Myelin plasticity does not significantly influence diffusion remodelling of the uninjured motor network after stroke

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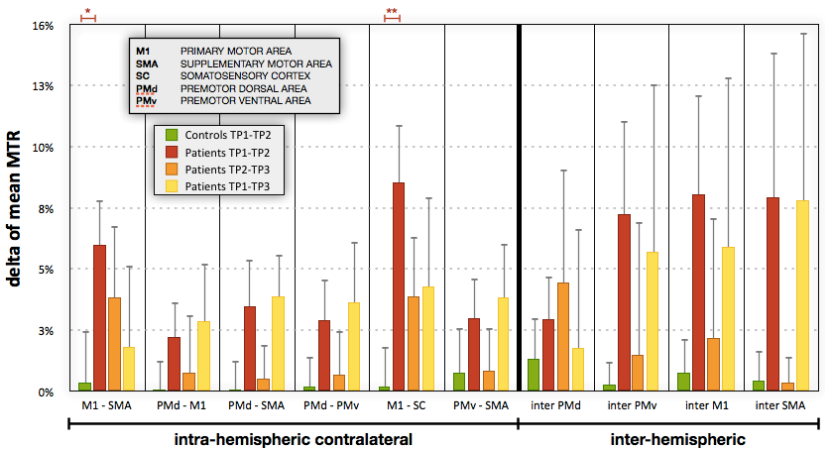
Introduction. Connectivity plasticity in the uninjured hemisphere after stroke has been reported in a number of experimental [1,2] and human [3-5] studies. Recently, we used Diffusion Spectrum Imaging (DSI) to explore longitudinal changes in the contra-lateral motor network of patients who suffered from stroke [6] and we showed that contra-lateral motor tracts changes in Generalized Fractional Anisotropy (GFA) correlated strongly with clinical scores. Furthermore, GFA measured in the acute phase together with a routine motor score and age proved to be strong predictors of motor outcome at six months (r^2=0.96, p=0.0002) [6]. Whether the observed changes in GFA are due to axonal remodeling or myelin plasticity remains however an open issue. GFA is the standard deviation of the diffusion process along different diffusion directions, representing fibre trajectories in tractography reconstructions [7]. Like Fractional Anisotropy, GFA can be influenced by axonal integrity and, to a lesser extent, by the properties of intra-axonal transport and myelin [8]. In this context, we wanted to study the behaviour of the Magnetisation Transfer Ratio (MTR) in the contra-lateral motor network and to correlate it to the longitudinal changes in GFA [6]. The MTR is a semi-quantitative parameter which increases with the content of myelin and the decreasing of water content along axonal fibers.

Methods. 10 patients (Age: 56.1±17.8; female:male=4:6) underwent 3 DSI and 3 MT scans, in the acute phase (within 1 week after the stroke onset, time point 1 or tp1), after 1 (±1 week, tp2) and 6 months (±15 days, tp3) after stroke, respectively. Patients benefitted of clinical assessment (NIHSS, FIM and RANKIN scores) at each time point. Ten healthy subjects (Age: 60.3±12.8; female:male=4:6) benefitted of DSI and MT scans twice within a 1 month interval (±1 week, tp1c and tp2c). DSI scans were performed as follow: TR/TE=6600/138 ms, FoV=212x212 mm, 34 slices, 2.2x2.2x3 mm^3 resolution, 257 diffusion directions, b_{max}=8000 s/mm^2 [6]. MT scans were performed using a multiple-echo Fast Low Angle SHot (FLASH) sequence with (MT) and without (M0) magnetization transfer preparation (TR/TE = 48/23 ms, FoV = 240x256x96, 2x2x2 mm^3 resolution, 8 echoes) as previously described [9]. Reconstruction of the motor network and GFA calculation was performed as in [6]. All measurements were performed at 3 T (Trio a Tim System, Siemens, Erlangen, Germany) using a 32-channel head coil. The following brain regions, and their corresponding connectivity, were considered: primary motor area (M1), secondary motor areas (SMA, PMv and PMd) and primary sensory area (SC). The connections between motor areas in the same hemisphere are named intra-hemispheric and the ones between motor areas and the corpus callosum were considered as inter-hemispheric. The myelin content in the connections between two cortical areas was measured using the ¨magnetisation transfer ration (MTR=M0-MT)/M0*100). Statistical analysis was performed using multivariate ANOVA to compare MTR in intra- and inter-hemispheric motor connections considering: (i) differences in MTR at tp1 and tp2 in patients vs controls, and (ii) longitudinal differences among time-points. Age, gender and the functional scores were used as covariates. Pearson's correlation was computed between deltas of MTR and GFA and between time points (tp1-tp2, tp2-tp3, tp1-tp3) and Bonferroni correction was used to correct for multiple comparisons.



Results. MTR changes in the contra-lesional motor tracts were found in all patients at the 3 time points; MTR changes between tp2 and tp1 differed significantly between patients and controls (see figure) in the M1-SMA (*: p<0.05) and M1-SC (**: p<0.01) connections. No significant differences were observed in patients when comparing the conditions tp1-tp2, tp2-tp3 and tp1-tp3. MTR changes in intra- and inter-hemispheric motor tracts between tp1 and tp2 had small correlation with GFA changes in controls ($R^2 \leq 0.13$, mean = 0.08). In patients, though, the correlations between MTR and GFA changes at tp1-tp2 ($R^2 \leq 0.47$, mean = 0.22), tp2-tp3 ($R^2 \leq 0.61$, mean = 0.22) and tp1-tp3 ($R^2 \leq 0.78$, mean = 0.30) were more pronounced than in controls, but did not reach significance.

Discussion and Conclusion. Our results show significant MTR differences between stroke patients and healthy controls at 1 month after stroke. This points to a remodeling of myelin in the motor network of the uninjured hemisphere. However, no significant correlation was found between MTR and GFA changes pointing to the fact that GFA is most probably originating from axonal remodeling (sprouting and degeneration) in the contra-lateral motor network.

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