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Original Article

Radiology Section

A Cross-sectional Study on Neuroimaging in Epilepsy: Diagnostic Value of T2 Relaxometry in Mesial Temporal Lobe Epilepsy

IFFATH MISBAH[1], JASMINE SHALIKA[2], SHAZIA FATHIMA[3], PAARTHIPAN NATARAJAN[4]

ABSTRACT

Introduction: The use of Magnetic Resonance Imaging (MRI) T2 relaxometry and spectroscopy has added new dimensions to the imaging of Temporal Lobe Epilepsy (TLE). Advanced techniques like MRI diffusion and MRI perfusion are new additions to the MRI protocol for epilepsy.

Aim: To study the diagnostic value of T2 relaxation time in Electroencephalogram (EEG) confirmed seizure cases.

Materials and Methods: A single-centre, cross-sectional study was conducted at Department of Radiodiagnosis, Saveetha Medical College, Saveetha Institute of Medical and Technical Sciences, Chennai, Tamil Nadu, India, from December 2020 to November 2022 at a tertiary care hospital. All patients were subjected to MRI with a special epilepsy protocol and T2 relaxometry. Hippocampal T2 relaxation values for each slice were measured by placing a Region of Interest (ROI) on the representative image obtained from the T2 relaxometry sequence, focusing on the hippocampus in both the control and study groups. The control group (n=30) consisted of healthy volunteers, whereas the case group (n=36) comprised patients presenting with a history of seizures with positive MRI and EEG findings. Mean T2 relaxation time was calculated in each ROI, and an average was derived. Mean and Standard Deviation (SD) were calculated for the continuous variables, while ratios and proportions were calculated for the categorical variables. To determine the association of T2 relaxometry values in the study and control groups, an unpaired t-test was used.

Results: The mean age of participants was 25.14±9.35 years (ranging from 9 to 51 years). The male-to-female ratio was 1.25:1. Hippocampal atrophy (32 out of 36 cases) and T2 signal alteration (30 out of 36 cases) were the most commonly identified features in Mesial Temporal Sclerosis (MTS). MRI without T2 relaxometry had a sensitivity of 94%. In two cases, where only mild hippocampal atrophy was identified in the conventional MRI sequence, making the diagnosis dubious, T2 relaxometry revealed increased T2 relaxation time in the head of the hippocampus and guided a proper diagnosis. EEG was able to lateralise seizures in 8 out of 13 right MTS cases (61.5%), 10 out of 17 left MTS cases (58.9%), and 5 out of 6 cases of bilateral MTS (83%).

Conclusion: T2 relaxometry allows quantification of hippocampal signal intensity, allowing the detection of even subtle changes in signal intensity that are difficult to perceive by visual assessment.

Keywords: Electroencephalogram, Hippocampal abnormalities, Lateralisation, Magnetic resonance imaging, T2 relaxometry

INTRODUCTION

A seizure is a paroxysmal alteration in neurological function resulting from abnormal excessive neuronal electrical activity. The pathophysiological basis of seizures is the loss of normal regulation of neuronal excitation and inhibition, resulting in a state of relative hyperexcitability [1]. Epilepsy, or "seizure disorder," is a chronic brain disorder that affects people in every country worldwide. There are over 50 million sufferers in the world today, 85% of whom live in developing countries; an estimated 2.4 million new cases occur each year globally. Roughly 60% of all cases of epilepsy are classified as partial epilepsy, and 30% are classified as generalised epilepsy [2]. Localisation of abnormalities in cases of partial seizures ranges from 28% to 80% as observed in different studies [2].

Localisation of the epileptogenic focus is most important in patients deemed surgical candidates. The term "epileptogenic lesion" refers to a structural abnormality found by imaging or pathology that causes the seizure disorder [3]. MRI, because of its ability to depict neuroanatomy, is ideally suited for identifying focal brain abnormalities and can detect structural lesions with a high degree of sensitivity. MRI is the most extensively used imaging technique for the evaluation of TLE [3].

