ADVANCED MAGNETIC RESONANCE IMAGING CORRELATES OF HISTOPATHOLOGICAL CHANGES IN AMYGDALA AND THE TEMPORAL NEOCORTEX IN MESIAL TEMPORAL SCLEROSIS

Dr. VISWANADH K S V G

DM NEUROIMAGING AND INTERVENTIONAL NEURORADIOLOGY THESIS

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A THESIS SUBMITTED BY

Dr. VISWANADH K S V G

TO

SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY, TRIVANDRUM.

IN PARTIAL FULFILMENT OF THE REQUIREMENTSFOR THE AWARD OF

DM NEUROIMAGING AND INTERVENTIONAL NEURORADIOLOGY

2021-2023

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The thesis entitled, "**Advanced Magnetic Resonance imaging correlates of Histopathological changes in Amygdala and the Temporal neocortex in Mesial Temporal Sclerosis**" was carried out under my direct supervision. No part of the thesis was submitted for the award of any degree or diploma prior to this date.

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APPROVAL OF THE THESIS

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TABLE OF CONTENTS

Table of contents	Page No
Declaration by the student	iii
Certificate by the research guide	iv
Acknowledgements	ix
Table of contents	x
List of figures	xi-xiii
List of Tables	xiv-xvii
List of Abbreviations	xviii-xix
Synopsis	xx-xxi
1.Introduction	1-3
2.Literature review	4-24
3.Materials and Methods	25-34
4.Results	35-92
5.Discussion	93-101
6.Summary and conclusions	102-103
7.References	104-116
Annexures	117-153

LIST OF FIGURES

Figure No	Figure Caption	Page No
Figure 3.1	Patient recruitment flowchart	27
Figure 3.2	Method for Quantitative analysis of ASL source images	33
Figure 4.1	Comparison of gender between MTS + NTC and MTS - NTC	35
Figure 4.2	Comparison of age(years) between MTS + NTC and MTS - NTC	36
Figure 4.3	Comparison of antecedent between MTS + NTC and MTS - NTC	37
Figure 4.4	Comparison of age at the onset of epilepsy(years) between MTS + NTC and MTS - NTC. (non-parametric variable, Box-whisker plot)	38
Figure 4.5	Comparison of age at surgery(years) between MTS + NTC and MTS - NTC	39
Figure 4.6	Comparison of duration of epilepsy(years) between MTS + NTC and MTS - NTC	40
Figure 4.7	Comparison of seizure frequency score between MTS + NTC and MTS - NTC	41
Figure 4.8	Comparison of number of anti-seizure medications between MTS + NTC and MTS - NTC	42
Figure 4.9	Comparison of secondary generalization between MTS + NTC and MTS - NTC	43
Figure 4.10	Comparison of aura between MTS + NTC and MTS - NTC	44
Figure 4.11	Comparison of sensory symptoms between MTS + NTC and MTS – NTC	45
Figure 4.12	Comparison of motor symptoms between MTS + NTC and MTS - NTC	46
Figure 4.13	Comparison of automatisms between MTS + NTC and MTS - NTC	47
Figure 4.14	Comparison of autonomic symptoms between MTS + NTC and MTS - NTC	48
Figure 4.15	Comparison of cognitive symptoms between MTS + NTC and MTS - NTC	49

Figure 4.16	Comparison of emotional symptoms between MTS + NTC and MTS - NTC	50
Figure 4.17	Comparison of antecedent type between MTS + NTC and MTS - NTC	51
Figure 4.18	Comparison of type of aura between MTS + NTC and MTS - NTC	53
Figure 4.19	Comparison of type of sensory symptoms between MTS + NTC and MTS - NTC	54
Figure 4.20	Comparison of type of motor symptoms between MTS + NTC and MTS - NTC	55
Figure 4.21	Comparison of type of automatisms between MTS + NTC and MTS - NTC	57
Figure 4.22	Comparison of type of autonomic symptoms between MTS + NTC and MTS - NTC	58
Figure 4.23	Comparison of type of cognitive symptoms between MTS + NTC and MTS - NTC	60
Figure 4.24	Comparison of type of emotional symptoms between MTS + NTC and MTS - NTC	61
Figure 4.25	Comparison of EEG between MTS + NTC and MTS - NTC	62
Figure 4.26	Comparison of type of I-EEG between MTS + NTC and MTS - NTC	63
Figure 4.27	Comparison of clinico-electrophysiological impression between MTS + NTC and MTS - NTC	64
Figure 4.28	Comparison of pathology side between MTS + NTC and MTS - NTC	65
Figure 4.29	Comparison of ASL (Hippocampus) between MTS + NTC and MTS - NTC	66
Figure 4.30	Comparison of ASL-SIR (Hippocampus) between MTS + NTC and MTS - NTC	67
Figure 4.31	Comparison of ASL (Amygdala) between MTS + NTC and MTS - NTC	68
Figure 4.32	Comparison of ASL-SIR (Amygdala) between MTS + NTC and MTS - NTC	69
Figure 4.33	Comparison of ASL (Anterior temporal lobe) between MTS + NTC and MTS - NTC	70
Figure 4.34	Comparison of ASL-SIR (Anterior temporal lobe) between MTS + NTC and MTS - NTC	71

Figure 4.35	Comparison of ASL-SIR (Temporal neocortex) between MTS + NTC and MTS - NTC	72
Figure 4.36	Comparison of histopathological findings between MTS + NTC and MTS - NTC	74
Figure 4.37	Association of clinico-electrophysiological impression with ASL (TN) in MTS + NTC	75
Figure 4.38	Association of histopathology- temporal lobe- FCD with ASL (Temporal neocortex) in MTS + NTC	76
Figure 4.39	Association of ASL-SIR (Temporal neocortex) with clinico-electrophysiological impression in MTS + NTC	77
Figure 4.40	Association of secondary generalization with T2/FLAIR (Anterior temporal lobe)	79
Figure 4.41	Association of motor symptoms with T2/FLAIR (Anterior temporal lobe)	80
Figure 4.42	Association of anterior temporal volume loss with T2/FLAIR (Anterior temporal lobe)	81
Figure 4.43	Association of secondary generalization with ASL (Anterior temporal lobe) in patients with anterior temporal lobe changes	82
Figure 4.44	Association of motor symptoms with ASL (Anterior temporal lobe) in patients with anterior temporal lobe changes	83
Figure 4.45	Association of ASL-SIR (Anterior temporal lobe) with secondary generalization in patients with anterior temporal lobe changes	84
Figure 4.46	Association of ASL-SIR (Anterior temporal lobe) with motor symptoms in patients with anterior temporal lobe changes	85
Figure 4.47	Illustrative case 1	91
Figure 4.48	Illustrative case 2	92

LIST OF TABLES

Table No	Table Caption	Page No
Table 2.1	Recommended 'HARNESS' epilepsy protocol MRI by ILAE	8
Table 3.1	Seizure frequency scoring	27
Table 3.2	Semiological features, evaluated according to ILAE 2017 terminology	29
Table 3.3	Acquisition parameters	32
Table 3.4	Interpretation of Kappa values	33
Table 4.1	Comparison of gender between MTS + NTC and MTS - NTC	35
Table 4.2	Comparison of age(years) between MTS + NTC and MTS – NTC	36
Table 4.3	Comparison of antecedent between MTS + NTC and MTS - NTC	37
Table 4.4	Comparison of age at the onset of epilepsy(years) between MTS + NTC and MTS - NTC	38
Table 4.5	Comparison of age at surgery(years) between MTS + NTC and MTS - NTC	39
Table 4.6	Comparison of duration of epilepsy(years) between MTS + NTC and MTS - NTC	40
Table 4.7	Comparison of seizure frequency score between MTS + NTC and MTS - NTC	41
Table 4.8	Comparison of number of anti-seizure medications between MTS + NTC and MTS - NTC	42
Table 4.9	Comparison of secondary generalization between MTS + NTC and MTS - NTC	43
Table 4.10	Comparison of aura between MTS + NTC and MTS - NTC	44
Table 4.11	Comparison of sensory symptoms between MTS + NTC and MTS - NTC	45
Table 4.12	Comparison of motor symptoms between MTS + NTC and MTS - NTC	46
Table 4.13	Comparison of automatisms between MTS + NTC and MTS - NTC	47

Table 4.14	Comparison of autonomic symptoms between MTS + NTC and MTS - NTC	48
Table 4.15	Comparison of cognitive symptoms between MTS + NTC and MTS - NTC	49
Table 4.16	Comparison of emotional or affective symptoms between MTS + NTC and MTS - NTC	52
Table 4.17	Comparison of antecedent type between MTS + NTC and MTS - NTC	51
Table 4.18	Comparison of type of aura between MTS + NTC and MTS - NTC	52
Table 4.19	Comparison of type of sensory symptoms between MTS + NTC and MTS - NTC	54
Table 4.20	Comparison of type of motor symptoms between MTS + NTC and MTS - NTC	55
Table 4.21	Comparison of type of automatisms between MTS + NTC and MTS - NTC	56
Table 4.22	Comparison of type of autonomic symptoms between MTS + NTC and MTS - NTC	58
Table 4.23	Comparison of type of cognitive symptoms between MTS + NTC and MTS - NTC	59
Table 4.24	Comparison of type of emotional or affective symptoms between MTS + NTC and MTS - NTC	61
Table 4.25	Comparison of EEG between MTS + NTC and MTS - NTC	62
Table 4.26	Comparison of type of Ictal-EEG between MTS + NTC and MTS - NTC	63
Table 4.27	Comparison of clinico-electrophysiological impression between MTS + NTC and MTS - NTC.	64
Table 4.28	Comparison of pathology side between MTS + NTC and MTS - NTC	65
Table 4.29	Comparison of ASL (Hippocampus) between MTS + NTC and MTS - NTC	66
Table 4.30	Comparison of ASL-SIR (Hippocampus) between MTS + NTC and MTS - NTC	67
Table 4.31	Comparison of ASL (Amygdala) between MTS + NTC and MTS - NTC	68
Table 4.32	Comparison of ASL-SIR (Amygdala) between MTS + NTC and MTS - NTC	69

Table 4.33	Comparison of ASL (Anterior temporal lobe) between MTS + NTC and MTS – NTC	70
Table 4.34	Comparison of ASL-SIR (Anterior temporal lobe) between MTS + NTC and MTS - NTC	71
Table 4.35	Comparison of ASL-SIR (Temporal neocortex) between MTS + NTC and MTS - NTC	72
Table 4.36	Comparison of histopathological findings between MTS + NTC and MTS - NTC.	73
Table 4.37	Association of clinico-electrophysiological impression with ASL (Temporal neocortex) in MTS + NTC	75
Table 4.38	Association of histopathology- temporal lobe- FCD with ASL (Temporal neocortex) in MTS + NTC	76
Table 4.39	Association of ASL-SIR (Temporal neocortex) with clinico-electrophysiological imp in MTS + NTC	77
Table 4.40	Univariate logistic regression to find out significant risk factors and associations of MTS + NTC	78
Table 4.41	Association of secondary generalization with T2/FLAIR (Anterior temporal lobe	79
Table 4.42	Association of motor symptoms with T2/FLAIR (Anterior temporal lobe)	80
Table 4.43	Association of anterior temporal volume loss with T2/FLAIR (Anterior temporal lobe).	81
Table 4.44	Association of secondary generalization with ASL (Anterior temporal lobe) in patients with anterior temporal lobe changes	82
Table 4.45	Association of motor symptoms with ASL (Anterior temporal lobe) in patients with anterior temporal lobe changes	83
Table 4.46	Association of ASL-SIR (Anterior temporal lobe) with secondary generalization in patients with anterior temporal lobe changes	84
Table 4.47	Association of ASL-SIR (Anterior temporal lobe) with motor symptoms in patients with anterior temporal lobe changes	85
Table 4.48	Inter rater kappa agreement between R1-T2/FLAIR (Temporal neocortex) and R2-T2/FLAIR (Temporal neocortex)	86
Table 4.49	Inter rater kappa agreement between R1-ASL (Temporal neocortex) and R2-ASL (Temporal neocortex)	87

Table 4.50	Inter rater kappa agreement between R1-T2/FLAIR (Anterior temporal lobe) and R2-T2/FLAIR (Anterior temporal lobe)	88
Table 4.51	Inter rater kappa agreement between R1-ASL (Anterior temporal lobe) and R2-ASL (Anterior temporal lobe	89
Table 4.52	Inter rater kappa agreement between R1-volume loss (Anterior temporal lobe) and R2-volume loss (Anterior temporal lobe)	90

LIST OF ABBREVIATIONS

S No	Abbreviation	Full Form
1.	ILAE	International League Against Epilepsy
2.	EEG	Electroencephalography
3.	MRI	Magnetic Resonance Imaging
4.	CT	Computed Tomography
5.	ASL	Arterial Spin Labeling
6.	PET	Positron Emission Tomography
7.	TLE	Temporal lobe epilepsy
8.	MTLE	Mesial Temporal lobe epilepsy
9.	NTLE	Neocortical Temporal lobe epilepsy
10.	HS	Hippocampal Sclerosis
11.	CA	Cornu Ammonis
12.	MTS	Mesial Temporal Sclerosis
13.	FLAIR	Fluid-Attenuated Inversion Recovery
14.	SLRE	Symptomatic localization related epilepsy
15.	EL	Epileptogenic lesion
16.	SOZ	Seizure onset zone
17.	EZ	Epileptogenic zone
18.	SZ	Symptomatogenic zone
19.	IZ	Irritative zone
20.	FDZ	Functional Deficit Zone
21.	AEDs	Anti-epileptic drugs
22.	HARNESS	Harmonized Neuroimaging of Epilepsy Structural Sequences
23.	CBF	Cerebral blood flow
24.	SNR	Signal to noise ratio
25.	PCASL	Pseudo continuous ASL
26.	DTI	Diffusion Tensor Imaging
27.	fMRI	Functional MRI
28.	MRS	Magnetic Resonance spectroscopy
29.	NAA	N-Acetyl Aspartate

30.	ATL + AH	Anterior Temporal lobectomy plus Amygdalohippocampectomy
31.	AH	Selective Amygdalohippocampectomy
32.	MTS + NTC	MTS plus Neocortical Temporal changes
33.	MTS-NTC	MTS minus Neocortical Temporal changes
34.	SIR	Signal Intensity Ratio

SYNOPSIS

The proper imaging evaluation of an Epilepsy patient however requires an epilepsy protocol MRI. Advanced MR imaging with ASL is a very useful adjunct in localization of the epileptogenic focus. The most common cause of mesial temporal epilepsy is Hippocampal sclerosis. The term Mesial Temporal sclerosis is more apt than Hippocampal sclerosis as the changes on histopathology and imaging are also seen to involve the rest of the mesial temporal lobe. These changes are also seen to extend in some patients into the anterior temporal pole and the lateral Temporal neocortex. The objectives of this study are to identify the T2, FLAIR and ASL MR imaging correlates of the histopathological changes in the Amygdala and Temporal neocortex in Mesial Temporal sclerosis, and to find the clinical and electrophysiological correlates of these changes.

This was a cohort study with prospective and retrospective arms. The retrospective arm was included 88 patients, and the prospective arm included 19 patients after fulfilling the inclusion criteria. They were divided into three groups based on the imaging findings in T2, FLAIR sequences. 63 patients were included in the mesial temporal sclerosis with neocortical changes group, 37 patients in the mesial temporal sclerosis without neocortical changes group and 7 controls. The clinical history, semiological features and electroencephalography findings were compared between the groups with and without neocortical temporal changes. The imaging data was analyzed and compared in four separate regions of the temporal lobe- the Hippocampus, the Amygdala, the anterior Temporal pole, and the Temporal neocortex. The corresponding histopathological data was compared in three regions- the Hippocampus, the Amygdala, and the Temporal neocortex.

There was no significant difference in the age, gender, presence of antecedent, duration of epilepsy and seizure frequency between the two groups ($P>0.05$). The age of onset of habitual seizures was earlier in the group with neocortical temporal changes, and this difference was statistically significant ($P=0.049$). On analysis of semiological features and electroencephalography, the group with neocortical temporal changes showed a higher incidence of neocortical epileptogenesis ($P<0.001$). Within the group with mesial temporal sclerosis and neocortical temporal changes, there was a statistically significant difference in the perfusion abnormality on qualitative analysis of ASL images between patients with neocortical epileptogenesis and those without ($P=0.015$). Histopathological analysis revealed the presence of diffuse astrogliosis in all patients, myelin loss in some patients and dysplasia

in a few patients. All patients with dysplastic changes in the temporal neocortex belonged to the neocortical temporal changes group and showed abnormality on qualitative analysis of ASL images.

The abnormality in the anterior temporal pole and temporal neocortex in mesial temporal sclerosis patients represents a continuum of changes outside the mesial temporal lobe. Presence of corresponding abnormality on ASL can predict neocortical epileptogenesis in patients with neocortical changes. MRI cannot predict the underlying histopathological make up. However, ASL sequence may be useful in predicting the presence of dysplastic neocortex. Preoperative prediction of this fact may be of significance in the treatment planning.

1. INTRODUCTION

The international league against epilepsy (ILAE) emphasizes on classification of seizures based on onset, which could be focal or generalized (Fisher, Cross, D'Souza, et al., 2017). When epilepsy is focal in onset, the goal of evaluation is to search for an underlying substrate which could be amenable to surgery in cases with pharmacological resistance (Schuele, 2019). The tools in the armamentarium for evaluation of epilepsy include semiological evaluation, electroencephalography (EEG), and imaging. Seizure semiology plays a simple and cost-effective role in the characterization of a seizure and the preliminary localization of underlying substrate (Jan and Girvin, 2008). Electrophysiological evaluation with EEG and Imaging with Magnetic resonance imaging (MRI) are vital in the presurgical evaluation of epilepsy. Computed tomography (CT) scan or a routine MRI (Magnetic resonance imaging) of the brain may suffice for a suspected acute symptomatic seizure but proper imaging evaluation of epilepsy requires an MRI Brain acquired in epilepsy protocol (Chen and Koubeissi, 2019; von Oertzen, 2002). Advanced MR imaging, with arterial spin labelling (ASL), an MR perfusion technique has become a valuable addition to structural MRI in the evaluation of epilepsy (Nagesh et al., 2018). The presurgical evaluation of focal onset epilepsy depends on the concordance between the clinical, electrophysiological, and imaging data (Rathore and Radhakrishnan, 2015). Positron emission tomography (PET) acts as a problem-solving modality in cases with discordance between the Clinico-electrophysiological and MRI data (Rathore and Radhakrishnan, 2015).

Temporal lobe epilepsy (TLE) which involves unprovoked seizures originating from the temporal lobe consists of Mesial Temporal lobe epilepsy (MTLE) and Lateral or neocortical Temporal lobe epilepsy (NTLE) (Ong and Department of Medicine, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia, 2019). The causes of TLE include Hippocampal sclerosis (HS), malformations of cortical development or dysplasias, neoplastic lesions, vascular malformations, sequelae to previous insults, inflammatory and infective processes (Al Sufiani and Ang, 2012). Mesial Temporal epilepsy is more common than lateral Temporal epilepsy accounting for more than 65% of the cases of TLE (Ong and Department of

Medicine, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia, 2019). It is also the most common cause of focal epilepsy (Sanon et al., 2012).

The commonest underlying pathological substrate for MTLE is HS (Sanon et al., 2012). Although the exact etiology is still unclear, antecedents like perinatal insults, status epilepticus and a history of febrile seizures in the past have been linked to HS (Liu et al., 1995). The mechanism is hypothesized to involve excitotoxicity at the hippocampus due to neurotransmitters like Glutamate in a developing brain, leading to the establishment of an epileptogenic substrate (Liu et al., 1995). Pathologically, Hippocampal sclerosis consists of neuronal loss and gliosis in all the sectors of the Hippocampus, most commonly in CA (Cornu Ammonis) 1 and CA4 (Al Sufiani and Ang, 2012). The term Mesial Temporal sclerosis (MTS) is more appropriate than HS as this pathology is often seen extending into adjacent structures like the Amygdala and the Dentate gyrus (Al Sufiani and Ang, 2012). In addition, it has been observed on imaging as well as on histopathological specimens that there are widespread changes involving the anterior temporal lobe and the lateral temporal neocortex in MTS patients (Mitchell et al., 2003; Thom et al., 2009). However, the pathological substrate for these imaging abnormalities and their clinical significance remains largely undefined.

There are hardly any studies in the literature utilizing advanced MR sequences like ASL in conjunction with conventional sequences like T2 and FLAIR in the evaluation of the temporal neocortex in patients with MTS. There are also very few studies that have comprehensively assessed the clinical, semiological, EEG, imaging, and histopathological findings in MTS patients with neocortical changes. The purpose of this study was to identify the advanced MR imaging correlates of neocortical changes and determine their clinico-electrophysiological, and histopathological features.

AIMS AND OBJECTIVES:

Null Hypothesis:

MRI-Brain cannot differentiate between the various types of histopathological changes in the temporal neocortex in patients with MTS

Aims and objectives:

1. Identification of the T2, FLAIR and ASL MR imaging correlates of histopathological changes in Amygdala and Temporal neocortex in Mesial Temporal sclerosis.

2. Identification of the clinical and electrophysiological correlates in MTS patients with neocortical Temporal changes.

2. LITERATURE REVIEW

A seizure is defined as abnormal sudden, synchronous, excessive electrical activity in the brain leading to transient clinical manifestations (Fisher et al., 2005). Epilepsy is defined as occurrence of two or more unprovoked seizures more than 24 hours apart or, as the high likelihood (more than 60 percent) to have another seizure after having a first one (Fisher et al., 2014).

Classification of seizures and epilepsy

The ILAE 2017 seizures and epilepsy classification consists of three levels:

1) seizure type,

2) epilepsy type, and

3) epilepsy syndrome.

The emphasis is on the onset of seizure. The first level, the seizure type can be classified as focal onset, generalized onset, or unknown onset. Focal seizures consist of abnormal discharges originating from a specific region of the brain before spreading along neuronal networks in one hemisphere, while generalized seizures consist of electrical discharges starting simultaneously from both the cerebral hemispheres (Fisher, Cross, French, et al., 2017). Unknown onset seizures are those that cannot be determined as focal or generalized due to lack of clinical or EEG evidence. The second level, epilepsy type, is also classified along similar lines. Additionally, epilepsy type can also be combined generalized and focal onset. The third level, epilepsy syndrome consists of a specific seizure type or types with consistent semiological features with associated characteristic findings on EEG (Scheffer et al., 2017; EC Wirrell et al., 2022).

Focal onset seizures or epilepsies can be motor or non-motor, can be associated with retained or impaired awareness. They can also be focal to bilateral tonic-clonic seizures, which is the newer terminology for the presence of secondary generalization (Fisher, Cross, D'Souza, et al., 2017). The classification also emphasizes on the determination of the cause of seizure and etiology of epilepsy for

proper prognostication and management (Fisher, Cross, French, et al., 2017; Scheffer et al., 2017). Etiology of epilepsy may be structural, genetic, infectious, metabolic, immune- mediated, or unknown. Focal onset epilepsy due to an underlying anatomical or pathological substrate is called as symptomatic localization related epilepsy (SLRE) (Nagesh et al., 2018).

Focal onset epilepsy

Description of a focal onset seizure as motor or non-motor depends on the first symptom in the semiology, called as 'rule of the first' (Fisher, Cross, French, et al., 2017; Fisher and Bonner, 2018). Loss of awareness is said to be present, if the patients lose their awareness at any point during the seizure. Focal seizures may originate in the Frontal, Temporal, Parietal, Occipital lobes, Insular region, or the Cingulate gyrus (Chowdhury et al., 2021). There are various zones of neuroparenchyma that are conceptualized in focal epilepsies. An 'Epileptogenic lesion (EL)' is the macroscopic lesion that is visible on the MRI responsible for the focal onset epilepsy (Chowdhury et al., 2021). The 'Seizure onset zone (SOZ)' is the region of cortex responsible for the origin of seizures. The 'Epileptogenic zone (EZ)' is needed for the seizurogenic potential. EZ can generate epileptiform discharges even in the absence of SOZ. This zone is to the target of resection or disconnection during epilepsy surgeries. The 'symptomatogenic zone (SZ)' is initially activated by the epileptiform discharges. It is responsible for the initial manifestations of the ictal semiology. It usually constitutes eloquent neuroparenchyma. The SZ is usually adjacent to the EZ but this may not always be the case and there may be no overlap between the two. The 'Irritative zone (IZ)' is the cortical area producing the epileptiform discharges on inter-ictal EEG. The 'functional deficit zone (FDZ)' is the region of the cortex with abnormal functionality in the interictal period (Rosenow and Luders, n.d.).

The ictal semiology refers to the chronological description of the signs and symptoms that occur during the evolution of a seizure (Alim-Marvasti et al., 2022). Interpretation of the seizure semiology has value in lateralization and localization of the symptomatic zone and consequently, the epileptogenic zone (Rossetti and Kaplan, 2010).

Focal seizures are more common than generalized onset seizures in both children and adults (Beghi, 2020). Focal epilepsies constitute about 60% of all epilepsies (Perucca, 2018). Focal epilepsies in children may be divided into those with known causes, those with unknown causes and those that have a constellation of clinical and EEG features, called as focal epilepsy syndromes (Nascimento et al., 2023). Known causes may be developmental structural causes like malformations of cortical development, acquired structural causes like perinatal brain injuries and HS, metabolic derangements due to inborn errors of metabolism, infectious or immune mediated/inflammatory pathologies. The etiological spectrum of focal epilepsies in adults is also similar (Nascimento et al., 2023). The most common site responsible for focal epilepsies is the temporal lobe (Al Sufiani and Ang, 2012).

Seizure and epilepsy evaluation

When a patient presents with a new-onset paroxysmal episode, the first step is to confirm of the occurrence of a seizure and not a seizure mimic (Gavvala and Schuele, 2016). History of provoking factors and clinical findings on preliminary examination are important (Schuele, 2019). Emergent imaging should be carried out in patients suspected of acute symptomatic seizure. An EEG is also done to look for epileptiform discharges (Chen and Koubeissi, 2019). Other facets of evaluation include routine blood investigations and a lumbar puncture in select cases.

If the patient has recurrent seizures, or is identified as having the tendency to have recurrent seizures, falling into the definition of epilepsy, a comprehensive evaluation for the underlying etiology of epilepsy needs to be carried out, including an epilepsy protocol MRI, usually on an elective basis (Bernasconi et al., 2011; Schuele, 2019; von Oertzen, 2002). Detailed elucidation of the clinical history and seizure semiology has great value not only in confirming that the recurrent events are seizures, but also in their characterization and classification (Jan and Girvin, 2008; Schuele, 2019). The tendency to have epilepsy is determined by the presence of inter-ictal epileptiform abnormality on EEG or a structural lesion on MRI (Schuele, 2019). The chances of demonstrating an inter-ictal EEG abnormality increases with the duration of the recording (Faulkner et al., 2012). A prolonged video-EEG (VEEG) after admission in a dedicated epilepsy monitoring unit (EMU) is more useful for

recording a seizure and localizing it, than inter-ictal EEG (Chen and Koubeissi, 2019). This is very important in presurgical evaluation when there is pharmacological resistance.

Role of imaging in seizure and epilepsy patients

Neuroimaging plays different roles in patients with new onset seizures, and in those with epilepsy. If acute symptomatic seizure is to be suspected, as mentioned earlier emergent neuroimaging is to be carried out (Cendes et al., 2016; Schuele, 2019). In most centers, CT-brain is the initial modality of choice, which may be sufficient to rule out certain causes like ischemic or hemorrhagic stroke, traumatic brain injury, neoplastic lesions, or infections. An MRI-brain with contrast is however needed, in most cases after urgent management and stabilization (Schuele, 2019). Routine CT or MRI brain may fail to detect more subtle structural lesions that may make the patient predisposed to have recurrent seizures (Schuele, 2019).

Neuroimaging is recommended in all patients with epilepsy. The exception is cases with the characteristic seizure semiology and EEG findings of a generalized epilepsy syndrome, with adequate response to anti-seizure medication (Cendes et al., 2016). Overall, an underlying epileptogenic lesion on neuroimaging is seen in only 20% of cases with new-onset seizures. This number rises to 50% in cases with new-onset focal seizures (Schuele, 2019). The chance of seizure remission with anti-epileptic drugs (AED) is greater when neuroimaging does not reveal an epileptogenic lesion (Nascimento et al., 2023). Neuroimaging is also very useful in the pre-surgical workup of patients with focal epilepsies resistant to AED (Yoo and Panov, 2019). Presence of a structural lesion on MRI confers a favorable outcome after surgery (Nascimento et al., 2023). The ILAE recommends that MRI is to be repeated in epilepsy patients, if the previous MRI was not acquired as per protocol. MRI is also to be repeated in children with focal epilepsy if a previous lesion-negative MRI was performed before one year of age (Bernasconi et al., 2019; Nascimento et al., 2023).

Epilepsy protocol MRI:

The rate of lesion detection in focal epilepsies also depends on the acquisition protocol and the experience of the neuroradiologist interpreting the scan (von Oertzen, 2002; Wang et al., 2020). The ILAE neuroimaging taskforce has given recommendations in epilepsy imaging (Bernasconi et al., 2019). Among these recommendations is the 'Harmonized Neuroimaging of Epilepsy Structural Sequences (HARNESS)' protocol with three mandatory sequences and two optional sequences (Bernasconi et al., 2019; Nascimento et al., 2023; Wang et al., 2020) (Table-2.1).

The mandatory sequences include:

1) A 3D T1-weighted sequence like the MPRAGE, BRAVO, SPGR or TFE

2) A 3D FLAIR sequence

3) A coronal high resolution T2 weighted sequence perpendicular to the long axis of the hippocampus

The optional sequences include:

1) A post-contrast 3D T1-weighted sequence

2) A susceptibility weighted (SWI) or a T2* gradient echo sequence (GRE)

Table-2.1: Recommended 'HARNESS' epilepsy protocol MRI by ILAE

	Mandatory sequences			Optional sequences	
Sequences	3D T1 weighted sequence	3D FLAIR	Coronal high resolution T2 spin echo	Post-contrast 3D T1 weighted sequence	SWI/T2* GRE
Recommended resolution	Isotropic voxels, 1x1x1 mm with no interslice gap	Isotropic voxels, 1x1x1 mm with no interslice gap	0.4x0.4 x2 mm. 2D images.	Isotropic voxels, 1x1x1 mm with no interslice gap	

The 3D sequences have isotropic voxels with an individual voxel size of 1 mm^3. This enhances the grey-white matter differentiation and increases the ability for detection of smaller lesions. The coronal high resolution T2W sequence has a very good in-plane resolution and exquisitely demonstrates the internal architecture of the hippocampus. The post-contrast MRI permits detection of leptomeningeal enhancement or intra-axial enhancing lesions (Nascimento et al., 2023). This sequence is particularly important when there are new-onset seizures in adults as there is a relatively increased possibility of the presence of an underlying neoplastic lesion (Englot et al., 2016; Kaur et al., 2018; Nascimento et al., 2023). SWI or T2* GRE is useful for the detection of lesions with blood products and calcifications. ILAE recommends that the epilepsy protocol MRI be done with 3T MRI machines although these sequences can be acquired with 1.5T MRI as well (Bernasconi et al., 2019; Nascimento et al., 2023).

Even with proper acquisition protocols, the interpretation is crucial. This is to be done by an experienced neuroradiologist in the context of the clinical localization and the electrophysiological impression. A previous study has shown that the sensitivity of standard MRI reports by a non-expert radiologist for localization of the source of focal onset epilepsies was 39%. This rose to 50% when the interpretation was by an expert radiologist. When a dedicated epilepsy-protocol MRI was interpreted by an expert radiologist, the sensitivity increased to 91%. About 85% of the patients, whose initial standard MRI was non-lesional, showed epileptogenic lesions in epilepsy protocol MRI (Schuele, 2019).

Arterial spin labeling (ASL):

ASL is a novel MR perfusion technique, that does not require the administration of exogenous contrast agents. The procedure involves magnetically tagging or labeling the arterial blood at the neck and acquisition of images, as this blood reaches the brain capillaries. The images called tagged images are acquired after the labeling process, after the certain delay called the post-labeling delay. Another set of images, called as control images are also acquired, without the tagging process. This is followed by post-processing, consisting of subtraction of labeled

images from control the images, to generate perfusion weighted images and cerebral blood flow (CBF) maps of the brain (Ferré et al., 2013).

The main advantage of ASL is its usage of an endogenous tracer that is freely diffusible across membranes. The main disadvantages are the inherently low signal to noise ratio (SNR) in the images due to the small quantity of tagged blood and a small difference in signal in the control and labeled images, and an increased scan time for repeated acquisition of two sets of images, to compensate for the poor SNR. This increased scan time also leads to increased chance of motion artifacts in the final image (Alsaedi et al., 2018).

There are three types of ASL sequences based on the labeling methods used. These include, the continuous ASL (CASL), pulsed ASL (PASL) and the pseudo continuous ASL (PCASL). In CASL, the continuous labeling radio frequency pulse lasts from 2 to 4 seconds. Although CASL has the advantage of higher SNR, it is associated with a high specific absorption ratio (SAR). It also has increased susceptibility to magnetization transfer effects, which can lead to further reductions in the SNR. PASL employs short labeling pulses. It is associated with low specific absorption ratio but also suffers from low SNR. PCASL is a compromise between CASL and PASL. Labeling is done with a train of radiofrequency pulses, to reduce the specific absorption ratio and magnetization transfer effects while also keeping the SNR high. The location of the labeling plane in PASL is located 2-4 cm below the inferior most slice of the acquisition volume, while in CASL and PCASL, this is 5-10 cm below the inferior most slice. Currently, 3D-Spin and Gradient echo-based stack of spirals readout techniques are used, that oversample the center of the K-space to increase the SNR. PCASL is the most used technique in the clinical setting (Ferré et al., 2013).

ASL has great value in epilepsy imaging. It has been shown to be useful for estimation of the EZ in SLRE (Nagesh et al., 2018). Imaging with ASL in epilepsy works on the principle of neurovascular coupling, i.e., increase in neuronal activity leads to a corresponding increase in the regional CBF (Huneau et al., 2015). Neurovascular coupling has been shown to be intact in the EZ (Stefanovic et al., 2005). ASL can therefore help in localization by showing interictal hypoperfusion and

peri-ictal hyper perfusion in the regions encompassing the EZ, the FDZ and the SZ (Nagesh et al., 2018). ASL alone has been shown to have a sensitivity of up to 70% for localization, as compared to the 90% sensitivity of clinico-electrophysiological evaluation (Kim et al., 2016, 2021). Therefore, ASL adds value when used in concert with semiological features, EEG, and structural MRI (Nagesh et al., 2018). There are certain pitfalls that need to be circumvented when using ASL in epilepsy. ASL images acquired in the peri-ictal period after a prolonged seizure, may show elevated CBF non-specifically in the hippocampus, irrespective of the location and focal or generalized onset of the seizure. Interval imaging may be used to monitor the development of hippocampal sclerosis (Nagesh et al., 2018). Peri-ictal ASL also shows increased CBF along the direction of seizure propagation, a phenomenon analogous to the clinical jacksonian march (Takahara et al., 2018). Apart from seizure related perfusion alterations confounding the localization, ASL may also show altered perfusion due to the underlying pathological process like infection or a neoplastic lesion, independent of the hemodynamic changes associated with the seizure itself (Amukotuwa et al., 2016; Haller et al., 2016). Interpretation in concert with structural MRI, including post-contrast sequences can help in this regard. Artifacts during labelling, acquisition, or readout processes of ASL images can also give rise to areas of spurious alterations in CBF (Amukotuwa et al., 2016; Jaganmohan et al., 2021). Areas of spuriously low CBF in a part of the brain parenchyma can be present in the arterial border zones, as a result of tortuous neck vessels and magnetic inhomogeneity at the tagging plane, abnormal tilt, flexion, or extension of the patient's head, in the upper most slices of the brain or due to magnetic susceptibility artifacts at a specific location in the imaging plane. Diffusely reduced signal in the brain parenchyma may be present as a result of acquisition of ASL images after administration of gadolinium-based contrast agents due to T1 shortening of the labeled blood. Spuriously elevated signal may be intravascular, and is not to be confused with elevated CBF in the cerebral cortex, especially if the arterial transit time is higher than the post labeling delay selected. Spurious elevation in cortical CBF can also occur in the occipital lobes and in medial frontal regions. In most cases, a knowledge about the mechanisms and sources of these signal abnormalities can help circumvent them, or consider them while interpretation in epilepsy cases (Amukotuwa et al., 2016; Jaganmohan et al., 2021).

Magnetic resonance spectroscopy, Diffusion tensor imaging (DTI) and fMRI:

Magnetic resonance spectroscopy (MRS) non-invasively measures certain metabolites in the tissues including the brain (Cendes et al., 2016). Proton MRS has shown value in localization of epileptogenic focus (Cendes et al., 2002; Thompson et al., 1998). This is because of changes in metabolites like elevation in lactate and reduction in NAA. In extratemporal focal onset epilepsy, these changes were seen with focal cortical dysplasias and polymicrogyria while MRS showed no significant abnormality with heterotopias (Cendes et al., 2002). A major limitation of MRS is bias due to limited sampling of neuroparenchyma.

MRI post-processing:

MRI post-processing may help, when the visual analysis is equivocal. Post-processing techniques may be used to perform quantitative analysis of various features like the T2-signal intensity of the hippocampus in the form of T2-relaxomtery or measurement of cortical thickness using voxel-based morphometry (Whitwell, 2009; Winston et al., 2017).

PET:

Positron emission tomography (PET) is useful as problem solving modality (Cendes et al., 2016; Ponisio et al., 2021). The hypometabolic area in the inter-ictal PET corresponds to the FDZ in focal epilepsy (Rosenow and Luders, n.d.). Coregistration with MRI with PET data or simultaneous acquisition of PET and MRI can further assist in localization (Ehman et al., 2017). The outcomes after surgery for focal onset epilepsy in patients who are lesion negative on MRI but show hypometabolism on PET are comparable to those patients with clearly demonstrated lesions on MRI (Carne et al., 2004; Cendes et al., 2016).

SPECT:

Single photon emission computed tomography (SPECT) done during or immediately after a seizure shows increased CBF in the SOZ (Cendes et al., 2016). Post-processing of SPECT by subtraction of ictal and interictal images and co-

registration with MRI (SISCOM) has been shown to be more sensitive in the focal epilepsies compared to SPECT alone (Foiadelli et al., 2020).

Pre-operative evaluation of epilepsy

In epilepsy patients, pharmacological resistance in epilepsy is defined as 'failure of adequate trials of two tolerated and appropriately used AEDs to achieve sustained seizure freedom.' An AED is considered effective, if the sustained seizure freedom lasts at least for one year or thrice the longest interval between seizures before treatment (Yoo and Panov, 2019). Surgery is considered in these focal epilepsy patients. Various studies have shown good efficacy of surgery for drug resistant epilepsy (Dwivedi et al., 2017; Stockman, 2013; Wiebe, 2001). Pseudo drug resistance is to be ruled out before a patient is evaluated for epilepsy surgery (Brodtkorb et al., 2016; Nascimento et al., 2023). The goal of pre-surgical evaluation in epilepsy is to delineate the possible extent of EZ, so that it can be resected or disconnected (Jehi, 2018; Rosenow and Luders, n.d.).

Drug resistant TLE due to MTS is the commonest substrate for resection (Boling, 2018). A successful outcome not only depends on the completeness of resection of the EZ but is also a fine balance between the extent of resection and sparing of eloquent neuroparenchyma (Al-Otaibi et al., 2012). The EZ itself cannot be delineated directly by most modalities and does not have clear anatomical boundaries. It must be inferred by concordance between the other zones (Rosenow and Luders, n.d.).

The main primary tools in the pre-surgical assessment of epilepsy include analysis of seizure semiology, EEG, neuropsychology, and neuroimaging with MRI (Nascimento et al., 2023; Rosenow and Luders, n.d.). PET is a problem-solving tool in MRI-negative and discordant cases as discussed early (Cendes et al., 2016; Ponisio et al., 2021). Clinical history localizes the symptomatogenic zone, neuropsychological assessment, inter-ictal PET- the FDZ, interictal EEG-the irritative zone, the ictal scalp EEG, ictal SPECT- the ictal onset zone and structural MRI-the epileptogenic lesion (Rosenow and Luders, n.d.). MR perfusion with ASL may demonstrate abnormality, in the EZ, SZ and the FDZ (Nagesh et al., 2018). fMRI and cortical stimulation are

useful for mapping out the eloquent functional areas adjacent to the possible area of resection and DTI is useful for visualizing important white matter tracts in the vicinity of this region (Leon-Rojas et al., 2021; Pittau et al., 2014; Szaflarski et al., 2017). Finally, post-operative neuropathological assessment of the resected specimen completes this evaluation (Blumcke et al., 2017).

Temporal lobe epilepsy and mesial temporal sclerosis

The temporal lobe consists of the three-layered archicortex in the hippocampus and parahippocampal gyrus and a six layered neocortex in the superior, middle, inferior temporal gyri, and the fusiform gyrus (Al-Otaibi et al., 2012; Khashper et al., 2014). The anterior temporal pole is the anterior most part of temporal lobe, with a boundary at its posterior limit formed by a line drawn, laterally from the limen insulae (Herlin et al., 2021).

Classification of temporal lobe epilepsy:

TLE is defined as focal onset unprovoked seizures originating in the temporal lobe. It is mainly classified into mesial temporal lobe epilepsy (MTLE) and lateral temporal lobe epilepsy or neocortical temporal epilepsy (NTLE) (Ong and Department of Medicine, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia, 2019). MTLE is more common than NTLE and accounts for more than two-thirds of the cases. The term temporal-plus epilepsy is used, when the EZ extends beyond the boundaries of the temporal lobe, to the neighboring structures including the insula, the opercular cortex, temporoparietal cortex and the temporoparietooccipital junction (Kahane et al., 2015; Toro-Perez et al., 2020). The temporal pole is a vital part of the temporal epileptogenic networks. The seizures originating from the anterior temporal pole may be hyper motor, or exhibit semiological features suggestive of mesial temporal seizures on account of the high intrinsic connectivity of the anterior temporal pole to the orbitofrontal region in addition to the insular and mesial temporal regions (Chabardès et al., 2005; Staack et al., 2011; Zhang et al., 2022).

Epidemiology:

The commonest cause of drug resistant epilepsy leading to surgery is TLE (Boling, 2018). In a published study consisting of 2200 epilepsy patients, 62.2 percent of them had SLRE. 66 percent of these cases had TLE (Semah et al., n.d.). Another study 291 patients who were operated for epilepsy resistant to Anti-epileptic drugs (AEDs), and 73 percent of these had TLE (Wass et al., 1996).

Etiology:

HS is the commonest cause of MTLE. The exact etiopathogenesis is still unclear. Retrospective studies show a high incidence of antecedents like perinatal insults, febrile seizures, status epilepticus, trauma and intracranial infections usually occurring before the age of 5 years (Compiled by Heinz-Gregor Wieser for the ILAE Commission on Neurosurgery of Epilepsy, 2004; Liu et al., 1995). Although no direct genetic factors are known, patients with the genetic predisposition for febrile seizures, may develop HS if they have prolonged seizures (Abou-Khalil et al., 2001). Familial MTLE patients have been observed to have increased incidence of HS. The genetic defect causing MTLE may subsequently lead to the HS (Kobayashi et al., 2002). In experimental studies, sodium channel defects in mice have been shown to cause HS (Kearney et al., 2001).

