PROJECT COMPLETION REPORT

1. Title of the project: Quantitative EEG and Multi-Model Neuro imaging biomarkers of Memory dysfunction in Epilepsy. (File No. DST/CSRI/2017/276 (G))

2. Principal Investigator(s) and Co-Investigator(s):

   PI: Prof. Ramshekhar N. Menon, Department of Neurology, SCTIMST, Trivandrum.
   Co- PI: Prof. C. Kesavadas, Deputy Director, SCTIMST, Trivandrum.
   Co- PI: Sri. Devanand P, Associate Director, Health Informatics and Software Technology Group, CDAC, Trivandrum.

3. Implementing Institution(s) and other collaborating Institution(s):

   (i) Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum.
   (ii) C-DAC, Trivandrum.

4. Date of commencement: 14-6-2019

5. Planned date of completion: 13-12-2022

6. Actual date of completion: 13-12-2022

7. Objectives as stated in the project proposal:

   a) To characterize the pattern of memory dysfunction of persons with TLE with IGE.
   b) To compare the pattern of memory dysfunction in persons with TLE with that of persons with IGE.
   c)To correlate the memory dysfunction with EEG and MRI characteristics of persons with epilepsy.

8. Deviation made from original objectives if any, while implementing the project and reasons thereof:

   The sample size was supposed to be in between 80-100 for patients and 50 healthy controls. But due to the outbreak of COVID pandemic, the sample size was restricted to 60 patients and 30 healthy controls. As part of neuro imaging, along with DTI and VBM, fMRI was also planned to be carried out. Demonstration trials were done in 3 healthy

controls in order to standardize. fMRI studies could not be completed in view of technical issues at site pertaining to memory fMRI signal acquisition and post processing.

9. Experimental work giving full details of experimental set up, methods adopted, data collected supported by necessary table, charts, diagrams & photographs:

Methodology

Setting: This study was carried out in the R. Madhavan Nayar Centre for Comprehensive Epilepsy Care in the Sree Chitra Tirunal Institute for Medical Sciences and Technology (SCTIMST). This is a tertiary care centre in India, where more than 10,000 persons with epilepsy attend on a yearly basis.

Population: This study is restricted to adult patients with Temporal Lobe Epilepsy (TLE) or Idiopathic Generalized Epilepsy (IGE) that scheduled for long term video EEG(VEEG) monitoring in the epilepsy program in SCTIMST. These cases are already well worked up for the epilepsy from clinical and imaging viewpoints. They are available for long observation over one week as they are already scheduled for one week in patient evaluation with long term video monitoring.

Inclusion criteria: Any patient with active epilepsy (one or more seizures in the past five years or seizure free on antiepileptic drugs) and age between 20 and 55 years and scheduled for a prolonged VEEG monitoring (for one to seven days) were screened

1. The patient should have TLE as suggested by two of the following: (a) typical seizure semiology consistent with complex partial seizure of temporal lobe origin. (b)Interictal epileptiform discharges in the EEG confined to the anterior or mid temporal electrodes. (c) MRI evidence of lesion in the temporal lobe – MTS, tumours or gliosis.
2. Patients should have IGE as suggested by two of the following: (a) Generalized seizures without any aura. (b) EEG diagnostic of generalized epilepsy (generalized IED, photoparoxysmal response, normal background activity). (c) Normal MRI Scan.

Exclusion criteria: Any patient with any of the following were excluded:

1. Progressive neurological disorders.
2. Lesions in the MRI in any location other than temporal lobe.
3. IQ less than 80.
4. Significant mental depression.
5. Pregnant women.
6. Other medical conditions that may interfere with the test procedures or may influence the outcome measures.

The potential candidates for the study were identified from the epilepsy service and would be briefed about the study and the procedures involved. An informed signed and witnessed consent were taken from every participant.

Sample: A sample size of 60 cases and a control group of 30 Healthy adults matched for age, sex and level of education were recruited for this study.

Methods: The clinical details of the patients related to epilepsy, use of antiepileptic drugs, other comorbidities and general life style of the patient are extracted from the medical records and from the personal interviews.

(a) Neuropsychological Evaluation

This study that has two parts, part 1 that attempts to capture the neuropsychological and memory functions in adults with epilepsy (temporal lobe epilepsy and idiopathic generalized epilepsy) and healthy control adults. The tests used are WAIS-IV Indian Edition (Intelligence test) for screening patients for recruiting patients for the project. Three memory tests are used. Rey Auditory Verbal Learning Test (RAVLT) for evaluating verbal memory, Rey Osterrieth Complex Figure test (ROCFT) for verbal memory assessment, and Autobiographical Memory Interview (AMI) for assessing the patient's ability to retain personal semantics and autobiographical incidents. WAIS- IV INDIA (Wechsler Adult Intelligence Scale) is the standardized Intelligence scale developed as per Indian norms. The test can be administered to individuals aged 16 – 90. It consists of four index scales and 10 subtests that come under them which are as follows: - 1. Verbal Comprehension Index Scale- Similarities, Vocabulary, Information. 2. Perceptual Reasoning Index Scale- Block Design, Matrix Reasoning, Visual Puzzles. 3. Working Memory Index Scale- Digit – span, Arithmetic. 4. Processing Speed Index Scale- Symbol Search, Coding. The testing takes about 60 to 90 minutes on average for each individual. RAVLT has a list of 15 unrelated words repeated to the participant over five different trials and are asked to repeat. Another list of 15 unrelated words is given as a distractor and the patient must again repeat the original list of 15 words and then again after 30 minutes. They are also asked to recognize the words from the original list while it is administered among words from the second list as well as words that are semantically or phonologically similar. In ROCFT, the patient is shown a figure and initially copies it as it is. After 3 minutes, the patient is asked to draw what they remember from memory to measure immediate recall and then after 30 minutes to assess delayed recall. Unlike studies done so far, RAVLT and ROCFT is carried out after a period of 5 to 7 days on the patients to record long term memory changes. With autobiographical memory

interview, the patient is asked questions that provide semantic information as well as one question that requires vivid emotional recollection of an event during different stages the individual's life. There are three main sections; Childhood, Early adult life and Recent life, which are further divided into a total of 10 subsections. The administration of the tests, beginning with WAIS IV India, takes up an average 3 to 4 hours per patient. The second part is the EEG and the MRI studies on these patients.

(b) EEG Acquisition

EEG was recorded using 32 channels Nicolet EEG system. The subjects were asked to relax and 19 channel resting state EEG data was acquired at a sampling rate of 500Hz using Ag electrodes according to the International 10-20 electrode settings. 10 minutes eyes closed and 10 minutes eyes open data were collected for each subject. The data from the EEG were extracted in ASCII format and handed over to CDAC for further digital processing and mathematical analysis.

Microstate Analysis Software development

EEG Microstate Analysis software was developed as part of the project. The software is a MATLAB based desktop software application developed using advanced digital signal processing and machine learning methods that can process multi-channel EEG signals using Microstate analysis as well as traditional time and frequency domain analysis methods. The software is equipped with machine learning based functionality for correlating EEG and MRI characteristics (provided by SCTIMST) for differentiating epilepsy patients from Healthy controls.

- Major features
  - The system has facilities to load and view multi electrode EEG data using different user defined settings.
  - The system has provisions to select and save required data epochs from a loaded EEG data.
  - The system is provided with various pre-processing filters.
  - The system has provisions to generate and view two-dimensional scalp topographical maps from EEG signals
  - The system is equipped with all functionalities to perform EEG Microstate analysis.
  - There are provisions to extract and view selected time domain and frequency domain features from EEG data.

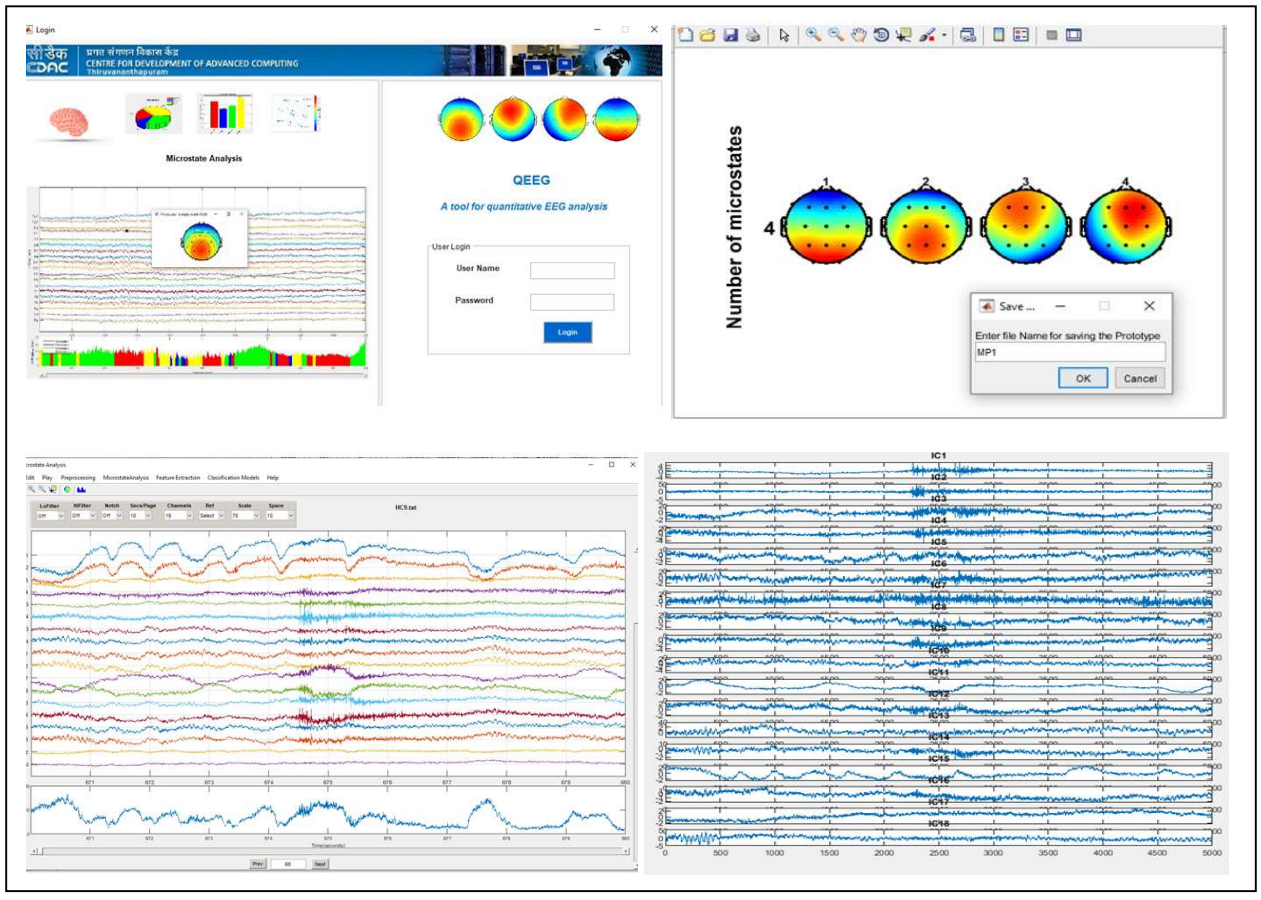
- Separate machine learning models are provided in the system for differentiating between groups using EEG Microstate statistics, VBM and DTI parameters (provided by SCTIMST).

