Structural and hemodynamic mouse spinal cord maturation assessed by high resolution diffusion tensor imaging (DTI) and arterial spin labeling (ASL).

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Introduction

Postnatal maturation of the spine has been described [1,2] and is marked by the ossification process and by changes in the shape of the vertebrae, discs and bone marrow. However, little has been published on the early organization and maturation of the spinal cord gray and white matters although they are an important factor for the sensory-motor development. In this work, we proposed to investigate these structures with an approach based on the combined use of *in vivo* high resolution diffusion and ASL-based perfusion MRI. Follow-up of mice from weanling (3 weeks) to young adult period (7 weeks) have been performed as a preliminary step for feasibility and sensitivity studies. The capability of measuring structural and hemodynamic developmental changes in spinal cord (SC) should enhance our knowledge of the normal spinal cord maturation and help as a basis for understanding atypical spine development and spine diseases.

Materials and Methods

Experiments were performed on anaesthetized C57BL/6J mice (n=3), on an 11.75T vertical Bruker system, using a 2-cm diameter transmitting/receiving birdcage coil. Both diffusion and perfusion experiments were performed using a 4-shots spin-echo EPI sequence [3] with: 128x128 acquisition matrix, 1.28x1.28 cm² field-of-view and 0.75-mm slice thickness. DTI acquisition parameters were: TE/TR 15.25/4500 ms, Δ/δ 6.82/2.3 ms, 6 diffusion encoding directions, b={0, 700} s/mm², 9 axial slices covering the overall cervical segments, 18 signal averaging and total acquisition time 38 minutes. DTI metrics (diffusivity, fractional anisotropy (FA), eigenvector) were calculated for each segment (C1-C7). Spinal cord blood flow (SCBF) measurements were obtained with a presaturated Flow sensitive Alternating Inversion Recovery (presat-FAIR) sequence adapted to the mouse SC investigation [4]. The acquisition parameters were: TE 10.7 ms, recovery time (τ) 3.5 s, inversion time (TI) 1.3 s, 1 axial slice (C3), 32 ΔM signal averaging and total acquisition time 20 minutes. Absolute SCBF values were obtained by solving the presat-FAIR equation extended to short coil [5]: $\Delta M = 2M_0.\alpha_0.(SCBF/\lambda).[(e^{-TI.R1^{app}} - e^{-TI.R1^a}) / (R1^a - R1^{app})]$ where λ is the water blood/tissue partition coefficient (0.9 ml/g) and $R1^a$ the longitudinal relaxation rate of arterial blood ($1/R1^a = 1/2.1\ s^{-1}$). M_0 (equilibrium magnetization), α_0 (inversion efficiency) and $R1^{app}$ (SC tissue apparent longitudinal relaxation rate) were determined with a slice selective inversion recovery prescan. Mice were followed every week, during 5 weeks. Minor and major diameters of the spinal cord (~ellipsoid) and mean length of the segments (C1-C7) were additionally derived from anatomic images at each MR examination. Spinal cord morphometrics and MR metrics were then compared to adulthood observations (15 weeks).

Results

Sagittal section, axial FA and SCBF maps at 3 different ages (3, 7 and 15 weeks) are shown on figure 1; the in-plane resolution for both diffusion and perfusion images was of 100x100 µm². From week 3 to week 7, all metrics were observed to continuously vary: FA values in white matter (WM) gradually increase from 0.72±0.04 to 0.79±0.04, FA in gray matter (GM) slightly increase from 0.25±0.02 to 0.29±0.02, SCBF values in GM decrease from 360±25 to 300±25 mL/100g/min and SCBF in WM vary from 116±14 to 109±16 mL/100g/min. Measurements obtained in week 7 were similar to those obtained in week 15. Morphometrics (SC diameters, mean segment length), as well as gray/white matter structural and hemodynamic metrics, are summarized on figure 2 for the weanling (3 weeks), young adult (7 weeks) and adult (15 weeks) periods.

