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Magnetic resonance imaging (MRI) volumetry in children with nonlesional epilepsy, does it help?

Ehab Ali Abdelgawad^{1*}, Samir M. Mounir², Marah M. Abdelhay¹ and Mohammed A. Ameen¹

Abstract

Background: Epilepsy is a chronic condition characterized by repeated spontaneous seizures. It affects up to 1% of the population worldwide. Children with magnetic resonance imaging (MRI) negative (or “nonlesional”) focal epilepsy constitute the most challenging pharmacoresistant group undergoing pre-neurosurgical evaluation. Volumetric magnetic resonance imaging (VMRI) is a non-invasive brain imaging technique done to measure the volume and structure of specific regions of the brain. It is useful for many things, but primarily for discovering atrophy (wasting away of body tissue) and measuring its progression. The aim of this study is to assess role of volumetric magnetic resonance imaging in evaluation of nonlesional childhood epilepsy in which no specific findings detected in conventional MRI.

Results: There were 20 children with normal MRI brain volumetry (33.3%) and 40 children (66.6%) with abnormal MRI brain volumetry.

Grey matter volume in the abnormal group was significantly higher (P value was 0.001*) than the normal group (mean \pm S.D 934.04 \pm 118.12 versus 788.57 \pm 57.71 respectively). White matter volume in the abnormal group was significantly smaller (P value was < 0.0001*) than in the normal group (mean \pm S.D 217.79 \pm 65.22 versus 418.07 \pm 103.76 respectively). Right hippocampus CA4-DG volume in the abnormal volume group was found to be significantly smaller (P value < 0.0001*) than that of the normal group volume (mean \pm S.D 0.095 \pm 0.04 versus 0.32 \pm 0.36 respectively). Right hippocampus subiculum volume in the abnormal volume group were found to be significantly smaller (P value was < 0.0001*) than that of the normal group volume (mean \pm S.D 0.42 \pm 0.11 versus 0.84 \pm 0.09 respectively). Thalamus volume in the abnormal group was significantly smaller (P value 0.048*) than in the normal group (mean \pm S.D 10.235 \pm 3.22 versus 11.82 \pm 0.75 respectively). Right thalamus was significantly smaller (P value was 0.028*) than in the normal group (mean \pm S.D 5.01 \pm 1.62 versus 5.91 \pm 0.39 respectively). The sensitivity of the right hippocampus subiculum volume and right hippocampus CA4-DG was 100%. The sensitivity of white matter volume and grey matter volume and thalamus was 85% and 75% and 55% respectively. The specificity of the right hippocampus subiculum volume and right hippocampus CA4-DG was 90% and 90% respectively. The specificity of the right hippocampus subiculum volume and right hippocampus CA4-DG and grey matter volume and white matter volume and total hippocampus and thalamus was 100%. The specificity of brain volume was 60%. The accuracy of the right hippocampus subiculum volume and right hippocampus CA4-DG was 100%. The specificity of white matter volume, grey matter volume, thalamus, total hippocampus, and brain volume

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was 97%, 87%, 65%, 61%, and 57% respectively.

Conclusion: Volumetric magnetic resonance imaging is a promising imaging technique that can provide assistance in evaluation of nonlesional pharmacoresistant childhood epilepsy.

Keywords: MRI, Volumetry, Children, Epilepsy

Background

Epilepsy is a chronic condition characterized by repeated spontaneous seizures. It affects up to 1% of the population worldwide [1].

Patients with magnetic resonance imaging (MRI) negative (or “nonlesional”) focal epilepsy constitute the most challenging pharmacoresistant group undergoing pre-neurosurgical evaluation [2].

The overall prevalence of nonlesional epilepsy in all surgical studies is ~26% [3].

Seizures are classified into either generalized or partial, with partial seizures being further divided into those without loss of consciousness (simple) and those where consciousness is lost or impaired (complex) [4].

Once patients have a diagnosis of epilepsy, it is critical to further classify these patients into lesional or nonlesional for treatment and prognostic reasons [5].

There is no standardized epilepsy imaging protocol in place among different institutions and hospitals; the primary clinical neuroimaging modality is MRI, with acquisition of a whole brain T1WI for imaging anatomy, and various T2-based acquisitions for detecting tissue pathology as FLAIR and GRE [5].

Volumetric magnetic resonance imaging (VMRI) is a non-invasive brain imaging technique done to measure the volume and structure of specific regions of the brain. It is useful for many things, but primarily for discovering atrophy (wasting away of body tissue) and measuring its progression [6].

Volumetric MRI, when used in conjunction with EEG, and neuropsychological studies enable patients with epilepsy to be treated in an appropriate, efficient, and cost-effective manner [7].

The aim of this study is to assess role of volumetric MRI in evaluation of nonlesional childhood epilepsy.

Methods

The institutional ethical committee board approved this prospective clinical study. A written consent was obtained for the current study, and the procedures were explained for parents. Total number of patients enrolled in this study was sixty epileptic patients (36 males and 24 females). Age range was (3–14 years old) (mean age 8.47 ± 3.15 years). The study was conducted in the time period from May 2019 to June 2020. Patients were clinically evaluated by parental interviewing and history

taking including onset of seizures, type, frequency, duration, medications, and response to drugs. Also, comprehensive clinical examination highlighting neurodevelopmental assessment was done. EEG with different montages was done for all patients using a Nihon Kohden 8-channel conventional EEG machine. Ten to 20 international systems of electrode placement for diagnosing epilepsy. MRI of the brain including volumetric measures was performed to all patients. Inclusion criteria were pediatric patients with both clinical- and EEG-suggested diagnosis of epilepsy, no structural abnormalities in conventional MRI, and no seizures at least 72 h before MRI imaging. Exclusion criteria included post-operative patients, post head trauma patients, febrile convulsions, patient with evidence of MRI structural lesion which may be the cause of seizures, contraindications to anesthesia before MRI technique, and contraindications to MRI technique itself as children with cochlear implants. No contrast material was given to any of our patients.