- Technology highlights: MATLAB, Machine learning, Signal processing
- Major outcome of the project (CDAC)

  A software to perform Quantitative EEG Analysis using EEG Microstates with the following features

  - UI to load and view multi-dimensional EEG signals
  - Preprocessing Filters
  - EEG Microstate Analysis
  - Time & Frequency domain Analysis
  - Machine learning models

- Screenshots of the software (Figure 1)



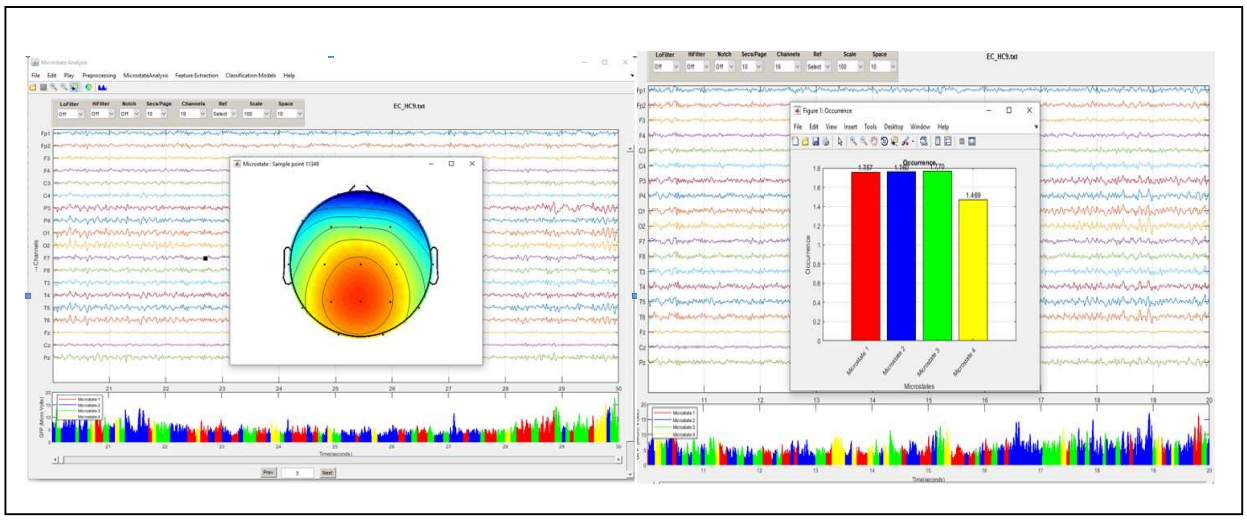


Figure 1. Screenshots of the software.

Preprocessing

The collected data were preprocessed using different preprocessing filters. Bad epochs and channels were removed either by manual inspection or by using ICA filters. 5 to 7 minutes of eyes closed resting state EEG data of each subject was selected for performing EEG Microstate analysis. The data was notch filtered to remove line noise 50 Hz and band pass filtered between 1-40 Hz. (Initially Microstate template maps were created for the following frequency bands 0.1-40 Hz,1-40 Hz,0.1-70 Hz,1-70Hz and 8-13 Hz. Finally, the band was fixed to 1-40 Hz for broad band EEG analysis after consultation with Dr Christoph M Michel, pioneer in the field.)

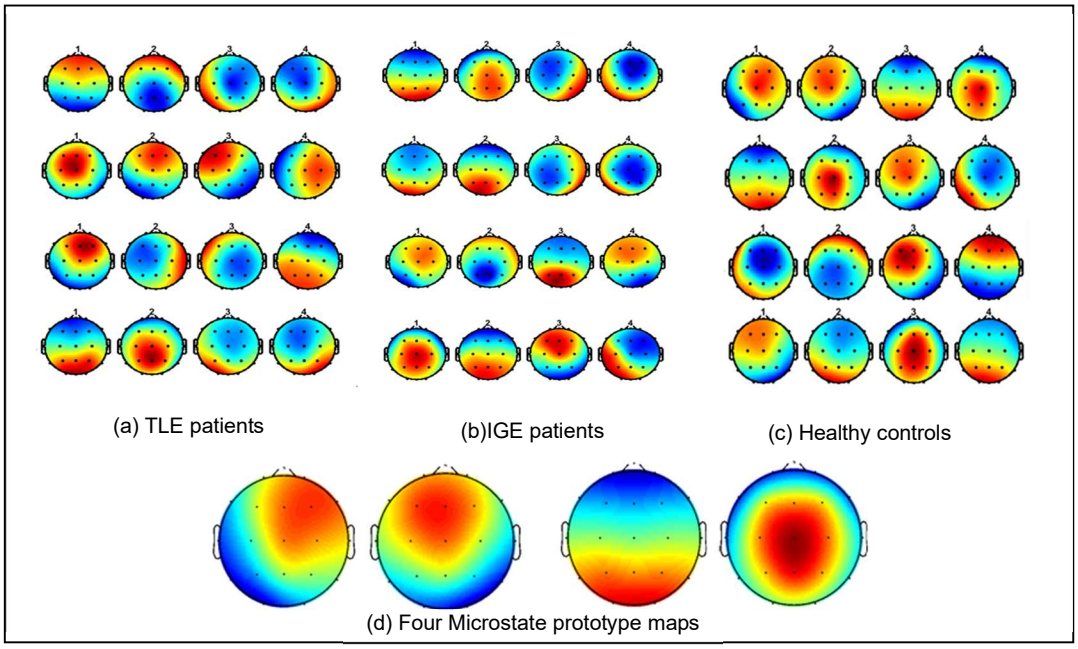


Figure 2. Microstate template maps obtained from (a) 4 individual TLE patients (b) 4 IGE patients and (c) 4 healthy controls (d) microstate prototypes created after second level spatial clustering.

Microstate Analysis

Global field power signal was calculated and the peaks where the signal to noise ratio (SNR) is high were identified. The scalp potential maps at the peaks were inputted to a modified k-means clustering algorithm and clustered into 4 microstate template classes. Half of the individual template maps were randomly picked from each group (15 HC, 15 TLE and 15 IGE) and were spatially clustered using k-means clustering to obtain the Microstate prototypes. The obtained microstate prototypes were similar to the archetypal maps found in the literature (Figure 2(d)).

Statistics Calculation

The generated four Microstate prototype maps were used to back fit onto the resting state EEG data of all the subjects (30 HCs, 30 TLE patients and 30 IGE patients) which provides a time series containing the dominant microstate map at each time point; thus, successive time points with the same map are termed “microstates.” This is achieved by correlating the spatial map at each time point with the four microstate prototype maps, and labeling each time point according to the map with the largest absolute correlation (absolute correlation is used to ensure polarity invariance of the back fitting). A temporal smoothing was used for removing noisy segments. From the back fitted microstate sequence the following Microstate Statistics were calculated for all the subjects.

1. Duration

   The mean duration of a microstate is the average duration of time in which a microstate does not shift and remains constant. It indicates the temporal stability of the underlying neuronal network that produces the microstate.

2. Occurrence

   Occurrence of a microstate is measured as the average number of times per second during the recording period that the specific microstate becomes dominant and could represent the inclination of its fundamental neural generators to become triggered.

3. Coverage

   The percentage of time spent in one microstate is indicated by this measure also known as Contribution or Functional Occupancy.

4. Spatial Correlation

   Mean Spatial correlation between a microstate and assigned EEG trials is calculated based on the strength independent topographical similarity.

5. Transition Probability

   The transition between microstates represents the sequential synchronized activity of different scattered neural networks. The transition probabilities represent the likelihood of

switching between different microstates.

(c) MRI Acquisition

MRI was performed to all patients to detect MTS and to exclude patients with other structural brain lesions. All MR images were acquired on a 3 Tesla MRI machine (GE Discovery MR750W Scanner) and it includes the following sequences:

1) Anatomical images using Ax FSPGR BRAVO iso sequence with Repetition time (TR)= 8.552ms, Time to Echo (TE)= 3.228ms, Inversion Time= 500ms, Flip angle 12^0, 176 slices, slice thickness= 1mm and 256 × 256 matrix size.

2) Diffusion Tensor Images using a single shot diffusion sequence (Ax DTI) in 64 encoding directions with a diffusion factor of 1000.57 s/mm^2, TR= 8975ms and TE= 103.1ms.

Image Processing

As the first step, using MRIconvert2.1.0 software the raw DICOM scans were converted into the Neuroimaging Informatics Technology Initiative format. VBM analysis was performed using CAT12.8.2 (Computational Anatomy Toolbox) which is an extension to SPM12 (Version 7771) (Statistical Parametric Mapping, Wellcome Department of Cognitive Neurology) in MATLAB-R2020A. Absolute volumes of CSF (Cerebrospinal Fluid), GM (Gray Matter) and WM (White Matter), TIV (Total Intracranial Volume), GM and WM volumes of the following 11 regions: Amygdala, Hippocampus, Entorhinal Area, Fusiform Gyrus, Inferior Temporal Gyrus, Middle Temporal Gyrus, Percuneus, Para Hippocampal Gyrus, Superior Temporal Gyrus, Temporal pole and Transverse Temporal Gyrus were calculated bilaterally. ROIs were defined using Neuromorphometrics atlas.

DTI Image Processing was performed using DSI studio(http://dsi_studio.labsolver.org). FA (Fractional Anisotropy) and MD (Mean Diffusivity) were calculated for regions of interest (ROI) and the software algorithm tracked the white matter tracts that passed through these ROIs. These values were measured bilaterally for the following 7 tracts: Fornix (FORX), Uncinate Fasciculus (UF), Inferior Longitudinal Fasciculus (ILF), Superior longitudinal Fasciculus (SLF), Arcuate Fasciculus (ARF), Para Hippocampal Cingulum (PHC) and for Corpus Callosum (CC). The fiber tractography of the individual tracts were obtained (Figure. 3).

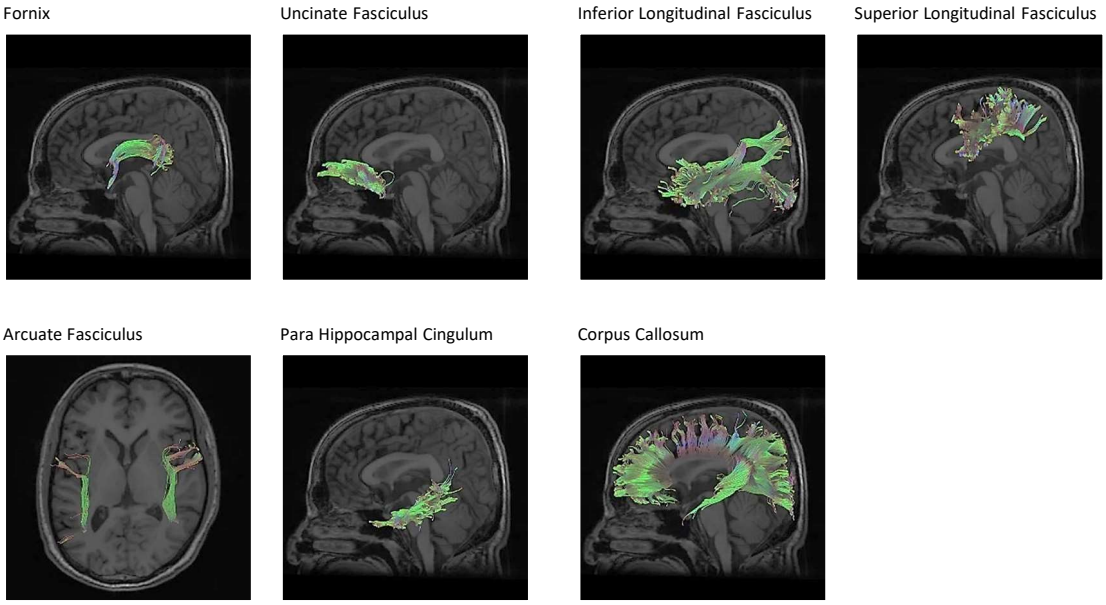


Figure.3. Diffusion tensor imaging (DTI) tractography of seven fiber tracts in a healthy control, 31-year-old male.

Statistical Methods: The data were coded and entered using the Statistical Package for Social Science version26, 2019. Mean, Standard deviation and significance values are derived using independent sample t test, to know the statistically significant difference between Healthy control and TLE, Healthy control and IGE, TLE and IGE in microstate, neuroimaging and neuropsychological parameters. Correlation analysis was also carried out to know the correlation between neuropsychological parameters with neuroimaging and microstate.

10. Detailed analysis of results indicating contributions made towards increasing the state of knowledge in the subject:

Demographic details are given in Table 1.

Table 1. Demographics of the studied groups.

Variables	HC (n=30)	TLE (n=30)	IGE (n=30)	p value
Age	31.63(8.17)	30.73(8.06)	30.97(8.81)	0.911
Education	16.1(2.43)	14.43(2.18)	14.83(2.69)	0.026
Male	17(56.7%)	15(50%)	8(26.7%)	0.049

p-value≥0.05 (non- significant), Values are expressed as the mean (SD) or number (percentage).