Pathogenesis:

There are no prospective studies to demonstrate the relationship of HS to the suspected antecedents. There are several theories that have been hypothesized for the pathogenesis of HS. Most of these suggest the role of glutamate excitotoxicity and mitochondrial dysfunction as a result of the antecedents leading to neuronal loss in the hippocampus. But the pathways that lead to the neuronal loss have not been defined (Compiled by Heinz-Gregor Wieser for the ILAE Commission on Neurosurgery of Epilepsy, 2004). A few studies have suggested that HS may be a developmental disorder. This hypothesis was based on the histopathological findings of persistent Cajal-Retzius cells, compromised reelin signaling pathways, presence of extrahippocampal white matter neurons and the incidence of dual pathology in patients with HS (Kaper et al., 1999; Bocti et al., 2003; Compiled by Heinz-Gregor

Wieser for the ILAE Commission on Neurosurgery of Epilepsy, 2004; Haas et al., 2002; Md et al., 2006). A few studies have suggested that the immature developing brain, when subjected to an insult is susceptible to the development of HS (Blümcke et al., 2001; Compiled by Heinz-Gregor Wieser for the ILAE Commission on Neurosurgery of Epilepsy, 2004; Rossetti and Kaplan, 2010). Various other studies have suggested that multiple acquired factors may be required leading to a double or a triple hit, where, the first hit like a seizure in febrile illness may lead to persistence of immature features in the brain while a second insult establishes the HS phenotype (Compiled by Heinz-Gregor Wieser for the ILAE Commission on Neurosurgery of Epilepsy, 2004). Astrogliosis that occurs in HS is believed to be responsible for glutamate imbalance leading to seizure generation (Al Sufiani and Ang, 2012).

Pathology:

According to ILAE, HS on histopathology consists of loss of pyramidal neurons from any sector of the Hippocampus, with associated astrogliosis. The neuronal loss and astrogliosis predominantly occurs from the CA1 and CA4 regions (Blümcke et al., 2013; Compiled by Heinz-Gregor Wieser for the ILAE Commission on Neurosurgery of Epilepsy, 2004). HS is also classified as types 1, 2 and 3 depending on the identification of the sector most effected by the neuronal loss and the astrogliosis. In this classification, the neuronal loss may also be classified semi-quantitatively as moderate and severe. Type 1 consists of neuronal loss mainly in the CA1 and CA4 regions. Type 2 has neuronal loss predominantly in the CA1 region, while type 3 predominantly in the CA4 region. Type 3 hippocampal sclerosis was previously called as 'End-folium sclerosis' (Al Sufiani and Ang, 2012; Blümcke et al., 2013). HS is more aptly described as mesial temporal sclerosis (MTS) as in most cases, the pathological changes of neuronal loss and astrogliosis extend beyond the hippocampus into the amygdala and the dentate gyrus (Al Sufiani and Ang, 2012). During the histopathological examination, along with the routine hematoxylin-eosin staining, NeuN is very useful to highlight the neuronal loss, immunohistochemistry for glial fibrillary acidic protein (GFAP) highlights the gliosis and luxol fast blue highlights the myelin changes (Al Sufiani and Ang, 2012; Thom, 2004).

According to ILAE, in an operated case with concordant clinico-electrophysiological and imaging data for HS, when the post-operative histopathological specimen demonstrating the neuronal loss and astrogliosis consists of only the CA1 and CA4 regions, rather than the entire hippocampus, the term 'probable hippocampal sclerosis' may be used (Blümcke et al., 2013). The term 'dual pathology' is used to describe the co-existence of HS with a second lesion, either within or outside the temporal lobe. Examples include neoplastic lesions, vascular malformations, sequelae of previous insults or focal cortical dysplasias type IIa or IIb. The term 'dual pathology' is not used however, when architectural abnormalities resembling focal cortical dysplasia type I are present in the ipsilateral temporal lobe along with MTS. Instead, this condition is called as focal cortical dysplasia type IIIa (Blümcke et al., 2011; Poyuran, n.d.).

Clinical presentation:

Most of the patients with MTS present with habitual seizures between 4 to 16 years of age, although earlier or later presentation is possible (Compiled by Heinz-Gregor Wieser for the ILAE Commission on Neurosurgery of Epilepsy, 2004). The existence of a 'latent period' has classically been described. However, some patients may not have a latent period and may present with habitual seizures immediately after the precipitating event. The seizures are initially responsive to AEDs. The response however wanes, and the seizures eventually become refractory possibly suggestive of progression of the underlying epileptogenic pathology. Eventually, seizures become medically refractory in 60 to 90 percentage of the patients with MTS (Compiled by Heinz-Gregor Wieser for the ILAE Commission on Neurosurgery of Epilepsy, 2004). MTLE and NTLE have different semiological features, although there may be an overlap when seizures originate from either of these regions due to the presence of interconnecting white matter tracts (Chowdhury et al., 2021; Rossetti and Kaplan, 2010).

MTS typically presents with focal onset seizures with a loss of awareness. The seizures have a characteristic aura, behavioral arrest, loss of awareness and automatisms. They may also have post-ictal amnesia and confusion, more commonly than lateral temporal epilepsy. The most common aura seen in MTLE is epigastric

sensation (Chowdhury et al., 2021). The probability of a seizure being of mesial temporal origin, when the aura is epigastric is almost 74 percent (Henkel et al., 2002). Other types of auras that may be seen in mesial temporal seizures include fear, experiential phenomena like déjà vu and jamais vu (Blair, 2012; Chowdhury et al., 2021; Tufenkjian and Lüders, 2012). Auras are less common in NTLE and when present, buzzing or ringing sounds constituting elementary auditory auras are characteristic. Vestibular auras in the form of vertiginous sensation before the onset of the seizure may also be present. Very rarely, the auditory auras in NTLE may also be complex like voices or songs indicating the involvement of the auditory association areas. Auditory auras also have a lateralizing value when unilateral, to the contralateral cerebral hemisphere (Blair, 2012; Chowdhury et al., 2021). Autonomic features like flushing, apnea, cyanosis, ictal retching, piloerection, and tachycardia are more commonly present in mesial temporal seizures and indicate a spread to the amygdala. Automatisms may be bimanual like picking at clothes or fidgeting, bipedal or oral, like lip-smacking or chewing. Rarely, automatisms may also involve ictal speech and vocalizations. Mesial temporal seizures are longer in duration compared to lateral temporal seizures and tend to spread to the frontal lobes less commonly (Chowdhury et al., 2021). The frequency of conversion from focal to bilateral tonic-clonic seizures is also lesser in MTLE relative to NTLE (Blair, 2012). Before bilateral tonic-clonic spread in either of these seizures, there is appearance of complex motor semiological features like head and eye aversion to the contralateral side and fencing posture suggestive of frontal lobe spread (Chowdhury et al., 2021). MTS is also commonly associated with psychiatric comorbidities like depression and anxiety. Cognitive abnormalities, learning and behavioral issues may also be present (Vinti et al., 2021).

EEG in MTS:

In the interictal EEG, unilateral anterior temporal spike and wave discharges are more characteristic of mesial temporal epilepsy, while cases with neocortical temporal epilepsy have paroxysmal discharges from posterior and mid temporal regions (Vinti et al., 2021). Both MTLE and NTLE mostly have inter-ictal discharges that are lateralized and localized to the temporal lobe. The presence of bilateral or

multifocal IEDs in MTS patients, correlates with the presence of bilateral or diffuse onset, on Ictal EEG and may suggest poor seizure freedom after surgery. In mesial temporal epilepsy, ictal EEG is characterized by bilateral hypersynchronous slow down, followed by focal theta range (5-9 Hz) rhythmic activity in the basitemporal electrodes (Vinti et al., 2021). Neocortical temporal epilepsy is characterized by the presence of fast beta activity (13-30Hz) over a wider distribution involving the inferior temporal regions at ictal onset (Lee et al., 2006).

MRI in MTS:

The main MRI findings in MTS include volume loss in the involved hippocampus associated with hyperintensity on T2, FLAIR sequences (Bronen, 1992; Palacios Bote et al., 2008). These changes can sometimes be subtle and correlate respectively with neuronal loss and astrogliosis on histopathology (Kuzniecky et al., 1987). Occasionally, either one of these changes may be absent in cases with MTS. Additional findings evaluated on T2, FLAIR sequences like hyperintensity of the amygdala and on 3D T1 weighted images like hippocampal head flattening with a loss of digitations and internal architecture loss can help in these cases. MTS may also be associated with findings outside the temporal lobe on MRI. These include atrophy of the fornix, mamillary body, cingulate gyrus, and thalamus on the side of involvement and contralateral cerebellar atrophy (Chan et al., 1997). Quantitative imaging using hippocampal volumetry and T2-relaxometry can help in equivocal cases and those with bilateral involvement. Hippocampal volumetry quantifies the hippocampal volume loss, while T2 relaxometry gives an objective measurement of the hippocampal T2, FLAIR hyperintensity (Lee et al., 1998; Jackson et al., 1993).

MRS has also shown value in TLE (Thompson et al., 1998). Although NAA is diffusely reduced in cases with focal onset epilepsies, it is significantly reduced in the region responsible for ictal onset. The asymmetry of NAA/Cr ratio between the temporal lobes could be used for lateralization with about 92 percent of the patients (Cendes et al., 1997). Proton MRS studies have also shown recovery of NAA levels in TLE cases ipsilaterally or contralaterally after removal of the epileptogenic zone (Hugg et al., 1996).

Extension of the abnormality in MTS beyond the medial temporal lobe

Various studies in MTS patients have reported the presence of electrophysiological and imaging abnormalities beyond the medial temporal lobe (Blümcke et al., 2013). Abnormalities on MRI are not only seen at the anterior temporal pole, but also involve the temporal neocortex to a variable extent (Mitchell et al., 1999; Blümcke et al., 2013; Mitchell et al., 2003). Various studies have described the MRI appearance of these changes as T2, FLAIR hyperintensity of the cortex and underlying white matter, blurred grey-white differentiation, and thinning of the cortex. Anterior temporal polar volume loss has also been described (Mitchell et al., 2003; Mueller et al., 2009).

The anterior temporal polar abnormality was previously evaluated in 50 TLE patients, including 36 HS patients. MRI evaluation in cases with MTS, apart from the findings of HS revealed temporal polar volume loss. Histopathological evaluation of the corresponding regions showed an increase in the glial cell nuclei. There was however, no statistically significant difference in the number of glial cell nuclei between patients with and without anterior temporal polar changes on MRI. Post-operative outcomes between the two groups also showed no difference. The study concluded that, these changes on imaging were not due to inflammatory or dysplastic etiology. They also stated that, myelin abnormality rather than the gliosis was a possible explanation for these changes (Mitchell et al., 1999).

Mitchell et al., in the year 2003 retrospectively evaluated 54 children with MTS. They stated that, apart from involvement of the hippocampus and parahippocampal structures, MR changes were also observed extending beyond the temporal pole into the anterior temporal lobe in MTS. They used the term ‘anterior temporal changes’ and found that, they were present in 57% of their patients. The side of MTS showed no correlation with the presence of these changes. The authors also performed follow up imaging in 7 patients with and 6 patients without these changes and found that there was no change in the incidence or appearance of anterior temporal changes on interval imaging. On comparison of the demographic and clinical features, the difference was significant in the age of onset of epilepsy with patients with anterior temporal changes presenting earlier with habitual seizures.

There was no difference in the incidence of antecedents between the cohorts (antecedents were seen in 87% of the patients with anterior temporal changes and in 74% without). However, the age of antecedent was lower in those with anterior temporal changes and the difference was statistically significant. The age at the onset of habitual seizures or the antecedent was more likely to be less than 2 years in those patients with anterior temporal changes. Definite histopathological opinion was not possible in the study. However, none of the resected temporal lobes showed dysplastic changes. The authors concluded that, anterior temporal changes are likely to be established at the initial insult itself, along with the mesial temporal sclerosis and that earlier cerebral insult or onset of habitual seizures at less than 2 years of age are more likely to be associated with these changes in MTS patients (Mitchell et al., 2003).

Lin et al., in the year 2007 quantitatively evaluated the cerebral cortex in MTS patients and compared them to controls. The authors conducted a retrospective study in 30 MTS patients and compared them to 19 controls with no MTS. Quantitative thickness analysis and fractal analysis of the surface complexity of the temporal neocortex was done and compared between the MTS cases and controls. It was found that there was widespread decrease in the neocortical thickness by about 30% in cases with MTS not only in the temporal neocortex, but also involving frontal poles, frontal operculum, orbitofrontal region, and occipital regions. The complexity of the gyral convolutions was also reduced in multiple lobes. A significant correlation between the epilepsy duration and the degree of reduction in the cortical thickness. It was concluded that these changes develop over a period due to chronic seizure propagation and were also influenced by the initial antecedent (Lin et al., 2007).

Barba et al., in the year 2007 conducted a retrospective analysis in 80 epilepsy patients. The authors divided the study subjects into those with temporal and temporal plus groups based on semiological and electrophysiological features. It was found that 17 patients in the temporal plus group (77.2%) had MRI findings suggestive of MTS and that, the groups did not show any difference in the incidence of MTS. They concluded that, temporal plus epilepsy may be seen in MTS cases and invasive EEG is necessary in these cases for careful delineation of epileptogenic zone prior to surgery (Barba et al., 2007).

Thom et al., in the year 2009 analyzed the neocortical histopathological changes in 272 cases with mesial temporal sclerosis. They found that, 30 cases (11%) showed loss of neurons in the layers 2 and 3 with laminar gliosis and additional architectural abnormalities with disordered neuronal orientation. They termed these changes as 're-organizational dysplasia' and concluded that, these changes were established early in life, by the same insult responsible for the HS. These changes also had a gradient, and were more present towards the anterior temporal pole. The remaining MTS cases in the study also showed histopathological changes in the form of preserved laminar architecture no significant neuronal loss and varying degrees of cortical and white matter gliosis. Review of MR images after blinding and showed no characteristic imaging findings in patients with the dysplasia. Outcome in terms of seizure freedom after surgery also showed no difference between the groups at follow up after 2 years. The authors deduced that; these changes occurred due to an interruption in cortical maturation due to the same pathophysiological process responsible for MTS (Thom et al., 2009).

Mueller et al., in 2009 conducted a retrospective study in 66 patients, including 15 TLE patients with MTS, 16 TLE patients without MTS and 35 controls. The authors used post processing of 3D T1 weighted gradient echo MR images (MPRAGE) to obtain quantitative measurements of the thickness of the temporal neocortex in their study group. They found that, there was reduced cortical thickness in TLE patients, both with and without MTS. However, the predominant thinning was observed in the medial and posterior temporal regions in patients with MTS, while it was observed in the lateral temporal and opercular regions in patients without MTS. It was concluded that different epileptogenic networks in these two epilepsy syndromes were responsible for these differences (Mueller et al., 2009).

Fauser et al., in the year 2006 published an article to characterize epileptogenic potential of the varying degrees of neocortical dysplasia in MTS. They retrospectively analyzed the invasive electrophysiological data of 12 patients with histologically proven MTS with neocortical dysplasia. In this study, only 3 patients had ictal onset from the mesial temporal lobe, while about 34.7% of the patients had ictal onset from the temporal neocortex. They described the dysplastic temporal

neocortex 'dual pathology' and concluded that, it was epileptogenic (Fauser and Schulze-Bonhage, 2006).

The diagnostic methods commission of ILAE published the clinical and pathological findings in various focal cortical dysplasias in 2011. The spectrum of histopathological findings in type IIIa focal cortical dysplasias of the temporal neocortex in MTS patients include architectural abnormalities falling under the purview of type I FCD, presence of temporal lobe sclerosis (TLS), TLS with sub-cortical white matter heterotopic neurons and TLS with lentiform heterotopias in the sub-cortical white matter. The term FCD type IIIa is not to be used, when neuronal loss is only seen in the mesial temporal lobe, for heterotopic neurons in the deep white matter or presence of other types of FCDs and pathologies in the temporal lobe (Blümcke et al., 2011).

Garbelli et al., in the year 2012 conducted a retrospective study in 32 MTS patients. All the patients had drug resistant TLE due to MTS and underwent surgery with a pre-operative 1.5T MRI scan. They were then divided into two cohorts, based on the presence or absence of temporal polar abnormalities on MRI. The clinical characteristics, histopathological findings and post-procedural 7T MRI findings were compared. Seizure frequency and the presence of antecedent did not differ between the groups. Habitual seizures started earlier, with a longer duration of epilepsy in patients with temporal polar abnormality. Patients with temporal polar changes also had a higher incidence of dystonic features on semiological evaluation. On histopathological evaluation, patients in both cohorts showed type IIIa dysplastic changes with no significant difference. Irrespective of the presence of MRI changes however, all the patients had variable degrees of gliosis in the white matter with myelination abnormality. Correlation with 7T MRI also revealed myelin loss in the patients with temporal polar changes. The authors concluded that the widespread gliosis was not responsible for the anterior temporal polar changes. Rather, the MRI abnormality could be explained by myelin abnormality (Garbelli et al., 2012).

The task force of ILAE diagnostic methods commission in 2013 reviewed the literature on the presence of pathology in the anterior temporal lobe and temporal neocortex in MTS patients, as evidenced by clinical, electrophysiological, imaging,

and histopathological data. They stated that ipsilateral temporal atrophy and anterior temporal blurred grey-white differentiation may be seen in up to 70 percent of cases with mesial temporal sclerosis and that the underlying histopathological abnormality translates to myelin loss, rather than the presence of dysplastic cortex. They also acknowledged the possibility of the presence of type IIIa FCD in the temporal neocortex, that could be acquired, due to the same etiological factors as MTS (Blümcke et al., 2013).

Surgical management of MTS

Epilepsy patients with resistance to AEDs are candidates for epilepsy surgery after a complete pre-surgical evaluation. MTS is the most common cause of medically refractory epilepsy subjected to epilepsy surgeries. Most of the cases with MTS show excellent response after surgery. The surgical techniques in TLE due to MTS include the anterior temporal lobectomy and amygdalo-hippocampectomy (ATL+AH) or selective amygdalo- hippocampectomy (AH). A few authors have recommended the ATL+AH in MTS patients as the standard procedure, since it has been observed by previous studies that, there are changes of uncertain pathology seen in the temporal neocortex as well. However, this has been debated as there are no prospective trials that clearly demonstrate its superiority over selective AH (Muzumdar et al., 2016).

ATL+AH is still preferred in a resource limited setting like India. This is because, the neocortex in some patients with MTS on histopathological evaluation has been found to harbor type 1 focal cortical dysplasia, which can cause neocortical temporal epileptogenesis. Even in the absence of dysplasia, the lateral neocortex most MTS patients has been found to be abnormal on histopathology.

3. MATERIALS AND METHODS

Study design

This was a cohort study with both prospective and retrospective arms. For the retrospective arm, MTS patients undergoing anterior temporal lobectomy with amygdalohippocampectomy (ATL +AH) from January 2017 to December 2021 were included, if they fulfilled the inclusion criteria. For the prospective arm of the study, TLE patients were consecutively recruited from the epilepsy out-patient clinic and neurosurgery wards, from January 2022 to December 2022 if they were scheduled to undergo ATL+AH and they satisfied the inclusion criteria.

Patients

Inclusion criteria:

Patients with TLE, who have undergone epilepsy protocol MRI-brain with a 3T MRI including the sequences T2, FLAIR and ASL, followed by ATL+AH with availability of histopathological analysis of specimen of the resected temporal lobe.

Exclusion criteria:

- Patients with bilateral Mesial Temporal sclerosis.
- Patients undergoing ATL + AH for mass lesions or other dual pathology in the Temporal lobe.
- Patients with unavailable or poor quality T2, FLAIR and/or ASL images.
- Patients with pre-operative MRI done from other hospitals or institutions before being referred to our institute for further management.
- Claustrophobic patients and patients who could not undergo MRI.
- MTS Patients, whose post-operative histopathological specimens were not available for analysis.

Study population:

The number of patients who had MRI for evaluation of temporal lobe epilepsy were 208 in the retrospective arm and 43 in the prospective arm. Two patients were excluded as due to non-availability of all the required MRI sequences, including ASL or on account of poor-quality MR images. Sixty-six cases were excluded as they had pre-operative MRI done from another hospital or institution with a lack of the necessary ASL source images. Four patients were excluded due to bilateral MTS. Seven patients were diagnosed with MTS on pre-operative MRI, but were excluded as histopathological assessment revealed no HS, only gliosis. Sixty-five patients were excluded, because they underwent ATL for causes other than MTS or had dual pathology in the temporal lobe. Finally, 88 patients were included in the retrospective arm and 19 patients in the prospective arm of the study (Figure 3.1).

The patients were divided into three cohorts for analysis of the data. The first group included 63 patients with MTS and neocortical temporal changes on pre-operative MRI (MTS+NTC group), the second group included 37 MTS patients without neocortical changes on pre-operative MRI (MTS-NTC group). The third group was 7 controls consisting of lesion-negative TLE patients without MTS and neocortical changes and with a normal pre-operative MRI, who underwent ATL+AH. The inclusion of the control group was to ensure that the visible neocortical changes were not artifactual in nature. The study was started only after the institutional ethics committee approval. Informed consent was waivered for the retrospectively included patients and it was obtained from the prospectively included patients.

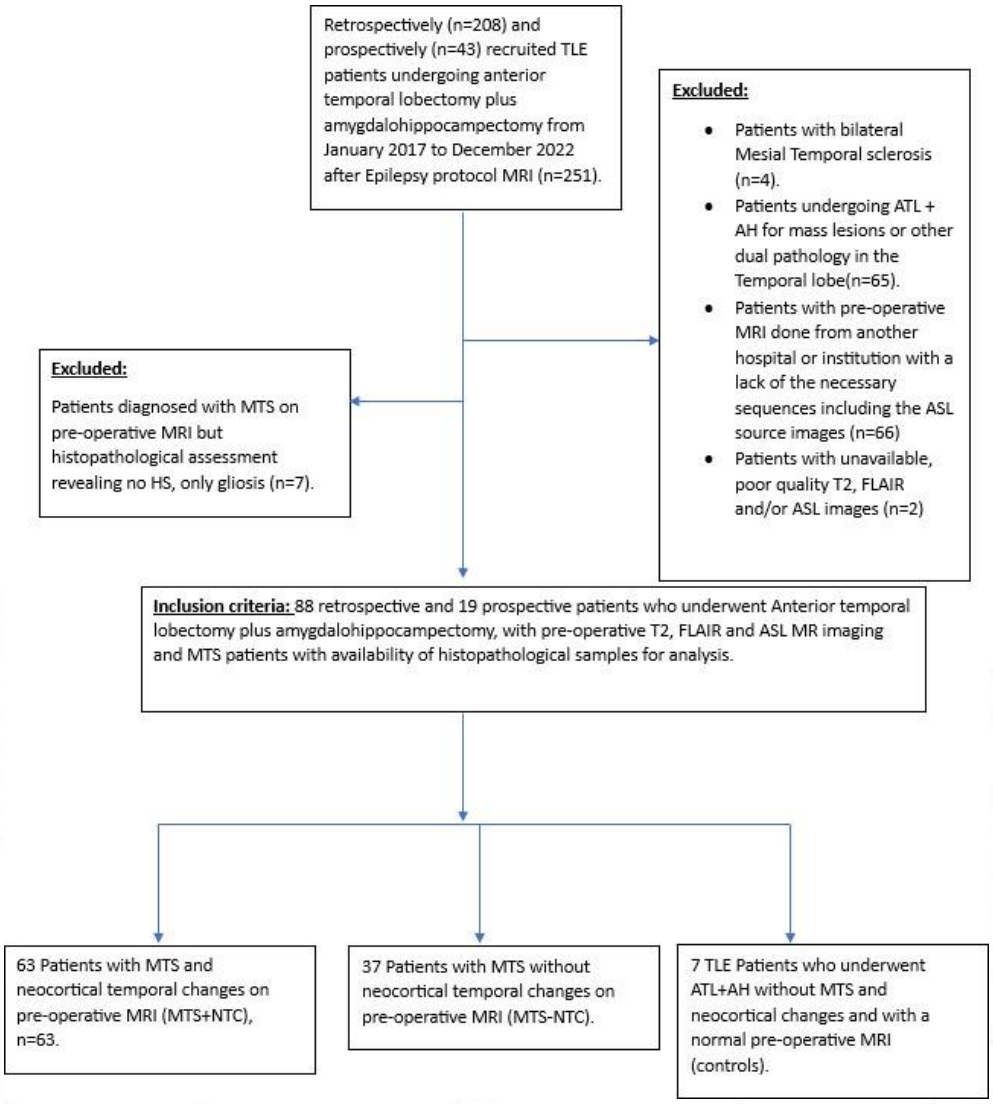


Figure 3.1: Patient recruitment flowchart

Demographics and clinical history

The gender and demographic characteristics were recorded for all patients. The clinical history and semiological data of the retrospectively included patients was retrieved from the electronic medical records (EMR). For the prospectively included patients, it was collected from the patients and their bystanders. The clinical history details recorded include the presence of an antecedent like febrile seizure, status epilepticus, perinatal hypoxia, meconium aspiration, meningoencephalitis, and head trauma. The age at which the antecedent occurred was also noted. The age of onset of epilepsy, age at surgery were documented. The duration of epilepsy was obtained by

subtracting the age at which the patient underwent ATL+AH from the age of onset of epilepsy. The seizure frequency one year prior to the presentation was scored for each patient, with a higher score corresponding to a higher frequency of seizures as in table-3.1.

Table 3.1: Seizure frequency scoring

Seizure (Sz) frequency score	Seizure frequency (Sz)
1	Sz free without AEDs
2	Sz free with uncertain necessity of AEDs
3	Sz free with necessity of AEDs
4	auras only
5	non disabling nocturnal seizures only
6	One to three seizures/year
7	Four to eleven seizures/year
8	One to three seizures/month
9	One to six seizures/week
10	One to three seizures/day
11	Four to ten seizures/day
12	>10 seizures/day

Clinical features

Presence or absence of focal to bilateral tonic-clonic progression was noted down for all patients. Rest of the semiological features were evaluated in detail for their presence or absence, and the type of manifestation. Nomenclature and categorization of the semiological features was in accordance with the instruction manual for ILAE 2017 classification of seizure types. Categories of semiological features, the respective features included in each category and other relevant features noted down are as in table-3.2.

Among the various semiological features, loss of awareness, motor symptoms and cognitive symptoms were only analyzed in those patients with no focal to bilateral tonic-clonic progression.

Electrophysiology

The electrodes for EEG recording were placed as per the international 10-20 system. When the discharges could not be obtained conventionally, anterior temporal and sphenoidal electrodes were used.

Invasive EEG recordings with depth and sub-dural electrodes were obtained in cases of doubtful lateralization or inconclusive scalp EEG data.

The interictal and ictal EEG findings were read by an epileptologist (HP) and the findings noted. The inter-ictal epileptiform spike and wave discharges (IEDs) were classified as either lateralized and localized, localized, or multifocal.

Similarly, the ictal EEG findings were classified as lateralized and localized, localized, or diffuse. The type of ictal EEG activity was also identified as either monomorphic theta, fast beta, or diffuse ictal onset. Monomorphic theta rhythm, with a frequency of 3.5 to 7.5 Hz was taken as indicative of mesial temporal epileptogenesis and fast beta rhythm, with a frequency of 13 to 30 Hz, was indicative of neocortical temporal epileptogenesis.

Table 3.2: Semiological features, evaluated according to ILAE 2017 terminology.

Semiological feature	Types
Aura	Epigastric sensation, fear, experiential, Auditory, vertiginous sensation, visual, foul-smelling, nausea, retching, cephalic sensation, palpitations, tiredness, cold sensation, premonition, chest discomfort and undescribable auras.
Loss of awareness	-
Sensory symptoms	Auditory, visual, vertiginous sensation,

	foul-smelling and cold sensation.
Motor symptoms	Head and eye adversion, upper limb posturing, lower limb posturing, inability to move, upper and lower limb posturing, hemiclonic jerks and dystonic posturing of upper limb and post-ictal Todd's paralysis.
Autonomic symptoms	Piloerection, palpitations, nausea, retching, salivation, epigastric sensation, abdominal pain, ictal cough, post-ictal cough, ictal swallow, and post-ictal sneezing.
Automatisms	Upper limb, bimanual, vocalization or ictal speech, oral, wandering behaviour, rubbing of ears, drinks water, violent behaviour, searching, ictal nose wiping, rubbing face, leaving behaviour, and pedaling movements of bilateral lower limbs.
Cognitive symptoms	Post-ictal confusion, post-ictal amnesia, post-ictal dysphagia, experiential phenomena, and post-ictal aphasia.
Emotional or affective symptoms	Fear and anger.

Clinico-electrophysiological impression

The clinico-electrophysiological opinion that was obtained from the detailed analysis of clinical history and VEEG findings at the multi-disciplinary patient management conferences was recorded. The presence or absence of neocortical epileptogenesis was deduced based on the presence of certain features either clinically, or on EEG. Red flags predictive of neocortical epileptogenesis were the presence of high frequency of focal to bilateral tonic clonic progression, increased

frequency of clustering or the presence of auras characteristic of neocortical seizures in the semiology. Neocortical epileptogenesis was also considered if the patient had fast beta rhythm on EEG.

Imaging (MRI) analysis

The MRI images were acquired on a 3T GE discovery 750W scanner (GE healthcare, Milwaukee, WI, USA). Our institute epilepsy protocol is in accordance with the HARNESS protocol prescribed by ILAE and includes the sequences 3D FLAIR, 3D SPGR, high resolution coronal T2, DWI, SWAN and ASL.

The acquisition parameters for the sequences used in the study- 3D FLAIR, high resolution coronal T2 and ASL are given in the table-3.3.

Pseudo continuous tagging was used for labeling in ASL. The labeling plane for ASL was in the upper part of the neck, 2 cm below lower most slice in the imaging plane. The average scan time for ASL was about 5 minutes. The MRI images were retrieved from PACS and were read by two Radiologists (VK and HK) after being blinded to the clinical, semiological and EEG findings. The T2 and FLAIR images were qualitatively analyzed for the presence or absence of hyperintensity in four regions. They were:

1) The hippocampus,

2) The amygdala,

3) The lateral temporal neocortex, and

4) The anterior temporal pole, defined as the anterior most part of the temporal lobe with an arbitrary posterior boundary formed by a laterally extending line drawn from the ipsilateral limen insulae.

Table 3.3: Acquisition parameters

	High resolution Coronal T2 FSE	3D FLAIR	3D PC-ASL
Slice thickness	3 mm	1 mm	4 mm
Field of View	16 x 16 cm	25 x 22.5 cm	24 x 24 cm
Matrix size	352 x 352	256 x 256	-
Voxel size	0.4 x 0.4 x 3 mm	1 x 1 x 1 mm	-
TR	8940 ms	7477 ms	4854 ms
TE	142.8 ms	115 ms	10.7 ms
TI	-	1993 ms	-
PLD	-	-	1025-1525 ms (children) 2025 ms (adults)

The qualitative analysis of images was performed at two levels. For the first level of interpretation, the images were reviewed independently for calculation of inter-observer agreement. The second level analysis was conducted by the radiologists in consensus to solve any disagreement. The results second level of analysis were used for classifying patients into the three cohorts.

The corresponding ASL images were also qualitatively analysed in these four regions for the presence or absence of perfusion abnormality. Perfusion abnormality corresponded to both hyper perfusion and hypoperfusion qualitatively.

Quantitative analysis of the ASL images was also done in these four regions. A region of interest (ROI) measuring about 7 to 15 mm2 in area was drawn in each region on ASL source images (figure 3.2). The ROI was drawn in such a way that, it encompassed the area of cortex in each region showing the perfusion abnormality. An ROI of similar size was placed in the homologous region of the cerebral cortex with no perfusion abnormality in the contralateral hemisphere. An ASL signal intensity ratio (SIR) was obtained, with the numerator being the signal intensity from the ROI on the involved side, and the denominator being the signal intensity from the ROI on

the normal side. Cases with increased perfusion on ASL were excluded from the quantitative analysis.

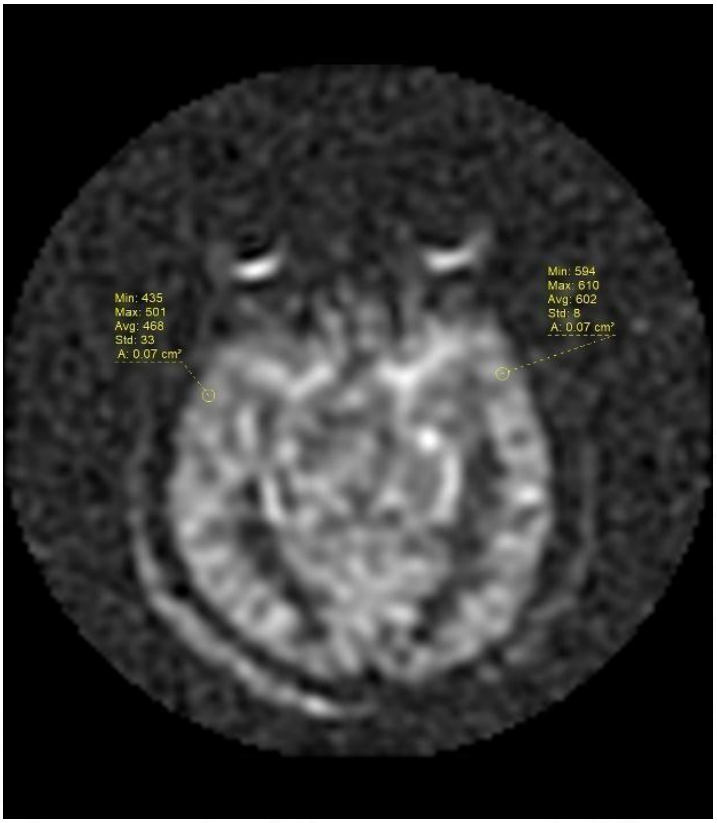


Figure 3.2: Method for Quantitative analysis of ASL source images

Histopathological analysis

The histopathological analysis of the resected specimens was done by two neuropathologists (DN and RP) in consensus, who were blinded to the clinical, electrophysiological and imaging data. The resected tissue specimens were processed and stained with NeuN for neuronal analysis. Immunohistochemistry with glial fibrillary acid protein (GFAP) was done for gliosis. Luxol fast blue staining for myelin was also done in select cases. The histopathological evaluation data was available in three regions:

1) The hippocampus
2) The amygdala
3) The temporal neocortex

Statistical analysis

Categorical variables were summarized as numbers and percentages. Continuous variables were summarized using mean +/- standard deviation and median with 25th and 75th percentiles (interquartile range). Normalcy of the data was assessed using the Kolmogorov-Smirnov test. When there was non-normal distribution of data, non-parametric tests were used. Normally distributed quantitative data was analysed with the independent t test. Non-normally distributed quantitative data was analysed using the Mann-Whitney U Test (for two groups). Qualitative variables were compared with the Chi-square test. When any cell had a count of less than 5, Fisher's exact test was used. Univariate logistic regression with the presence of neocortical changes in MTS as the dependent variable, and the independent variables being gender, age, presence of antecedents, age of antecedent, age of onset of epilepsy and duration of epilepsy. The inter-observer agreement was quantified using kappa values. Interpretation of Kappa values is as shown in table-3.4.

The data was collected and tabulated using a Microsoft EXCEL spreadsheet. Final statistical analysis was done using Statistical Package for Social Sciences (SPSS) software, IBM, Chicago, USA, version 25.0.

A p -value < 0.05 was considered statistically significant.

Table 3.4: Interpretation of Kappa values

Kappa value	Strength of agreement
< 0.20	Poor
0.21 - 0.40	Fair
0.41 - 0.60	Moderate
0.61 - 0.80	Good
0.81 - 1.00	Very good

4. RESULTS

Table 4.1: Comparison of gender between MTS + NTC and MTS - NTC.

Gender	MTS + NTC(n=63)	MTS - NTC(n=37)	Total	P value
Female	29 (46.03%)	20 (54.05%)	49 (49%)	0.438†
Male	34 (53.97%)	17 (45.95%)	51 (51%)	
Total	63 (100%)	37 (100%)	100 (100%)	

† **Chi square test**

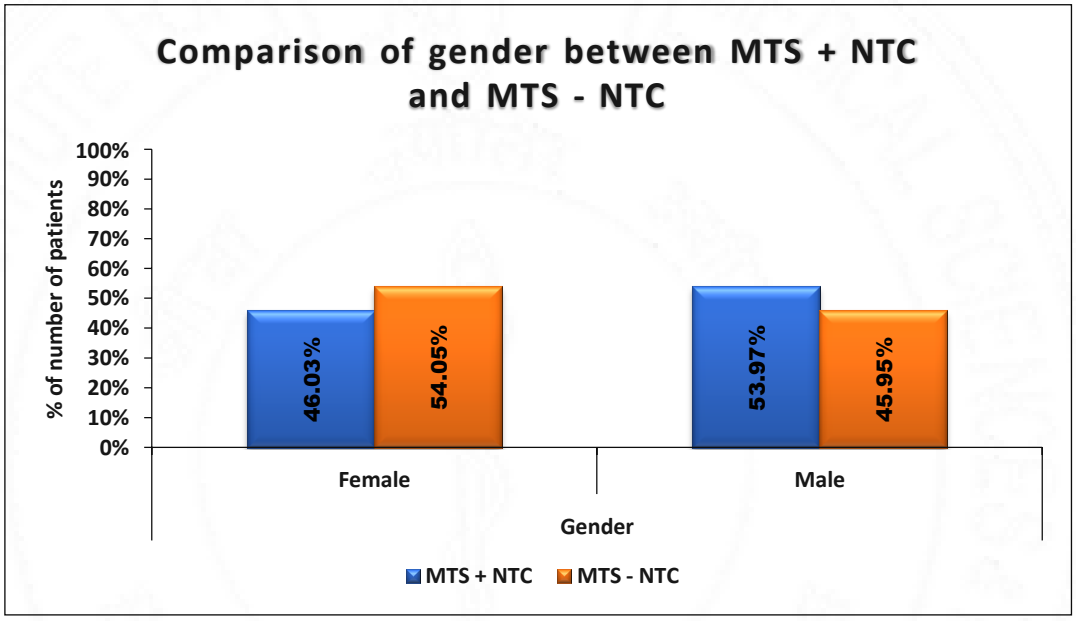


Figure 4.1: Comparison of gender between MTS + NTC and MTS - NTC.

Distribution of gender was comparable between MTS + NTC and MTS - NTC. (Female:- 46.03% vs 54.05% respectively, Male:- 53.97% vs 45.95% respectively) (p value=0.438).(Table 4.1, figure 4.1).

Table 4.2: Comparison of age(years) between MTS + NTC and MTS - NTC.

Age(years)	MTS + NTC(n=63)	MTS - NTC(n=37)	Total	P value
<=10	3 (4.76%)	2 (5.41%)	5 (5%)	
11-20	19 (30.16%)	8 (21.62%)	27 (27%)	
21-30	28 (44.44%)	17 (45.95%)	45 (45%)	0.748*
31-40	11 (17.46%)	7 (18.92%)	18 (18%)	
>40	2 (3.17%)	3 (8.11%)	5 (5%)	
Mean ± SD	23.7 ± 9.21	25.95 ± 9.48	24.53 ± 9.33	
Median(25th-75th percentile)	22(17.5-29.5)	26(20-31)	24(18-30)	0.247‡
Range	3-51	8-50	3-51	

‡ **Independent t test,** * **Fisher's exact test**

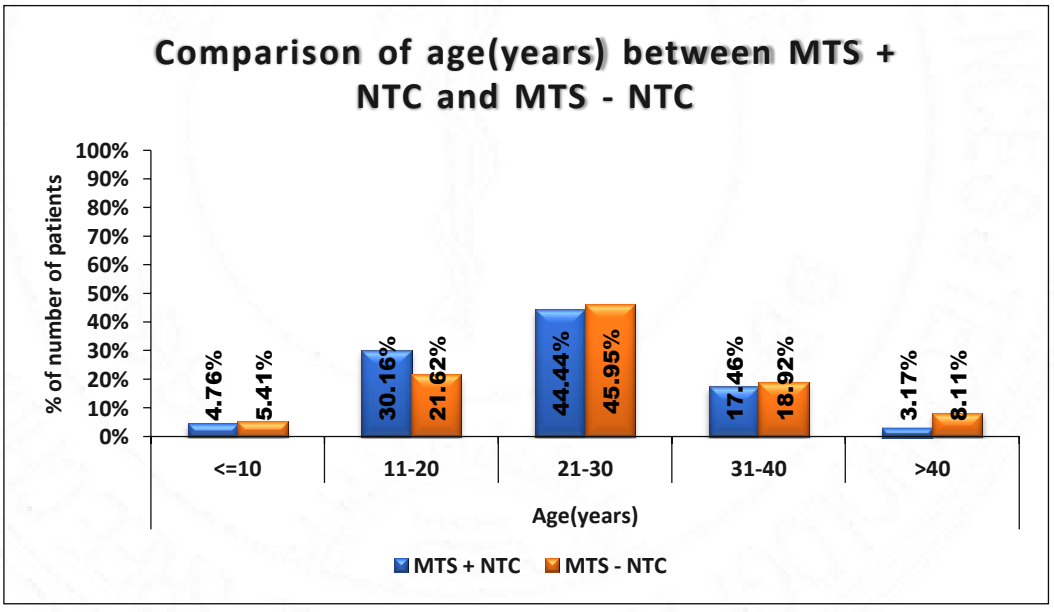


Figure 4.2: Comparison of age(years) between MTS + NTC and MTS - NTC.

Distribution of age(years) was comparable between MTS + NTC and MTS - NTC. (<=10 years: - 4.76% vs 5.41% respectively, 11-20 years:- 30.16% vs 21.62%

respectively, 21-30 years:- 44.44% vs 45.95% respectively, 31-40 years:- 17.46% vs 18.92% respectively, >40 years:- 3.17% vs 8.11% respectively) (p value=0.748).

Mean ± SD of age(years) in MTS + NTC was 23.7 ± 9.21 and in MTS - NTC was 25.95 ± 9.48 with no significant difference between them. (p value=0.247) (Table 4.2, figure 4.2).

Table 4.3: Comparison of antecedent between MTS + NTC and MTS - NTC.

Antecedent	MTS + NTC(n=63)	MTS - NTC(n=37)	Total	P value
Absent	23 (36.51%)	17 (45.95%)	40 (40%)	0.352†
Present	40 (63.49%)	20 (54.05%)	60 (60%)	
Total	63 (100%)	37 (100%)	100 (100%)	

† **Chi square test**

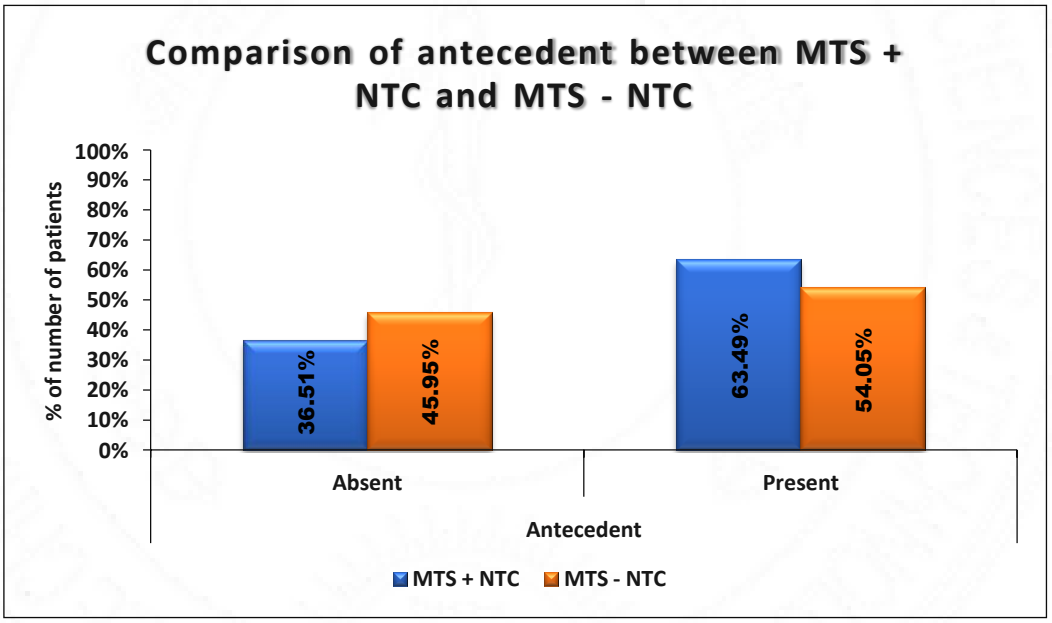


Figure 4.3: Comparison of antecedent between MTS + NTC and MTS - NTC.

