European Journal of Radiology 83 (2014) 2196–2202

Contents lists available at ScienceDirect

European Journal of Radiology

journal homepage: www.elsevier.com/locate/ejrad

Age-related changes of the diffusion tensor imaging parameters of the normal cervical spinal cord

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ARTICLE INFO

Article history:
Received 27 June 2014
Received in revised form 2 September 2014
Accepted 11 September 2014

Keywords:
Magnetic resonance imaging
Cervical spinal cord
Intervertebral space
Diffusion tensor imaging
Apparent diffusion coefficient
Fractional anisotropy

ABSTRACT

Background: The diffusion tensor imaging (DTI) parameters of the cervical spinal cord (CSC) changes with age. However, previous studies only examined specific CSC areas.
Objectives: To analyze the DTI parameters in all intervertebral space levels of the whole normal CSC and to study the impact of age on these parameters in a Chinese population.
Methods: Thirty-six healthy subjects aged 20–77 years were recruited. DTI parameters were calculated for gray matter (GM) and white matter (WM) funiculi in all the CSC intervertebral spaces (C1/2-C6/7). Age-related changes of DTI parameters were analyzed for the GM and WM funiculi.
Results: Fractional anisotropy (FA) and mean diffusivity (MD) were lower in GM than in WM. MD and FA values were lower in the WM in the lower CSC compared with the upper CSC (all $P < 0.05$), but no difference was observed in GM. In ventral funiculi, MD increased with age, while FA decreased (all $P < 0.001$). In lateral and dorsal funiculi, MD and FA decreased with age (all $P < 0.001$). In GM, MD and FA decreased with age (all $P < 0.001$). Significant age-related changes were observed in FA and MD from GM and WM funiculi. FA was correlated with age in all funiculi (ventral: $r = -0.733$; lateral: $r = -0.468$; dorsal: $r = -0.607$; GM: $r = -0.724$; all $P < 0.01$).
Conclusion: Important changes in MD and FA were observed with advancing age at all levels of CSC in Chinese patients. DTI parameters may be useful to assess CSC pathology, but the influence of age and segments need to be taken into account in diagnosis.

1. Introduction

The diameter of the human cervical spinal cord (CSC) is only about 13 mm. Its cross-section is characterized by a butterfly-shaped gray mater (GM) surrounded by white mater (WM). The WM can be divided into dorsal, lateral, and ventral funiculi (DF, LF and VF, respectively). Funiculi carry distinct ascending somatosensory and descending motor spinal cord tracts [1]. Previously studies [2–6] revealed that the dorsomedian tract, the Burdach's tract and the medial part of the LF were thin, while the fiber bundles on the outside of the VF and LF were coarse. Therefore, DTI characteristics of different WM funiculi might be different. A precise characterization of the properties of these funiculi might be of importance to improve our understanding of pathologies involving specific funiculi.

Diffusion tensor imaging (DTI) is an advanced magnetic resonance imaging (MRI) technique based on diffusion weighted imaging (DWI) that measures at least six diffusion directions and offers the possibility to evaluate the scalar properties of the diffusion of extracellular water molecules within WM fibers [7]. DTI enables the quantitative assessment of the integrity of the WM using the fractional anisotropy (FA) and mean diffusivity (MD) values [8]. The FA values reflect the global anisotropy of the analyzed structure [9]. Disturbances (restriction or increase) of diffusion may be assessed quantitatively using mean diffusivity (MD) values.

In 1999, Clark et al. [10] first reported that water diffusion in the human cervical spinal cord (CSC) was anisotropic. DTI studies in normal CSC showed that there were significant differences between different segments and different age groups, and that DTI parameters of the CSC were sensitive to age-related microstructural changes [11–14]. However, these studies focused only on specific parts of the CSC.

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http://dx.doi.org/10.1016/j.ejrad.2014.09.010
0720-048X/

With the increasing use of DTI in patients with cervical cord pathologies, it is essential to determine the DTI parameters in the whole CSC. The aim of the present study was to analyze DTI parameters in all intervertebral space levels of the CSC and to study the impact of age on these parameters in healthy Chinese subjects. Assessing the correct impact of age at all intervertebral space levels of the CSC could provide better insights in factors that could bias the diagnosis of CSC pathologies.

2. Materials and methods

2.1. Subjects

Thirty-six healthy subjects were enrolled between May 2013 and May 2014 at Orthopedics Department of Changhai Hospital Affiliated to Second Military Medical University (Shanghai, China). Subjects were approached during a routine health examination. All subjects considered themselves to be healthy, and were without any past history of neck or back injuries, spine surgeries, or neurological disorders. The lack of any spinal cord compression of the cervical spine was confirmed by MRI in all subjects. The study was approved by the local ethical review board, and written informed consent was obtained from each subject.

2.2. Study design

DTI parameters were determined in all 36 subjects at six intervertebral space levels. DTI parameters were compared between different CSC levels and between different age groups.