Neuropsychological test findings

Intelligence quotient, verbal memory, visual memory and Autobiographical memory index have been tested among 30 TLE and 30 IGE patients and 30 Healthy controls.

(a) Between Healthy controls and TLE:

Mean values of healthy controls are higher than TLE patients in almost all variables except omission and commission errors and their 7 days recall (Table 2). As per t test results, there is statistically significant difference among verbal comprehensive index (VCI), Working memory index (WMI), processing speed index (PSI) (sub-dimension of IQ), full scale IQ, sum of RAVLT score (SRAVLT), 30 minutes delayed recall RAVLT (30MDRECALLRAVLT), recognition RAVLT (RECOGRAVLT), Omission error RAVLT (OERAVLT), 7 days recall RAVLT (7DRECALRAVLT) 7 day recognition RAVLT (7DRECOG), 7 day omission error RAVLT (7DOERAVLT), 7 day commission error RAVLT (7DCERAVLT), immediate recall RCFT(IRERCFT), 30 minutes delayed recall RCFT (30MDRERCFT), 7 day RCFT (7DRCFT), recent life personal semantic AMI (RLPSAMI), total personal semantic AMI (TPSAMI), early adult life autobiographical incidents AMI (EALAIAMI), total AMI (TAMI) between Healthy controls and TLE (all $p < 0.05$). Verbal memory and working memory is more affected for TLE patients as compared to healthy controls.

Table 2. Mean, Standard Deviation and p- values of Intelligence and memory parameters of healthy control and TLE groups.

Variables	HC (n=30) Mean (SD)	TLE (n=30) Mean (SD)	p-value
VCI	**101.93(7.32)**	**92.43(11.59)**	**<0.001**
PRI	98.67(12.38)	93.5(11.34)	0.097
WMI	**96.03(10.25)**	**88.5(15.2)**	**0.028**
PSI	**102.7(9.86)**	**94.2(9.32)**	**0.001**
FSIQ	**99.7(7.74)**	**90.4(9.67)**	**<0.001**
SRAVLT	**55.53(6.99)**	**49.97(12.41)**	**0.036**
30MDRECALLRAVLT	**12.17(2.41)**	**9.33(3.08)**	**<0.01**
RECOGRAVLT	**14.33(0.96)**	**13.37(1.85)**	**0.014**
OERAVLT	**0.67(0.96)**	**1.63(1.85)**	**0.014**
CERAVLT	0.63(0.77)	1.7(3.01)	0.065
7DRECALLRAVLT	**9.14(2.96)**	**5.07(2.88)**	**<0.001**
7DRECOG	**13.62(1.45)**	**11.77(2.21)**	**<0.001**
7DOERAVLT	**1.17(1.31)**	**3.23(2.21)**	**<0.001**
7DCERAVLT	**2.14(2.89)**	**5.1(4.45)**	**0.007**
CRCFT	31.92(0.23)	30.78(4.08)	0.135
IRERCFT	**22.7(6.28)**	**17.53(6.54)**	**0.003**
30MDRERCFT	**23.85(5.71)**	**17.87(6.89)**	**0.001**
7DRCFT	**20.33(7.7)**	**13.05(7.73)**	**0.002**
CPSAMI	20.7(1.11)	20.18(1.48)	0.132
EALPSAMI	20.87(0.55)	20.48(1.29)	0.133
RLPSAMI	**20.92(0.27)**	**19.02(2.02)**	**<0.001**
TPSAMI	**62.49(1.68)**	**59.68(3.9)**	**0.001**
CAIAMI	8.78(0.69)	8.35(1.22)	0.096

EALAIAMI	**9(0)**	**8.42(1.47)**	**0.034**
RLAIAMI	8.97(0.18)	8.7(0.87)	0.105
TAIAMI	26.88(0.74)	25.47(2.83)	0.01
TAMI	**89.38(2.29)**	**85.15(6.51)**	**0.001**

p value≥0.05 not significant, and p value < 0.001 highly significant. VCI= Verbal Comprehensive Index, PRI= Perceptual Reasoning Index, WMI= Working Memory Index, PSI= Processing Speed Index, FSIQ= Full scale IQ, RAVLT= Rey Auditory Verbal Learning Test, ROCFT= Rey Osterrieth Complex Figure test, AMI= Autobiographical Memory Interview, SRAVLT= Sum RAVLT, 30MDRECALLRAVLT= 30 minutes delayed recall RAVLT, RECOGRAVLT= Recognition RAVLT, OERAVLT= omission error RAVLT, CERAVLT= commission error RAVLT, 7DRECALLRAVLT= 7 day recall RAVLT, 7DRECOG= 7day recognition RAVLT, 7DOERAVLT=7day omission error RAVLT, 7DCERAVLT= 7day commission error RAVLT, CRCFT= Copy RCFT, IRERCFT= immediate recall RCFT, 30MDRERCFT= 30minutes delayed recall RCFT, 7DRCFT=7day RCFT, CPSAMI= Childhood personal semantic AMI, EALPSAMI= Early adult life personal semantic AMI, RLPSAMI= Recent life personal semantic AMI, TPSAMI= Total personal semantic AMI, CAIAMI= Childhood autobiographical incidents AMI, EALAIAMI= Early adult life autobiographical incidents AMI; RLAIAMI= Recent life autobiographical incidents AMI, TAIAMI= Total autobiographical incidents AMI, TAMI= Total AMI.

(b) Between Healthy controls and IGE:

Mean and SD values are almost similar between healthy controls and IGE (Table 3). Most of the IGE patients are well educated as compared to TLE patients and had similar IQ scores to that of healthy controls. There is statistically significant difference in verbal comprehensive index (VCI), Perceptual processing speed (PSI), full scale IQ (FSIQ), 30 minutes delayed recall RCFT (30MDRERCFT), 7day RCFT (7DRCFT), Childhood personal semantic AMI (CPSAMI), recent life personal semantic AMI (RLPSAMI), total personal semantic AMI (TPSAMI), childhood autobiographical incidents AMI (CAIAMI), total autobiographical incidents AMI (TAIAMI) and total AMI (AMI) between healthy controls and IGE patients. There is no significant difference in the verbal memory parameters of RAVLT between the two categories.

Table 3. Mean, Standard Deviation and p- values of Intelligence and memory parameters of healthy control and IGE groups.

Variables	HC (n=30) Mean (SD)	IGE (n=30) Mean (SD)	p-value
VCI	**101.93(7.32)**	**93.53(11.97)**	**0.002**
PRI	98.67(12.38)	94.03(9.59)	0.11
WMI	96.03(10.25)	91.4(13.23)	0.135
PSI	**102.7(9.86)**	**97.2(10.84)**	**0.044**
FSIQ	**99.7(7.74)**	**92.33(9.81)**	**0.002**
SRAVLT	55.53(6.99)	52.07(8.58)	0.092
30MDRECALLRAVLT	12.17(2.41)	11.1(3.03)	0.137
RECOGRAVLT	14.33(0.96)	14.27(1.08)	0.801

OERAVLT	0.67(0.96)	0.77(1.1)	0.709
CERAVLT	0.63(0.77)	1.3(2.15)	0.115
7DRECALLRAVLT	9.14(2.96)	7.87(3.56)	0.16
7DRECOG	13.62(1.45)	13.77(1.36)	0.584
7DOERAVLT	1.17(1.31)	1.37(1.85)	0.75
7DCERAVLT	2.14(2.89)	2.67(3.02)	0.671
CRCFT	31.92(0.23)	31.62(0.8)	0.052
IRERCFT	22.7(6.28)	20.38(5.75)	0.14
30MDRERCFT	**23.85(5.71)**	**20.36(6.1)**	**0.026**
7DRCFT	**20.33(7.7)**	**15.4(6.04)**	**0.029**
CPSAMI	**20.7(1.11)**	**19.93(1.27)**	**0.016**
EALPSAMI	20.87(0.55)	20.8(0.45)	0.574
RLPSAMI	**20.92(0.27)**	**19.12(1.59)**	**<0.01**
TPSAMI	**62.49(1.68)**	**59.85(2.23)**	**<0.01**
CAIAMI	**8.78(0.69)**	**8.1(1.43)**	**0.022**
EALAIAMI	9(0)	8.95(0.2)	0.179
RLAIAMI	8.97(0.18)	8.72(0.78)	0.094
TAIAMI	**26.88(0.74)**	**25.57(2.16)**	**0.003**
TAMI	**89.38(2.29)**	**85.42(3.84)**	**<0.01**

p value≥0.05 not significant, and p value < 0.001 highly significant. VCI= Verbal Comprehensive Index, PRI= Perceptual Reasoning Index, WMI= Working Memory Index, PSI= Processing Speed Index, FSIQ= Full scale IQ, RAVLT= Rey Auditory Verbal Learning Test, ROCFT= Rey Osterrieth Complex Figure test, AMI= Autobiographical Memory Interview, SRAVLT= Sum RAVLT, 30MDRECALLRAVLT= 30 minutes delayed recall RAVLT, RECOGRAVLT= Recognition RAVLT, OERAVLT= omission error RAVLT, CERAVLT= commission error RAVLT, 7DRECALLRAVLT= 7 day recall RAVLT, 7DRECOG= 7day recognition RAVLT, 7DOERAVLT=7day omission error RAVLT, 7DCERAVLT= 7day commission error RAVLT, CRCFT= Copy RCFT, IRERCFT= immediate recall RCFT, 30MDRERCFT= 30minutes delayed recall RCFT, 7DRCFT=7day RCFT, CPSAMI= Childhood personal semantic AMI, EALPSAMI= Early adult life personal semantic AMI, RLPSAMI= Recent life personal semantic AMI, TPSAMI= Total personal semantic AMI, CAIAMI= Childhood autobiographical incidents AMI, EALAIAMI= Early adult life autobiographical incidents AMI; RLAIAMI= Recent life autobiographical incidents AMI, TAIAMI= Total autobiographical incidents AMI, TAMI= Total AMI.

(c) Between TLE and IGE patients:

Mean and SD are mostly higher for IGE patients as compared to that of TLE patients (Table 4). There is statistically significant difference in 30 minutes delayed recall RAVLT (30MDRECALLRAVLT), recognition RAVLT (RECOGRAVLT), Omission error RAVLT (OERAVLT), 7 days recall RAVLT (7DRECALRAVLT) 7day recognition RAVLT (7DRECOG), 7day omission error RAVLT (7DOERAVLT), 7day commission error RAVLT (7DCERAVLT), immediate recall RCFT(IRERCFT) and early adult life autobiographical incidents AMI (EALAIAMI) between TLE and IGE patients. There is no significant difference in intelligence

quotient between the two categories. Also, there is no significant difference in visual memory parameters other than immediate recall.

Table 4. Mean, Standard Deviation and p- values of Intelligence and memory parameters of TLE and IGE groups.

