Strong correlation between hippocampal volume and integrity of inferior cingulum bundle in patients with mesial temporal lobe epilepsy

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Introduction

Hippocampal sclerosis (HS) is the common abnormality observed in patients with mesial temporal lobe epilepsy (MTLE). Previous morphometric studies showed that hippocampal and extrahippocampal atrophies were associated with MTLE [1]. MTLE affects the networks of regions that are anatomically connected to the hippocampus [2]. Inferior cingulum bundle (CB) is a bundle of axons projecting from posterior cingulate gyrus to entorhinal cortex. Since the hippocampus is a terminal node of the inferior CB pathway, we hypothesized that the integrity of the inferior CB is related to the atrophy of the hippocampus. In this study, we evaluated the integrity of white matter by diffusion spectrum imaging (DSI) and the atrophy of hippocampus by the volume measurement according to the T1-weighted image, and investigated their relationship.

Methods

The subjects consisted of 8 adults (3 males and 5 females) with clinical diagnosis of MTLE with left HS and 8 age-, sex- and handedness-matched healthy adult controls. DSI was performed on a 3T magnetic resonance imaging system (TIM Trio, Siemens) using a twice-refocused balanced echo diffusion echo planar imaging (EPI) sequence, TR/TE = 9600/130 ms, FPV = 200 x 200 mm, image matrix size = 80 x 80, and slice thickness = 2.5 mm. A total of 102 diffusion encoding gradients with the maximum diffusion sensitivity bmax = 4000 s/mm^2 were sampled on the grid points in the 3D q-space with $|q| \leq 3.6$ units [3]. T1-weighted image with 1 mm isotropic voxels was acquired in the coronal plane by 3-dimesion magnetization prepared rapid gradient echo sequence (3-D MPRAGE) with following parameters: TR/TE = 2000/2.98 ms, flip angle = 9°, FOV = 256 x 256 mm. To reconstruct white matter tracts of bilateral inferior CB, we placed regions of interest (ROI) at bilateral posterior cingulate cortex (PCC) and ventral potion of hippocampus by WFU pickatlas [4] (Fig. 1). The ROIs were transformed from Montreal Neurological Institute (MNI) space through the DSI template performed by large deformation diffeomoffic metric mapping (LDDMM) [5] to the individual brains. The mean generalized fractional anisotropy (GFA), an index representing the white matter integrity, was measured by calculating the weighted sum of the GFA sampled along each tract bundle. The volume measurement of bilateral hippocampus was conducted by FreeSurfer [6]. The volume-based stream of FreeSurfer consists of five stages: affine registration with Talairach space, initial volumetric labeling, correction of the B1 bias field, nonlinear volumetric alignment to the Talairach atlas, and labeling of the volume [7]. Mann-Whitney U test was used to compare the fiber integrity of each tract bundle between the two groups. To evaluate the relationship between GFA of bilateral inferior CB and the volume of hippocampus, both indices were used to compute the correlation coefficients using Pearson correlation.

Results

Patients showed lower GFA in both left and right inferior CBs than controls. In the left inferior CB, GFA was decreased significantly in patients ($p = 0.007$, uncorrected). Volume reduction of bilateral hippocampus was found in patients, with the left hippocampus showing significant reduction ($p = 0.007$, uncorrected). Moreover, patients' GFA of the left inferior CB showed strong positive correlation with the volume of left hippocampus ($r = 0.87$, $p = 0.05$; Fig. 2). No correlation between GFA of the inferior CB and hippocampal volume was found in patients' right side and controls' bilateral sides.

Conclusion

The present study demonstrates the relationship between the integrity of the inferior CB and the volume of hippocampal gray matter. Strong positive correlation was found in the lesion side of patients with HS. The findings are consistent with previous DTI studies [8], with more specific implication that the severity of the inferior CB is gauged by the hippocampal atrophy. Previous studies have reported that patients with MTLE exhibit a network of atrophy, involving mesial temporal lobe and limbic lobe [9]. It is known that PCC is responsible for episodic memory function and self-referencing, and that the inferior CB is the main pathway interconnecting PCC and hippocampus. We postulate that the impaired integrity of inferior CB might affect the memory function and other cognitive function in patients. Therefore, it warrants further study on the correlation between integrity of inferior CB and cognitive functions related to PCC.

References

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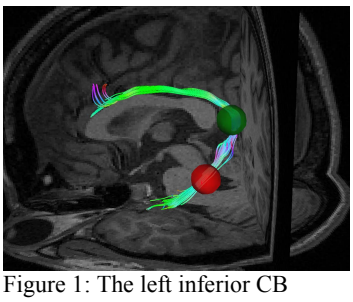

Figure 1: The left inferior CB (PCC is indicated by a green sphere with radius = 2 mm and the ventral portion of the hippocampus is indicated by a red sphere with radius = 2mm).

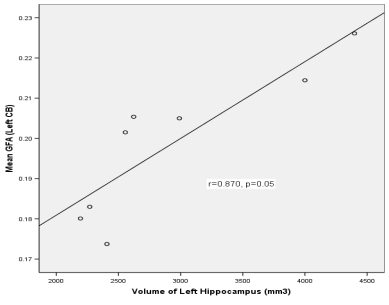

Figure 2: The scatter plot of the volumes of left hippocampus (*X* axis) and mean GFA of the left inferior CB (*Y* axis) in patients with left HS ($r = 0.87$, $p = 0.05$, uncorrected).