The Egyptian Journal of Radiology and Nuclear Medicine xxx (xxxx) xxx–xxx

Contents lists available at ScienceDirect

The Egyptian Journal of Radiology and Nuclear Medicine

journal homepage: www.elsevier.com/locate/ejrnm

Original Article

Correlation of diffusion tensor imaging findings and episodic memory impairment in temporal lobe epilepsy

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ARTICLE INFO

Keywords:
DTI
Episodic memory
Temporal lobe epilepsy

ABSTRACT

Purpose: Our aim was to evaluate the utility of diffusion tensor imaging (DTI) in exploration of white matter tracts microstructure changes and clarify their relation to episodic memory in temporal lobe epilepsy (TLE).
Materials and methods: DTI was performed on 30 (18 left, 12 right) TLE patients and 20 healthy controls. Fractional anisotropy (FA) and apparent diffusion coefficient (ADC) were calculated for six fiber tracts; the parahippocampal cingulum (PHC), superior longitudinal fasciculus (SLF), inferior longitudinal fasciculus (ILF), fornix (FORX), uncinate fasciculus (UF) and corpus callosum (CC). Assessment for episodic memory (visual and verbal) was performed at least 48 h after the last seizure.
Results: All TLE patients had episodic memory impairment. Left TLE patients demonstrated more verbal memory affection, whereas right TLE patients demonstrated more visual memory affection ($p < 0.05$). Abnormal DTI parameters (decreased FA and increased ADC) were detected in most of the white matter tracts ($p < 0.001$) compared to control group. In left TLE patients, there was significant correlation between DTI parameters of left (PHC, SLF, UF, FORX) and verbal memory. Whereas, in right TLE patient, we found significant correlation between DTI parameters of right ILF and visual memory.
Conclusions: TLE patients had multiple micro-structural white matter tracts abnormalities and episodic memory impairment. Both are structurally and functionally related.

1. Introduction

Temporal lobe epilepsy (TLE) is the most common complex partial seizure [1]. It is usually accompanied by mesial temporal lobe sclerosis (MTS), characterized by neuronal loss and gliosis of the hippocampus, amygdala, and entorhinal cortex [2]. Widespread white matter abnormalities were reported in TLE patients [3–6] specifically ipsilateral to the epileptogenic focus [6].

Episodic memory enables storing and recalling events that were actually lived through and experienced by a person [7] and it is frequently impaired in TLE with the left temporal structures are more related to verbal memory, while the right temporal structures are more involved in visuospatial memory [8,9].

Diffusion tensor imaging (DTI) is an MRI technique detecting microstructural and functional abnormalities of tissues through fractional anisotropy (FA) and Apparent diffusion coefficient (ADC) [10] FA measures the preferred orientation of diffusion within white matter tissues [11] with tightly paralleled white matter fascicles provide strong coherence (high FA) while poorly organized fascicle reveals (low FA) [12], ADC refers to the mean diffusivity in a voxel with high ADC in area of more pronounced diffusion abnormality and low ADC in area of less diffusion abnormality [13,14].

DTI tractography provides an in vivo method for quantifying and visualizing the integrity of white matter tracts and its relation to memory impairment [15].

White matter tracts play a crucial role in linking cortical processing networks of memory [16]. Thus, its injury leads to memory impairment [17] and these white matter tracts changes was detected by DTI in TLE patients correlated to memory functions especially the episodic memory [18–21].

The purpose of this study is to evaluate the utility of DTI to explore white matter tracts microstructure changes and clarify their relation to episodic memory in TLE.

Peer review under responsibility of The Egyptian Society of Radiology and Nuclear Medicine.
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https://doi.org/10.1016/j.ejrnm.2017.12.013
Received 10 September 2017; Accepted 25 December 2017

2. Materials and methods

2.1. Materials

The study was approved by the hospital ethical committee. Informed consent was obtained from all patients. From December 2014 to October 2016 we prospectively evaluated 30 adult patients with TLE and 20 healthy control subjects matched for age, sex and level of education. They were diagnosed as TLE according to international league classification against epilepsy (ILAE) [22] EEG compliant to the 10–20 international system was done for all patients under standard conditions and they were subdivided into left TLE (n = 18) and right TLE group (n = 12) according to lateralization by EEG and seizure semiology.

Selected patients had to have a score > 24 on Mini-mental state examination (MMSE) to exclude dementia [23] and had the ability to read, write and do simple calculations. Patients should be seizure-free at least 48-h before MRI examination.

Patients with a history of substance abuse, head trauma, major psychiatric disorder or any concomitant medical or metabolic illness known to alter the cognition as well as patients with bilateral EEG epileptic focus and patients with MRI brain showing structural lesion apart from MTS are excluded from the study.