Variables	TLE (n=30) Mean (SD)	IGE (n=30) Mean (SD)	p-value
VCI	92.43(11.59)	93.53(11.97)	0.719
PRI	93.5(11.34)	94.03(9.59)	0.845
WMI	88.5(15.2)	91.4(13.23)	0.434
PSI	94.2(9.32)	97.2(10.84)	0.255
FSIQ	90.4(9.67)	92.33(9.81)	0.445
SRAVLT	49.97(12.41)	52.07(8.58)	0.449
30MDRECALLRAVLT	**9.33(3.08)**	**11.1(3.03)**	**0.029**
RECOGRAVLT	**13.37(1.85)**	**14.27(1.08)**	**0.025**
OERAVLT	**1.63(1.85)**	**0.77(1.1)**	**0.031**
CERAVLT	1.7(3.01)	1.3(2.15)	0.556
7DRECALLRAVLT	**5.07(2.88)**	**7.87(3.56)**	**0.001**
7DRECOG	**11.77(2.21)**	**13.77(1.36)**	**<0.01**
7DOERAVLT	**3.23(2.21)**	**1.37(1.85)**	**0.001**
7DCERAVLT	**5.1(4.45)**	**2.67(3.02)**	**0.016**
CRCFT	30.78(4.08)	31.62(0.8)	0.277
IRERCFT	**17.53(6.54)**	**20.38(5.75)**	**0.079**
30MDRERCFT	17.87(6.89)	20.36(6.1)	0.143
7DRCFT	13.05(7.73)	15.4(6.04)	0.194
CPSAMI	20.18(1.48)	19.93(1.27)	0.486
EALPSAMI	20.48(1.29)	20.8(0.45)	0.209
RLPSAMI	19.02(2.02)	19.12(1.59)	0.832
TPSAMI	59.68(3.9)	59.85(2.23)	0.84
CAIAMI	8.35(1.22)	8.1(1.43)	0.47
EALAIAMI	**8.42(1.47)**	**8.95(0.2)**	**0.054**
RLAIAMI	8.7(0.87)	8.72(0.78)	0.938
TAIAMI	25.47(2.83)	25.57(2.16)	0.878
TAMI	85.15(6.51)	85.42(3.84)	0.847

p value≥0.05 not significant, and p value < 0.001 highly significant. VCI= Verbal Comprehensive Index, PRI= Perceptual Reasoning Index, WMI= Working Memory Index, PSI= Processing Speed Index, FSIQ= Full scale IQ, RAVLT= Rey Auditory Verbal Learning Test, ROCFT= Rey Osterrieth Complex Figure test, AMI= Autobiographical Memory Interview, SRAVLT= Sum RAVLT, 30MDRECALLRAVLT= 30 minutes delayed recall RAVLT, RECOGRAVLT= Recognition RAVLT, OERAVLT= omission error RAVLT, CERAVLT= commission error RAVLT, 7DRECALLRAVLT= 7 day recall RAVLT, 7DRECOG= 7day recognition RAVLT, 7DOERAVLT=7day omission error RAVLT, 7DCERAVLT= 7day commission error RAVLT, CRCFT= Copy RCFT, IRERCFT= immediate recall RCFT, 30MDRERCFT= 30minutes delayed recall RCFT, 7DRCFT=7day RCFT, CPSAMI= Childhood personal semantic AMI, EALPSAMI= Early adult life personal semantic AMI, RLPSAMI= Recent life personal semantic AMI, TPSAMI= Total personal semantic AMI, CAIAMI= Childhood autobiographical incidents AMI,

EALAIAMI= Early adult life autobiographical incidents AMI; RLAIAMI= Recent life autobiographical incidents AMI, TAIAMI= Total autobiographical incidents AMI, TAMI= Total AMI.

Microstate Results

The following are the 4 microstates obtained after analyzing the data (Figure.4).

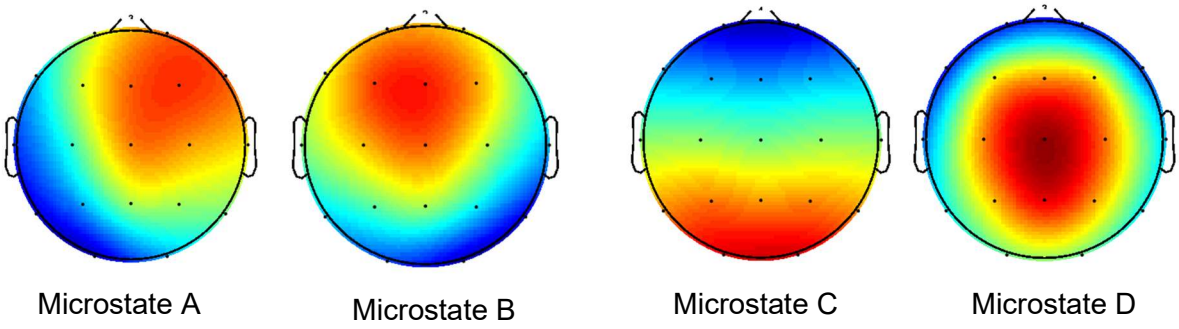


Figure 4: Microstate prototypes A, B, C, D.

Microstates and their functional significance

Microstate A
- Related to phonological /auditory processing

Microstate B
- Related to visual processing

Microstate C
- Related to autonomic processing and salience network

Microstate D
- Related to attention related processing/fronto-parietal network

The statistical evaluation of results of Microstate statistics (30 HC- Healthy Controls, 30 TLE- Temporal Lobe Epilepsy patients and 30 IGE- Idiopathic generalized Epilepsy patients) using ANOVA yielded the following results. Significant differences were found between HC, TLE and IGE in all microstate statistical parameters Duration, Occurrence, Coverage, Spatial Correlation and Transition Probabilities (TP).

(a) Between Healthy Controls and TLE:

Duration, Occurrence and Time Coverage of Microstate D were significantly lower compared to healthy controls in TLE patients (Table 5). Attention is often impaired in TLE due to impaired vigilance networks. As Microstate D is related to attention related processing the lower values in parameters related to it underlines slowdown or aberrations in attention related processing in TLE patients. Mean spatial correlation of microstate A and microstate B were significantly higher in TLE patients. Transition probabilities from B to D, D to A and A to C were lower in

TLE patients when compared to healthy Controls. But transition probability from B to A was higher for TLE patients when compared with Healthy controls.

Table 5. Mean, Standard Deviation and p- values of microstate parameters of healthy control and TLE groups.

Variables	HC(n=30) Mean(SD)	TLE(n=30) Mean(SD)	p-value
Duration_ (D)	138.96(11.40)	128.02(12.98)	0.001
Duration_ (B)	164.13(32.03)	176.00(53.12)	0.299
Duration_ (A)	152.30(16.22)	155.94(15.22)	0.373
Duration_ (C)	146.41(22.68)	141.57(25.08)	0.437
Occurence_ (D)	1.57(0.31)	1.34(0.38)	0.016
Occurence_ (B)	1.77(0.23)	1.87(0.21)	0.068
Occurence_ (A)	1.70(0.26)	1.77(0.35)	0.407
Occurence_ (C)	1.51(0.26)	1.48(0.32)	0.673
TimeCoverage_(D)	0.22(0.06)	0.18(0.07)	0.006
TimeCoverage_ (B)	0.29(0.08)	0.33(0.10)	0.130
TimeCoverage_ (A)	0.26(0.06)	0.28(0.07)	0.303
TimeCoverage_ (C)	0.23(0.07)	0.22(0.08)	0.603
SpatialCorrelation_ (D)	0.52(0.03)	0.52(0.03)	0.656
SpatialCorrelation_ (B)	0.52(0.04)	0.56(0.04)	0.003
SpatialCorrelation_ (A)	0.51(0.03)	0.54(0.03)	0.001
SpatialCorrelation_ (C)	0.61(0.04)	0.61(0.04)	0.532
TP12(D →B)	0.31(0.06)	0.27(0.08)	0.022
TP13(D→A)	0.32(0.07)	0.26(0.09)	0.010
TP14(D→C)	0.31(0.07)	0.25(0.08)	0.003
TP21(B→D)	0.35(0.07)	0.38(0.08)	0.121
TP23(B→A)	0.40(0.08)	0.44(0.10)	0.045
TP24(B→C)	0.37(0.09)	0.41(0.12)	0.125
TP31(A→D)	0.35(0.07)	0.35(0.10)	0.920
TP32(A→B)	0.38(0.07)	0.41(0.08)	0.107
TP34(A→C)	0.32(0.06)	0.34(0.08)	0.283
TP41(C→D)	0.30(0.08)	0.27(0.08)	0.137
TP42(C→B)	0.32(0.09)	0.33(0.12)	0.683
TP43(C→A)	0.29(0.06)	0.29(0.08)	0.621

(b) Between Healthy Controls and IGE:

Duration, Occurrence and Time Coverage of Microstate B was significantly higher compared to healthy controls in IGE patients (Table 6). Impaired visual habituation and different visual information processing style has been reported in IGE patients in recent studies. As Microstate B is related to vision related processing this may indicate aberrations in visual processing in IGE patients. Mean spatial correlation of microstate A and microstate B were higher in IGE patients which are in line with that found in TLE patients. Transition probabilities from Microstate

B to all other microstates (A, C, D) were higher in IGE when compared to healthy Controls. But transition probabilities from D to C and A to C were lower for IGE patients when compared with Healthy controls.

Table 6. Mean, Standard Deviation and p- values of microstate parameters of healthy control and IGE groups.

Variables	HC(n=30) Mean (SD)	IGE(n=30) Mean (SD)	p-value
Duration_ (D)	138.96(11.40)	135.93(19.35)	0.462
Duration_ (B)	164.13(32.03)	190.34(61.92)	**0.044**
Duration_ (A)	152.30(16.22)	149.42(17.55)	0.513
Duration_ (C)	146.41(22.68)	147.06(28.14)	0.922
Occurence_ (D)	1.57(0.31)	1.34(0.54)	0.051
Occurence_ (B)	**1.77(0.23)**	**1.89(0.24)**	**0.046**
Occurence_ (A)	1.70(0.26)	1.55(0.35)	0.073
Occurence_ (C)	1.51(0.26)	1.44(0.29)	0.347
TimeCoverage_ (D)	0.22(0.06)	0.19(0.10)	0.134
TimeCoverage_ (B)	**0.29(0.08)**	**0.36(0.11)**	**0.010**
TimeCoverage_ (A)	0.26(0.06)	0.23(0.07)	0.102
TimeCoverage_ (C)	0.23(0.07)	0.22(0.08)	0.685
SpatialCorrelation_ (D)	0.52(0.03)	0.52(0.03)	0.852
SpatialCorrelation_ (B)	0.52(0.04)	0.56(0.05)	0.002
SpatialCorrelation_ (A)	0.51(0.03)	0.53(0.04)	0.037
SpatialCorrelation_ (C)	0.61(0.04)	0.61(0.04)	0.467
TP12(D →B)	0.31(0.06)	0.28(0.11)	0.279
TP13(D→A)	0.32(0.07)	0.27(0.11)	0.074
TP14(D→C)	0.31(0.07)	0.26(0.12)	0.027
TP21(B→D)	0.35(0.07)	0.40(0.07)	0.015
TP23(B→A)	0.40(0.08)	0.46(0.12)	0.017
TP24(B→C)	0.37(0.09)	0.46(0.13)	0.003
TP31(A→D)	0.35(0.07)	0.31(0.09)	0.077
TP32(A→B)	0.38(0.07)	0.37(0.10)	0.801
TP34(A→C)	**0.32(0.06)**	**0.29(0.07)**	**0.045**
TP41(C→D)	0.30(0.08)	0.29(0.09)	0.630
TP42(C→B)	0.32(0.09)	0.35(0.12)	0.267
TP43(C→A)	0.29(0.06)	0.27(0.09)	0.384

(c) Between TLE and IGE patients:

A comparative study between TLE and IGE revealed the following results (Table 7). The Occurrence and Time Coverage of Microstate A was lower in IGE patients when compared to TLE patients. This may be the reason for selective impairment of auditory attention processing in idiopathic generalized epilepsies as Microstate A is related to audiological processing. Also transitions from Microstate A to C were significantly lower for IGE patients when compared with TLE patients.

Table 7. Mean, Standard Deviation and p- values of microstate parameters of TLE and IGE groups.