Apart from the visual analysis of routine MRI sequences, the use of MRI T2 relaxometry and spectroscopy has added new dimensions to the imaging of TLE [4]. Advanced techniques like MRI diffusion and MRI perfusion are new additions to the MRI protocol for epilepsy. Further advancements include image processing algorithms that aid in detecting these lesions [5]. Functional MRI has become an essential part of the presurgical evaluation of epileptic patients for eloquent cortex mapping and language lateralisation. Here, lateralisation refers to the side of the brain involved. The primary objective of the present study was to investigate the diagnostic significance of T2 relaxation time in individuals with confirmed mesial TLE through EEG findings.

MATERIALS AND METHODS

A single-centre cross-sectional study was conducted within Department of Radiodiagnosis, Saveetha Medical College, Saveetha Institute of Medical and Technical Sciences, Chennai, Tamil Nadu, India, from December 2020 to November 2022 and received approval from the Institutional Ethics Committee (IEC-Reference number: 089/12/2020/IEC/SMCH). The sample size of the study was 66 by convenient sampling method.

Inclusion criteria: Patients of both sexes and any age group with a history of epilepsy who reported to the MRI section of the Radiology Department and were willing to participate in the present study were included in the study.

Exclusion criteria: Patients presenting with seizures due to intracranial Space-occupying Lesions (SOLs), meningoencephalitis, granulomatous, and demyelinating diseases were excluded from the study.

Study Procedure

The study involved two groups:

- **Case group:** This consists of 36 patients presenting with a history of seizures with positive MRI and EEG findings.
- **Control group:** This consists of 30 healthy volunteers who visited the hospital (15 males and 15 females) without any neurological or psychiatric complaints, with normal EEG and MRI brain.

The demographic details of both groups were collected, and individuals were subjected to MRI brain study with a special epilepsy protocol using the Siemens Magnatom Avanto 1.5T MR system. The following images were obtained: Axial and sagittal T1-weighted (W) Fast Spin Echo (FSE), axial and sagittal T2W FSE, axial Fluid-attenuated Inversion Recovery (FLAIR), coronal oblique fast FLAIR images, coronal oblique T2 FSE images, oblique coronal 3D T1 inversion recovery images, and T2 relaxometry.

The T2 relaxometry involves measuring the T2 relaxation time in the ROI. For the computation of T2 values, images were acquired in the coronal plane, ranging from the frontal lobe anteriorly to the fornix posteriorly, using a spin-echo pulse sequence. Flow-compensated gradients were applied in all three directions, and slices were aligned orthogonally to the hippocampal body's axis. Each individual's T2 relaxation time for the left and right hippocampus (HT2) was calculated using averages from eight slices covering the head, body, and tails of the hippocampus.

Hippocampal T2 relaxation values for each slice were measured by placing an ROI on the representative image obtained from the T2 relaxometry sequence, focusing on the hippocampus in both the control and study groups. The mean T2 relaxation time was calculated in each ROI, and an average was derived. The values from the control population were utilised to establish a standardised normal range for the machine.

STATISTICAL ANALYSIS

Data were collected and compiled using Microsoft excel, analysed using SPSS version 23.0. Mean and SD were calculated for the continuous variables, while ratios and proportions were calculated for the categorical variables. To determine the association of T2 relaxometry values in the study and control groups, an unpaired t-test was used. A p-value less than 0.05 was considered statistically significant.

RESULTS

The age distribution shows the maximum occurrence of mesial temporal sclerosis in the 2nd and 3rd decades of life [Table/Fig-1].

Hippocampal atrophy (32 out of 36 cases) and T2 signal alteration (30 out of 36) were the most commonly identified features in mesial temporal sclerosis. Among the extratemporal changes, fornix atrophy was most commonly seen in seven patients, followed by Mammillary body atrophy and one case of thalamic atrophy [Table/Fig-2].

