Original Article

The Evaluation of the Brain Alterations in Epileptic Patients Using Structural Magnetic Resonance Imaging.

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Abstract

Purpose: The purpose of this study is to evaluate the brain alterations in epileptic patients and normal adults in order to help differential diagnosis using volumetric Magnetic Resonance Imaging (MRI).

Materials and Methods: The study case group included 11 subjects, 6 patients of whom with focal and secondary generalized seizures and 5 of whom were healthy people as a control group. Measurements and evaluations of the brain important regions were performed with volBrain software within 4 different pipelines.

Results: Statistical results showed that the significant quantitative assessments were observed in the areas as follows: right Hippocampus (P-value<0.05), right cerebellar (P-value<0.1), thalamus Asymmetry (P-value<0.1), right CA1 (P-value<0.1), left SR-SL-SM (P-value<0.1), right subiculum (P-value<0.1), left cerebellum cortical thickness (P-value<0.05) and some cerebellar lobules.

Conclusion: Structural MRI demonstrated significant brain alterations in epileptic subjects comparing normal adults. Assessment of brain lesions did not show any defect in Brain which implies that patients have disappearing lesions caused by seizures. Significant quantitative assessments were shown in the right lobule III, lobule IX mean cortical thickness, right cerebellum grey matter, right hippocampus and right cerebellar areas.

1. Introduction

Epilepsy is one of the most common and disabling neurologic conditions with recurrent unprovoked seizures striking about 50 new cases per year per 100,000 populations globally [1]. A seizure is a paroxysmal change of neurologic function caused by the inordinate, hyper synchronous discharge of human brain neurons [2]. Recently the International League Against Epilepsy (ILAE) has updated the epilepsy and seizure classification with Focal seizure as one division. Focal seizures are episodes of highly unruly brain activity, which are considered to be appeared in local areas of pathological abnormalities in the brain. Determination of the exact focal origin in a given patient is crucial for the clinical management of their epilepsy.

A seizure can begin from a site and later generalize to other areas of the brain [3]. Complex partial seizures usually arise from the frontal or temporal lobes but they spread to broader areas frequently in the bilateral patterns which are associated with impairment in consciousness [4, 5]. Over 70% of patients with focal epilepsy occasionally experience secondary generalization seizures, as the other subtype of the current issue [6]. These seizures can appear as a simple or complex partial seizure. According to the origination of the seizure, signal in ordination spreads to the entire cortex, thalamus, and midbrain, leading to a tonic-clonic seizure. There has been a growing investigation yielding that seizure-induced neuronal damages in chronic epilepsy can cause alterations in synaptic reorganization and connectivity

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[7]. Identification of the specific cortical and subcortical areas involved in focal seizures will be conclusive to reach a better understanding of the seizure related mechanisms and consequently impairment of brain regions, and may also help identify targets for improved prevention or treatment of this seizure type [8]. Beside EEG, neuroimaging techniques are especially sensitive for structural lesions of central nervous system including cortical and subcortical areas. MRI is more likely to illustrate a disease origination in a patient with focal seizures, extraordinary neurologic findings, or abnormal focal signals on Electroencephalography (EEG). CT is less sensitive than MRI, therefore this imaging method is preferred, most importantly for the detection of cortical malformation, digenesis, or hippocampal sclerosis [3].

In addition, investigations remark that the volumetric MRI has been successful in the evaluation of hippocampal and amygdaloidal damage in Focal seizures [9-11]. It is worth to say that quantitative, computer-assisted volume analysis of the temporal lobes may detect asymmetries that are not readily apparent on visual analysis of the scan [3]. Quantification of hippocampal volume has advantages over visual assessment for the detection of subjective and bilateral hippocampal and amygdala abnormalities which are the markers of epilepsy diagnosis [10, 12]. Appropriate diagnosis using Structural MRI will enable patients with focal epilepsy to be treated in a suitable, impressive, and cost-effective manner [11]. The goal of this study is to quantify the evaluation of the brain alterations in patients with epilepsy using structural MRI.

2. Materials and Methods

2.1. Subjects

The study case group included 6 patients with focal and secondary generalized seizures and 5 normal subjects as healthy control group which were recruited through local advertisements. The inclusion criteria in this study were:

- Detecting epilepsy in patients for at least one year: It takes time to appear the effects of epilepsy in the brain of the patient.

- Use of anticonvulsants during the study: In order to neutralize the effect of the drug as a disturbing variable, this criterion is considered as an inclusion criteria for all patients to be the same in this respect.

