Left hippocampal volume reduction is strongly coupled with structural and functional connectivity in patients with left mesial temporal lobe epilepsy

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Introduction

The hippocampal sclerosis (HS) is the general abnormality observed in patients with mesial temporal lobe epilepsy (MTLE). Our previous study has demonstrated the strong positive correlation between the integrity of the inferior cingulate bundle (CB) and the volume of hippocampal gray matter in left MTLE [1]. Inferior CB is a bundle of axons projecting from posterior cingulate cortex (PCC) to the ventral side of hippocampus (HP). We have confirmed the altered structural connectivity related to HS or hippocampal atrophy in left MTLE, however, the functional connectivity between these two regions is still unclear. In this study, we applied the general linear model (GLM) with PCC seed to examine the strength of functional connectivity in HP on SPM platform [2]. We hypothesized that there were relationships existed between structural and functional connectivity caused by HS.

Methods

The subjects consisted of 8 adults with clinical diagnosis of MTLE with left HS and 8 age-, sex-, and handedness-matched healthy adult controls. All images were performed on a 3T MRI system (TIM Trio, Siemens). DSI was acquired using a twice-refocused balanced echo diffusion echo planar imaging (EPI) sequence, TR/TE = 9000/130 ms, FOV 200 mm, image matrix size 80 x 80, and s 2.5 mm slice thick. A total of 102 diffusion encoding gradients with the maximum diffusion sensitivity bmax = 4000 s/mm² were sampled on the grid points in the 3D q-space with |g| ≤ 3.6 units [3]. Functional images in the resting state were acquired using the following parameters: TR/TE = 2000/24 ms, flip angle = 90 deg, 34 slices, 3 mm thick with no gap interleaved, FOV 256 mm, matrix size 64 x 64, and 180 volumes per run with additional 2 volumes of dummy scans in advance. We discarded the first 3 volumes and used the remaining 177 volumes. T1-weighted image with 1 mm isotropic voxels was acquired in the coronal plane by 3D MPRAGE with following parameters: TR/TE = 2000/2.98 ms, flip angle = 9 deg, FOV 256 mm. To reconstruct white matter tracts of bilateral inferior CB, we placed regions of interest (ROI) at bilateral PCC and HP by from automated anatomical (ANCOVA) with PCC seed to examine the strength of functional connectivity in HP on SPM platform [2]. We hypothesized that there were relationships existed between structural and functional connectivity caused by HS.

Results

Patients showed the volume of left HP was positively correlated to mGFA of left inferior CB (r = 0.905, p = 0.002), and negatively correlated to bilateral HP’s Z-scores (left HP: r = -0.095, p = 0.022; right HP: r = -0.881, p = 0.004). For the relationship between structural and functional connectivity, patients showed strong negative correlation between mGFA of left inferior CB and left HP's averaged Z-score (r = -0.857, p = 0.007); mGFA of right inferior CB was positively correlated to both sides of HP’s averaged Z-scores (left: r = 0.810, p = 0.015; right: r = 0.738, p = 0.037) (Table 1). These relationships were absent in controls. In addition, both groups showed the positive correlation between left and right HP’s Z-scores (patients: r = 0.786, p = 0.021; controls: r = 0.714, p = 0.047). For group comparison, there was no significant difference in the averaged Z scores of bilateral HP between groups. However, for the second level group comparison using ANCOVA, patients showed decreased functional connectivity in bilateral superior and middle temporal gyrus compared to healthy controls (Figure 1).

Conclusion

The present study reveals the relationships among the integrity of the inferior CB, the volume of hippocampal gray matter and the strength of functional connectivity in the lesion side of patients with HS. It indicates that the reduced HP volume and the impaired integrity of the inferior CB are quite related to the enhanced functional connectivity between HP and PCC. We also demonstrated that patients with left MTLE declined functionally in the superior and middle temporal gyrus.

Table 1. The correlation coefficients among HP volume, GFA of inferior CB, and averaged Z score in HP

<table>
<thead>
<tr>
<th>HP volume (L)</th>
<th>mGFA in CB (L)</th>
<th>mGFA in CB (R)</th>
<th>Averaged Z score in HP (L)</th>
<th>Averaged Z score in HP (R)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(L) (mm³)</td>
<td>r = 0.190</td>
<td>r = 0.905**</td>
<td>r = 0.962*</td>
<td>r = -0.905**</td>
</tr>
<tr>
<td>(R) (mm³)</td>
<td>r = 0.595</td>
<td>r = 0.017</td>
<td>r = 0.871**</td>
<td>r = -0.881**</td>
</tr>
<tr>
<td>mGFA in CB (L)</td>
<td>r = -0.143</td>
<td>r = 0.000</td>
<td>r = 0.333</td>
<td>r = -0.000</td>
</tr>
<tr>
<td>(R) (mm³)</td>
<td>r = 0.452</td>
<td>r = 0.000</td>
<td>r = 0.420</td>
<td>r = 0.000</td>
</tr>
<tr>
<td>Averaged Z score in HP (L)</td>
<td>r = -0.333</td>
<td>r = 0.095</td>
<td>r = 0.709</td>
<td>r = 0.786*</td>
</tr>
<tr>
<td>(R) (mm³)</td>
<td>r = -0.595</td>
<td>r = 0.017</td>
<td>r = 0.420</td>
<td>r = 0.017</td>
</tr>
</tbody>
</table>

Note. N = 8 for each group. HP: hippocampus. L: left; R: right. *: p < 0.05. **: p < 0.01. The correlation coefficients marked with * indicates patients with left MTLE; blue color indicates healthy controls.

References


Figure 1: The group comparison result using SPM 8 (N=8 for each group, p < 0.05). The blue arrows indicate the peak activations in bilateral superior and middle temporal gyrus. L: hemisphere.