Identifying the Start of Multiple Sclerosis Tissue Injury: A Longitudinal DTI Study

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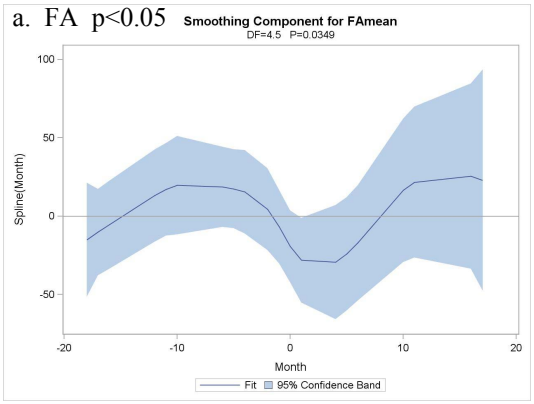
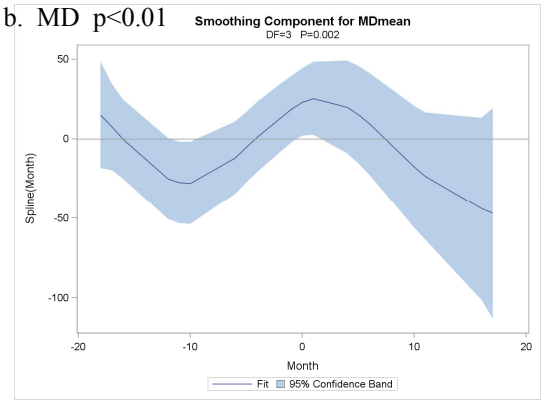
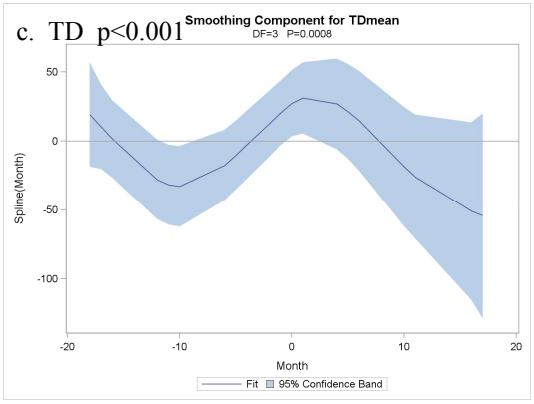
Objective: To use diffusion tensor imaging (DTI) to investigate changes in multiple sclerosis brain tissue prior to gadolinium enhancement.

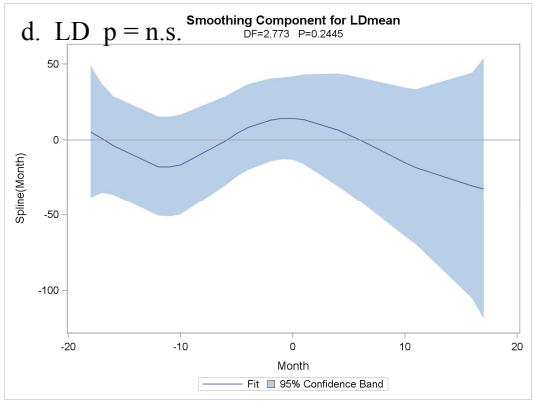
Background: It is unknown when MS pathology starts in any individual brain region. Changes in pre-lesional brain tissue have been described previously using magnetization transfer imaging[1] and simple diffusion-weighted imaging.[2] No such investigation has been carried out using DTI. DTI offers the advantage of relative differentiation of myelin and axonal integrity.[3, 4]

Design/Methods: 21 patients with relapsing remitting multiple sclerosis underwent serial imaging for 12-18 months after starting natalizumab therapy on a Siemens Trio 3 tesla scanner with standard 12-channel head coil (Siemens Medical Solutions, Erlangen Germany) with a HARDI acquisition[5] (104x104 matrix, 260x260mm FOV, 48 2.5mmthick slices, TE=95msec, 5/8 partial fourier factor, 2290 Hz/pixels bandwidth, 71 diffusion gradients with b=2000sec/mm^2 and 8 b=0 acqusitions). Regions of interest (ROIs) were outlined for normal appearing brain (grey and white) tissue (NABT) and gadolinium enhancing lesions (gad) on T2-weighted and T1-MPRAGE images, respectively, and coregistered to the mean b=0 image. Average values within each ROI were derived for fractional anisotropy (FA), longitudinal diffusivity (LD), transverse diffusivity (TD), and mean diffusivity (MD). Analysis was performed using a non parametric regression model based on cubic smoothing splines.[6]









Results: 31 gad lesions were identified over the course of follow-up, 4 of which were re-enhancing lesions. A progressive decrease in FA was observed the 10 months prior to gad development ($p < 0.035$). A progressive increase in both MD ($p < 0.002$) and TD ($p < 0.0008$) was observed over the same period. AD remained unchanged ($p > 0.2$). DTI measures in NABT remained unchanged.

Figure: Evolution of DTI measures before and after development of gadolinium enhancement a. FA; b. MD; c. TD; d. LD. 0 value in each graph represents the average of all measures over the observation period.

Conclusions/Relevance: Our data show a significant change in DTI measures of brain tissue integrity 10 months prior to gadolinium enhancement. Changes in FA were driven by TD, with little contribution from AD. This study provides evidence for impaired myelin integrity up to 10 months prior to development of gadolinium enhancement.

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