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/mm2) 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 (CSTabove). For CMF, mGFA was calculated for each side of CMF divided by a mid sagittal line measuring CST integrity, mean generalized fractional anisotropy (mGFA) was obtained for the segment of CST tractography above and mGFA of affected 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.

References:

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

<table>
<thead>
<tr>
<th>Dependent variable</th>
<th>Independent variable</th>
<th>R²</th>
<th>Adjusted R²</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FMA score</td>
<td>age + affected CST mGFA</td>
<td>.547</td>
<td>.457</td>
<td>.019</td>
</tr>
<tr>
<td>FMA score</td>
<td>age + affected CST mGFA + affected CMF mGFA</td>
<td>.684</td>
<td>.579</td>
<td>.012</td>
</tr>
</tbody>
</table>

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