White matter reorganization and functional recovery following stroke in adult rat

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Purpose:
The brain appears to have the capacity, after stroke, to compensate the tissue damage in order to permit functional recovery. Functional improvement is thought to be due to adaptation of neuronal networks to generate and to use new connections for compensation of the lost function represented by the neurons damaged by stroke. For this reason, we have investigated the correlation between the functional recovery and the structural reorganisation after stroke in adult rats, observed with fMRI and diffusion spectrum imaging (DSI), respectively. DSI protocol was applied in vivo for an optimal fiber tracking analysis including distinction and assessment of crossing fibers.

Materials and methods:
A 60 min transient occlusion of the middle cerebral artery was induced in male Wistar rats (n=10). Four healthy rats were studied additionally for stability and reproducibility of fiber tracking results. In all animals, DSI experiments were acquired at 11.7T, before, one and four weeks after stroke. fMRI was recorded before and five weeks after stroke. For DSI data, twelve DTI-EPI scans were acquired with different b-values and directions to achieve a total of 203 diffusion gradient vectors with following parameters: four shot EPI scans, TR/TE = 3000/37.9 ms, resolution = 0.2x0.2x0.5 mm^3, Δ/δ = 25/5 ms. The fMRI paradigm was electrical forepaw stimulation, consisting of five blocks composed of 45 s resting period and 15 s stimulation period and resulting in a total of 115 images. A single-shot gradient-echo EPI sequence was used with the following parameters: TR/TE = 2840/17.5 ms, resolution = 0.3x0.3x1.2 mm^3. After the last MRI acquisition, rats were sacrificed and brains prepared for luxol fast blue tissue staining to observe myelin.

Results:
At 4 weeks after stroke, an area characterized by a high fraction of anisotropy (FA) value was observed located between the ischemic territory and lateral ventricle (approximately, bregma -0.8 to -1.4), in all stroke animals. In agreement with earlier reports (Jiang et al., 2006 and Li et al., 2009), this area is interpreted as white matter tissue based on the positive myelin staining. At 5 weeks after stroke, all ischemic rats, except one animal, showed a BOLD signal in the ischemic cortex S1 (figure1.A). Using the area characterized by higher FA as seeding zone for tractography, a connection between both hemispheres via the corpus callosum was observed (figure 1.B, green arrow). In the animal without functional BOLD recovery, this transhemispheric fiber connection was missing (figure 1.B, white arrow).

Conclusion:
These observations indicate that the functional recovery after transient stroke could be linked to the white matter reorganization as previously proposed (Jiang et al., 2006 and Li et al., 2009) but also, as suggested by our results, maybe to the presence of this fiber connection between both hemispheres. The results of this investigation underline the importance and suitability of fiber tracking to distinguish early structural correlates of functional deficit and recovery. It allows new insights into functionally relevant restructuring and re-organization of the brain in response to focal lesions.

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References: Jiang et al., Neuroimage, 2006; 32:1080-9
Li et al., Stroke, 2009; 40:936-41

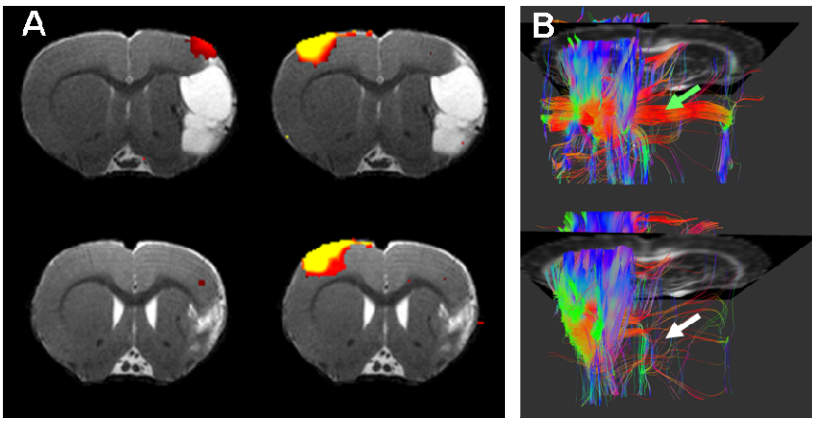

Figure 1 : Representations of the BOLD signal observed in two stroke rats (one rat per line) following of the stimulation of the right (right column) and the left (left column) forepaw at 5 weeks after stroke (A) and the tractography results of these rats at 4 weeks after stroke (B). The fiber-tracking permitted to visualize the presence (green arrow) or the absence (white arrow) of the transhemispheric fiber connection.