Variables	TLE(n=30) Mean(SD)	IGE(n=30) Mean(SD)	p-value
Duration_ (D)	128.02(12.98)	135.93(19.35)	0.068
Duration_ (B)	176.00(53.12)	190.34(61.92)	0.340
Duration_ (A)	155.94(15.22)	149.42(17.55)	0.130
Duration_ (C)	141.57(25.08)	147.06(28.14)	0.429
Occurence_ (D)	1.34(0.38)	1.34(0.54)	0.977
Occurence_ (B)	1.87(0.21)	1.89(0.24)	0.749
Occurence_ (A)	**1.77(0.35)**	**1.55(0.35)**	**0.022**
Occurence_ (C)	1.48(0.32)	1.44(0.29)	0.654
TimeCoverage_ (D)	0.18(0.07)	0.19(0.10)	0.506
TimeCoverage_ (B)	0.33(0.10)	0.36(0.11)	0.302
TimeCoverage_ (A)	**0.28(0.07)**	**0.23(0.07)**	**0.018**
TimeCoverage_ (C)	0.22(0.08)	0.22(0.08)	0.925
SpatialCorrelation_ (D)	0.52(0.03)	0.52(0.03)	0.507
SpatialCorrelation_ (B)	0.56(0.04)	0.56(0.05)	0.714
SpatialCorrelation_ (A)	0.54(0.03)	0.53(0.04)	0.274
SpatialCorrelation_ (C)	0.61(0.04)	0.61(0.04)	0.906
TP12(D →B)	0.27(0.08)	0.28(0.11)	0.490
TP13(D→A)	0.26(0.09)	0.27(0.11)	0.700
TP14(D→C)	0.25(0.08)	0.26(0.12)	0.868
TP21(B→D)	0.38(0.08)	0.40(0.07)	0.435
TP23(B→A)	0.44(0.10)	0.46(0.12)	0.560
TP24(B→C)	0.41(0.12)	0.46(0.13)	0.131
TP31(A→D)	0.35(0.10)	0.31(0.09)	0.119
TP32(A→B)	0.41(0.08)	0.37(0.10)	0.115
TP34(A→C)	**0.34(0.08)**	**0.29(0.07)**	**0.009**
TP41(C→D)	0.27(0.08)	0.29(0.09)	0.326
TP42(C→B)	0.33(0.12)	0.35(0.12)	0.527
TP43(C→A)	0.29(0.08)	0.27(0.09)	0.228

(d) Right TLE and left TLE:

No significant differences were found in any microstate statistical parameters between right TLE and left TLE patients.

Neuroimaging Results

(i) VBM:

(a) Between Healthy controls and TLE:

Mean and SD are high for almost all variables in healthy control than that of TLE patients (Table 8). There is statistically significant difference among grey matter volumes in left and

right Hippocampus and left Percuneus between HC and TLE patients. There is no significant difference among absolute volumes and white matter volumes between the two groups.

Table 8. The mean, standard deviation and p-value of volumes of different regions in Control and TLE groups.

Variables	HC (n=30) Mean(SD)	TLE (n=30) Mean(SD)	p-value
Abs_Vol_CSF	251.83(39.38)	246.03(60.24)	0.661
Abs_Vol_GM	625.60(47.81)	603.20(84.85)	0.213
Abs_Vol_WM	487.93(57.22)	475.17(55.00)	0.382
TIV	1365.17(126.25)	1334.33(144.29)	0.382
VGM_R_Amy	0.80(0.08)	0.82(0.13)	0.521
VGM_L_Amy	0.82(0.09)	0.84(0.10)	0.510
VGM_R_Hip	3.30(0.26)	3.03(0.45)	**0.006**
VGM_L_Hip	3.09(0.24)	2.91(0.40)	**0.041**
VGM_R_Ento	1.81(0.22)	1.84(0.30)	0.713
VGM_L_Ento	1.74(0.20)	1.79(0.23)	0.320
VGM_R_Fusi	6.38(0.64)	6.30(0.89)	0.665
VGM_L_Fusi	5.99(0.53)	6.09(0.72)	0.560
VGM_R_ITG	10.09(1.09)	10.07(1.37)	0.941
VGM_L_ITG	9.79(1.07)	9.77(1.25)	0.965
VGM_R_MTG	12.68(1.25)	12.33(1.50)	0.339
VGM_L_MTG	12.00(1.18)	11.76(1.46)	0.474
VGM_R_Per	9.39(1.02)	8.95(1.37)	0.165
VGM_L_Per	9.22(1.00)	8.52(1.48)	**0.035**
VGM_R_PHG	2.67(0.29)	2.65(0.37)	0.741
VGM_L_PHG	2.80(0.27)	2.81(0.35)	0.838
VGM_R_STG	6.12(0.65)	6.00(0.78)	0.536
VGM_L_STG	5.63(0.58)	5.75(0.80)	0.513
VGM_R_TP	7.98(0.89)	7.90(1.16)	0.773
VGM_L_TP	8.03(1.04)	8.13(1.10)	0.725
VGM_R_TTG	0.99(0.16)	0.99(0.17)	0.935
VGM_L_TTG	1.09(0.19)	1.08(0.23)	0.887
VWM_R_Amy	0.02(0.02)	0.02(0.03)	0.351
VWM_L_Amy	0.02(0.03)	0.02(0.02)	0.963
VWM_R_Hip	0.18(0.06)	0.20(0.07)	0.204
VWM_L_Hip	0.15(0.06)	0.15(0.06)	0.694
VWM_R_Ento	0.16(0.07)	0.16(0.05)	0.724
VWM_L_Ento	0.15(0.06)	0.13(0.04)	0.304
VWM_R_Fusi	1.25(0.32)	1.17(0.38)	0.415
VWM_L_Fusi	1.11(0.27)	1.02(0.24)	0.201
VWM_R_ITG	2.26(0.35)	2.23(0.44)	0.748
VWM_L_ITG	1.94(0.37)	1.98(0.40)	0.700
VWM_R_MTG	1.88(0.27)	1.84(0.37)	0.691
VWM_L_MTG	2.03(0.32)	1.93(0.38)	0.316

VWM_R_Per	1.48(0.30)	1.34(0.31)	0.067
VWM_L_Per	1.41(0.29)	1.30(0.27)	0.114
VWM_R_PHG	0.36(0.07)	0.35(0.11)	0.610
VWM_L_PHG	0.38(0.07)	0.37(0.09)	0.859
VWM_R_STG	0.81(0.15)	0.80(0.16)	0.803
VWM_L_STG	0.83(0.18)	0.84(0.17)	0.830
VWM_R_TP	1.03(0.22)	0.94(0.22)	0.162
VWM_L_TP	0.97(0.21)	0.95(0.22)	0.728
VWM_R_TTG	0.18(0.06)	0.16(0.05)	0.180
VWM_L_TTG	0.22(0.10)	0.19(0.08)	0.268

p value≥0.05 not significant. Abs_Vol= Absolute Volume in cm^3, CSF= Cerebral Spinal Fluid, TIV= Total Intracranial Volume in cm^3, VGM= Grey Matter Volume in mm^3, VWM= White Matter Volume in mm^3, L= Left, R= Right, Amy= Amgydala, Hip= Hippocampus, Ento= Entorhinal area, Fusi= Fusiform Gyrus, ITG= Inferior Temporal Gyrus, MTG= Middle Temporal Gyrus, Per= Percuneus, PHG= Para-hippocampal Gyrus, STG= Superior Temporal Gyrus, TP= Temporal Pole, TTG= Transeverse Temporal Gyrus.

(b) Between Healthy Controls and IGE:

The mean and standard deviation of grey matter and white matter volumes in all regions are high for healthy control than that of IGE patients (Table 9). There is statistically significant difference among absolute grey matter and white matter volumes, total intracranial volume, grey matter volumes in left and right hippocampus and percuneus, right superior temporal gyrus, left transverse temporal gyrus, white matter volumes in left and right middle temporal gyrus and superior temporal gyrus between controls and TLE patients.

Table 9. The mean, standard deviation and p-value of volumes of different regions in Control and IGE groups.

Variables	HC (n=30) Mean(SD)	IGE (n=30) Mean(SD)	p-value
Abs_Vol_CSF	251.83(39.38)	252.13(53.80)	0.980
Abs_Vol_GM	625.60(47.81)	597.30(52.33)	**0.033**
Abs_Vol_WM	487.93(57.22)	453.57(47.03)	**0.014**
TIV	1365.17(126.25)	1303.03(109.60)	**0.046**
VGM_R_Amy	0.80(0.08)	0.79(0.09)	0.646
VGM_L_Amy	0.82(0.09)	0.80(0.11)	0.401
VGM_R_Hip	3.30(0.26)	3.11(0.27)	**0.010**
VGM_L_Hip	3.09(0.24)	2.92(0.25)	**0.011**
VGM_R_Ento	1.81(0.22)	1.74(0.19)	0.169
VGM_L_Ento	1.74(0.20)	1.68(0.21)	0.238
VGM_R_Fusi	6.38(0.64)	6.10(0.75)	0.119
VGM_L_Fusi	5.99(0.53)	5.81(0.59)	0.208
VGM_R_ITG	10.09(1.09)	9.64(1.13)	0.116
VGM_L_ITG	9.79(1.07)	9.32(1.12)	0.105
VGM_R_MTG	12.68(1.25)	12.03(1.26)	0.050
VGM_L_MTG	12.00(1.18)	11.48(1.33)	0.109

VGM_R_Per	9.39(1.02)	8.80(1.03)	**0.031**
VGM_L_Per	9.22(1.00)	8.63(1.03)	**0.028**
VGM_R_PHG	2.67(0.29)	2.58(0.27)	0.207
VGM_L_PHG	2.80(0.27)	2.70(0.28)	0.197
VGM_R_STG	6.12(0.65)	5.77(0.60)	**0.038**
VGM_L_STG	5.63(0.58)	5.45(0.72)	0.277
VGM_R_TP	7.98(0.89)	7.53(0.94)	0.066
VGM_L_TP	8.03(1.04)	7.65(1.07)	0.164
VGM_R_TTG	0.99(0.16)	0.93(0.14)	0.138
VGM_L_TTG	1.09(0.19)	0.99(0.17)	**0.037**
VWM_R_Amy	0.02(0.02)	0.01(0.01)	0.317
VWM_L_Amy	0.02(0.03)	0.02(0.02)	0.482
VWM_R_Hip	0.18(0.06)	0.15(0.05)	0.074
VWM_L_Hip	0.15(0.06)	0.13(0.06)	0.245
VWM_R_Ento	0.16(0.07)	0.15(0.06)	0.842
VWM_L_Ento	0.15(0.06)	0.14(0.06)	0.577
VWM_R_Fusi	1.25(0.32)	1.19(0.24)	0.423
VWM_L_Fusi	1.11(0.27)	1.11(0.23)	0.978
VWM_R_ITG	2.26(0.35)	2.11(0.39)	0.114
VWM_L_ITG	1.94(0.37)	1.93(0.34)	0.923
VWM_R_MTG	1.88(0.27)	1.71(0.30)	**0.023**
VWM_L_MTG	2.03(0.32)	1.77(0.35)	**0.006**
VWM_R_Per	1.48(0.30)	1.38(0.26)	0.159
VWM_L_Per	1.41(0.29)	1.28(0.23)	0.059
VWM_R_PHG	0.36(0.07)	0.33(0.06)	0.084
VWM_L_PHG	0.38(0.07)	0.37(0.09)	0.673
VWM_R_STG	0.81(0.15)	0.73(0.15)	**0.046**
VWM_L_STG	0.83(0.18)	0.74(0.15)	**0.048**
VWM_R_TP	1.03(0.22)	1.00(0.20)	0.573
VWM_L_TP	0.97(0.21)	0.96(0.22)	0.870
VWM_R_TTG	0.18(0.06)	0.17(0.06)	0.597
VWM_L_TTG	0.22(0.10)	0.18(0.07)	0.122

p value≥0.05 not significant. Abs_Vol= Absolute Volume in cm^3, CSF= Cerebral Spinal Fluid, TIV= Total Intracranial Volume in cm^3, VGM= Grey Matter Volume in mm^3, VWM= White Matter Volume in mm^3, L= Left, R= Right, Amy= Amgydala, Hip= Hippocampus, Ento= Entorhinal area, Fusi= Fusiform Gyrus, ITG= Inferior Temporal Gyrus, MTG= Middle Temporal Gyrus, Per= Percuneus, PHG= Para-hippocampal Gyrus, STG= Superior Temporal Gyrus, TP= Temporal Pole, TTG= Transeverse Temporal Gyrus.

(c) Between TLE and IGE patients:

There is no statistically significant difference in volumes of regions except grey matter volume in left entorhinal cortex and white matter volumes in right amygdala, right hippocampus and left superior gyrus between these two categories (Table 10).

Table 10. The mean, standard deviation and p-value of volumes of different regions in TLE and IGE groups.