2.3. Image acquisition

Imaging was performed using a 3.0 MRI system (Signa HDxt, GE Healthcare, Waukesha, WI, USA) with a maximum gradient strength of 40 mT/m and an 8-channel NV-full neck coil (GE Healthcare, Waukesha, WI, USA). The head of the patient was fixed to the table using padding and a strap. Patients were asked to avoid swallowing during image acquisition. The imaging protocol began with the acquisition of a coronal T2-weighted preview, then a sagittal T2-weighted fast spin echo (FSE) sequence [field of view 240 mm × 240 mm; image matrix 320 × 224; section thickness 3 mm; repetition time/echo time (TR/TE) 3200 ms/121 ms] and a sagittal T1-weighted flair sequence (field of view 240 mm × 240 mm; image matrix 320 × 224; section thickness 3 mm; TR/TE 2698 ms/25.8 ms). A sequence of FSE, axial, T2-weighted images (field of view 180 mm × 180 mm; image matrix 288 × 224; section thickness 4 mm; TR/TE 3200 ms/121 ms) was obtained throughout the cervical spine cord (C1-T1). Subsequently, a sequence of axial sensitivity-encoding echo-planar DTI (field of view 240 mm × 240 mm; image matrix 130 × 128; 29 sections, 4.0 mm thick; TR/TE 8000 ms/87.6 ms; gradient directions, 15; and b values, 0 and 1000 s/mm^2) was obtained at C1-T1. The acquisition time of DTI was 5 min per participant.

2.4. Image processing

Images were analyzed using the Functool software 9.4 (GE Healthcare, Waukesha, WI, USA). Before performing tensor estimation, a GE correction procedure was applied to the DTI dataset to correct distortions related to eddy currents induced by the large diffusion-sensitizing gradients. Mean values of MD and FA were measured at six intervertebral levels (C1/C2, C2/C3, C3/C4, C4/C5, C5/C6 and C6/C7). The cervical cord was divided into three segmental groups: upper cord (C1/C2 and C2/C3 levels), middle cord (C3/C4 and C4/C5 levels), and lower cord (C5/C6 and C6/C7 levels) (Fig. 1).

2.5. Regions of interest

MD and FA were measured at six levels (C1/C2-C6/C7) of the CSC. The regions of interest (ROI) were drawn manually to set the spinal cord at the most accurate axial b0 image, which matched the size of the transverse spinal cord. ROIs for the WM (VF, LF, DF) and GM were traced manually, as previously described [15] (Fig. 2). The ROI-based measurement has been shown to be valuable and reproducible for the measurements of DTI parameters [16,17].

Thus, eight ROIs were defined at each of the six levels, for a total of 48 (12 DV, 12 LF, 12 VF, and 12 GM) ROIs in each subject. FA and MD were measured at each of these 48 ROIs. The measurements from the both sides of WM funiculi and GM were averaged, and the mean values were used for analysis, as previously reported [1]. The tracing of the ROIs was performed to exclude at least two voxels outside the cord, thereby minimizing the risk of partial volume effects due to the cerebrospinal fluid (CSF).

2.6. Statistical analysis

Data were analyzed using SPSS 18.0 (SPSS Inc., Chicago, IL, USA). Continuous data are reported as means ± standard deviation (SD). DTI parameters from different sides, different segments and different age groups were compared using one-way analysis of variance (ANOVA) with the Student–Newman–Keuls (SNK) post hoc test. Generalized linear models (GLM) were used for analyzing the interaction effects between segments and age. Linear regression was used to test for correlations between age and DTI parameters. P-values <0.05 were considered significant.

3. Results

3.1. Subjects' characteristics

Table 1 shows the subjects' characteristics. All subjects were healthy Han individuals, including 22 men and 14 women. There was no difference in sex distribution across the groups. Mean age was 51.3 years (range: 20–77 years). All age groups contained 5–7 subjects.

3.2. DTI parameters between the GM and WM

Table 2 shows that the MD values were higher in the WM compared with the GM (VF: 1.067 ± 0.049; LF: 1.092 ± 0.067; DF: 1.311 ± 0.112 vs. GM: 1.032 ± 0.058; all P < 0.05). The same was observed for FA values (VF: 0.715 ± 0.037; LF: 0.793 ± 0.04; DF: 0.711 ± 0.086 vs. 0.589 ± 0.039; all P < 0.05).

3.3. DTI parameters according to the CSC segment

Table 3 and Fig. 3A and B shows that MD and FA values were lower in the WM of the lower CSC compared with the upper CSC (all P < 0.05). In addition, MD in VF, FA in LF and MD in DF were lower in the WM of the lower CSC compared with the middle CSC. No difference was observed in the GM.

Table 1
Subjects' characteristics (n = 36).

Group	Age (years)	Males	Females	Total	Mean age
A	20–30	3	2	5	24.60 ± 3.36
B	30–40	3	3	6	35.83 ± 2.79
C	40–50	3	2	5	45.40 ± 2.88
D	50–60	4	3	7	54.57 ± 2.88
E	60–70	5	2	7	69.00 ± 2.83
F	>70	4	2	6	73.17 ± 2.40