The average T2 relaxation value was 103.7 ms for the right hippocampus and 104.6 for the left hippocampus, with a mean of 104.15±2.0 ms. A value of 3SD above the mean (110 ms) was taken as the cut-off value for normal T2 relaxation for this study [Table/Fig-3].

The mean T2 relaxation value in the right and left abnormal hippocampi was 119 and 118.5 ms, respectively, and the values were more than 110 ms, above the mean of the control group (104.15), with a p-value (<0.0001) [Table/Fig-4].

On comparison between the qualitative analysis of the hippocampus on conventional MRI sequences and MRI with T2 relaxometry, conventional MRI alone was able to diagnose 34 out of 36 cases with confidence; however, with the addition of T2 relaxometry, all cases were diagnosed [Table/Fig-5].

Characteristics	No. of patients	
	Cases n (%)	Control n (%)
Age groups (in years)		
<10	1 (2.8)	1 (3.3)
11-20	11 (30.6)	1 (3.3)
21-30	16 (44.4)	18 (60)
31-40	5 (13.9)	4 (13.33)
41-50	2 (5.6)	3 (10)
> 50	1 (2.8)	3 (10)
Mean age (mean±SD)	25.14±9.35 years	26.42±6.76 years
Gender		
Male	20 (55.5)	15 (50)
Female	16 (44.5)	15 (50)
Age of seizure onset (in years)		
0-10	5 (13.8)	
11-20	22 (61.2)	
20-30	6 (16.6)	
>30	3 (8.4)	
Mean±SD	15.56±5.92 years	
Duration of seizures		
6-12 months	2 (5.5)	
1-6 years	10 (27.7)	
7-12 years	17 (47.3)	
13-20 years or above	7 (19.5)	
Mean±SD	9.4±4.7 years	

[Table/Fig-1]: General characteristics of case and control group.

Signs in MRI	n (%)
Hippocampal atrophy	32 (88.9)
T2/FLAIR signal alterations	30 (83.3)
Loss of internal architecture and hippocampal head digitations	24 (66.7)
Thinning of collateral white matter in parahippocampal gyrus	22 (61.2)
Dilation of temporal horn	27 (75)
Temporal lobe atrophy	5 (13.9)
Extra temporal changes-Fornix atrophy	7 (19.5)
Mammillary body atrophy	4 (11.1)
Thalamic atrophy	1 (2.7)

[Table/Fig-2]: Conventional MRI in mesial temporal sclerosis.

Variable	Right-side	Left-side	Mean	Cut-off T2 value (>3SD)
Hippocampus	103.7	104.6	104.15±2.0	110

[Table/Fig-3]: T2 relaxometry (in ms) in control group.

T2 relaxation time (Average)	Right hippocampus (only abnormal 19 hippocampus included)	Left hippocampus (only abnormal 23 hippocampus included)
T2 relaxation time in study group	120.57	119.43
T2 relaxation time in control group	103.70	104.60
p-value	<0.0001	<0.0001

[Table/Fig-4]: Association of T2 relaxometry values (ms) in study and control group. Unpaired t-test was used

Modality	Number (n)	Percentage (%)
Conventional MRI	34	94
MRI with T2 relaxometry	36	100
Total	36	100

[Table/Fig-5]: Comparison of conventional MRI and MRI with T2 relaxometry in detection of mesial temporal sclerosis.

In the present study, 13 out of 36 cases involved the right hippocampus, 17 out of 36 cases involved the left hippocampus, and six cases had asymmetrical bilateral hippocampi involvement [Table/Fig-6].

Side of involvement	Unilateral involvement		Bilateral involvement
	Right-side	Left-side	
Number (n)	13	17	6.0
Percentage (%)	36.1	47.2	16.7

[Table/Fig-6]: Laterality of hippocampal lesion.