MRI examination

No special preparation was needed. The examination was fully explained to the parents. All MRI studies were carried out using the same MRI machine Philips Ingenia 1.5 T, 16 channels coil, Philips medical systems. Scan time was about 12 min.

The epilepsy-dedicated research protocol included the following pulse sequences: T1WI 3D: sT1W_3D_TFE, FOV: covering whole brain (230 mm), voxel $1 \times 1 \times 1$ mm isotropic, SNR = 1, Echo pulse sequence: gradient, flip angle 30, TE 3.4 ms, TR 7.3 ms; T2W_3D_DRIVE: FOV: covering whole brain (230 mm), voxel $1 \times 1 \times 1$ mm isotropic, SNR = 1, TE 245 ms, TR 1500 ms, SNR = 1; 3D FLAIR: FOV 230, voxel $1.16 \times 1.44 \times 5$ mm, TR 11,000 ms, TE140 ms, SNR = 1

Image analysis

Conventional assessment was done using Philips ISP (Intellispace portal v. 9), for primary reporting.

Volumetric and segmentation reporting

A compressed T1WI dataset in NIFTI (Neuroimaging Informatics Technology Initiative) format was uploaded to online MRI-brain volumetric system at www.volbrain.com (VolBrain version 1.0 for whole brain segmentation

and HIPS version 1.0 hippocampus segmentation). When automatic process is complete, a PDF report is created containing volumetric data about the grey matter, white matter, CSF, and subcortical grey matters as well as hippocampus segmentations.

We validate NIFTI files using the ITK-SNAP Version 3.4.0 software for all cases; full description of VolBrain pipe-line was published by Manjon and Coupé [8].

Once the process is finished, we were notified by e-mail, so we were able to download a package including some image files and two (CSV and PDF) reports gathering all the volumetry values calculated from the segmentations. In each report, volumes were measured such as: (1) volBrain report: parenchyma, brain tissues, macro-structure, and subcortical structure volumes measured such as volumes of the main intracranial cavity (ICC) tissues (that is, cerebrospinal fluid (CSF), grey matter (GM), and white matter (WM)). It also provides volume information of some macroscopic areas such as brain hemispheres, cerebellum, brainstem, and thalamus, finally, automatic subcortical structure segmentation and also asymmetry indexes. (2) Lesion brain report: lesion classes, volumes, and their locations; (3) hippocampus report: subfield volumes of hippocampus CA1-3, CA4-DG, and subiculum. The report also includes several snapshots from the different labeling results as a quality control. All the volumes were presented in absolute value (measured in cm^3) and in relative value (measured in relation to the ICV). The asymmetry index is calculated as the difference between the right and left volumes divided by their mean (in percent). Values between brackets show expected limits (95%) of normalized volume in function of sex and age for each measure for reference purpose. Green and red values indicate that the volume is above or under the expected volume limits respectively.

Statistical analysis of the data

Data were fed to the computer and analyzed using the SPSS software package version 20.0. Cleaning of data as a first step was done to detect missing values and invalid responses. Qualitative data were described using frequency, number, and percent. Quantitative data were described using mean, standard deviation, and range (minimum and maximum). Significance of the obtained results was judged at the 5% level.

Used tests

The Chi-square test and Fisher exact test “used if more than 20% of cells are less than 5” were used to compare between proportions. Student’s *t* test was used to compare two means.

Diagnostic accuracy was represented using the term sensitivity, specificity, positive predictive value, negative

predictive value, and overall accuracy. *P* value less than 0.05 was considered statistically significant, and all statistical tests were 2 tailed.

Results

According to the volumetric results, we classified epileptic patients who had shown normal conventional brain MR imaging into two groups: abnormal volume group (group A) and normal volume group (group B).

Group A included 40 patients (66.6%) and group B included 20 patients (33.3 %). The mean age for group A was 7.25 ± 3.39 (*P* 0.39) and mean age for group B was 8.2 ± 2.48 . Generalized epilepsy was more common than focal epilepsy in group A (75% generalized epilepsy versus 25% focal epilepsy). On the other hand in group B patients, generalized epilepsy was 30% versus 70% focal epilepsy. Volumetric measures of different brain regions in the studied group A (*N* = 40) are given in Table 1. Volumetric measures of different brain regions in group B (*N* = 20) are given in Table 2.

Seizure frequency was 1.8 ± 0.85 with a range of attacks from 1 to 3 attacks/week and seizure duration ranged from 15 to 45 s. Seizure frequency in group A was significantly higher than in group B (mean \pm S.D 2.05 ± 0.89 versus 1.30 ± 0.48 respectively). Age and sex showed no statistically significant difference between both groups.

