



MANUAL TRACING QUANTIFICATION OF HIPPOCAMPI TO PREDICT THE LATERALIZATION OF THE SEIZURE FOCUS IN TEMPORAL LOBE EPILEPSY PATIENTS

Radiology

Dr. Sofia Bansal MD Radiology, Chettinad Hospital and Research Institute.

Dr. Aena Bansal MBBS

Dr Tharamel

Moideen MBBS MDRD, Chettinad Hospital and Research Institute *Corresponding Author

Muhuesein*

ABSTRACT

This study was aimed to determine the ability of manual tracing quantification of hippocampi to predict the lateralization of the seizure focus in TLE patients and establish a normative data for Indian population. **Materials And Method:** The study was conducted in the Department of Radiology, Chettinad Hospital and Research Institute. It was a hospital based prospective double blinded study. It was approved by the human ethical committee of our institution and was performed after getting informed, written consent from all the patients referred from Neurology department of Chettinad Hospital and Research Institute, Kelambakkam. The data collection for the study was done for an 18 months' period between February 2019 and August 2020. **Results:** 35 patients with clinical and EEG proven temporal lobe epilepsy patients underwent MRI brain. In 32 (91%) patients, HA was detected on quantitative volumetry as opposed to visual inspection which could detect only 26 (74%) cases out of 35. The difference was statistically significant (p -value <0.1). The mean HV was calculated to be 2.64709 cm³ (SD - 0.0879). The mean RHV was 2.659 cm³ and the mean LHV was 2.634 cm³. Using 95% confidence intervals (2SD), the upper and lower limits for HV were calculated to be 2.822 cm³ and 2.471 cm³, respectively. Mean RHV of 2.683 in males and 2.627 in females was obtained. The difference was statistically significant ($P < 0.1$). **Conclusion:** The most common findings documented in evaluation of TLE with MRI in the current study were hippocampal sclerosis and hippocampal atrophy.

KEYWORDS

INTRODUCTION

Hippocampus, embedded deep within the temporal lobe, is a part of the limbic system. With an archaic three-layered histology, it is involved in primordial lower order emotional processing, memory and temporal consciousness.⁽¹⁾ Although its precise functionality is still the subject of several competing speculations. Two folded sheets of gray matter are folded over one another called the cornu ammonis and the dentate gyrus. Neural plasticity or long-term potentiation occurring in hippocampi is the main mechanism of memory storage.⁽²⁾

Damage to this structure occurs mainly in Alzheimer's disease, inflammatory/ infectious etiologies, hypoxic events and temporal lobe epilepsy.⁽³⁾

Temporal lobe epilepsy (mesial type) being the most common form of partial epilepsy, is one of the most researched aspects related to the hippocampus.⁽⁴⁾ Gross hippocampal atrophy is easy to detect on MR imaging using specific sequences, however, more subtle changes in intensity as well as volume of hippocampi require more detail-oriented tools like quantitative volume measurement.⁽⁵⁾ Correlation between quantitative volumetry (manual tracing) and histological hippocampus is already established.⁽⁶⁾

MATERIALS AND METHOD

A total of 35 patients fulfilling inclusion criteria mentioned below were included in this study for MR Brain and volumetry. Investigation was done after attaining institutional human ethical committee clearance and informed consent from the patients who were subjected for this investigation. The study was performed using 1.5 Tesla SIGNA GE HDXT MRI scanner and the images obtained were subjected to radiological analysis and interpretation.

Sample for the study included control (healthy) subjects (total - 70; mean age - 30 yrs $\pm$ 9.0 [standard deviation]; range - 15 to 45 yrs; 40 men [mean age - 29.8 yrs $\pm$ 9; 15 to 45 yrs], 30 women [mean age - 30.6 yrs $\pm$ 9.0; 15 to 45 years]) and patients with clinically proven medically refractory TLE (total - 35; mean age, 27.6 years $\pm$ 9.7; 15 to 45 years; 20 men [mean age, 28.6 years $\pm$ 10.6; 15 to 45 years], 15 women [mean age 26.2 years $\pm$ 8.7; 15 to 45 years]).

EEG monitoring was done for all suspected patients at Chettinad Hospital and Research Institute to record the seizure activity. Patients within the age group 15 to 45 were included who had medically refractory disease, and had unilateral temporal lobe seizure activity as

diagnosed during EEG, as assessed by an experienced neurologist. Patients with extra-hippocampal disease/lesions at MR imaging or bilateral seizure activity were excluded. Patients were divided into two categories ie. left lateralized TLE ($n = 20$) or right lateralized TLE ($n = 15$) on the basis of the EEG.