The MRI without T2 relaxometry had a sensitivity of 94%. In two cases where only mild hippocampal atrophy was identified in the conventional MRI sequence, making the diagnosis dubious, T2 relaxometry revealed increased T2 relaxation time in the head of the hippocampus and guided a proper diagnosis.

Interictal EEG was able to lateralise the epileptogenic focus in 23 (63.9) of the cases of clinically suspected mesial temporal sclerosis. EEG showed high sensitivity for the detection of bilateral disease. It was unable to lateralise 13 out of 36 cases. However, there was no false-positive report by EEG. EEG was able to lateralise seizures in eight out of 13 right MTS cases (61.5%), 10 out of 17 left MTS cases (58.9%), and 5 out of 6 cases of bilateral MTS (83%).

DISCUSSION

Temporal Lobe Epilepsy (TLE) is the most common epileptogenic focus in the brain. Furthermore, mesial TLE contributes to 80% of the TLE [6]. In the present study, the mean age of cases was 25.14±9.35 years (ranging from 9 to 51 years). Smith AP et al., in their study of 21 patients, showed the mean age of presentation at 28 years [7]. Janszky J et al., studied 153 patients with intractable epilepsy and found the mean age of presentation to be 33.5 years [8].

The sex distribution in the present study revealed a male to female ratio of 1.25:1 (55% male and 45% female), representing no significant sex variation of the disease. Studies by Conz L et al., and Bonilha L et al., do not show any obvious sex difference in their studies [9,10]. MRI evaluation of 36 cases revealed hippocampal atrophy and T2/FLAIR hyperintensity of the hippocampus as the most commonly identified abnormality in the study group. Patients with longer seizure durations were noted to have a significantly smaller hippocampus ipsilateral to the seizure and more secondary signs of hippocampal sclerosis.

Jafari-Khouzani K et al., in their study of 36 definitive cases of Mesial Temporal Lobe Epilepsy (MTLE), identified a correct localisation of 83% by hippocampal atrophy alone and 86% by FLAIR hyperintensity on coronal images [11]. Hakyemez B et al., studied 32 cases of pathologically proven mesial temporal sclerosis and found that 27 out of 32 patients with IR sequence (84%) had atrophy, and 28 out of 32 patients (88%) had increased signal intensity on FLAIR sequence [12].

YH Kim et al., studied 57 consecutive patients with histologically proven mesial temporal sclerosis and hippocampal atrophy in 96% of cases, concluding that atrophy of the hippocampus is the most common and consistent MR imaging finding [13]. Jackson GD et al., studied 18 cases of MTLE retrospectively and described increased hippocampal signal on T2-weighted images seen in 77%, hippocampal atrophy in 83%, decreased signal on T1-weighted images in 83%, and disruption of the internal hippocampal structure in 89% [14].

Briellmann RS et al., studied 30 control and 20 patients with partial seizures for the evaluation of T2 relaxometry values [15]. They found that the mean hippocampal T2 relaxation time was 98±2.8 ms in the control group. From the 15 patients with pathologically proven hippocampal sclerosis, the mean hippocampal T2 relaxation times were 118±7 ms ($p<0.0001$) on the ipsilateral side and 101±4 ms ($p=0.005$) on the contralateral side. The definition of a normal hippocampus is precise, and the diagnosis does not depend on a side-to-side comparison [4].

Conventional MRI alone was able to diagnose 34 out of 36 cases with confidence, with a sensitivity of 94%; however, with the addition of T2 relaxometry, all cases were diagnosed. Cheon JE et al., found a sensitivity of 86% in the visual assessment of hippocampal sclerosis [16]. In this study, EEG was able to lateralise the epileptiform discharges to the involved temporal lobe in 63.9% of clinically suspected cases.

Olivia M et al., found that 21/34 patients (62%) dipoles for the interictal spikes localised to the epileptogenic temporal lobe [17]. Velioglu SK et al., conducted a prospective interictal EEG study in 80 patients and found a 70% success rate in localising epileptic discharges in TLE [18]. They also found that the abnormal imaging incidence in patients with unilateral EEG findings was significantly greater than in patients with bilateral EEG findings.