Distribution of antecedent was comparable between MTS + NTC and MTS - NTC. (63.49% vs 54.05% respectively) (p value=0.352). (Table 4.3, figure 4.3).

Table 4.4: Comparison of age at the onset of epilepsy(years) between MTS + NTC and MTS - NTC.

Age at the onset of epilepsy(years)	MTS + NTC(n=63)	MTS - NTC(n=37)	Total	P value
Mean ± SD	7.82 ± 6.19	11.12 ± 8.16	9.04 ± 7.12	**0.049**§
Median (25th-75th percentile)	6.5(2-12)	10(5-15)	8(3-13.25)	
Range	0.08-22	0.08-34	0.08-34	

§ **Mann Whitney test**

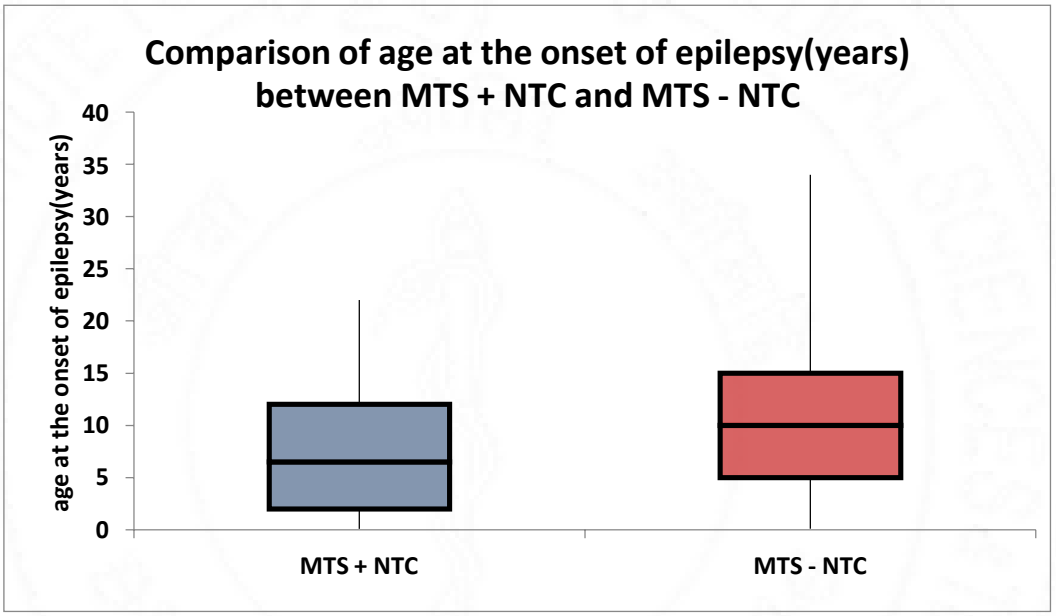


Figure 4.4: Comparison of age at the onset of epilepsy(years) between MTS + NTC and MTS - NTC. (non-parametric variable, Box-whisker plot)

Median (25th-75th percentile) of age at the onset of epilepsy(years) in MTS - NTC was 10(5-15) which was significantly higher as compared to MTS + NTC (6.5(2-12)). (p value=0.049) (Table 4.4, figure 4.4).

Table 4.5: Comparison of age at surgery(years) between MTS + NTC and MTS - NTC.

Age at surgery(years)	MTS + NTC(n=63)	MTS - NTC(n=37)	Total	P value
Mean ± SD	23.56 ± 9.19	25.89 ± 9.57	24.42 ± 9.35	0.23‡
Median (25^{th} - 75^{th} percentile)	22(17.5-29.5)	26(20-31)	24(18-30)	
Range	3-51	8-50	3-51	

‡ **Independent t test**

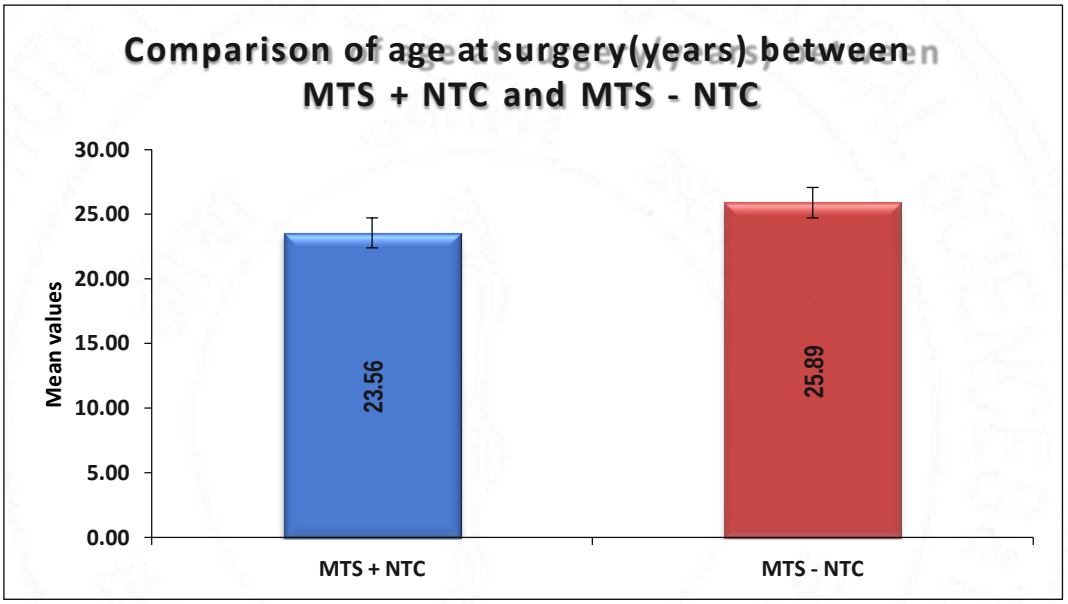


Figure 4.5: Comparison of age at surgery(years) between MTS + NTC and MTS - NTC.

Mean ± SD of age at surgery(years) in MTS + NTC was 23.56 ± 9.19 and in MTS - NTC was 25.89 ± 9.57 with no significant difference between them. (p value=0.23) (Table 4.5, figure 4.5).

Table 4.6: Comparison of duration of epilepsy (years) between MTS + NTC and MTS - NTC

Duration of epilepsy(years)	MTS + NTC(n=63)	MTS - NTC(n=37)	Total	P value
Mean ± SD	15.85 ± 9.08	14.11 ± 8.96	15.2 ± 9.03	0.355‡
Median(25th-75th percentile)	13.5(8-22.5)	12(8-20)	13(8-21.125)	
Range	1-35.5	1-37	1-37	

‡ **Independent t test**

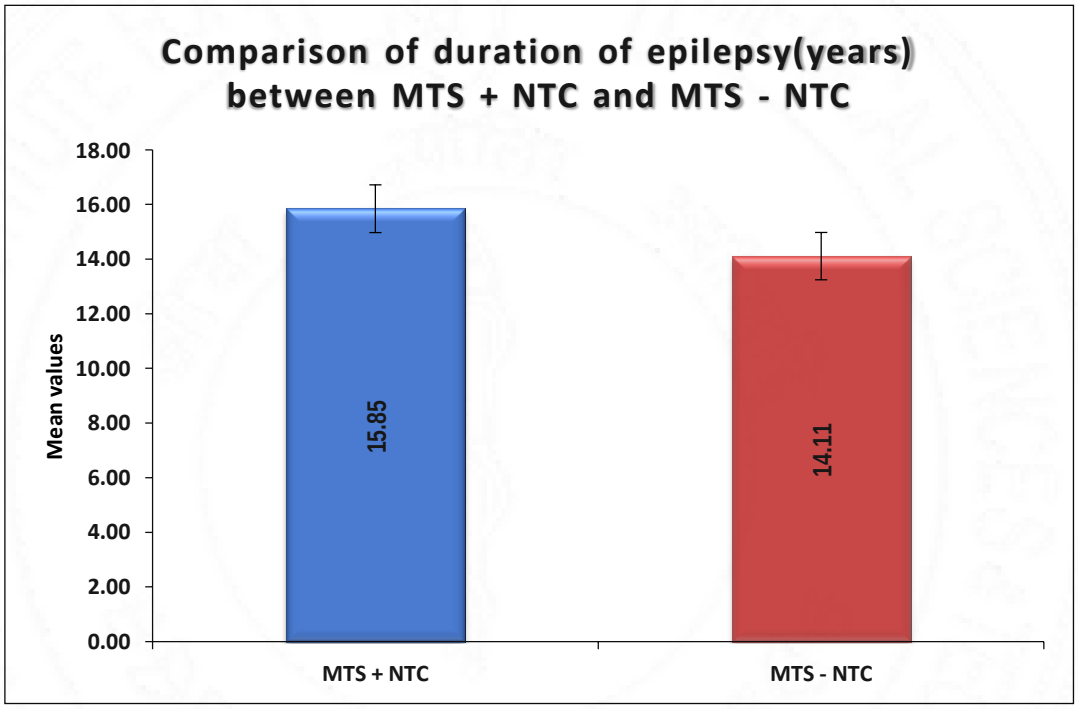


Figure 4.6: Comparison of duration of epilepsy(years) between MTS + NTC and MTS - NTC

Mean ± SD of duration of epilepsy(years) in MTS + NTC was 15.85 ± 9.08 and in MTS - NTC was 14.11 ± 8.96 with no significant difference between them. (p value=0.355) (Table 4.6, figure 4.6).

Table 4.7: Comparison of seizure frequency score between MTS + NTC and MTS - NTC

Seizure frequency score	MTS + NTC(n=63)	MTS - NTC(n=37)	Total	P value
Mean ± SD	7.57 ± 0.84	7.27 ± 0.93	7.46 ± 0.88	0.099‡
Median(25th-75th percentile)	7(7-8)	7(7-8)	7(7-8)	
Range	6-10	5-9	5-10	

‡ **Independent t test**

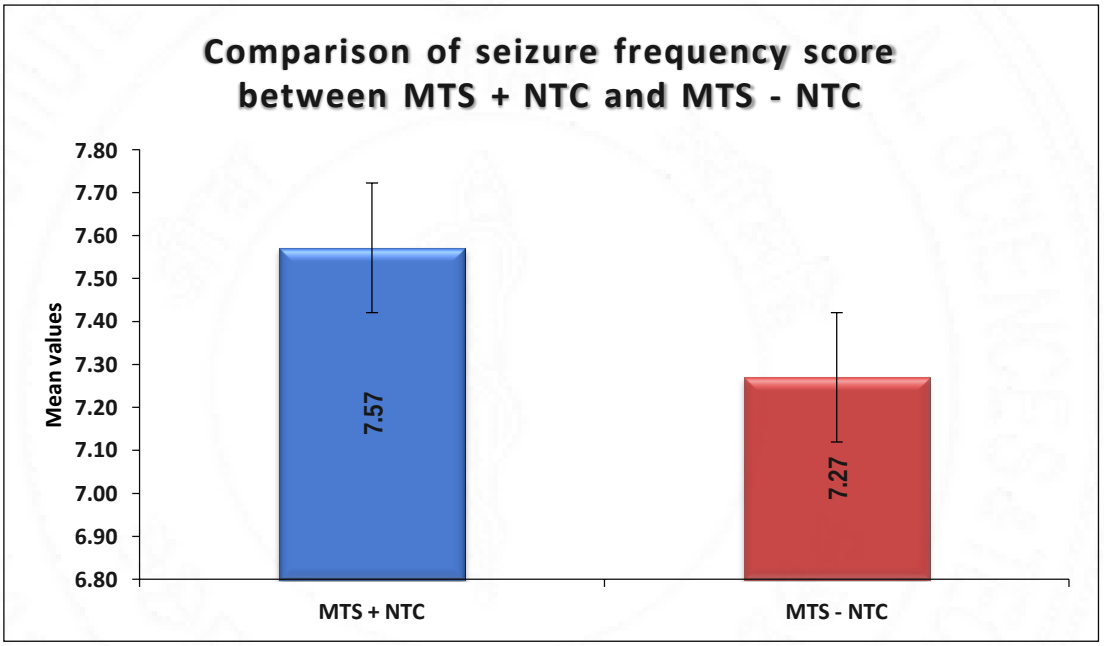


Figure 4.7: Comparison of seizure frequency score between MTS + NTC and MTS – NTC

Mean ± SD of seizure frequency score in MTS + NTC was 7.57 ± 0.84 and in MTS - NTC was 7.27 ± 0.93 with no significant difference between them. (p value=0.099) (Table 4.7, figure 4.7).

Table 4.8: Comparison of number of anti-seizure medications between MTS + NTC and MTS - NTC

Number of anti-seizure medications	MTS + NTC(n=63)	MTS - NTC(n=37)	Total	P value
Mean ± SD	2.65 ± 0.77	2.51 ± 0.77	2.6 ± 0.77	0.389‡
Median(25th-75th percentile)	2(2-3)	2(2-3)	2(2-3)	
Range	2-5	1-4	1-5	

‡ **Independent t test**

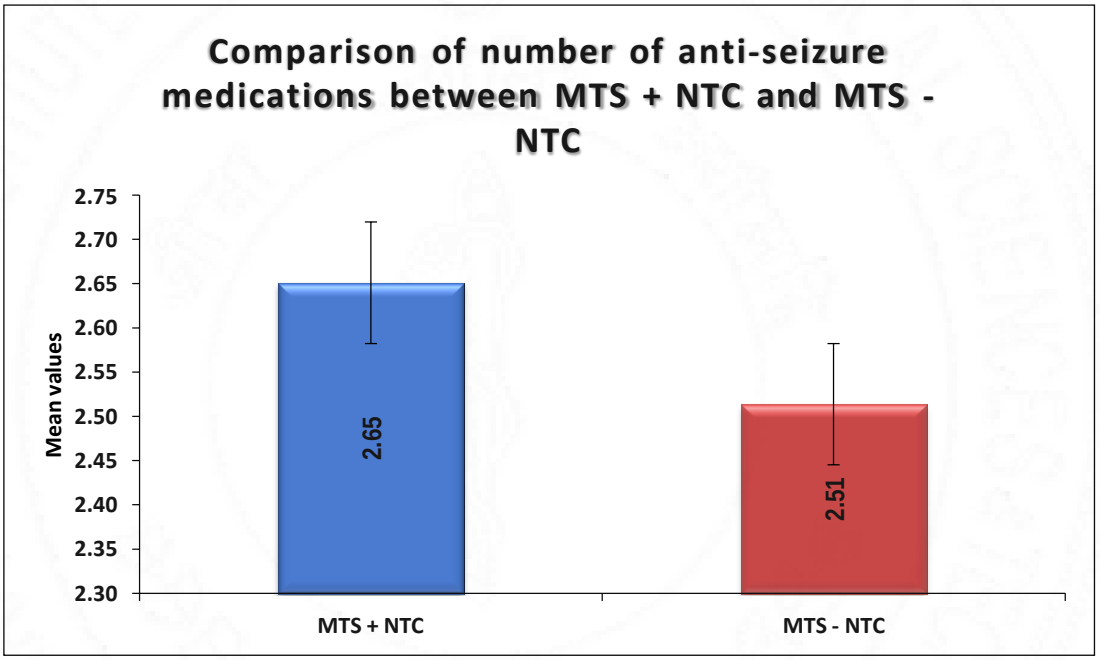


Figure 4.8: Comparison of number of anti-seizure medications between MTS + NTC and MTS - NTC

Mean ± SD of number of anti-seizure medications in MTS + NTC was 2.65 ± 0.77 and in MTS - NTC was 2.51 ± 0.77 with no significant difference between them. (p value=0.389) (Table 4.8, figure 4.8).

Table 4.9: Comparison of secondary generalization between MTS + NTC and MTS - NTC

Secondary generalization	MTS + NTC(n=63)	MTS - NTC(n=37)	Total	P value
Absent	34 (53.97%)	24 (64.86%)	58 (58%)	
Present	29 (46.03%)	13 (35.14%)	42 (42%)	0.286†
Total	63 (100%)	37 (100%)	100 (100%)	

† **Chi square test**

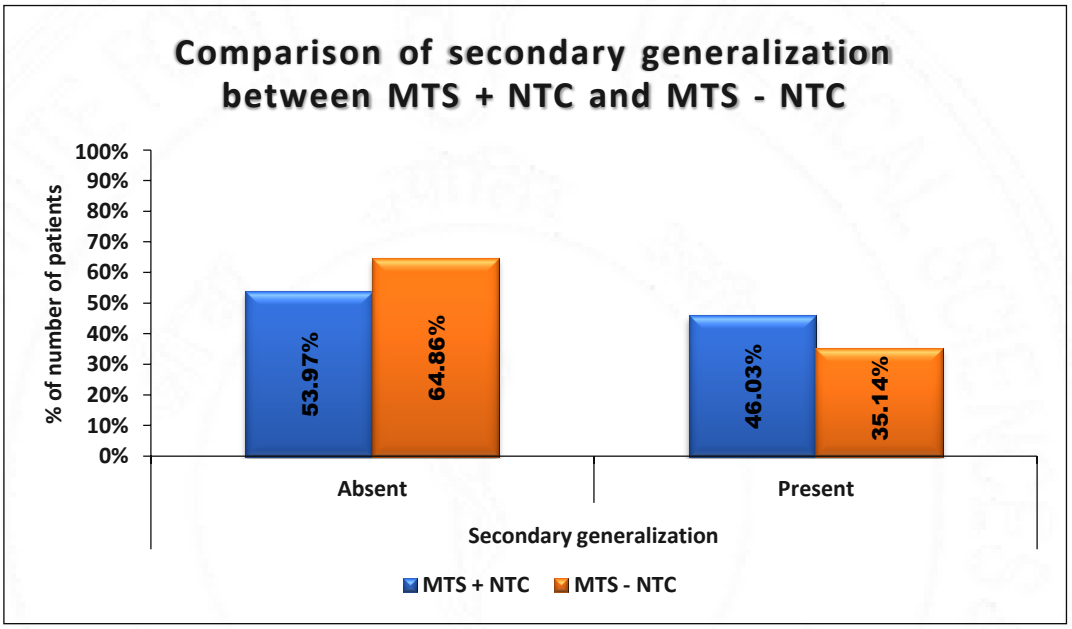


Figure 4.9: Comparison of secondary generalization between MTS + NTC and MTS - NTC

Distribution of secondary generalization was comparable between MTS + NTC and MTS - NTC. (46.03% vs 35.14% respectively) (p value=0.286).(Table 4.9, figure 4.9).

Table 4.10: Comparison of aura between MTS + NTC and MTS - NTC

Aura	MTS + NTC(n=63)	MTS - NTC(n=37)	Total	P value
No	13 (20.63%)	13 (35.14%)	26 (26%)	0.11†
Yes	50 (79.37%)	24 (64.86%)	74 (74%)	
Total	63 (100%)	37 (100%)	100 (100%)	

† **Chi square test**

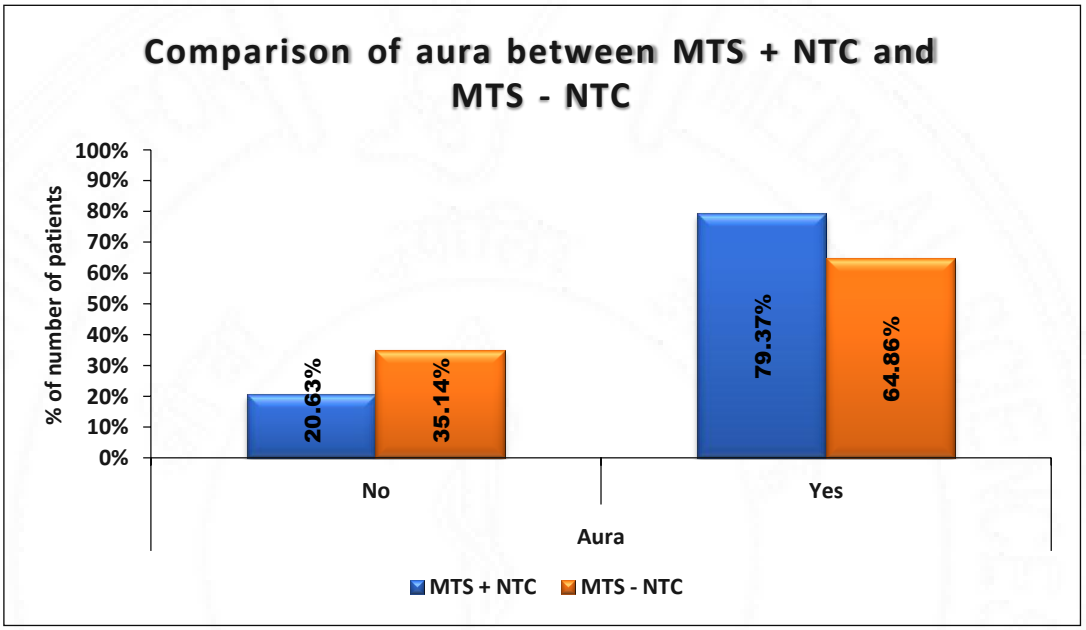


Figure 4.10: Comparison of aura between MTS + NTC and MTS - NTC

Distribution of aura was comparable between MTS + NTC and MTS - NTC. (79.37% vs 64.86% respectively) (p value=0.11).(Table 4.10, figure 4.10).

Table 4.11: Comparison of sensory symptoms between MTS + NTC and MTS - NTC

Sensory symptoms	MTS + NTC(n=63)	MTS - NTC(n=37)	Total	P value
Absent	52 (82.54%)	36 (97.30%)	88 (88%)	**0.03***
Present	11 (17.46%)	1 (2.70%)	12 (12%)	
Total	63 (100%)	37 (100%)	100 (100%)	

* **Fisher's exact test**

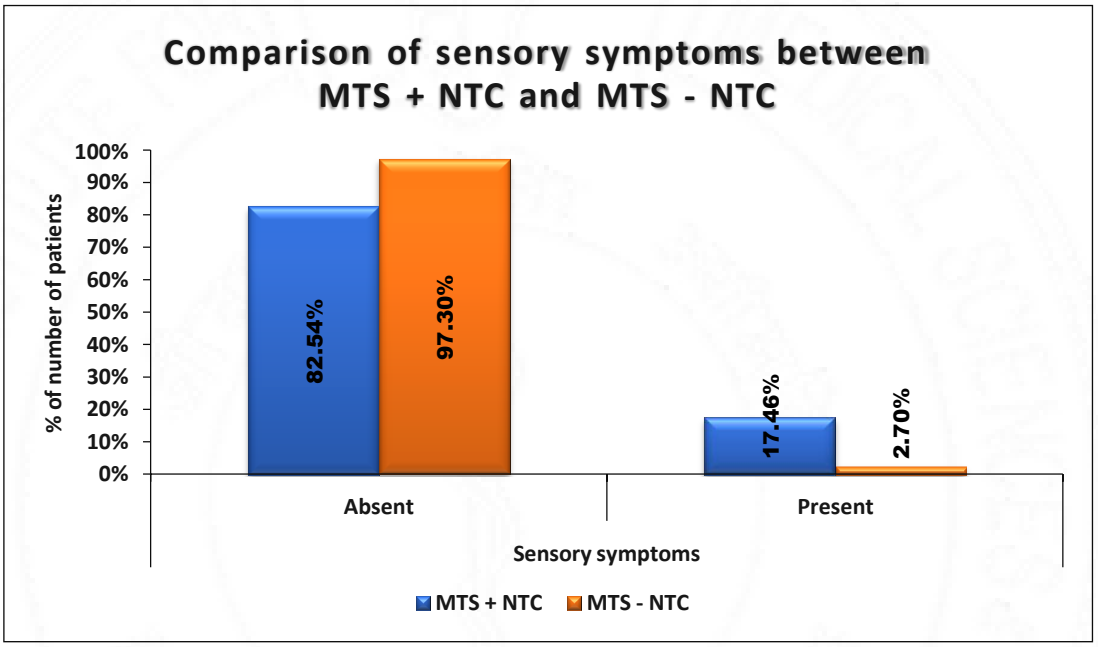


Figure 4.11: Comparison of sensory symptoms between MTS + NTC and MTS - NTC.

Proportion of patients with sensory symptoms was significantly higher in MTS + NTC as compared to MTS - NTC. (17.46% vs 2.70% respectively). (p value=0.03) (Table 4.11, figure 4.11).

Table 4.12: Comparison of motor symptoms between MTS + NTC and MTS - NTC

Motor symptoms	MTS + NTC(n=34)	MTS - NTC(n=24)	Total	P value
Absent	16 (47.06%)	14 (58.33%)	30 (51.72%)	0.397†
Present	18 (52.94%)	10 (41.67%)	28 (48.28%)	
Total	34 (100%)	24 (100%)	58 (100%)	

† **Chi square test**

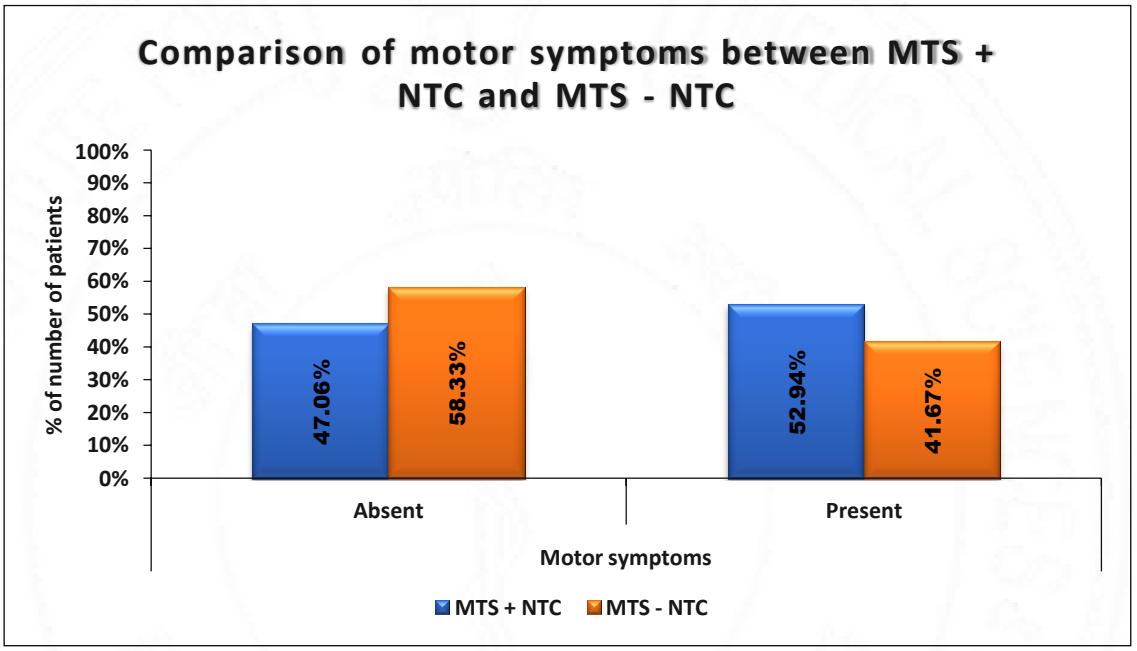


Figure 4.12: Comparison of motor symptoms between MTS + NTC and MTS - NTC.

Distribution of motor symptoms was comparable between MTS + NTC and MTS - NTC. (52.94% vs 41.67% respectively) (p value=0.397).(Table 4.12, figure 4.12).

Table 4.13: Comparison of automatisms between MTS + NTC and MTS - NTC

Automatisms	MTS + NTC(n=63)	MTS - NTC(n=37)	Total	P value
Absent	13 (20.63%)	6 (16.22%)	19 (19%)	0.587†
Present	50 (79.37%)	31 (83.78%)	81 (81%)	
Total	63 (100%)	37 (100%)	100 (100%)	

† **Chi square test**

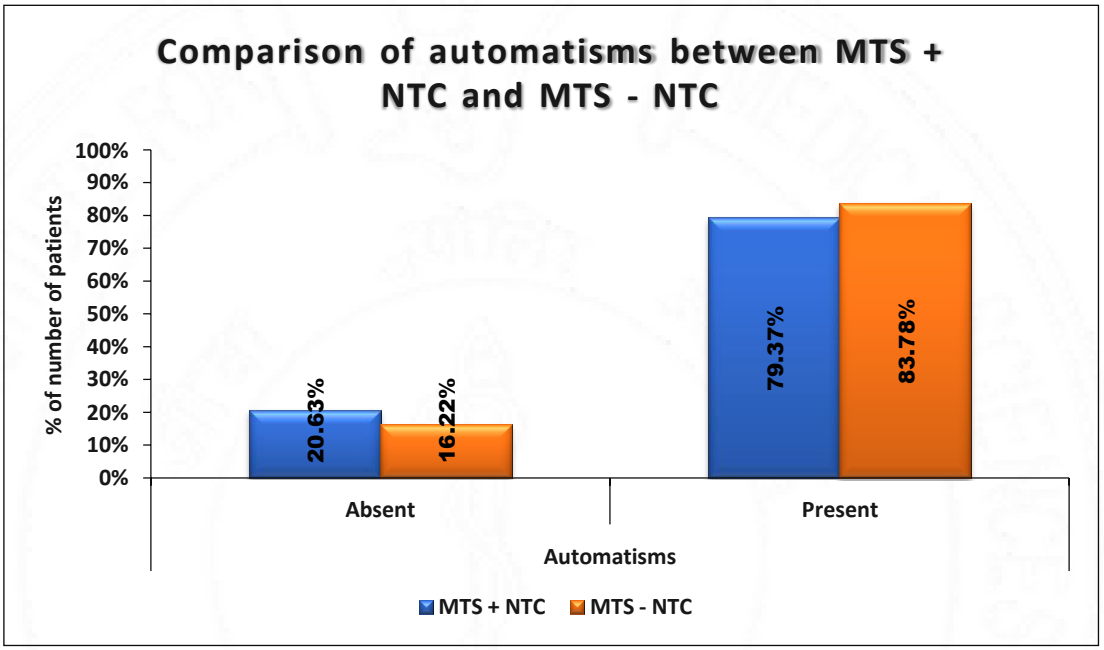


Figure 4.13: Comparison of automatisms between MTS + NTC and MTS - NTC.

Distribution of automatisms was comparable between MTS + NTC and MTS - NTC. (79.37% vs 83.78% respectively) (p value=0.587).(Table 4.13, figure 4.13).

Table 4.14: Comparison of autonomic symptoms between MTS + NTC and MTS - NTC

Autonomic symptoms	MTS + NTC(n=63)	MTS - NTC(n=37)	Total	P value
Absent	43 (68.25%)	23 (62.16%)	66 (66%)	0.535†
Present	20 (31.75%)	14 (37.84%)	34 (34%)	
Total	63 (100%)	37 (100%)	100 (100%)	

† **Chi square test**

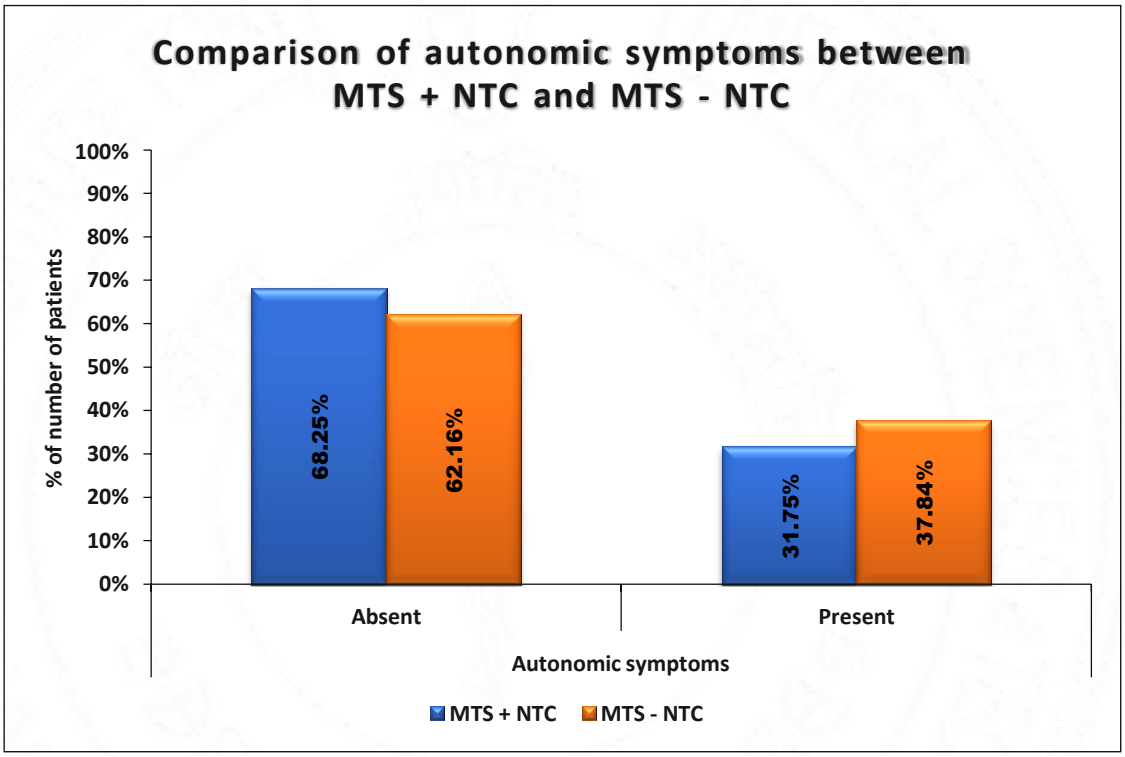


Figure 4.14: Comparison of autonomic symptoms between MTS + NTC and MTS - NTC

Distribution of autonomic symptoms was comparable between MTS + NTC and MTS - NTC. (31.75% vs 37.84% respectively) (p value=0.535).(Table 4.14, figure 4.14).

Table 4.15: Comparison of cognitive symptoms between MTS + NTC and MTS - NTC

Cognitive symptoms	MTS + NTC(n=34)	MTS - NTC(n=25)	Total	P value
Absent	19 (55.88%)	13 (52%)	32 (54.24%)	0.767†
Present	15 (44.12%)	12 (48%)	27 (45.76%)	
Total	34 (100%)	25 (100%)	59 (100%)	

† **Chi square test**

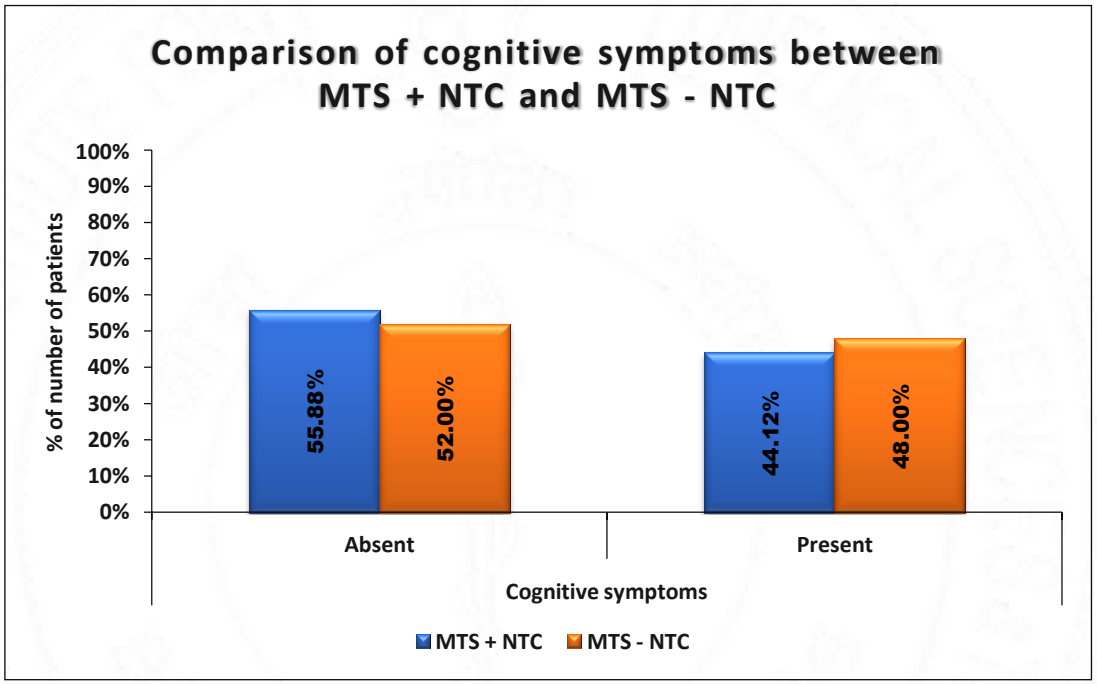


Figure 4.15: Comparison of cognitive symptoms between MTS + NTC and MTS - NTC.

Distribution of cognitive symptoms was comparable between MTS + NTC and MTS - NTC. (44.12% vs 48% respectively) (p value=0.767).(Table 4.15, figure 4.15).

Table 4.16: Comparison of emotional or affective symptoms between MTS + NTC and MTS - NTC

Emotional or affective symptoms	MTS + NTC(n=63)	MTS - NTC(n=37)	Total	P value
Absent	38 (60.32%)	26 (70.27%)	64 (64%)	0.317†
Present	25 (39.68%)	11 (29.73%)	36 (36%)	
Total	63 (100%)	37 (100%)	100 (100%)	

† **Chi square test**

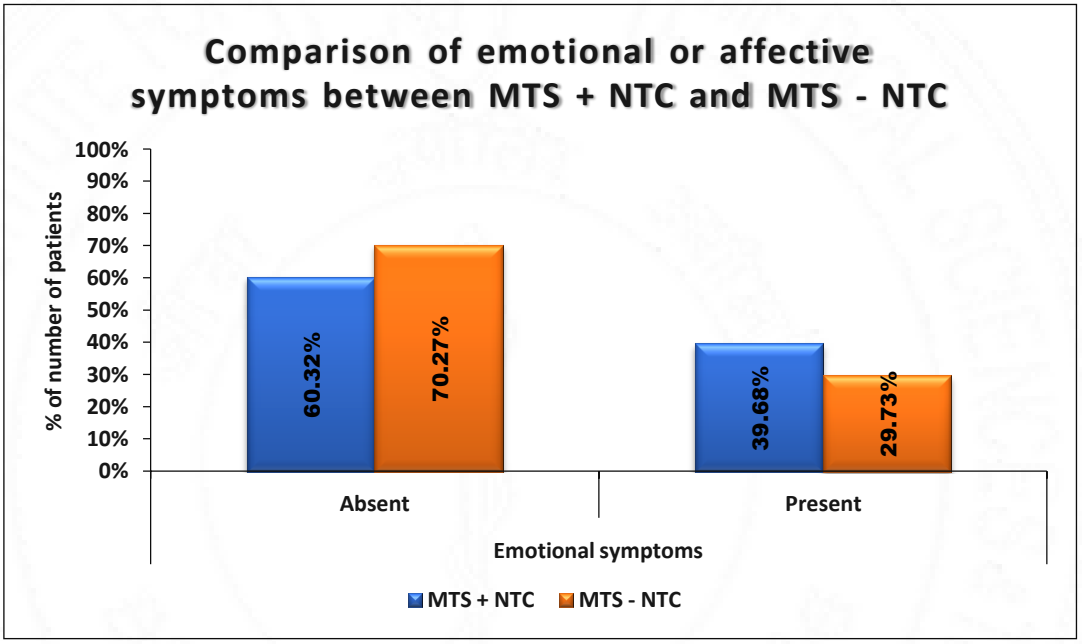


Figure 4.16: Comparison of emotional or affective symptoms between MTS + NTC and MTS - NTC

Distribution of emotional symptoms was comparable between MTS + NTC and MTS - NTC. (39.68% vs 29.73% respectively) (p value=0.317).(Table 4.16, figure 4.16).

Table 4.17: Comparison of antecedent type between MTS + NTC and MTS - NTC

Antecedent type	MTS + NTC(n=40)	MTS - NTC(n=20)	Total	P value
Febrile seizure	29 (72.50%)	17 (85%)	46 (76.67%)	0.623*
Febrile status	2 (5%)	0 (0%)	2 (3.33%)	
Head trauma	0 (0%)	1 (5%)	1 (1.67%)	
Meconium aspiration	1 (2.50%)	0 (0%)	1 (1.67%)	
Meningoencephalitis	3 (7.50%)	1 (5%)	4 (6.67%)	
Perinatal hypoxia	5 (12.50%)	1 (5%)	6 (10%)	
Total	40 (100%)	20 (100%)	60 (100%)	

* **Fisher's exact test**

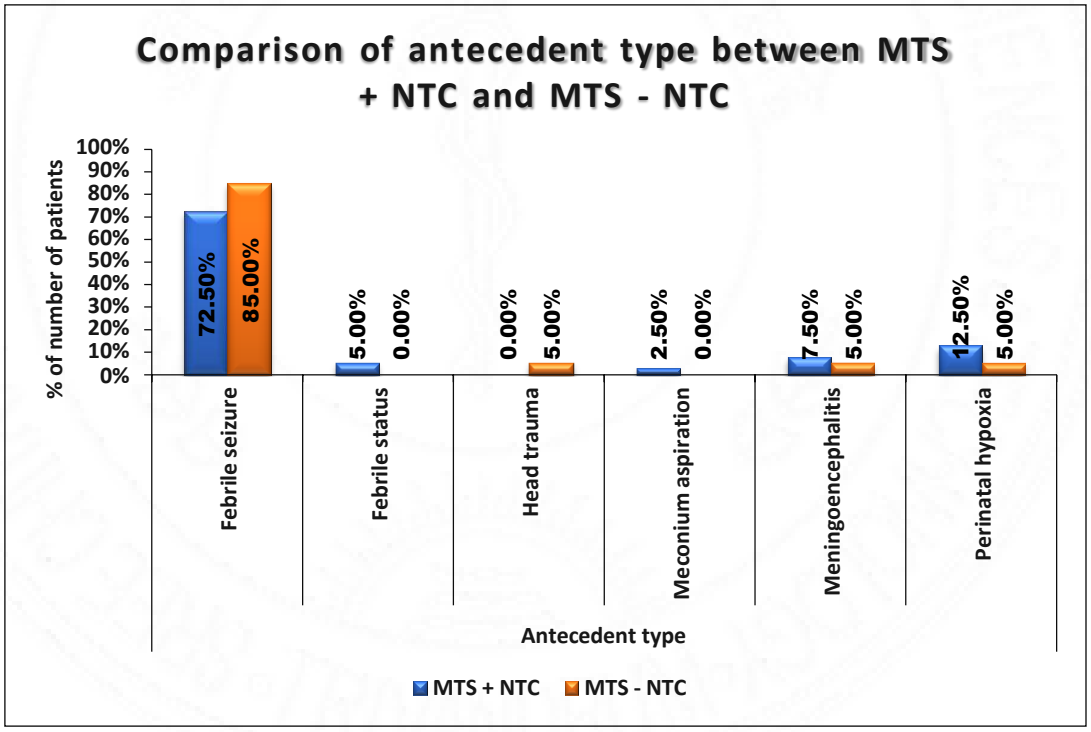


Figure 4.17: Comparison of antecedent type between MTS + NTC and MTS - NTC

Distribution of antecedent type was comparable between MTS + NTC and MTS - NTC. (Febrile seizure:- 72.50% vs 85% respectively, Febrile status:- 5% vs 0% respectively, Head trauma:- 0% vs 5% respectively, Meconium aspiration:- 2.50% vs 0% respectively, Meningoencephalitis:- 7.50% vs 5% respectively, Perinatal hypoxia:- 12.50% vs 5% respectively) (p value=0.623).(Table 4.17, figure 4.17).

