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Characterization of Hippocampus in Epileptic Sudanese Children using MRI

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Abstract- Seizures are the most noticeable clinical manifestations of epilepsy; measurement of the hippocampus on magnetic resonance (MR) images of the brain has been useful for the assessment of patients with seizures. Therefore this study aimed to diagnose subjects who had developed epilepsy by measuring the RT and LT hippocampus area and volume considering epilepsy duration, seizure frequency, EEG results, T2 signal intensity, treatment, and children ages as well as to correlate the MRI findings with EEG findings. This Study was conducted at Gezira University- MRI Diagnostic center –Khartoum –Sudan during the period from 2010up to2011using Siemens 0.5 Tesla MRI machine. A total of 29 Sudanese children of both genders with clinical history of generalized seizures, and 17 normal children who were selected as control group at different ages were involved in this study. Children with head injury or organic lesion found on MR images were excluded.

Keywords: *epilepsy, siezers, hippocampus.*

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Characterization of Hippocampus in Epileptic Sudanese Children using MRI

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Abstract- Seizures are the most noticeable clinical manifestations of epilepsy; measurement of the hippocampus on magnetic resonance (MR) images of the brain has been useful for the assessment of patients with seizures. Therefore this study aimed to diagnose subjects who had developed epilepsy by measuring the RT and LT hippocampus area and volume considering epilepsy duration, seizure frequency, EEG results, T2 signal intensity, treatment, and children ages as well as to correlate the MRI findings with EEG findings. This Study was conducted at Gezira University- MRI Diagnostic center –Khartoum –Sudan during the period from 2010up to2011using Siemens 0.5 Tesla MRI machine. A total of 29 Sudanese children of both genders with clinical history of generalized seizures, and 17 normal children who were selected as control group at different ages were involved in this study. Children with head injury or organic lesion found on MR images were excluded.

The hippocampus was characterized in the coronal MR images; the area and volume of the right and Left sides were found to be reduces significantly in the diseased sample comparing with the control group; there was relationship between patient's age and seizure duration and frequency as well as hippocampus area and volume. Significant differences were detected in the hippocampus area and volume in children who have got treatment and none treated children.T2 weighted images showed hyper signal intensity in the hippocampuses of the diseased sample. No significant differences were detected in males and females measurements. EEG failed in diagnoses of 12 (41.4%) cases of the sample, and new formulas were established for prediction of EEG findings regarding the hippocampus area and epilepsy duration.MRI has a great value in characterization hippocampus in epileptic Sudanese children.

Keywords: epilepsy, siezers, hippocampus.

I. Introduction

Epilepsy is a chronic brain disorder that is characterized by repeated spontaneous seizures, and increased risk of mortality.[Wilner AN et al.,2010] Epilepsy is one of the most common neurologic disorders encountered in clinical practice. Epilepsy is more common among the elderly, higher incidence in men than women.

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[Hesdorffer DC et al., 2011, Banerjee PN et al .,2009], more common among racial or ethnic minorities or among low-income populations. [Banerjee PN et al., 2009].

Seizures are the most obvious clinical manifestations of epilepsy; it refers to the changes in physical findings that occur in relation to abnormal electrical activity within the brain [Fisher RS et al., 2005] The electroencephalogram (EEG), can measures changes in brain electrical activity, and identify brain regions where seizures are most likely to originate. More recently, imaging technologies such as magnetic resonance imaging (MRI), has become indispensable tool in evaluating patients with epilepsy and other seizure disorders, because of it's superior soft tissues contrast, and ability of viewing variety of planes, providing greater sensitivity and accuracy for the identification of underlying lesions in patients with epilepsy .According to guidelines from the American College of Radiology (ACR), MRI is considered appropriate for all epilepsy evaluations, and become the standard for brain imaging in patients with seizures.[www.acr.org 2011].

A systematic approach to the evaluation of seizure disorders is essential to ensure that patients receive appropriate treatment and to rule out the many other medical conditions that may resemble epilepsy [Noe KHet al., 2011].

Common MRI protocols used in the evaluation of epilepsy include volumetric T1-weighted sequencing; proton-density, T2-weighted and fluid-attenuated inversion recovery (FLAIR) sequences in oblique coronal and axial planes; and gradient echo sequences. [Duncan JS. ,2010].

