DIFFUSION SPECTRUM IMAGING AFTER STROKE SHOWS STRUCTURAL CHANGES IN THE CONTRA-LATERAL MOTOR NETWORK CORRELATING WITH FUNCTIONAL RECOVERY.

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Introduction. There is growing interest in understanding the role of the non-injured contra-lateral hemisphere in stroke recovery. In the experimental field, histological evidence has been reported that structural changes occur in the contra-lateral connectivity[1] and circuits[2] during stroke recovery. In humans, some recent imaging studies indicated that contra-lateral sub-cortical pathways[7] and functional and structural cortical networks[8, 9] are remodeling after stroke. Structural changes in the contra-lateral networks, however, have never been correlated to clinical recovery in patients.

To determine the importance of the contra-lateral structural changes in post-stroke recovery, we selected a population of patients with motor deficits after stroke affecting the motor cortex and/or sub-cortical motor white matter. We explored i) the presence of Generalized Fractional Anisotropy[3] (GFA) changes indicating structural alterations in the motor network of patients' contra-lateral hemisphere as well as their longitudinal evolution ii) the correlation of GFA changes with patients' clinical scores, stroke size and demographics data iii) and a predictive model.

Methods. 12 patients (Age: 58.4±17; F:M=7:5) underwent 3 serial DSI scans (i) within 1 week (tp1), (ii) after 1 month (± 1 week, tp2) and (iii) 6 months (± 15 days, tp3) after stroke. Patients also underwent clinical assessments (NIHSS, FIM and RANKIN scores) at each time point. 12 healthy subjects (Age: 57.2±14.5; F:M=7:5) had two serial DSI scans within a 1 month interval (± 1 week, tp1c and tp2c). All DSI measurements (TR/TE=6600/138 ms, FoV=212x212 mm, 34 slices, 2.2x2.2x3 mm resolution, 258 diffusion directions, b=8000 s/mm^2) were performed at 3T (Magnetom Trio a Tim System, Siemens, Erlangen, Germany) using a 32 channel head coil. Orientation distribution functions were reconstructed using Diffusion Toolkit (*www.trackvis.org/dtk*). Fiber-tracking was performed using in-house software based on the classical streamline algorithm. High-resolution MPRAGE images (TR/TE=2400/3 ms, voxel=1x1x1.2 mm, FoV=256x240 mm) were acquired for anatomical reference and linearly registered to T2 images (TR/TE=3000/84 ms, voxel=0.5x0.5x3 mm). Subsequently, non-linear registration was used to register T2 to diffusion space in order to reduce EPI spatial distortions. All registrations were performed using FSL (*www.fmrib.ox.ac.uk/fsl*). Primary and secondary motor cortical regions were mapped from MPRAGEs images using Freesurfer (*surfer.nmr.mgh.harvard.edu*) to define intra- and inter-hemispheric connections using DSI-based tractography. The connectivity between two cortical areas was measured using the mean GFA along the tracts. Stroke volumes were evaluated using in-house software based on the MPRAGEs images. Statistical analysis was performed using multivariate ANOVA to compare GFA in all motor connections considering: (i) patients tp1 vs controls and (ii) time-points differences in patients. Using a generalized linear model (GLM), clinical scores, lesion volume and demographic information were used to model GFA changes between time points.
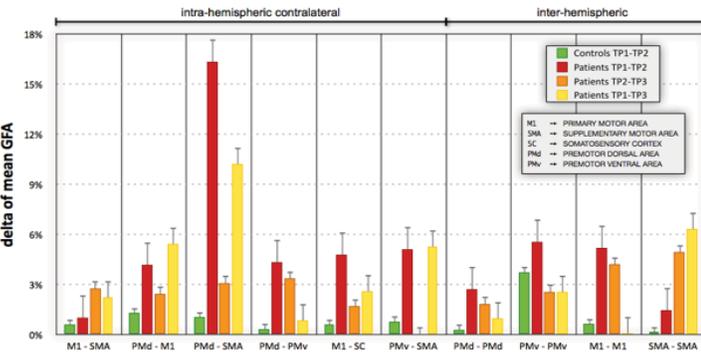

Figure 1: delta of the mean GFA between time-points calculated along the connections between motor areas in patients and controls.

Results. Average patients' stroke size was: 64.3 ± 68.9 cm^3, mean ± SD. The delta of GFA in tp1 and tp2 in the contra-lateral motor connections was significantly different from the delta GFA between tp1c and tp2c (p <0.05) both for intra- and inter-hemispheric motor connections (figure 1). GFA longitudinal changes in the inter-hemispheric motor connections correlated with age (p<0.01), functional scores (NIHSS, p<0.001) and stroke size (p<0.001) and in the intra-hemispheric motor connections with age (p<0.0001). The GLM analysis revealed that, using clinical scores (NIHSS, RANKIN, FIM), stroke size and patients gender, 26 out of 30 temporal GFA evolution combinations (tp1-tp2, tp2-tp3, tp1-tp3) in all investigated connections (s. Fig 1) could be modeled between p ≤ 0.0005 and p ≤ 0.05 .

Discussion and Conclusion. This longitudinal DSI study of stroke patients with motor deficits shows that the contra-lateral motor network undergoes structural changes during recovery of the motor function. Those changes, using the GFA metric, were age dependent (intra- and inter-hemispheric connections), correlated with functional scores (NIHSS) and with stroke size (inter-hemispheric connections), and could be modeled for the majority of investigated connections and time-points differences. Our patients' data confirm that the contra-lateral hemisphere plays an important role in the recovery of the motor function after stroke and suggest that diffusion MRI can provide complementary information to clinical scores. These findings may become particular interesting for outcome prediction and post-stroke rehabilitation.

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