Table 4.18: Comparison of type of aura between MTS + NTC and MTS - NTC

Type of aura	MTS + NTC(n=63)	MTS - NTC(n=37)	Total	P value
Fear	25 (39.68%)	12 (32.43%)	37 (37%)	0.468†
Anger	1 (1.59%)	0 (0%)	1 (1%)	1*
Experiential (Deja vu, Jamis vu),Visual	5 (7.94%)	5 (13.51%)	10 (10%)	0.369†
Auditory	4 (6.35%)	0 (0%)	4 (4%)	0.294*
Vertigenous sensation	6 (9.52%)	0 (0%)	6 (6%)	0.082*
Visual	6 (9.52%)	0 (0%)	6 (6%)	0.082*
Foul-smell	0 (0%)	1 (2.70%)	1 (1%)	0.37*
Nausea	1 (1.59%)	1 (2.70%)	2 (2%)	1*
Retching	1 (1.59%)	0 (0%)	1 (1%)	1*
Epigastric sensation	11 (17.46%)	11 (29.73%)	22 (22%)	0.153†
Cephalic sensation	6 (9.52%)	1 (2.70%)	7 (7%)	0.255*
Palpitations	1 (1.59%)	1 (2.70%)	2 (2%)	1*
Tiredness	1 (1.59%)	0 (0%)	1 (1%)	1*
Cold sensation	2 (3.17%)	0 (0%)	2 (2%)	0.529*
Undescribable	2 (3.17%)	1 (2.70%)	3 (3%)	1*
Premonition	1 (1.59%)	0 (0%)	1 (1%)	1*
Chest discomfort	0 (0%)	1 (2.70%)	1 (1%)	0.37*

*** Fisher's exact test, † Chi square test**

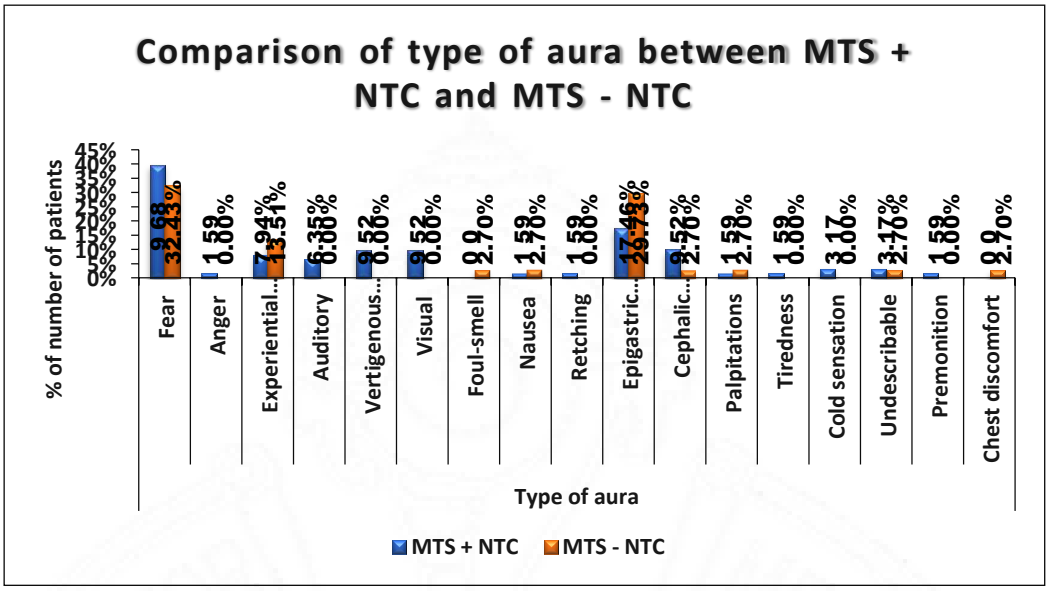


Figure 4.18: Comparison of type of aura between MTS + NTC and MTS - NTC

Distribution of type of aura was comparable between MTS + NTC and MTS - NTC. (Fear:- 39.68% vs 32.43% respectively (p value=0.468), Anger:- 1.59% vs 0% respectively (p value=1), Experiential (Deja vu, Jamis vu),Visual:- 7.94% vs 13.51% respectively (p value=0.369), Auditory:- 6.35% vs 0% respectively (p value=0.294), Vertigenous sensation:- 9.52% vs 0% respectively (p value=0.082), Visual:- 9.52% vs 0% respectively (p value=0.082), Foul-smell:- 0% vs 2.70% respectively (p value=0.37), Nausea:- 1.59% vs 2.70% respectively (p value=1), Retching:- 1.59% vs 0% respectively (p value=1), Epigastric sensation:- 17.46% vs 29.73% respectively (p value=0.153), Cephalic sensation:- 9.52% vs 2.70% respectively (p value=0.255), Palpitations:- 1.59% vs 2.70% respectively (p value=1), Tiredness:- 1.59% vs 0% respectively (p value=1), Cold sensation:- 3.17% vs 0% respectively (p value=0.529), Undescribable:- 3.17% vs 2.70% respectively (p value=1), Premonition:- 1.59% vs 0% respectively (p value=1), Chest discomfort:- 0% vs 2.70% respectively (p value=0.37)).(Table 4.18, figure 4.18).

Table 4.19: Comparison of type of sensory symptoms between MTS + NTC and MTS - NTC

Type of sensory symptoms	MTS + NTC(n=63)	MTS - NTC(n=37)	Total	P value
Auditory	4 (6.35%)	0 (0%)	4 (4%)	0.294*
Vertigenous sensation	6 (9.52%)	0 (0%)	6 (6%)	0.082*
Visual	4 (6.35%)	0 (0%)	4 (4%)	0.294*
Foul-smell	0 (0%)	1 (2.70%)	1 (1%)	0.37*
Cold sensation	1 (1.59%)	0 (0%)	1 (1%)	1*

* **Fisher's exact test**

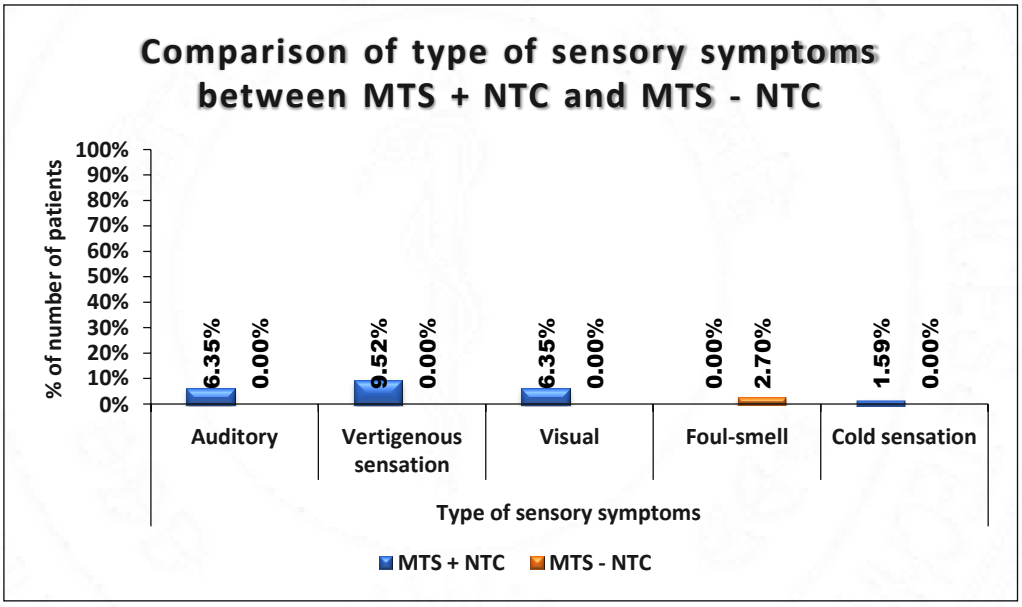


Figure 4.19: Comparison of type of sensory symptoms between MTS + NTC and MTS - NTC

Distribution of type of sensory symptoms was comparable between MTS + NTC and MTS - NTC. (Auditory:- 6.35% vs 0% respectively (p value=0.294), Vertigenous sensation:- 9.52% vs 0% respectively (p value=0.082), Visual:- 6.35% vs 0%

respectively (p value=0.294), Foul-smell:- 0% vs 2.70% respectively (p value=0.37), Cold sensation:- 1.59% vs 0% respectively (p value=1)).(Table 4.19, figure 4.19).

Table 4.20: Comparison of type of motor symptoms between MTS + NTC and MTS - NTC

Type of motor symptoms	MTS + NTC(n=34)	MTS - NTC(n=25)	Total	P value
Post-ictal todds	2 (5.88%)	0 (0%)	2 (3.39%)	0.503*
Inability to move	1 (2.94%)	0 (0%)	1 (1.69%)	1*
Head and eye adversion	8 (23.53%)	3 (12%)	11 (18.64%)	0.325*
Upper limb posturing	6 (17.65%)	7 (28%)	13 (22.03%)	0.343†
Lower limb posturing	0 (0%)	0 (0%)	0 (0%)	NA
Upper and lower limb posturing	3 (8.82%)	0 (0%)	3 (5.08%)	0.255*
Hemiclonic jerks	3 (8.82%)	2 (8%)	5 (8.47%)	1*
Dystonic posturing of upper limb	2 (5.88%)	1 (4%)	3 (5.08%)	1*

*** Fisher's exact test, † Chi square test**

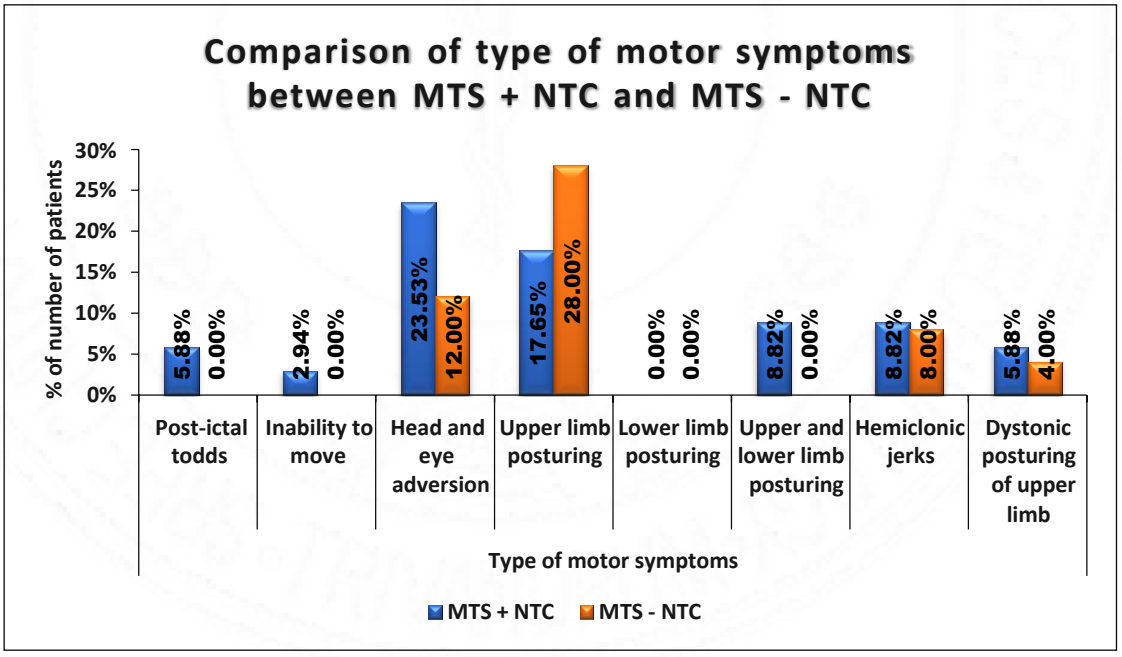


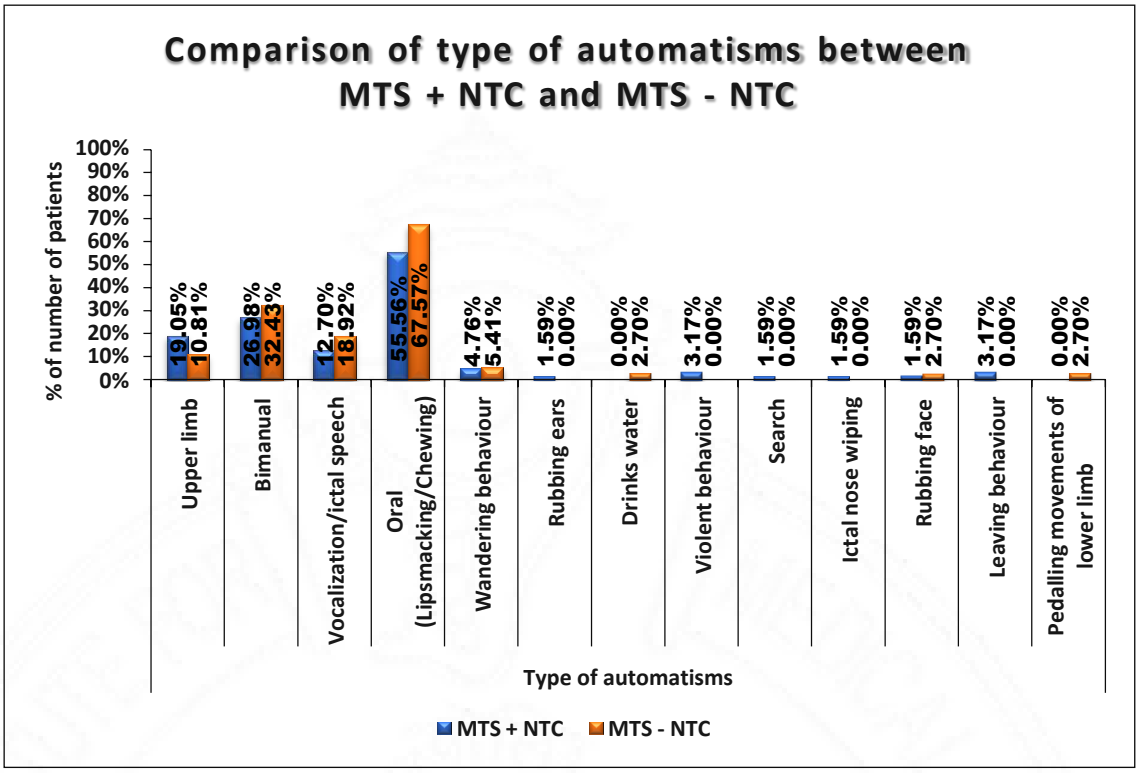
Figure 4.20: Comparison of type of motor symptoms between MTS + NTC and MTS - NTC

Distribution of type of motor symptoms was comparable between MTS + NTC and MTS - NTC. (Post-ictal todds:- 5.88% vs 0% respectively (p value=0.503), Inability to move:- 2.94% vs 0% respectively (p value=1), Head and eye adversion:- 23.53% vs 12% respectively (p value=0.325), Upper limb posturing:- 17.65% vs 28% respectively (p value=0.343), Lower limb posturing:- 0% vs 0% respectively, Upper and lower limb posturing:- 8.82% vs 0% respectively (p value=0.255), Hemiclonic jerks:- 8.82% vs 8% respectively (p value=1), Dystonic posturing of upper limb:- 5.88% vs 4% respectively (p value=1)) (Table 4.20, figure 4.20).

Table 4.21: Comparison of type of automatisms between MTS + NTC and MTS - NTC

Type of automatisms	MTS + NTC(n=63)	MTS - NTC(n=37)	Total	P value
Upper limb	12 (19.05%)	4 (10.81%)	16 (16%)	0.399*
Bimanual	17 (26.98%)	12 (32.43%)	29 (29%)	0.562†
Vocalization/ictal speech	8 (12.70%)	7 (18.92%)	15 (15%)	0.4†
Oral (Lipsmacking/Chewing)	35 (55.56%)	25 (67.57%)	60 (60%)	0.236†
Wandering behaviour	3 (4.76%)	2 (5.41%)	5 (5%)	1*
Rubbing ears	1 (1.59%)	0 (0%)	1 (1%)	1*
Drinks water	0 (0%)	1 (2.70%)	1 (1%)	0.37*
Violent behaviour	2 (3.17%)	0 (0%)	2 (2%)	0.529*
Search	1 (1.59%)	0 (0%)	1 (1%)	1*
Ictal nose wiping	1 (1.59%)	0 (0%)	1 (1%)	1*
Rubbing face	1 (1.59%)	1 (2.70%)	2 (2%)	1*
Leaving behaviour	2 (3.17%)	0 (0%)	2 (2%)	0.529*
Pedalling movements of lower limb	0 (0%)	1 (2.70%)	1 (1%)	0.37*

*** Fisher's exact test, † Chi square test**



<u>Figure 4.21:</u> Comparison of type of automatisms between MTS + NTC and MTS - NTC

Distribution of type of automatisms was comparable between MTS + NTC and MTS - NTC. (Upper limb:- 19.05% vs 10.81% respectively (p value=0.399), Bimanual:- 26.98% vs 32.43% respectively (p value=0.562), Vocalization/ictal speech:- 12.70% vs 18.92% respectively (p value=0.4), Oral (Lipsmacking/Chewing):- 55.56% vs 67.57% respectively (p value=0.236), Wandering behaviour:- 4.76% vs 5.41% respectively (p value=1), Rubbing ears:- 1.59% vs 0% respectively (p value=1), Drinks water:- 0% vs 2.70% respectively (p value=0.37), Violent behaviour:- 3.17% vs 0% respectively (p value=0.529), Search:- 1.59% vs 0% respectively (p value=1), Ictal nose wiping:- 1.59% vs 0% respectively (p value=1), Rubbing face:- 1.59% vs 2.70% respectively (p value=1), Leaving behaviour:- 3.17% vs 0% respectively (p value=0.529), Pedalling movements of lower limb:- 0% vs 2.70% respectively (p value=0.37)).(Table 4.21, figure 4.21).

Table 4.22: Comparison of type of autonomic symptoms between MTS + NTC and MTS - NTC

Type of autonomic symptoms	MTS + NTC(n=63)	MTS - NTC(n=37)	Total	P value
Piloerection	2 (3.17%)	0 (0%)	2 (2%)	0.529*
Palpitations	2 (3.17%)	1 (2.70%)	3 (3%)	1*
Nausea	0 (0%)	1 (2.70%)	1 (1%)	0.37*
Vomiting, Retching	3 (4.76%)	1 (2.70%)	4 (4%)	1*
Salivation	1 (1.59%)	2 (5.41%)	3 (3%)	0.553*
Epigastric sensation	11 (17.46%)	11 (29.73%)	22 (22%)	0.153†
Abdominal pain	1 (1.59%)	0 (0%)	1 (1%)	1*
Post-ictal cough	0 (0%)	1 (2.70%)	1 (1%)	0.37*
Ictal cough	1 (1.59%)	0 (0%)	1 (1%)	1*
Ictal swallow	1 (1.59%)	0 (0%)	1 (1%)	1*
Post-ictal sneezing	1 (1.59%)	0 (0%)	1 (1%)	1*

* **Fisher's exact test,** † **Chi square test**

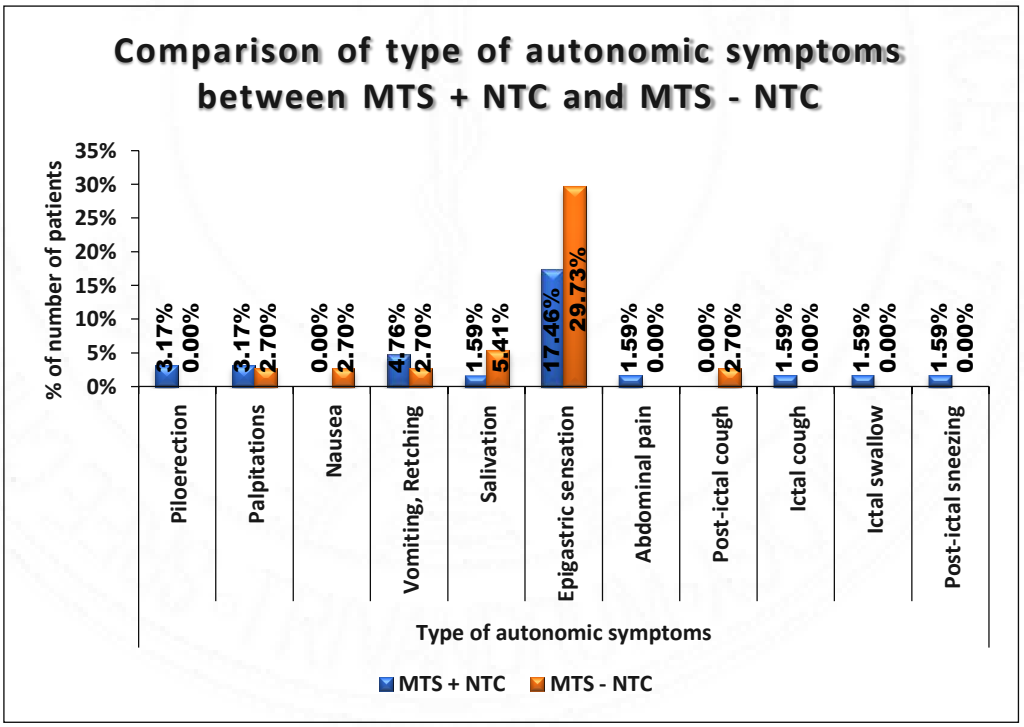


Figure 4.22: Comparison of type of autonomic symptoms between MTS + NTC and MTS - NTC

Distribution of type of autonomic symptoms was comparable between MTS + NTC and MTS - NTC. (Piloerection:- 3.17% vs 0% respectively (p value=0.529), Palpitations:- 3.17% vs 2.70% respectively (p value=1), Nausea:- 0% vs 2.70% respectively (p value=0.37), Vomiting, Retching:- 4.76% vs 2.70% respectively (p value=1), Salivation:- 1.59% vs 5.41% respectively (p value=0.553), Epigastric sensation:- 17.46% vs 29.73% respectively (p value=0.153), Abdominal pain:- 1.59% vs 0% respectively (p value=1), Post-ictal cough:- 0% vs 2.70% respectively (p value=0.37), Ictal cough:- 1.59% vs 0% respectively (p value=1), Ictal swallow:- 1.59% vs 0% respectively (p value=1), Post-ictal sneezing:- 1.59% vs 0% respectively (p value=1)).(Table 4.22, figure 4.22).

Table 4.23: Comparison of type of cognitive symptoms between MTS + NTC and MTS - NTC

Type of cognitive symptoms	MTS + NTC(n=34)	MTS - NTC(n=25)	Total	P value
Post-ictal confusion	2 (5.88%)	6 (24%)	8 (13.56%)	0.061*
Post-ictal amnesia	9 (26.47%)	4 (16%)	13 (22.03%)	0.526*
Post-ictal dysphagia	1 (2.94%)	0 (0%)	1 (1.69%)	1*
Experiential phenomena	2 (5.88%)	3 (12%)	5 (8.47%)	0.641*
Post-ictal aphasia	2 (5.88%)	0 (0%)	2 (3.39%)	0.503*

* **Fisher's exact test**

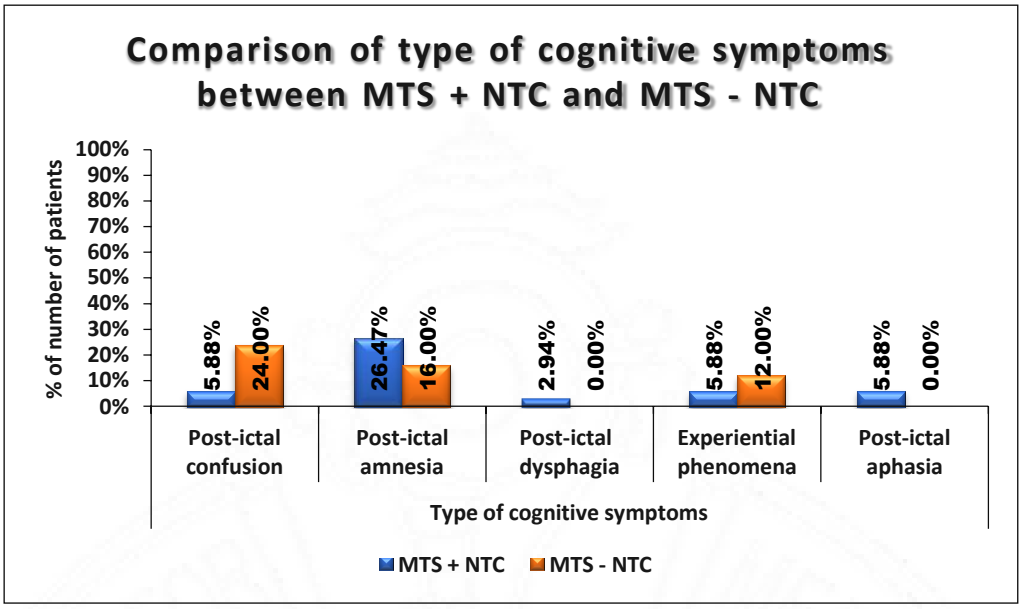


Figure 4.23: Comparison of type of cognitive symptoms between MTS + NTC and MTS - NTC

Distribution of type of cognitive symptoms was comparable between MTS + NTC and MTS - NTC. (Post-ictal confusion:- 5.88% vs 24% respectively (p value=0.061), Post-ictal amnesia:- 26.47% vs 16% respectively (p value=0.526), Post-ictal dysphagia:- 2.94% vs 0% respectively (p value=1), Experiential phenomena:- 5.88% vs 12% respectively (p value=0.641), Post-ictal aphasia:- 5.88% vs 0% respectively (p value=0.503)).(Table 4.23, figure 4.23).

Table 4.24: Comparison of type of emotional or affective symptoms between MTS + NTC and MTS - NTC

Type of emotional or affective symptoms	MTS + NTC(n=25)	MTS - NTC(n=11)	Total	P value
Anger	1 (4%)	0 (0%)	1 (2.78%)	1*
Fear	24 (96%)	11 (100%)	35 (97.22%)	
Total	25 (100%)	11 (100%)	36 (100%)	

* **Fisher's exact test**

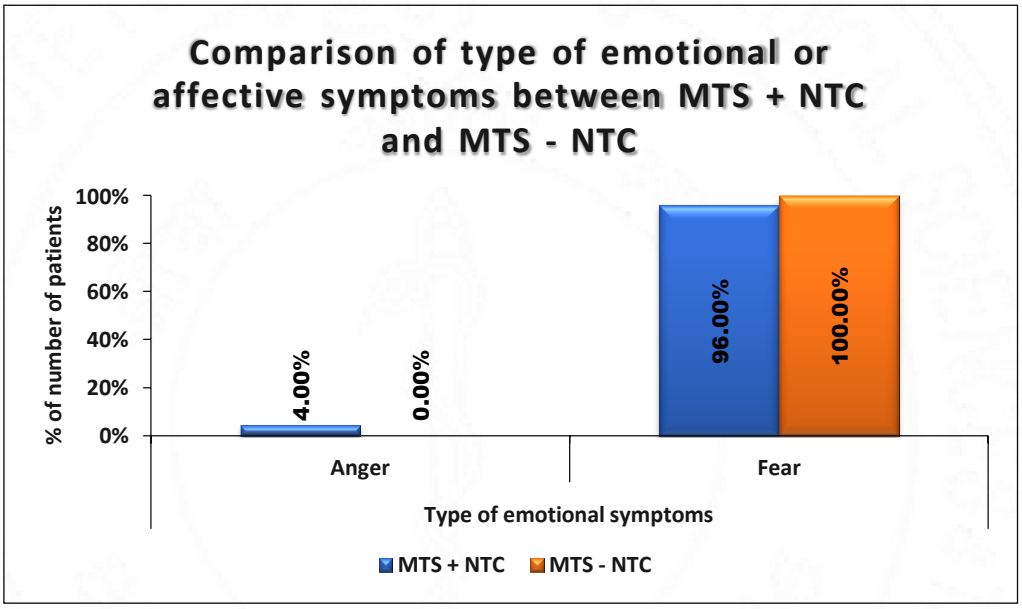


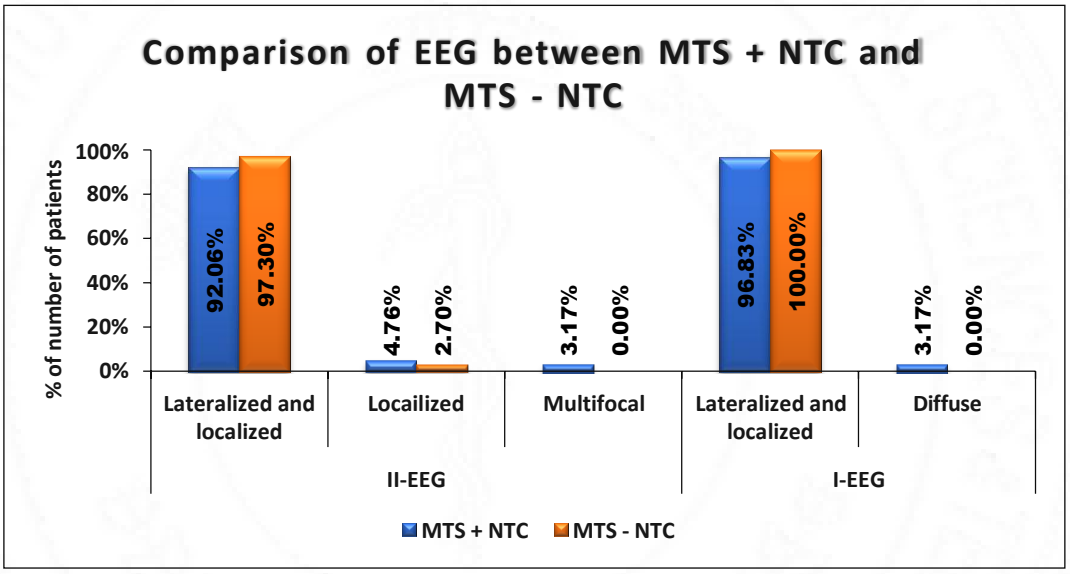
Figure 4.24: Comparison of type of emotional symptoms between MTS + NTC and MTS - NTC

Distribution of type of emotional or affective symptoms was comparable between MTS + NTC and MTS - NTC. (Anger: - 4% vs 0% respectively, Fear: - 96% vs 100% respectively) (p value=1). (Table 4.24, figure 4.24).

Table 4.25: Comparison of EEG between MTS + NTC and MTS - NTC

EEG	MTS + NTC(n=63)	MTS - NTC(n=37)	Total	P value
II-EEG				
Lateralized and localized	58 (92.06%)	36 (97.30%)	94 (94%)	0.667*
Localized	3 (4.76%)	1 (2.70%)	4 (4%)	
Multifocal	2 (3.17%)	0 (0%)	2 (2%)	
I-EEG				
Lateralized and localized	61 (96.83%)	37 (100%)	98 (98%)	0.529*
Diffuse	2 (3.17%)	0 (0%)	2 (2%)	

* **Fisher's exact test, I-EEG: Ictal EEG, II-EEG: Interictal EEG**



I-EEG: Ictal EEG, II-EEG: Interictal EEG

Figure 4.25: Comparison of EEG between MTS + NTC and MTS - NTC

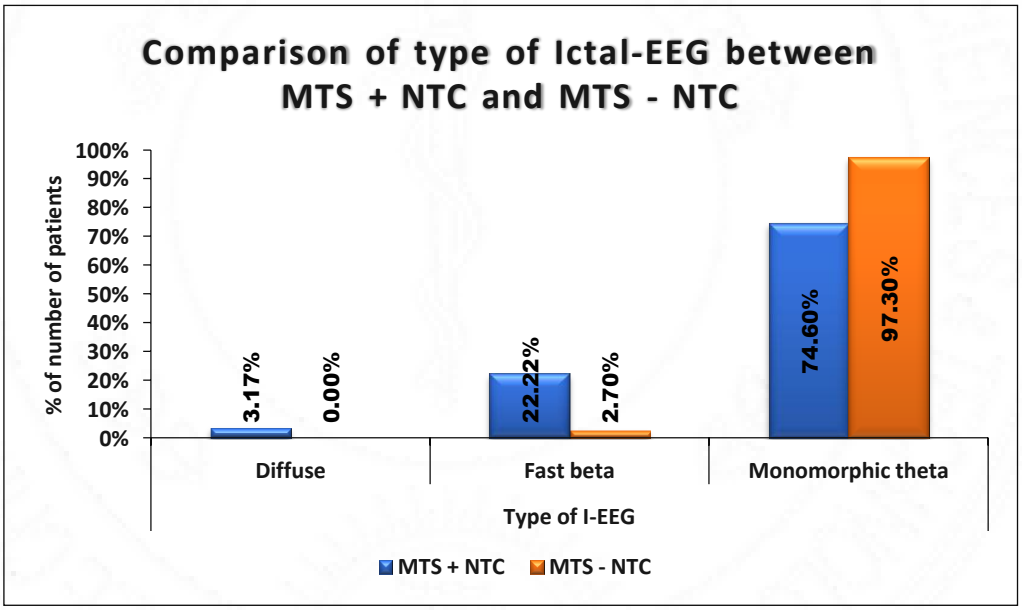
Distribution of II-EEG (Interictal-EEG) was comparable between MTS + NTC and MTS - NTC. (Lateralized and localized:- 92.06% vs 97.30% respectively, Localized:- 4.76% vs 2.70% respectively, Multifocal:- 3.17% vs 0% respectively) (p value=0.667).

Distribution of I-EEG (Ictal-EEG) was comparable between MTS + NTC and MTS - NTC. (Lateralized and localized:- 96.83% vs 100% respectively, Diffuse:- 3.17% vs 0% respectively) (p value=0.529).(Table 4.25, figure 4.25).

Table 4.26: Comparison of type of Ictal-EEG between MTS + NTC and MTS - NTC

Type of I-EEG	MTS + NTC(n=63)	MTS - NTC(n=37)	Total	P value
Diffuse	2 (3.17%)	0 (0%)	2 (2%)	**0.007***
Fast beta	14 (22.22%)	1 (2.70%)	15 (15%)	
Monomorphic theta	47 (74.60%)	36 (97.30%)	83 (83%)	
Total	63 (100%)	37 (100%)	100 (100%)	

*** Fisher's exact test, Ictal-EEG: Ictal EEG**



I-EEG: Ictal EEG

Figure 4.26: Comparison of type of I-EEG between MTS + NTC and MTS - NTC

Proportion of patients with type of I-EEG:- diffuse, fast beta was significantly higher in MTS + NTC as compared to MTS - NTC. (Diffuse:- 3.17% vs 0% respectively,

Fast beta:- 22.22% vs 2.70% respectively). Proportion of patients with type of I-EEG:- monomorphic theta was significantly lower in MTS + NTC as compared to MTS - NTC. (Monomorphic theta:- 74.60% vs 97.30% respectively). (p value=0.007) (Table 4.26, figure 4.26).

Table 4.27: Comparison of clinico-electrophysiological impression between MTS + NTC and MTS - NTC

Clinico-electrophysiological impression	MTS + NTC(n=63)	MTS - NTC(n=37)	Total	P value
Neocortical seizures absent	21 (33.33%)	32 (86.49%)	53 (53%)	<.0001†
Neocortical seizures present	42 (66.67%)	5 (13.51%)	47 (47%)	
Total	63 (100%)	37 (100%)	100 (100%)	

† **Chi square test**

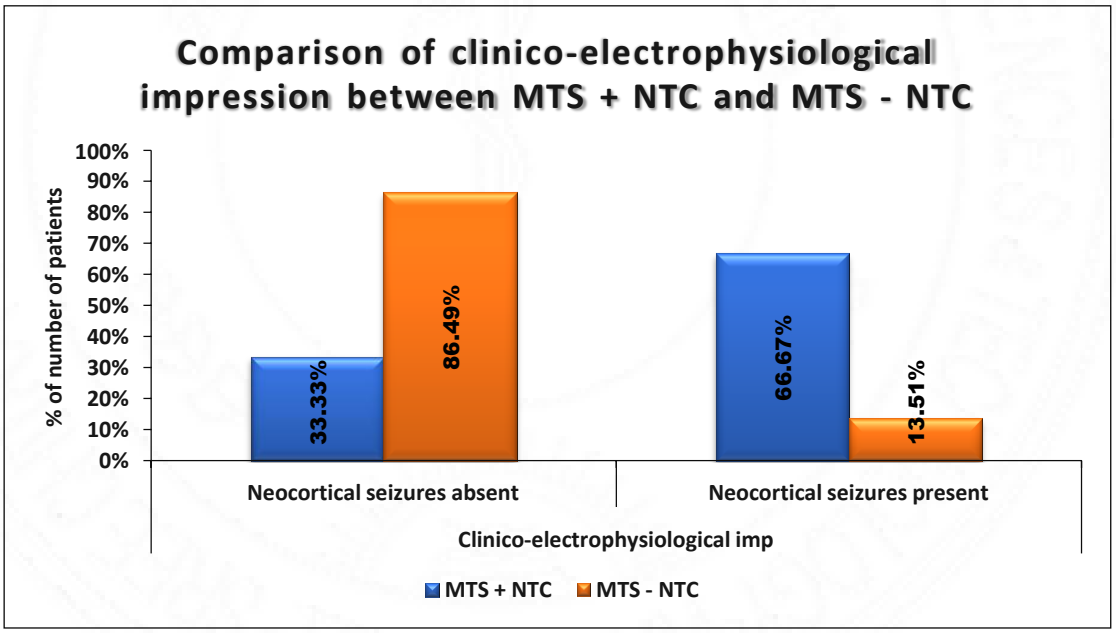


Figure 4.27: Comparison of clinico-electrophysiological impression between MTS + NTC and MTS - NTC

Proportion of patients with neocortical seizures was significantly higher in MTS + NTC as compared to MTS - NTC. (66.67% vs 13.51% respectively). (p value <0.0001) (Table 4.27, figure 4.27).

Table 4.28: Comparison of pathology side between MTS + NTC and MTS - NTC.

Pathology side	MTS + NTC(n=63)	MTS - NTC(n=37)	Total	P value
Left	40 (63.49%)	15 (40.54%)	55 (55%)	**0.026**†
Right	23 (36.51%)	22 (59.46%)	45 (45%)	
Total	63 (100%)	37 (100%)	100 (100%)	

† **Chi square test**

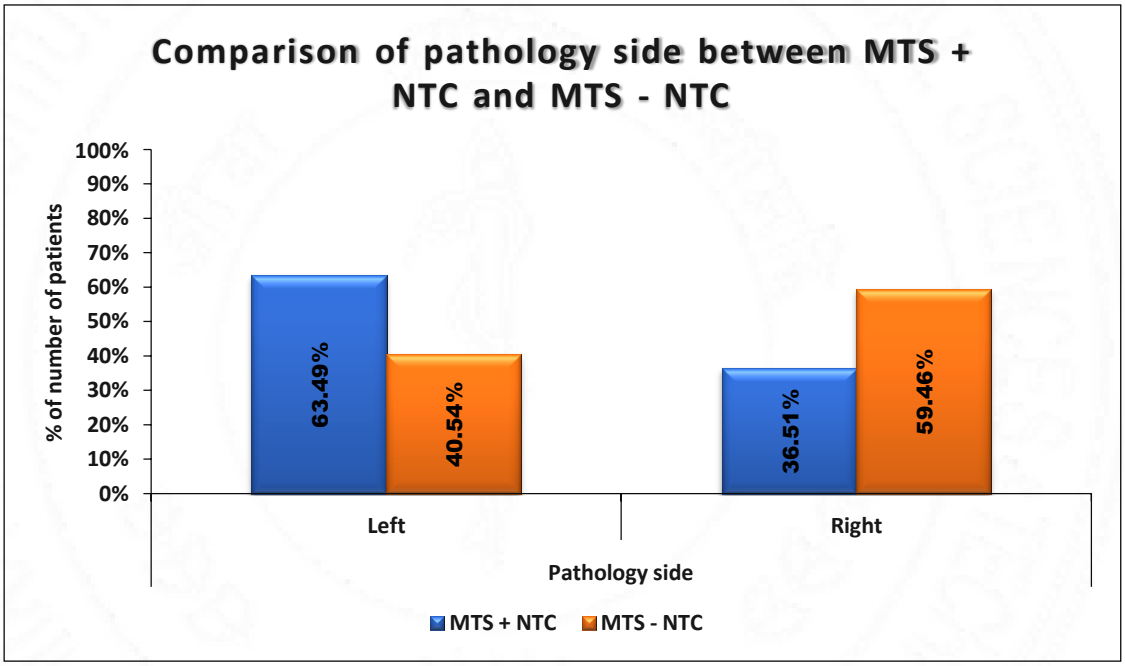


Figure 4.28: Comparison of pathology side between MTS + NTC and MTS - NTC

Proportion of patients with pathology side:- left was significantly higher in MTS + NTC as compared to MTS - NTC. (Left:- 63.49% vs 40.54% respectively). Proportion of patients with pathology side:- right was significantly lower in MTS + NTC as

compared to MTS - NTC. (Right:- 36.51% vs 59.46% respectively). (p value=0.026) (Table 4.28, figure 4.28).

