Smoking Influences White Matter Alterations In Clinically Isolated Syndrome As Revealed By DTI

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Purpose:

Cigarette smoking has been reported to lead increased risk for multiple sclerosis and progression of the disease [1,2]. Quantitative MR imaging evidence on the influence of smoking on demyelinating diseases remains insufficient. We hypothesized that smoker patients with clinically isolated syndrome (CISs) would yield different pattern and extent of white matter (WM) abnormalities than nonsmoker patients (CISns) revealed by DTI.

Material and Methods:

IRB was obtained for this study and all the participants gave signed consent form.

Subjects

17 patients with CISns (M/F: 9/8; 29.71±6.95 years), 14 nonsmoker healthy controls (nsHC) (M/F: 7/7; 29.85±6.60 years) (t-test; p>0.5) and 16 patients with CISs (M/F:8/8; 30.31±8.94 years) and 13 smoker HC (sHC) (M/F:7/6; 30.76±7.46 years) (t-test; p>0.5) were included in the study. All patients in each group had diagnosis of CIS based on clinical, electrophysiological, CSF and MR studies.

Image Acquisition

All participants underwent MRI on a 3T scanner (Trio, Siemens, Germany). Imaging protocol included T1-weighted 3D high resolution images with 0.9 mm isotropic voxels (MPRAGE) (TR/TE: 1900/3.4 ms; FA: 90; FOV: 256mm; matrix: 224x256; distance factor: %50) and isotropic high resolution DTI of the whole brain (single-shot EPI; TR/TE: 8020 /83 ms, max. b factor: 1000s/mm^2, 60 independent directions, FOV: 256 mm, matrix: 128×128, 64 axial sections with 2 mm thickness without intersection gap, voxel size: 2x2x2 mm).

Data Processing and Analysis

For comparative DTI analysis of the groups, we used tract-based spatial statistics (TBSS), a part of FSL. Preprocessing of the diffusion weighted data including head motion and eddy current correction, and diffusion tensor fitting (FSL DTIFit) were performed. Fractional anisotropy (FA), and mean diffusivity (MD) maps were computed. FA maps were registered and aligned to the average space as input for TBSS, and the thinned mean FA skeleton was computed. Then voxelwise statistics were performed using the permutation-based inference with 500 permutations. The resulting TFCE output was corrected for multiple comparisons by controlling the family-wise error rate and thresholded at significance level $p < 0.05$. We used standard cluster-based thresholding corrected for multiple comparisons with a t threshold of 1.5 and obtained the contiguous clusters of supra-threshold voxels using 26-neighbour connectivity. Region-of-interest (ROI) s with significant change of FA were outlined from WM clusters on the resultant TBSS maps, registered to Montreal Neurological Institute (MNI) anatomical template, and labeled using Johns Hopkins University WM tractography and the International Consortium for Brain Mapping DTI-81 WM atlases included in FSL. Mean FA of the ROIs were calculated for each subject and groups. Correlation between nicotine consumption (pack/year) and DTI metrics was also searched by Spearman's correlations.

Results:

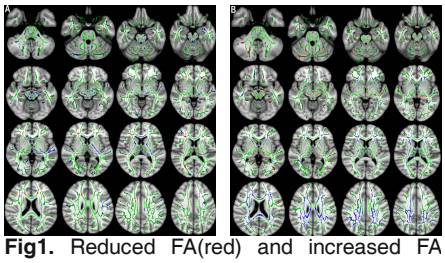

Fig1. Reduced FA(red) and increased FA (blue) (A) and reduced MD (red) and increased MD (blue) in CISns (B) compared to nsHC.

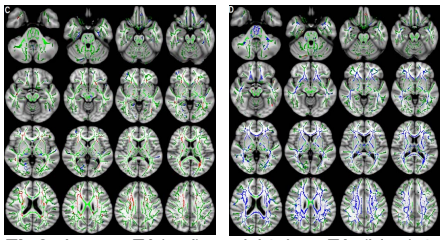

Fig2. Lower FA(red) and higher FA (blue) in CISs (C) and Lower MD (red) and higher MD (blue) in CISs (D) compared to sHC.

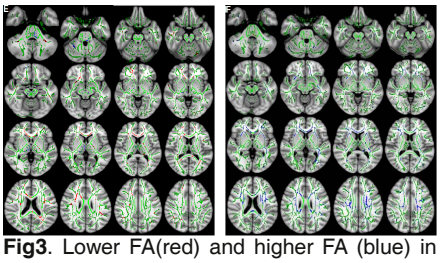

Fig3. Lower FA(red) and higher FA (blue) in patients with CISs (E) and Lower MD(red) and higher MD (blue) in CISs (F) compared to CISns are seen.

When compared to the matched healthy controls, TBSS analysis revealed greater extent of increased FA and MD in WM of CISns (Fig.1), reduced FA and increased MD in CISs groups when compared to matched control subjects (Fig. 2). In TBSS of CISs vs. CISns, CISs patients showed predominantly lower FA in the corpus callosum, internal capsules, superior and inferior longitudinal fasciculi, middle cerebellar peduncles, and higher MD in the corpus callosum, internal and external capsules, middle cerebellar peduncles, uncinate fasciculi, superior and inferior longitudinal fasciculi than CISns (Fig.3). FA and MD values obtained from ROIs did not real any correlation with cigarette consumption.

Conclusions:

Smoker and nonsmoker patients with CIS displayed different pattern and extent of WM abnormalities as revealed by TBSS analysis of DTI. By exerting a significant influence on WM alteration in CIS, smoking status of the patients may also affect long-term prognosis in this disease.

References:

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2. Arikanoglu A, Shugaiv E, Tüzün E, Eraksoy M. Impact of Cigarette Smoking on Conversion from Clinically Isolated Syndrome to Clinically Definite Multiple Sclerosis. Int J Neurosci. 2013 Jan 10.