Mesial temporal sclerosis or hippocampal sclerosis is a highly epileptogenic abnormality associated with MTLE. Recognition of this condition is important as it tends to be refractory to treatment with antiepileptic drugs but responds well to surgery. MRI is the radiological investigation of choice for diagnosing mesial temporal sclerosis among all age groups [19,20]. Optimised high-resolution MRI of the temporal lobes with a specific epilepsy protocol and spectroscopy [21,22] is required for reliable detection of mesial temporal sclerosis. Special oblique coronal thin sections perpendicular to the plane of the hippocampus have high sensitivity and specificity for mesial temporal sclerosis. Coronal T2W and FLAIR images are the most sensitive for detecting MTS.

Limitation(s)

The limitations of the study include a small sample size, lack of randomisation, and also the lack of elimination of observer bias.

CONCLUSION(S)

The T2 relaxometry allows quantification of hippocampal signal intensity, allowing the detection of even subtle changes in signal intensity that are difficult to perceive by visual assessment. It can be best applied in cases of bilateral hippocampal abnormalities when MR visual could not pick up bilateral abnormalities. In bilateral disease, T2 relaxometry can indicate the side of severity, which helps to determine the side to be operated on. By comparison with the range of values obtained for healthy control volunteers, quantification allows an objective determination of whether abnormalities are present in a particular patient. MR imaging findings, along with EEG data, strongly guide the workup of TLE patients.

REFERENCES

[1] Friedl RJ, Bronen RA. Magnetic resonance imaging of epilepsy. Edelman Clinical MRI. 3rd edition, Ch 47, pp 1366-1391.
[2] Alves IS, Coutinho AM, Vieira AP, Rocha BP, Passos UL, Gonçalves VT, et al. Imaging aspects of the hippocampus. Radiographics. 2022;42(3):822-40.
[3] Hogan RE, Mark KE, Wang L, Joshi S, Miller MI, Bucholz RD. Mesial temporal sclerosis and temporal lobe epilepsy: MR imaging deformation-based segmentation of the hippocampus in five patients. Radiology. 2000;216(1):291-97.
[4] Granados Sanchez AM, Orejuela Zapata JF. Diagnosis of mesial temporal sclerosis: Sensitivity, specificity and predictive values of the quantitative analysis of magnetic resonance imaging. The Neuroradiology Journal. 2018;31(1):50-59.
[5] Strnad BS, Orlowski HL, Parsons MS, Salter A, Dahiya S, Sharma A. An image processing algorithm to aid diagnosis of mesial temporal sclerosis in children: A case-control study. Pediatr Radiol. 2020;50(1):98-106.
[6] Tatum WO IV. Mesial temporal lobe epilepsy. J Clin Neurophysiol. 2012;29(5):356-65.
[7] Smith AP, Sani S, Kanner AM, Stoub T, Morrin M, Palac S, et al. Medically intractable temporal lobe epilepsy in patients with normal MRI: Surgical outcome in twenty-one consecutive patients. Seizure. 2011;20(6):475-79.
[8] J Janszky, R Schulz, I Janszky, A Ebner. Medial temporal lobe epilepsy: Gender differences. J Neurol Neurosurg Psychiatry. 2004;75(5):773-75.
[9] Conz L, Morita ME, Coan AC, Kobayashi E, Yasuda CL, Pereira AR, et al. Longitudinal MRI volumetric evaluation in patients with familial mesial temporal lobe epilepsy. Front Neurol. 2011;2:5.

