Research Article

Role of Volumetric Magnetic Resonance Imaging in Evaluation of Nonlesional Childhood Epilepsy

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Abstract
Introduction: Epilepsy, one of the oldest recorded diseases, is a chronic condition characterized by repeated spontaneous seizures. It is considered as one of the most common neurological disorders and represents a major health problem. **Patients and Methods:** This prospective clinical study included 30 epileptic patients (18 males and 12 females). The range of age for the cases was (3-12 years old); the mean age was (7.57±3.15years) with clinically diagnosed epilepsy who were referred from pediatric neurological clinic to magnetic resonance imaging unit at Radiology Department, Minia University Hospital in the time period from May 2019 to March 2020. Magnetic Resonance Imaging (MRI) of the brain including volumetric measures was performed to all the patients included in this study. **Results:** This study was carried out on 30 epileptic patients. The range of age for the cases was (3-12 years old); the mean age was (7.57±3.15 years). According to the volumetric results epileptic patients was divided into two groups: Abnormal volume group (20 cases) and normal volume group (10 cases).
Key words: volumetry, MRI, Nonlesional Childhood Epilepsy.

Introduction
Epilepsy, one of the oldest recorded diseases, is a chronic condition characterised by repeated spontaneous seizures. It is considered as one of the most common neurological disorders and represents a major health problem.[(1)] Epilepsy is a condition affecting up to 1% of the population worldwide.[(2)]

Patients with magnetic resonance imaging (MRI) negative (or 'nonlesional') pharmacoresistant focal epilepsy constitute the most challenging group undergoing presurgical evaluation.[(3)] The overall prevalence of nonlesional epilepsy in all surgical studies is ~26%.[(4)] The aim of this study was to assess role of volumetric magnetic resonance imaging in evaluation of nonlesional childhood epilepsy.

Patient and Methods
This prospective clinical study included 30 epileptic patients (18 males and 12 females). The range of age for the cases was (3-12 years old); the mean age was (7.57±3.15 years) with clinically diagnosed epilepsy who were referred from pediatric neurological clinic to magnetic resonance imaging unit at Radiology Department, Minia University Hospital in the time period from May 2019 to March 2020.
Magnetic Resonance Imaging (MRI) of the brain including volumetric measures was performed to all the patients included in this study. Inclusion criteria were: Pediatric patient with convulsion, pediatric patients with abnormal EEG, no structural abnormalities revealed on MR images, no seizure at least 72 hours before MR imaging.

Exclusion criteria were
Post-operative patients, post traumatic patients, febrile convulsions, patient with ence of structural lesion which may be the cause of seizures, patient with MRI contraindications.

All the patients were subjected to:
1) Thorough detailed history regarding age of patients, duration of seizure in minutes and frequency of seizures per week.
2) Detailed clinical examination
3) EEG
4) MRI examination:

No special preparation was needed. The examination was fully explained to the parents. The same MRI was done for all the patients at MR

unit at Radiology Department of Faculty of Medicine, Minia University Hospitals using Philips Ingenia 1.5T, 16 channels coil. No contrast material was given.

The epilepsy-dedicated research protocol included the following Pulse sequences:

i.

ii. **i. T1WI 3D:** sT1W_3D_TFE, FOV: covering whole brain (230mm), voxel: 1x1x1 mm isotropic, SNR= 1, Echo pulse sequence: Gradient, Flip angle: 30, TE: 3.4ms, TR: 7.3ms.

iii.

iv. **T2WI: T2W_3D_DRIVE**: FOV: covering whole brain (230mm), voxel: 1x1x1 isotropic, SNR=1 TE: 245ms, TR: 1500ms, SNR=1.

iii. FLAIR: FOV: 230, voxel: 1.16x1.44x5mm, TR: 11000ms, TE:140ms, SNR=1

Image analysis:

Conventional assessment: using Philips ISP (intellspace portal v. 9), for primary reporting.

Volumetric and segmentations reporting: A compressed T1WI dataset in NIFTI (Neuroimaging Informatics Technology Initiative) format was uploaded to online MRI-brain volumetric system at www.volbrain.com (Vol Brain version 1.0 for whole brain segmentation & 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 ITK-SNAP Version 3.4.0 software for all cases. VolBrain is not inferior to other software such as Freesurfer or SPM in volumetric analysis regarding reproducibility and accuracy.

Statistical analysis of the data:

Data were fed to the computer and analyzed using 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.

The 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, was. Student 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 signifycant and all statistical tests were 2 tailed.

