Vascular Alterations and Recruitment in Spinal Cord Injury Revealed by Multislice Arterial Spin Labeling (ASL) Perfusion Imaging

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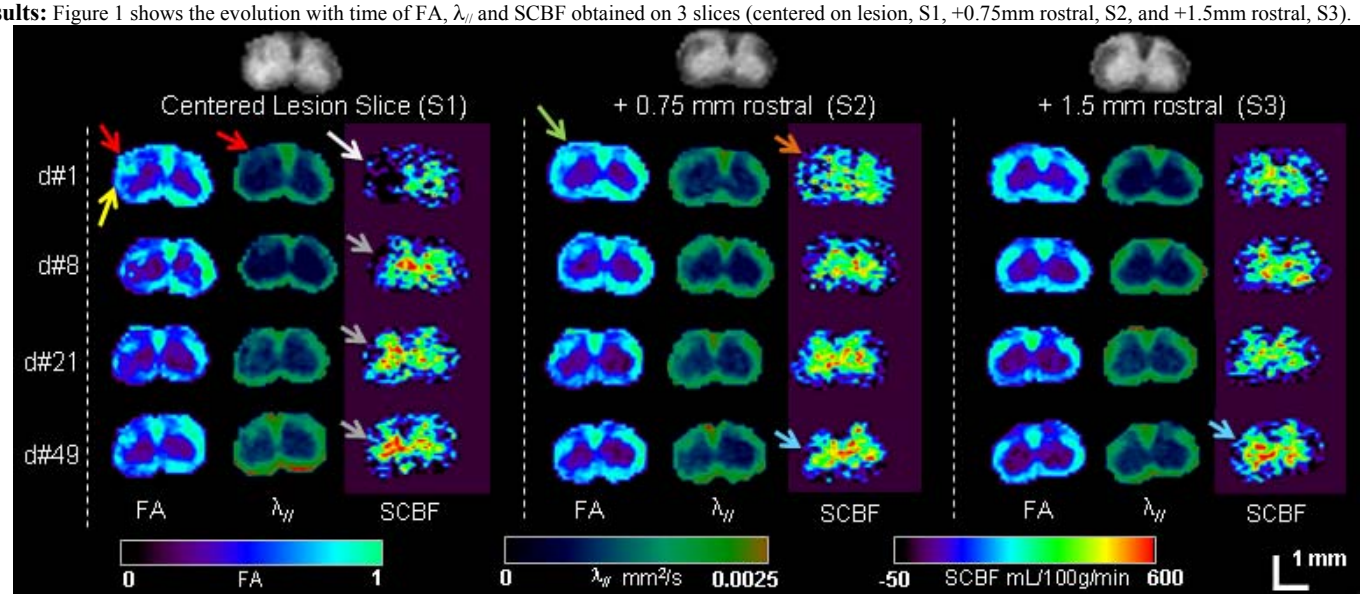
Introduction: In spinal cord injury (SCI) investigation, the combination of diffusion tensor imaging (DTI) and perfusion imaging has the potential to be a useful tool in the detection of functional impairments, white matter tract disruption and deficient tissue blood supply, but also in the evaluation of functional recovery and tissue repair[1]. Whereas multislice DTI is widely used for SCI models investigation, allowing then a large volume coverage per imaging session, assessment of mouse SC blood flow (SCBF) by MRI, which has recently been demonstrated to be feasible[2,3], currently relies on the use of a single slice arterial spin labeling (ASL) technique (presaturated FAIR[4]). To better characterize the lesion (regional extension), and to be able to detect potential secondary injury, it would be important to match perfusion with multislice DTI. Multislice ASL in a single imaging session was achieved by the modification of the original presat-FAIR sequence to a presat-FAIR-QUIPSSII[5] sequence, optimized to mouse SC. Multislice DTI and ASL were then applied in a follow-up study performed over time on mice having received SCI (compression) at the cervical level. Resulting DTI metrics and SCBF values were additionally correlated to functional assessment tests.

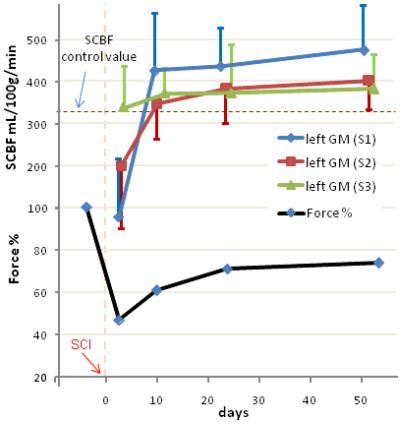
Methods: ***SCI model and functional assessment:*** Experiments were performed on C57Bl/6J mice (age 10 weeks, 20g). The spinal cord compression was induced by inflation (10 mm^3, 2.5 bar, 10s duration) of a balloon connected to a catheter and inserted at the C4 epidural space of the SC. Following the compression, mice suffered from left fore-limb paralysis. Grasping test, performed with a Bioseb® apparatus (incline grid connected to a strength gauge), measured the developed fore-limb force.

