DTI PARAMETER CHANGES IN AXONAL LOSS DUE TO MULTIPLE SCLEROSIS

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ABSTRACT

Multiple sclerosis (MS) is a chronic inflammatory demyelinating disease of central nervous system with presumed autoimmune origin. It is largely accepted that the inflammatory induced loss of axons and neurons is the underlying cause of disability in multiple sclerosis patients.
Diffusion tensor imaging (DTI) is a new neuroimaging technique based on MRI, used for quantification of water diffusion in tissues.
We performed DTI to 12 MS patients in order to assess idiffusion parameters (fractional anisotropy, mean diffusivity, longitudinal diffusivity (F1) and transversal diffusivities (F2, F3). We foud that F1 may be used as an indicator of axonal loss in human as well, proving a good correlation with degree of disability.

Key words: multiple scleorsis (MS), diffusion tensor imaging (DTI), axonal loss, disability

BACKGROUND

MS it is characterized clinically by episodes of focal disorders of the optic nerves, spinaol cord and brain, which remit to a varyng extend and recur over a period.

Multiple sclerosis (MS) is a chronic inflammatory demyelinating disease of central nervous system with presumed autoimmune origin

Autoimmune demyelination follows different patterns and is either macrophage mediated (pattern I), antibody mediated (pattern II), characterised by distal oligodendrogliopathy and apoptosis (pattern III) or primary oligodendrocyte degeneration (pattern IV). MS is a demyelinative disease. Both axon and myelin degeneration may have impact on the disability severity of patients with white matter disorder, but it is now largely accepted that the inflammatory induced loss of axons and neurons is the underlying cause of disability in multiple sclerosis patients.

Diffusion tensor imaging (DTI) is a a new neuroimaging technique based on MRI, used for quantification of water diffusion in tissues. Since the introduction of this methodology in 1994 (Basser et al.) it has been used to study the white matter architecture and integrity of the normal and diseased brains (multiple sclerosis, stroke, aging, dementia, schizophrenia, etc.).

The molecules of any substance in a continuous media have a random movement determined by their thermal energy.

The diffusion can be either:

- **isotropic –** being the same in all directions in space, or,
- **anisotropic** – when has barriers against diffusion for some directions.

DTI assess diffusion using **parameters**:

- **FA** (fractional anisotropy) – measures the degree of the preference for a single direction of diffusion.
- **ADC** (apparent diffusion coefficient) – estimates total diffusion for each voxel analyzed and will increase if biological tissues are affected (no diffusion hinders).

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Lambda 1, **2** or **3 (F 1, 2, 3)** reviews magnitude of diffusion along most preferred direction (1) to least favored diffusion (space) direction (3).

Myelin is unique to white matter and is therefore believed to be one of the main effectors of the DTI signal. Water molecules' motion or diffusion was found to be much faster along the white matter fibers than perpendicular to them. The difference between these two motions (parallel and perpendicular to the fibers, also termed diffusion anisotropy) is the basis of DTI. In nervous tissues (white matter), water diffuses preferentially along axons and nerve fiber bundles. In the absence of myelin there is a reduced diffusion anisotropy.

Diffusion tensor imaging measures the displacement of water molecules on the micron scale and yields information about white matter fibers that pass within a pixel. DTI uses additional MRI sequences and processing for computing directional water diffusion maps.

INTRODUCTION

Directional diffusivities derived from diffusion tensor imaging (DTI) have been previously proposed as potential markers to differentiate axon and myelin degeneration (1-4). It has been proved that axonal degeneration will mainly result in a detectable variation of longitudinal diffusivity (F1) (1).

Growing evidence suggests that axonal degeneration rather than demyelination is the pathological substrate underlying disability in multiple sclerosis (MS) (2).

In a post-mortem study, Tallantyre et al. proved that axonal loss is the pathological substrate of disability in multiple sclerosis (motor disability did not correlate with degree of demyelination) (2).

Our hypothesis was that motor disability in patients with MS correlate better with F1 than any other diffusion parameters.

OBJECTIVE

To determine DTI parameters in MS patients admitted at the Bucharest University Hospital – Neurology Department, and to find correlations of these parameters with the disability of the patients (EDSS score).

METHODS

Twelve patients with diagnosed MS were implied in our study.

Neurological examination and EDSS score was performed in each patient.

For diffusion tensor imaging acquisition, a Genesis Signa 1,5T MR system was used equiped with an head coil, an EP/SE scanning sequence, FOV = 240mm, 25 gradient directions, b value = 1.000, TR/TE = 9.999/113 ms, RF pixel bandwidth = 625 Hz, spatial resolution = 1.87mm.