Measuring hippocampus volume with MRI has provided important information about several neuropsychiatric disorders, smaller hippocampus volu-mes have been reported in epilepsy [Geuze et al., 2009].

Measurement of hippocampus volumes has been found to be the most accurate approach to evaluate the hippocampus pathology [Bronen RA.,1991]. This has found its greatest clinical application in the assessment of patients with seizures [Ashtari M et al., 1991, Jack CR.,1990]. Other factors may also help identify hippocampal sclerosis: quantitative evidence of increased T2 values; and visual assessment of the disruption of internal architecture, volume loss, and

intensity elevation [Jackson GD., 1990, Kuzniecky R., 1987].

This study aimed to diagnose subjects who had developed epilepsy by measuring the RT and LT hippocampus area and volume considering epilepsy duration, seizure frequency, EEG results, T2 signal, treatment, and children ages as well as to correlate the MRI findings with EEG findings.

II. Material and Methods

This Study was conducted at Gezira University-MRI Diagnostic center-Khartoum-Sudan during the period from 2010up to2011.

MRI machine: Siemens 0.5 Tesla

Patients: A total of 29 children in both genders with clinical history of generalized seizures, and 17 were normal as control group at different ages were involved in this study. The ethics and research committee approved the study.

Exclusion criteria: Subjects who were normal, with head injury or organic lesion found on MR images were excluded.

MRI technique and Hippocampus area and volume measurements

MRI Brain was done first axial T1, T2, FLAIR and sagittal images; it is used as screening for presence of mass lesion or other abnormalities. Sagittal image was used as a guide to obtain perpendicular plane to temporal lobe. T1, T2 of coronal 3mm slice thickness, images perpendicular to the long axis of the temporal lobe were taken.

Volume measurement

The whole hippocampal volume was measured. Measurement of hippocampal body and tail included subicular complex, the hippocampus proper, the dentate gyrus, the alveus and hippocampal fimbria. ROI-manually traced with computer mouse, right and left sides were measured individually. The measures were done three times for each ROI and the average was taken. Summation of the average of each slice = the total area of hippocampus for each side.

Volume of the hippocampal complex (cm3)=total area of the hippocampal complex (cm2) X the slice thickness (cm)

III. Results

The 29 subjects studied consist of 11(37.9%) males and 18(62.1%) females. The mean ages of the subjects were 14.79±6.01 years. The mean age of the seizure onset was found to be 12.4±5.7and frequency of 6.6±4.35.

Table 1 : The mean and standard deviation of the hippocampus volume and area measurements for epileptic patients

	Area (RT) Cm^2	Volume (RT) cm^3	Area (LT) Cm^2	Volume (LT) cm^3
Mean	2.75	2.47	2.62	2.36
Std. Deviation	±0.23	±0.21	±0.21	±0.19

Table 2 : Shows the frequency of epilepsy duration in the sample

Epilepsy duration (minutes)	Frequency	Percent%
2	7	24.1
3	5	10.3
4	5	13.8
5	5	6.9
8	1	3.4

9	3	10.3
11	1	3.4
13	2	6.9
Total	29	100.0

Table 3 : Shows the frequency of EEG results

		Frequency	Percent%
EEG	Consigned with MRI (negative epileptic findings)	7	24.1
	Adverse findings with MRI	12	41.4
	Consigned with MRI (positive epileptic findings)	10	34.5
	Total	29	100.0

Table 4 : Shows the frequency of T2 signal classified as (iso signal intensity& hyper signal intensity)

		Frequency	Percent%
Signal intensity	Iso intense	7	24.1
	Hyper intensity	22	75.9
	Total	29	100.0

Table 5 : Shows frequency of not treated & treated patients

		Frequency	Percent%
Treatment	Not treated	23	79.3
	Treated	6	20.7
	Total	29	100.0

Table 6 : Shows correlation between seizure frequency & Treatment

Model	Un-standardized Coefficients		Standardized Coefficients	Sig.
	B	Std. Error	Beta	
(Constant)	-.099	.124		.432
Seizures Frequency	.047	.016	.492	.007