MR imaging examination for participants utilized an seizure imaging protocol ie. a coronal oblique T2-weighted FSE sequence (TR/TE: 4880/102; slice thickness: 5 mm; FOV: 22 cm; matrix: 320*192) and a coronal T1-weighted Spoiled Gradient Recalled (SPGR) sequence (TR/TE: 8.1/3.5; number of slices: 26; slice thickness: 1 mm; FOV: 22 cm; matrix: 256*224; and voxel resolution: $0.6 \times 0.7 \times 1$ mm).

All MRI studies were inspected by a postgraduate student and an experienced radiologist for detection of hippocampal atrophy and the exclusion of extra hippocampal disease followed by volumetry by manual hippocampal tracing according to the protocol established by Watson et al. 1992.⁽⁷⁾

The mean and standard deviation for right and left HV were calculated. Using 95% confidence intervals (2 standard deviation), the upper and lower limits were calculated. We used t-test analysis to assess the effect of age and sex on hippocampal volume. To study the effect of age, we divided the control subjects into two groups based on age (15-30 and 31-45).

Patients with TLE meeting clinical and EEG criteria, with medically refractory TLE, age - 15 to 45 years were included in this study.

Patients with evidence of extra hippocampal disease at clinical MR imaging, claustrophobic, with metallic implants, cardiac pacemakers, cochlear implants, early pregnancy were excluded from study.

Equipment: Signa contour GE 1.5 Tesla whole body MR scanner

Protocol: Table 1

RESULTS

Normative Data

A total of 70 healthy control subjects were included in the study.

The number of people with the age less than 30 were 35 (50 %) and with the age greater than 30 were 35 (50 %). (Table 2, & fig. 1)

No statistically significant variation was detected when comparing the

two age groups with equal variances (as illustrated in Table 3).

Out of 70 subjects, 30 (42.9 %) were females and 40 (57.1%) were males. (Table 4 & fig.2)

Male RHV - 2.683 +/- 0.1646, Female RHV - 2.627 +/- 0.1312, Male LHV - 2.654 +/- 0.204, Female LHV - 2.609 +/- 0.1528 (Table 5)

The mean HV was calculated to be 2.64709 cm³ (SD - 0.0879). The mean RHV was 2.659 cm³ and the mean LHV was 2.634 cm³. Using 95% confidence intervals (2SD), the upper and lower limits for HV were calculated to be 2.822 cm³ and 2.471 cm³, respectively. Mean RHV of 2.683 in males and 2.627 in females was obtained. The difference was statistically significant ($P < 0.1$). Similar significant results were obtained for the LHV, with a mean of 2.654 in males and 2.609 in females ($P < 0.1$). (Table 6).

Temporal Lobe Epilepsy Patients

On EEG recording and clinical examination, 35 patients were diagnosed with unilateral TLE with 20 patients exhibiting left laterality (57%) and 15 with right laterality (43%). Apart from these, 7 patients were excluded from the study due to dual disease/extra hippocampal disease detected on MR imaging. (Table 7 & fig.3)

On visual inspection, 26 patients (74%) were confirmed for hippocampal atrophy ie. 15 were left lateralized (58%) and 11 were right lateralized (42%) (fig. 4).

On quantitative volumetry, 32 (91%) were detected with reduced hippocampal volume. 18 patients (56%) had left laterality out of which 2 had bilateral disease while 14 (44%) had right laterality out of which 2 had bilateral disease. Hippocampal volume was normal for 3 patients (2 with left lateralization and 1 with right lateralization on EEG). (fig.5).

Concordance of visual inspection findings with EEG findings

Visual inspection of the MR imaging demonstrated 74% agreement (26 of 35). In nine cases of hippocampal atrophy, asymmetry was overlooked by the radiologist but 6 out of them were identified at volumetric MR imaging. In almost all the cases (except 3), the consistency between EEG and quantitative volumetry in detecting asymmetry was significant, which was considered the standard for lateralization.

Concordance of visual inspection findings with quantitative MR imaging findings

Agreement between volumetric MR imaging and visual assessment of the MRI studies was 82% (26 of 32). In six cases, asymmetry was overlooked on visual assessment but was caught at quantitative MR imaging. In three cases, EEG demonstrated laterality that was overlooked at quantitative volumetric MR imaging.

Concordance of quantitative MR volumetry findings with EEG findings

Concordance between quantitative MR imaging and EEG was 91% (32 of 35). In three cases, hippocampal asymmetry was overlooked on quantitative MR volumetry as normal volumes were obtained.

When each method was compared with EEG recordings, lateralization accuracy was 91% with volumetric MR imaging (32 of 35) and 74% with visual assessment of MRI studies (26 of 35).

