A diffusion and perfusion EPI-based MR protocol for the characterization of rodent spinal cord diseases.

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Introduction

Correct diagnosis of SC pathology would, in theory, requires the entire spine to be imaged, anatomical views, as well as diffusion-weighted images and perfusion measurements early in the course of the pathology to document white matter integrity and potential ischemia. So far, such a characterization has not been possible, because of the lack of SC perfusion measurement method as well as the too long DTI (diffusion tensor imaging) acquisition scan-time required to collect spatially resolved images with good signal-to-noise ratio in mouse models.

In this study, we propose to perform Diffusion Tensor Imaging (DTI) and quantitative perfusion imaging (PI) of the mouse spinal cord, with an in-plane resolution of 133x133 µm² and a total scan-time of 90 minutes. Imaging was performed at the cervical level, where spinal cord injury, infarction or tumor may easily occur. DTI covers the overall cervical segments and perfusion (based on arterial spin labeling (ASL)) was performed at 2 different levels, mimicking the possibility of studying the perfusion state up and downstream a pathology.

Materials and Methods

C57BL/6J mice (25-30 g) were anaesthetized with an isoflurane+air mixture and placed in a transmitting/receiving birdcage coil (diameter 2 cm, homogeneous length 3 cm). All experiments were performed on an 11.75T vertical Bruker Avance 500 WB system, in agreement with the guide for care and use of laboratory animals. Both DTI and PI experiments were performed using a 4-shots spin-echo EPI sequence [1], a 128x128 acquisition matrix, 1.7x1.7 cm² field-of-view, and 0.75-mm slice thickness. DTI acquisition parameters were as follow: TE/TR 14.25/500 ms, Δ/δ 6.82/2.3 ms, 6 diffusion encoding directions, b={0, 700} s/mm², 6 axial slices (fig. 1), 8 signal averaging (NEX), total acquisition time 11.2 minutes. DTI metrics (diffusivity, fractional anisotropy (FA), eigenvector) and fiber tracking were analyzed with BrainVisa software. Spinal cord blood flow (SCBF) measurements were obtained with a presaturated Flow sensitive Alternating Inversion Recovery (presat-FAIR) experiment adapted to the mouse SC investigation [2].The acquisition parameters were: TE 10.6ms, recovery time (τ) 3.5s, inversion time (TI) 1.3 s, 32 presat-FAIR signal (ΔM) averaging. Absolute SCBF values were obtained by solving the presat-FAIR equation [3] $\Delta M = 2M_0.\alpha_0.(SCBF/\lambda).[(e^{-TI.R1^{app}} - e^{-TI.R1^a}) / (R1^a - R1^{app})]$, where λ is the water blood/tissue partition coefficient (0.9 ml/g) and $R1^a$ the longitudinal relaxation rate of arterial blood ($1/R1^a = 1/2.1\ s^{-1}$). The M_0 (equilibrium magnetization), α_0 (inversion efficiency) and $R1^{app}$ (SC tissue apparent longitudinal relaxation rate) parameters were determined with a slice selective inversion recovery prescan. The acquisition time for the perfusion investigation of the two cervical segments was 60 minutes.

Results

In-plane resolutions of 133x133 µm² were obtained for both PI and DTI images. The total scan time needed to perform the entire protocol (localizer, EPI adjustments, T1-weighted, perfusion and diffusion data collection) was equal to 90 minutes. Examples of T_1-w images, SCBF, diffusivity and eigenvector maps, as well as fiber tracking reconstructions, are given on figure 2. Absolute perfusion values, as well as mean diffusivities or FA values can be derived from these maps. For instance, in a ROI that covers the overall gray matter of the C5 segment, SCBF value was found equal to (345±80) mL/100g/min, longitudinal and transversal diffusivities equal to $(1.09\pm0.15).10^{-3}$ and $(0.94\pm0.14).10^{-3}$mm²/s and FA (0.24±0.07). In white matter, diffusivities were evaluated to $(1.95\pm0.11).10^{-3}$ and $(0.40\pm0.06).10^{-3}$ mm²/s and FA to (0.86±0.09).