Results

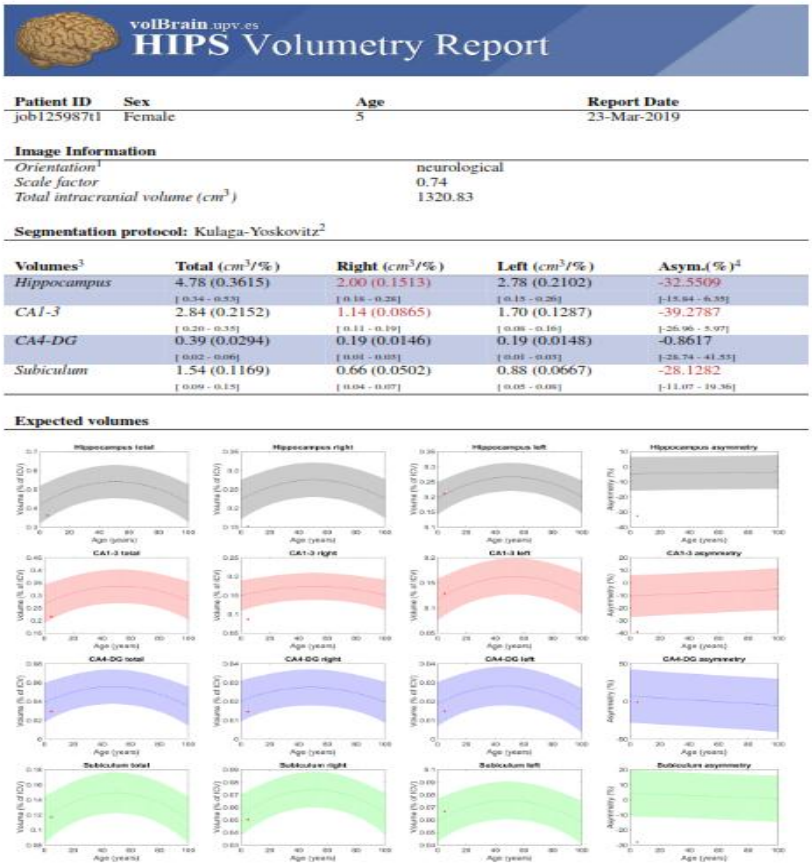
This study was carried out on 30 epileptic patients. The range of age for the cases was (3-12 years old); the mean age was (7.57±3.15 years). According to the volumetric results epileptic patients was divided into two groups: Abnormal volume group (20 cases) and normal volume group (10 cases).

Table (1): Significance of volumetric changes for the nonlesional conventional MRI between abnormal and normal volume group (N=30).

Items	Abnormal volume group (n=20) (Mean±SD)	Normal volume group (n=10) (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*
Total hippocampus volume	5.42±1.50	5.94±0.79	0.23
Right hippocampus CA4-DG volume	0.095±0.04	0.32±0.36	<0.0001*
Right hippocampus subiculum volume	0.42±0.11	0.84±0.09	<0.0001*
Thalamus volume	10.23±3.22	11.82±0.75	0.048*
Right thalamus volume	5.01±1.62	5.91±0.39	0.028*

Table (1): shows a significance of volumetric changes for the nonlesional conventional MRI between abnormal and normal volume group (N=30). We found a significant difference in the grey matter volume, white matter volume, right hippocampus CA4-DG and right hippocampus subiculum volumes, thalamus volume and right thalamus volume with P value were **0**.001*, <0.0001*, <0.0001*, <0.0001*, 0.048* and P value 0.028* respectively.

Table (2): Results of receiver operating curves (ROC curves) for volumetric changes among the nonlesional conventional MRI studied groups (N=30).



volBrain.upv.es
HIPS Volumetry Report

Patient ID	Sex	Age	Report Date
job125987t1	Female	5	23-Mar-2019

Image Information

Orientation[1]	neurological
Scale factor	0.74
Total intracranial volume (cm^3)	1320.83

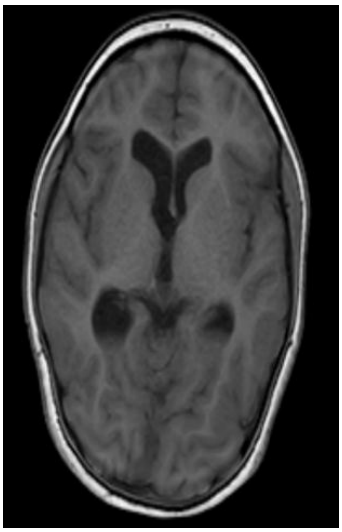
Segmentation protocol: Kulaga-Yoskovitz[2]

