Diffusion Spectrum Imaging Tractography Study in Chronic Alcoholics Found Marked Deficit of White Matter Integrity in the Posterior Cingulate Cortex

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Introduction
Chronic excessive alcohol consumption is associated with significant shrinkage of the cortical tissue and degradation of fibers that carry information between neurons. Previous studies have shown widespread fractional anisotropy (FA), a measure of diffusion orientation and coherence, deficits in the white matter [1]. However, the areas showing the most significant deficit of FA and the corresponding white matter tracts are still lacking. Here we used voxel base morphometry (VBM) to identify the most significant areas, and used diffusion spectrum imaging (DSI) tractography to determine the affected tracts and analyzed the change in FA values along these tracts.

Materials and Methods
Subjects Ten alcoholics (age range: 37–52 years; mean±SD: 43.9±4.8 years) and 8 healthy controls (age range: 38–52 years; mean±SD: 44.0±5.1 years) were recruited in the study. All subjects were right-handed male. DSI acquisition and analysis MRI scans were performed on a 3.0 T MRI scanner (Trio, Siemens, Erlangen, Germany). Both T2-weighted structure images and DSI were acquired with the same slice orientation and the same scan range. The T2-weighted images were acquired using a turbo spin echo sequence, TR/TE = 920/102 ms, matrix size = 256x256, spatial resolution = 0.98x0.98 mm2, and slice thickness = 3.9 mm. DSI was performed using a twice-refocused balanced echo diffusion echo planar imaging sequence, TR/TE = 9100/142 ms, image matrix size = 128x128, spatial resolution = 2.9x2.9 mm2, and slice thickness = 2.9 mm. A total of 203 diffusion encoding gradients with the maximum diffusion sensitivity bmax = 6000s/mm2 were sampled on the grid points in the 3D q-space with |q| ≤ 3.6 units. DSI analysis was performed based on the relationship that the echo signal S(q) and the diffusion probability density function P(r) were a Fourier pair [2]. The orientation distribution function (ODF) was determined by computing the second moment of P(r) along each radial direction [3]. The orientations of individual crossing fibers were determined by decomposing the original ODF into several constituent ODFs [4]. The crossing fiber vectors were used for tractography reconstruction. Generalized fraction anisotropy (GFA) at each voxel was quantified based on the shape of the original ODF [5].

Co-registration and normalization We used MARINA (Bender Institute of Neuroimaging) to define posterior cingulate cortex (PCC) on the MNI (Montreal Neurobiology Institute). Linear and non-linear transformations from the image coordinates of individual participants’ brains to the MNI coordinates were computed. The coordinates of the PCC defined in the MNI template were then mapped onto individual participants’ brains through the calculated inverse transformations. The transformation from individual brains to MNI template was performed using SPM5 (Wellcome Department of Imaging Neuroscience).

VBM of GFA The GFA maps of the individual brains were normalized to MNI template via the computed transformations as described above. VBM analysis was performed by comparing the average GFA maps between control and alcoholic groups. FWER threshold of P=7.6519 was used to present the regions of significant difference [6].

Cingulate bundle tractography reconstruction and GFA analysis Tractography was reconstructed based on a simple algorithm adapted for DSI data. One of the decomposed fiber vectors in the white matter pixels was used as a seed vector to produce one fiber tract. A step of 0.4 pixel was tracked forward from the seed vector, and all vectors in the nearest voxels were evaluated to determine the proceeding orientation for the next step. A vector with closest orientation to the starting vector was chosen if it was within 45° deviation. Tracking stopped if no such vectors were found in the nearest voxels. The procedure of the fiber tracking was iterated by randomly selecting the seed vectors in the pixels covering the cingulate cortex. Cingulate bundle (CB) tractography was produced by selecting fiber tracts that passed through the ROI at PCC. This ROI was also used to divide the three different parts of CB, i.e. anterior part, middle part, and posterior part. The anterior part was the bundle anterior to ROI, the middle part was that inside ROI, and the posterior part was that posterior to the ROI. GFA values within each part of CB were averaged. Comparison was performed between control and alcoholic groups using two-tailed t-test, the difference was considered statistically significant if p<0.05.

Results
VBM showed that there was significant difference of GFA located in bilateral PCC (FWER, P>7.6519). Tractography analysis showed that GFA in the middle part of CB was reduced in the alcoholic group compared to the control group (left: 0.1809±0.0140 [control] vs. 0.1517±0.0214 [alcoholic], p=0.0032; right: 0.1692±0.0229 vs. 0.1494±0.0174, p=0.0653) (Fig.1).

In chronic alcoholics, we found that the most significant GFA deficit was located at PCC, corresponding to the middle part of CB. Our findings suggest that the degradation of white matter at PCC might be the core lesion in chronic alcoholics. The significance of this core lesion in cognitive function impairment warrants further investigation.

References