OPTIMIZING DIFFUSION MEASUREMENTS FOR LARGE-SCALE MULTI-CENTRE TRIALS: A MAGNIMS DT MRI SEQUENCE.

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Introduction

Diffusion tensor (DT) magnetic resonance imaging (MRI) has the ability to quantify disease related changes of brain tissue. DT MRI-derived measures may represent a desirable paraclinical outcome in treatment trials, but the issue of DT MRI measurements variability has not been addressed yet. The aims of the present study were: a) the development of an optimal acquisition scheme for multi-centre trials (considering the time issue in the context of "multi-sequence scans"), and b) the evaluation of both the feasibility of the sequence set-up on various scanners and the inter-centre reproducibility of DT-derived metrics

Methods

Twenty-nine healthy subjects were studied in 7 MRI centres. The following MRI scanners were used: centre A: 1.5 Tesla, Sonata, Siemens; centre B: 1.5 Tesla, Avanto, Siemens; centre C: 1.5 Tesla, Avanto, Siemens; centre D: 1.5 Tesla, Intera, Philips; centre E: 3.0 Tesla, Allegra, Siemens; centre F: 3.0 Tesla, Intera, Philips; centre G: 3.0 Tesla, TrioTim, Siemens. Table 1 reports the demographic characteristics of subjects enrolled at each centre. The following template was established for the DT-MRI sequence to be used: Pulsed Gradient Spin Echo Single Shot Echo Planar , TR[ms]:5000-9000, TE[ms]: 90-125, FOV [mm]: 320, matrix: 128x96, %FOV: 75, %sampling: 100, half Fourier: no, receiver bandwidth [Hz / pixel]: 2000-2500, slices: 50, slice thickness [mm]: 2.5; diffusion-encoding gradients directions: 30 (1), b-value [s/mm^2]: 900; number of acquisitions with b=0: 4-6. A high-resolution dual echo (DE) sequence was also acquired.

DW images were first corrected for distortions induced by eddy currents; then the DT was estimated by linear regression (2). In order to standardize a region of interest (ROI)-based analysis approach, native images were coregistered onto the MNI standard space using the T2-weighted image to drive an affine transformation (3). This native-to-standard transformation was used to obtain fractional anisotropy (FA) and mean diffusivity (MD) (4) maps in standard space. Two ROIs were positioned on the genu and the splenium of the corpus callosum using the T2-weighted atlas; ROIs were then transferred onto the transformed FA maps and eventually moved to avoid CSF contamination. Mean FA and MD values were calculated. Histograms of MD/FA values were also created and analysed to provide measures not influenced by ROIs choice/positioning. First, DE scan s were segmented (SPM2) to produce maps of grey (GM) and white matter (WM) . Then, the b=0 T2 weighted image was deformed (5) onto the TSE-T2-weighted scan to compensate for distortions typical of the EPI acquisition and this transformation was applied to the diffusion-derived maps. After masking, FA and MD histograms from the whole brain (WB) tissue, the WM and the GM were created, normalized and mean MD/FA, peak height and position values derived. The inter-centre heterogeneity was assessed for 1.5 T and 3T scanner separately using a Kruskal-Wallis test. A comparison between 1.5 and 3 T scanners was assessed only on the same five subjects undergoing the scan procedure at the centres B and E, using the Wilcoxon signed rank test.

Table 1

Centre	A	B	C	D	E	F	G
N	4	5	3	3	5	5	4
Mean age [years] (STD)	36 (10)	34 (5.5)	36 (5.9)	28 (3.5)	34 (5.5)	31 (7.1)	34 (2.4)
M/F	1/3	3/2	1/2	1/2	3/2	3/2	1/3

Results

Table 2 reports mean and standard deviation of MD and FA values per centre and table 3 the results of the statistical analysis . The analysis of histogram peak height and position values gave similar results (data not shown).

Table 2. Mean and standard deviation (STD) values of FA and MD per centre.

Centre		A	B	C	D	E	F	G
Genu CC	FA	0.81 (0.03)	0.79 (0.03)	0.83 (0.11)	0.88 (0.04)	0.85 (0.02)	0.80 (0.04)	0.86 (0.06)
	MD	0.68 (0.05)	0.65 (0.03)	0.70 (0.07)	0.75 (0.05)	0.80 (0.05)	0.86 (0.04)	0.70 (0.03)
Splenium CC	FA	0.83 (0.07)	0.77 (0.06)	0.84 (0.05)	0.89 (0.05)	0.81 (0.03)	0.84 (0.03)	0.88 (0.04)
	MD	0.68 (0.01)	0.66 (0.05)	0.75 (0.01)	0.75 (0.05)	0.76 (0.04)	0.82 (0.02)	0.77 (0.10)
Whole brain	FA	0.27 (0.01)	0.29 (0.01)	0.30 (0.01)	0.27 (0.01)	0.30 (0.01)	0.25 (0.01)	0.32 (0.01)
	MD	0.87 (0.03)	0.83 (0.01)	0.84 (0.02)	0.93 (0.02)	0.92 (0.03)	0.94 (0.02)	0.90 (0.02)
White matter	FA	0.46 (0.02)	0.47 (0.02)	0.47 (0.01)	0.44 (0.03)	0.49 (0.04)	0.39 (0.01)	0.49 (0.02)
	MD	0.73 (0.02)	0.69 (0.02)	0.74 (0.01)	0.78 (0.02)	0.79 (0.03)	0.80 (0.01)	0.78 (0.01)
Grey matter	MD	0.90 (0.04)	0.85 (0.01)	0.86 (0.02)	0.96 (0.03)	0.94 (0.03)	0.97 (0.02)	0.92 (0.04)

Table 3. Chi-squares (p values) for heterogeneity analysis and Z scores (p values) for between-group comparisons.

		ROI-based analysis				Histograms-based analysis				
		Genu CC		Splenium CC		Whole brain		White matter		Grey matter
	age	FA	MD	FA	MD	FA	MD	FA	MD	MD
Intercentre 1.5 T chi^2 (p)	2.64 (0.45)	5.60 (0.13)	6.53 (0.09)	5.87 (0.13)	9.53 (0.02)	8.57 (0.04)	10.43 (0.01)	2.64 (0.45)	11.76 (0.01)	9.82 (0.02)
Intercentre 3 T chi^2 (p)	0.87 (0.65)	6.10 (0.05)	8.54 (0.01)	3.34 (0.18)	4.98 (0.08)	10.26 (0.01)	5.40 (0.07)	9.23 (0.01)	2.44 (0.29)	3.88 (0.14)
Between group comparison 1.5 vs 3T Z (p)	-	-2.02 (0.04)	-2.02 (0.04)	-1.75 (0.08)	-2.02 (0.04)	-2.02 (0.04)	-2.02 (0.04)	-0.67 (0.50)	-2.02 (0.04)	-2.02 (0.04)

Conclusions

A careful standardization of DT MRI sequences allowed us to achieve a low inter-scanner variability of DT-derived quantities, which seems to be lower for anisotropy measures when using 1.5 T magnets. This might be due to a stronger presence of artefacts at 3T or because the 1.5 T group is less influenced by inter-manufactures variability than the 3 T one.

References

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