DISCUSSION

Imaging of medial temporal lobe in patients with temporal lobe epilepsy is consistently developing with headway of imaging advancements. However, most tertiary centres in India still function on 1.5 T machines which have lower sensitivity for detecting hippocampal atrophy on visual inspection. Moreover, most centres aren't equipped with expensive volume evaluating softwares. Establishment of normative data for Indian population, defining hippocampal boundaries and evaluating sensitivity and accuracy of various modalities for lateralizing seizure foci becomes important.

Medial temporal lobe, known for its complexity of structures and ambiguous boundaries between individual structures, has been a subject of research for a very long time.

Current study was attempted in two parts.

First part dealt with establishing normative data for Indian population

in control subjects subjected to MRI. As per this study, hippocampal volume was evaluated for 70 control subjects who underwent MRI brain. Mean HV came out to be 6.4709 +/- 0.1758. 40 subjects were male and 30 were female. Age distribution was uniform with 35 subjects in both age groups ie. 15-30 and 31-45 years of age. Mean male RHV and LHV is 2.683 +/- 0.1646 and 2.654 +/- 0.204 respectively. Mean female RHV and LHV is 2.627 +/- 0.1312 and 2.609 +/- 0.1528 respectively. No statistically significant variation was detected when comparing the two age groups. However, p-value was significant for gender where male HV was slightly more than female HV.

It was in concordance with the study performed by Aravind Narayan Mohandas et al. where mean HV of 2.411 cm³ (SD=0.299) was found with HV higher in males than in females and no statistically significant difference between age groups. (8) Second part of the study dealt with the pathology. 35 patients with clinical and EEG proven temporal lobe epilepsy patients underwent MRI brain. As per current study findings, in 32 (91%) patients, HA was detected on quantitative volumetry as opposed to visual inspection which could detect only 26 (74%) cases out of 35. The difference was statistically significant ($p\text{-value} < 0.1$). Visual inspection led to only 74% agreement with EEG while MR volumetry had 91% agreement.

The result was in concordance with the study performed by Nikdokht Farid et al. Volumetric MRI data was assessed for 34 patients and 116 control subjects. In comparison with video EEG recordings, lateralization accuracy was 88% with quantitative MR volumetry and 76% with visual assessment of MRI studies. (9)

Another study performed by A.C.Coan et al. found atrophy by the method of volumetry in 95% of patients with visually detected sclerosis and 13% with visually normal MR imaging findings. In conclusion, hippocampal volume and signal can increase detection by 28% while we established the proportion to be 22%. (10)

Table 1: MR Imaging epilepsy protocol for the current study

MRI Sequences	T1 FLAIR	T2 FLAIR	T2	SPGR	DWI	GRE	3D FIESTA
Imaging Planes	Axial and Sagittal	Axial and Coronal	Axial and Coronal	Coronal	Axial	Axial	Axial
TR/TE (msec)	1042/25	8002/85	4880/102	8.1/3.5	7520/97	500/15	4.5/1.7
FOV	25	22	22	22	26	25	24
Section thickness/spacing (mm)	5	5	5	1	5	5	1
Matrix	320*192	256*160	320*192	256*224	128*160	512*224	320*224

Table 2: Descriptive analysis of AGE GROUP in control group (N=70)

AGE GROUP	Frequency	Percentage
15-30	35	50
31-45	35	50

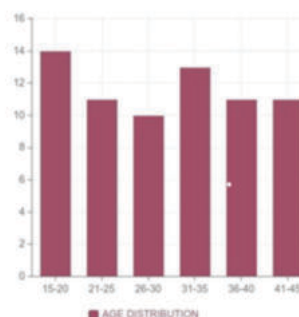


Figure 1: Bar chart of AGE GROUP distribution in study group (N=70)

t-test for equality of means				
	Mean	T	Df	Significance (2-tailed)
RHV with age				
15 to 30 years (35)	2.652	0.6974	68	0.4879
31 to 45 years (35)	2.6654			
LHV with age				
15 to 30 years (35)	2.635	0.0044	68	0.9965
31 to 45 years (35)	2.6349			

Table 4: Descriptive analysis of SEX in study group (N=30)

SEX	Frequency	Percentage
Female	30	42.9
Male	40	57.1

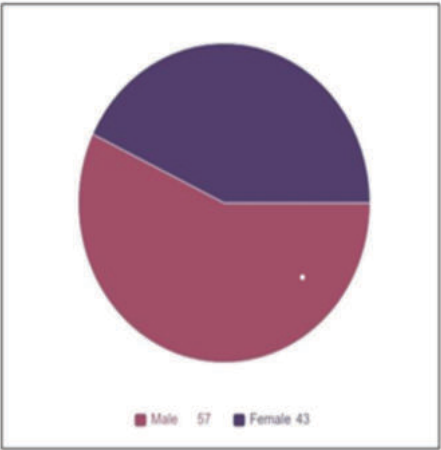


Figure 2: Pie chart of SEX distribution in study group (N=70)

t-test for equality of means				
	Mean	T	Df	Significance (2-tailed)
RHV with gender				
Male (40)	2.683	3.0657	68	<0.1
Female (30)	2.627			
LHV with gender				
Male (40)	2.654	2.0235	68	<0.1
Female (30)	2.609			

