Visualization of Vascular Modifications Occuring during Spinal Cord Injury (SCI) Recovery using High-Resolution Arterial Spin Labeling (ASL)

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Introduction: Diffusion and perfusion MRI might be among the techniques of choice for the characterization of spinal cord injury (SCI). The combination of the two modalities should allow the detection of functional impairments, white matter tract disruption, deficient tissue blood supply, as well as a better characterization of the extension of the lesion from the primary site of injury. This combination may additionally play an important role in the evaluation of functional recovery or regenerative therapeutic strategy [1]. Nowadays, diffusion tensor imaging (DTI) is a common tool for SCI investigation, whereas the possibility of assessing SC perfusion by MRI has only been demonstrated recently with the use of a pulsed arterial spin labeling (PASL) technique [2]. Vascular aspects (tissue blood supply deficiency, reperfusion...) of SCI have therefore not been investigated by MRI so far. In this work we present a follow-up study with high resolution DTI and perfusion-ASL MRI performed over time on mice which have received a spinal cord injury (compression) at the cervical level (C2). The quantitative MRI parameters derived from these studies were additionally correlated to functional assessment test (grasping test).

Methods:

SCI model: Experiments were performed in anesthetized mice (C57Bl/6J, age 14 weeks, 25g). A balloon connected to an air-filled syringe was inserted between the C1-C2 vertebras and advanced caudally, so that the center of the balloon rested at the C2 epidural space of the spinal cord. The compression was induced without laminectomy by a rapid inflation of the balloon (volume 10 mm^3, pressure 2.5 bar, duration 10s). Following the compression, mice suffered from left fore-limb paralysis.

MR Imaging: Experiments were performed on an 11.75T vertical MR system (Bruker, AV 500WB). High sensitivity was obtained by the use of a small transmitter/receiver volumic coil (∅ 2cm, length 3cm), well adapted to the mouse SC imaging. An optimized 4-shot SE-EPI sequence [3] (matrix 128x128, FOV=1.5x1.5cm^2, slice thickness 0.5mm) was used for all the images acquisition. High-resolution DTI imaging was obtained using a standard Stejskal-Tanner sequence (TR/TE=4500/15.2 ms, δ/Δ =2.3 ms/6.8 ms, b-values {0,700} s/mm^2, 7 slices and 6 diffusion-encoding directions, NEX=15, acq. time=30 min) [4]. High-resolution absolute quantitative perfusion imaging was obtained by PASL, using a presaturated-FAIR sequence [5] adapted to SC [2] (TE=10.7ms, inversion time TI=1.3s, recovery time τ=3.5s, NEX=40, acq. time=40m min).