Volumes[3]	Total (cm^3/%)	Right (cm^3/%)	Left (cm^3/%)	Asym.(%)[4]
Hippocampus	4.78 (0.3615) [0.34 - 0.53]	2.00 (0.1513) [0.18 - 0.28]	2.78 (0.2102) [0.15 - 0.26]	-32.5509 [-15.84 - 6.35]
CA1-3	2.84 (0.2152) [0.20 - 0.35]	1.14 (0.0865) [0.11 - 0.19]	1.70 (0.1287) [0.08 - 0.16]	-39.2787 [-26.96 - 5.97]
CA4-DG	0.39 (0.0294) [0.02 - 0.06]	0.19 (0.0146) [0.01 - 0.03]	0.19 (0.0148) [0.01 - 0.03]	-0.8617 [-26.74 - 41.55]
Subiculum	1.54 (0.1169) [0.09 - 0.15]	0.66 (0.0502) [0.04 - 0.07]	0.88 (0.0667) [0.05 - 0.08]	-28.1282 [-11.07 - 19.36]

Expected volumes

Table (2): shows Results of receiver operating curves (ROC curves) for volumetric changes among the nonlesional conventional MRI studied groups (N=30). The sensitivity of right hippocampus subiculum volume and right hippocampus CA4-DG were 100%. The sensitivity of white matter volume and grey matter volume and thalamus were 85% and 75% and 55% respectively. The specificity of right hippocampus subiculum volume and right hippocampus CA4-DG were 90% and 90% respectively. The specificity of right hippocampus subiculum volume and right hippocampus CA4-DG and grey matter volume and white matter volume and total hippocampus and thalamus were 100%. The specificity of brain volume was 60%. The accuracy of 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 were 97%, 87% and 65%, 61% and 57% respectively.

Case Presentation:



Case presentation: Shows MR volumetry of the thalamus in a 5 years female patient with focal epilepsy, right thalamus was 2 cm^3 and left thalamus was 2.78 cm^3.

Discussion

Epilepsy is a common chronic neurological disorder that is characterized by recurrent unprovoked seizures. These seizures are transient signs and/or symptoms due to abnormal, excessive or synchronous neuronal activity in the brain.[5]

Patients with nonlesional epilepsy constitute the most challenging group undergoing presurgical evaluation.[3]

Routine MRI studies are not adequate for the evaluation of these patients with nonlesional epilepsy.[6] Volumetric MRI has been fundamental in the diagnosis and management of drug-resistant epilepsy, allowing the detection of subtle abnormalities of brain tissue that are difficult or impossible to reveal on visual inspection.[7]

On comparison between abnormal volume and normal volume group patients **(Table 6)** regarding seizure frequency, we found that patients with abnormal volume group epilepsy had highly frequent seizures than normal volume group patients (mean frequency per week was 2.05±0.89 versus 1.30±0.48, p value = **0.006**).
Regarding seizure type**,** our study demonstrated that generalized epilepsy was more common than focal epilepsy in the abnormal volume group (75% generalized epilepsy versus 25% focal epilepsy). On the other hand in the normal volume group generalized epilepsy was 30% versus 70% focal epilepsy.

In our study, we proved a big role of volumetry in the diagnosis of epileptic patients that although they are nonlesional childhood epilepsy and their conventional MRI give no pathology we can diagnose them by the sensitivity of right hippocampus subiculum volume and right hippocampus CA4-DG were 100%. The sensitivity of white matter volume and grey matter volume and thalamus were 85% and 75% and 55% respectively.

In agreement with high sensitivity of volumetric MRI in detection of hippocampus volume in epileptic patients was the study in 2012 of Giorgio and his colleagues that 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%.[7] Another study in 2013, Farid et al., and his colleagues found that quantitative MR imaging–derived hippocampal asymmetries discriminated patients with TLE from control subjects with high sensitivity (86.7%–89.5%) and specificity (92.2%–94.1%).[8]

In our study we compared between abnormal volume epileptic patients and normal volume epileptic patients regarding the volumetric measurements **(table 7),** and we found a significant reduction in the volume of most of the measured areas including white matter, hippocampus CA4-DG and hippocampus subiculum, and thalamus. But we found a significant increase in the volume of grey matter.

Our results are in concordance with many volumetric studies that focused on these different brain regions in epileptic patients.

The studies in hippocampus region are such as: In 2016, Daichi Sone and his colleagues found that Automatic segmentation hippocampal subfields (ASHS) and Free Surfer detected severe volume loss of ipsilateral CA1 and CA4/DG.[9]

In 2017, Caihong Ji and his colleagues found reduced volumes in all hippocampal subregions in epileptic patients.[10]

In 2018, Ji Hyun Kim and his colleagues revealed hippocampus and thalamic volumes reduction in epilepstic patients.[11]

In 2019, James Allebone and his colleagues revealed volume reduction in posterior hippocampus especially with psychosis in epilepsy[12]

Conclusion

Magnetic resonance imaging (MRI) has become the method of choice for the examination of macroscopic neuroanatomy in vivo due to excellent levels of image resolution and tissue contrast.

Unfortunately, Routine MRI studies are not adequate for the evaluation of these patients with nonlesional. Hence arises the need to add more criteria such as those provided by Volumetric Magnetic Resonance Imaging which 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.

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