[10] Bonilha L, Kobayashi E, Rorden C, Cendes F. Medial temporal lobe atrophy in patients with refractory temporal lobe epilepsy J Neurol Neurosurg Psychiatry. 2003;74(12):1627-30.
[11] Jafari-Khouzani K, Elisevich K, Patel S, Smith B, Soltanian-Zadeh H. FLAIR signal and texture analysis for lateralizing mesial temporal lobe epilepsy. Neuroimage. 2010;49(2):1559-71.
[12] Hakyemez B, Yucel K, Bora A. MRI findings in patients with temporal lobe epilepsy: Clinical diagnostic value of quantitative and qualitative. Turk J Diagn Interv Radiol. 2003;9(2):157-65.
[13] Kim YH, Chang KH, Park SW. Hippocampal sclerosis: Correlation of MR imaging findings with surgical outcome. Korean J Radiol 2001;2(2):63-67.
[14] Jackson GD, Berkovic SF, Duncan JS, Connelly A. Optimizing the diagnosis of hippocampal sclerosis using MR imaging. AJNR Am J Neuroradiol. 1994;14(3):753-62.
[15] Briellmann RS, Syngeniotis A, Fleming S, Kalnins RM, Abbott DF, Jackson GD. Increased anterior temporal lobe T2 times in cases of hippocampal sclerosis: A multi-echo T2 relaxometry study at 3 T. Am J Neuroradiol. 2004;25(3):389-94.
[16] Cheon JE, Chang KH, Kim HD. MR of hippocampal sclerosis: Comparison of qualitative and quantitative assessments AJNR Am J Neuroradiol. 1998;19(3):465-68.
[17] Oliva M, Meckes-Ferber S, Roten A. EEG dipole source localization of interictal spikes in non-lesional TLE with and without hippocampal sclerosis. Epilepsy Res. 2010;92(2-3):183-90.
[18] Velioğlu SK, Ozmenoğlu M, Komsuoğlu SS. EEG investigation of temporal lobe epilepsy. Clin Electroencephalogr. 1997;28(2):121-26.
[19] Gupta S, Razdan R, Hanumanthu R, Tomycz L, Ghesani N, Pak J, et al. MRI based composite parameter of multiple tissue types for improved patient-level hemispheric and regional level lateralization in pediatric epilepsy. Magn Reson Imaging. 2022;94:174-80.
[20] Sarkar P, Sherwani P, Dev R, Tiwari A. Role of T2 relaxometry in localization of mesial temporal sclerosis and the degree of hippocampal atrophy in patients with intractable temporal lobe epilepsy: A cross-sectional study. Hippocampus. 2023;33(11):1189-96.
[21] Jamalipour Soufi G, Hekmat Nia A, Hajalikhani P, Mehvari-Habibabadi J, Chit Saz N. Correlation of magnetic resonance spectroscopy and magnetic resonance imaging with findings of electroencephalography in patients with temporal lobe epilepsy. J Med Radiat Sci. 2024;71(1):51-56. Doi: 10.1002/jmrs.718.
[22] Chen H, Yu G, Wang J, Li F, Li G. Application of T2 relaxometry in lateralization and localisation of mesial temporal lobe epilepsy and corresponding comparison with MR volumetry. Acta Radiol. 2016;57(9):1107-13.

PARTICULARS OF CONTRIBUTORS:
1. Resident, Department of Radiodiagnosis, Saveetha Medical College, Saveetha Institute of Medical and Technical Sciences, Chennai, Tamil Nadu, India.
2. Consultant, Aarthi Scans, Chennai, Tamil Nadu, India.
3. Assistant Professor, Department of Oral Pathology and Microbiology, Ragas Dental College and Hospital, 2I IO2, East Coast Road, Uthandi, Chennai, Tamil Nadu, India; PhD Student, Centre of Molecular Medicine and Diagnostics (COMMAND), Department of Biochemistry, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences, Chennai, Tamil Nadu, India.
4. Head, Department of Radiodiagnosis, Saveetha Medical College, Saveetha Institute of Medical and Technical Sciences, Chennai, Tamil Nadu, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Iffath Misbah,
No. 22, E-Block, Anna Nagar East, Chennai-600102, Tamil Nadu, India.
E-mail: Iffathmisbahcp@gmail.com

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