Table 4.29: Comparison of ASL (Hippocampus) between MTS + NTC and MTS - NTC

ASL (Hippo)	MTS + NTC(n=63)	MTS - NTC(n=37)	Total	P value
ASL abnormality absent	3 (4.76%)	0 (0%)	3 (3%)	0.294*
ASL abnormality present	60 (95.24%)	37 (100%)	97 (97%)	
Total	63 (100%)	37 (100%)	100 (100%)	

* **Fisher's exact test**

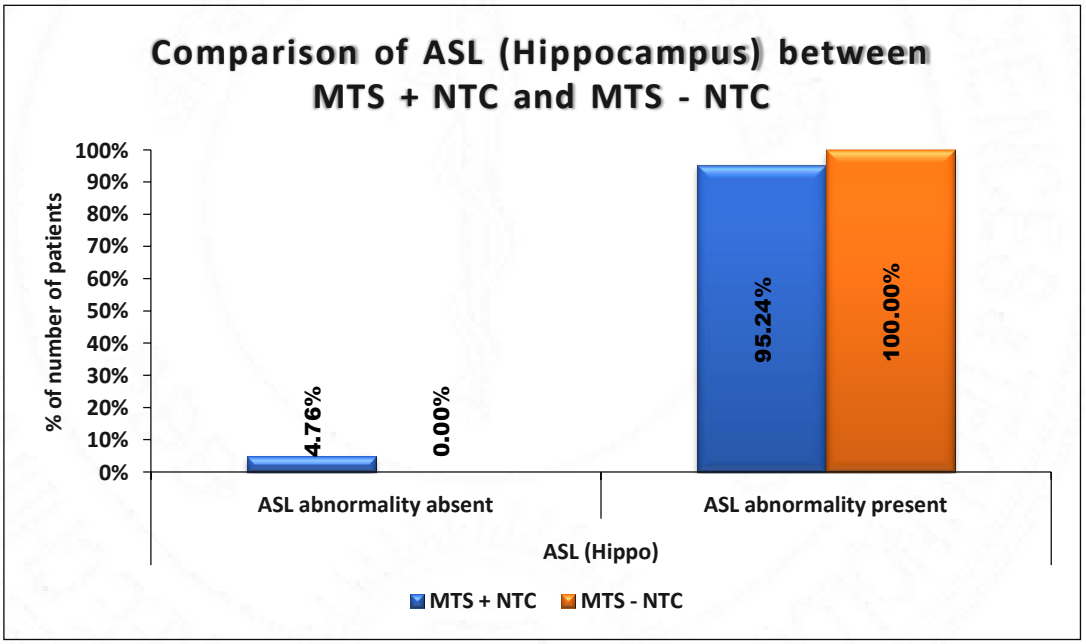


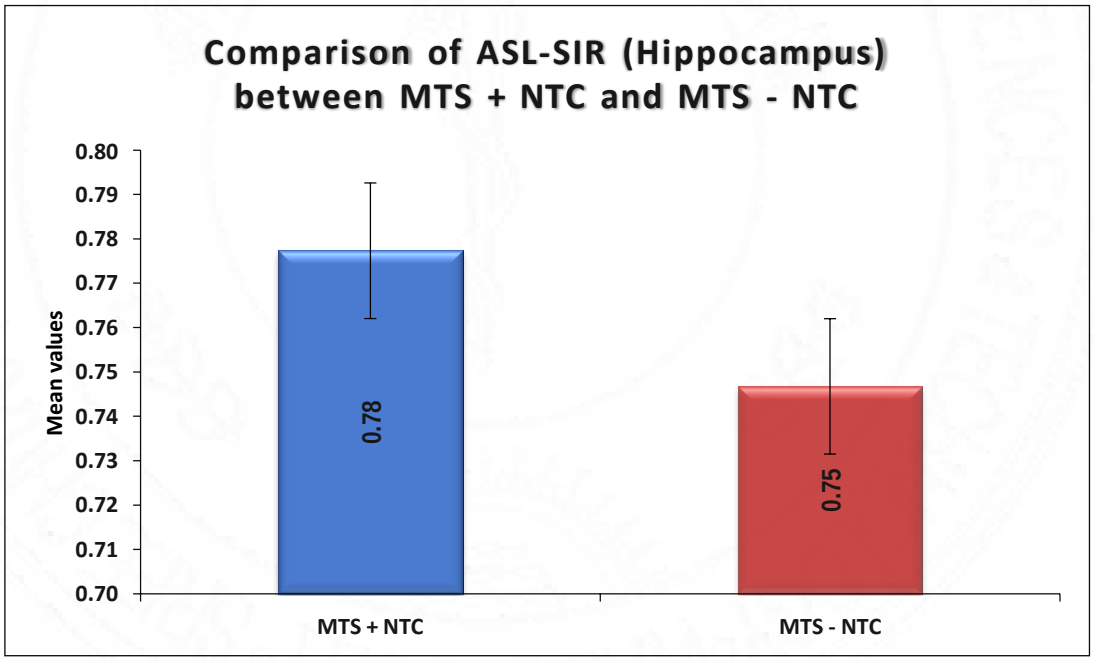
Figure 4.29: Comparison of ASL (Hippocampus) between MTS + NTC and MTS - NTC

Distribution of ASL (Hippocampus) was comparable between MTS + NTC and MTS - NTC. (ASL abnormality absent:- 4.76% vs 0% respectively, ASL abnormality present:- 95.24% vs 100% respectively) (p value=0.294).(Table 4.29, figure 4.29).

Table 4.30: Comparison of ASL-SIR (Hippocampus) between MTS + NTC and MTS - NTC

ASL-SIR (Hippocampus)	MTS + NTC(n=63)	MTS - NTC(n=37)	Total	P value
Mean ± SD	0.78 ± 0.16	0.75 ± 0.09	0.77 ± 0.14	0.286‡
Median(25th-75th percentile)	0.74(0.7-0.8)	0.74(0.68-0.78)	0.74(0.698-0.78)	
Range	0.6-1.54	0.6-1.2	0.6-1.54	

‡ **Independent t test, ASL-SIR: ASL-signal intensity ratio**



ASL-SIR: ASL-signal intensity ratio

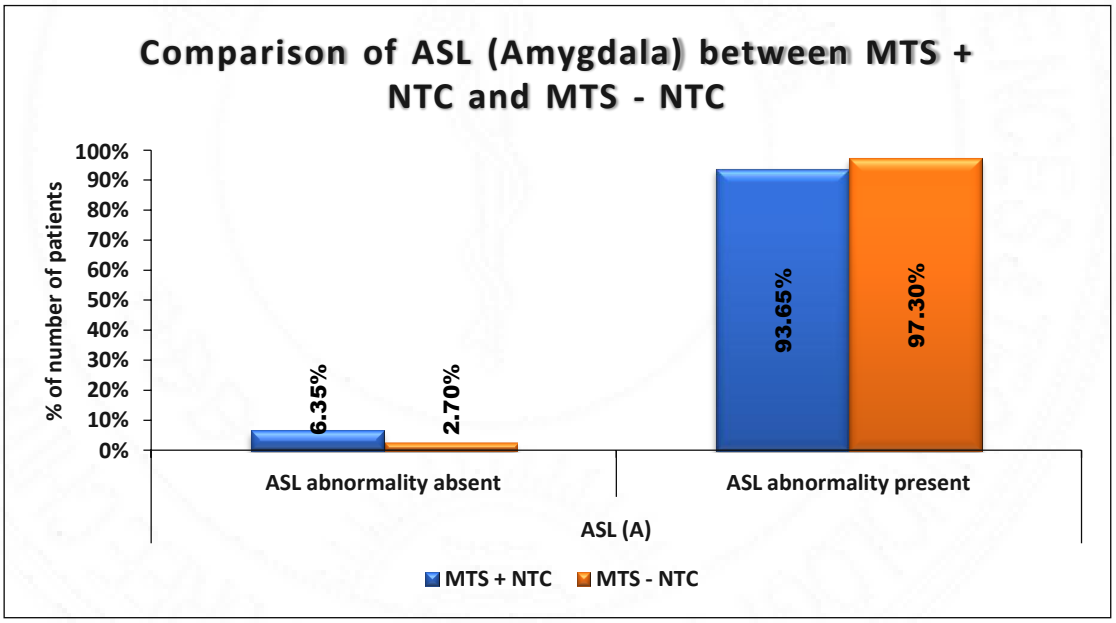
Figure 4.30: Comparison of ASL-SIR (Hippocampus) between MTS + NTC and MTS - NTC

Mean ± SD of ASL-SIR (Hippo) in MTS + NTC was 0.78 ± 0.16 and in MTS - NTC was 0.75 ± 0.09 with no significant difference between them. (p value=0.286) (Table 4.30, figure 4.30).

Table 4.31: Comparison of ASL (Amygdala) between MTS + NTC and MTS - NTC

ASL (Amygdala)	MTS + NTC(n=63)	MTS - NTC(n=37)	Total	P value
ASL abnormality absent	4 (6.35%)	1 (2.70%)	5 (5%)	0.649*
ASL abnormality present	59 (93.65%)	36 (97.30%)	95 (95%)	
Total	63 (100%)	37 (100%)	100 (100%)	

* **Fisher's exact test**



ASL (A): ASL (Amygdala)

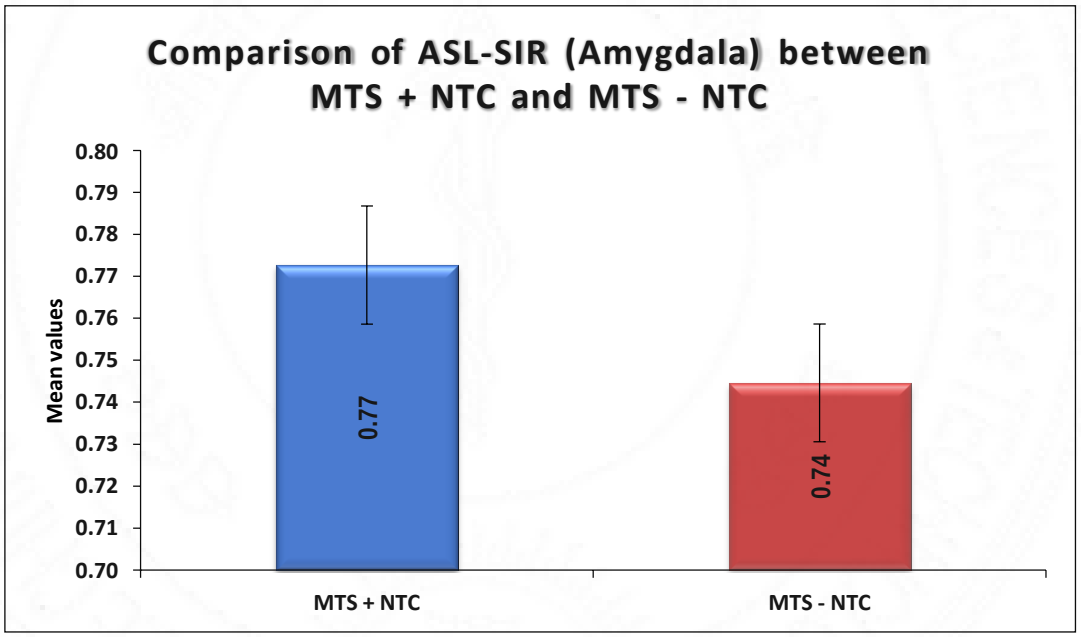
Figure 4.31: Comparison of ASL (Amygdala) between MTS + NTC and MTS - NTC

Distribution of ASL (Amygdala) was comparable between MTS + NTC and MTS - NTC. (ASL abnormality absent:- 6.35% vs 2.70% respectively, ASL abnormality present:- 93.65% vs 97.30% respectively) (p value=0.649).(Table 4.31, figure 4.31).

Table 4.32: Comparison of ASL-SIR (Amygdala) between MTS + NTC and MTS - NTC.

ASL-SIR (Amygdala)	MTS + NTC(n=63)	MTS - NTC(n=37)	Total	P value
Mean ± SD	0.77 ± 0.15	0.74 ± 0.11	0.76 ± 0.13	0.316‡
Median(25th - 75th percentile)	0.76(0.68-0.8)	0.74(0.68-0.78)	0.74(0.68-0.8)	
Range	0.6-1.6	0.62-1.2	0.6-1.6	

‡ **Independent t test, ASL-SIR: ASL-signal intensity ratio**



ASL-SIR: ASL-signal intensity ratio

Figure 4.32: Comparison of ASL-SIR (Amygdala) between MTS + NTC and MTS - NTC.

Mean ± SD of ASL-SIR (Amygdala) in MTS + NTC was 0.77 ± 0.15 and in MTS - NTC was 0.74 ± 0.11 with no significant difference between them. (p value=0.316) (Table 4.32, figure 4.32).

Table 4.33: Comparison of ASL (Anterior temporal lobe) between MTS + NTC and MTS - NTC.

ASL (Anterior temporal lobe)	MTS + NTC(n=63)	MTS - NTC(n=37)	Total	P value
ASL abnormality absent	6 (9.5%)	26 (70.3%)	32 (32%)	<.00001†
ASL abnormality present	57 (90.5%)	11 (29.7%)	68 (68%)	
Total	63 (100%)	37 (100%)	100 (100%)	

† **Chi square test**

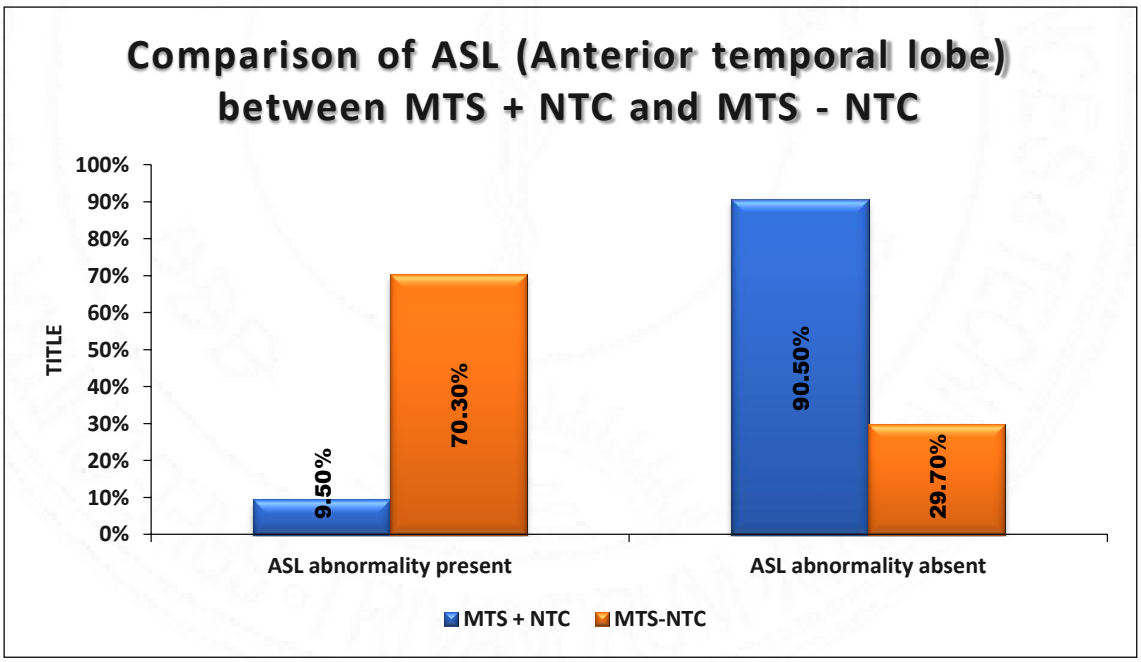


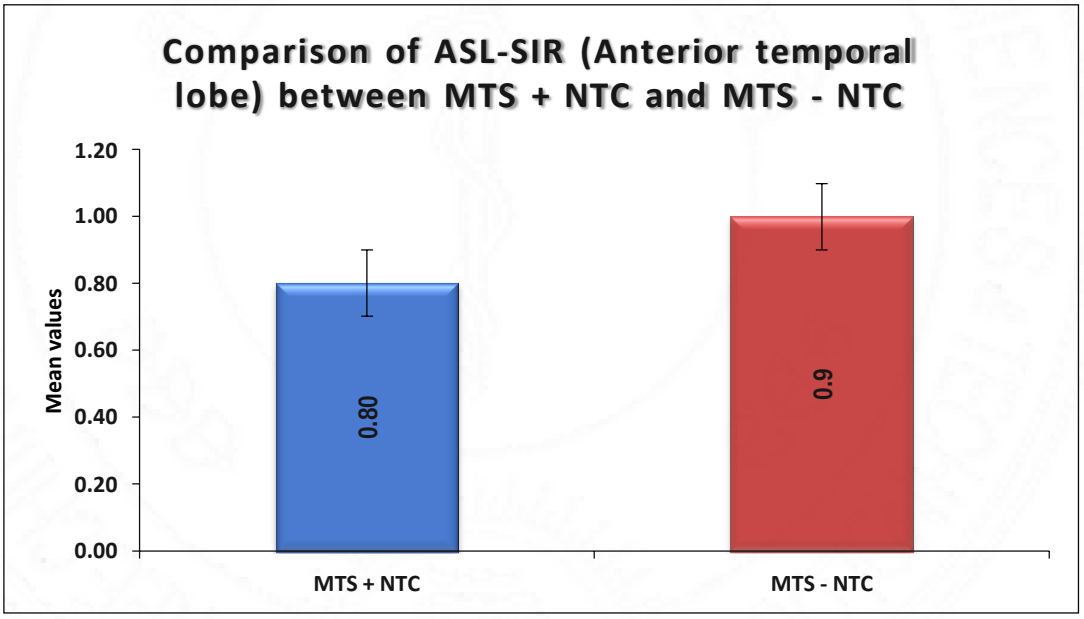
Figure 4.33: Comparison of ASL (Anterior temporal lobe) between MTS + NTC and MTS - NTC

Abnormality on ASL in the anterior temporal lobe was present in 90.5% of the patients in MTS + NTC group and in 29.7 % of the patients in the MTS – NTC group and this difference was statistically significant (p value <.00001) (Table 4.33, Figure 4.33).

Table 4.34: Comparison of ASL-SIR (Anterior temporal lobe) between MTS + NTC and MTS - NTC.

ASL-SIR (Anterior temporal lobe)	MTS+NTC (n=63)	MTS-NTC (n=37)	Total	P value
Mean ± SD	0.8 ± 0.15	0.9 ± 0.14	0.83 ± 0.15	**<.0001**‡
Median (25^{th} - 75^{th} percentile)	0.78 (0.7-0.8)	0.98 (0.78-1.01)	0.8 (0.72-0.98)	
Range	0.62-1.7	0.6-1.02	0.6-1.7	

‡ **Independent t test, ASL-SIR: ASL-signal intensity ratio**



ASL-SIR: ASL-signal intensity ratio

Figure 4.34: Comparison of ASL-SIR (Anterior temporal lobe) between MTS + NTC and MTS - NTC.

Mean ± SD of ASL-SIR (anterior temporal lobe) in MTS - NTC was 0.9 ± 0.14 which was significantly higher as compared to MTS + NTC (0.8 ± 0.15). (p value <.0001) (Table 4.34, figure 4.34).

Table 4.35: Comparison of ASL-SIR (Temporal neocortex) between MTS + NTC and MTS - NTC.

ASL-SIR (Temporal neocortex)	MTS + NTC(n=63)	MTS - NTC(n=37)	Total	P value
Mean ± SD	0.8 ± 0.17	1 ± 0.04	0.87 ± 0.16	**<.0001‡**
Median (25^{th} - 75^{th} percentile)	0.75(0.68-0.905)	1.01(0.98-1.01)	0.93(0.72-1.01)	
Range	0.6-1.3	0.9-1.1	0.6-1.3	

‡ Independent t test, ASL-SIR: ASL-signal intensity ratio

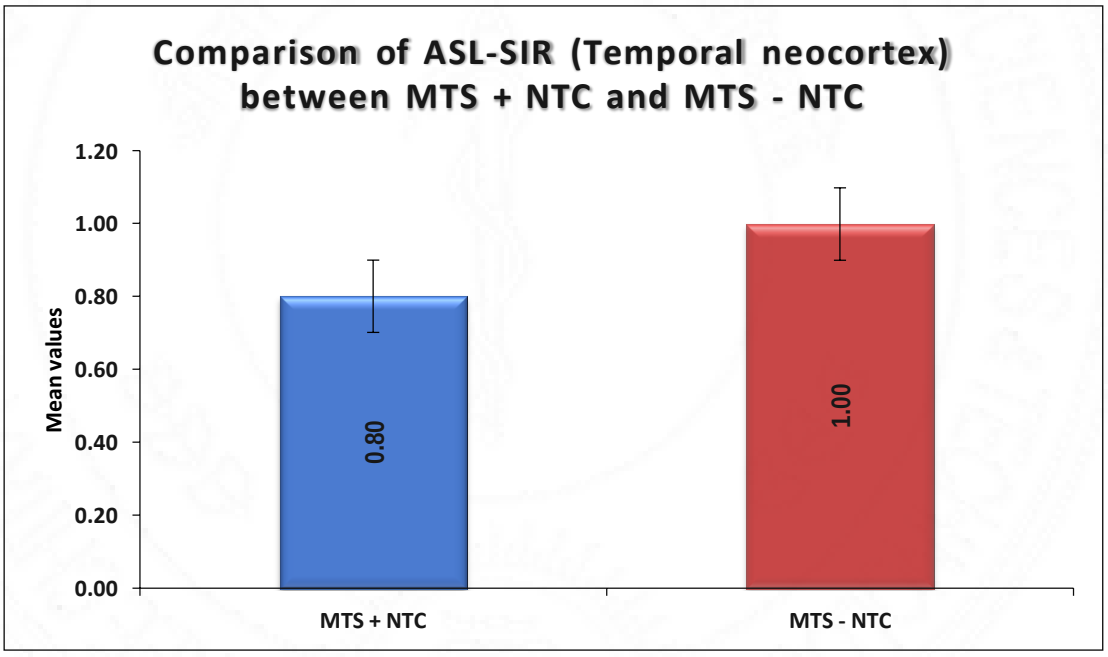


Figure 4.35: Comparison of ASL-SIR (Temporal neocortex) between MTS + NTC and MTS - NTC.

Mean ± SD of ASL-SIR (Temporal neocortex) in MTS - NTC was 1 ± 0.04 which was significantly higher as compared to MTS + NTC (0.8 ± 0.17).(p value <.0001) (Table 4.35, figure 4.35).

Table 4.36: Comparison of histopathological findings between MTS + NTC and MTS - NTC.

Histopathological findings	MTS + NTC(n=63)	MTS - NTC(n=37)	Total	P value
Hippocampus- neuN (type of HS)				
Probable HS	3 (4.76%)	2 (5.41%)	5 (5%)	0.937*
HS type 1	57 (90.48%)	32 (86.49%)	89 (89%)	
HS type 2	2 (3.17%)	2 (5.41%)	4 (4%)	
HS type 3	1 (1.59%)	1 (2.70%)	2 (2%)	
Hippocampus- astrogliosis				
Moderate	11 (17.46%)	5 (13.51%)	16 (16%)	0.603†
Severe	52 (82.54%)	32 (86.49%)	84 (84%)	
Temporal lobe- LFB- grey-white bluring				
Absent	38 (60.32%)	22 (59.46%)	60 (60%)	0.933†
Present	25 (39.68%)	15 (40.54%)	40 (40%)	
Temporal lobe- FCD				
Absent	58 (92.06%)	36 (97.30%)	94 (94%)	0.408*
Present	5 (7.94%)	1 (2.70%)	6 (6%)	

*** Fisher's exact test, † Chi square test, LFB: Luxol fast blue, FCD: focal cortical dysplasia**

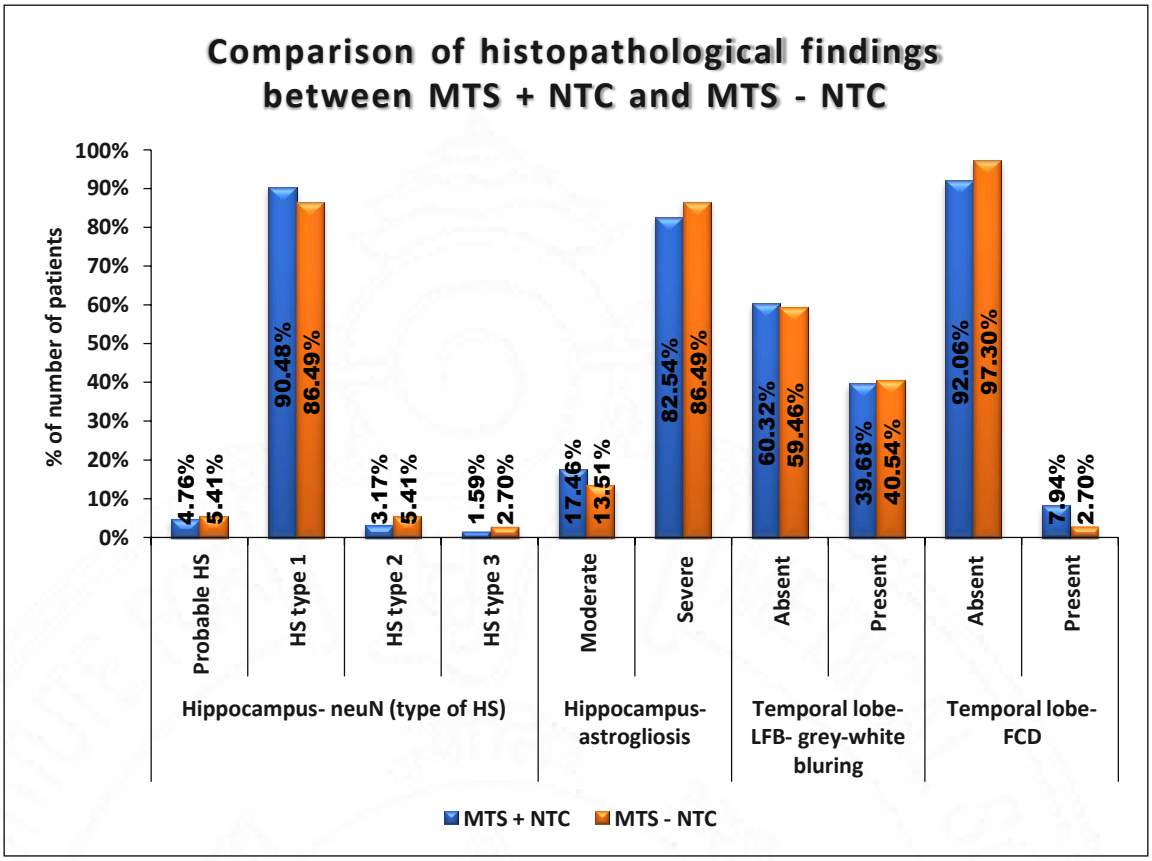


Figure 4.36: Comparison of histopathological findings between MTS + NTC and MTS - NTC.

Distribution of hippocampus- neuN (type of HS) was comparable between MTS + NTC and MTS - NTC. (Probable HS:- 4.76% vs 5.41% respectively, HS type 1:- 90.48% vs 86.49% respectively, HS type 2:- 3.17% vs 5.41% respectively, HS type 3:- 1.59% vs 2.70% respectively) (p value=0.937).

Distribution of hippocampus- astrogliosis was comparable between MTS + NTC and MTS - NTC. (Moderate:- 17.46% vs 13.51% respectively, Severe:- 82.54% vs 86.49% respectively) (p value=0.603).

All the specimens of Amygdala showed diffuse neuronal loss and astrogliosis with no specific lesion. All patients showed diffuse astrogliosis in the Temporal cortex. Distribution of temporal lobe- LFB- grey-white blurring was comparable between MTS + NTC and MTS - NTC. (Absent:- 60.32% vs 59.46% respectively, Present:- 39.68% vs 40.54% respectively) (p value=0.933).

Distribution of temporal lobe- FCD was comparable between MTS + NTC and MTS - NTC. (Absent:- 92.06% vs 97.30% respectively, Present:- 7.94% vs 2.70% respectively) (p value=0.408).(Table 4.36, figure 4.36).

Table 4.37: Association of clinico-electrophysiological impression with ASL (Temporal neocortex) in MTS + NTC.

Clinico-electrophysiological impression	ASL abnormality absent(n=13)	ASL abnormality present(n=50)	Total	P value
Neocortical seizures absent	8 (61.54%)	13 (26%)	21 (33.33%)	**0.015†**
Neocortical seizures present	5 (38.46%)	37 (74%)	42 (66.67%)	
Total	13 (100%)	50 (100%)	63 (100%)	

† **Chi square test**

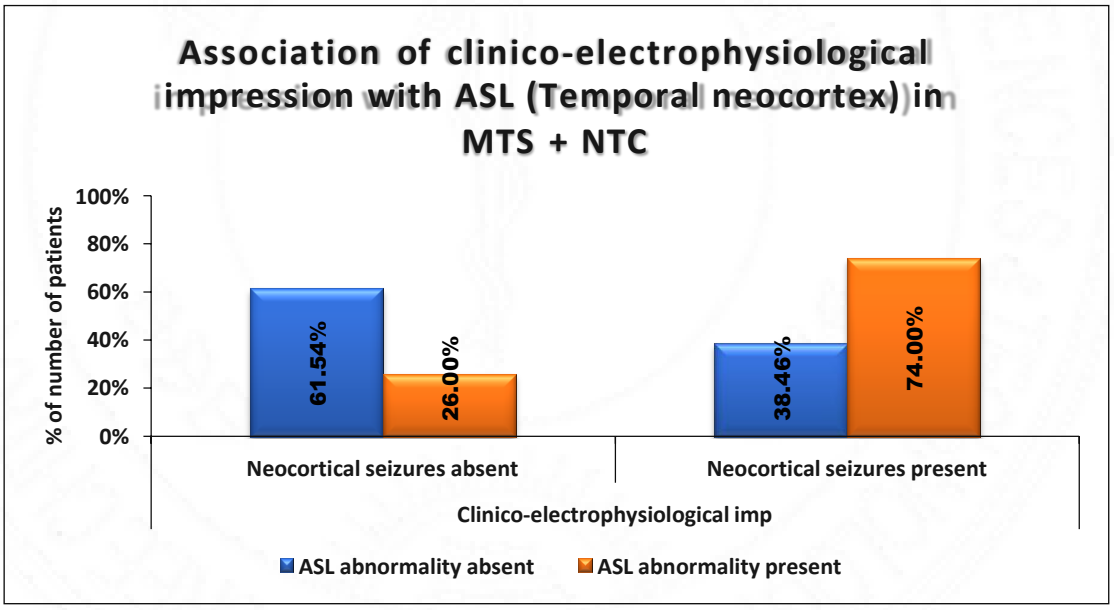


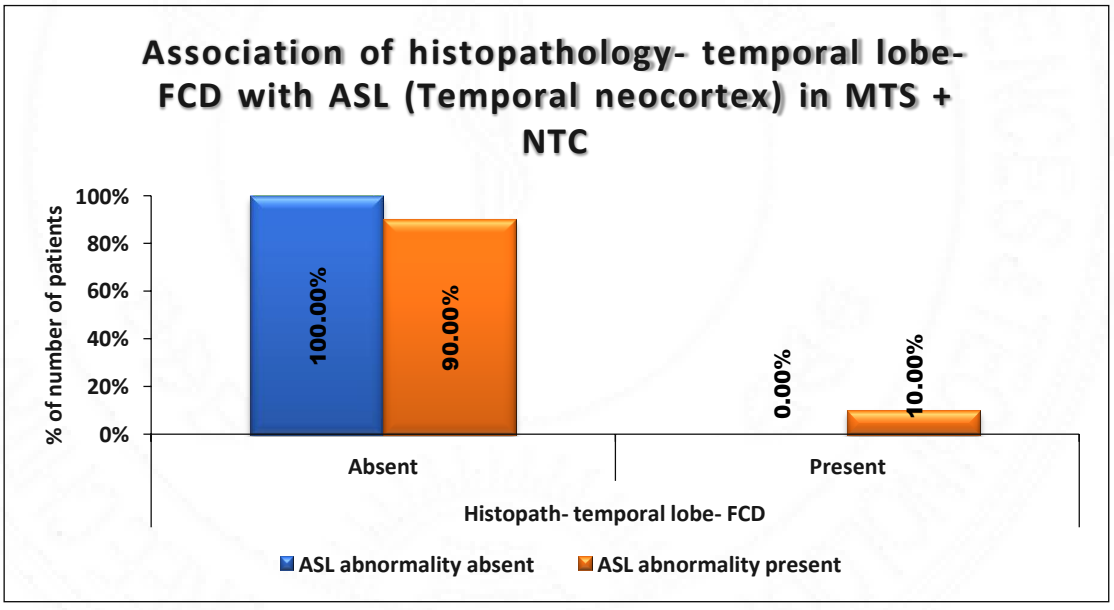
Figure 4.37: Association of clinico-electrophysiological impression with ASL (TN) in MTS + NTC.

Proportion of patients with neocortical seizures was significantly lower in without ASL abnormality as compared to with ASL abnormality. (38.46% vs 74% respectively). (p value=0.015)(Table 4.37, figure 4.37).

Table 4.38: Association of histopathology- temporal lobe- FCD with ASL (Temporal neocortex) in MTS + NTC.

Histopathology- temporal lobe- FCD	ASL abnormality absent(n=13)	ASL abnormality present(n=50)	Total	P value
Absent	13 (100%)	45 (90%)	58 (92.06%)	0.574*
Present	0 (0%)	5 (10%)	5 (7.94%)	
Total	13 (100%)	50 (100%)	63 (100%)	

* **Fisher's exact test, FCD: focal cortical dysplasia**



FCD: focal cortical dysplasia

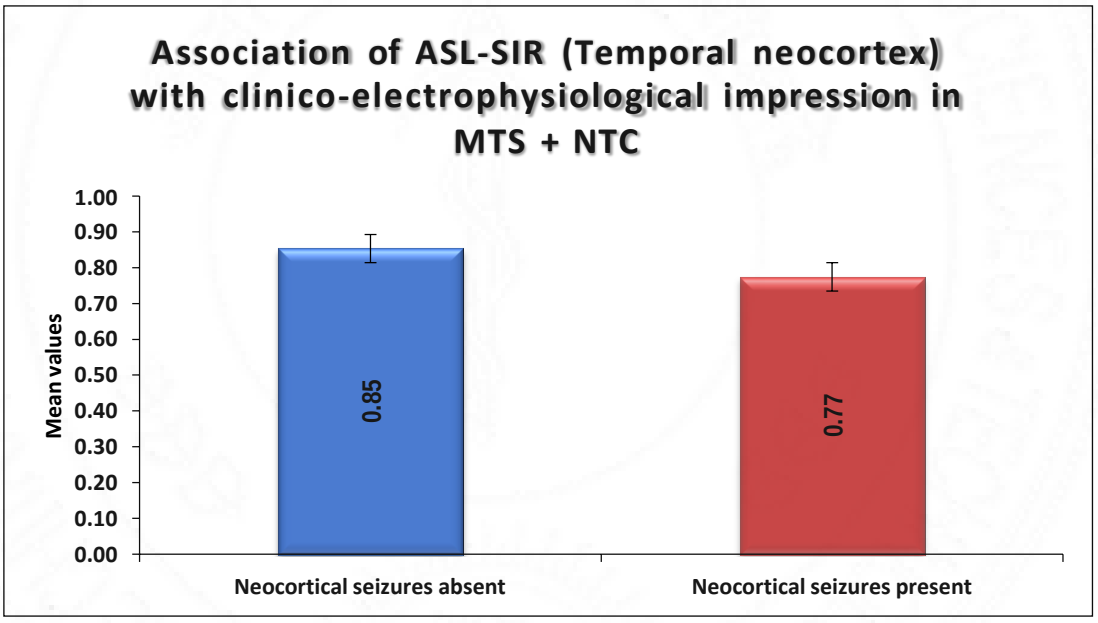
Figure 4.38: Association of histopathology- temporal lobe- FCD with ASL (Temporal neocortex) in MTS + NTC.

Distribution of histopathology- temporal lobe- FCD was comparable without and with ASL (Temporal neocortex) in MTS + NTC. (0% vs 10% respectively) (p value=0.574). (Table 4.38, figure 4.38).

Table 4.39: Association of ASL-SIR (Temporal neocortex) with clinico-electrophysiological imp in MTS + NTC.

ASL-SIR (Temporal neocortex)	Neocortical seizures absent(n=21)	Neocortical seizures present(n=42)	Total	P value
Mean ± SD	0.85 ± 0.12	0.77 ± 0.18	0.8 ± 0.17	0.075‡
Median (25^{th} - 75^{th} percentile)	0.84 (0.78-0.95)	0.72 (0.64-0.81)	0.75 (0.68-0.905)	
Range	0.66-1.1	0.6-1.3	0.6-1.3	

‡ **Independent t test, ASL-SIR: ASL-signal intensity ratio**



ASL-SIR: ASL-signal intensity ratio

Figure 4.39: Association of ASL-SIR (Temporal neocortex) with clinico-electrophysiological impression in MTS + NTC.

Mean ± SD of ASL-SIR (Temporal neocortex) in patients without neocortical seizures was 0.85 ± 0.12 and in patients with neocortical seizures was 0.77 ± 0.18 with no significant association between them. (p value=0.075) (Table 4.39, figure 4.39).

Table 4.40: Univariate logistic regression to find out significant risk factors and associations of MTS + NTC

Variable	Beta coefficient	Standard error	P value	Odds ratio	Odds ratio Lower bound (95%)	Odds ratio Upper bound (95%)
Age(years)	-0.025	0.022	0.263	0.975	0.933	1.019
Age of antecedent(years)	0.109	0.187	0.561	1.115	0.772	1.609
Age at the onset of epilepsy (A)	-0.064	0.030	0.035	0.938	0.884	0.995
Seizure frequency score	0.390	0.250	0.119	1.477	0.904	2.412
Duration of epilepsy (years)	0.021	0.024	0.375	1.021	0.975	1.070
Gender						
Female				1.000		
Male	0.314	0.415	0.449	1.369	0.607	3.087
Antecedent	0.386	0.421	0.359	1.471	0.645	3.354

On performing univariate regression, age at the onset of epilepsy (A) had a significant association with MTS + NTC. Age of onset of epilepsy (A) was lower in the MTS + NTC group with odds ratio of 0.938(0.884 to 0.995). (Table 4.40)

Table 4.41: Association of secondary generalization with T2/FLAIR (Anterior temporal lobe)

Secondary generalization	HI absent(n=18)	HI present(n=82)	Total	P value
Absent	11 (61.11%)	47 (57.32%)	58 (58%)	0.768†
Present	7 (38.89%)	35 (42.68%)	42 (42%)	
Total	18 (100%)	82 (100%)	100 (100%)	

† **Chi square test**

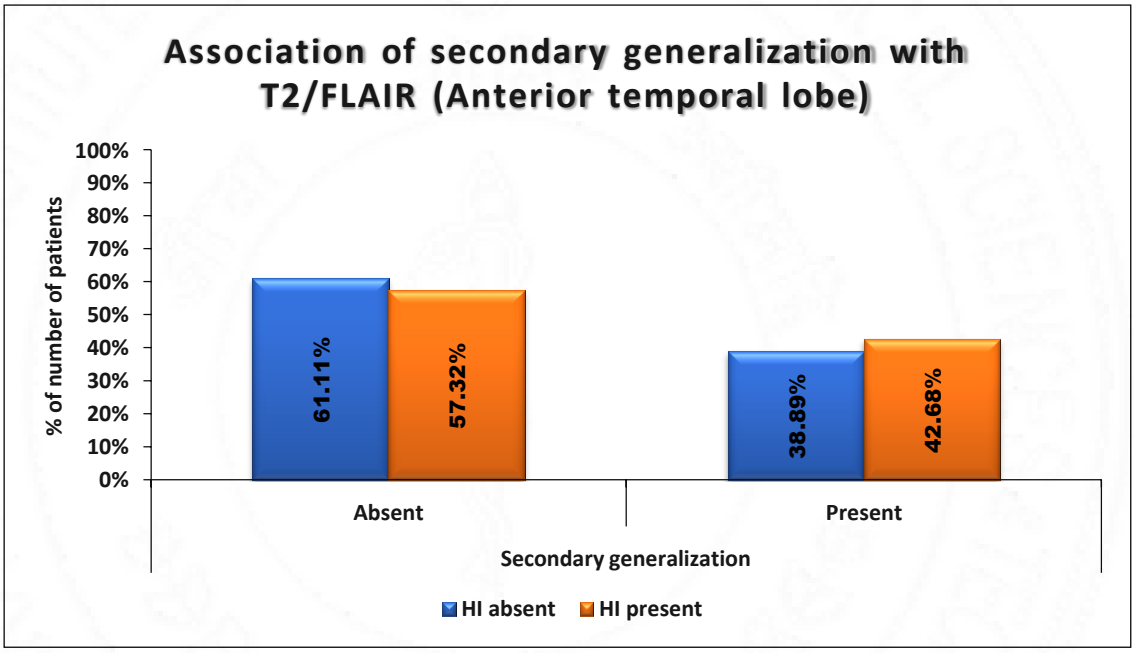


Figure 4.40: Association of secondary generalization with T2/FLAIR (Anterior temporal lobe).

Distribution of secondary generalization was comparable in patients without and with HI {T2/FLAIR (Anterior temporal lobe)}. (38.89% vs 42.68% respectively) (p value=0.768).(Table 4.41, figure 4.40).

Table 4.42: Association of motor symptoms with T2/FLAIR (Anterior temporal lobe)

Motor symptoms	HI absent(n=11)	HI present(n=47)	Total	P value
Absent	6 (54.55%)	24 (51.06%)	30 (51.72%)	0.835†
Present	5 (45.45%)	23 (48.94%)	28 (48.28%)	
Total	11 (100%)	47 (100%)	58 (100%)	

† **Chi square test**

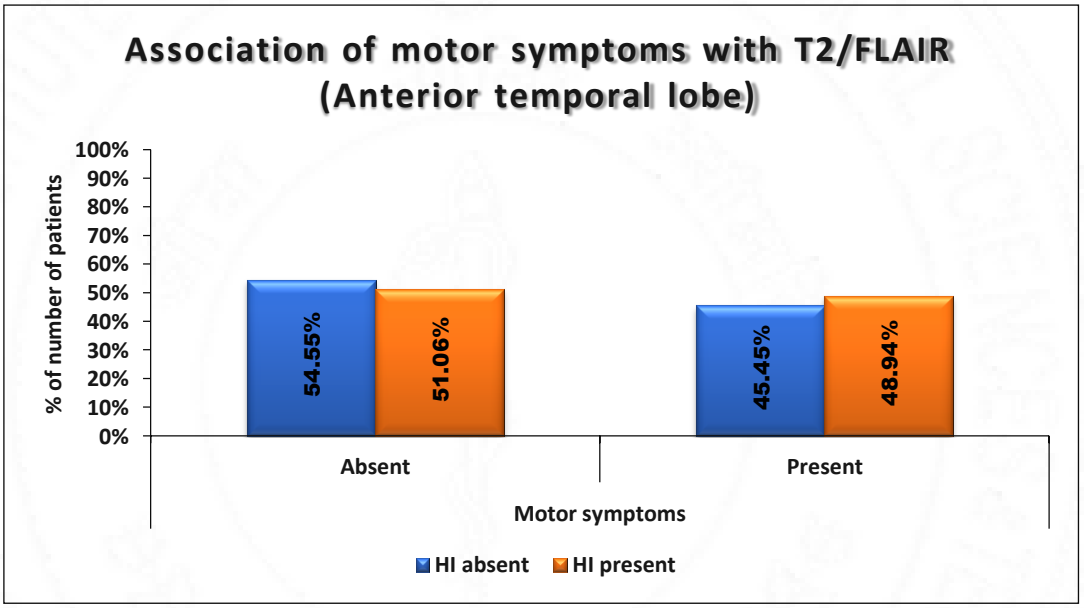


Figure 4.41: Association of motor symptoms with T2/FLAIR (Anterior temporal lobe).

Distribution of motor symptoms was comparable in patients without and with HI {T2/FLAIR (Anterior temporal lobe)}. (45.45% vs 48.94% respectively) (p value=0.835).(Table 4.42, figure 4.41).

Table 4.43: Association of anterior temporal volume loss with T2/FLAIR (Anterior temporal lobe)

Anterior temporal volume loss	HI absent(n=18)	HI present(n=82)	Total	P value
Absent	16 (88.89%)	3 (3.66%)	19 (19%)	<.0001*
Present	2 (11.11%)	79 (96.34%)	81 (81%)	
Total	18 (100%)	82 (100%)	100 (100%)	

* **Fisher's exact test**

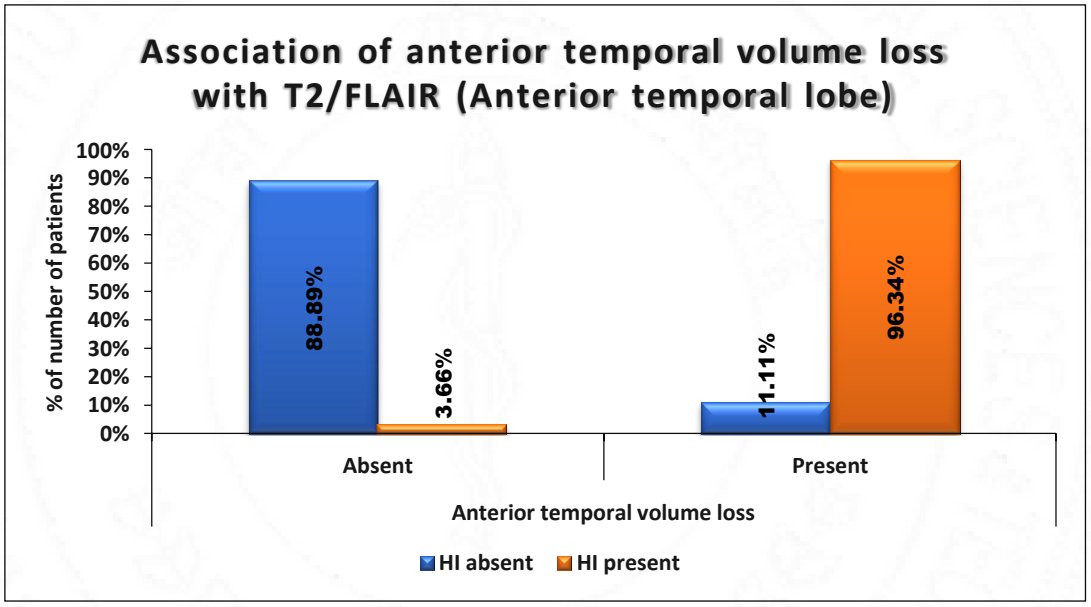


Figure 4.42: Association of anterior temporal volume loss with T2/FLAIR (Anterior temporal lobe).