**This table showed that the seizures frequency decreased by .099 according to the treatment*

Table 7 : Shows correlation among EEG, Epilepsy duration, LT Hippocampus area in both genders

gender	Model	Un-standardized Coefficients		Standardized Coefficients	Sig.
		B	Std. Error	Beta	
Male	(Constant)	-3.229	1.924		.105
	Area (LT) Cm^2	1.570	.730	.388	.041
Female	(Constant)	-4.125	1.812		.032
	Area (LT) Cm^2	1.726	.676	.427	.017
	Epilepsy Duration	.101	.043	.397	.025

+here also EEG results can be related to the area (LT) and epilepsy duration as follow:
EEG = [(area (LT) × 1.726) + (epilepsy duration × 0.101)] – 4.13

Table 8 : Shows correlation among EEG, Epilepsy duration, RT Hippocampus area in both genders

gender	Model	Un-standardized Coefficients		Standardized Coefficients	Sig.
		B	Std. Error	Beta	
Male	(Constant)	-2.336	1.026		.126
	Area (RT) Cm^2	1.679	.680	.372	.036
Female	(Constant)	-3.236	1.789		.029
	Area (RT) Cm^2	1.624	.457	.496	.028
	Epilepsy Duration	.101	.043	.397	.025

**here also EEG results can be related to the area (RT) and epilepsy duration as follow:*
EEG = [(area (RT) × 1.624) + (epilepsy duration × 0.101)] – 3.24

Table 9 : Shows T-Test Difference between male & female measurement of the area and Volume as mean, Std. Deviation and *P*-value

	gender	N	Mean	Std. Deviation	Sig. (2-tailed)
Area (RT) cm^2	Male	11	2.7182	.21442	.607
	Female	18	2.7650	.24677	.595
Volume (RT) cm^3	Male	11	2.4473	.19267	.616
	Female	18	2.4883	.22150	.604

Area (LT) cm^2	Male	11	2.6173	.19571	.906
	Female	18	2.6272	.22862	.902
Volume (LT) cm^3	Male	11	2.3564	.17614	.891
	Female	18	2.3667	.20594	.887

Table 10 : Shows the measured area and volume (comparison between none treated & treated measurement in mean &Std. Deviation and *P*-value

	Treatment	N	Mean	Std. Deviation	Sig. (2-tailed)
Area (RT) cm^2	No treated	23	2.7322	.22682	.504
	Treated	6	2.8050	.26569	.558
Volume (RT) cm^3	No treated	23	2.4583	.20252	.473
	Treated	6	2.5283	.24128	.534
Area (LT) cm^2	No treated	23	2.6061	.20701	.400
	Treated	6	2.6900	.24331	.464
Volume (LT) cm^3	No treated	23	2.3474	.18663	.409
	Treated	6	2.4217	.21885	.471

Table 11 : Shows the T2 signal status in normal & abnormal patients as mean Std. Deviation and *P*-val Ue

	T2 Signal	N	Mean	Std. Deviation	Sig. (2-tailed)
Area (RT) Cm2	Normal	7	2.6186	.15291	.093
	Abnormal	22	2.7882	.24073	.043
Volume (RT) cm3	Normal	7	2.3586	.14053	.097
	Abnormal	22	2.5091	.21580	.048
Area (LT) Cm2	Normal	7	2.5200	.14059	.143
	Abnormal	22	2.6564	.22413	.074
Volume (LT) cm3	Normal	7	2.2700	.12490	.145
	Abnormal	22	2.3923	.20225	.073

Table 12 : Shows mean and standard Deviation of the epileptic subjects and control group for RT and LT area and volume measurement (*p*-value at 0.05)

	Area (sample) (RT) cm^2	Area (control) (RT) cm^2	Volume (sample) (RT) cm^3	Volume (control) (RT) cm^3	Area (sample) (LT) cm^2	Area (control) (LT) cm^2	Volume (sample) (LT) cm^3	Volume (control) (LT) cm^3
Mean	2.7	2.9	2.47	3.01	2.62	2.8	2.4	3.21
STDV	±.23	±.26	±.21	±.21	±.21	±.32	±.19	±.21
p-value	0.0423		0.059		0.0563		0.034	