Variables	TLE (n=30) Mean(SD)	IGE (n=30) Mean(SD)	p-value
Abs_Vol_CSF	246.03(60.24)	252.13(53.80)	0.681
Abs_Vol_GM	603.20(84.85)	597.30(52.33)	0.747
Abs_Vol_WM	475.17(55.00)	453.57(47.03)	0.107
TIV	1334.33(144.29)	1303.03(109.60)	0.348
VGM_R_Amy	0.82(0.13)	0.79(0.09)	0.338
VGM_L_Amy	0.84(0.10)	0.80(0.11)	0.158
VGM_R_Hip	3.03(0.45)	3.11(0.27)	0.366
VGM_L_Hip	2.91(0.40)	2.92(0.25)	0.910
VGM_R_Ento	1.84(0.30)	1.74(0.19)	0.138
VGM_L_Ento	1.79(0.23)	1.68(0.21)	**0.038**
VGM_R_Fusi	6.30(0.89)	6.10(0.75)	0.354
VGM_L_Fusi	6.09(0.72)	5.81(0.59)	0.104
VGM_R_ITG	10.07(1.37)	9.64(1.13)	0.185
VGM_L_ITG	9.77(1.25)	9.32(1.12)	0.145
VGM_R_MTG	12.33(1.50)	12.03(1.26)	0.399
VGM_L_MTG	11.76(1.46)	11.48(1.33)	0.441
VGM_R_Per	8.95(1.37)	8.80(1.03)	0.641
VGM_L_Per	8.52(1.48)	8.63(1.03)	0.737
VGM_R_PHG	2.65(0.37)	2.58(0.27)	0.447
VGM_L_PHG	2.81(0.35)	2.70(0.28)	0.185
VGM_R_STG	6.00(0.78)	5.77(0.60)	0.207
VGM_L_STG	5.75(0.80)	5.45(0.72)	0.128
VGM_R_TP	7.90(1.16)	7.53(0.94)	0.184
VGM_L_TP	8.13(1.10)	7.65(1.07)	0.091
VGM_R_TTG	0.99(0.17)	0.93(0.14)	0.168
VGM_L_TTG	1.08(0.23)	0.99(0.17)	0.086
VWM_R_Amy	0.02(0.03)	0.01(0.01)	**0.047**
VWM_L_Amy	0.02(0.02)	0.02(0.02)	0.420
VWM_R_Hip	0.20(0.07)	0.15(0.05)	**0.003**
VWM_L_Hip	0.15(0.06)	0.13(0.06)	0.144
VWM_R_Ento	0.16(0.05)	0.15(0.06)	0.548
VWM_L_Ento	0.13(0.04)	0.14(0.06)	0.669
VWM_R_Fusi	1.17(0.38)	1.19(0.24)	0.852
VWM_L_Fusi	1.02(0.24)	1.11(0.23)	0.162
VWM_R_ITG	2.23(0.44)	2.11(0.39)	0.268
VWM_L_ITG	1.98(0.40)	1.93(0.34)	0.623
VWM_R_MTG	1.84(0.37)	1.71(0.30)	0.117
VWM_L_MTG	1.93(0.38)	1.77(0.35)	0.096
VWM_R_Per	1.34(0.31)	1.38(0.26)	0.552
VWM_L_Per	1.30(0.27)	1.28(0.23)	0.846
VWM_R_PHG	0.35(0.11)	0.33(0.06)	0.411
VWM_L_PHG	0.37(0.09)	0.37(0.09)	0.824

VWM_R_STG	0.80(0.16)	0.73(0.15)	0.089
VWM_L_STG	0.84(0.17)	0.74(0.15)	**0.026**
VWM_R_TP	0.94(0.22)	1.00(0.20)	0.351
VWM_L_TP	0.95(0.22)	0.96(0.22)	0.857
VWM_R_TTG	0.16(0.05)	0.17(0.06)	0.407
VWM_L_TTG	0.19(0.08)	0.18(0.07)	0.667

Abs_Vol= Absolute Volume in cm^3, CSF= Cerebral Spinal Fluid, TIV= Total Intracranial Volume in cm^3, VGM= Grey Matter Volume in mm^3, VWM= White Matter Volume in mm^3, L= Left, R= Right, Amy= Amgydala, Hip= Hippocampus, Ento= Entorhinal area, Fusi= Fusiform Gyrus, ITG= Inferior Temporal Gyrus, MTG= Middle Temporal Gyrus, Per= Percuneus, PHG= Para-hippocampal Gyrus, STG= Superior Temporal Gyrus, TP= Temporal Pole, TTG= Transeverse Temporal Gyrus.

(d) Between left and right TLE patients:

There is no statistically significant difference in volumes of regions except grey matter volume in left hippocampus between the two TLE categories (Table 11). The mean value of grey matter volume in left hippocampus is low for left TLE patients when compared with right TLE patients.

Table 11. The mean, standard deviation and p-value of volumes of different regions in Left and Right TLE groups.

Variables	RTLE (n=15) Mean(SD)	LTLE (n=15) Mean(SD)	p-value
Abs_Vol_CSF	246.33(62.18)	245.73(60.41)	0.979
Abs_Vol_GM	628.47(79.61)	577.93(84.89)	0.104
Abs_Vol_WM	484.07(59.69)	466.27(50.34)	0.385
TIV	1358.73(165.16)	1309.93(120.73)	0.363
VGM_R_Amy	0.83(0.16)	0.80(0.10)	0.546
VGM_L_Amy	0.87(0.11)	0.80(0.08)	0.059
VGM_R_Hip	2.99(0.50)	3.06(0.42)	0.661
VGM_L_Hip	3.08(0.34)	2.74(0.40)	**0.021**
VGM_R_Ento	1.87(0.34)	1.81(0.27)	0.639
VGM_L_Ento	1.86(0.22)	1.73(0.23)	0.125
VGM_R_Fusi	6.30(1.06)	6.29(0.72)	0.984
VGM_L_Fusi	6.18(0.87)	6.00(0.56)	0.506
VGM_R_ITG	10.27(1.63)	9.87(1.06)	0.440
VGM_L_ITG	10.08(1.51)	9.46(0.88)	0.177
VGM_R_MTG	12.36(1.59)	12.30(1.47)	0.906
VGM_L_MTG	12.17(1.72)	11.35(1.06)	0.127
VGM_R_Per	9.12(1.61)	8.78(1.12)	0.505
VGM_L_Per	8.89(1.77)	8.14(1.05)	0.170
VGM_R_PHG	2.67(0.45)	2.62(0.29)	0.693
VGM_L_PHG	2.90(0.37)	2.73(0.31)	0.185
VGM_R_STG	6.17(0.79)	5.83(0.76)	0.247
VGM_L_STG	5.93(0.88)	5.57(0.69)	0.228
VGM_R_TP	7.92(1.28)	7.88(1.07)	0.913
VGM_L_TP	8.47(1.03)	7.78(1.08)	0.084

VGM_R_TTG	0.99(0.15)	0.98(0.19)	0.803
VGM_L_TTG	1.10(0.24)	1.06(0.22)	0.660
VWM_R_Amy	0.02(0.03)	0.02(0.02)	0.642
VWM_L_Amy	0.02(0.02)	0.02(0.02)	0.745
VWM_R_Hip	0.23(0.06)	0.18(0.07)	0.089
VWM_L_Hip	0.16(0.06)	0.15(0.07)	0.617
VWM_R_Ento	0.16(0.06)	0.17(0.05)	0.785
VWM_L_Ento	0.14(0.04)	0.12(0.03)	0.101
VWM_R_Fusi	1.17(0.45)	1.18(0.31)	0.915
VWM_L_Fusi	0.99(0.29)	1.05(0.19)	0.524
VWM_R_ITG	2.23(0.55)	2.22(0.33)	0.923
VWM_L_ITG	2.08(0.44)	1.87(0.34)	0.147
VWM_R_MTG	1.78(0.34)	1.91(0.40)	0.320
VWM_L_MTG	1.96(0.40)	1.91(0.37)	0.695
VWM_R_Per	1.32(0.37)	1.36(0.24)	0.729
VWM_L_Per	1.34(0.31)	1.26(0.23)	0.437
VWM_R_PHG	0.35(0.10)	0.35(0.12)	0.855
VWM_L_PHG	0.39(0.08)	0.35(0.10)	0.250
VWM_R_STG	0.80(0.15)	0.80(0.17)	0.943
VWM_L_STG	0.85(0.18)	0.83(0.16)	0.690
VWM_R_TP	0.92(0.19)	0.97(0.25)	0.489
VWM_L_TP	0.97(0.24)	0.92(0.19)	0.555
VWM_R_TTG	0.16(0.05)	0.15(0.05)	0.598
VWM_L_TTG	0.19(0.10)	0.19(0.07)	0.985

p value≥0.05 not significant. Abs_Vol= Absolute Volume in cm^3, CSF= Cerebral Spinal Fluid, TIV= Total Intracranial Volume in cm^3, VGM= Grey Matter Volume in mm^3, VWM= White Matter Volume in mm^3, L= Left, R= Right, Amy= Amgydala, Hip= Hippocampus, Ento= Entorhinal area, Fusi= Fusiform Gyrus, ITG= Inferior Temporal Gyrus, MTG= Middle Temporal Gyrus, Per= Percuneus, PHG= Para-hippocampal Gyrus, STG= Superior Temporal Gyrus, TP= Temporal Pole, TTG= Transeverse Temporal Gyrus.

(ii) DTI:

(a) Between healthy controls and TLE:

There is statistically significant difference in fractional anisotropy in all tracts except superior longitudinal fasciculus 1 left, superior longitudinal fasciculus 2 right and corpus callosum forceps minor between healthy control and TLE patients (Table 12). Among these tracts, some of the tracts show highly significant difference in fractional anisotropy and mean diffusivity ($p<0.001$). There is no significant difference in mean diffusivity in fornix left, uncinate fasciculus left, superior longitudinal fasciculus 1 left and arcuate fasciculus right between the two categories.

Table 12. The mean, standard deviation and p-value of FA and MD in different tracts of Control and TLE groups.

Variables	HC(n=30) Mean(SD)	TLE(n=25) Mean(SD)	p-value
fa_F_L	0.38(0.03)	0.34(0.04)	**0.002**
md_F_L	1.80(0.33)	1.83(0.34)	0.679
fa_F_R	0.39(0.03)	0.37(0.04)	**0.041**
md_F_R	1.62(0.20)	1.78(0.28)	**0.016**
fa_UF_L	0.42(0.03)	0.38(0.05)	**0.002**
md_UF_L	0.85(0.03)	0.93(0.23)	0.051
fa_UF_R	0.45(0.02)	0.40(0.07)	**0.001**
md_UF_R	0.82(0.03)	0.94(0.23)	0.007
fa_ILF_L	0.53(0.03)	0.49(0.06)	**0.002**
md_ILF_L	0.83(0.03)	0.86(0.03)	**<0.001**
fa_ILF_R	0.51(0.02)	0.49(0.04)	**0.021**
md_ILF_R	0.81(0.03)	0.84(0.04)	**0.006**
fa_SLF1_L	0.47(0.06)	0.48(0.06)	0.778
md_SLF1_L	0.77(0.03)	0.86(0.19)	0.331
fa_SLF2_L	0.45(0.02)	0.43(0.03)	**0.007**
md_SLF2_L	0.77(0.03)	0.79(0.03)	**0.033**
fa_SLF3_L	0.45(0.03)	0.41(0.06)	**0.004**
md_SLF3_L	0.79(0.03)	0.82(0.05)	**0.015**
fa_SLF2_R	0.46(0.03)	0.46(0.03)	0.267
md_SLF2_R	0.73(0.02)	0.75(0.03)	**0.001**
fa_SLF3_R	0.49(0.03)	0.44(0.06)	**<0.001**
md_SLF3_R	0.73(0.02)	0.79(0.04)	**<0.001**
fa_CC_FM	0.55(0.02)	0.52(0.06)	0.061
md_CC_FM	0.80(0.03)	0.86(0.12)	**0.009**
fa_CC_B	0.58(0.02)	0.54(0.08)	**0.021**
md_CC_B	0.79(0.03)	0.88(0.16)	**0.005**
fa_CC_T	0.62(0.03)	0.56(0.06)	**<0.001**
md_CC_T	0.95(0.10)	1.12(0.19)	**<0.001**
fa_CC_FJ	0.64(0.02)	0.61(0.05)	**0.014**
md_CC_FJ	0.78(0.03)	0.82(0.05)	**0.001**
fa_PHC_L	0.39(0.04)	0.35(0.04)	**<0.001**
md_PHC_L	0.91(0.07)	0.99(0.18)	**0.048**
fa_PHC_R	0.43(0.04)	0.37(0.04)	**<0.001**
md_PHC_R	0.89(0.06)	1.05(0.20)	**<0.001**
fa_ARF_L	0.49(0.03)	0.46(0.05)	**0.021**
md_ARF_L	0.78(0.02)	0.82(0.08)	**0.029**
fa_ARF_R	0.50(0.03)	0.47(0.05)	**0.048**
md_ARF_R	0.75(0.04)	0.77(0.04)	0.077

p value≥0.05 not significant, and p value < 0.001 highly significant.
fa= fractional anisotropy, md= mean diffusivity, L= Left, R= Right, F= Fornix, UF= Uncinate Fasciculus, ILF= Inferior Longitudinal Fasciculus, SLF (1,2,3) = Superior Longitudinal Fasciculus (1,2,3), PHC= para-hippocampal cingulum, CC (FM, B, T, FJ) = corpus callosum (Forceps minor, Body, Tapetum, Forceps Minor), ARF= Arcuate Fasciculus.