Proportion of patients with anterior temporal volume loss was significantly lower in without HI as compared to with HI. (11.11% vs 96.34% respectively). (p value <0.0001) (Table 4.43, figure 4.42).

Table 4.44: Association of secondary generalization with ASL (Anterior temporal lobe) in patients with anterior temporal lobe changes

Secondary generalization	ASL abnormality absent(n=14)	ASL abnormality present(n=68)	Total	P value
Absent	7 (50%)	40 (58.82%)	47 (57.32%)	0.543†
Present	7 (50%)	28 (41.18%)	35 (42.68%)	
Total	14 (100%)	68 (100%)	82 (100%)	

† **Chi square test**

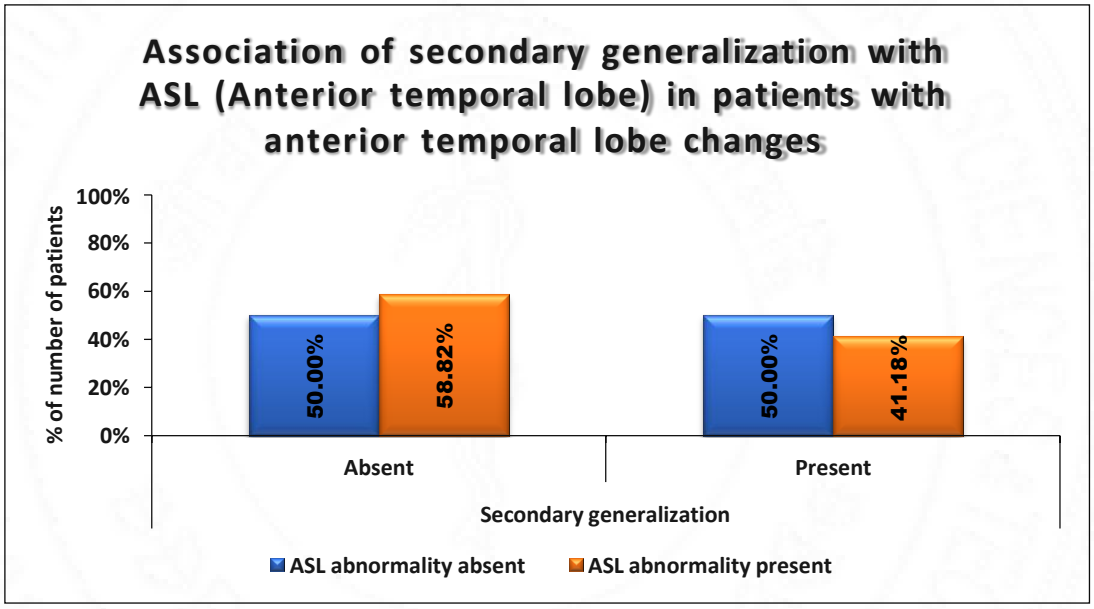


Figure 4.43: Association of secondary generalization with ASL (Anterior temporal lobe) in patients with anterior temporal lobe changes.

Distribution of secondary generalization was comparable in patients without and with ASL abnormality. (50% vs 41.18% respectively) (p value=0.543).(Table 4.44, figure 4.43).

Table 4.45: Association of motor symptoms with ASL (Anterior temporal lobe) in patients with anterior temporal lobe changes.

Motor symptoms	ASL abnormality absent(n=7)	ASL abnormality present(n=40)	Total	P value
Absent	4 (57.14%)	20 (50%)	24 (51.06%)	1*
Present	3 (42.86%)	20 (50%)	23 (48.94%)	
Total	7 (100%)	40 (100%)	47 (100%)	

* **Fisher's exact test**

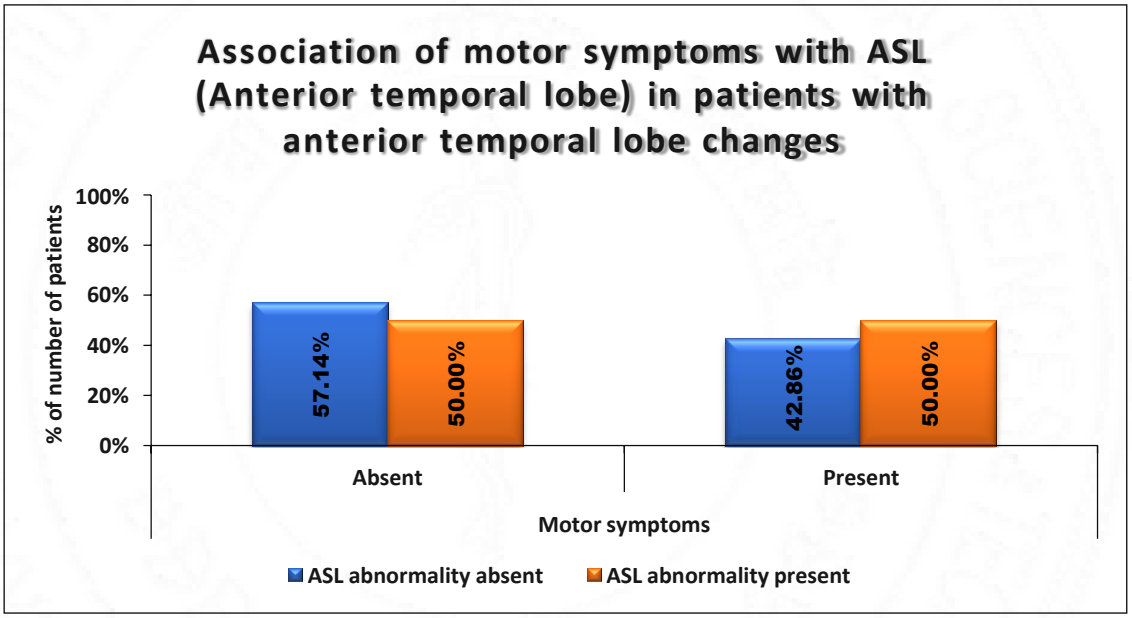


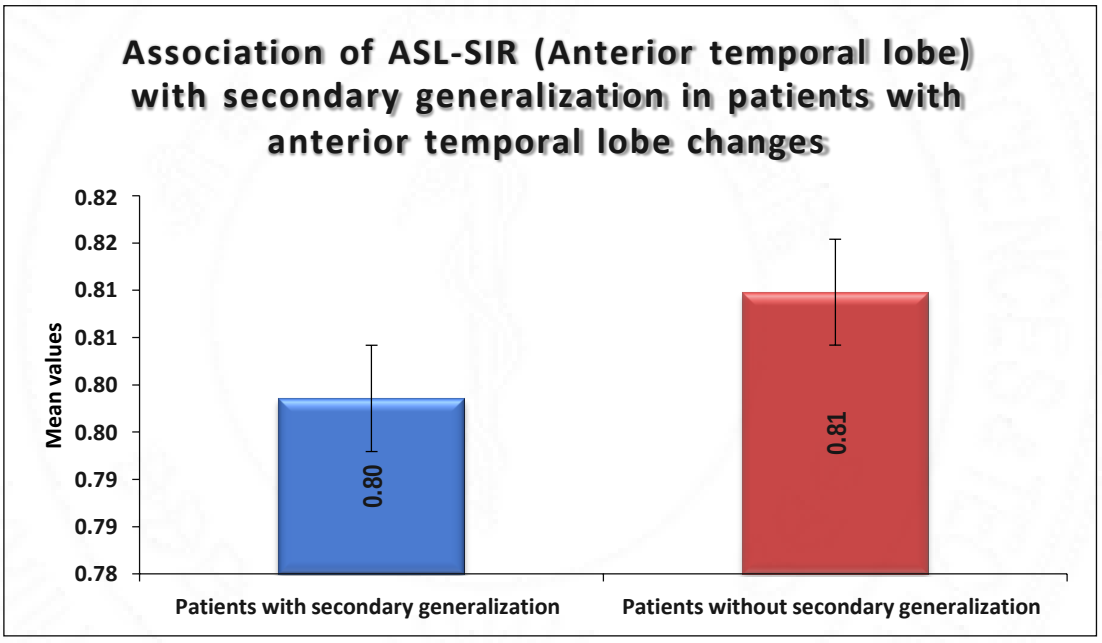
Figure 4.44: Association of motor symptoms with ASL (Anterior temporal lobe) in patients with anterior temporal lobe changes.

Distribution of motor symptoms was comparable in patients without and with ASL abnormality. (42.86% vs 50% respectively) (p value=1).(Table 4.45, figure 4.44).

Table 4.46: Association of ASL-SIR (Anterior temporal lobe) with secondary generalization in patients with anterior temporal lobe changes.

ASL-SIR (Anterior temporal lobe)	Patients with secondary generalization (n=35)	Patients without secondary generalization (n=47)	Total	P value
Mean ± SD	0.8 ± 0.15	0.81 ± 0.16	0.8 ± 0.16	0.75‡
Median(25^{th} - 75^{th} percentile)	0.78 (0.7-0.81)	0.78 (0.72-0.82)	0.78 (0.7-0.82)	
Range	0.6-1.2	0.6-1.7	0.6-1.7	

‡ **Independent t test, ASL-SIR: ASL-signal intensity ratio**



ASL-SIR: ASL-signal intensity ratio

Figure 4.45: Association of ASL-SIR (Anterior temporal lobe) with secondary generalization in patients with anterior temporal lobe changes.

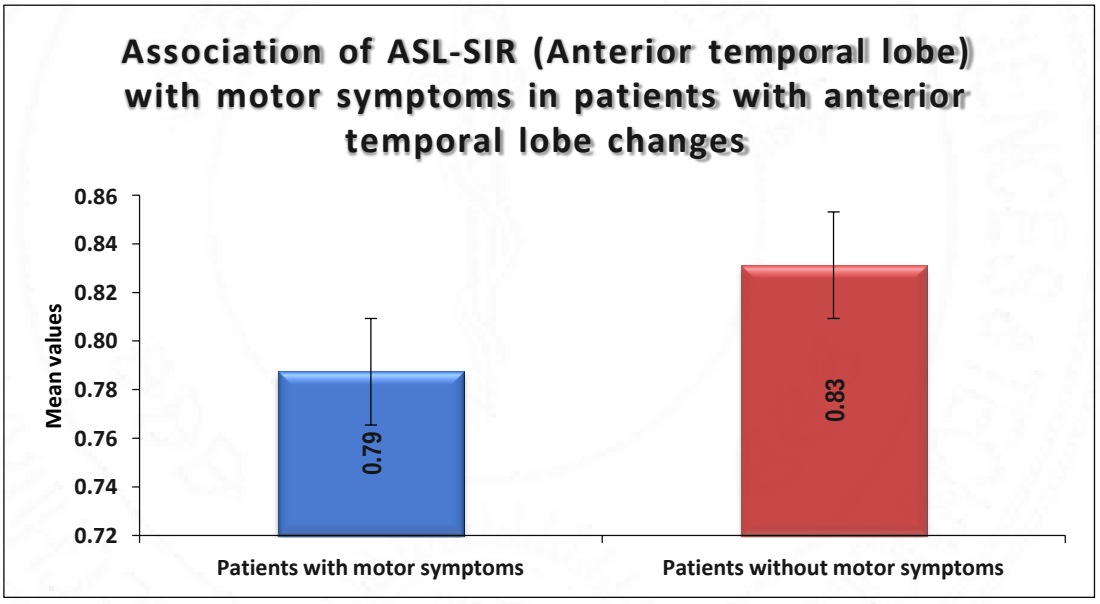
Mean ± SD of ASL-SIR (Anterior temporal lobe) in patients with secondary generalization was 0.8 ± 0.15 and in patients without secondary generalization was

0.81 ± 0.16 with no significant association between them. (p value=0.75)(Table 4.46, figure 4.45).

Table 4.47: Association of ASL-SIR (Anterior temporal lobe) with motor symptoms in patients with anterior temporal lobe changes.

ASL-SIR (Anterior temporal lobe)	Patients with motor symptoms(n=23)	Patients without motor symptoms(n=24)	Total	P value
Mean ± SD	0.79 ± 0.09	0.83 ± 0.21	0.81 ± 0.16	0.368‡
Median (25^{th} -75^{th} percentile)	0.8 (0.74-0.81)	0.78 (0.7-0.84)	0.78 (0.72-0.82)	
Range	0.6-0.99	0.68-1.7	0.6-1.7	

‡ **Independent t test, ASL-SIR: ASL-signal intensity ratio**



ASL-SIR: ASL-signal intensity ratio

Figure 4.46: Association of ASL-SIR (Anterior temporal lobe) with motor symptoms in patients with anterior temporal lobe changes.

Mean ± SD of ASL-SIR (AT) in patients with motor symptoms was 0.79 ± 0.09 and in patients without motor symptoms was 0.83 ± 0.21 with no significant association between them. (p value=0.368) (Table 4.47, figure 4.46).

Inter rater agreement between the radiologists:

On analysis of the images after blinding, none of the patients in the control group with normal pre-operative MRI were found to have MTS changes by both radiologists. None of these patients without MTS had neocortical or anterior temporal polar changes.

All the patients in the study were also found to have T2, FLAIR hyperintensity of the hippocampus and the amygdala by both the readers.

Table 4.48: Inter rater kappa agreement between R1-T2/FLAIR (Temporal neocortex) and R2-T2/FLAIR (Temporal neocortex).

R1-T2/FLAIR (Temporal neocortex)	R2-T2/FLAIR (Temporal neocortex)		Total	P value	Kappa
	Hyperintensity absent(n=39)	Hyperintensity present(n=61)			
Hyperintensity absent	34 (34.00%)	6 (6.00%)	40 (40.00%)	**<0.0001**	**0.770**
Hyperintensity present	5 (5.00%)	55 (55.00%)	60 (60.00%)		
Total	39 (39.00%)	61 (61.00%)	100 (100.00%)		

R1: Radiologist 1, R2: Radiologist 2

Good agreement exists between R2 (Radiologist 2)-T2/FLAIR (Temporal neocortex) and R1 (Radiologist 1)-T2/FLAIR (Temporal neocortex) with kappa 0.77 and p value <.0001.

Among 39 patients diagnosed as hyperintensity absent via R2-T2/FLAIR (Temporal neocortex), 34 patients had similar findings in R1-T2/FLAIR (Temporal neocortex). Among 61 patients diagnosed as hyperintensity present via R2-T2/FLAIR

(Temporal neocortex), 55 patients had similar findings in R1-T2/FLAIR (Temporal neocortex). Overall concordance rate was 89.00% and overall discordance rate was 11.00% between R2-T2/FLAIR (Temporal neocortex) and R1-T2/FLAIR (Temporal neocortex). (Table 4.48)

Table 4.49: Inter rater kappa agreement between R1-ASL (Temporal neocortex) and R2-ASL (Temporal neocortex).

R1-ASL (Temporal neocortex)	R2-ASL (Temporal neocortex)		Total	P value	Kappa
	ASL abnormality absent(n=53)	ASL abnormality present(n=47)			
ASL abnormality absent	44 (44.00%)	7 (7.00%)	51 (51.00%)	**<0.0001**	**0.680**
ASL abnormality present	9 (9.00%)	40 (40.00%)	49 (49.00%)		
Total	53 (53.00%)	47 (47.00%)	100 (100.00%)		

R1: Radiologist 1, R2: Radiologist 2

Good agreement exists between R2-ASL (Temporal neocortex) and R1-ASL (Temporal neocortex) with kappa 0.68 and p value <.0001.

Among 53 patients diagnosed as ASL abnormality absent via R2-ASL (Temporal neocortex), 44 patients had similar findings in R1-ASL (Temporal neocortex). Among 47 patients diagnosed as ASL abnormality present via R2-ASL (Temporal neocortex), 40 patients had similar findings in R1-ASL (Temporal neocortex). Overall concordance rate was 84.00% and overall discordance rate was 16.00% between R2-ASL (Temporal neocortex) and R1-ASL (Temporal neocortex). (Table 4.49)

Table 4.50: Inter rater kappa agreement between R1-T2/FLAIR (Anterior temporal lobe) and R2-T2/FLAIR (Anterior temporal lobe).

R1-T2/FLAIR (Anterior temporal lobe)	R2-T2/FLAIR (Anterior temporal lobe)		Total	P value	Kappa
	Hyperintensity absent(n=15)	Hyperintensity present(n=85)			
Hyperintensity absent	13 (13.00%)	3 (3.00%)	16 (16.00%)	**<0.0001**	**0.809**
Hyperintensity present	2 (2.00%)	82 (82.00%)	84 (84.00%)		
Total	15 (15.00%)	85 (85.00%)	100 (100.00%)		

R1: Radiologist 1, R2: Radiologist 2

Very good agreement exists between R2-T2/FLAIR (Anterior temporal lobe) and R1-T2/FLAIR (Anterior temporal lobe) with kappa 0.809 and p value <.0001.

Among 15 patients diagnosed as Hyperintensity absent via R2-T2/FLAIR (Anterior temporal lobe), 13 patients had similar findings in R1-T2/FLAIR (Anterior temporal lobe). Among 85 patients diagnosed as hyperintensity present via R2-T2/FLAIR (Anterior temporal lobe), 82 patients had similar findings in R1-T2/FLAIR (Anterior temporal lobe). Overall concordance rate was 95.00% and overall discordance rate was 5.00% between R2-T2/FLAIR (Anterior temporal lobe) and R1-T2/FLAIR (Anterior temporal lobe). (Table 4.50).

Table 4.51: Inter rater kappa agreement between R1-ASL (Anterior temporal lobe) and R2-ASL (Anterior temporal lobe).

R1-ASL (Anterior temporal lobe)	R2-ASL (Anterior temporal lobe)		Total	P value	Kappa
	ASL abnormality absent(n=27)	ASL abnormality present(n=73)			
ASL abnormality absent	24 (24.00%)	5 (5.00%)	29 (29.00%)	**<0.0001**	**0.802**
ASL abnormality present	3 (3.00%)	68 (68.00%)	71 (71.00%)		
Total	27 (27.00%)	73 (73.00%)	100 (100.00%)		

R1: Radiologist 1, R2: Radiologist 2

Very good agreement exists between R2-ASL (Anterior temporal lobe) and R1-ASL (Anterior temporal lobe) with kappa 0.802 and p value <.0001.

Among 27 patients diagnosed as ASL abnormality absent via R2-ASL (Anterior temporal lobe), 24 patients had similar findings in R1-ASL (Anterior temporal lobe). Among 73 patients diagnosed as ASL abnormality present via R2-ASL (Anterior temporal lobe), 68 patients had similar findings in R1-ASL (Anterior temporal lobe). Overall concordance rate was 92.00% and overall discordance rate was 8.00% between R2-ASL (Anterior temporal lobe) and R1-ASL (Anterior temporal lobe). (Table 4.51)

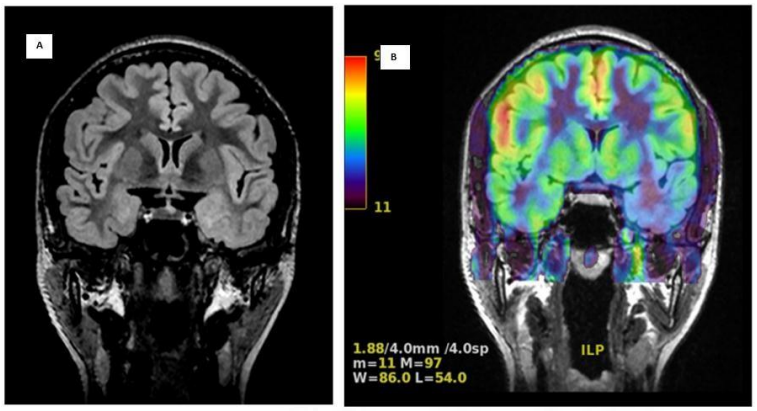
Table 4.52: Inter rater kappa agreement between R1-volume loss (Anterior temporal lobe) and R2-volume loss (Anterior temporal lobe).

R1-volume loss (Anterior temporal lobe)	R2-volume loss (Anterior temporal lobe)		Total	P value	Kappa
	Absent(n=17)	Present(n=83)			
Absent	16 (16.00%)	2 (2.00%)	18 (18.00%)	<0.0001	0.896
Present	1 (1.00%)	81 (81.00%)	82 (82.00%)		
Total	17 (17.00%)	83 (83.00%)	100 (100.00%)		

R1: Radiologist 1, R2: Radiologist 2

Very good agreement exists between R2-volume loss (Anterior temporal lobe) and R1-volume loss (Anterior temporal lobe) with kappa 0.896 and p value <.0001.

Among 17 patients diagnosed as absent via R2-volume loss (Anterior temporal lobe), 16 patients had similar findings in R1-volume loss (Anterior temporal lobe). Among 83 patients diagnosed as present via R2-volume loss (Anterior temporal lobe), 81 patients had similar findings in R1-volume loss (Anterior temporal lobe). Overall concordance rate was 97.00% and overall discordance rate was 3.00% between R2-volume loss (Anterior temporal lobe) and R1-volume loss (Anterior temporal lobe). (Table 4.52)



(A): Coronal FLAIR showing left MTS+NTC

(A): Coronal ASL showing left Temporal reduced CBF

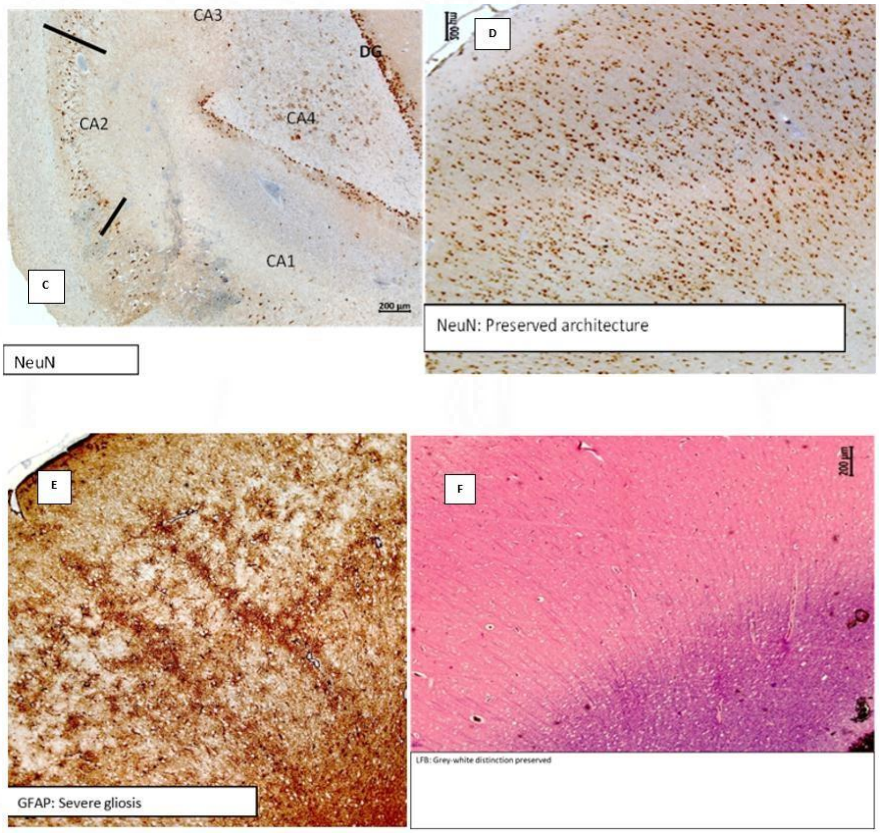
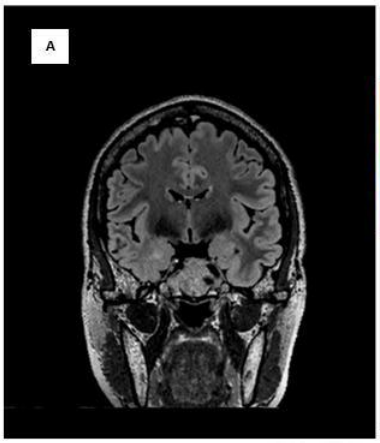
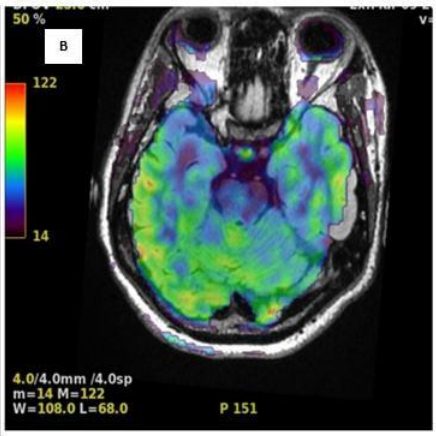


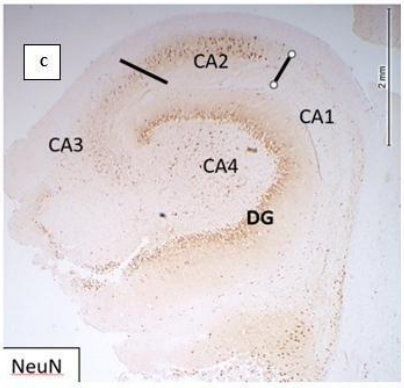
Figure 4.47: Illustrative case 1: A left MTS case with left temporal neocortical epileptogenesis on electrophysiological evaluation, left temporal neocortical changes on T2/FLAIR (A) with a corresponding reduced CBF on ASL (B). Histopathology showing neuronal loss predominantly in the CA1 and CA4 regions of the Hippocampus (C), preserved laminar architecture in the temporal neocortex, suggestive of no dysplastic changes (D),diffuse gliosis in the left temporal neocortex (E) and grey-white matter distinction preservation on Luxol fast stain (F) NeuN: Neuronal nuclear protein for neuronal staining, GFAP: Glial fibrillary acid protein for gliosis, LFB: Luxol fast blue staining for myelin, CA: Cornu Ammonis and DG: Dentate gyrus.

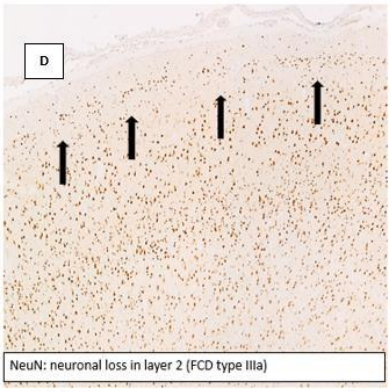


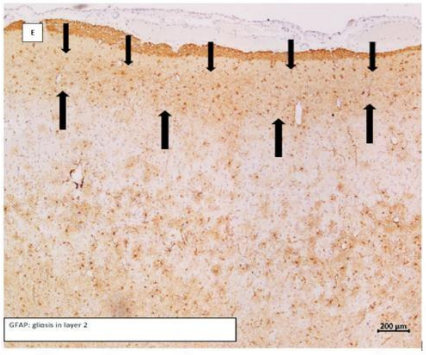
(A): Coronal FLAIR showing right MTS+NTC



(A): Axial ASL showing right Temporal reduced CBF







<u>Figure 4.48:</u> Illustrative case 2: A right MTS case with right sided temporal neocortical epileptogenesis on clinico-electrophysiological evaluation, right temporal neocortical changes on T2/FLAIR (A) with a corresponding reduced CBF on ASL (B). Histopathology showing neuronal loss predominantly in the CA1, CA3 and CA4 regions of the hippocampus (C), loss of laminar architecture (black arrows) with type IIIa dysplastic changes (D) and diffuse gliosis (black arrows) in the right temporal neocortex (E). NeuN: Neuronal nuclear protein for neuronal staining, GFAP: Glial fibrillary acid protein for gliosis, CA: Cornu Ammonis and DG: Dentate gyrus.

5. DISCUSSION

Evidence from various studies clarifies that MTS may be associated with abnormality in the anterior temporal lobe and temporal neocortex as evidenced by clinical, electrophysiological, imaging, and histopathological findings. It has already been shown that, this abnormality on imaging is not artifactual in nature (Garbelli et al., 2012). This has also been confirmed in our study as none of the patients in the control group without MTS were found to have neocortical or anterior temporal lobe MRI changes by both the Radiologists. We evaluated patients with MTS for the presence of anterior temporal polar changes on MRI. We defined anterior temporal changes as T2, FLAIR cortical and white matter hyperintensity, with a blurring of grey-white matter differentiation in accordance with published literature (Mitchell et al., 2003; Mueller et al., 2009). Almost all the patients in our study with temporal polar changes on MRI, also had anterior temporal volume loss. In addition, MR images were also assessed for 'temporal neocortical changes' which involved extension of the T2, FLAIR hyperintensity into the lateral temporal lobe, with grey-white matter border blurring at the lateral temporal neocortex and the fusiform gyrus. We also performed MR perfusion with ASL to look at the associated abnormalities in these patients.

MTS patients with, and without neocortical temporal changes on these sequences were also assessed to look for differences in the age of onset of epilepsy, presence of antecedent, age of antecedent, duration of epilepsy, seizure frequency score, degree of AED resistance, semiological features, the presence of focal to bilateral tonic-clonic progression, ictal, inter-ictal EEG findings, clinico-electrophysiological impression regarding the presence of neocortical temporal seizures, imaging, and histopathology. The conventional MR and ASL evaluations were done in four regions- the hippocampus, amygdala, temporal pole, and the temporal neocortex. The corresponding histopathological assessment was only done in three of these regions, as the temporal pole was not available for assessment. There was good to very good agreement between both Radiologists for all the parameters analyzed on T2/FLAIR and ASL sequences in our study (Tables 4.48-4.52).

Analysis of the imaging and histopathological abnormality

In the current study, Imaging assessment revealed the presence of T2/FLAIR abnormality in the amygdala in all patients with MTS. Anterior temporal polar changes were seen in 82% of the patients, while neocortical temporal changes were present in 63% of the patients in the study. ASL abnormality within the hippocampus was present in 97% of the patients, while it was present in 95% of the patients in the Amygdala, in 82% of the patients with anterior temporal polar changes, and in 79.3% of the patients with neocortical temporal changes.

The histopathological assessment of the resected temporal lobes revealed the presence of Type 1 HS in 89 % of the patients, type 2 HS in 4 % of the patients, type 3 HS in 2 % of the patients. 5 % of the patients were diagnosed as probable HS on account of the lack of availability of the complete hippocampus for histopathological assessment. The degree of astrogliosis in the hippocampus was moderate in 16 % of the patients and severe in 84 % of the patients. There was no difference in the degree of astrogliosis in the hippocampus in patients with and without neocortical temporal changes. All the specimens of Amygdala showed diffuse neuronal loss and gliosis with no specific lesion. When the temporal neocortex was evaluated, all the patients showed diffuse astrogliosis in the cortex and underling white matter irrespective of the changes seen on MRI. Staining with Luxol fast blue showed myelin abnormality, with grey-white matter blurring in 60.32 % of the patients with neocortical changes and 59.46 % of the patients without neocortical changes, with no significant difference. Dysplastic cortex was seen in 6 cases, 5 of whom has T2, FLAIR temporal neocortical and anterior temporal polar hyperintensity, with a corresponding reduced CBF in these regions on ASL. In the remaining case with dysplasia, the T2, FLAIR hyperintensity with reduced CBF was restricted to the anterior temporal pole (Table 4.36, 4.38; Figures 4.36, 4.48).

Our findings suggest that the extra-hippocampal imaging abnormality in patients with MTS not only extends into the other mesial temporal structures like the amygdala, but also into the anterior temporal pole. This abnormality in most patients extended further into the temporal neocortex. This is in concert with the results in literature published by Mitchell et al., stating that MR changes in MTS patients are

not only restricted to the anterior temporal pole, but extend further posteriorly. They used the term 'anterior temporal changes' in their study (Mitchell et al., 2003). This is also in agreement with the findings of Lin et al., and Mueller et al., who found that there was diffuse neocortical abnormality on MR imaging in patients with MTS (Lin et al., 2007; Mueller et al., 2009). Thom et al., also found in 272 MTS cases that, the temporal neocortex exhibited histopathological abnormality (Thom et al., 2009). The ASL abnormality in our study was present in 97% of the patients in the hippocampus and in 95% of the patients with amygdala. The sensitivity of ASL for the detection of epileptogenic focus in SLRE has been described to be 74 % (Kim et al., 2021).

When the histopathological specimens were evaluated in the current study to find the underlying substrate that could be responsible for these imaging changes, we found three distinct findings. Diffuse lateral temporal cortical and white matter gliosis in all patients, myelination abnormality in the temporal lobe of some evaluated patients, and dysplastic temporal neocortex in a few patients. Our results also show that, neither the presence of diffuse astrogliosis, nor the myelination abnormality differed between the groups with and without neocortical changes on MRI. In other words, MR imaging cannot predict these histopathological changes in the temporal lobe preoperatively. 5/6 (83.33%) patients with dysplastic temporal neocortex had abnormality in both T2/FLAIR and ASL sequences (Table 4.38, figure 4.38; Illustrative case 2 in figure 4.48). Statistically significant difference was absent, when compared with the T2/FLAIR and ASL findings of those patients without dysplasia, probably due to the fewer patients with dysplasia in our cohort. These results are only partly in agreement with Mitchell et al., who suggested that, the imaging abnormality in the anterior temporal lobe may be caused by myelination abnormality, and that gliosis, although commonly present, has no bearing with respect to the imaging appearance. They also stated that dysplasia is unlikely to be present in the temporal lobe of MTS patients (Mitchell et al., 1999; Mitchell et al., 2003). The results published by Thom et al., are more aligned with our results. In their cohort of MTS patients, on histopathological analysis of the temporal neocortex, they found that, about 11 percent cases had dysplasia. The remaining patients also showed diffuse gliosis of the cortex and underlying white matter. MRI could not be used to differentiate between cases with and without dysplastic neocortex in their study

(Thom et al., 2009). Garbelli et al., only analyzed the anterior temporal pole in their study. They found that the imaging abnormality in the anterior temporal pole was due to an underlying myelin pathology in the temporal lobe. Astrogliosis, although diffusely present in all patients in their study did not influence the imaging appearance of the temporal pole. There was also no significant difference in the MR appearance of this region with or without underlying dysplastic changes (Garbelli et al., 2012). The dysplastic neocortex was initially labelled as 'dual pathology' in MTS patients. The task force of ILAE diagnostic methods confirmed in 2011, that this was not to be called as dual pathology. Rather, they classified it as focal cortical dysplasia type IIIa, the diagnosis of which is based on histopathological criteria (Blümcke et al., 2011). This task force in 2013 published a summary of the additional pathology that has been shown to be present in the rest of the temporal lobe in MTS patients. They stated that, the anterior temporal changes on MRI in these patients were most likely caused by myelin loss. They also detailed that, type IIIa dysplastic changes may be present in the temporal neocortex in these patients (Blümcke et al., 2013).

It is noteworthy that, none of the studies in the literature used advanced MR imaging with ASL to evaluate these patients. It is apparent that, the underlying histopathological abnormality in the anterior temporal pole and temporal neocortex in MTS cases can be a very heterogenous mixture, that can vary from patient to patient. We noticed that the imaging findings outside the medial temporal lobe, in these patients extend not only to the anterior temporal pole, but also into the temporal neocortex, to a variable degree. The underlying histopathological substrate for these anomalies, is possibly a combination of gliosis in all patients, myelin loss in some patients and the presence of dysplasia in a few patients. Although it is difficult to predict the exact underlying histopathological makeup with conventional MRI using T2, FLAIR sequences, our results show that ASL abnormality was present almost all the patients with dysplasia (Table 4.38). Although, this difference could not reach statistical significance, due probably to a smaller sample size of dysplasias in the cohort. There might be a possibility of the MTS patient having associated dysplastic temporal neocortex if there is abnormality of the temporal neocortex, on both the structural MRI (T2/FLAIR) and ASL sequences. This may be of clinical interest and needs to be evaluated further in future studies.

Demographic features and clinical history

We found that, patients with neocortical temporal seizures more commonly had left sided involvement, although the reason for this is unclear (Table 4.28). Our results also show that, demographic features, presence of antecedent, age of incidence of the antecedent, duration of epilepsy, seizure frequency and the AED resistance were not different between the two groups. Our results are partly concordant with the study done by Garbelli et al. who found that there was no difference in MTS patients with and without anterior temporal polar changes, for characteristics like the presence of antecedent and seizure frequency (Garbelli et al., 2012). They also stated that, a longer duration of epilepsy was associated with anterior temporal polar changes, which does not agree with our results. This study results are also in contrary to that published by Mitchell et al., in 2003; i.e., MTS patients with anterior temporal changes on MRI had a lower age of antecedent incidence (Mitchell et al., 2003). The presence of an initial antecedent and the duration of epilepsy influenced the degree of neocortical pathology in MTS patients, as opined by Lin et al (2006). Thom et al., found that, a history of febrile seizure was more common in MTS cases with 're-organizational dysplasia' in the temporal neocortex, than those without (Thom et al., 2009).

We also found that, patients with neocortical changes on MRI, had an earlier onset of habitual seizures (Table 4.4, Figure 4.4). This association was found on logistic regression analysis as well (Table 4.41). Previously published studies also claim that, habitual seizures started early in patients with anterior temporal changes (Mitchell et al., 2003; Muzumdar et al., 2016). The task force for ILAE diagnostic methods opined that the type IIIa FCD that is seen in patients with MTS is probably caused by the same etiopatholgical factors that were responsible for MTS and is established at the same point in time (Blümcke et al., 2013).

We think that, the pathological changes in the anterior temporal lobe and the lateral temporal neocortex share the same etiological factor, and is established at the same time as MTS. The pathophysiological pathway by which, the antecedent causes the neocortical temporal changes along with the MTS is still obscure. The factors that are responsible for the differential involvement of the temporal neocortex in different

patients with MTS are also unclear. It is already known that, certain genetic factors, although not directly responsible, may predispose patients to have MTS, by increasing their propensity for febrile seizures or temporal lobe seizures (Compiled by Heinz-Gregor Wieser for the ILAE Commission on Neurosurgery of Epilepsy, 2004). It is possible that, genetic factors that are yet to be identified, may explain why only some patients with MTS have neocortical temporal changes on MRI. Habitual seizures started early in patients with these changes, compared to their counterparts, possibly due to the epileptogenic potential of this region.

Clinical and electrophysiological assessment

We also assessed these neocortical changes for their epileptogenic activity and evolution in MTS patients. There was no significant difference between patients with neocortical changes and those without, in the incidence of individual semiological features like, aura, motor symptoms, automatisms, autonomic, cognitive, and emotional symptoms. Sensory symptoms however, showed a statistically significant difference with greater presence in MTS patients with neocortical changes (Table 4.11, Figure 4.11). The most common sensory symptoms that were present in the study group were auditory and vertiginous auras (Table 4.19, Figure 4.19), which are characteristic of neocortical epileptogenesis. There was also no difference in the incidence of focal to bilateral tonic-clonic progression and inter-ictal EEG findings between the groups. Both groups showed that the inter-ictal discharges and ictal onset was mostly localized and lateralized. Analysis of ictal EEG patterns showed that, patients without neocortical temporal changes mostly had monomorphic theta waveforms, while 22.22% patients with neocortical temporal changes had fast beta waveforms, more characteristic of neocortical ictal onset (Table 4.26, Figure 4.26). Two patients with neocortical temporal changes group had diffuse ictal onset on EEG, out of which one patient had dysplastic temporal neocortex. The clinical and electrophysiological opinions were assessed in concert in the patient management conference for pre-surgical formation of a hypothesis on the location of the EZ. The red flags that were considered for the epileptogenesis outside the medial temporal lobe were the presence of high degree of clustering, high frequency of secondary generalization, auras characteristic of neocortical seizures and the presence of beta

rhythm on ictal EEG. 66.67% of patients with neocortical temporal changes had neocortical epileptogenesis, while 13.51% of the patients without these changes on MRI had ictal onset from the temporal neocortex, and this difference was statistically significant (Table 4.27, figure 4.27). Interestingly, when we looked at the imaging findings in the cohort of MTS patients with neocortical changes, we found that, presence of abnormality within the temporal neocortex on T2/FLAIR and ASL sequences, was associated with neocortical epileptogenesis relative to the presence of abnormality on T2/FLAIR alone (Table 4.37, figure 4.37). On quantitative analysis of ASL images, there was a statistically significant difference in the ASL-SIR in the anterior temporal pole and temporal neocortex, between patients with and without neocortical temporal changes (Tables 4.34,4.35; figures 4.34,4.35). There was however, no difference in these values in the temporal neocortex, between those patients with neocortical epileptogenesis and those without, within the cohort with neocortical changes Table 4.39, Figure 4.39). This could probably be due to the poor spatial resolution of ASL. We also found that, the presence of anterior temporal polar changes was not associated with any specific semiological features.

Our results are concordant with those published by Barba et al., who in their study performed a retrospective review of 80 temporal lobe epilepsy patients. They found that, a significant number (77.2 percent) of patients with semiological and electrophysiological features suggestive of ictal onset outside the medial temporal lobe, had MRI findings suggestive of MTS (Barba et al., 2007). Fauser et al., in 2006 analyzed MTS patients with histologically proven dysplasia in the neocortex. On invasive EEG recordings, 34.7 percent of MTS patients had ictal onset from the temporal neocortex (Fauser and Schulze-Bonhage, 2006). Garbelli et al. found that patients with temporal polar changes had a higher incidence of dystonic features on semiological evaluation (Garbelli et al., 2012).

We think that the temporal neocortex in a significant number of MTS patients is not a passive bystander in the epileptogenic network. Although the heterogenous mixture of pathological changes in the temporal neocortex, apart from dysplasia are poorly predicted by MRI, interpretation of T2/FLAIR and ASL sequences together could help predict the role of lateral temporal cortex in seizure generation in these

patients. ASL has been already shown to have good predictive value for localization in SLRE (Nagesh et al., 2018). This utility of ASL could also be applied to MTS patients. ASL, is therefore a valuable addition to epilepsy protocol MRI brain. Interpretation of clinical, electrophysiological, structural MRI and ASL findings in concert could prove to be quite valuable to approximate the extent of epileptogenic zone in MTS patients, which could be targeted for resection. However, this needs to be validated further with larger future studies. Although the benefit of anterior temporal lobectomy relative to selective amygdalohippocampectomy is controversial in literature, few authors have suggested that anterior temporal lobectomy is better than selective amygdalohippocampectomy, especially in resource limited settings like in India (Muzumdar et al., 2016). When there is a suggestion of neocortical epileptogenesis in the pre-surgical evaluation with various modalities including imaging with conventional sequences and ASL, anterior temporal lobectomy might provide better seizure freedom after surgery, than selective amygdalohippocampectomy. The extent of safe lateral temporal neocortical resection has been published in literature to be up to 5.5 cm from the temporal pole in the non-dominant hemisphere, and 4.5 cm from the temporal pole in the dominant hemisphere (Muzumdar et al., 2016). Alternatively, intra-operative electrocorticography may be used, to tailor the extent of this resection. But pre-operative prediction of this need might be of great help in planning MTLE surgery.

Limitations of the study

Our study has a few limitations:

1. Previously published literature on involvement of the temporal neocortex in quantitative imaging analysis has shown a diffuse reduction in the thickness. We did not perform a quantitative analysis of the same, in the current study

2. DTI images could have been used for quantification of the myelin abnormality in the temporal white matter seen on histopathology. We could not calculate the fractional anisotropy values from DTI due to the lack of availability of high-resolution DTI images in our retrospectively studied patients.