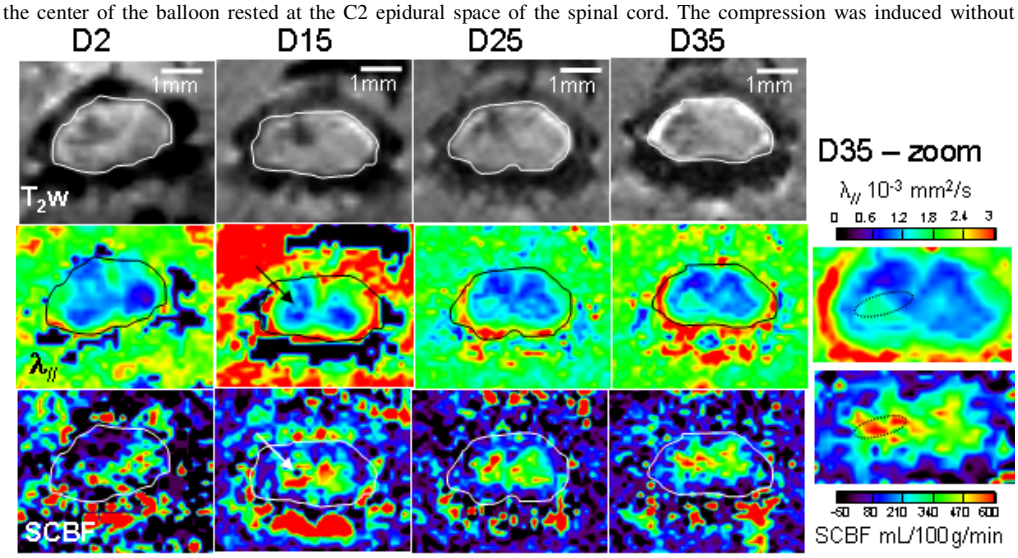

Figure 1: Diffusion/Perfusion imaging of a mouse SCI model

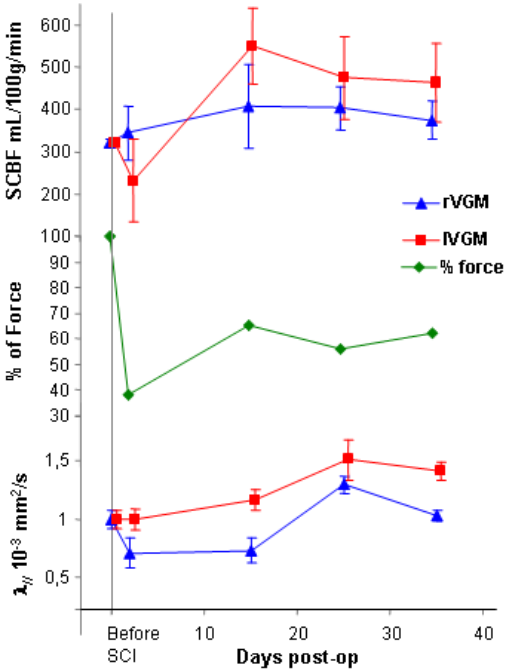

Figure 2: MR and functional parameters follow-up

Functional assessment: Grasping test was performed before every MR exam using a Bioseb® apparatus (incline grid connected to a strength gauge) to measure the developed fore-limb force (5 trials repeated every 30 seconds). Force tests, DTI metrics and absolute SCBF values were evaluated at 2, 15, 25 and 35 days after the SC injury.

Results: Figure 1 shows T_{2w} images, $\lambda_{//}$ and SCBF maps obtained for the 4 investigated days. $\lambda_{//}$ represents the mean diffusivity along the principal axis (spinal cord axis). The lesion resulting from the SCI is clearly visible on T_{2w} images and is characterized by hyposignal in the left dorsal and ventral horns GM (dGM and vGM) and upper left WM. At day 2, the lesion is characterized by abnormal $\lambda_{//}$ in upper left WM, heterogeneous diffusivities in the GM and very low perfusion values in left GM. At day 15, $\lambda_{//}$ map shows abnormal low values in upper left WM as well as a localized region of high $\lambda_{//}$ in the vGM (arrow). The high-$\lambda_{//}$ area pointed by the arrow corresponds, on the SCBF map, to a region surrounded by very high perfusion values. At days 25 and 35, this high-$\lambda_{//}$/very-high-SCBF "effect" in left vGM is enhanced (zoom, D35). The evolution with time of the quantitative DTI metrics and absolute SCBF values confirm the qualitative information seen on the maps (figure2, ROIs selected in left and right vGM). After the dramatic drop, 2 days post-injury, a recovery of the perfusion in the left vGM can be observed with time (red curves, 232±98mL/100g/min at day 2, and 463±93 mL/100g/min at day 35). The same dynamic was obtained for the percentage of developed force (green curve, 38% at day 2, 62% at day 25). An increase of $\lambda_{//}$ is also observed ($\lambda_{//}$=0.99±0.08.10^{-3} mm^2/s at day 2 and $\lambda_{//}$=1.41±0.08.10^{-3} mm^2/s at day 35).

Discussion: High resolution SC DTI and perfusion images obtained in this study allowed to precisely characterizing the lesion affecting upper left WM and vGM after SCI. The strong vascular effects, observed and characterized by local very high SCBF values in vGM, at days 15, 25 and 35 might be linked to the slow functional recovery (increase of the percentage of fore-limbs developed-force). To our knowledge, this study is the first MR investigation that demonstrates the presence and the importance of a vascular role in SCI. In this model, the variation of the perfusion values were accurately detected and measured with the presat-FAIR technique, highlighting then the potentiality of ASL in SCI characterization. In the next future, additional histologic evaluation will be performed, in order to verify evolution the presence of vascular recruitment (suspected by high perfusion values in SCBF maps) and to understand the tissue restructuration (characterized by high $\lambda_{//}$ values) occurring in the gray matter.

References: *[1] Xiaowei et al., Spinal Cord (2006). [2] Duhamel et al., MRM (2008) [3] Callot et al., Magma (2007) [4] Callot et al., NMR Biomed (2008) [5] Pell et al, MRM (1999)*