Frontal-Subcortical pathways for working memory: DTI fiber pathway reduction in healthy older subjects

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Introduction The dorsal lateral prefrontal cortex (DLPFC) and basal ganglia are all essential components of the verbal working memory network [1, 2]. Functional and structural changes may occur in these regions with advancing age. Based on region of interests (ROI) derived from functional MRI, total number of DTI fiber tracking pathways were compared between healthy young and old subjects in the present study. We found that in the basal ganglia and left prefrontal regions, the DTI fiber pathways are disproportionally reduced in the old subjects, while their fiber pathways in the right prefrontal region are kept relatively intact. This preliminary data suggests a non-uniform reduction of structural connectivity in the working memory associated brain network, which may provide some neurobiological basis of the HAROLD (Hemispheric Asymmetry Reduction in Older Adults) effect [3].

Method Fourteen young (age 22±2.6) and seventeen old (age 73±5.9) neurologically normal, right-handed, native English speaking women participated in the present study. The DTI data were collected with a 3T Siemens scanner (12 directions with b value of 1000s/mm^2, TR/TE/FOV=6500ms/90ms/220mm, flip angle=90^o, Matrix=256×256, 24 axial 3.5mm slices with 0mm gap, 6 averages). Function MRI data were also collected while subjects performed a verbal working memory task (results shown elsewhere).

DTI data were pre-processed in the "AFNI" software package (http://afni.nimh.nih.gov) for brain volume registration, diffusion tensor calculation, and stereotaxic Talairach transformation. The diffusion tensor data were then imported into the "DTI-Query" software package (http://graphics.stanford.edu/projects/dti/dti-query) for tractography path computing and displaying. The "TEND" fiber tracing algorithm (path step size=2mm, space between seeds=4mm, FA/angle termination threshold=0.15/45^o, min/max path length=5mm/300mm) was adopted, which uses the tensor at each point to multiply the incoming path vector, resulting a new vector that is deflected toward the principal direction of diffusion [4]. Three cubical ROIs were selected, with their centers/volumes matching those of the fMRI activations, in the basal ganglia (x/y/z=-0.2/5.3/10.5mm, volume=9569mm^3) and bilateral DLPFC (left x/y/z=41.4/-15.1/30.1mm, volume=15053mm^3; right x/y/z=-40.6/-18.5/33.7mm, volume=4620mm^3). For the old subjects' whole brain and each of the ROIs, the number of passing through pathways (length > 6mm and average FA > 0.3) was firstly scaled with the young data (old/young). This scaled data of the three local ROIs, which indicate the relative reduction level, were then compared with the whole brain average value through within subject paired t-test.

Result In the old subjects, there is a clear reduction in both the local ROI pathway numbers and the whole brain total pathway number. Fig.1 shows the pathway computation result for a young subject and an old subject. Quantitative comparison of old/young pathway number ratios is shown in the bar graph. In addition to the general whole brain reduction, pathway numbers in the basal ganglia and left DLPFC are disproportionally more reduced in the older subjects. In contrast, the reduction for the right DLPFC is relatively mild and similar to the average reduction of the whole brain.

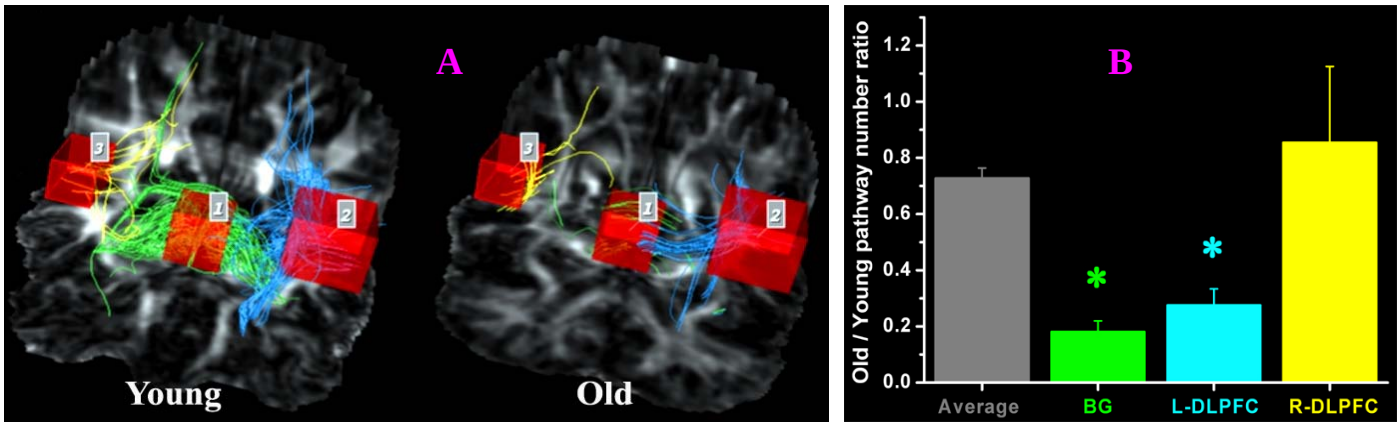

Fig.1. (A) Pathway computation result for a young and an old subject in the basal ganglia (1), left (2), and right (3) prefrontal areas. (B) Quantitative comparison of old/young pathway number ratio between the 3 local ROIs and the whole brain average value. The asterisks depict a significant (p<0.0001) disproportional regional reduction relative to the average brain reduction. The error bars represent standard error. BG: Basal ganglia; L / R-DLPFC: Left / Right Dorsal Lateral Prefrontal Cortex; Average: the whole brain average reduction.

Conclusions Age associated reductions of structural connectivity are not uniform in the whole brain. The less/milder degraded right prefrontal region may provide a compensational support to the verbal working memory function in aged individuals, which has been reported in fMRI studies as the HAROLD effect.

References [1] D'Esposito et al., Exp. Brain Res. (2000) 133:3. [2] Chang et al., Neuroimage. (2007) 34:1253. [3] Cabeza, Psychol. Aging. (2002) 17:85. [4] Lazar et al., Hum. Brain Mapp. (2003) 18:306.

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