3. The post-operative outcome, assessed by seizure freedom ATL + AH was not compared, between MTS patients with, and without neocortical temporal changes.

Future studies may be performed to quantitatively analyze MR images for a more precise correlation of imaging, histopathological and clinico-electrophysiological characteristics of the MTS patients with temporal neocortical changes. Analysis of outcome after surgery may be a more definitive criterion for the evaluation of the capability of ASL in delineating the epileptogenic zone.

6. SUMMARY AND CONCLUSION

1. The imaging abnormality in MTS patients outside the medial temporal lobe consisted of anterior temporal polar abnormality, visible as T2/FLAIR hyperintensity of the cortex and underlying white matter, with a blurring of grey-white differentiation. Almost all patients with anterior temporal polar changes had anterior temporal volume loss. This abnormality also had a variable extension into the temporal neocortex posteriorly.

2. Patients with neocortical temporal changes on MRI have an earlier onset of habitual seizures.

3. The structural MRI features in some patients, were accompanied by perfusion abnormalities in the corresponding regions on ASL with hypoperfusion in the inter-ictal period, and hyper-perfusion in the peri-ictal period.

4. The underlying histopathological changes responsible for these changes, were a mixture of variable degree of gliosis in all patients, myelin loss in some patients and dysplasia in a few patients.

5. Gliosis of the cortex and underling white matter in the anterior temporal pole, extending beyond to a variable extent into the lateral temporal lobe, was present in all the patients irrespective of the presence or absence of temporal neocortical changes on MRI. There is also no significant difference in the imaging findings in patients with and without myelin abnormality. Although no statistical significance was attained, all except one patient with neocortical temporal dysplasia had abnormality on both T2/FLAIR and ASL sequences.

6. Higher number of patients with neocortical epileptogenesis had abnormality on T2/FLAIR and ASL, than on T2/FLAIR alone.

To conclude, the MRI changes at the anterior temporal pole and temporal neocortex in patients with MTS represents a continuum, and consists of hyperintensity on T2/FLAIR sequences in the cortex and underlying white matter with blurring of grey-white matter differentiation. They may share a common etiological factor, and

may be established at the same time as MTS. The pathophysiological mechanisms are not clear. The presence of these changes is associated with an earlier onset of habitual seizures in MTS patients. The underlying histopathological substrate is usually a mixture of gliosis in all patients, myelin loss in some patients and dysplasia in a few patients. As hypothesized, MRI is a poor predictor of the underlying histopathological make up. Addition of ASL to epilepsy protocol MRI may help predict the presence of associated dysplasia. Future studies may be done to evaluate the role of ASL in this regard, with a larger sample size. Presence of neocortical temporal changes on MRI is associated with a higher rate of neocortical epileptogenesis. Addition of ASL enhanced the capability of MRI to predict neocortical seizures in these patients. This concordance of abnormality on T2/FLAIR, ASL and clinico-electrophysiology in such patients suggests that, the temporal neocortex is possibly a part of the epileptogenic zone and needs to be targeted during surgery. Preoperative prediction of this fact may be of significance in the treatment planning.

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resection: *Hyperkinetic Seizures in Temporal Lobe Epilepsy*. *Epilepsia* 52(8): 1439–1446. DOI: 10.1111/j.1528-1167.2011.03100.x.

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ANNEXURES

Curriculum vitae (CV)- Dr. Viswanadh K S V G

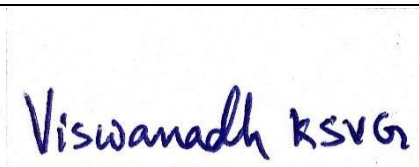
Last Name -K S V G	**First Name** - VISWANADH	
Date of Birth (dd/mm/yy)- 24/04/1990		**Sex**- MALE
Current affiliation- Senior resident in DM Neuroimaging and interventional neuroradiology at Sree Chitra Tirunal institute of medical sciences and Technology		
Address		
Dr VISWANADH K S V G, DEPT. OF IMAGING SCIENCES AND INTERVENTIONAL RADIOLOGY, SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY, THIRUVANANTHAPURAM, KERALA, INDIA-695011		
Phone number-8106645664		**Alternative Number**- 9496937773
		Email- viswanath2481990@gmail.com
Academic Qualifications (Most recent qualification first)		
Degree/Certificate	Year	Institution, Country
MD RADIO DIAGNOSIS	2016-2019	GUNTUR MEDICAL COLLEGE, GUNTUR, ANDHRA PRADESH
MBBS	2008-2014	SRI VENKATESWARA MEDICAL COLLEGE, TIRUPATI, ANDHRA PRADESH

Current and previous positions (most recent position first)		
Month and Year	Title	Institution/Company, Country
JAN 2021 to current	SENIOR RESIDENT	SCTIMST, THIRUVANANTHAPURAM, INDIA
2019 to 2020	SENIOR RESIDENT	KAMINENI ACADEMY OF MEDICAL SCIENCES AND RESEARCH CENTRE, HYDERABAD.

Brief summary of relevant research experience:

Presented a poster titled Evaluation of arteriovenous malformations of the brain with CT Angiography: A case report at AOCR 2018

1. MRI evaluation of traumatic ACL and associated injuries of knee with arthroscopy correlation; Balaji Varaprasad Mallula, Annapurna S, Srinadh Boppana, Ravi Raja Sankuri, Viswanadh KSVG and Jaya Prasad PS; International Journal of Radiology and Diagnostic Imaging

Signature: 	Date: 05-01-2023 Place: THIRUVANANTHAPURAM

CV- Dr. Bejoy Thomas

Format for CV of the Investigators

Last Name **Thomas**	First Name **Bejoy**	Middle Name
Date of Birth (dd/mm/yy) **23.05.1969**		Sex **Male**
Study Site Affiliation (e.g. Principal Investigator, Co-Investigator, Coordinator) PI, Co PI		
Professional Mailing Address (Include Institution name)		Study Site Address (Include Institution name)
Professor, Department of Imaging Sciences and Interventional Radiology, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum, Kerala, India, 695011.		**Department of Imaging Sciences and Interventional Radiology, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum, Kerala, India, 695011.**
Telephone (Office): **+ 91 471 2524117**		Mobile Number:**+ 91 9447719481**
Telephone (Residence):**+ 91 471 2440687**		Email bejoy@sctimst.ac.in
Academic Qualifications (Most recent qualification first)		
Degree/Certificate	Year	Institution, Country
Clinical Fellowship, Pediatric Neuroradiology	2009	The Hospital for Sick Children, University of Toronto, ON, **Canada**
BOYSCAST' Fellowship	2004	University Hospital, Gasthuisberg, Katholieke Universiteit Leuven, **Belgium.**
PDCC (Neuro and Vascular Radiology)	1998	Sree Chitra Tirunal Institute for Medical Sciences and Technology, Thiruvananthapuram, **India**
DNB (Radiodiagnosis)	1997	National Board of Examinations, **India**
MD (Radiodiagnosis)	1997	N.H.L. Municipal Medical College, Gujarat University, **India**
MBBS	1993	Government Medical College Kottayam, Mahatma Gandhi University, Kottayam, Kerala, **India.**
Details of professional registration : (MCI/State Registration/Bar Council/DCI/etc including Registration Number and Year of Registration **TCM Reg No: 20483 year 1993**		

Current and previous positions (most recent position first)		
Month and Year	Title	Institution/Company, Country
July 2012	**Professor**	Department of Imaging Sciences and Interventional Radiology, Sree Chitra Tirunal Institute for Medical Sciences and Technology (SCTIMST), Kerala, India
April 2009	**Additional Professor**	"
April 2005	**Associate Professor**	"
April 2001	**Assistant Professor**	"

Brief summary of relevant research experience:

Advanced Neuroimaging, Quantitative Image Analysis, Functional and Metabolic Neuroimaging, Medical devices innovation

Current project/s at hand:
rsfMRI in DAVF (prospective)
Brain perfusion changes under GA measured using ASL (retrospective)
Development of a prototype vein viewer and extravasation prevention system

Signature: S/d	Date: 28. 09. 2018 Place: Thiruvananthapuram

CV- Dr. Ashalatha Radhakrishnan

Last Name: **Radhakrishnan**	First Name: **Dr Ashalatha**	Middle Name
Date of Birth (dd/mm/yy): 13/05/1970		Sex: Female
Study Site Affiliation (e.g. Principal Investigator, Co-Investigator, Coordinator) Principal Investigator		
Professional Mailing Address(Include Institution name)		Study Site Address (Include Institution name)
Professor of Neurology, Department of Neurology, Sree Chitra Tirunal Institute for Medical Sciences andTechnology (SCTIMST), Medical College P.O, Thiruvananthapuram - 695011		SCTIMST, Medical College P.O, Thiruvananthapuram
Telephone (Office): 91-471-2443520		Mobile Number: 9847416321
Telephone (Residence):		Email:drashalatha@sctimst.ac.in
Academic Qualifications (Most recent qualification first)		
Degree/Certificate	Year	Institution, Country
Fellow of American Neurological Association (FANA) Fellow of Royal College of Physicians (Glasgow) MBA(Hospital Administration & HRD)	2017 -18	The Royal College of Physicians and Surgeons ofGlasgow, Scotland
Training in Stereo EEG for utilization in surgical evaluation ofrefractory Epilepsy	2016	Montreal, Canada
Training in EEG co-registered MRIfor application in refractory epilepsy	2012	Queen Square Hospital, UniversityCollege, London
Fellowship in Epilepsy & SleepMedicine	2007-2008	Austin Health, Melbourne, Victoria, Melbourne University, Australia (under supervision of Prof. Samuel F Berkovic and Rob J Pearce, University of Melbourne)
M.D General Medicine	1999	Govt. Medical College, Alappuzha, University of Kerala
MBBS	1994	Govt. Medical College, Alappuzha, University of Kerala

Details of professional registration : (MCI/State Registration/Bar Council/DCI/etc including RegistrationNumber and Year of Registration: TCMC-21956/1994

Current and previous positions (most recent position first)

Month and Year	Title	Institution/Company, Country
January 2016-continuing	Professor	SCTIMST, Trivandrum
2015-2017	Additional Professor	SCTIMST, Trivandrum
January 2009 - 2015	Associate Professor	SCTIMST, Trivandrum
June 2008 – December 2008	Consultant in Neurology(Sleep Project)	SCTIMST, Trivandrum
January 2007-May 2008	Fellowship Training in Epilepsy and Sleep Medicine	SCTIMST, Trivandrum
August 2006 – February 2007	Assistant Professor	SCTIMST, Trivandrum
June 2003 – July 2006	Ad Hoc Consultant in Neurology and Epilepsy Program	SCTIMST, Trivandrum

Brief summary of relevant research experience:

The applicant has been working as a faculty member in the Department of Neurology, Sree Chitra Tirunal Institute and Medical Sciences (an institute of national importance under the Department of Science and Technology, Govt. of India) since 2003 after completing the graduation in Neurology in the same institute. She is devoting 70% of her time in the R. Madhavan Nayar Center for Comprehensive Epilepsy Care which is the largest of its kind in the country with state of the art facilities catering to patients with epilepsy headed by Dr. Sanjeev Thomas, Professor of Neurology and a renowned epileptologist. During this period she has focused in the evaluation and management of medically refractory epilepsy and its surgical management by developing new neuroimaging techniques like functional MRI-coregistered EEG, diffusion tensor imaging and fiber tracking, voxel based morphometry etc related to epilepsy.

Functional MRI-EEG coregistration technique aids in the pre-surgical workup of epilepsy patients when other investigation tools fail to localize the area of epileptogenic focus. Dr Ashalatha along with her colleagues in Neuroradiology and Biomedical technology wing standardized the procedure of EEG- fMRI for the first time in the country which is now in the process of being utilized in the field of pre-surgical evaluation of refractory cases of epilepsy.

In conventional MRI negative epilepsy patients, she along with computer scientists has developed newer computational software for detection of subtle cortical dysplasia by a method called voxel based morphometry (VBM) which was presented for the first time from India in the International Conference on Epilepsy at Melbourne, Australia in October,2010. Newer sequences have been applied for the clinical problem. These methods are now going to be utilized for the detection of such subtle lesions like focal cortical dysplasias which may aid the epileptologist to proceed with better treatment for epilepsy.

The applicant has also applied advanced neuroimaging protocols such as diffusion tensor imaging with fiber tracking of white matter tracts aiding in the mapping of white matter tracts in the pre-surgical evaluation of patients with epilepsy. This will aid the surgeon to plan out his surgery at or close to eloquent areas in order to avoid untoward complications like hemiparesis, speech difficulty etc which are the major hindrances in selection of candidates for brain surgery. This work is not being done in any other parts of the country and author won the Young Investigator award for this pioneering work at the 100th International Congress of Epilepsy at Budapest, Hungary in 2009.

Current project/s at hand:

1. Multimodal imaging in pre surgical evaluation of extra temporal lobe epilepsy-(PI)
2. Utility of 3D pseudo continuous ASL perfusion in pre- surgical evaluationof focal temporal and Extratemporal epilepsy -(Co- PI)
3. Prevalence of sleep disordered breathing (SDB) in children with attention deficit hyperactivity disorder (ADHD) and its response to treatment in school going children in Thiruvanathapuramdistrict-(PI)
4. A genetic association for severe hyponatremia and central pontinemyelinolysis-(PI)
5. Genome-Wide Association and Blood Marker study in Narcolepsy and Hypersomania-(PI)
6. Association of Pulmonary arterial hypertension (PAH) and cardiac arrhythmias in patients of Obstructive sleep apnea (OSA) and possible therapeutic benefit with CPAP treatment-(PI)
7. Clinical profile and outcome in patients with autoimmune encephalitis-(PI)

8. Global audit of treatment of refractory Status Epilepticus-(PI) **9.** Development of intracranial electrodes for use in acute and chronic electrocorticography-(Co-PI) **10.** Indigenous Intracranial electrode manufacture (TRC) – (DST Funded) - (Co–PI) **11.** Model the effect of Mutations of HCN Channels in Neuronal Excitability and impact of GABABR onGIRK and HCN mutations using NEURON - (DBT Funded) – (Co-PI) **12.** Validation of memory fMRI paradigms and its utility in pre-surgical evaluation of patients with refractory TLE – (Co-PI) **13.** A resting state fMRI and task based fMRI study: Optimization, language lateralization, memory lateralization and connectivity in normal subjects versus patientswith epilepsy - (DBT Funded) – (Co_PI)
Signature:  Date: 31/08/2021 Place: Thiruvananthapuram

CV-Dr. Deepti A.N.

AN	Deepti	
Last Name	First Name	Middle Name
Date of Birth (dd/mm/yy): 17/07/1974		Sex: Female
Study Site Affiliation (e.g. Principal Investigator, Co-Investigator, Coordinator): Co-Investigator		
Professional Mailing Address: (Include Institution name)		Study Site Address (Include Institution name)
Department of Pathology SCTIMST, Trivandrum		Department of Pathology SCTIMST, Trivandrum
Telephone (Office): 0471-2524594		Mobile Number: 9481036933
Telephone (Residence): -		Email: akkihebbal@sctimst.ac.in

Academic Qualifications (Most recent qualification first)

Degree/Certificate	Year	Institution, Country
PhD	2014	Université catholique de Louvain, Belgium
Postdoctoral fellowship in Neuropathology	2005-2006	National Institute of Mental Health and Neurosciences, Bangalore, India
MD (Pathology)	2004	Christian Medical College, Vellore, Tamil Nadu, India
MBBS	1998	Karnatak University, Dharwad, Karnataka, India

Details of professional registration : (MCI/State Registration/Bar Council/DCI/etc including Registration Number and Year of Registration

Tamil Nadu Medical Council Registration Number: 67785 Year: 2008

Current and previous positions (most recent position first)

Month and Year	Title	Institution/Company, Country
December 2015 till date	Associate Professor (Pathology)	SCTIMST, Trivandrum
	Lecturer, Department of	Christian Medical College,

June 2006 to June 2008	General Pathology	Vellore
June 2004 to June 2005	Demonstrator (Non-PG), Department of General Pathology	Christian Medical College, Vellore
Brief summary of relevant research experience: Experience in Neuropathology, immunohistochemistry, molecular techniques (PCR, including RT-PCR; FISH), in silico analysis (gene expression profiling, microarray-based)		
Current project/s at hand: -		
Signature:		Date: 27-09-2018 Place: Thiruvananthapuram

CV-Dr. Rajalakshmi P

P	RAJALAKSHMI	
Last Name	**First Name**	
Date of Birth (dd/mm/yy): 19/03/1984		**Sex:** F
Study Site Affiliation: Assistant Professor, Department of Pathology, SCTIMST		
Professional Mailing Address(Include Institution name)		**Study Site Address (Include Institution name)**
Department of PathologySCTIMST Trivandrum- 695011		Department of PathologySCTIMST Trivandrum- 695011
Telephone (Office): 0471 2524494		**Mobile Number:** 9620643510
Telephone (Residence):		**Email:** rajalakshmi.p.19@gmail.com

Academic Qualifications (Most recent qualification first)

Degree/Certificate	**Year**	**Institution, Country**
PDF- Neuropathology	2015	NIMHANS, Bangalore, India
MD- Pathology	2011	Mysore medical College and Research Institute, Mysore, India
MBBS	2005	JIPMER, Puducherry, India

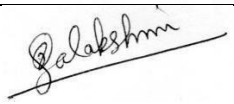
Details of professional registration : (MCI/State Registration/Bar Council/DCI/etc includingRegistration Number and Year of Registration
Registration no: 80327 Year of registration: 2007
Tamil Nadu Medical Council

Current and previous positions (most recent position first)

Month and Year	**Title**	**Institution/Company, Country**
Aug 2016 till date	Assistant Professor	SCTIMST, Trivandrum, India
Jan 2016 to June 2016	Senior Resident	NIMHANS, Bangalore, India
Aug 2015 to Dec 2015	Junior Consultant	Bangalore Hospital, Bangalore, India
Aug 2014 to June 2015	PDF-Neuropathology	NIMHANS, Bangalore, India
March 2013 to June 2014	Senior Resident	JIPMER, Puducherry, India
July 2011 to March 2013	Assistant Professor	Sri Manakula Vinayagar Medical Collegeand Hospital, Puducherry, India

Brief summary of relevant research experience: Nil

Current project/s at hand: Nil

Signature: 	Date: 31.01.2019 Place: Trivandrum

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APPENDIX-A-IEC Approval form

श्री चित्रा तिरुनाल आयुर्विज्ञान और प्रौद्योगिकी संस्थान, त्रिवेन्द्रम
तिरुवनन्तपुरम - ६९५०११, केरल, इंडिया
SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY, TRIVANDRUM
Thiruvananthapuram - 695 011, Kerala, India
(An Institute of National Importance under Govt. of India)
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Institutional Ethics Committee

(IEC Regn No. ECR/189/Inst/KL/2013/RR-21)

SCT/IEC/1776/NOVEMBER/2021 27.12.2021

Dr. Viswanadh KSVG
Senior Resident
Department of IS & IR
SCTIMST, Thiruvananthapuram

Dear Dr. Viswanadh,

The Institutional Ethics Committee held on 26th November, 2021, reviewed and discussed your application to conduct the study titled "**ADVANCED MR IMAGING CORRELATES OF HISTOPATHOLOGICAL CHANGES, IN AMYGDALA AND THE TEMPORAL NEOCORTEX IN MESIAL TEMPORAL SCLEROSIS**" (IEC/1776).

The following members of the Ethics Committee were present at the meeting held on 26th November, 2021 at Residences and Offices of IEC Members via Video Conference

SL. No.	Member Name	Highest Degree	Gender	Scientific /Non Scientific	Affiliation with Institution(s)
1.	Prof. C.C. Kartha	MBBS,MD	Male	Basic Medical Scientist (Chairman)	No
2.	Dr. Kala Kesavan P	MBBS,MD	Female	Basic Medical Scientist	No
3.	Smt. Sathi Nair	MA (English Literature)	Female	Lay Person	No
4.	Dr. Pradeep S	MBBS, MD	Male	Basic Medical Scientist	No
5.	Adv. N Anand	BAL, L.LB	Male	Legal Expert	No
6.	Adv. Priya Kaimal	LL.M, MBL	Female	Legal Expert	No
7.	Dr. Achuth Sankar S. Nair	Ph.D (i.Engineering ii.Music)	Male	Social Scientist	No
8.	Dr. Harikrishna Varma P. R	Ph.D (Materials Sciences)	Male	Medical Technology	Yes
9.	Dr. Narayanan Namboodiri. K.K	MBBS,MD,DM	Male	Clinician	Yes
10.	Dr. Manikandan.S	MBBS,MD,PDCC	Male	Clinician	Yes
11.	Dr. Ashalatha R	MBBS, MD,DM	Female	Clinician	Yes
12.	Dr. Biju Soman	MBBS,MD, DPH, MSc, DLSHTM	Male	Basic Medical Scientist	Yes
13.	Dr. Srinivas G	PhD	Male	Basic Medical Scientist (Member Secretary)	Yes

SCT/IEC/1776/NOVEMBER-2021

The following documents were reviewed:

Original submission

1. *Checklist Form*
2. *Covering letter addressed to the Chairperson, IEC, SCTIMST dated 07.10.2021*
3. *IEC Application Form*
4. *Project Proposal*
5. *Declaration Form*
6. *Informed Consent Form in English and Malayalam*
7. *Patient Information Sheet in English and Malayalam*
8. *CV of PI and Co-PIs*
9. *Proforma*
10. *SRC Approval Letter*

Revised submission

1. *Checklist Form*
2. *Covering letter addressed to the Chairperson, IEC, SCTIMST dated 24.12.2021*
3. *IEC Application Form*
4. *Project Proposal*
5. *Declaration Form*
6. *Informed Consent Form in English and Malayalam*
7. *Patient Information Sheet in English and Malayalam*
8. *CV of PI and Co-PIs*
9. *Proforma*

IEC Decision

The IEC approved the conduct of the study in the present form.

Remarks:
The Institutional Ethics Committee expects to be informed about the progress of the study, any SAE occurring in the course of the study, any changes in the protocol and patient information/informed consent and asks to be provided a copy of the final report.

There was no member of the study team who participated in voting / decision making process. The ethics committee is organized and operated according to the requirements of Good Clinical Practice and the requirements of the Indian Council of Medical Research (ICMR).

Sincerely,

G. Srinivas
Member Secretary, IEC

SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES & TECHNOLOGY
INSTITUTIONAL ETHICS COMMITTEE (IEC)
SCTIMST
THIRUVANANTHAPURAM

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE (IEC)
SCTIMST, THIRUVANANTHAPURAM

APPENDIX B

Supplementary table-1

PROFORMA

Sree Chitra Tirunal Institute for Medical Sciences and Technology
Thiruvananthapuram, Kerala-695011

TITLE OF THE STUDY: Advanced MR imaging correlates of Histopathological changes in Amygdala and the Temporal neocortex in Mesial Temporal Sclerosis.

1. Patient demographic data:

1.1 Serial number:

1.2 Patient gender:

1.3 Age (in years):

2. Clinical History:

2.1 History of Antecedent: Present (1)/absent (0)

2.2 Antecedent type: (F)-Febrile seizure, (FS)- Febrile status, (H)- Perinatal hypoxia, (MAS)- Meconium aspiration, (ME)-Meningoencephalitis, (HE)-Head trauma

2.3 Age of antecedent (in years):

2.4 Age of onset of epilepsy (in years):

2.5 Age at surgery (in years):

2.6 Duration of epilepsy (in years):

2.7 Seizure frequency score:

2.8 Number of anti-epileptic drugs:

3. Semiological features:

3.1 Secondary generalization: Present (1)/absent (0)

3.2 Aura: Present (1)/absent (0)

3.3 Type of aura: (F)- Fear, (A)-Anger, (E)- Experiential (Deja vu, Jamis vu), (AU)- Auditory, (VE)-Vertiginous sensation, (V)-Visual, (FS)-Foul-smell, (N)-Nausea, (R)- Retching, (E)-Epigastric sensation, (CE)- Cephalic sensation, (P)-Palpitations, (T)-Tiredness, (C)-Cold sensation, (U)-Undescribable, (PR)-Premonition, (CH)-Chest discomfort.

3.4 Sensory symptoms: Present (1)/absent (0)

3.5 Type of sensory symptoms: (AU)-Auditory, (VE)-Vertiginous sensation, (V): Visual, (FS)- Foul-smell, (C)- Cold sensation

3.6 Motor symptoms: Present (1)/absent (0)

3.7 Type of Motor symptoms: (PT)-Post-ictal todds, (I)- Inability to move, (HE)-Head and eye adversion, (ULP)-Upper limb posturing, (LLP)- Lower limb posturing, (ULLP)- Upper and lower limb posturing, (HC)- Hemiclonic jerks, (DUL)-Dystonic posturing of upper limb

3.8 Automatisms: Present (1)/absent (0)

3.9 Type of Automatisms: (UL)- Upper limb, (B)- Bimanual, (V)-Vocalization/ictal speech, (O)- Oral (Lip-smacking/Chewing), (W)-Wandering behaviour, (R)- Rubbing ears, (D)- Drinks water, (VI)- Violent behaviour, (S)- Search, (IN)- Ictal nose wiping, (RF)- Rubbing face, (L)-Leaving behaviour, (PL)- Pedaling movements of lower limb

3.10 Autonomic symptoms: Present (1)/absent (0)

3.11 Type of Autonomic symptoms: (PI)- Piloerection, (PA)-Palpitations, (N)-Nausea, (R)- Retching, (S)- Salivation, (EP)- Epigastric sensation, (AB)-Abdominal pain, (PICO)- Post-ictal cough, (ICO)- Ictal cough, (IS)- Ictal swallow, (PIS)- Post-ictal sneezing

3.12 Cognitive symptoms: Present (1)/absent (0)

3.13 Type of Cognitive symptoms: (PIC)- Post-ictal confusion, (PIA)- Post-ictal amnesia, (PID)- Post-ictal dysphagia, (E)- Experiential phenomena, (PIAP)- Pot-ictal aphasia

3.14 Affective/emotional symptoms: Present (1)/absent (0)

3.15 Type of Affective/emotional symptoms: (F)- Fear, (A)- Anger

4. Electroencephalography (EEG):

4.1 Inter-ictal EEG: (1)-Lateralized and localized, (2)-Localized, (3)-Multifocal

4.2 Ictal EEG: (1)-Lateralized and localized, (2)-Localized, (3)-Diffuse

4.3 Type of Ictal EEG recording: (T)-Monophasic theta, (B)-Fast beta, (D)-Diffuse

4.4 Clincal-electrophysiological impression: (0)-Neocortical seizures absent, (1)-Neocortical seizures present

5. Imaging (MRI) analysis:

5.1 Pathology side: (L)-Left, (R)-Right

5.2 T2/FLAIR Hippocampus: (1)-Hyperintensity present, (0)- Hyperintensity absent

5.3 ASL Hippocampus: (1)-ASL abnormality present, (0)- ASL abnormality absent

5.4 ASL signal intensity ratio (Hippocampus):

5.5 T2/FLAIR Amygdala: (1)-Hyperintensity present, (0)- Hyperintensity absent

5.6 ASL Amygdala: (1)-ASL abnormality present, (0)- ASL abnormality absent

5.7 ASL signal intensity ratio (Amygdala):

5.8 T2/FLAIR Temporal neocortex: (1)-Hyperintensity present, (0)-Hyperintensity absent

5.9 ASL Temporal neocortex: (1)-ASL abnormality present, (0)- ASL abnormality absent

5.10 ASL signal intensity ratio (Temporal neocortex):

5.11 T2/FLAIR Anterior Temporal pole: (1)-Hyperintensity present, (0)-Hyperintensity absent

5.12 ASL Anterior Temporal pole: (1)-ASL abnormality present, (0)-ASLabnormality absent

5.13 ASL signal intensity ratio (Anterior Temporal pole):

5.14 Radiologist-1 (T2, FLAIR abnormality in the Temporal neocortex): Present (1)/absent (0)

5.15 Radiologist-2 (T2, FLAIR abnormality in the Temporal neocortex): Present (1)/absent (0)

5.16 Radiologist-1 (ASL abnormality in the Temporal neocortex): Present (1)/absent (0)

5.17 Radiologist-2 (ASL abnormality in the Temporal neocortex): Present (1)/absent (0)

5.18 Radiologist-1 (T2, FLAIR abnormality in the Anterior Temporal pole): Present (1)/absent (0)

5.19 Radiologist-2 (T2, FLAIR abnormality in the Anterior Temporal pole): Present (1)/absent (0)

5.20 Radiologist-1 (ASL abnormality in the Anterior Temporal pole): Present (1)/absent (0)

5.21 Radiologist-2 (ASL abnormality in the Anterior Temporal pole): Present (1)/absent (0)

5.22 Radiologist-1 (Anterior Temporal pole volume loss): Present (1)/absent (0)

5.23 Radiologist-2 (Anterior Temporal pole volume loss): Present (1)/absent (0)

6. Histopathological analysis:

6.1 Hippocampus (NeuN): Hippocampal sclerosis type-1 (HS type-1)/HS type-2/HS type-3/Probable HS

6.2 Hippocampus (Astrogliosis): Moderate/severe

6.3 Amygdala (Neuronal loss): Present/Absent

6.4 Amygdala (Astrogliosis): Present/Absent

6.5 Temporal lobe-Luxol fast blue-grey-white blurring: Present/Absent

6.6 Temporal lobe-Focal cortical dysplasia: Present/Absent

APPENDIX B-data

S.no	Gender	Age	Antecedent	Antecedent type	Age of antecedent	Age at the onset of epilepsy (A)	Age at surgery (B)	Duration of epilepsy (B-A)	Seizure frequency score	Number of Anti-epileptic drugs	Secondary generalization	Aura	Type of aura 1	Type of aura 2	Type of aura 3	Sensory	Type of sensory 1	Type of sensory 2	Motor	Type of motor 1	Type of motor 2	Automatisms	Type of automatisms 1	Type of automatisms 2	Type of automatisms 3	Autonomic	Type of autonomic 1	Type of autonomic 2	Type of autonomic 3	Cognitive	Type of cognitive	Type of cognitive 2	Emotional	Type of emotional	III-EEG (A)	I-EEG	Type
1	F	39	0			22	32	10	8	2	1	0				0						1	B	V		1	PIS						0		1	1	T
2	F	33	0			14	34	20	7	4	1	1	EP			0						1	O			1	EP						0		3	3	D
3	M	37	0			5	40	35	7	3	0	1	F			0			0			1	O			0				1	PIAP		1	F	1	1	T
4	M	18	1	F	1.5	4.5	18	13.5	7	2	0	1	CE			0			1	HC		1	O			0				0			0		1	1	T
5	F	36	0			5	36	31	7	2	0	1	CE			0			1	HE	ULP	1	B	S	V	0				1	PIC		0		1	1	T
6	F	15	1	F	0.67	4	15	11	7	2	0	1	F			0			0			1	B	O		0				0			1	F	1	1	B
7	M	19	0			11	19	8	8	2	1	1	AU			1	AU					1	O			0							0		1	1	T
8	F	15	1	ME	0.75	6.5	15	9.5	8	3	0	1	U	N	R	0			0			1	V			1	R			0			0		1	1	T
9	F	42	0			14	42	28	8	3	0	1	CE			0			1	ULP		1	B	IN		0				1	PIAP		0		1	1	T
10	M	30	0			9	30	21	8	4	1	1	AU	V		0						0				0							0		1	1	T
11	F	28	1	F	1	5	28	23	8	3	0	1	F			0			1	HE		1	UL			0				0			0		1	1	T
12	M	10	1	F	0.75	1	11	10	7	2	0	1	F			0			0			1	UL			0				0			1	F	1	1	T
13	M	29	1	F	5	6	29	23	7	2	1	1	F			0						0				0							1	F	2	1	B
14	M	30	1	F	3	7	30	23	7	4	0	1	F	EP		0			1	ULP		1	UL			1	EP			1	PIA		1	F	1	1	T
15	F	24	0			2.5	24	21.5	7	2	1	1	F			0						1	O			0							0		1	1	T
16	F	23	1	F	0.5	18	23	5	9	2	0	1	F			0			0			1	V			0				1	PIA		1	F	1	1	T
17	F	16	0			1	16	15	8	2	0	0				0			1	HE	ULP	0				0				0			0		1	1	T
18	M	15	0			4	15	11	7	3	1	1	F	E	V	1	V					0				1	AB						1	F	1	1	B
19	M	24	1	F	2	18	24	6	7	3	0	1	F	V	VE	1	V	VE	1	HC		1	UL	V	VI	1	IS			0			1	F	1	1	T
20	F	25	0			19	25	6	8	3	1	1	F			0						1	O	B		1	EP	ICO					1	F	2	1	B
21	F	18	1	FS	0.16	3	18	15	8	3	0	1	F	EP		0			1	ULLP		1	O	UL		1	R			0			1	F	1	1	T
22	F	18	1	F	1.5	9	18	9	7	2	1	0				0						1	O	B	W	0							0		1	1	T
23	F	27	0			9	27	18	7	2	1	1	P	E		0						1	O			1	PA						0		1	1	T
24	F	12	1	F	2	5	13	8	9	2	0	0				0			0			1	O	B	VI	0				0			0		1	1	T
25	M	26	1	F	3	16	26	10	7	3	1	0				0						1	O			0							0		1	1	T
26	M	22	1	F	0.16	1.5	22	20.5	7	3	1	1	AU			1	AU					0				0							0		1	1	T
27	M	35	1	H	0.08	0.08	33	33	7	4	1	0				0						0				0							0		1	1	B
28	M	15	0			11	15	4	7	2	1	1	F			0						1	O	B		0							1	F	1	1	T
29	M	21	0			12	21	9	10	2	1	1	PR	E	VE	1	VE					1	UL	O		0							1	F	1	1	T
30	M	12	1	H	0.08	0.75	12	11.3	7	2	0	0				0			1	HE	HC	0				0				1	PIA		0		1	1	T

31	M	21	0			10	21	11	6	4	1	0				0						1	V			0							0		1	1	T
32	M	29	0			6	29	23	8	2	0	1	U			0			0			1	O	B		0				1	PIA		0		1	1	T
33	M	19	1	ME	0.58	18	19	1	7	2	0	1	EP	E		0			0			1	L			1	EP			1	E	PIA	0		1	1	T
34	F	31	1	F	2	12	31	19	8	3	0	1	VE			1	VE		1	HE	DUL	1	O			0				0			0		1	1	B
35	M	34	0			2	34	32	8	4	0	1	V	VE		1	V	VE	1	HE	DUL	1	O			0				0			0		1	1	T
36	M	24	0			17	24	7	8	2	1	1	EP			0						1	O			1	EP						0		1	1	T
37	M	15	1	H	0.08	2	15	13	8	2	1	0				0						1	RF			0							0		1	1	B
38	M	22	1	F	0.25	11	20	9	8	3	0	0				0			0			1	O	UL		0				0			0		1	1	T
39	M	16	1	F	2	10	16	6	9	2	0	1	EP			0			0			1	O	UL		1	EP			0			0		1	1	T
40	M	22	0			10	22	12	10	2	0	1	F	T		0			1	PT		1	B	V		0				0			1	F	1	1	T
41	M	23	1	H	0.08	0.67	23	22	9	2	0	1	F			0			0			0				1	PI			0			1	F	1	1	T
42	M	22	1	F	1.5	7	22	15	7	3	0	1	F			0			0			1	B	O		0				1	PID		1	F	1	1	T
43	M	51	1	F	5	17	51	34	8	3	0	1	F	E		0			1	I		0	NA			1	PI			1	E		1	F	1	1	T
44	F	17	1	F	1	10	17	7	8	2	0	1	F			0			0			1	B	O		0				1	PIA		1	F	2	1	T
45	F	25	1	ME	9	19	25	6	6	2	1	0				0						1	B	O		0							0		3	3	D
46	M	13	1	F	5	13	8	8	8	3	0	1	F			0			1	HE		1	O	V	W	1	PA			0			1	F	1	1	T
47	F	12	1	F	1	2	13	11	8	3	0	1	V	C		1	AU		0			1	O	R		0				0			0		1	1	B
48	F	3	1	MAS	0.08	0.67	3	2	8	2	0	0				0			1	ULP	PT	1	UL			0				0			0		1	1	T
49	M	9	1	F	0.75	0.75	9	8	7	3	0	1	EP			0	NA		1	HE	ULP	1	UL	O	W	1	S	R	EP	0			0		1	1	T
50	M	40	1	F	1	21	40	19	7	2	1	1	VE	A		1	VE					1	B	O		0							1	A	1	1	B
51	F	11	1	FS	3	4	11	7	6	4	1	1	F			0						1	O			0							1	F	1	1	B
52	F	39	1	F	2.5	3.5	39	35.5	9	5	1	1	EP	AU	VE	1	AU	VE				1	O			1	EP						0		1	1	B
53	F	22	1	F	3	14	22	8	8	3	1	0				0						1	O			0							0		1	1	B
54	F	26	1	F	0.5	2.5	26	23.5	7	2	0	1	V	C		1	V	C	1	ULLP		0				0				1	PIC		0		1	1	B
55	F	22	1	H	0.08	1	22	21	7	2	1	1	EP			0						1	O	B		1	EP						0		1	1	T
56	M	21	1	F	0.75	0.91	21	20	7	3	0	1	F			0			0			1	O	UL		0				1	PIA		1	F	1	1	T
57	F	37	1	F	0.5	13	37	24	7	4	1	1	F			0						0				0							1	F	1	1	T
58	F	21	1	F	1	7	21	8	7	3	0	1	CE			0			1	ULLP		1	UL	O		0				1	PIA		0		1	1	T
59	F	20	0			1.5	20	18.5	8	2	1	1	EP			0						1	O	B		1	EP						0		1	1	T
60	M	33	0			1.5	33	31.5	7	3	1	1	CE			0						0				0							0		1	1	B
61	M	30	0			2	30	28	8	2	1	1	F			0						0				0							1	F	1	1	T
62	M	25	1	F	0.5	1	25	24	7	2	0	1	F	EP		0			0			1	O			1	EP			1	PIA		1	F	1	1	T
63	F	24	0			8	24	16	7	3	1	1	CE	F		0						1	B	L		0							1	F	1	1	T
64	F	22	1	F	2	10	22	12	8	2	0	0				0			0			1	B	O		0				0			0		1	1	T
65	M	21	1	H	0.08	3	23	20	7	2	0	1	F	EP		0			0			1	O			1	EP			0			1	F	1	1	B
66	F	28	1	F	0.41	10	28	18	7	2	0	1	E			0			1	ULP		1	V			0				1	E		0		1	1	T
67	F	18	1	F	1	4	18	14	8	2	1	1	F	EP		0			0			1	B	O		1	EP			0			1	F	1	1	T

68	M	37	0			1	37	36	8	4	1	1	F			0						1	B	O		0							1	F	1	1	T
69	M	30	1	F	0.67	2	30	28	7	3	0	1	E			0			0			1	UL	O		0				1	E		0		1	1	T
70	F	31	1	F	0.5	11	31	20	5	2	0	1	F	EP		0			0			1	B	O		1	EP			1	PIA		1	F	1	1	T
71	F	22	1	F	1	12	22	10	7	2	0	1	F	EP		0			0			1	B	O	V	0				0			0		1	1	T
72	M	38	0			8	38	30	7	2	1	1	EP			0						0				1	EP						0		1	1	T
73	M	26	1	F	3	6	26	20	8	3	0	1	F	P	E	0			0			1	UL			1	PA	EP		0			1	F	1	1	T
74	F	8	0			1	8	7	7	2	0	0	NA			0			1	HC		1	B			0				0			0		1	1	T
75	F	26	1	F	3	19	26	7	8	3	0	1	F			0			1	ULP		1	O	B		0				1	PIA		1	F	1	1	T
76	F	26	1	F	0.5	0.5	26	25	8	3	1	1	F			0						1	O	V		1	PICO						1	F	1	1	T
77	F	34	1	F	2	21	34	13	7	2	1	0	NA			0						1	O	D	W	0							0		1	1	T
78	F	33	1	F	3	21	33	12	7	2	0	1	EP	F	E	0			0			1	B	O	RF	1	EP			1	E	PIC	1	F	1	1	T
79	F	27	1	F	3	5	27	22	7	2	0	1	F			0			1	HE	ULP	1	O			0				1	PIC		1	F	1	1	T
80	M	13	0			7	13	6	8	3	0	0				0			1	HC		1	PL	V		1	S			0			0		1	1	T
81	M	10	0			5	10	2	7	4	1	1	CH			0						0				0							0		1	1	T
82	M	19	1	F	0.5	4	18	14	8	3	0	1	EP			0			0			1	O			1	EP			0			0		1	1	T
83	F	15	1	F	0.08	0.08	15	14	7	2	0	0				0			0			1	O	UL		0				0			0		1	1	T
84	M	22	0			14	22	8	8	3	0	0				0			0			1	O			0				1	PIA		0		1	1	T
85	F	25	1	ME	0.58	11	25	14	6	1	0	0				0			1	DUL		1	B	O		0				0			0		1	1	T
86	F	22	0			11	22	11	9	3	0	0				0			0			1	O			0				1	PIC		0		1	1	T
87	F	15	1	HE	1	14	15	1	8	2	0	1	F			0			1	ULP		1	O	B		0				0			1	F	1	1	T
88	M	50	0			30	50	20	7	2	0	0				0			0			1	O	B	W	0				1	PIC		0		1	1	T
89	M	16	1	F	1	4	15	11	8	3	1	1	EP			0						1	UL			1	EP						0		1	1	T
90	M	26	0			13	26	13	7	2	0	1	EP			0			1	HE	ULP	0				1	EP			0			0		1	1	T
91	F	27	0			23	27	4	6	2	1	1	E			0						0				0							0		1	1	T
92	M	25	1	F	2	15	25	10	6	2	1	1	U			0						1	O	V		0							0		1	1	T
93	M	25	0			16	25	9	7	2	0	1	FS	N		1	FS		0			1	O			1	N	R		1	PIC		0		2	1	T
94	F	33	0			8	33	5	7	4	1	0				0						1	O	B		0							0		1	1	T
95	F	45	0			8	45	37	7	3	0	1	CE			0			1	ULP		1	V			0				1	PIC		0		1	1	T
96	M	30	0			20	30	10	5	4	1	0				0						1	O			0							0		1	1	T
97	F	16	0			8	14	6	9	2	0	1	F	EP		0			1	ULP	HE	0				1	EP	S		1	PIA		1	F	1	1	T
98	M	42	0			20	42	22	7	4	1	0				0						1	O			0							0		1	1	T
99	F	20	0			12	20	8	9	2	0	1	EP			0			0			0				1	EP			0			0		1	1	T
100	M	37	1	F	1	34	37	3	7	2	1	0				0						1	O	V		0							0		1	1	T

