Introduction

Most patients suffering from temporal lobe epilepsy (TLE) are associated with mesial temporal sclerosis (MTS). Patients with unilateral MTS were shown to have extensive gray matter (GM) and white matter (WM) abnormalities ipsilateral and contralateral to the seizure onset area [1]. Previous diffusion tensor imaging (DTI) study have demonstrated different epileptic networks in TLE patients with and without MTS, suggesting WM alterations in patients with MTS is more extensive than patients without MTS [2]. The widespread abnormalities in MTS are due to the secondary generalization in other brain areas [3]. However, these DTI studies are limited to analytic methods and only focus on a few fiber tracts. The changes of the whole brain WM tracts in MTS still remain unclear. In this study, we proposed a new method to perform tract-specific analysis over the whole brain, named tract-based automatic analysis (TBAA), using a diffusion spectrum imaging (DSI) template and a tract atlas. We hypothesized that left and right MTS would affect WM tract integrity over the whole brain and have different epileptic networks.

Methods

The subjects consisted of 21 adults with clinical diagnosis of TLE with unilateral MTS (left MTS 12, age 35.5±7.98 years; right MTS 9, age 34.89±5.11 years) and 19 age-, sex- and handedness-matched healthy adult controls (age 34.79±6.89 years). MR scanning was performed on a 3T MRI system (TIM Trio, Siemens) with a 32 channel phased-array head coil. DSI was acquired using a twice-refocused balanced echo diffusion echo planar imaging (EPI) sequence, TR/TE = 9600/130 ms, FOV 200 mm, image matrix size 80 x 80, and s 2.5 mm slice thick. A total of 12 diffusion encoding gradients with the maximum diffusion sensitivity bmax = 4000 s/mm² were sampled on the grid points in a half sphere of the 3D q-space with |q| ≤ 3.6 units [4]. The TBAA method requires two pieces of information, a high quality DSI template and a whole brain white matter tract atlas. The DSI template was constructed by coregistering 122 healthy participants’ DSI datasets (Male: Female = 63:59) in the Montreal Neurobiology Institute (MINI) space using the Large Defomation Diffeomorphic Metric Mapping (LDDMM) method [5]. Whole brain WM tracts were reconstructed on the DSI template by an expert using multiple regions of interest (ROIs) and whole brain seeding. A total of 119 tracts were reconstructed from 60 ROIs defined in the Automatic Anatomical Labeling system. Each reconstructed tract was subdivided into multiple steps with even spacing and the step coordinates along tract bundles were saved as sampling coordinates. The procedures of TBAA method were as follows. 1) Study subjects (controls, left MTS, and right MTS) were coregistered to create a study specific template (SST) using LDDMM. 2) The SST was coregistered to the DSI template. 3) Sampling coordinates were transformed from the DSI template to individual DSI datasets via the transformation matrix between DSI template and SST as well as the matrix between SST and individual DSI. 4) The generalized fractional anisotropy (GFA) values were sampled in the native DSI space using the transformed sampling coordinates and the mean GFA value (mGFA) was then computed for each tract. Kruskal–Wallis test (K-W test) was used to test the between-group differences in those significant tracts.

Results

As shown in Fig. 1, we found 10 fiber tracts (4 association fibers, 5 projection fibers, and 1 commissural fiber), namely right inferior frontal occipital fasciculus (IFOF_R), left inferior longitudinal fasciculus (ILF_L), bilateral uncinate fasciculus (UF_L and UF_R), left caudate–inferior orbital frontal, left spinohalamic tract, left thalamus–inferior orbital frontal, left thalamus–middle frontal, left thalamus–superior middle frontal, and genu of corpus callosum (Genu), showing significant differences among groups (p < 0.05, corrected). Patients with left MTS and right MTS showed significantly lower mGFA in these tracts except left spinohalamic tract which was only shown in right MTS. The mGFA of the left spinohalamic tract in right MTS was significantly higher than that of both control group and left MTS. The widespread abnormalities in MTS are due to the secondary generalization in other brain areas (orbitofrontal, frontal and occipital lobes) via temporal lobe, suggesting that MTS lesions may affect other brain areas via these fiber tracts. The mGFA reduction in genu might explain in part the involvement of tracts in bilateral hemispheres. The 5 abnormal projection fibers which were projected from thalamus or caudate to the cortical regions might be associated with the GM atrophy in the limbic system, postcentral gyrus, frontal, and orbitofrontal cortex [8,9]. In addition, we found that right MTS showed more extensive WM alteration than left MTS by involving additional UF_R and left thalamus–middle frontal, and the affected tracts were located more in the left hemisphere than the right hemisphere. Previous study reported that patients with right MTS had more extensive, bilateral WM abnormalities than patients with left MTS [2]. We speculate that the GM atrophy in hippocampus-amygdala structure affects the tracts connecting to the temporal region in the first stage; the secondary generalization then causes atrophy in the thalamus and caudate and affects the related projection fibers. Furthermore, previous studies reported that these fiber tracts were related to variable cognitive dysfunctions in patients with MTS, such as episodic memory encoding, emotion, executive function, and egocentric memory [2, 6-9]. In conclusion, we successfully identified different epileptic networks in left and right MTS, and found more extensive WM alterations in right MTS than in left MTS.

Discussion and conclusion

In the present study, we proposed a whole brain tract-specific analysis to investigate epileptic networks in both left and right MTS groups. Some results were consistent with previous studies in which reduced mGFA in IFOF, ILF, UF, and Genu was observed in MTS patients [2,6,7]. The association fibers (IFOF, ILF, and UF) connect with other brain areas (orbitofrontal, frontal and occipital lobes) via temporal lobe, suggesting that MTS lesions may affect other brain areas via these fiber tracts. The mGFA reduction in genu might explain in part the involvement of tracts in bilateral hemispheres. The 5 abnormal projection fibers which were projected from thalamus or caudate to the cortical regions might be associated with the GM atrophy in the limbic system, postcentral gyrus, frontal, and orbitofrontal cortex [8,9]. In addition, we found that right MTS showed more extensive WM alteration than left MTS by involving additional UF_R and left thalamus–middle frontal, and the affected tracts were located more in the left hemisphere than the right hemisphere. Previous study reported that patients with right MTS had more extensive, bilateral WM abnormalities than patients with left MTS [2]. We speculate that the GM atrophy in hippocampus-amygdala structure affects the tracts connecting to the temporal region in the first stage; the secondary generalization then causes atrophy in the thalamus and caudate and affects the related projection fibers. Furthermore, previous studies reported that these fiber tracts were related to variable cognitive dysfunctions in patients with MTS, such as episodic memory encoding, emotion, executive function, and egocentric memory [2, 6-9]. In conclusion, we successfully identified different epileptic networks in left and right MTS, and found more extensive WM alterations in right MTS than in left MTS.

References