A MULTI CENTER LONGITUDINAL STUDY OF DIFFUSION TENSOR MRI CHANGES IN HEALTHY VOLUNTEERS AND PEOPLE WITH MS

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Introduction

Diffusion tensor (DT) MRI allows the quantification of disease-related changes of brain tissue in patients with multiple sclerosis (MS) and measures derived from this technique are likely to be useful in monitoring the efficacy of experimental treatment. With this goal, it is necessary to assess the longitudinal variability from data acquired with different MR systems, manufacturers, and magnetic field strengths, with a standard acquisition protocol. In the present study, we analyzed DT-derived metrics acquired at baseline and after 6 months with the aim of assessing: a) the longitudinal stability in a group of healthy subjects, and b) the sensitivity to microstructure tissue changes in MS patients.

Methods

Thirty-one healthy subjects and 22 MS patients with low disability (EDSS $\leq$3.5) were studied at baseline and after 6 months in 7 MRI centers, part of the MAGNIMS network (http://www.magnims.eu). Table 1 reports the number of subjects enrolled at each center, their average age and the average follow-up duration. The MRI scanners used were: centers A and B: 1.5 T, Avanto, Siemens; center C: 1.5 T, Sonata, Siemens; center D: 3.0 T, Intera, Philips; center E: 3.0 T, Allegra, Siemens; centers F and G: 3.0 T, TrioTim, Siemens.

The acquisition parameters of the DT-MRI sequence were: pulsed gradient spin echo single shot echo planar, TR[ms]:7000-8000, TE[ms]: 90-105, FOV [mm]: 320, matrix: 128x96, %FOV: 75, receiver bandwidth [Hz / pixel]: 2000-2300, slices: 50, slice thickness [mm]: 2.5; diffusion-encoding gradients directions: 30 (NEX=1) and 12 (NEX=2), b-value [s/mm^2]: 900. High-resolution dual spin-echo images were also acquired.

DT images were first corrected for distortions induced by eddy currents; then the DT was estimated by linear regression (1) and mean diffusivity (MD) and fractional anisotropy (FA) maps derived. Mean FA and MD were calculated from the corpus callosum (CC), as seen on the midsagittal slice, after rigid transformation to the mid-point between baseline and follow-up (2). To this aim a region of interest was drawn on the average of the transformed baseline and follow-up FA images which was then used on each individual MD and FA images to segment the CC (Figure 1).

The longitudinal stability was assessed on health subjects using a multifactor ANOVA test for repeated measures, including the acquisition center as a between-subject factor and the follow-up duration as a covariate. The sensitivity to tissue changes in MS patients was assessed using the same model by adding the factor group to the analysis.

Table 1. Demographic characteristics

Center		A	B	C	D	E	F	G	ALL
Ctrls	N	4	3	6	5	4	4	5	31
	Age (SD) [years]	34.5 (6.1)	36.2 (5.9)	33.8 (8.7)	30.8 (7.0)	34.5 (6.1)	32.2 (3.9)	30.3 (5.1)	33.0 (6.1)
	FU (SD) [months]	5.8 (0.3)	6.4 (0.6)	5.6 (0.4)	7.2 (1.2)	5.8 (0.3)	7.1 (1.2)	10.3 (1.3)	6.9 (1.8)
MS	N	-	2	3	5	6	2	4	22
	Age (SD) [years]		33.6 (1.4)	40.5 (8.6)	36.9 (6.9)	36.8 (10.1)	32.6 (1.7)	33.9 (11.7)	35.9 (8.1)
	FU (SD) [months]		7.5 (0.2)	6.4 (0.2)	6.6 (0.2)	6.5 (0.8)	6.8 (1.6)	10.0 (2.4)	7.2 (1.7)

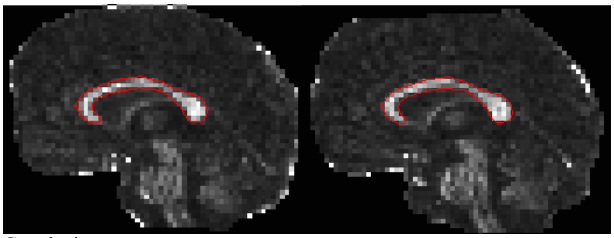
Results

Table 2 reports absolute percentage changes of FA and MD values between baseline and follow-up, averaged across healthy subjects at each center. Statistical analysis showed that longitudinal changes of MD values were statistically significant in healthy subjects (ANOVA, p=0.016), with an interaction with the follow-up duration and the acquisition center, whereas FA values were found to be stable. When patients were included, neither FA nor MD longitudinal changes were significant (Figure 2).

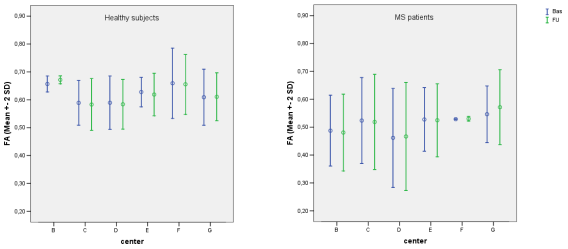
Table 2. Percentage changes between baseline and follow-up (healthy subjects): mean of absolute values, (mean ± standard deviation).

	A	B	C	D	E	F	G	ALL
FA	2.0% (1.1±2.4)	2.7% (2.3±3.0)	1.5% (-1.1±1.5)	0.9% (-0.9±0.8)	2.0% (-1.5±2.4)	3.6% (-0.4±4.4)	1.1% (0.3± 1.6)	1.9% (-0.2±2.4)
MD	2.1% (1.6±2.4)	2.7% (-2.7±2.0)	3.7% (2.8±2.9)	1.5% (0.9±2.9)	0.9% (0.4±1.1)	3.5% (-1.6±4.1)	2.6% (2.5±2.6)	2.5% (0.9±3.0)

Figure 1. Baseline (left) and follow-up (right) FA maps of a healthy subject after coregistration to the mid-point. In red, the region of interest drawn on the corpus callosum.



2. Fractional anisotropy mean and standard deviation at baseline (blue) and follow-up (green) in health controls (left) and MS patients (right).



Conclusions

MD and FA longitudinal changes in healthy subjects ranged from 1% to 3.7%, depending on the acquisition center. In healthy subjects, although the small number included per center, FA was stable over time, while MD showed small, but statistically significant changes. However, neither of the two measures considered was sensitive to the possible changes associated to disease evolution in MS. This might be due to the relatively short follow-up of this study and suggests a longer time period would be necessary for this technique to be able to detect tissue changes in MS.

References

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