(b) Between Healthy controls and IGE:

There is statistically significant difference in fractional anisotropy in uncinate fasciculus left, uncinate fasciculus right, inferior longitudinal fasciculus left, superior longitudinal fasciculus 3 right, corpus callosum forceps major and para-hippocampal cingulum right between healthy control and IGE patients (Table 13). There is no significant difference in mean diffusivity in tracts except uncinate fasciculus right, superior longitudinal fasciculus 2 left, superior longitudinal fasciculus 3 right, corpus callosum forceps minor, corpus callosum body and corpus callosum forceps major between the two categories. The mean diffusivity in superior longitudinal fasciculus 3 right and corpus callosum forceps major are highly significant between these groups.

Table 13. The mean, standard deviation and p-value of FA and MD in different tracts of Controls and IGE groups.

Variables	HC(n=30) Mean(SD)	IGE(n=30) Mean(SD)	p-value
fa_F_L	0.38(0.03)	0.36(0.05)	0.068
md_F_L	1.80(0.33)	1.80(0.35)	0.934
fa_F_R	0.39(0.03)	0.37(0.04)	0.185
md_F_R	1.62(0.20)	1.69(0.31)	0.300
fa_UF_L	0.42(0.03)	0.40(0.04)	**0.014**
md_UF_L	0.85(0.03)	0.87(0.12)	0.236
fa_UF_R	0.45(0.02)	0.42(0.06)	**0.042**
md_UF_R	0.82(0.03)	0.89(0.15)	**0.022**
fa_ILF_L	0.53(0.03)	0.49(0.05)	**0.002**
md_ILF_L	0.83(0.03)	0.85(0.04)	0.056
fa_ILF_R	0.51(0.02)	0.50(0.03)	0.220
md_ILF_R	0.81(0.03)	0.84(0.06)	0.077
fa_SLF1_L	0.47(0.06)	0.47(0.06)	0.913
md_SLF1_L	0.77(0.03)	0.86(0.29)	0.524
fa_SLF2_L	0.45(0.02)	0.44(0.03)	0.143
md_SLF2_L	0.77(0.03)	0.78(0.04)	0.419
fa_SLF3_L	0.45(0.03)	0.44(0.04)	0.136
md_SLF3_L	0.79(0.03)	0.80(0.03)	0.255
fa_SLF2_R	0.46(0.03)	0.46(0.03)	0.249
md_SLF2_R	0.73(0.02)	0.75(0.03)	**0.028**
fa_SLF3_R	0.49(0.03)	0.46(0.04)	**0.003**
md_SLF3_R	0.73(0.02)	0.77(0.04)	**<0.001**
fa_CC_FM	0.55(0.02)	0.54(0.05)	0.373
md_CC_FM	0.80(0.03)	0.84(0.07)	**0.014**
fa_CC_B	0.58(0.02)	0.56(0.06)	0.189
md_CC_B	0.79(0.03)	0.83(0.10)	**0.049**
fa_CC_T	0.62(0.03)	0.60(0.04)	0.092
md_CC_T	0.95(0.10)	0.98(0.16)	0.305
fa_CC_FJ	0.64(0.02)	0.62(0.03)	**0.001**

md_CC_FJ	0.78(0.03)	0.84(0.07)	**<0.001**
fa_PHC_L	0.39(0.04)	0.38(0.03)	0.499
md_PHC_L	0.91(0.07)	0.91(0.07)	0.911
fa_PHC_R	0.43(0.04)	0.40(0.04)	**0.003**
md_PHC_R	0.89(0.06)	0.93(0.09)	0.105
fa_ARF_L	0.49(0.03)	0.48(0.04)	0.330
md_ARF_L	0.78(0.02)	0.79(0.04)	0.136
fa_ARF_R	0.50(0.03)	0.45(0.10)	0.050
md_ARF_R	0.75(0.04)	0.74(0.16)	0.708

p value≥0.05 not significant, and p value < 0.001 highly significant. fa= fractional anisotropy, md= mean diffusivity, L= Left, R= Right, F= Fornix, UF= Uncinate Fasciculus, ILF= Inferior Longitudinal Fasciculus, SLF (1,2,3) = Superior Longitudinal Fasciculus (1,2,3), PHC= para-hippocampal cingulum, CC (FM, B, T, FJ) = corpus callosum (Forceps minor, Body, Tapetum, Forceps Minor), ARF= Arcuate Fasciculus.

(c) Between TLE and IGE patients:

There is statistically significant difference in fractional anisotropy in corpus callosum tapetum, para-hippocampal cingulum left and para-hippocampal cingulum right between TLE and IGE patients (Table 14). There is statistically significant difference in mean diffusivity in inferior longitudinal fasciculus left, corpus callosum tapetum, para-hippocampal cingulum left and para-hippocampal cingulum right between the two categories.

Table 14. The mean, standard deviation and p-value of FA and MD in different tracts of TLE and IGE groups.

Variables	TLE(n=25) Mean(SD)	IGE(n=30) Mean(SD)	p-value
fa_F_L	0.34(0.04)	0.36(0.05)	0.285
md_F_L	1.83(0.34)	1.80(0.35)	0.743
fa_F_R	0.37(0.04)	0.37(0.04)	0.497
md_F_R	1.78(0.28)	1.69(0.31)	0.272
fa_UF_L	0.38(0.05)	0.40(0.04)	0.297
md_UF_L	0.93(0.23)	0.87(0.12)	0.241
fa_UF_R	0.40(0.07)	0.42(0.06)	0.158
md_UF_R	0.94(0.23)	0.89(0.15)	0.331
fa_ILF_L	0.49(0.06)	0.49(0.05)	0.594
md_ILF_L	0.86(0.03)	0.85(0.04)	**0.047**
fa_ILF_R	0.49(0.04)	0.50(0.03)	0.218
md_ILF_R	0.84(0.04)	0.84(0.06)	0.905
fa_SLF1_L	0.48(0.06)	0.47(0.06)	0.827
md_SLF1_L	0.86(0.19)	0.86(0.29)	0.995
fa_SLF2_L	0.43(0.03)	0.44(0.03)	0.229
md_SLF2_L	0.79(0.03)	0.78(0.04)	0.260
fa_SLF3_L	0.41(0.06)	0.44(0.04)	0.101
md_SLF3_L	0.82(0.05)	0.80(0.03)	0.124

fa_SLF2_R	0.46(0.03)	0.46(0.03)	0.926
md_SLF2_R	0.75(0.03)	0.75(0.03)	0.336
fa_SLF3_R	0.44(0.06)	0.46(0.04)	0.085
md_SLF3_R	0.79(0.04)	0.77(0.04)	0.191
fa_CC_FM	0.52(0.06)	0.54(0.05)	0.381
md_CC_FM	0.86(0.12)	0.84(0.07)	0.334
fa_CC_B	0.54(0.08)	0.56(0.06)	0.293
md_CC_B	0.88(0.16)	0.83(0.10)	0.159
fa_CC_T	0.56(0.06)	0.60(0.04)	**0.006**
md_CC_T	1.12(0.19)	0.98(0.16)	**0.007**
fa_CC_FJ	0.61(0.05)	0.62(0.03)	0.662
md_CC_FJ	0.82(0.05)	0.84(0.07)	0.365
fa_PHC_L	0.35(0.04)	0.38(0.03)	**0.002**
md_PHC_L	0.99(0.18)	0.91(0.07)	**0.042**
fa_PHC_R	0.37(0.04)	0.40(0.04)	**0.007**
md_PHC_R	1.05(0.20)	0.93(0.09)	**0.004**
fa_ARF_L	0.46(0.05)	0.48(0.04)	0.144
md_ARF_L	0.82(0.08)	0.79(0.04)	0.187
fa_ARF_R	0.47(0.05)	0.45(0.10)	0.553
md_ARF_R	0.77(0.04)	0.74(0.16)	0.405

p value≥0.05 not significant, and p value < 0.001 highly significant.
fa= fractional anisotropy, md= mean diffusivity, L= Left, R= Right, F= Fornix, UF= Uncinate Fasciculus, ILF= Inferior Longitudinal Fasciculus, SLF (1,2,3) = Superior Longitudinal Fasciculus (1,2,3), PHC= para-hippocampal cingulum, CC (FM, B, T, FJ) = corpus callosum (Forceps minor, Body, Tapetum, Forceps Minor), ARF= Arcuate Fasciculus.

(d) Between left and right TLE patients:

Mean and standard deviation are almost similar for left and right TLE patients (Table 15). There is no statistically significant difference in fractional anisotropy in all tracts between left and right TLE patients. Similarly, there is no significant difference in mean diffusivity in all tracts except para-hippocampal cingulum left between the these two TLE categories. The mean value of mean diffusivity in left para-hippocampal cingulum is high for left TLE patients when compared with right TLE patients.

Table 15. The mean, standard deviation and p-value of FA and MD in different tracts of left and right TLE groups.

Variables	RTLE(n=15) Mean(SD)	LTLE(n=15) Mean(SD)	p-value
fa_F_L	0.34(0.04)	0.35(0.03)	0.608
md_F_L	1.81(0.40)	1.86(0.27)	0.761
fa_F_R	0.36(0.04)	0.37(0.04)	0.681
md_F_R	1.78(0.32)	1.78(0.24)	0.978
fa_UF_L	0.39(0.05)	0.38(0.06)	0.735
md_UF_L	0.88(0.08)	0.98(0.33)	0.287

fa_UF_R	0.40(0.07)	0.40(0.07)	0.801
md_UF_R	0.96(0.30)	0.92(0.12)	0.629
fa_ILF_L	0.49(0.06)	0.48(0.07)	0.702
md_ILF_L	0.86(0.02)	0.87(0.03)	0.286
fa_ILF_R	0.49(0.04)	0.49(0.04)	0.734
md_ILF_R	0.84(0.03)	0.84(0.04)	0.853
fa_SLF1_L	0.49(0.03)	0.46(0.09)	0.586
md_SLF1_L	0.80(0.10)	0.95(0.27)	0.235
fa_SLF2_L	0.43(0.03)	0.43(0.03)	0.983
md_SLF2_L	0.79(0.03)	0.79(0.04)	0.805
fa_SLF3_L	0.41(0.06)	0.42(0.07)	0.875
md_SLF3_L	0.81(0.04)	0.83(0.06)	0.278
fa_SLF1_R	0.48(0.04)	0.43(0.10)	0.362
md_SLF1_R	0.75(0.04)	0.83(0.06)	0.141
fa_SLF2_R	0.45(0.03)	0.47(0.02)	0.091
md_SLF2_R	0.75(0.03)	0.76(0.03)	0.448
fa_SLF3_R	0.44(0.06)	0.44(0.05)	0.702
md_SLF3_R	0.78(0.03)	0.79(0.04)	0.232
fa_CC_FM	0.54(0.04)	0.51(0.08)	0.248
md_CC_FM	0.83(0.04)	0.90(0.16)	0.108
fa_CC_B	0.56(0.03)	0.52(0.11)	0.263
md_CC_B	0.85(0.07)	0.90(0.22)	0.426
fa_CC_T	0.56(0.07)	0.57(0.02)	0.594
md_CC_T	1.15(0.25)	1.08(0.09)	0.360
fa_CC_FJ	0.62(0.07)	0.61(0.03)	0.904
md_CC_FJ	0.83(0.06)	0.82(0.05)	0.706
fa_PHC_L	0.36(0.04)	0.34(0.04)	0.134
md_PHC_L	0.92(0.04)	1.06(0.24)	**0.042**
fa_PHC_R	0.37(0.03)	0.37(0.04)	0.619
md_PHC_R	1.03(0.21)	1.07(0.20)	0.690
fa_ARF_L	0.46(0.05)	0.46(0.06)	0.751
md_ARF_L	0.79(0.03)	0.84(0.11)	0.229
fa_ARF_R	0.48(0.03)	0.46(0.05)	0.418
md_ARF_R	0.75(0.02)	0.78(0.05)	0.230

p value≥0.05 not significant, and p value < 0.001 highly significant.
fa= fractional anisotropy, md= mean diffusivity, L= Left, R= Right, F= Fornix, UF= Uncinate Fasciculus, ILF= Inferior Longitudinal Fasciculus, SLF (1,2,3) = Superior Longitudinal Fasciculus (1,2,3), PHC= para-hippocampal cingulum, CC (FM, B, T, FJ) = corpus callosum (Forceps minor, Body, Tapetum, Forceps Minor), ARF= Arcuate Fasciculus.

