Tract-based assessment of the subcortical motor network plasticity after stroke

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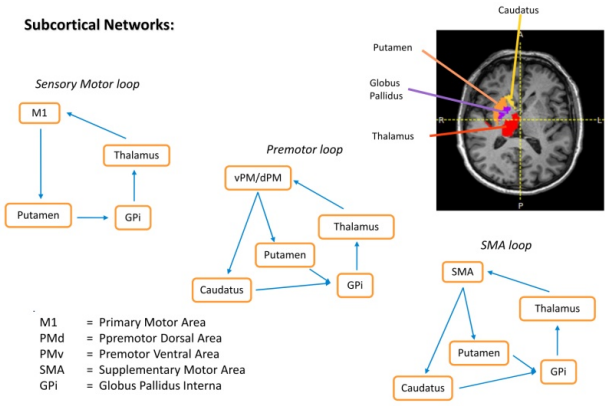
Introduction. We previously established that uninjured cortical motor network is remodeling in stroke patients with motor deficits [1.2]. Both axonal [1] and myelin plasticity [2] were, in fact, observed during 6 months longitudinal follow-up. However, the contribution of uninjured subcortical motor circuits in stroke recovery has not been studied yet. Therefore, in this study, we aimed at investigating myelin and axonal plasticity in the subcortical motor networks (SC-MN) contralateral to stroke by applying diffusion spectrum and magnetization transfer imaging. The SC-MS is constituted by connections between the cortical motor area, the basal ganglia and the thalamus, and it essentially consists in three major subcortical networks (figure 1): i) the sensory-motor sub-loop (primary and sensory motor areas -putamen-globus pallidus-ventral lateral thalamic nucleus-motor cortex), ii) the premotor sub-loop (premotor dorsal and ventral areas (dPM, vPM)-caudate nucleus-putamen, globus pallidus-ventral anterior thalamic nuleus-premotor cortex iii) the supplementary motor area (SMA) sub-loop (SMA - putamen and caudatus - globus pallidus-ventral anterior and the ventro-lateral thalamic nuclei-SMA).

Methods Ten patients (age: 58.4±17; female:male=7:5) underwent 3 DSI scans, in the acute phase (within 1 week after the stroke onset, time point 1 or tp1), 1 week (± 1 week, tp2) and 6 months (±15 days, tp2) after stroke. Patients benefitted of clinical assessment (NIHSS, FIM and RANKIN scores) at each time point. Ten healthy subjects (Age: 57.2±14.5; female:male=7:5) benefitted of DSI twice within a 1 month interval (± 1 week, tp1c and tp2c). All measurements were performed at 3T (Trio a Tim System, Siemens, Erlangen, Germany) using a 32 channel head coil (TR/TE=6600/138 ms, FoV=212x212 mm, 34 slices, 2.2x2.2x3 mm resolution, 258 diffusion directions, b=8000 s/mm^2). High resolution MPRAGE images were also acquired to extract the region of interest corresponding to the basal ganglia, thalamus (figure 1) and cortical motor regions (M1, SMA, PMd and PMv) using Freesurfer (http://surfer.nmr.mgh.harvard.edu/). The orientation distribution functions (ODF) were reconstructed using the Diffusion Toolkit (www.trackvis.org/dtk). Fiber-tracking was performed using a streamline-based algorithm following the two major ODF directions [3-5]. Magnetization transfer ratio (MTR) values were calculated as percent of the ratio (MT-M0)/M0 and extracted for each fiber. Generalized Fractional Anisotropy (GFA) was derived from DSI scans as descried in [6]. Subsequently, MTR and GFA histograms were calculated for each fiber bundle in order to assess between groups differences. For each histogram, the following feature-based histogram descriptors were extracted: mean, variance, skewness, kurtosis, peak height and peak location. Furthermore, distances between histograms were used (Mean Square Error, Kullbach-Leibler, Hausdorff). Variation of feature based and distance based parameters of subcortical motor connections (belonging to the 3 subnetworks) at tp1-tp2 and tp1-tp3 were compared between patients and HC using multivariate ANOVA and false discovery rate (FDR) correction for multiple comparisons.



GFA Analysis	Significance Stroke vs HC (tp1-tp2)	Significance Stroke vs HC (tp1-tp3)
FEATURE-BASED		
Mean	P < 0.001	P < 0.001
Variance	P < 0.001	P < 0.001
Skewness	P < 0.05	P < 0.001
Kurtosis	P < 0.05	P < 0.001
Peak Height	ns	ns
Peak Location	ns	ns
DISTANCE-BASED		
Kullbach-Leibler	P ≤ 0.005	P < 0.001
Mean Square Error	P < 0.05	P < 0.05
Hausdorff	ns	ns

MTR Analysis	Significance Stroke vs HC (tp1-tp2)	Significance Stroke vs HC (tp1-tp3)
FEATURE-BASED		
Mean	P < 0.001	P < 0.001
Variance	P < 0.001	P < 0.001
Skewness	ns	P ≤ 0.01
Kurtosis	ns	P < 0.005
Peak Height	ns	P < 0.001
Peak Location	ns	ns
DISTANCE-BASED		
Kullbach-Leibler	P < 0.01	P < 0.01
Mean Square Error	P < 0.005	P < 0.005
Hausdorff	ns	ns

Results. Between groups comparison of MTR and GFA variations are reported in Tables 1 (a) and (b), respectively. Both feature-based and distance-based histogram descriptors appeared to be sensitive measures of MTR and GFA differences between patients and controls. However, a larger number of feature-based parameters evidenced differences in GFA than in MTR within 1 month after stroke and peak location appeared to be the less sensitive feature-based measure. As to distance based characteristics, both Kullbach-Leiber and Mean Square error were sensitive differentiators between patients and controls but not Hausdorff distance.

Discussion and Conclusions. Overall, results suggest both short term (1 month) and mid term (6 months) axonal and myelin plasticity in the uninjured cortico-subcortical motor circuits of stroke patients with motor deficits. The impact of the observed remodeling in patients clinical recovery will be assessed in the next future.

References. [1] C. Granziera, et al. Neurology, 2012. [2] , Y.C. et al., ISMRM 2013. [3] Obertino et al., ISMRM DPTM Workshop 2013. [4] P. Hagmann, et al, PLoS ONE, 2007.[5] J. Wedeen, et al, NeuroImage, 2008. [6] A. Daducci, et al, PLoS ONE, 2012. [6] D. Tuch, Magn. Res. in Medicine 52:1358–1372 (2004).