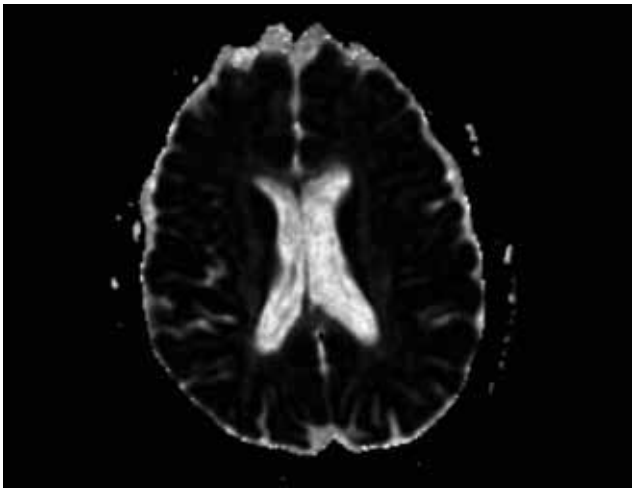
After MR-DTI acquisition (Based on Pierpaoli and Basser paper principle), the corticospinal tract was reconstructed and its diffusion parameters (fractional anisotropy, mean diffusivity, longitudinal diffusivity) (F1) and transversal diffusivities (F2, F3) were obtained. MedInria software (http://www-sop.inria.fr/asclepios/software/MedINRIA) was used for obtaining diffusion maps and tractography.

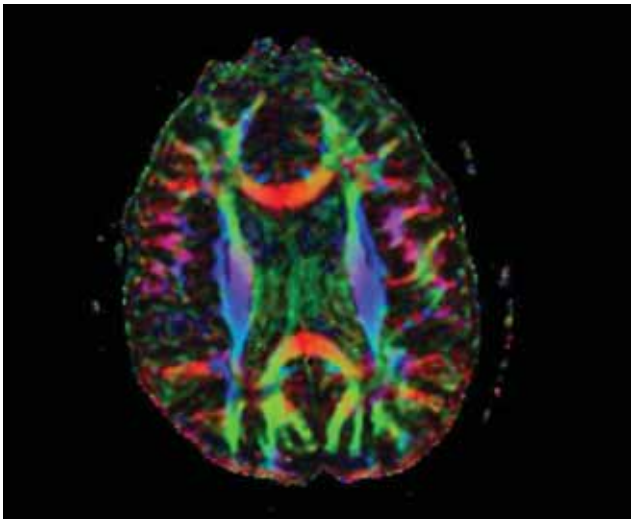
RESULTS

Cerebral FA, F1, F2, F3 maps were obtained in all volunteers (Fig. 1a, b).

A region of interest (ROI) at the level of internal capsule was selected in order to get the seeding points for the corticospinal tract generation (Fig. 1c).

Correlation between disability degree (EDSS score) and diffusion parameters was checked by





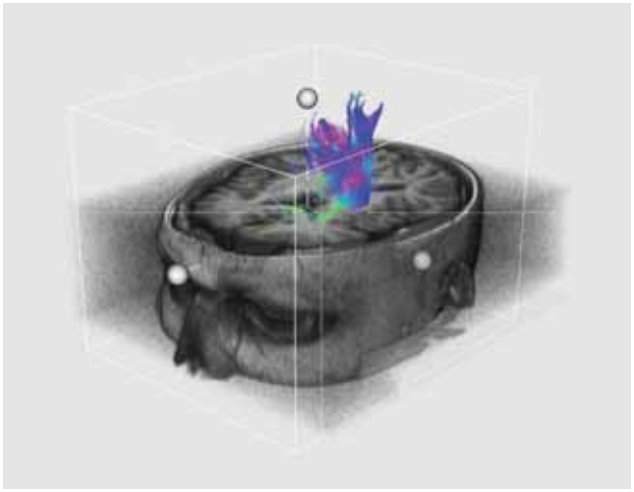


Figure 1. *Longitudinal diffusivity (1) map (a), fractional anisotropy map (b) and reconstructed corticospinal tract (c)*

calculating the Spearman coefficient for each patient. The highest correlation was found between disability degree and F1 (corr. coeff. = 0.67) (Fig. 2b).

Transversal diffusivities (F2, F3) correlation coefficients to EDSS score were found to be equal to 0.6 and 0.58 while the FA correlation coefficient to EDSS score was found to be negative, as expected (corr. coeff. = – 0.58) (Fig. 2a, c, d).