- No seizure occurrence at least 24 hours before imaging: Short-term changes in the brain may occur when a seizure happens that is apart from long-term and durable changes. To prevent the interference of short-term effects, this criterion has been considered.

- Absence of other neurological diseases: Other neurological diseases cause known effects on the brain. While we are studying the effects of epilepsy on the brain, so other neurological diseases as a disturbing variable should be eliminated.

- No Drug and alcohol abuse: Drug and alcohol abuse has known effects on the brain. While we are studying the effects of epilepsy on the brain, this variable as a disturbing variable should be eliminated.

- No history of cardiac arrest: Cardiac arrest leads to a lack of blood supply to the heart and structural damage, so this variable as a disturbing variable should be eliminated.

- No history of brain surgery: Any manipulation of the brain tissue causes changes in the structure and function of the brain and as a disturbing variable should be eliminated.

- Right handed: Lateralization in the brain of right handed and left handed people is different, so in order to assimilate all cases, only right handed patients are included.

2.2. Data Acquisition and Analysis

2.2.1. MRI Protocols

Participants underwent an imaging protocol including three-dimensional (3D) T1-weighted, T2-weighted, and FLAIR sequences, using a 3.0T Prisma MRI (Siemens, Germany) with a 64-channel head coil. Whole-brain T1-weighted images were obtained with the following imaging parameters: TR = 1810ms, TE = 3.47ms, TI = 1110ms, Voxel size = 1 × 1 × 1mm, FOV (Field Of View) = 256mm, Flip angle = 7 degree and Slice thickness = 1mm with no gap. FLAIR sequence parameters were: TR = 9120ms, TE = 83ms, TI = 2513.7ms, Slice thickness = 3mm with 2 mm gap.

2.2.2. MRI Analysis

In this study we used T1-weighted and T2 FLAIR images in order to assess general brain alterations from volumes and lesions points of view. Measurements and evaluations of the important brain regions were performed with volBrain software with 4 different pipelines including volBrain 1.0, CERES 1.0, HIPS 1.0 and lesion Brain 1.0.

3. Results

Right Hippocampus (P-value<0.05), right cerebellar (P-value<0.1), thalamus Asymmetry (P-value<0.1), right CA1 (P-value<0.1), left SR-SL-SM (P-value<0.1), right subiculum (P-value<0.1), left cerebellum cortical thickness (P-value<0.05) and some cerebellar lobules.

Table 1. VolBrain pipeline (whole brain volumetry)

Tissue	p-value	Mean	SD
Right Hippocampus	0.04	3.81	0.403
Right cerebellar	0.09	452.23	154.271
Thalamus Asymmetry	0.09	-1.96	3.296

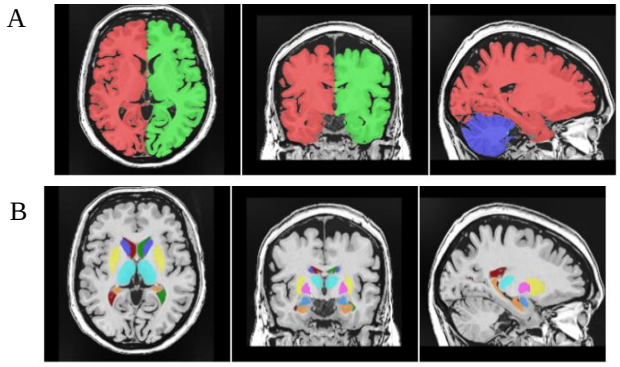

Figure 1. (A) Macrostructures and (B) subcortical structures were shown in volBrian pipeline

Table 2. HIPS pipeline (Hippocampal subfields volumetry)

Tissue	p-value	Mean	SD
Right CA1	0.09	0.93	0.196
Left SR-SL-SM	0.09	0.49	0.059
Right Subiculum	0.09	0.23	0.052

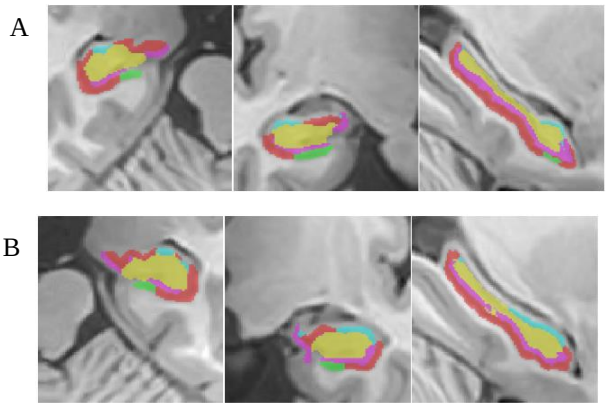

Figure 2. Hippocampal subfields segmentation was shown in HIPS pipeline. (A) Left Hippocampus. (B) Right Hippocampus