Grey matter volume in group A was significantly higher (*P* value was 0.001*) than group B (mean \pm S.D 934.04 ± 118.12 versus 788.57 ± 57.71 respectively) (Fig. 4). White matter volume in group A was significantly smaller (*P* value was <0.0001*) than in group B (mean \pm S.D 217.79 ± 65.22 versus 418.07 ± 103.76 respectively) (Fig. 1). Right hippocampus CA4-DG volume in group A was found to be significantly smaller (*P* value <0.0001*) than that of group B (mean \pm S.D 0.095 ± 0.04 versus 0.32 ± 0.36 respectively) (Fig. 2). Right hippocampus subiculum volume in group A was found to be significantly smaller (*P* value was <0.0001*) than that of group B (mean \pm S.D 0.42 ± 0.11 versus 0.84 ± 0.09 respectively). Thalamus volume in group A was significantly smaller (*P* value 0.048*) than in group B (mean \pm S.D 10.235 ± 3.22 versus 11.82 ± 0.75 respectively) (Fig. 3). Right thalamus was significantly smaller (*P* value was 0.028*) than that found in group B (mean \pm S.D 5.01 ± 1.62 versus 5.91 ± 0.39 respectively). Comparison between group A and B regarding volumetric measures is given in Table 3.

There was significant difference between EEG abnormalities and the volumetric measurements in the white matter volume and in the right hippocampus CA4-DG volume in the studied groups (*P* value was 0.03* and 0.02* respectively).

Table 1 Volumetric measures of different brain regions in the studied abnormal volume group ($N = 20$)

Different brain regions	Volumetric measures (mean \pm SD)
Brain volume	1151.84 \pm 160.27
Grey matter volume	934.04 \pm 118.12
White matter volume	217.79 \pm 65.22
Hippocampus volume	
Total hippocampus volume	5.42 \pm 1.50
Right hippocampus volume	2.69 \pm 0.79
Left hippocampus volume	2.74 \pm 0.77
Right hippocampus CA1-3 volume	1.71 \pm 0.54
Left hippocampus CA1-3 volume	1.68 \pm 0.48
Right hippocampus CA4-DG volume	0.095 \pm 0.04
Left hippocampus CA4-DG volume	0.26 \pm 0.11
Right hippocampus subiculum volume	0.42 \pm 0.11
Left hippocampus subiculum volume	0.78 \pm 0.23
Thalamus volume	
Thalamus volume	10.235 \pm 3.22
Right thalamus volume	5.01 \pm 1.62
Left thalamus volume	5.28 \pm 1.55

Table 2 Volumetric measures of different brain regions in the studied normal volume group ($N = 40$)

Different brain regions	Volumetric measures (mean \pm SD)
Brain volume	1206.63 \pm 157.77
Grey matter volume	788.57 \pm 57.71
White matter volume	418.07 \pm 103.76
Hippocampus volume	
Total hippocampus volume	5.94 \pm 0.79
Right hippocampus volume	3.07 \pm 0.38
Left hippocampus volume	2.85 \pm 0.45
Right hippocampus CA1-3 volume	1.88 \pm 0.26
Left hippocampus CA1-3 volume	1.67 \pm 0.29
Right hippocampus CA4-DG volume	0.32 \pm 0.36
Left hippocampus CA4-DG volume	0.31 \pm 0.45
Right hippocampus subiculum volume	0.84 \pm 0.09
Left hippocampus subiculum volume	0.87 \pm 0.17
Thalamus volume	
Thalamus volume	11.82 \pm 0.75
Right thalamus volume	5.91 \pm 0.39
Left thalamus volume	5.91 \pm 0.37

There was a fair to moderate positive correlation between most of the volume measured structures and the frequency of seizures reaching a significant level at brain volume (P 0.04), grey matter volume (P 0.0001), total hippocampus volume (0.03), left hippocampus volume (0.01), and left hippocampus CA1-3 volume (0.006).

The sensitivity of right hippocampus subiculum volume and right hippocampus CA4-DG was 100%. The sensitivity of white matter volume and grey matter volume and thalamus was 85% and 75% and 55% respectively. The specificity of the right hippocampus subiculum volume and right hippocampus CA4-DG was 90% and 90% respectively. The specificity of the right hippocampus subiculum volume and right hippocampus CA4-DG and grey matter volume and white matter volume and total hippocampus and thalamus was 100%. The specificity of brain volume was 60%. The accuracy of the right hippocampus subiculum volume and right hippocampus CA4-DG was 100%. The specificity of white matter volume, grey matter volume, thalamus, total hippocampus, and brain volume was 97%, 87%, 65%, 61%, and 57% respectively (Table 4).

Discussion

Epilepsy is a chronic neurological disorder characterized by recurrent unprovoked seizures. These seizures are transient signs and/or symptoms due to abnormal, excessive, or synchronous neuronal activity in the brain [9]. Patients with nonlesional epilepsy constitute the most challenging group undergoing presurgical evaluation [2].

Volumetric MRI allows detection of subtle abnormalities of the brain that are difficult or impossible to reveal on visual inspection [10].

Several recent software tools have been developed to automatically obtain volumetric measures using different strategies. volBrain is a new software pipeline for volumetric brain analysis. This pipeline provides automatically volumetric brain information at different scales in a very simple web-based interface not requiring any installation or advanced computational requirements [8].

In the current study, volumetric and segmentation reporting were done using an online MRI-brain volumetric system at www.volbrain.com (volBrain version 1.0 for whole brain segmentation and HIPS version 1.0 hippocampus segmentation) using the automated method. Once the automatic process is complete, a PDF report was created containing volumetric data.