CONCLUSION

Taking into account previously proved correlation between axonal loss and disability in MS (2) and considering Song et al. small animal studies conclusion that F1 may be an indicator of axonal injury (1), our study suggest that F1 may be used as an indicator of axonal loss in human as well, proving a good correlation (corr. coeff., 0.67) with degree of disability (EDSS score).

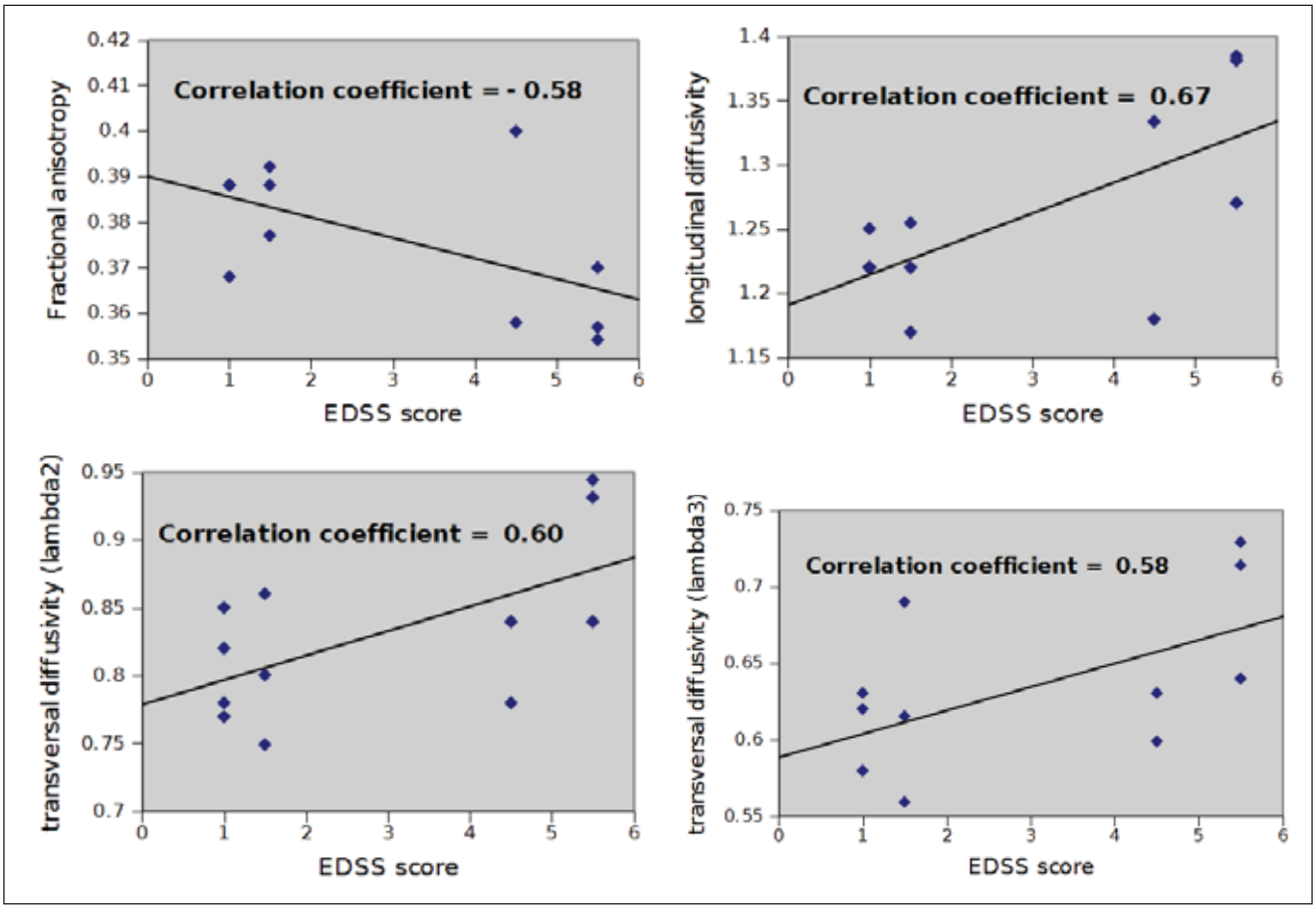


Figure 2. *Fractional anisotropy, longitudinal diffusivity, transversal difusivities dependencies on EDSS score and corresponding correlation factors are depicted in a,b,c,d.*

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