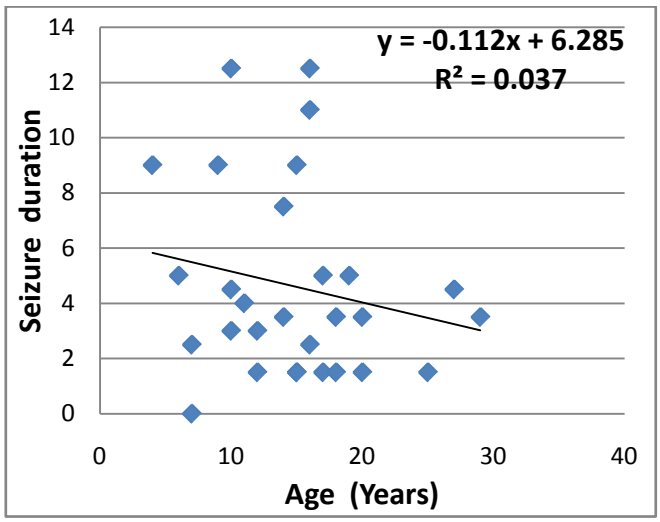

Figure 1 : The relation between the Seizure duration and the age

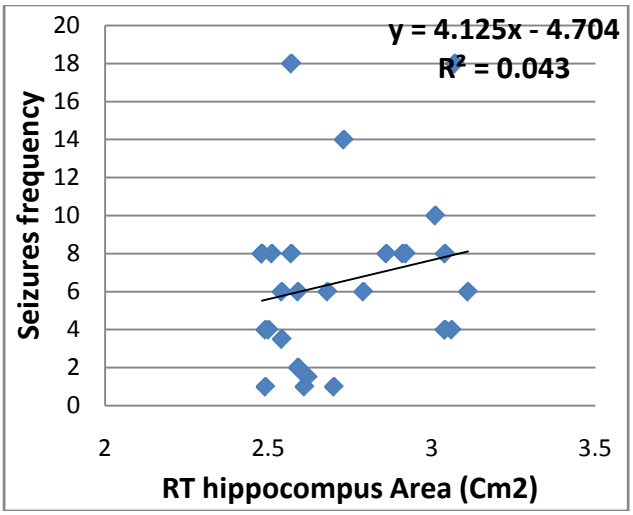

Figure 3 : The relation between the Seizure frequency and the RT hippocampus area

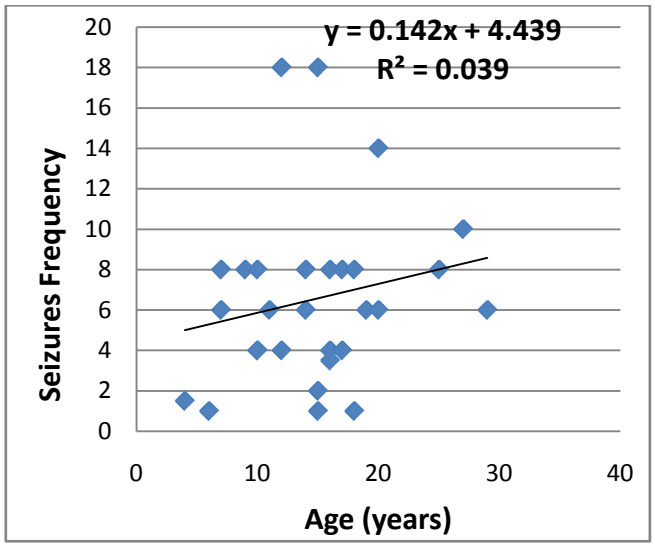

Figure 2 : The relation between the Seizure frequency and the age

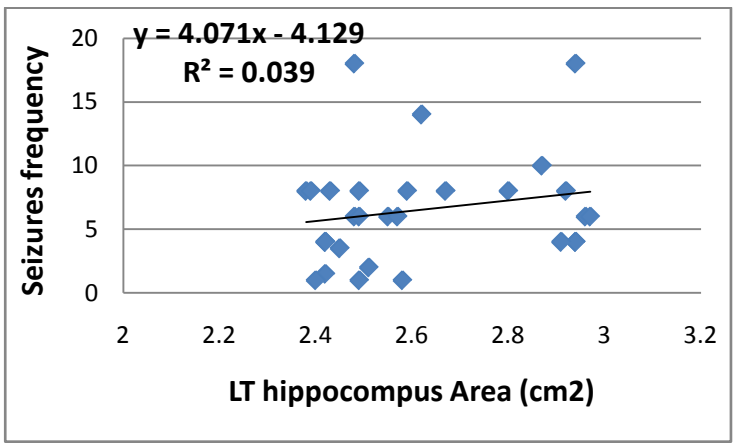

Figure 4 : The relation between the Seizure frequency and the LT hippocampus area