In the current study and on comparison between abnormal volume (group A) and normal volume group patients (group B) and regarding seizure frequency, we found that patients in group A have highly frequent seizures than those in group B.

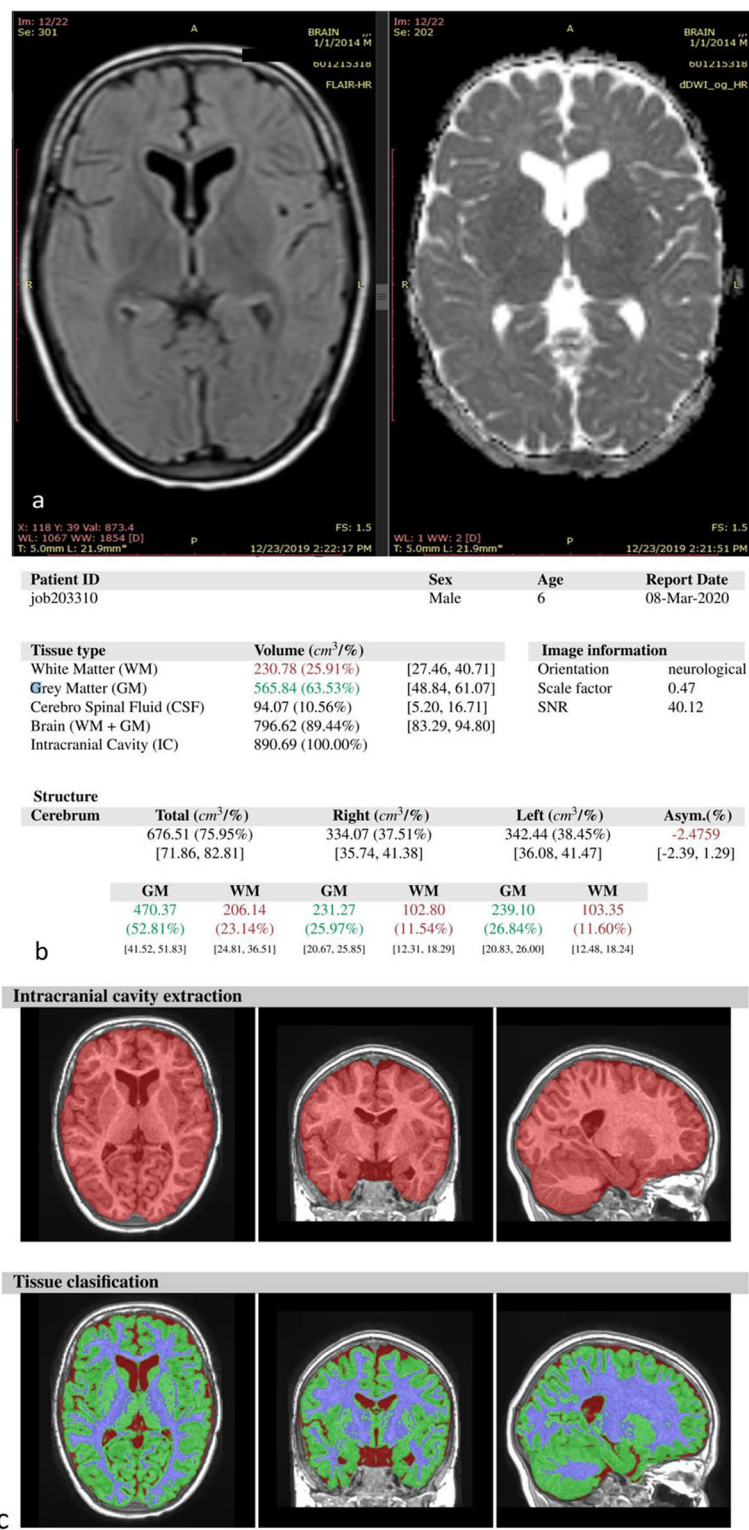


Fig. 1 Conventional MRI images (**a**) show no evident signal or structural changes, **b** and **c** are images from MRI volumetry showing increase in the GM volume marked in green numbers and decrease in the WM volume marked in red numbers. Green is grey matter, blue is white matter, and red is the whole brain

