About "Axial" and "Radial" Diffusivities

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Introduction

Diffusion Tensor Imaging (DTI) allows the quantitative assessment of diffusion anisotropy in tissue. The DT can be diagonalised to determine three eigenvectors, $\mathbf{V}_1$, $\mathbf{V}_2$ and $\mathbf{V}_3$ and their corresponding eigenvalues, λ_1, λ_2 and λ_3. It is well known that these eigenvalues depend on the underlying tissue structure and that their direction is affected by uncertainty[1,2]. Recently the attention has shifted from comparing rotationally invariant anisotropy measurements, such as Fractional Anisotropy (FA), which are insensitive to the eigenvectors sorting, towards comparing the individual eigenvalues. The introduction of the terms "axial" and "radial" diffusivities associated to λ_1 and the average of λ_2 and λ_3 respectively, and the results of post-mortem studies have started a debate on the interpretation of the biophysics of these indices in terms of myelin and axons density[3]. The problem that arises is that potentially encouraging correlations between the eigenvalues and histological measures of myelin and axonal degeneration are shadowing the fact that the eigenvectors $\mathbf{V}_1$, $\mathbf{V}_2$ and $\mathbf{V}_3$ associated with the eigenvalues λ_1, λ_2 and λ_3 may not be aligned with the underlying structure in the same way in different subjects and therefore comparing "axial" and "radial" diffusivity indices across different subjects/samples can be misleading. We strongly recommend that current and future studies that deal with "axial" and "radial" diffusivities are accompanied by a thorough investigation of the associated directions of the eigenvectors, with particular emphasis on areas characterised by low anisotropy, partial volume or an oblate diffusion ellipsoid. To support our pledge, we have shown a practical example of what sort of errors could occur when analysing the eigenvalues, neglecting the eigenvectors.

Methods

Two healthy controls (females, 35 (HC_{ref}) and 37 (HC) years old) and two patients with relapsing remitting Multiple Sclerosis (MS) (a female, aged 34 (MS_{p1}), disease duration = 1.5 years, EDSS (Expanded Disability Status Scale) = 2.5 and a male, aged 55 (MS_{p2}), disease duration = 7 years, EDSS = 5.5)) were scanned on a 1.5T MRI scanner using a dual echo fast spin echo (FSE; $TR/TE_1/TE_2$=2300/17/103ms) and a pulsed-gradient single shot spin echo EPI sequence (cardiac gated with TR=20RR≅20s, TE=85ms, 61 distributed directions[4] interleaved with 7 non-diffusion weighted b≅0 acquisitions, maximum b factor=1200smm^{-2}, voxel size=2.3mm^3). The DTI data were first realigned and corrected for eddy currents using a 3D affine transformation[5]; the tensor was fitted to the data, and FA was calculated. Using HC_{ref} as the reference, FA images of all subjects were co-registered and the transformation was applied to the components of the tensor using the preservation of principal direction algorithm[6]. The eigenvectors and eigenvalues of the rotated tensor were then derived. In every voxel we computed the dot product of the principal eigenvectors of two subjects, yielding maps of cos(θ), where θ is the angle subtended between them. To discern areas where the principle eigenvector is not aligned with the underlying tissue structure in the same way as the principle eigenvector of the reference data, we thresholded the maps to highlight voxels where θ>45º.

Results

Fig 1 shows the voxels where θ>45º between HC_{ref} and HC (left), between HC_{ref} and MS_{p1} (centre) and between HC_{ref} and MS_{p2} (right). There is good agreement between the direction of the principal eigenvector in the major white matter tracts of HC_{ref} and HC, while grey matter areas, voxels affected by partial volume and a few sparse voxels in white matter areas of low FA show misalignment > 45 º. Areas of misalignment are more widespread in MS_{p1}, and these areas do not coincide necessarily with MS lesions. Many areas of white matter that are characterised by a change in the direction of the principal eigenvector are evident in MS_{p2} and are involving lesion sites too.

Discussion

This study confirms that the principal eigenvalue of the DT, λ_1, and therefore the second and third ones, λ_2 and λ_3, can represent different underlying structures in different datasets because of a different orientation of the corresponding principal eigenvector, $\mathbf{V}_1$. This different directionality of the diagonalised DT eigenvectors in different subjects may be due to a real inter-subjects anatomical difference, but it may also be caused by a change of the main underlying structure or by the presence of a sorting bias introduced by noise or by the shape of the ellipsoid in that particular area. Whatever the reason, the point is that it underpins the rationale behind the definition of "axial" and "radial" diffusivities and their interpretation in relation to histology results of myelin content and axonal density measures. In view of this well known problem, we cannot stress enough that analysis which are using the eigenvalues themselves must include the eigenvectors as well.

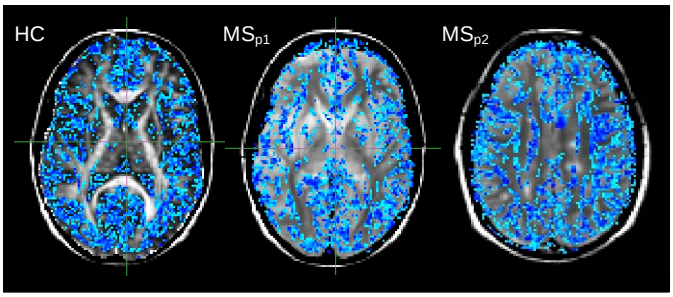

Fig 1.Voxels in blue are those were the angle between the principal eigenvector of a given subject and HC_{ref} differ by more than 45º.

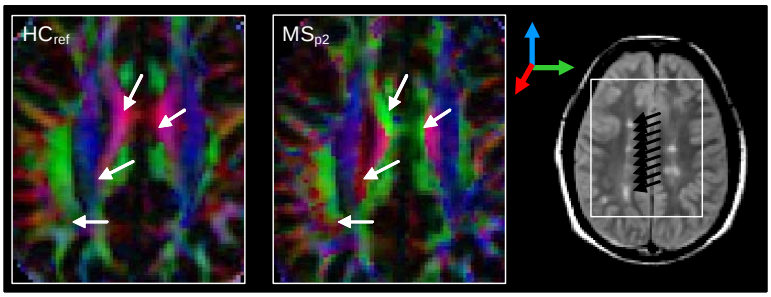

Fig 2. Areas of $\mathbf{V}_1$ changes between MS_{p2} and HC_{ref}.The colour coding represents the direction of $\mathbf{V}_1$. The T_2-weighted image shows lesions in MS_{p2}.

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