<u>Correlations between neuropsychology, EEG and neuroimaging data</u>:

Microstate and Neuropsychology correlation:

In duration M1, there is a negative correlation between 7day omission error RAVLT and positive correlation between full scale IQ and 7day recognition RAVLT. In spatial correlation M2, there

is negative correlation between recent life personal semantic AMI. Between spatial correlation M3 and 7day omission error RAVLT there is a positive correlation and a negative correlation between 7day recall RAVLT and total personal semantic AMI. In TP34, there is a negative correlation with recognition RAVLT and positive correlation with omission error RAVLT.

VBM and Neuropsychology correlation:

Absolute white matter volume shows negative correlation with 30 minutes delayed recall RAVLT, 7day recall RAVLT and 7day recognition RAVLT (verbal memory parameters). There is a positive correlation between absolute white matter volume and 7day omission error RAVLT (7DOERAVLT). There is a positive correlation between grey matter volume in right hippocampus and visual memory parameters such as immediate recall RCFT, 30minutes delayed recall RCFT, autobiographical memory parameters such as early adult life autobiographical incident, total autobiographical incidents and total AMI. The white matter volume in right hippocampus is negatively correlated with verbal memory parameters such as 30 minutes delayed recall RAVLT, recognition RAVLT, 7day recall RAVLT and 7day recognition RAVLT and positively correlated with omission error RAVLT, 7day omission error RAVLT, 7day commission error RAVLT. Between white matter volume in left middle temporal gyrus and 7day recognition of verbal memory there is a negative correlation and between 7day omission error RAVLT there is a positive correlation.

DTI and Neuropsychology correlation:

There is a positive correlation between autobiographical memory parameters (RLPSAMI, TPSAMI, EALAISAMI, TAIAMI, TAMI) and fractional anisotropy in left fornix. Fractional anisotropy in left fornix, right uncinate fasciculus, right para-hippocampal cingulum, corpus callosum forceps major and tapetum shows negative correlation and mean diffusivity in right para-hippocampal cingulum and corpus callosum forceps tapetum shows positive correlation with 7day omission error RAVLT (7DOERAVLT). Fractional anisotropy in left and right uncinate fasciculus shows positive correlation with visual memory recall parameters (IRERCFT, 30MDRERCFT, 7DRCFT) and recent life personal semantic autobiographical memory (RLPSAMI). The verbal memory 7day recall (7DRECALLRAVLT) shows positive correlation with fractional anisotropy in left fornix, left uncinate fasciculus and left inferior longitudinal fasciculus. The visual memory 7day recall (7DRCFT) shows a positive correlation with fractional anisotropy and a negative correlation with mean diffusivity in left inferior longitudinal fasciculus. There is a positive correlation between verbal-visual recognition-recall parameters (RECOGRAVLT, 7DRECALLRAVLT, 7DRECOG, IRERCFT, 30MDRERCFT, 7DRCFT) and fractional anisotropy in right superior longitudinal fasciculus 3. The recent life personal semantic autobiographical memory (RLPSAMI) shows a positive correlation with fractional anisotropy

and a negative correlation with mean diffusivity in right superior longitudinal fasciculus 3. Fractional anisotropy in corpus callosum forceps major and tapetum is positively correlated and also mean diffusivity in these regions is negatively correlated with verbal-visual memory recall parameters (30MDRECALLRAVLT, 7DRECALLRAVLT, IRERCFT, 30MDRERCFT, 7DRCFT) and autobiographical memory parameters (RLPSAMI, TPSAMI, TAMI). The visual memory recall parameters (IRERCFT, 30MDRERCFT, 7DRCFT) are positively correlated with fractional anisotropy in left and right para-hippocampal cingulum. The fractional anisotropy in right para-hippocampal cingulum shows positive correlation and mean diffusivity in this region shows negative correlation with 7day recognition of verbal memory (7DRCFT). The autobiographical memory parameters (RLPSAMI, TPSAMI, TAMI) are also positively correlated with fractional anisotropy in right para-hippocampal cingulum.

Machine Learning Based evaluation

Machine Learning models were built to classify Healthy Controls, IGE and TLE patients. Using the 17 statistically significant parameters obtained from the group analysis (a p-value <0.05 was considered statistically significant), machine learning classifiers were built using Support Vector Machines (SVM) and K Nearest Neighbour (KNN) algorithms. 4 separate machine learning models were built for differentiating between HC-TLE, HC-IGE, TLE-IGE and HC-TLE-IGE. The accuracy of each model was calculated using 9-fold cross validation. MATLAB's Machine learning app was used for creating and validating Machine learning models. All models performed with accuracy greater than 70% which is considered a very good model performance (Table 16).

Table 16. Machine learning (ML) model accuracy

Sl. No.	ML Model	Classifier Accuracy	
		SVM	KNN
1	HC_TLE	78%	76.7%
2	HC_IGE	72%	70%
3	TLE_IGE	71%	73.3%
4	HC_TLE_IGE	70%	74.4%

11. Conclusions summarizing the achievements and indication of scope for future work:

Our study results show that resting state EEG Microstates are capable of differentiating between HC, TLE and IGE patients with a very good accuracy. Hence, they can be used as potential biomarkers for classifying HC, TLE and IGE patients. Our work focuses on data of 90 subjects but the results need to be validated with more data. The software developed as part of this project: -

- Can be used to explore and analyze EEG data for any neurological disorder
- Can be used to find potential biomarkers for neuropsychiatric disorders
- Can be an efficient a clinical research tool for quantitative EEG analysis

Based on our neuroimaging findings, there are extensive bilateral grey matter volume and white matter tract abnormalities in some regions in TLE and IGE patients compared to control groups. We observed a more significant correlation between visual-verbal and autobiographical memory parameters with volumetric changes, fractional anisotropy, and mean diffusivity in certain regions of the brain in IGE patients than in TLE patients. In order to decipher significant differences in memory patterns between the epilepsy patients and controls, we need more advanced imaging techniques like functional MRI to incorporate into this study, and more participants should also be included.

12. S&T benefits accrued:

i. List of Research publications

Sr.	Authors	Title of paper	Name of the Journal	Volume	Pages	Year
1	Balaji B. Seshachala, Manna Jose, Arya M. Lathikakumari, Sruthy Murali, Arjun S. Kumar, Sanjeev V. Thomas	Valproate usage in pregnancy: An audit from the Kerala Registry of Epilepsy and Pregnancy	Epilepsia	62	1141-1147	2021
2	Sanjeev V. Thomas, Panniyamakal Jeemon, Rajit Pillai, Manna Jose, Arya M. Lathikakumari, Sruthy Murali, Arjun Sanalkumar,	Malformation risk of new anti-epileptic drugs in women with epilepsy; observational data from the Kerala registry of epilepsy and	Seizure: European Journal of Epilepsy	93	127-132	2021

	Reshma A. Salini, Veena Pavithran	pregnancy (KREP)				

* Paper titled “Accelerated Long-term Forgetting and autobiographical amnesia in Temporal Lobe Epilepsy patient” presented by Dr. Pavan Rudrabhatla at ECON 2020 in Award Paper Section at Hyatt Regency, Ahmedabad on January 18th,2020.

* Paper titled "Juvenile myoclonic hospital-based epilepsy: Outcome beyond three decades from onset- A cohort study" presented by Dr. Harini Pavuluri at 34" International Epilepsy Congress, Paris 2021 on 28th August 2021.

** One review paper submitted by CDAC in Clinical EEG and Neuroscience journal.

** Two articles from SCTIMST (Neuroimaging, Neuropsychology) and an article from CDAC (Microstate analysis) are in preparation.

ii. Manpower trained on the project

a) Research Scientists or Research Associates: Nil

b) No. of Ph.D. produced: Nil

c) Other Technical Personnel trained: 2

iii. Patents taken, if any: NA

iv. Any other outcome. NA

13. Financial Position:

(a) SCTIMST

Sr.	Budget Head	Funds Sanctioned	Expenditure	% of Total cost
1.	Manpower	23,63,500	26,64,886	112.75%
2.	Consumables	8,05,200	3,00,572	37.33%
3.	Contingencies	70,000	57,653	82.36%
4.	Travel	52,500	29,296	55.80%
5.	Others, if any	-	-	-
6.	Overhead Expenses	3,78,000	3,78,000	100%
7.	Equipment	4,50,000	4,50,000	100%
	Total	Rs. 41,19,200/-	Rs. 38,80,407/-	**94.20%**

(b) CDAC

Sr.	Budget Head	Funds Sanctioned	Expenditure	% of Total cost
1.	Manpower	18,31,500/-	18,31,500/-	100%
2.	Consumables	0/-	0/-	0
3.	Contingencies	1,00,000/-	1,00,000/-	100%
4.	Travel	1,00,00/-	1,00,00/-	100%
5.	Others, if any	0/-	0/-	0
6.	Overhead Expenses	2,00,000/-	2,00,000/-	100%
7.	* Equipment	1,50,000/-	1,44,270/-	96.18%

* Balance capital amount of Rs. 5, 730/- is refunded to DST with the transaction ref. number: 1811200000690, dated 18 Nov 2020, 9.59 AM, via bharatkosh.gov.in.

14. Procurement/Usage of Equipment

(i) SCTIMST

a)

Sr.	Name of Equipment	Make/ Model	Cost (FE/ Rs.) in lakhs	Date of Installation	Utilization Rate (%)	Remarks regarding maintenance/ breakdown
1	Work Station	Dell Precision 3630 Tower with twin monitors, additional hard drives	1.80176	06-12-2019	100	Replaced RAM and Motherboard.
2	Neuropsychological test battery	WAIS IV, document processor license, Printed test batteries	0.97748	17-08-2020	100	NA
3	MRI software	MRI processing softwares	1.12612.41	30-12-2020	100	NA

b) Plans for utilizing the equipment facilities in future

The equipment procured as part of this project will be kept at SCTIMST Thiruvananthapuram for continuing the research activity in neuroimaging for memory dysfunction analysis and other neurological conditions.

(ii) CDAC

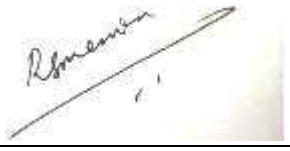
a)

Sr.	Name of Equipment	Make/ Model	Cost (FE/ Rs.) in lakhs	Date of Installation	Utilization Rate (%)	Remarks regarding maintenance/ breakdown
1	Workstation (For CDAC)	Yes, HP Z2 Tower G4	137400.00	Yes	100 %	Workstation is kept at CDAC

b) Plans for utilizing the equipment facilities in future

The equipment procured as part of this project will be kept at CDAC Thiruvananthapuram for continuing the research activity in Microstate Analysis for Memory dysfunction analysis and other neurological conditions.

Name and Signature with Date



Prof. Ramshekhar N. Menon

(Principal Investigator)

22/03/23