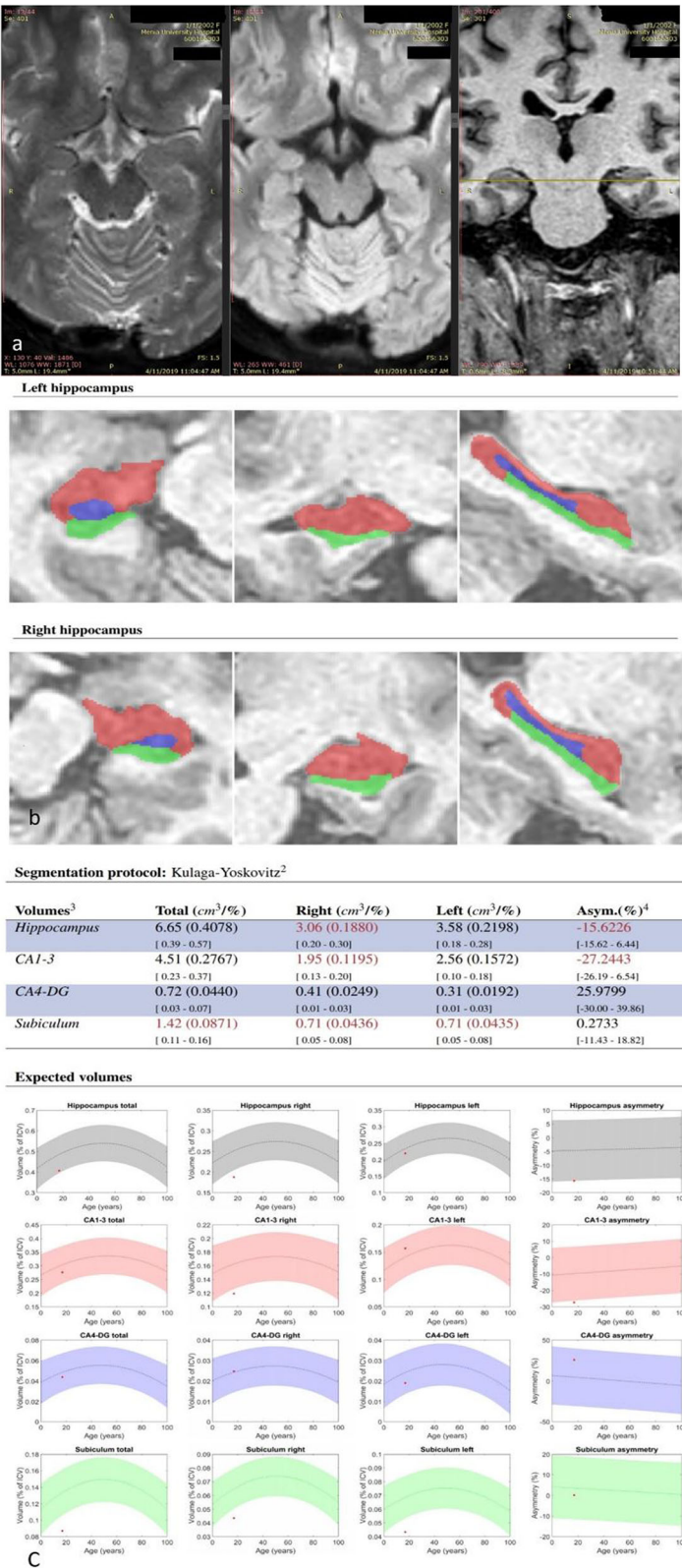
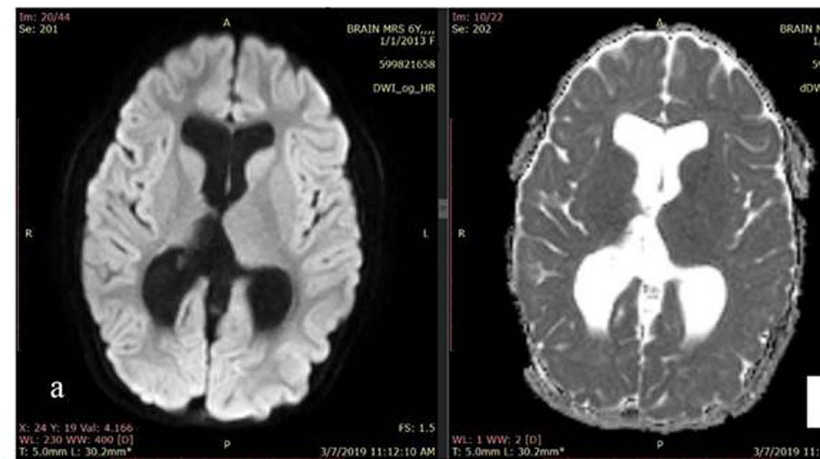
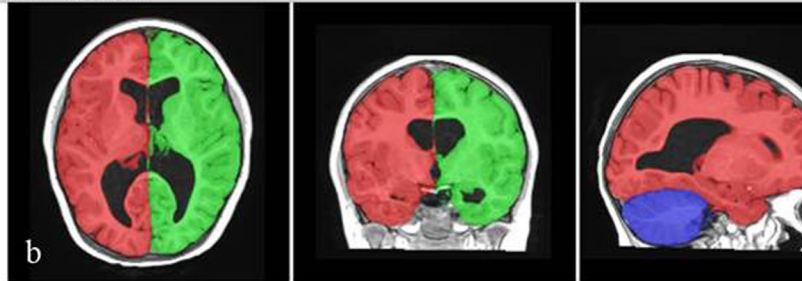


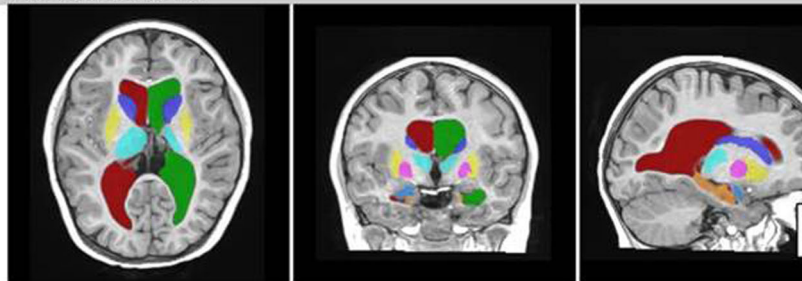
Fig. 2 Conventional MRI images **(a)** show no evident signal or structural changes in the hippocampus, **b** and **c** are images form MRI volumetry showing decreased volume of the right hippocampus written in green numbers compared with the normal volume of the left hippocampus. Red color is CA1-3, blue is CA4-DG, and green is subiculum