Table 3. CERES pipeline (Cerebellum lobules volumetry)

Tissue	p-value	Mean	SD
Right Lobule III	0.02	0.64	0.134
Lobule IX Mean Cortical Thickness	0.02	4.44	0.327
Right Cerebellum Grey Matter	0.02	41.97	7.812
Left Lobule I-II	0.04	0.05	0.013
Lobule III Total	0.04	1.26	0.246
Lobule VIIIA Total	0.04	7.60	2.860
Left Lobule VIIIA	0.04	3.65	1.352
Lobule VIIIB Asymmetry	0.04	4.72	10.480
Right Lobule IX Cortical Thickness	0.04	4.21	0.695
Left Cerebellum Cortical Thickness	0.04	4.77	0.230

Table 4. Lesion Brain pipeline (Evaluation of the Brain Lesions)

Lesion	p-value	Mean	SD
Total Lesion Count	0.10	4.60	3.921
Periventricular Count	0.14	2.70	1.059

This pipeline did not show significant alterations between the two healthy control and patient groups.

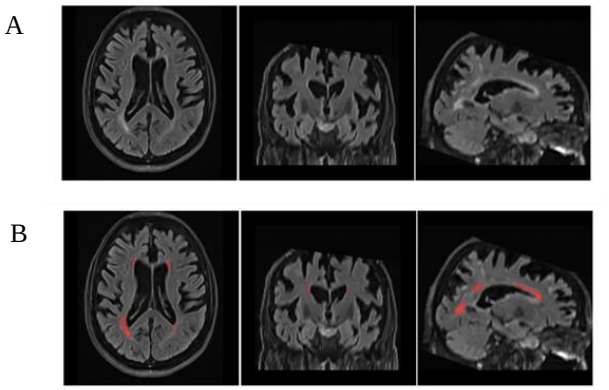

Figure 4. (A) FLAIR Images and (B) level of Lesions were shown in an Epileptic patient with Lesion Brain pipeline

4. Conclusion

The results of this study indicate that adults with focal and secondary generalized epilepsy tend to show alteration in hippocampal volume, both in right and left hemisphere but most significantly in right hippocampus volume loss, in comparison with healthy controls. Volume reductions were also found in right cerebral hemisphere, yielding that right part of brain is under the influence of seizures. Thalamus volume asymmetry was also observed. The medial dorsal nucleus of the thalamus has been associated with focal epilepsy specifically with Mesial Temporal Lobe Epilepsy (MTLE). Animal models of the MTLE have shown that the thalamus is a central contributor to seizure onset and perhaps acts as a regulator of secondary generalization of seizure from the medial temporal lobe to distant neocortical area [13]. In our investigation, also morphological changes of cerebellar subfields played role as a discriminator between epileptic subjects and healthy controls. Cerebellar atrophy is frequently debated in patients with epilepsy [14-16]. Previous studies showed that the cerebellar lobules volume alterations are routinely reported to occur in a subset of patients with secondary generalized epilepsy, the rate varying across studies [17, 18]. Ipsilateral reduction of cerebellar whole gray matter volume regardless of seizure focus in temporal lobe epilepsy was observed by several investigations [19]. Lateralized cerebellar alterations related to the side of the epileptic focus were illustrated by Keller *et al.*[20] There is coincidence in gray matter volume reduction of the whole cerebellum and the posterior cerebellar lobe, however, white matter volume changes seem to be insignificant in the present study [21]. The cerebellum itself might not be the initiator, but only another structure experiencing detrimental epileptic activity. Cerebellar damage can also indirectly cause epileptic seizures. Patients with epilepsy may have abnormal brain imaging. Lesions showed on CT or MRI often yielded the underlying cause of the seizures [22]. Our employing pipeline for assessing brain lesions did not show any defect in brain, which implies that patients have disappearing lesions caused by seizures. With this evidences, our multi-method assessments have demonstrated that some brain alterations can make differentiation between epileptic patients and normal adults using structural MRI.

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