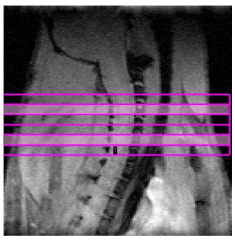

Fig.1 – Sagittal scout, representing the 6 DTI and 2 PI (shaded) slice locations.

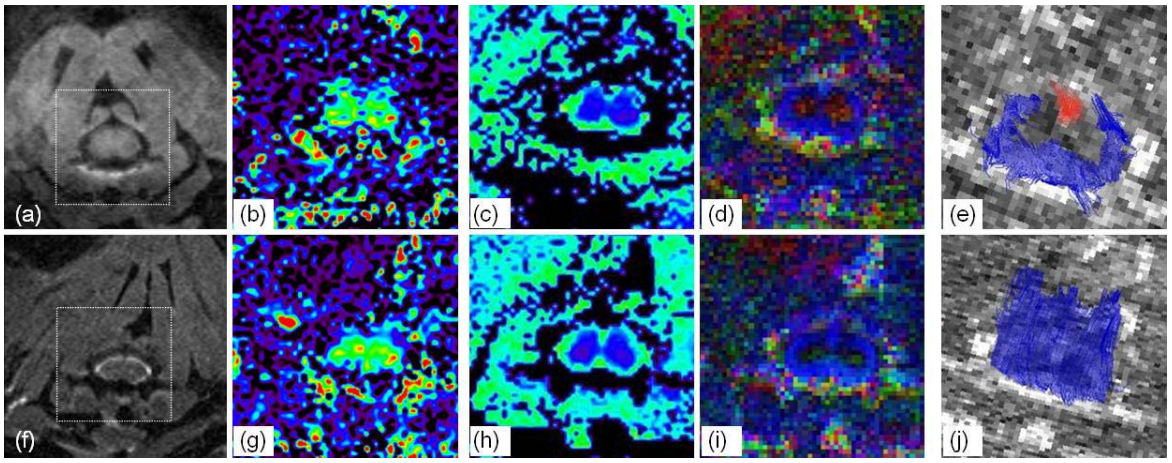

Fig. 2 – DTI and PI at the level of C3 (top) and C5 (bottom). (a,f) T1-w images, (b,g) SCBF, (c,h) diffusivity ($\lambda_{//}$) and (d,i) eigenvector maps. (e,j) fiber tracking.

Discussion

Diffusion tensor imaging gives morphological and structural information that are now widely used to assess the integrity of the tissue, whereas perfusion imaging gives regional and quantitative hemodynamic information that help to characterize the adequacy of the tissue blood supply. The combination of both methods has already proved useful in cerebral vascular accident where perfusion-diffusion mismatch represents the tissue at risk. In spinal cord pathology, such a combination may also help to greatly improve the diagnosis, allowing the detection of functional impairments, white matter tract disruption, deficient tissue blood supply, and extension or evolution of the lesion from the primary site. Moreover, this combined protocol may also play a role in the evaluation of functional recovery or to study regenerative therapeutic strategy as revascularization has already been described to precede tissue repair and nerve regeneration in the dorsal columns [4].

In this work, both DTI and PI acquisitions lead to relevant and reliable measurements, within acceptable scan time (90 minutes) with in-ROI standard deviations in the order of 15 and 25% respectively. These variations should permit to detect and follow pathological tissue changes. This has to be further investigated by applying the protocol to pathological cases.

Conclusion

The purpose of this work was to give an experimental MR procedure that may be used to better characterize spinal cord diseases in which structural tissue damage and deficient blood supply are involved. Our combined diffusion/perfusion EPI protocol provided good images quality and functional measurements of the mouse cervical spinal cord within 90 minutes. This DTI-PI protocol may open new and great perspectives in the pathological description of rodent (and eventually human) SC diseases.

References

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