Macrostructures



Subcortical structures



Structure	Total (cm ³ /%)	Right (cm ³ /%)	Left (cm ³ /%)	Asymmetry (%)
Lateral ventricles	88.72 (6.72%) [0.00, 2.33]	47.88 (3.63%) [0.00, 1.11]	40.84 (3.09%) [0.00, 1.27]	15.8881 [-76.8427, 46.05]
Caudate	7.66 (0.58%) [0.48, 0.70]	3.88 (0.29%) [0.24, 0.35]	3.78 (0.29%) [0.24, 0.35]	2.5671 [-8.7276, 11.16]
Putamen	7.49 (0.57%) [0.57, 0.80]	3.56 (0.27%) [0.28, 0.40]	3.93 (0.30%) [0.29, 0.41]	-9.6738 [-8.7830, 3.92]
Thalamus	7.16 (0.54%) [0.82, 1.05]	2.20 (0.17%) [0.40, 0.52]	4.96 (0.38%) [0.41, 0.53]	-77.3294 [-7.7761, 5.20]
Globus Pallidus	2.41 (0.18%) [0.14, 0.23]	1.18 (0.09%) [0.07, 0.11]	1.22 (0.09%) [0.07, 0.12]	-3.3323 [-23.1548, 8.22]
Hippocampus	4.59 (0.35%) [0.42, 0.61]	1.72 (0.13%) [0.22, 0.31]	2.86 (0.22%) [0.20, 0.30]	-49.5631 [-4.5746, 16.46]
Amygdala	0.78 (0.06%) [0.09, 0.15]	0.34 (0.03%) [0.05, 0.08]	0.44 (0.03%) [0.04, 0.07]	-24.3243 [-9.3708, 24.74]
Accumbens	0.29 (0.02%) [0.04, 0.09]	0.14 (0.01%) [0.02, 0.04]	0.15 (0.01%) [0.02, 0.05]	-10.4167 [-42.6441, 12.13]

Fig. 3 Conventional MRI images (a...R = R) shows decreased size of the right thalamus and lentiform nucleus compared to the left one, **b** and **c** are images from MRI volumetry (R = L) showing significant decrease in the size of the right thalamus and lentiform nucleus marked by red numbers. There were global involutinal changes of the right hemisphere compared to the left one

Table 3 Comparison between normal and abnormal groups regarding volumetric measures.

Items	Abnormal volume group (n = 40) (mean ± SD)	Normal volume group (n = 20) (mean ± SD)	P value
Brain volume	1151.84 ± 160.27	1206.63 ± 157.77	0.38
Grey matter volume	934.04 ± 118.12	788.57 ± 57.71	0.001*
White matter volume	217.79 ± 65.22	418.07 ± 103.76	< 0.0001*
Hippocampus volume			
Total hippocampus volume	5.42 ± 1.50	5.94 ± 0.79	0.23
Right hippocampus volume	2.69 ± 0.79	3.07 ± 0.38	0.09
Left hippocampus volume	2.74 ± 0.77	2.85 ± 0.45	0.68
Right hippocampus CA1-3 volume	1.71 ± 0.54	1.88 ± 0.26	0.36
Left hippocampus CA1-3 volume	1.68 ± 0.48	1.67 ± 0.29	0.94
Right hippocampus CA4-DG volume	0.095 ± 0.04	0.32 ± 0.36	< 0.0001*
Left hippocampus CA4-DG volume	0.26 ± 0.11	0.31 ± 0.45	0.16
Right hippocampus subiculum volume	0.42 ± 0.11	0.84 ± 0.09	< 0.0001*
Left hippocampus subiculum volume	0.78 ± 0.23	0.87 ± 0.17	0.24
Thalamus volume			
Thalamus volume	10.235 ± 3.22	11.82 ± 0.75	0.048*
Right thalamus volume	5.01 ± 1.62	5.91 ± 0.39	0.028*
Left thalamus volume	5.28 ± 1.55	5.91 ± 0.37	0.096

Regarding seizure type, our study demonstrated that generalized epilepsy was more common than focal epilepsy in group A (75% generalized epilepsy versus 25% focal epilepsy). On the other hand, in group B patients, generalized epilepsy was 30% versus 70% focal epilepsy. The aforementioned results come in concordance with the study done by Debourdeau et al. [11]; in their study, they reported that generalized epilepsy was more common than partial epilepsy.

In our study, an abnormal EEG was found both in abnormal volume and normal volume group patients. This finding strengthens the fact that EEG is used in the diagnosis of epilepsy and continues to play a central role in both diagnosis and management of patients with seizure disorders.

The higher percentage of abnormal EEG in our study may be attributed to the highly frequent seizures that were recorded in our study as Farid et al. [12] stated that there are many factors that influence the recording of interictal epileptiform discharge in epileptic patients; among these factors is the frequency of seizures.

We proved a big role of volumetry in the diagnosis of epileptic patients that if their conventional MRI gives no pathology, we can diagnose them by volumetric MRI. In our study, the sensitivity of the right hippocampus subiculum volume and right hippocampus CA4-DG was 100%. The sensitivity of white matter volume and grey matter volume and thalamus was 85% and 75% and 55% respectively.