MR Imaging: Experiments were performed on an 11.75T vertical MR system (Bruker, AV 500WB) with a transmitter/receiver volume coil (∅ 2cm, length 3cm). A 4-shot SE-EPI sequence was used for high resolution imaging (100x100μm^2, slice thickness 0.75mm). DTI was obtained using a standard Stejskal-Tanner sequence with parameters described in [6]. Multislice (4 slices) perfusion imaging was obtained with a presat-FAIR-QUIPSSII sequence, for which timing parameters were previously optimized on healthy mice. Unlike in human studies, the global inversion pulse labeled almost all the blood, making then possible the use of long inversion time (TI1=1.0s), which is beneficial for SNR considerations[5]. The delay ΔTI after the saturation was optimized to 0.2s. This value ensured that the entire tagged bolus released from the tagging region was delivered to the imaging slices at time TI2 (TI2=TI1+ΔTI). Under these conditions the following equation applied for quantitative SCBF values measurements[5]: $\Delta M = 2M_b^0/\lambda.SCBF.\alpha.e^{-TI2.R1app}/(R_{1app}-R_{1a}).(e^{-TI1.(R1a-R1app)}-1)$, with λ =0.9 ml/g (water blood/tissue partition coefficient) and R_{1a}=1/2.1 s^{-1} (blood longitudinal relaxation rate). M_b^0 (equilibrium magnetization), α (inversion efficiency) and R_{1app} (SC tissue apparent longitudinal relaxation rate) were determined with a slice-selective inversion recovery prescan[3]. Magnetization difference ΔM was averaged during 45 minutes leading to a maximum total experimental time (EPI-adjustment, DTI and ASL) of 2 hours. Force tests, DTI metrics (FA, $\lambda_{//}$, $\lambda_{\perp}$) and absolute SCBF values were evaluated 1, 8, 21 and 49 days after the SCI.

Results: Figure 1 shows the evolution with time of FA, $\lambda_{//}$ and SCBF obtained on 3 slices (centered on lesion, S1, +0.75mm rostral, S2, and +1.5mm rostral, S3).



One day post-injury, the lesion was clearly identified on slice S1 in the left lateral white matter (lWM, low FA values, yellow arrow) and left dorsal gray matter (dGM, red arrows). Lesion in left lWM and dGM is also visible on the +0.75mm rostral slice (green arrow) whereas the +1.5mm rostral slice presents normal pattern. With time, the FA values in left lWM (S1) slightly increased whereas a pronounced increase of $\lambda_{//}$ values in total left GM for both S1 and S2 slices can be noticed. At day#1, strong perfusion alteration could be seen in S1 on the total left GM (white arrow). Right GM was also affected and reduced SCBF values were observed. The vascular alterations propagated to S2 slice GM (orange arrow) whereas for S3, SCBF values were similar to control values[2,3] (see graph). After the initial drop, SCBF values of S1 clearly increased with time, revealing an area of very high perfusion around the lesion location (gray arrows). Similar increase with time was also observed for S2 and S3 (blue arrows). The graph reports the evolution of total left GM SCBF values for the 3 slices along with the force tests results expressed in percent of the initial developed force. A good correlation (R^2>0.85) was measured between the evolution of the force and the S1, S2 GM SCBF values.



Discussion: Vascular modifications arising in the days following the SCI were clearly observed and accurately quantified. In particular, multislice quantitative perfusion imaging permitted to show that after an initial drop, GM SCBF significantly and progressively increased around the lesion sites in S1 and S2, but also rostrally (S3) whereas no initial perfusion deficit was noticed. In the mean time, a significant increase of the fore-limbs developed-force was measured. We hypothesized the observed large area of vascular recruitment being part of the process of endogenous tissue repair which led to progressive functional recovery.

References**:** *[1] Xiaowei et al., Spinal Cord (2006). [2,3] Duhamel et al., MRM (2008, 2009) [4]Pell et al., MRM (1999) [5]Wong et al.,MRM (1998) [6] Callot et al, NMR in biomed (2008)*