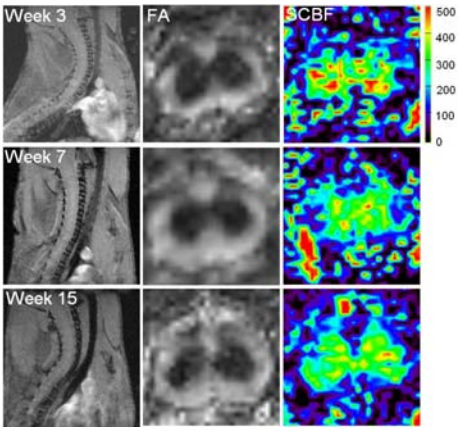

Fig.1 – Sagittal anatomic images (left), FA (middle) and SCBF (in mL/100g/min, right) maps at weanling (top), young adult (middle) and adulthood (bottom) periods.

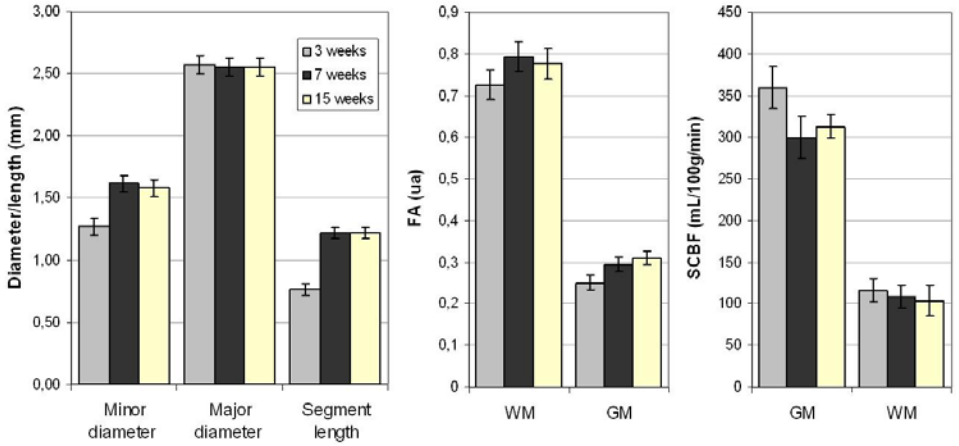

Fig. 2 –Morphometrics and MR metrics (FA, SCBF) measured on healthy mice aged of 3, 7 and 15 weeks.

Discussion

The development of the brain has already been relatively well-depicted [6] whereas little has been published on developmental spinal cord. This study reports a preliminary investigation on changes of diffusion and perfusion patterns accompanying normal SC development from weanling to young adult age. High-resolution images have been obtained and sensitivity was sufficient to observe evolution of the metrics with time. Although non-significantly different due to the small number of animals currently included in the study (n=3), the structural and hemodynamic variations observed in the SC are in agreement with recent reports on the brain growth pattern: FA increases potentially in relation with myelination process [7] and SCBF decreases, potentially in relation with less "fuel" demand during myelination [8].
Next studies will investigate postnatal development in the first 3 weeks, which is probably the most dynamic phase of development, and the number of animal will be increased so as to constitute a normative database of MR maturation patterns.

Conclusion

This work was a preliminary investigation and a prerequisite for further diffusion and perfusion spinal cord studies. The combination of both diffusion and perfusion methods may foster a better understanding of the normal spinal cord (SC) maturation and offer new perspectives to understand pathologic disorders.

References

[1] Byrd, Neurosurg Clin N Am (2007); [2] Dias, Neurosurg Clin N Am (2007); [3] Callot *et al.*, Magn Reson Mater Phy, Magma (2007); [4] Duhamel *et al.,* Magn Res Med (2008)*;* [5] Pell *et al.,* Mag Res Med (1999)*;* [6] Garcl, Springer-Verlag (2004), [7] Chahboune et al., NMR biomed (2007); [8] Biagi et al., JMRI (2007).