Transsynaptic effect on degeneration of callosal motor fibers in patients with stroke using diffusion spectrum imaging

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Background and purpose: Upper extremity (UE) motor impairment is a major issue in stroke rehabilitation. Corticospinal tract (CST) structural integrity has been found to be moderately correlated with the severity of UE motor impairment after stroke.[1] Callosal motor fibers (CMF) is the largest tissue for communication of bilateral hemispheres, which may mediate patients' UE motor control. However, evidence remains unclear whether the structural integrity of CMF is affected secondary to an ischemic lesion involving CST only.[2] Animal model suggests CMF and CST are connected through layer III (pre-synaptic) and layer V (post-synaptic) pyramids.[3] Therefore, the purpose of the study was to examine whether CMF structural integrity is affected secondary to a CST lesion and whether CMF structural integrity contributes to UE motor control. We hypothesized that CMF integrity decreased due to transsynaptic degeneration effect.

Methods: 13 patients with chronic stroke (6 male, 60.2 ± 9.8 years, 14.2 ± 12.9 months after stroke onset) and 13 age- and gender-matched healthy controls (61.5 ± 10.1 years) were recruited. All lesions were confirmed to involve CST but not CMF by T1 and T2 weighted images. Imaging data acquisition was performed on 3T magnetic resonance imaging system (TIM Trio, Siemens). Diffusion spectrum imaging was acquired using a twice-refocused balanced echo diffusion echo planar imaging (EPI) sequence, with 102 diffusion-encoding directions (bmax of 4000s/mm^2) corresponding to grid points filled in the half sphere of the 3D q-space.[4] For measuring CST integrity, mean generalized fractional anisotropy (mGFA) was obtained for the segment of CST tractography above the posterior limb of internal capsule (CST_{above}). For CMF, mGFA was calculated for each side of CMF divided by a mid sagittal line of the brain. The mGFA of white matter tracts in the affected/unaffected hemispheres in patients were compared with the average mGFA of bilateral tracts in the healthy control group using two sample t-test. To investigate the transsynaptic effect on CMF, CMF of the affected hemisphere was further divided into medial and lateral part by a saggital line tangential to the edge of lateral ventricle in a coronal view. Partial correlation coefficients were computed for mGFA of affected CMF, affected lateral CMF, and affected medial CMF with affected CST_{above}, respectively, after controlling for the age effect. Multiple regression analysis was conducted to examine the contribution of affected CMF integrity to the UE motor control, in addition to affected CST integrity. UE subscale of Fugl-Meyer motor assessment (0 - 66) was used to assess UE motor control.[5]

Results: Patients with stroke had significantly lower mGFA of affected CST_{above} (p = .001) and affected lateral CMF (p = .017) than the control group. Figure 1 shows that the CST integrity decreased in patients with stroke and that the CMF integrity became more asymmetric in the patient with more severe UE motor impairment. High correlation was found between mGFA of affected CST_{above} and mGFA of affected CMF (r = .85, p = .001), as well as mGFA of affected lateral CMF (r = .80, p = .002), but not affected medial CMF (r = .45, p = .145). Multiple regression analysis revealed that the CMF integrity explained 13.7% variance of UE motor impairment in addition to CST integrity (Table 1).

Conclusion: This study shows the degeneration of CMF progressing from lateral to medial after ischemic lesion on CST, supporting the transsynaptic degeneration effect hypothesis. Moreover, the degeneration of CMF contributed to patients' UE motor impairment in addition to CST injury. The results could help clinicians make prognosis of patients' motor function, as well as future research on developing interventions that may prevent the transsynaptic degeneration effect.

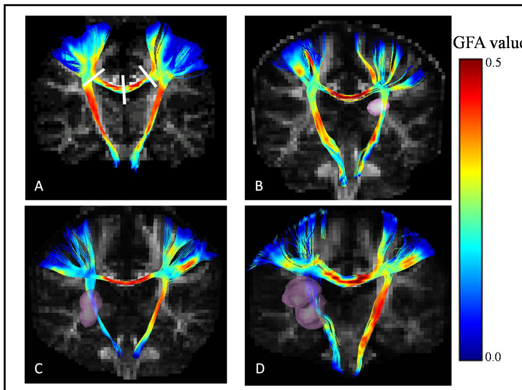

Figure 1: GFA-code tractography of CMF and CST of a healthy adult (A) and patients with stroke with mild (B), modete (C), and severe (D) upper extremity motor impairment. Purple regions represent infarct areas.

Table 1. Multiple regression analysis of upper extremity motor impairment (n=13)

Dependent variable	Independent variable	R^2	Adjusted R^2	P value
FMA score	age + affected CST mGFA	.547	.457	.019
FMA score	age + affected CST mGFA + affected CMF mGFA	.684	.579	.012

FMA: = Fugl-Meyer motor assessment, CST = corticospinal tract, mGFA = mean generalized fractional anisotropy, CMF = callosal motor fiber

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