Table 6: Mean hippocampal volumes

Mean hippocampal volume : 2.64709 +/- 0.1758		
	RHV (cm3)	LHV (cm3)
Male	2.683	2.654
Female	2.627	2.609

Table 7: Number of TLE patients as detected by the three modalities

	Left-lateralized	Right-lateralized	Bilateral with left laterality	Bilateral with right laterality
EEG proven (35)	20	15	0	0
Visual Inspection (26/35)	15	11	0	0
Quantitative volumetry (32/35)	16	12	2	2

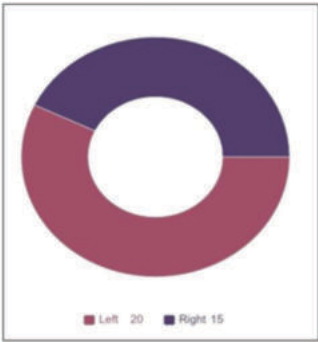


Figure 3: Doughnut chart demonstrating seizure laterality on EEG.

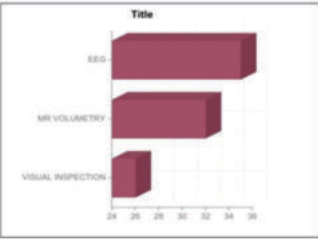


FIGURE 4: Chart showing accuracy of different modalities in lateralizing epileptic foci.

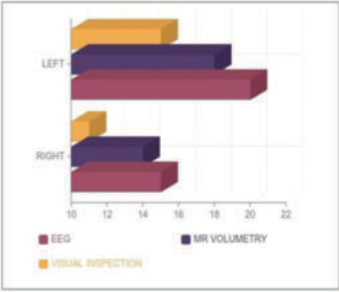


FIGURE 5: Chart comparing the three modalities, EEG, MRI volumetry, and visual inspection, for left and right sides.

CONCLUSION

The most common findings documented in evaluation of TLE with MRI in the current study were hippocampal sclerosis and hippocampal atrophy. Even though there were no statistically significant differences observed between different age groups, males tend to have significantly higher hippocampal volume as compared to females. The accuracy rates for detecting hippocampal atrophy were significantly higher for MR volumetry in comparison to visual detection using 1.5 T machines.

REFERENCES

1. Margerison JH, Corsellis JA. Epilepsy and the temporal lobes. A clinical, electroencephalographic and neuropathological study of the brain in epilepsy, with particular reference to the temporal lobes. Brain 1966;89(3):499–530.
2. Cuingnet, R., et al., Automatic classification of patients with Alzheimer's disease from structural MRI: A comparison of ten methods using the ADNI database, NeuroImage (2010), doi:10.1016/j.neuroimage.2010.06.013.
3. B. Hakyemez et al. "Qualitative and quantitative MRI findings in temporal lobe epilepsy," Tanisal ve Girişimsel Radyoloji, vol. 9, no. 2, pp. 157–165, 2003.
4. Bronen RA, Fulbright RK, Kim JH, Spencer SS, Spencer DD, al-Rodhan NR. Regional distribution of MR findings in hippocampal sclerosis. AJNR Am J Neuroradiol1995;16(6):1193–1200.
5. Salmenperä T et al. Hippocampal damage caused by seizures in temporal lobe epilepsy. Lancet 1998;351:35.
6. Fuerst D et al. Volumetric MRI, pathological, and neuropsychological progression in hippocampal sclerosis. Neurology 2001;57:184-8.
7. C. Watson, F. Andermann, P. Gloor et al., "Anatomic basis of amygdaloid and hippocampal volume measurement by magnetic resonance imaging," Neurology, vol. 42, no. 9, pp. 1743–1750, 1992.
8. Aravind Narayan Mohandas et al. Hippocampal volumetry: Normative data in the Indian population. Annals of Indian Academy of Neurology. 2014 Jul-Sep; 17(3): 267–271.
9. Nikdokht Farid et al. Temporal Lobe Epilepsy: Quantitative MR Volumetry in Detection of Hippocampal Atrophy. PMC Radiology 2012 Aug; 264(2): 542–550.
10. Coan AC, Kubota B, Bergo FP, Campos BM, Cendes F. 3T MRI quantification of hippocampal volume and signal in mesial temporal lobe epilepsy improves detection of hippocampal sclerosis. American journal of neuroradiology. 2014 Jan 1;35(1):77-83.