Multimodality Imaging in Cerebro-Cerebeller Verbal Working Memory

W-Y. Chiang[1], J-S. Yu[2], S-H. A. Chen[2], and W-Y. I. Tseng[3]

[1]Research Institute, The Methodist Hospital, Houston, TX, United States, [2]Department of Psychology, National Taiwan University, Taipei, Taiwan, [3]Center for Optoelectronic Biomedicine, National Taiwan University College of Medicine, Taipei, Taiwan

Introduction A protocol of combining structural and functional images is proposed to localize the specific white matter connections between multiple activation areas. A cerebro-cerebellar framework for verbal working memory has been proposed based on neuroanatomical projections from cortico-ponto [1], and ponto-cerebellar [2] in primates. Functional MRI data showed that the superior region of right cerebellum contribute to the articulatory control system of working memory, and the inferior cerebellum link to the phonological storage [2-4]. The present work makes it possible to visualize the specific white-matter connections of each circuit involved in the working memory task for in *vivo* human brain which has not yet been done before. We choose diffusion spectrum image (DSI) [5] and functional magnetic resonance image (fMRI) to look at two different circuits of articulatory control and phonological storage involved in cerebro-cerebullar working memory.

Materials and Methods 5 female and 5 male university students ranging from 20 to 26 years old has been studied for whole-brain fMRI and DSI scan via a 3T MRI scanner (Trio, SIEMENS). Sternberg verbal working memory task was used for fMRI with parameters of TR/TE = 2700/24 ms, flip angle = 90°, isotropic resolution of 3.8 mm and 40 slices. For DSI scan, a twice-refocused balanced single-shot diffusion EPI was used with parameters of 203 diffusion-encoding gradients, maximum b-value = 6000 s/mm^2, TR/TE = 9100/142 ms, isotropic resolution of 2.9 mm and 45 slices. All fMRI were preprocessed using SPM5. GLM was used to obtain individual subject's high vs. low contrast maps. Activation areas were extracted via SPM5 "cluster function" and served as ROI for latter DSI tractography. Additional ROI such as thalamus and pons are defined on MNI template using MARINA and MRIcron software. Individual white-matter mask are calculated from B_0 image of DSI via SPM5 and served as seeding area. All of these ROI and seeding area were transformed to voxel space of DSI to perform native-space tractography via custom-made software package. For the circuit of articulatory control, we used ROI of activations in Broca's area, activations in superior cerebellum and mask of thalamus and mask of pons. We tracked the circuit of phonological storage using ROI of activations in inferior parietal lobe, activations in inferior cerebellum, mask of thalamus and mask of pons.

Results Figure 1 shows individual tractography for one of our volunteers (Male No.2). For white matter which involves in articulatory control shown as blue lines, it passes through the medial part of pons shown as green volume in (h). The red lines which intersect with lateral part of pons shown in (h) indicate the white matter connections involved in the process of phonological storage. We smoothed the intersections of white-matter tracts around pons to form probability-like map to exam the distribution of white matter involved for these two functional tasks in (i, j). Both circuits of articulatory control and phonological storage go around anterior, ventral anterior or ventral lateral part of thalamus, but we are not yet able to exactly determine which nucleus is involved in each circuit due to the limited precision of transforming nucleus from template to individual.

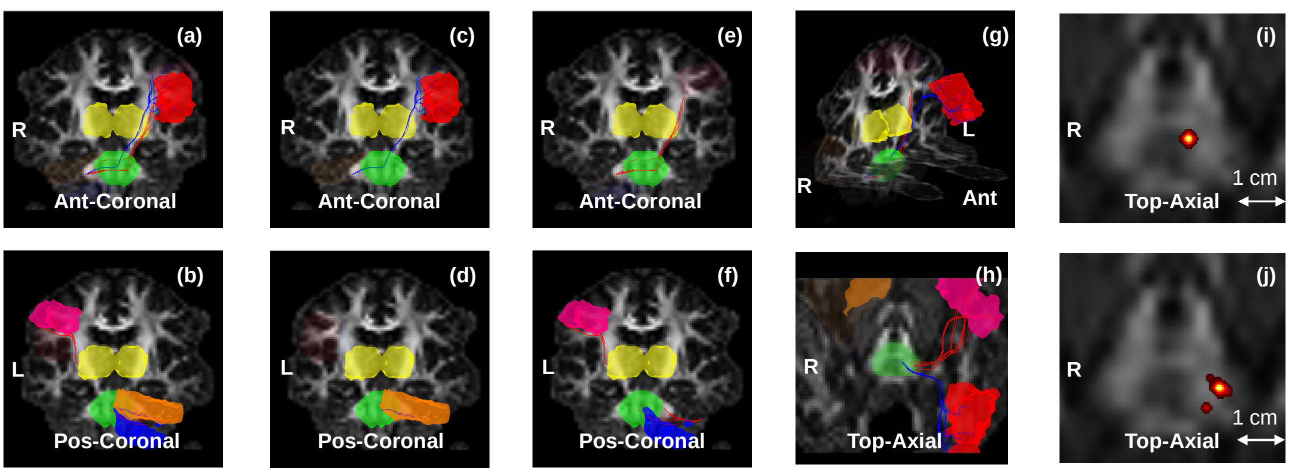

Figure 1. Individual Tractography for Male No. 2 with background of GFA index (red/magenta/orange/blue volume: activations in Broca's area/inferior parietal lobe/superior cerebellum/inferior cerebellum; yellow/green volume: mask of thalamus/pons; blue/red lines: white-matter tracts for articulatory control/phonological storage). (a, b) Combined circuits of articulatory control and phonological storage in coronal view. (c, d) Circuits of articulatory control only. (e, f) Circuits of phonological storage only. (g) Combined circuits with background of coronal and axial GFA map in angled view. (h) Combined circuits in axial view centered around pons. (i) Probability-like intersections through pons with background of GFA map for circuits of articulatory control, and (j) through pons for circuits of phonological storage.

Conclusions This protocol integrates fMRI and DSI techniques which is utilized to localize the white matter connections involved in different functional activations. Fig 1(i) and (j) indicate that we can discriminate adjacent white matter tracts involved in different functional tasks even if their distance in between is only 1 cm. Although this is a long-connection situation and there are multiple crossing-fiber areas involved in this model of working memory, DSI and deterministic (streamline) tractography enable us to successfully discriminate different white-matter tracts involved in different functional tasks. In this protocol, because all the masks are generated from MNI template, we are able to parameterize all the processes needed to calculate tractography, such as calculating white-matter mask for seeding area and functional activation areas for ROI. Therefore, we reduced the differences of subjective decisions between each subject. In generating white-matter mask, we also found that GFA-threshold method is not sufficient because of the drop of GFA for white matter in crossing areas, and, therefore, we choose SPM5 for segmentation. Better segmentation may be achieved through software other than SPM in the future. This in *vivo* technique not only enables us to discriminate the difference of adjacent white-matter structures involve in different stages of functional activations, but also prospects the vision of looking at the dynamic involvements of white-matter connections during different neuronal activities.

References [1] Schmahmann, 1996. [2] Brodal, 1979. [3] Desmond, 1997. [4] Chen & Desmond, 2005. [5] Wedeen, 2005.