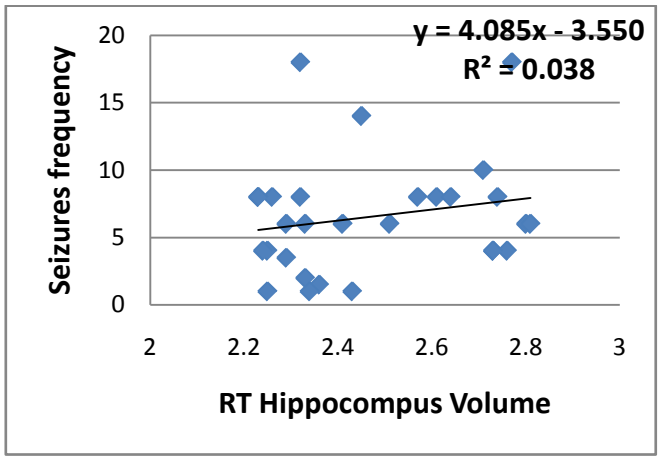

Figure 5 : The relation between the Seizure frequency and the RT hippocampus volume

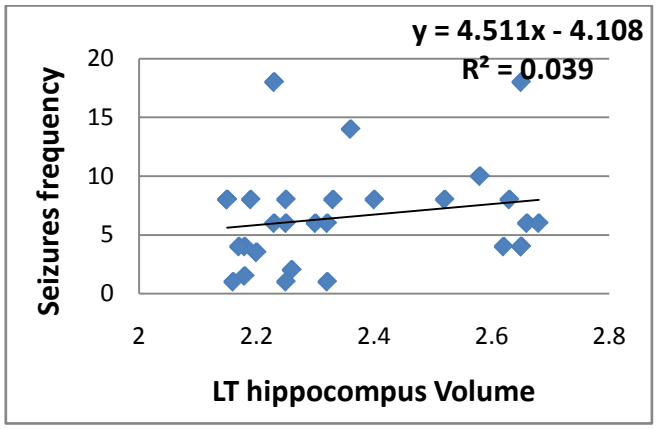

Figure 6 : The relation between the Seizure frequency and the LT hippocampus Volume

IV. Discussion

This study reported the MR findings in a group of patients with documented temporal lobe epilepsy. The diagnosis of temporal lobe epilepsy was based on typical clinical seizure characteristic. In epilepsy researches and in temporal lobe epilepsy in particular, hippocampal volumetry with MRI were mainly used in the determination of hippocampal atrophy and hippocampal sclerosis.The clinical features of this study of 29 epileptic children with temporal lobe epilepsy were in line with four cross sectional previous studies (L.E. Betting et al.,2006; Idil Cavus et al.,2008; Mai Hanamiya et al.,2009; Douglas E et al.,2010).Females were affected more often than males (18 females, 11 males) . This gender results were consistently seen in our studies, supporting the hypothesis that the cause could be a biological phenomenon rather than a research entity.Table1showed the measurements of hippo-campus area and duration and table 2 showed the duration of seizures (minutes)in the sample Abnormalities on MR images were detected in 22 (75.9%), hippocampal sclerosis being the most common lesion. EEG confirmation was present in 10 (34.5%) regarding 7 (24.1%) had normal EEG and 12 cases were reported adverse results from the MRI findings as presented in table(3). Overall agreement between the two observers was fair, indicating that hippocampal sclerosis and other lesion can be detected reliably on MR images. The reported MR features of hippocampal sclerosis included hippocampal atrophy, increased signal intensity on T2, loss of internal architecture of the hippocampus, and loss of singnal intensity on T1 weighted images. In our study only the first two were used as criteria for diagnosis of hippocampal sclerosis.

No lesion was detectable on MR images of 7(24.1%) concordant with 7(24.1%) whom EEG result was normal as the T2 signal intensity was found to be iso intense and patients were diagnosed as normal but the abnormal signal was detected in 22(75.9%) of the sample showing hyper signal intensity and were diagnosed as abnormal this was presented in table (4). The epilepsy was usually mild and responsive to medication this was presented in table (5). 23 out of 29 (79.3%) were on no treatment at the time of study. 6 out of 29 (20.7%) had good seizure control with a single anti-epileptic drug. The seizures frequency decreased by 0.99 according to treatment and the relation is significant between the frequency of seizures and cases administrated with drugs at *p* value 0.007; this was presented in table (6).