Table 4 Results of receiver operating curves (ROC curves) for volumetric changes among the nonlesional conventional MRI studied groups (N = 60)

Volumetric changes	Indices							
	Sensitivity	Specificity	PPV	NPV	Accuracy	Cutoff value	AUC	P value
Brain volume	65%	60%	76.5%	46%	57%	1200	0.575	0.38
Grey matter	75%	100%	100%	66.7%	87%	875.27	0.865	0.001*
White matter	85%	100%	100%	76.9%	97%	270.84	0.970	< 0.0001*
Total hippocampus	25%	100%	100%	40%	61%	≤ 3.71	0.612	0.23
Hippocampus CA4-DG	100%	100%	100%	100%	100%	≤ 0.15	1	< 0.0001*
Hippocampus subiculum	100%	100%	100%	100%	100%	≤ 0.62	1	< 0.0001*
Thalamus	55%	100%	100%	52%	65%	≤ 10.8	0.650	0.048*

In agreement with high sensitivity of volumetric MRI in detection of hippocampus volume in epileptic patients was the study of Giorgio and his colleagues [10] which found that volumetric MRI was useful in the presurgical evaluation of the epileptogenic site in TLE, showing asymmetry of the hippocampal volume ipsilateral to the seizure focus with a sensitivity up to 95%.

Another study in 2012 done by Farid et al. [12] found that quantitative MR imaging-derived hippocampal asymmetries discriminated patients with temporal lobe epilepsy from control subjects with high sensitivity (86.7–89.5%) and specificity (92.2–94.1%).

We compared between groups A and B patients regarding the volumetric measurements, and we found a significant reduction in the volume of most measured areas including white matter, hippocampus CA4-DG and hippocampus subiculum, and thalamus; we also found a significant increase in the volume of grey matter.

Lee and his colleagues [13] investigated the possible associations between cognitive dysfunctions and regional grey matter/white matter volumes in patients with newly diagnosed pediatric epilepsy; they found that the most prominent structural abnormalities observed in newly diagnosed pediatric epilepsy were decreased GM volumes in the bilateral frontal areas, especially the left inferior frontal and right middle frontal gyri.

Beheshti and his colleagues [14] reported significant grey matter and white matter volume reductions in temporal lobe epilepsy patients with hippocampal sclerosis; they also observed a slight grey matter amygdala swelling in the right temporal lobe epilepsy patients without hippocampal sclerosis.

Bernasconi and his colleagues [15] reported that the hippocampal head, body, and the entorhinal and perirhinal cortices in epileptic patients were significantly reduced.

Guimarães and his colleagues [16] revealed that volume reduction in the hippocampus has been demonstrated in pediatric localization-related epilepsy, including mesial temporal lobe epilepsy (TLE) and extratemporal lobe epilepsy.

Our results are in concordance with many volumetric studies that focused on hippocampal brain region and revealed hippocampal volume reduction in epileptic patients [17–20].

There are many volumetric studies focused on thalamic brain region and revealed thalamic volume reduction and dysfunction in epileptic patients [15–23].

It has been reported that the thalamus as a part of the limbic network has well-developed anatomic connection with mesial temporal lobe structures [21], so it has been suggested that the thalamus plays an important role in the amplification and distribution of limbic seizures and

hence the volumetric abnormalities that can be detected in the thalamus could be concluded as a result of recurrent seizures [22].

Bonilha and his colleagues [24] reported that juvenile myoclonic epilepsy patients exhibited significant volume reductions in thalamus. In 2018, Yoong and his colleagues [25] revealed that cognitive impairment in early onset epilepsy is associated with reduced thalamic volume. In our study, the thalamus had no significant difference in abnormal volume group of patients with generalized seizures than in the other groups of the study.

The observed volumetric changes of the thalamus in our study and others were congruent with the reported data which points to an increase in blood oxygenation level-dependent signal in both thalami during interictal epileptiform activity in idiopathic generalized epilepsy [26, 27]. These volumetric changes which were confined to the thalamus were explained by Aghakhani et al. [26] as the thalamus mediates motor functions via connections from the ventral anterior and lateral nuclei to the motor cortex, basal ganglia, and cerebellum.

On comparison between abnormal volume group and normal volume group patients with partial seizures regarding volumetric measurements, we found a smaller hippocampal volume and its parts and white matter volume in abnormal volume group patients than that of normal volume group (Fig. 4). Our result was in keeping with an Australian follow-up study which focused on epileptic diagnosed cases and demonstrated a significant hippocampal volume loss over a period of time [28]. Szabo et al. [22] found that patients with chronic temporal lobe epilepsy tend to have hippocampal volume loss. On the other hand, Liu et al. [29] found no relevant difference in hippocampal volume or other brain pathology after a period of time from follow-up.

Holtkamp et al. [30] concluded in their follow-up study of patients with focal epilepsy that recurrent seizures do not cause hippocampal volume change. This difference may be argued to the different methodological approaches that had been employed.

In our study, the correlation between seizure frequency and volumetric measurements of patients with partial epilepsy revealed significant correlation between the seizure frequency and brain volume, grey matter volume, and hippocampus.

The results of Pulsipher and colleagues [31] found a significant correlation between seizure frequency and hippocampal volume in patients with temporal lobe epilepsy. We only detected a significant decrease in hippocampus volume on the epileptogenic side. This observation was consistent with prior findings [32].

