red are the areas where significant lower FA values were present in the patients compared to the control group. No significant areas were found where the FA was higher in the patient group compared to the control group.

Discussion

The diffuse differences between the SLE patients and the healthy controls do not suggest a specific location of susceptibility to reduction in FA values of white matter tracts in SLE patients. Our results rather suggest a more widespread involvement of the white matter, which could be compatible with generalized vasogenic edema or other subtle widespread forms of white matter involvement. However, the number of directions used in this study is relatively small. Increased quality of acquisition, i.e. more directions, could therefore reveal more selective involvement of the connections in the limbic system.

References

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