EEG results can be related to the left hippocampus area and epilepsy duration as: EEG = [(area (LT) × 1.726) + (epilepsy duration × 0.101)] – 4.13,where EEG results can be related to the right hippocampus area and epilepsy duration as: EEG = [(area (RT) × 1.624) + (epilepsy duration × 0.101)] – 3.24.as presented in tables (7)and(8).

No significant differences were detected between males and females mean measurements for the hippocampus area and volume as presented in table (9).

The hippocampal volume for treated patient were RT 2.53±0.24, LT 2.42±0.22 and for none treated were RT2.46±0.2, LT 2.35±0.19 respectively table (10). The difference at T test (*P*. value = 0.05) was found to be insignificant for both RT&LT as to be for RT (0.47, 0.53).

Table (4) showed that 7 (24.1%) in the group of patients had normal hippocampus T2 signal, 22 (75.9%) showed high signal intensity on T2. The hippocampal volume of normal T2 signal were RT 2.36±0.14, LT 2.27±0.12 were the volume for high signal intensity RT 2.51±0.21, LT 2.39±0.2 respectively table (11). T- test showed that the difference at (*P-value 0.05)* was to be insignificant for the normal and abnormal T2 signal for hippocampus volume as (0.97, 0.15) for RT and (0.5, 0.73) for LT respectively, but the difference was to be

significant for the normal T2 signal of the RT hippocampus area when compared with the abnormal T2 signal for the same area.

Previous investigations using volumetry showed that hippocampal atrophy is a reliable marker of hippocampal sclerosis (L.E. Betting et al.,2006; Mai Hanamiya et al.,2009). In an investigation of patients with temporal lobe epilepsy, 22 (75.9%) patients with hippocampal sclerosis pathologically proven had atrophy in the MRI evaluation.

In another volumetric evaluation of patients with idiopathic generalized epilepsy, no hippocampal atrophy had been detected but the hippocampal hyper intense T2 signal was present (Mai Hanamyia et al., 2009).

A significant reduction had been detected in the right and left hippocampus area and volume of the epileptic children when compared with the control group as presented in table (12).

The reduced hippocampus volumes described herein were slightly different from the typical findings of hippocampal sclerosis. Ipsilateral reduction of the fornix is associated with hippocampal atrophy in most of the patients with unilateral hippocampal atrophy. Hippocampal hyperintense T2 signal was present in 22(75.9%) similar findings were mentioned by (L.E. Betting et al., 2006).

The justification is that a disturbance in the blood and oxygen supply during epileptic attacks causes destruction of hippocampal nerve cells and that the sclerosis, or scarring, is the end result of this process Margerison J. H. ,et al2010).The tendency for the damage to occur preferentially in certain parts of the hippocampus, is attributed either to a special sensitivity of these areas to lack of oxygen, or to their exceptional need for oxygen through increased cellular activity at a time when it is liable to be in short supply. This discriminating susceptibility may be due to variations in the chemical make-up of its different parts, (Purpura and Gonzalez-Monteagudo,1960), the researchers suggested that these were the causes of changing the signal intensity in T2 weighted images.

EEG failed in diagnosing of 12 patients where MRI images showed a significant reduction and changing in the T2 signal intensity.

The study also noted that as the children ages increased the seizure duration was also decreased by 0.11 starting from 6.4minutes, but the frequency increased by0.14 as the children ages increased, this was presented in figure(1)and figure(2).

As the RT and LT hippocampus areas increased; the seizures frequency was also increased at R^2 0.04 and 0.039,this was presented in figures (3,4)as well as the RT and LT hippocampus volume ;it increased at R^2 0.038,0.039 respectively and this was presented in the figures5and6.

Regarding the results, the routine electroencephalogram (EEG) is often helpful in diagnosing epilepsy because it can detect the abnormal electrical discharges in the brain that indicate epilepsy. However, the EEG is very often normal in patients with proven epilepsy, so it cannot be used alone to exclude epilepsy. MRI is an excellent imaging modality used to characterize the hippocampus by measuring its area and volume as well as to evaluate the signal intensity as these articles are very important to evaluate patients with neurological disorders.

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