Altered Integrity and Asymmetry of Association White Matter Tracts in Epilepsy with Mesial Temporal Sclerosis: Preliminary
Results Using Diffusion Spectrum Imaging

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Introduction Human epilepsy is a chronic neurological disorder which is characterized by different seizure types, a variable age of onset, and range of effective treatments. Temporal lobe epilepsy (TLE), one of the partial-onset epilepsies, is the most common type for adult patients. To date, it is possible to analyze the structural connectivity and white matter abnormalities of patients with TLE noninvasively using diffusion tensor imaging (DTI). Previous findings using DTI suggest that TLE patients have decreased fractional anisotropy in the hippocampal formation ipsilateral to the seizure focus [1]. Here, we investigated three association fibers connecting the medial frontal cortex (MFC), posterior cingulate cortex (PCC), inferior parietal lobe (IPL) and mesial temporal lobe, namely superior fronto-occipital fasciculus [SFOF], cingulum bundles [CG], uncinate fasciculus [UF], by diffusion spectrum imaging (DSI) [Figure 1] and calculated their generalized fractional anisotropy (GFA). Further, we hypothesized that tract’s GFAs of the lesion side are lower than healthy side with TLE patients.

Materials and Methods Seven right-handed Taiwanese adults with left TLE and mesial temporal sclerosis (MTS) (3 males and 4 females), as well as seven age and gender matched, right handed neurotypical participants were examined using DSI. The patients have all been diagnosed with MTS in the left hemisphere by neurological examination and neuroimage studies. Images were acquired on a 3T MRI system with a 32-channel head coil (TIM Trio, Siemens, Erlangen, Germany). DSI was performed using a twice-refocused balanced echo diffusion echo planar imaging (EPI) sequence, TR/TE = 9600/130 ms, image matrix size = 80 x 80, spatial resolution = 2.5 x 2.5 mm², and slice thickness = 2.5 mm. 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 |q| ≤ 3.6 units [2]. DSI analysis was based on the relationship between the echo signal S(q) and the diffusion probability density function P(r). S(q) and P(r) could be depicted in Fourier relation, i.e., S(q)=FT[P(r)]. The orientation distribution function (ODF) was determined by computing the second moment of P(r) along each radial direction. The intravoxel fiber orientations were determined by decomposing the original ODF into several constituent ODFs [3]. Further, those primary fiber orientations were used to reconstruct fiber tracking. GFA at each voxel was quantified based on the shape of the original ODF [4]. In this study, the targeted tracts were selected by specific regions-of-interest (ROIs) based on Brodmann’s area. The mean path analysis projected the targeted white matter tracts and analyzed local changes in the microstructure coherence along the individual tract bundles [5]. The GFA of superior and inferior portions of CG, UF, and SFOF were compared between normal controls and patients.

Results Patients were higher than neurotypical participants in GFA in all association fibers except the inferior portion of the left CG [Figure 2]. In neurotypical participants, we found that the GFA of the left CG was higher than that of the right CG. Patients with left TLE, however, did not demonstrate such a leftward asymmetry. Rather, they demonstrated a rightward asymmetry, especially in the inferior portion of the CG [Figure 2].

Discussion In this study, we have characterized the alteration of GFA in three association fiber tracts in patients with TLE and MTS. Our findings include: 1) there is a tendency of increased structural connectivity in all association fiber tracts except the inferior portion of the left CG, and 2) the CG changed its asymmetry from leftward to rightward. The inferior portion of the CG is known to pass through the hippocampus, and patients with TLE and MTS have been shown to have hippocampal sclerosis [6]. It is reasonable to suspect that the integrity of the left CG ipsilateral to MTS is affected directly, leading to the decrease in GFA and the change in asymmetry. The increased structural connectivity in all other tracts might suggest a mechanism of white matter plasticity. Further studies are warranted to increase the number of subjects and explore other fiber tracts that also pass through the hippocampus.


Figure 1 Two association fibers passing through the mesial temporal lobe in the left hemisphere: 1, cingulum bundles (CG), 2, uncinate fasciculus (UF) and 3, hippocampus. The inferior portion of the CG passes through the hippocampus.