2.2. Methods

2.2.1. MRI imaging acquisition

MRI was performed to all patients to detect MTS and to exclude patients with other structural brain lesions. All MRI examinations were performed using 1.5 Tesla MRI machine (Achiva, Philips Medical system, Netherlands) with head coil and it included the following sequence:

- Sagittal T1WI, T2WI, Axial T1WI, T2WI and Fluid Attenuated Inversion Recovery (FLAIR), Coronal T2WI and FLAIR. All coronal images were obtained along a plane perpendicular to the long axis of the hippocampus.
- Diffusion weighted image (DWI) using single shot spin-echo echo planner sequence at b value of 0 and 1000 s/mm^2
- -Diffusion tensor imaging (DTI) using single shot spin-echo echo planar sequence in 25 encoding directions and diffusion factor of 800 s/mm^2.

2.2.2. Image processing

All MR images were transferred to an independent workstation (Philips MR extend workspace, software version 2009). The maps obtained were; ADC map, FA maps and directionally-encoded color maps as well as fiber tractography of the individual tracts (Fig. 1).

FA and ADC values were measured through application of multiple color-coded regions of interest (ROI) that were drawn manually as seeds in the portions of the white matter tracts and the software algorithm tracked the white matter tracts that passed through these ROIs.

FA and ADC values were measured bilaterally for the following 5 tracts; parahippocampal cingulum (PHC), superior longitudinal (arcuate) fasciculus (SLF), inferior longitudinal fasciculus (ILF), fornix (FORX), uncinate fasciculus (UF) and for corpus callosum (CC) as a whole.

2.2.3. Neuropsychological evaluation

It was done for all subjects in one session for each individual by an experienced trained neurologist.

A. Visual episodic memory: a subtests of Wechsler memory scale – revised (WMS-R) [24] including: Figural memory, Visual Paired Associates I & II and Visual Reproduction I & II both for immediate and delayed visual recall and Visual Memory Span which is a visual-spatial analog of the digit span subtest.
B. Verbal episodic memory: Logical memory I & II subtests of WMS-R were used for immediate and delayed verbal memory.

2.2.4. Statistical methods

The data were coded and entered using: the statistical package for social science version 15 (SPSS v15). Student *t*-test was used for comparison between means of two groups of quantitative variables. One way analysis of variance (ANOVA) test with posthoc multiple 2-group comparisons in comparing more than 2 groups. Chi square test was used for comparison between two groups of categorical data or frequency of events. Pearson correlation coefficient (r) was used to describe the degree of relationship between two variables. The sign of correlation coefficient (+, −) defines the direction of the relationship, either positive or negative. The probability/significance value (P value) ≥ 0.05 is not statistically significant and < 0.05 is statistically significant.

3. Results

Demographic data, seizure frequency, seizure duration and EEG, structural MRI findings, are summarized in Table 1.

3.1. Tractography findings

The mean FA values of the examined tracts were lower in both TLE groups than the control group. Only the mean FA value of the corpus callosum showed no statistically significant difference between the TLE groups and control group (Table 2). Also, There was no statistical significant difference of the FA values of the all tracts between the left and right TLE groups (all p > 0.05).

The mean ADC values were significantly higher in both TLE groups than the control group in the following tracts: (PHC, SLF, UF, FORX) except for the left ILF and corpus callosum which showed no statistically significant difference (Table 3).

On comparing the mean ADC values between the left and right TLE groups: the left TLE group had a significantly higher ADC value of left SLF (p < 0.001) whereas, the right TLE group had significantly higher ADC values of right (PHC, ILF and UF) (p < 0.01).

3.2. Neuropsychological tests characteristics

The mean values of the score of all the psychometric tests were lower in both TLE groups than control group (all P < 0.001). On comparing psychometric test results between both epileptic groups, the left TLE group had a significantly lower mean values of the Logical memory I (p = 0.02) and the difference approached significance (p = 0.05) regarding logical memory II subtest. While, the right TLE had a significantly lower mean values in the scores of visual memory subtests of WMS-R (visual paired associate II (p = 0.02) and visual memory span (p = 0.01) and the difference approached significance (p = 0.05) regarding visual paired associate I subtest (see Table 4).

3.3. Correlative results of tractography and neuropsychological tests

In the control group: There was no statistically significant correlation between the mean values of either FA or ADC and any of the scores of the psychometric tests of all tracts (all P > 0.05).

In the left TLE group: There was a significant positive correlation between each of verbal memory subtests (logical memory I &II) and FA of left PHC, SLF, UF, FORX with p values of (0.02), (0.000), (0.002), (0.007) and (0.01), (0.03), (0.005), (0.001) respectively.

There was a significant negative correlation between each of verbal memory subtests (logical memory I &II) and ADC of left PHC, SLF, UF, FORX with p values of (0.01), (0.006), (0.000), (0.008) and (0.02), (0.000), (0.01), (0.01) respectively.

Also, significant negative correlation between logical memory I and