CAN WHOLE BRAIN DKI DETECT REGIONAL CHANGES IN MULTIPLE SCLEROSIS PATIENTS?

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Introduction

Pathologic changes of tissue microstructure of the brain parenchyma are difficult to measure by conventional magnetic resonance imaging (MRI) techniques. Diffusion kurtosis imaging (DKI) (1-3) has shown its potential for tissue characterization (4,5) by investigating the non-Gaussian diffusion pattern of water thereby indicating changes of microstructural complexity. Pathologic microstructural tissue changes were found in patients with multiple sclerosis by using DTI measures in regions of normal appearing tissue based on conventional MR imaging (6). The purpose of this study was to evaluate whether the DKI technique is able to detect differences between multiple sclerosis patients and healthy controls when performed as a whole brain high resolution study.

Methods

In this IRB approved and patient consented study we examined 25 patients with known MS and 23 healthy controls (patients 21 w, 2 m; controls 10 w, 12m). Scans were performed on a 3T scanner equipped with a 32 channel head coil, using a dual spin echo sequence (TR 18500, TE 101ms, parallel imaging factor 3, one average, 2mm isotropic resolution, 80 slices with whole brain coverage, three b values [0, 500, 1500, 2500], 30 directions). An anatomic 3D-FLAIR and 3D-T1 scan reasons were acquired for reference, total scanning time 50min. We compared diffusional measures of axial, radial and mean kurtosis (axK, radK, MK), axial, radial and mean diffusivity (axD, radD, MD), DTI-model based radD, axD and MD (MD_dti, radD_dti and axD_dti) as well as fractional anisotropy (FA, FA_dti) data in 15 regions (manually placed regions of interest (ROI) with radius of 3mm; midline positions for rostrum and splenium corporis callosi as well as medulla oblongata; middle of cingulate gyrus, globus pallidum, posterior limb of internal capsule, middle cerebellar peduncle, posterior thalamus on both hemispheres) using the software MRIcron (Chris Rordon, www.mricro.com). ROI's with 4mm size were placed on the intraorbital optic nerve on each side. The multivariate ANOVA with age as covariate was used to test for group differences.

Results

Due to quality reasons (motion artifacts, noise, metal implant related distortions) we had to exclude 6 scans, so that scans of 23 patients (21w, 2m, mean age 47.2 +/-10.7) and 15 controls (7w, 8m, mean age 41.2 +/-12) were analyzed. We found significant ($p<0.05$) overall differences in 50 parameters in 9 regions when comparing both groups, but we also found significant differences within the control group comparing both sexes (overall 17 parameters in 6 regions, in 5 regions several near significant differences).
We therefore compared the women of both groups, showing mainly significant differences in the rostrum of corpus callosum (all parameters), the splenium of the corpus callosum (axD, axD_dti, axK) and the right cingulate gyrus (all three kurtosis parameters and MD_dti) (see Table 1). Only 1 parameter showed a significant difference in the right cerebellar peduncle (FA, control vs. patients 0.57±0.03/0.54±0.03), and the medulla oblongata (radK, 1.51±0.17/1.30±0.12). For the optic nerves we found large data deviations mainly due to image distortion, which was not corrected for.

Conclusions

Diffusional kurtosis imaging with high resolution whole brain coverage is feasible and can detect microstructural tissue differences between MS patients and healthy controls, showing regional differences for instance within the corpus callosum indicating axonal as well myelin damage rostrally and only axonal damage in the posterior part of the corpus callosum. DKI can also detect sex related microstructural differences of the brain in different regions, which has to be accounted for in future analyses. Further studies have to show whether distortion correction and noise reduction of DW images can improve detection of group differences. The differences we found have to be correlated with clinical information of the patients.

ROI	**Rostrum c.c.**	**Splenium c.c.**	**Cingulate gyrus right**
Parameter	Controls / Patients	Controls / Patients	Controls / Patients
axD	1.57±0.07 / 1.77±0.14 (*)	1.37±0.08 / 1.65±0.17	-
axD_dti	1.12±0.06 / 1.25±0.08 (*)	1.00±0.08 / 1.16±0.12	-
MD	0.88±0.06 / 1.04±0.14 (*)	-	-
MD_dti	0.61±0.03 / 0.72±0.08 (*)	-	0.62±0.04 / 0.66±0.04
radD	0.53±0.07 / 0.68±0.15 (*)	-	-
radD_dti	0.36±0.04 / 0.45±0.09 (*)	-	-
FA	0.61±0.05 / 0.55±0.07 (*)	-	-
FA_dti	0.62±0.05 / 0.57±0.07 (*)	-	-
axK	0.76±0.03 / 0.68±0.05	0.88±0.05 / 0.73±0.08	1.01±0.06 / 0.95±0.05 (*)
MK	1.37±0.10 / 1.22±0.13 (**)	-	1.14±0.07 / 1.09±0.08
radK	2.13±0.25 / 1.85±0.30 (*)	-	1.42±0.14 / 1.36±0.17

Table 1: Mean values of all parameters with significant differences in three ROIs ± standard deviation. Apparent diffusion coefficients in μm²/ms. (*) $p<0.005$; (**) $p<0.001$. c.c. = corpus callosum

References

1. Jensen JH, Helpern JA. Quantifying Non-Gaussian Water Diffusion by Means of Pulsed-Field-Gradient MRI.; 2003; Toronto, Canada. p 2154.
2. Jensen JH, Helpern JA, Ramani A, Lu H, Kaczynski K. Diffusional kurtosis imaging: the quantification of non-gaussian water diffusion by means of magnetic resonance imaging. Magn Reson Med 2005;53(6):1432-1440.
3. Tabesh A, Jensen JH, Ardekani BA, Helpern JA. Estimation of tensors and tensor-derived measures in diffusional kurtosis imaging. Magn Reson Med 2011;65(3):823-836.
4. Falangola MF, Jensen JH, Babb JS, Hu C, Castellanos FX, Di Martino A, Ferris SH, Helpern JA. Age-related non-Gaussian diffusion patterns in the prefrontal brain. J Magn Reson Imaging 2008;28(6):1345-1350.
5. Raab P, Hattingen E, Franz K, Zanella F, Lanfermann H. Diffusional kurtosis imaging of cerebral gliomas – analysis of microstructural differences. Radiology (in Press) 2009.
6. Roosendaal SD, Geurts JJ, Vrenken H, Hulst HE, Cover KS, Castelijns JA, Pouwels PJ, Barkhof F. Regional DTI differences in multiple sclerosis patients. Neuroimage 2009;44(4):1397-1403.