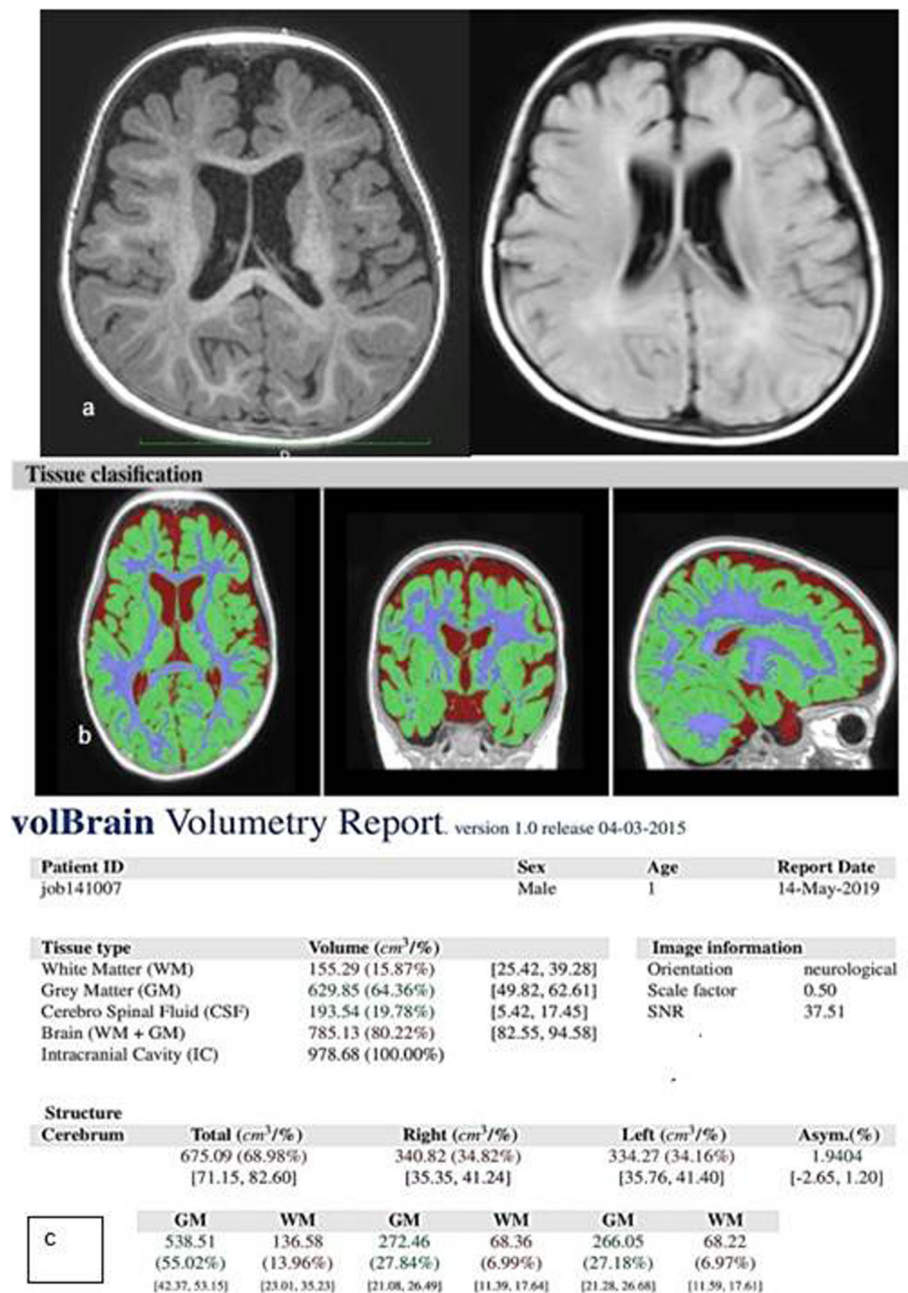


Fig. 4 Conventional MRI images (R = R) including conventional 3D T1 and FLAIR images show no evident abnormality detected, **b** is tissue classification, and **c** is a volumetry report showing decrease in the volume of the white matter volume and increased volume of the grey matter volume

Conclusion

Volumetric magnetic resonance imaging is a promising imaging technique that can provide assistance in evaluation of nonlesional childhood epilepsy that may change prognosis and line of management. Future prospective studies applying volumetric magnetic resonance imaging on a larger number of children are recommended to confirm the results of the present study and to establish the diagnostic accuracy of this technique, and the

validation of the MRI volumetry tool is recommended in epileptic children as early as possible to detect any volumetric changes.

Abbreviations

MRI: Magnetic resonance imaging; FLAIR: Fluid-attenuated inversion recovery; ICC: Intracranial cavity; GM: Grey matter; WM: White matter; TLE: Temporal lobe epilepsy; CA: Cornu ammonis; DG: Dentate gyrus; EEG: Electroencephalography; NIFTI: Neuroimaging Informatics Technology Initiative

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Authors' contributions

All authors have read and approved the current manuscript. EA: design of the study, data collection, CT image interpretation, and manuscript drafting. MA, MM: CT image interpretation, manuscript writing, statistical analysis, sequence alignment. SM: patient referral, manuscript editing, sequence alignment. EA, MA, MM, and SM: all authors read and approved the final manuscript

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

This study was approved by the Research Ethics Committee of the Faculty of Medicine at Minia University in Egypt on 2019 (reference number is not applicable). All patients included in this study gave written informed consent to participate in this research.

Consent for publication

All patients included in this research gave written informed consent to publish the data contained within this study.

Competing interests

The authors declare that they have no competing interests.

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