Clinico-electrophysiological imp	Pathology side	T2/FLAIR (Hippo)	ASL (Hippo)	ASL-SIR (Hippo)	T2/FLAIR (A)	ASL (A)	ASL-SIR (A)	T2/FLAIR (TN)	ASL (TN)	ASL-SIR (TN)	T2/FLAIR (AT)	ASL (AT)	ASL-SIR (AT)	VL (AT)	R1-T2/FLAIR (TN)	R2-T2/FLAIR (TN)	R1-ASL (TN)	R2-ASL (TN)	R1-T2/FLAIR (AT)	R2-T2/FLAIR (AT)	R1-ASL (AT)	R2-ASL (AT)	R1-VL (AT)	R2-VL (AT)	Histopath- Hippocampus-neuN (type of HS)	Histopath- Hippocampus-astrogliosis	Amygdala (neuronal loss)	Amygdala (Astrogliosis)	Histopath- temporal lobe-LFB- grey-white bluring	Histopath- temporal lobe-FCD
0	L	1	1	0.87	1	1	0.89	1	1	0.75	1	1	0.8	1	1	1	1	1	1	1	1	1	1	1	HS type 1	severe	Present	Present	absent	absent
1	R	1	1	0.88	1	1	0.84	1	1	0.74	1	0	1.03	1	1	1	1	1	1	1	1	0	0	1	1	HS type 1	moderate	Present	Present	absent	absent
0	L	1	1	0.94	1	1	0.87	1	1	0.84	1	1	0.8	1	1	1	1	0	1	1	1	1	1	1	HS type 1	moderate	Present	Present	absent	absent
1	L	1	1	0.74	1	1	0.78	1	1	0.61	1	1	0.8	1	1	1	1	1	1	1	1	1	1	1	HS type 1	moderate	Present	Present	absent	absent
0	L	1	1	0.9	1	1	0.86	1	1	0.91	1	1	0.87	1	1	1	1	1	1	1	1	1	1	1	HS type 1	severe	Present	Present	absent	absent
1	L	1	1	0.76	1	1	0.82	1	1	0.89	1	1	0.9	1	1	1	1	1	1	1	1	1	1	1	HS type 1	severe	Present	Present	absent	absent
0	L	1	1	0.68	1	1	0.78	1	1	0.88	1	1	0.8	1	0	1	1	1	1	1	1	1	1	1	HS type 1	severe	Present	Present	absent	absent
0	R	1	1	0.68	1	1	0.72	1	1	0.74	1	1	0.82	1	1	1	1	1	1	1	1	1	1	1	HS type 1	severe	Present	Present	absent	absent
0	L	1	1	0.74	1	1	0.68	1	0	1.02	1	0	0.98	1	1	1	1	0	1	1	1	0	1	1	HS type 1	severe	Present	Present	absent	absent
1	L	1	1	0.74	1	1	0.78	1	1	0.76	1	1	0.78	1	1	1	1	1	1	1	1	1	1	1	HS type 1	severe	Present	Present	absent	absent
1	L	1	1	0.68	1	1	0.64	1	1	0.72	1	1	0.74	1	1	0	1	0	1	1	1	1	1	1	HS type 1	severe	Present	Present	absent	absent
0	L	1	1	0.64	1	1	0.68	1	0	0.98	1	1	0.78	1	1	1	1	0	1	1	1	1	1	1	HS type 1	moderate	Present	Present	absent	absent
1	L	1	1	0.74	1	1	0.78	1	1	0.78	1	1	0.8	1	1	1	1	1	1	1	1	1	1	1	HS type 1	severe	Present	Present	present	absent
0	R	1	1	0.64	1	1	0.68	1	1	0.78	1	1	0.74	1	0	1	1	1	1	1	1	1	1	1	HS type 1	severe	Present	Present	absent	absent
0	L	1	1	0.64	1	1	0.72	1	0	0.98	1	1	0.68	1	1	1	1	0	1	1	1	1	1	1	HS type 1	severe	Present	Present	present	absent
0	R	1	1	0.7	1	1	0.65	1	1	0.66	1	1	0.68	1	1	1	1	1	1	1	1	1	1	1	HS type 1	severe	Present	Present	absent	absent
1	L	1	1	0.6	1	1	0.6	1	1	0.6	1	1	0.7	1	1	1	1	1	1	1	1	1	1	1	HS type 1	severe	Present	Present	absent	absent
1	L	1	1	0.7	1	1	0.7	1	1	0.6	1	1	0.7	1	1	1	1	1	1	1	1	1	1	1	HS type 1	severe	Present	Present	absent	absent
1	R	1	1	0.7	1	1	0.7	1	1	0.7	1	1	0.8	1	1	1	1	1	1	1	1	1	1	1	HS type 1	severe	Present	Present	absent	absent
1	L	1	1	0.7	1	1	0.8	1	1	0.6	1	1	0.7	1	1	1	1	1	1	1	1	1	1	1	HS type 1	severe	Present	Present	absent	absent
0	R	1	1	0.8	1	1	0.76	1	0	0.9	1	0	0.9	1	1	1	0	1	1	1	1	0	1	1	HS type 1	severe	Present	Present	absent	absent
0	L	1	1	0.7	1	1	0.8	1	1	0.8	1	1	0.8	1	0	1	1	1	1	1	1	1	1	1	HS type 1	moderate	Present	Present	absent	absent
1	L	1	1	0.8	1	1	0.8	1	1	0.7	1	1	0.8	1	1	1	1	1	1	1	1	1	1	1	HS type 1	moderate	Present	Present	absent	present
0	R	1	1	0.64	1	1	0.68	1	1	0.8	1	1	0.7	1	1	1	1	1	1	1	1	1	1	1	HS type 1	moderate	Present	Present	absent	absent
0	L	1	1	0.68	1	1	0.72	1	0	0.98	1	0	1.01	1	1	1	1	0	1	1	1	0	1	1	HS type 1	moderate	Present	Present	present	absent
1	L	1	0	0.99	1	1	0.78	1	0	1.02	1	0	1.01	1	1	1	0	0	1	1	0	1	1	1	HS type 1	severe	Present	Present	absent	absent
1	L	1	1	0.76	1	1	0.68	1	1	0.64	1	1	0.62	1	1	0	1	1	1	1	1	1	1	1	HS type 1	severe	Present	Present	absent	absent
1	L	1	1	0.68	1	1	0.62	1	1	0.72	1	1	0.82	1	1	1	1	1	1	1	1	1	1	1	HS type 1	moderate	Present	Present	absent	absent
1	R	1	1	0.72	1	1	0.68	1	1	0.82	1	1	0.78	1	1	1	0	1	1	1	1	1	1	1	probable H	moderate	Present	Present	absent	absent
1	R	1	1	0.69	1	1	0.78	1	1	0.74	1	1	0.8	1	1	1	1	0	1	1	1	1	1	1	HS type 1	severe	Present	Present	absent	absent

1	L	1	1	0.7	1	1	0.68	1	1	0.76	1	1	0.78	1	1	1	1	1	1	1	1	1	1	1	HS type 1	severe	Present	Present	absent	absent
0	R	1	1	0.78	1	1	0.68	1	1	0.69	1	1	0.72	1	1	1	1	1	1	1	1	1	1	1	HS type 1	severe	Present	Present	present	absent
1	L	1	1	0.68	1	1	0.69	1	1	0.7	1	1	0.78	1	0	1	1	1	1	1	1	1	1	1	HS type 1	severe	Present	Present	absent	absent
1	L	1	1	0.78	1	1	0.72	1	0	0.97	1	1	0.8	1	1	1	0	0	1	1	1	1	1	1	HS type 1	severe	Present	Present	present	absent
1	L	1	1	0.76	1	1	0.78	1	0	0.98	1	1	0.77	1	1	1	0	0	1	1	1	1	1	1	HS type 1	severe	Present	Present	absent	absent
1	L	1	1	0.76	1	1	0.78	1	1	0.74	1	1	0.78	1	1	1	1	1	1	1	1	1	1	1	HS type 1	severe	Present	Present	absent	absent
1	R	1	1	0.78	1	1	0.64	1	1	0.98	1	1	0.7	1	1	1	1	0	1	1	1	1	1	1	HS type 1	severe	Present	Present	present	absent
1	L	1	1	0.78	1	1	0.77	1	1	0.64	1	1	0.7	1	1	1	1	1	1	1	1	1	1	1	probable H	severe	Present	Present	present	absent
1	L	1	1	0.7	1	1	0.68	1	0	0.99	1	1	0.7	1	1	1	0	0	1	1	1	1	1	1	HS type 1	severe	Present	Present	present	absent
0	R	1	1	0.8	1	1	0.78	1	1	0.68	1	1	0.8	1	1	1	1	1	1	1	1	1	1	1	HS type 1	severe	Present	Present	present	absent
0	R	1	1	0.7	1	1	0.8	1	1	0.8	1	1	0.77	1	1	1	1	1	1	1	1	1	1	1	HS type 1	severe	Present	Present	present	absent
0	L	1	1	0.8	1	1	0.8	1	0	0.9	1	1	0.68	1	1	1	0	0	1	1	1	1	1	1	HS type 1	severe	Present	Present	present	absent
1	R	1	1	0.8	1	1	0.8	1	1	0.7	1	1	0.76	1	1	1	1	1	1	1	1	1	1	1	HS type 1	severe	Present	Present	present	absent
0	L	1	1	0.64	1	0	0.94	1	0	0.95	1	1	0.8	1	1	1	0	0	1	1	1	1	1	1	HS type 1	severe	Present	Present	present	absent
1	R	1	1	0.8	1	1	0.8	1	1	0.66	1	1	0.66	1	1	1	1	1	1	1	1	1	1	1	HS type 2	severe	Present	Present	absent	present
0	L	1	1	0.8	1	1	0.85	1	0	1.1	1	1	0.82	1	1	1	0	1	1	1	1	1	1	1	HS type 2	severe	Present	Present	absent	absent
1	R	1	1	1.54	1	1	1.6	1	1	1.23	1	1	1.7	0	1	1	1	1	1	1	1	1	0	0	HS type 1	severe	Present	Present	present	absent
1	R	1	1	0.74	1	1	0.68	1	1	0.65	1	1	0.72	1	1	1	1	1	1	1	1	1	1	1	HS type 1	severe	Present	Present	present	Present
0	L	1	0	0.96	1	0	0.98	1	1	0.78	1	1	0.8	1	1	0	1	1	1	1	1	1	1	1	HS type 1	severe	Present	Present	present	absent
1	R	1	1	1.3	1	0	0.98	1	1	1.3	1	0	1.1	1	1	1	0	1	1	1	0	1	1	1	HS type 1	severe	Present	Present	present	absent
1	L	1	1	0.7	1	1	0.68	1	1	0.64	1	1	0.72	0	1	1	1	1	1	1	1	1	1	0	HS type 1	severe	Present	Present	absent	absent
1	L	1	1	1.2	1	1	1.2	1	1	1.2	1	1	1.2	1	1	1	1	1	1	1	1	1	1	1	HS type 1	severe	Present	Present	present	absent
1	L	1	1	0.8	1	1	0.7	1	1	0.6	1	1	0.8	1	1	1	1	1	1	1	1	1	1	1	probable H	severe	Present	Present	present	present
1	L	1	1	0.7	1	1	0.8	1	1	0.62	1	1	0.8	1	1	1	0	1	1	1	1	1	1	1	HS type 3	severe	Present	Present	present	present
1	R	1	1	0.8	1	1	0.76	1	1	0.72	1	1	0.68	1	1	1	1	1	1	1	1	1	1	1	HS type 1	severe	Present	Present	absent	absent
1	L	1	1	0.72	1	1	0.68	1	1	0.71	1	1	0.77	1	1	1	1	0	1	1	1	1	1	1	HS type 1	severe	Present	Present	present	absent
1	R	1	1	0.74	1	1	0.72	1	1	0.64	1	1	0.62	1	1	1	1	1	1	1	1	1	1	1	HS type 1	moderate	Present	Present	absent	absent
1	L	1	0	1.04	1	0	1.01	1	0	1.01	1	1	0.82	1	1	1	0	1	1	1	1	1	1	1	HS type 1	severe	Present	Present	absent	absent
1	L	1	1	0.74	1	1	0.69	1	1	0.72	1	1	0.76	1	1	1	0	1	1	1	1	1	1	1	HS type 1	severe	Present	Present	present	absent
1	L	1	1	0.68	1	1	0.64	1	1	0.62	1	1	0.71	0	1	1	1	1	1	1	1	1	0	0	HS type 1	severe	Present	Present	present	absent
1	R	1	1	0.64	1	1	0.68	1	1	0.78	1	1	0.72	1	1	1	1	1	1	1	1	1	1	1	HS type 1	severe	Present	Present	absent	absent
1	R	1	1	0.76	1	1	0.74	1	1	0.68	1	1	0.72	1	1	1	1	1	1	1	1	1	1	1	HS type 1	severe	Present	Present	present	absent
1	R	1	1	0.72	1	1	0.68	1	1	0.64	1	1	0.7	1	1	0	0	0	1	1	1	1	1	1	HS type 1	severe	Present	Present	present	absent
0	L	1	1	0.82	1	1	0.88	0	0	1.02	0	0	0.9	0	0	0	0	0	0	0	0	0	0	1	HS type 1	severe	Present	Present	absent	absent
1	R	1	1	0.77	1	1	0.76	0	0	0.98	1	1	0.78	1	0	0	0	0	1	1	1	1	1	1	HS type 1	severe	Present	Present	absent	absent
0	L	1	1	0.68	1	1	0.78	0	0	0.9	0	0	1.01	0	0	0	0	0	0	0	0	0	0	0	HS type 1	severe	Present	Present	absent	
1	L	1	1	0.68	1	1	0.64	0	0	0.97	0	0	1.01	0	0	0	0	0	0	0	0	1	0	1	HS type 2	moderate	Present	Present	absent	absent

0	R	1	1	0.78	1	1	0.74	0	0	0.96	1	0	1.02	1	0	0	0	0	1	1	0	0	1	1	HS type 1	severe	Present	Present	absent	absent
0	R	1	1	0.68	1	1	0.64	0	0	1.02	1	0	1.01	1	0	0	0	0	1	1	0	1	1	1	HS type 1	severe	Present	Present	absent	absent
0	R	1	1	0.78	1	1	0.78	0	0	1.01	1	0	0.98	1	1	0	0	0	1	1	0	0	1	1	HS type 1	severe	Present	Present	absent	absent
0	R	1	1	0.78	1	1	0.76	0	0	1.02	0	0	1.01	1	0	0	0	0	1	0	0	1	1	1	HS type 2	severe	Present	Present	absent	absent
0	R	1	1	0.78	1	1	0.68	0	0	0.99	1	1	0.78	1	0	0	0	0	1	1	1	1	1	1	HS type 1	severe	Present	Present		absent
0	R	1	1	0.74	1	1	0.72	0	0	1.01	0	0	0.99	0	0	0	0	0	0	0	0	0	0	0	HS type 1	moderate	Present	Present	absent	absent
0	L	1	1	0.7	1	1	0.68	0	0	1.1	1	1	0.6	1	0	0	0	0	1	1	1	1	1	1	HS type 1	moderate	Present	Present	present	absent
0	R	1	1	0.7	1	1	0.7	0	0	1	0	0	0.9	1	0	0	0	0	1	0	0	0	1	1	HS type 1	severe	Present	Present	absent	absent
1	R	1	1	0.6	1	1	0.62	0	0	0.9	1	1	0.6	1	0	0	0	0	1	1	1	1	1	1	HS type 1	severe	Present	Present	absent	absent
1	R	1	1	0.8	1	1	0.8	0	0	1	1	0	0.9	1	0	0	0	0	1	1	0	0	1	1	HS type 1	severe	Present	Present	absent	absent
0	R	1	1	0.74	1	1	0.64	0	0	1.01	1	0	0.96	1	0	0	0	0	1	1	0	0	1	1	HS type 1	moderate	Present	Present	absent	absent
0	L	1	1	0.78	1	1	0.62	0	0	1.01	0	0	1.02	0	0	1	0	0	0	0	0	0	0	0	HS type 1	severe	Present	Present	absent	absent
0	R	1	1	0.64	1	1	0.74	0	0	0.98	0	0	1.02	0	0	0	0	0	0	1	0	0	0	0	HS type 1	severe	Present	Present	absent	absent
0	R	1	1	0.72	1	1	0.76	0	0	0.98	1	1	0.64	1	0	0	0	0	1	1	1	1	1	1	HS type 1	severe	Present	Present	absent	absent
0	L	1	1	0.78	1	1	0.72	0	0	1.01	1	1	0.7	1	0	0	0	0	1	1	1	1	1	1	HS type 1	severe	Present	Present	present	absent
0	L	1	1	0.74	1	1	0.7	0	0	0.99	0	0	1.01	0	0	0	0	0	0	1	0	0	0	0	HS type 1	severe	Present	Present	present	absent
0	L	1	1	0.72	1	1	0.68	0	0	1.01	1	1	0.7	1	0	0	0	0	1	1	1	1	1	1	HS type 1	severe	Present	Present	present	absent
0	L	1	1	0.68	1	1	0.72	0	0	0.99	1	0	0.99	1	0	1	0	0	1	1	0	0	1	1	HS type 1	severe	Present	Present	absent	absent
0	R	1	1	0.76	1	1	0.77	0	0	1.01	1	1	0.78	1	0	0	0	0	1	1	1	1	1	1	HS type 1	severe	Present	Present	present	absent
0	R	1	1	0.78	1	1	0.8	0	0	1.02	1	1	0.78	1	0	0	0	0	1	1	1	1	1	1	probable H	severe	Present	Present	present	absent
0	R	1	1	0.72	1	1	0.74	0	0	1.01	0	0	1.01	0	0	0	0	0	0	0	0	0	0	0	HS type 1	severe	Present	Present	present	absent
0	L	1	1	0.78	1	1	0.8	0	0	1.02	0	0	0.98	0	0	0	0	0	0	1	0	0	0	0	HS type 1	severe	Present	Present	present	absent
0	R	1	1	0.68	1	1	0.7	0	0	0.99	0	0	1.01	0	0	0	0	0	0	0	0	0	0	0	HS type 1	severe	Present	Present	present	absent
0	R	1	1	0.8	1	1	0.8	0	0	1.1	0	0	1.01	0	0	0	0	0	0	0	0	0	0	0	probable H	severe	Present	Present	present	absent
0	R	1	1	0.8	1	0	0.98	0	0	0.95	1	0	0.95	1	0	0	0	0	1	1	0	0	1	1	HS type 1	severe	Present	Present	present	absent
0	R	1	1	1.2	1	1	1.2	0	0	0.98	0	0	0.97	0	0	0	0	0	0	0	0	0	0	0	HS type 1	severe	Present	Present	absent	absent
0	L	1	1	0.76	1	1	0.78	0	0	0.99	0	0	1.01	0	0	0	0	0	0	0	0	0	0	0	HS type 1	severe	Present	Present	absent	absent
0	L	1	1	0.68	1	1	0.72	0	0	1.02	1	1	0.68	1	0	0	0	0	1	1	1	1	1	1	HS type 1	severe	Present	Present	present	present
0	L	1	1	0.68	1	1	0.74	0	0	1.01	0	0	1.02	0	0	0	0	0	0	0	0	0	0	0	HS type 1	severe	Present	Present	present	absent
0	R	1	1	0.68	1	1	0.64	0	0	1.01	1	1	0.64	1	0	0	0	0	1	1	1	1	1	1	HS type 1	severe	Present	Present	present	absent
0	R	1	1	0.78	1	1	0.7	0	0	0.99	0	0	1.02	0	0	0	0	0	0	0	0	0	0	0	HS type 1	severe	Present	Present	absent	absent
0	L	1	1	0.72	1	1	0.68	0	0	0.98	1	0	1.02	1	0	0	0	0	1	1	0	0	1	1	HS type 3	moderate	Present	Present	absent	absent
1	L	1	1	0.72	1	1	0.74	0	0	1.01	0	0	1.02	0	0	0	0	0	0	0	0	0	0	0	HS type 1	severe	Present	Present	present	absent

Supplementary table-3

SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY, THIRUVANANTHAPURAM, KERALA - 695011

INFORMED CONSENT FORM

Title of Study:

Advanced magnetic resonance imaging correlates of histopathological changes in amygdala and the temporal neocortex in mesial temporal sclerosis

Principal Investigator:

Dr Viswanadh K S V G, Senior resident, Department of imaging sciences and interventional radiology, SCTIMST

Co-Principal Investigators:

Dr Bejoy Thomas, Professor & HOD, Department of imaging sciences and interventional radiology, SCTIMST.

Dr Ashalatha. R, Professor, Department of Neurology, SCTIMST.

Dr Deepthi A N., Associate professor, Department of Pathology, SCTIMST.

Co-Investigator:

Dr Rajalakshmi P, Assistant professor, Department of Pathology, SCTIMST.

Please tick the following points:

I agree to participate as a participant in the study described in the Participant Information Sheet attached to this form.	[ ]
I acknowledge that I have read the Participant Information Sheet, which explains why I have been selected, the aims of the study and the nature and the possible risks of the investigation, and the information sheet has been explained to me to my satisfaction.	[ ]
Before signing this consent form, I have been given the opportunity of asking any questions relating to any possible physical and mental harm I might suffer as a result of my participation and I have received	[ ]

satisfactory answers.	
I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.	[ ]
I agree that research data gathered from the results of the study may be published, provided that I cannot be identified.	[ ]
I understand that if I have any questions relating to my participation in this research, I may contact my doctor, who will be happy to answer them.	[ ]
I acknowledge receipt of a copy of this Consent Form and the Participant Information Sheet attached to this form	[ ]

_____
Name of Participant

_____
Signature of Participant

_____
Name of Caretaker or Next of Kin
(If patient not directly consented)

_____
Relationship with the patient

_____ _____
Signature of Caretaker or Next of Kin

_____
Name of Witness

_____ _____
Signature of Witness

_____
Name of Person conducting Informed Consent discussion

_____ _____ _____
Signature of Person conducting Informed Consent discussion Date Time

Supplementary table-4

INFORMED CONSENT-Malayalam

ശ്രീ ചിത്ര തിരുനാൾ ഇൻസ്റ്റിറ്റ്യൂട്ട് ഫോർ മെഡിക്കൽ സയൻസസ് ആന്റ് ടെക്നോളജി,
തിരുവനന്തപുരം, കേരളം – 695011
മസ്തിഷ്ക്കാഘാത പരിചരണത്തിനായുള്ള സമഗ്ര പരിപാടി

കാര്യബോധത്തോടെയുള്ള സമ്മതപത്രം

പഠനശീർഷകം:
മീസിയൽ ടെമ്പോറൽ സ്ലിറോസിസിൽ അമിഗ്ഡുലയിലും ടെമ്പോറൽ നിയോകോർടെക്സിലുമുള്ള മാറ്റങ്ങളുടെ രോഗനിദാനശാസ്ത്രവും (ഹിസ്റ്റോപതോളജി) എംആർ ഇമേജിംഗും തമ്മിലുള്ള പാരസ്പര്യം.

പ്രധാനഗവേഷകൻ
ഡോ. വിശ്വനാഥ് കെ എസ് വിജി, സീനിയർ റെസിഡന്റ്, ഡിപ്പാർട്ടമെന്റ് ഓഫ് ഇമേജിംഗ് സയൻസസ് ആന്റ് ഇന്റർവെൻഷണൽ റേഡിയോളജി, SCTIMST
സഹ പ്രധാനഗവേഷകൻ
ഡോ. ബിജോയ് തോമസ്, പ്രൊഫസർ & ഹെഡ്, ഡിപ്പാർട്ടമെന്റ് ഓഫ് ഇമേജിംഗ് സയൻസസ് ആന്റ് ഇന്റർവെൻഷണൽ റേഡിയോളജി, SCTIMST
ഡോ. ആശാലത ആർ, പ്രൊഫസർ, ന്യൂറോളജി ഡിപ്പാർട്ട്മെന്റ്, SCTIMST
ഡോ. ദീപ്തി എ എൻ, അസോസിയേറ്റ് പ്രൊഫസർ, പതോളജി ഡിപ്പാർട്ടമെന്റ്, SCTIMST
സഹ ഗവേഷക:
ഡോ. രാജലക്ഷ്മി പി, അസിസ്റ്റന്റ് പ്രൊഫസർ, പതോളജി ഡിപ്പാർട്ടമെന്റ്, SCTIMST

(കോളങ്ങളിൽ അടയാളപ്പെടുത്തുക)

ഈ പത്രികയോടൊപ്പമുള്ള, പങ്കെടുക്കുന്നവർക്കുള്ള കാര്യവിവരണപത്രത്തിൽ വിശദീകരിക്കുന്ന പഠനത്തിൽ പങ്കെടുക്കാൻ ഞാൻ സമ്മതിക്കുന്നു.	[ ]
എന്നെ എന്തുകൊണ്ട് തിരഞ്ഞെടുത്തു, പഠനത്തിന്റെ ഉദ്ദേശം, സ്വഭാവം, പരിശോധനയിൽ ഉണ്ടാവാനിടയുള്ള അപായങ്ങൾ എന്നിവ വിവരിക്കുന്ന പങ്കെടുക്കുന്നവർക്കുള്ള കാര്യവിവരണപത്രം വായിച്ചതായും എന്റെ തൃപ്തിയ്ക്കനുസരിച്ച് വിശദീകരിച്ചുതന്നതായും ഞാൻ സമ്മതിക്കുന്നു.	[ ]
സമ്മതപത്രത്തിൽ ഒപ്പു വയ്ക്കുന്നതിനുമുമ്പ്, ഈ പഠനത്തിൽ പങ്കെടുക്കുന്നതുകൊണ്ട് ശാരീരികവും മാനസികവുമായ എന്തെങ്കിലും ഹാനി എനിക്ക് ഉണ്ടാകാൻ സാദ്ധ്യതയുണ്ടോ എന്നതുമായി ബന്ധപ്പെട്ട ചോദ്യങ്ങൾ ചോദിക്കാൻ എനിക്ക് അവസരം ഉണ്ടാവുകയും തൃപ്തികരമായ മറുപടി ലഭിക്കുകയും ചെയ്തു	[ ]
എന്റെ പങ്കാളിത്തം സ്വമേധയായാണെന്നും, കാരണമൊന്നും നൽകാതെയും എന്റെ വൈദ്യപരിചരണത്തെ ബാധിക്കാതെയും ഏതു സമയത്തും എനിക്ക് പിൻമാറാൻ സ്വാതന്ത്ര്യമുണ്ടെന്നും മനസ്സിലാക്കുന്നു.	[ ]
പഠനഫലമായി ശേഖരിച്ച വിവരങ്ങൾ പ്രസിദ്ധീകരിക്കുമ്പോൾ എന്നെ തിരിച്ചറിയാനിടയാകുന്നതൊന്നും വെളിപ്പെടുത്തുകയില്ലെന്ന് ഞാൻ മനസ്സിലാക്കുന്നു.	[ ]
ഗവേഷണത്തിൽ പങ്കെടുക്കുന്നതുമായി ബന്ധപ്പെട്ട് എനിക്ക് ചോദ്യങ്ങളുണ്ടെങ്കിൽ എനിക്ക് ഡോക്ടറെ ബന്ധപ്പെടാമെന്നും ഉത്തരം തരുന്നതിൽ അദ്ദേഹത്തിന് സന്തോഷമേയുള്ളൂവെന്നും ഞാൻ മനസ്സിലാക്കുന്നു.	[ ]
ഈ പത്രികയോടൊപ്പം നൽകിയിട്ടുള്ള പങ്കാളികൾക്കുള്ള വിവരണപത്രവും സമ്മതപത്രവും കിട്ടിയതായി ഞാൻ അറിയിക്കുന്നു.	[ ]

പങ്കെടുക്കുന്നയാളുടെ പേര്

പങ്കെടുക്കുന്നയാളുടെ ഒപ്പ് തീയതി സമയം

പരിചരിക്കുന്നയാളുടെ അല്ലെങ്കിൽ അടുത്തബന്ധുവിന്റെ പേര്
(രോഗി നേരിട്ടല്ല സമ്മതം തരുന്നതെങ്കിൽ)

രോഗിയുമായുള്ള ബന്ധം

പരിചരിക്കുന്നയാളുടെ അല്ലെങ്കിൽ അടുത്തബന്ധുവിന്റെ ഒപ്പ് തീയതി സമയം

സാക്ഷിയുടെ പേര്

സാക്ഷിയുടെ ഒപ്പ് തീയതി സമയം

സമ്മതപത്രത്തെപ്പറ്റി ചർച്ച ചെയ്തയാളുടെ പേര്

സമ്മതപത്രത്തെപ്പറ്റി ചർച്ച ചെയ്തയാളുടെ ഒപ്പ് തീയതി സമയം

Supplementary table-5

SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY, THIRUVANANTHAPURAM, KERALA - 695011

PATIENT INFORMATION SHEET

Title of the study:
Advanced magnetic resonance imaging correlates of histopathological changes in amygdala and the temporal neocortex in mesial temporal sclerosis

Principal Investigator:
Dr Viswanadh K S V G, Senior resident, Department of imaging sciences and interventional radiology, SCTIMST

Co-Principal Investigators:
Dr Bejoy Thomas, Professor & HOD, Department of imaging sciences and interventional radiology, SCTIMST.
Dr Ashalatha. R, Professor, Department of Neurology, SCTIMST.
Dr Deepthi A N., Associate professor, Department of Pathology, SCTIMST.

Co-Investigator:
Dr Rajalakshmi P, Assistant professor, Department of Pathology, SCTIMST.

Sir/ Madam,
We invite you to take part in our study titled *"Advanced MR imaging correlates of Histopathological changes in Amygdala and the Temporal neocortex in Mesial Temporal Sclerosis"* an observational study. Before you agree to participate in this research study, it is important that you read and understand this information sheet which will provide you with all the information needed for participation in this study so that you can make a well informed and considered decision about participation. In addition, should you have any questions, the investigator and his team members will be happy to answer them and explain to you more about this research study, the procedure involved and the related issues. You may ask them any questions you may have regarding the study, or ask them to explain any word or information that you don't clearly understand.

Study Overview

You are invited to take part in this study as you have epilepsy due to a condition called mesial Temporal sclerosis in the brain and you will be undergoing a surgery called anterior temporal lobectomy and amygdalohippocampectomy for this condition. As a part of investigative workup, epilepsy protocol MRI including a special sequence called arterial spin labelling (ASL) is also done for diagnostic information about the cause of your seizures and the extent of the disease. Patients who are diagnosed with epilepsy due to mesial Temporal sclerosis and are to undergo the surgical procedure of anterior Temporal lobectomy with Amygdalohippocampectomy after epilepsy protocol MRI at SCTIMST will be included in the study.

Purpose of this study

The purpose of this study Identify the advanced MRI sequence imaging correlates of histopathological changes in additional parts of the brain called Amygdala and Temporal neocortex seen in Mesial Temporal sclerosis patients and also to identify clinical, electrophysiological (EEG) correlates in MTS patients with neocortical Temporal changes.

Study Procedures

If you are willing to participate, you/your bystanders will be interviewed by the doctor performing the study, clinical findings will be noted. This will be done when you are admitted and evaluated for epilepsy due to Mesial Temporal sclerosis and are to undergo the surgical procedure of anterior Temporal lobectomy with amygdalohippocampectomy. As a part of your management plan, you will have to undergo epilepsy protocol MRI brain including ASL sequence. The data from the clinical findings, MRI findings, histopathological findings after surgery will be used in this study.

Risks and Discomfort

This study involves only a structured interview by the doctor along with MR imaging and histopathological examination done as a part of standard management protocol. There are no additional risks or costs associated with the study.

Benefits

Taking part in this research may not benefit you. However, we do hope that this study will shed light on additional aspects of pathology in epilepsy patients with mesial Temporal sclerosis as demonstrated by MRI, thus helping in better management and patient care.

Confidentiality

Your privacy is very important to us and the results of the tests performed on you will be treated as highly confidential, and nobody other than the investigators listed above will be knowing the test results. Your name or any other identifiable details will not be published in any research paper or scientific presentation arising out of the study.

Rights

Your participation in the trial is voluntary. You do not have to take part in this study if you are unwilling and you will not be losing any of your rights as a patient if you choose not to participate. You will also be at the liberty to withdraw from the study at any stage (even after signing this consent form) of the study in case you want to withdraw.

Contact Information

- When you read this information, your treating doctor will be available to discuss and answer any questions you may have. If you have any queries please contact:

  Dr Viswanadh K S V G
  Senior Resident, Department of Imaging sciences and interventional Radiology,
  Sree Chitra Tirunal Institute for Medical Sciences and Technology
  Tel: +91 9496937773, Email: viswanath248@sctimst.ac.in

- If you have any questions, concerns or complaints about the research please contact:

  Dr. Srinivas G
  Member Secretary, Institutional Ethics Committee,
  Sree Chitra Tirunal Institute for Medical Sciences and Technology
  Tel: 0471- 2524689, Email: iec.mem.sec@sctimst.ac.in

Supplementary table-6

PATIENT INFORMATION SHEET-Malayalam

ശ്രീ ചിത്ര തിരുനാൾ ഇൻസ്റ്റിറ്റ്യൂട്ട് ഫോർ മെഡിക്കൽ സയൻസസ് ആന്റ് ടെക്നോളജി, തിരുവനന്തപുരം, കേരളം – 695011
മസ്തിഷ്ക്കാഘാത പരിചരണത്തിനായുള്ള സമഗ്ര പരിപാടി

രോഗിക്കുള്ള കാര്യവിവരണപത്രം

പഠനശീർഷകം:
മീസിയൽ ടെമ്പോറൽ സ്ലീറോസിസിൽ അമിഗ്ഡുലയിലും ടെമ്പോറൽ നിയോകോർടെക്സിലുമുള്ള മാറ്റങ്ങളുടെ രോഗനിദാനശാസ്ത്രവും (ഹിസ്റ്റോപതോളജി) എംആർ ഇമേജിംഗും തമ്മിലുള്ള പാരസ്പര്യം.

പ്രധാനഗവേഷകൻ
ഡോ. വിശ്വനാഥ് കെ എസ് വിജി, സീനിയർ റെസിഡന്റ്, ഡിപ്പാർട്ടമെന്റ് ഓഫ് ഇമേജിംഗ് സയൻസസ് ആന്റ് ഇന്റർവെൻഷണൽ റേഡിയോളജി, SCTIMST
സഹ പ്രധാനഗവേഷകൻ
ഡോ. ബിജോയ് തോമസ്, പ്രൊഫസർ & ഹെഡ്, ഡിപ്പാർട്ടമെന്റ് ഓഫ് ഇമേജിംഗ് സയൻസസ് ആന്റ് ഇന്റർവെൻഷണൽ റേഡിയോളജി, SCTIMST

ഡോ. ആശാലത ആർ, പ്രൊഫസർ, ന്യൂറോളജി ഡിപ്പാർട്ട്മെന്റ്, SCTIMST
ഡോ. ദീപ്തി എ എൻ, അസോസിയേറ്റ് പ്രൊഫസർ, പതോളജി ഡിപ്പാർട്ടമെന്റ്, SCTIMST
സഹഗവേഷക:
ഡോ. രാജലക്ഷ്മി പി, അസിസ്റ്റന്റ് പ്രൊഫസർ, പതോളജി ഡിപ്പാർട്ടമെന്റ്, SCTIMST

ശ്രീ/ശ്രീമതി,

മീസിയൽ ടെമ്പോറൽ സ്ലീറോസിസിൽ അമിഗ്ഡുലയിലും ടെമ്പോറൽ നിയോകോർടെക്സിലുമുള്ള മാറ്റങ്ങളുടെരോഗനിദാനശാസ്ത്രവും എംആർ ഇമേജിംഗും തമ്മിലുള്ള പാരസ്പര്യം എന്ന പഠനത്തിൽ പങ്കെടുക്കൻ താങ്കളെ ഞങ്ങൾ ക്ഷണിക്കുന്നു.
ഈ പഠനത്തിൽ പങ്കെടുക്കുവാൻ താങ്കൾ സമ്മതിക്കുന്നതിനുമുമ്പ് ഈ പഠന സംബന്ധമായി അറിയേണ്ടുന്ന പ്രസക്തമായ എല്ലാ വിവരങ്ങളും നൽകുന്ന ഈ കാര്യവിവരണപത്രം വായിക്കുകയും മനസ്സിലാക്കുകയും ചെയ്യേണ്ടത് കാര്യബോധത്തോടെ സമ്മതം നൽകാൻ തീരുമാനമെടുക്കുന്നതിൽ പ്രധാനമാണ്. അതിനൊപ്പം താങ്കൾക്കെന്തെങ്കിലും ചോദ്യങ്ങളുണ്ടെങ്കിൽ അവ വിശദീകരിച്ചുതരുവാൻ ഗവേഷകയും സംഘാംഗങ്ങളും സന്തോഷത്തോടെ തയാറാകുകയും ഗവേഷണ പഠനം, ഉൾപ്പെട്ട നടപടികൾ ബന്ധപ്പെട്ട വിഷയങ്ങൾ എന്നിവയെപ്പറ്റി കൂടുതൽ വിശദീകരണം നൽകുകയും ചെയ്യും. പഠനത്തെപ്പറ്റി താങ്കൾക്കെന്തെങ്കിലും ചോദ്യങ്ങളോ വ്യക്തമായി മനസ്സിലാകാത്ത ഏതെങ്കിലും വാക്കുളോ വിവരങ്ങളോ ഉണ്ടെങ്കിൽ പഠനം നടത്തുന്നവരോട് ചോദിക്കുക.

പഠന അവലോകനം
താങ്കളുടെ തലച്ചോറിൽ മീസിയൽ ടെമ്പോറൽ സ്ലീറോസിസ് എന്ന അവസ്ഥയുടെ ഫലമായുള്ള അപസ്മാരമുള്ളതിനാലും അതിനായി ആന്റീഇയൽ ടെമ്പോറൽ ലോബോട്ടമിക്കും അമിഗ്ഡലോഹിപ്പോകാമ്പക്ടമിക്കും വിധേയമാകാൻ പോകുന്നു എന്നതിനാലാണ് താങ്കളെ ഈ പഠനത്തിലേയ്ക്ക് ക്ഷണിക്കുന്നത്. പരിശോധനാനടപടികളുടെ ഭാഗമായി താങ്കളുടെ കോച്ചിപ്പിടുത്തത്തിന്റെ കാരണവും രോഗത്തിന്റെ വ്യാപ്തിയും രോഗനിർണ്ണയവിവരങ്ങളും ലഭിക്കാൻ അപസ്മാരത്തിനായുള്ള എംആർഐ നടപടിക്രമങ്ങളിൽ ആർട്ടീഇയൽ സ്പിൻ ലേബലിംഗും (എഎസ്എൽ) ചെയ്യും. ഈ പഠനത്തിൽ പരിശോധനാനടപടികളുടെ ഭാഗമായി രോഗികളുടെ കോച്ചിപ്പിടുത്തത്തിന്റെ കാരണവും രോഗത്തിന്റെ വ്യാപ്തിയും രോഗനിർണ്ണയവിവരങ്ങളും ലഭിക്കാൻ SCTIMSTയിൽ അപസ്മാരത്തിനായുള്ള SCTIMST നടപടിക്രമങ്ങൾ പ്രകാരമുള്ള എംആർഐ ചെയ്യുന്നവരെ ഉൾപ്പെടുത്തും..

പഠനത്തിന്റെ ഉദ്ദേശം

മീസിയൽ ടെമ്പോറൽ സ്ലീറോസിസിൽ (എംറ്റിഎസ്) കാണപ്പെടുന്ന തലച്ചോറിന്റെ ഭാഗങ്ങളായ അമിഗ്ഡുലയിലും ടെമ്പോറൽ നിയോകോർടെക്സിലുമുള്ള മാറ്റങ്ങളുടെ രോഗനിദാനശാസ്ത്രവും എംആർ ഇമേജിംഗും തമ്മിലുള്ള പാരസ്പര്യവും ക്ലിനിക്കൽ ഇലക്ട്രോഫിസിയോളജിക്കൽ (ഇഇജി) പാരസ്പര്യവും എംറ്റിഎസ് രോഗികളിൽ കണ്ടെത്തുക എന്നതാണ് ഈ പഠനത്തിന്റെ ഉദ്ദേശം.

പഠന നടപടികൾ

താങ്കൾ/കൂടെ പരിചരണത്തിനുള്ളയാളുകൾ പങ്കെടുക്കാൻ സമ്മതിക്കുകയാണെങ്കിൽ, താങ്കളുമായി/കൂടെ പരിചരണത്തിനുള്ളയാളുകളുമായി അഭിമുഖം നടത്തുകയും പരിശോധിക്കുകയും ക്ലിനിക്കൽ കണ്ടെത്തലുകൾ രേഖപ്പെടുത്തുകയും ചെയ്യും. താങ്കളെ ആശുപത്രിയിൽ പ്രവേശിപ്പിക്കുകയും വിലയിരുത്തുകയും ചെയ്തശേഷം താങ്കളുടെ തലച്ചോറിൽ മീസിയർ ടെമ്പോറൽ സ്ലീറോസിസ് എന്ന അവസ്ഥയുടെ ഫലമായുള്ള അപസ്മാരമുള്ളതിനാലും അതിനായി ആന്റീഇയർ ടെമ്പോറൽ ലോബോട്ടമിക്കും അമിഗ്ഡലോഹിപ്പോകാമ്പക്ടമിക്കും വിധേയമാകാൻ എങ്കിലാണ് ഇത് ചെയ്യുക. താങ്കളുടെ ചികിത്സാർഥം തലച്ചോറിന്റെ എംആർഐയുടെ ആപസ്മാര പരിശോധനാ നടപടിക്രമപ്രകാരം എഎസ്എൽ പരമ്പരയും ചെയ്യും. ശസ്ത്രക്രിയയ്ക്കു ശേഷമുള്ള ക്ലിനിക്കൽ, എംആർഐ, ഹിസ്റ്റോപതോളജി കണ്ടെത്തലുകൾ എന്നിവയുടെ വിവരങ്ങൾ, പഠനത്തിനായി ഉപയോഗിക്കും.

അപായങ്ങളും അസ്വസ്ഥതകളും

താങ്കൾ അംഗീകൃത നടപടിക്രമവും ചികിത്സാപദ്ധതിയും പ്രകാരം വിധേയമായ എംആർ ഇമേജിംഗിന്റെയും ഹിസ്റ്റോപതോളജിക്കൽ പരിശോധനയുടെയും ഒപ്പം സുഘടിതമായ ഒരഭിമുഖവും മാത്രമാണ് ഈ പഠനത്തിലുള്ളത്. ഈ പഠനവുമായി ബന്ധപ്പെട്ട് കൂടുതൽ അപായമോ ചിലവോ ഇല്ല.

നേട്ടങ്ങൾ

ഗവേഷണത്തിൽ പങ്കെടുക്കുന്നതുകൊണ്ട് താങ്കൾക്ക് നേട്ടമൊന്നും ഉണ്ടായേക്കില്ല. എന്നിരുന്നാലും, എംആർഐയിൽ പ്രദർശിപ്പിക്കപ്പെടുന്നതുപോലെ മീസിയർ ടെമ്പോറൽ സ്ലീറോസിസ് ഉള്ള അപസ്മാരരോഗികളിലെ രോഗനിദാനവശങ്ങളിൽ കൂടുതൽ വെളിച്ചം വീശാനും അതുവഴി ചികിത്സയിലും രോഗീപരിചരണത്തിലും ഈ പഠനം സഹായകമാകും എന്ന് ഞങ്ങൾ പ്രതീക്ഷിക്കുന്നു.

രഹസ്യാത്മകത

താങ്കളുടെ സമ്മതം ഞങ്ങൾക്ക് വളരെ പ്രധാനമായതിൽ പരിശോധനാഫലങ്ങൾ വളരെ രഹസ്യസ്വഭാവത്തോടെ സൂക്ഷിക്കും. മുകളിൽ പറഞ്ഞവരൊഴികെ മറ്റാരും പരിശോധനാവിവരങ്ങൾ അറിയില്ല. പഠനഫലം ഒരു വൈദ്യശാസ്ത്ര പ്രസിദ്ധീകരണത്തിൽ പ്രസിദ്ധീകരിക്കുമെങ്കിലും താങ്കളെ പേരുകൊണ്ട് തിരിച്ചറിയാനിടയാക്കുന്നതൊന്നും പ്രസിദ്ധീകരണത്തിലോ പ്രദർശനത്തിലോ ഉണ്ടാകില്ല.

അവകാശങ്ങൾ

താങ്കളുടെ പങ്കാളിത്തം സ്വമേധയായാണ്.. താങ്കൾക്ക് സമ്മതമില്ലെങ്കിൽ ഈ പഠനത്തിൽ പങ്കെടുക്കേണ്ടതില്ല. പങ്കെടുക്കാതിരിക്കുന്നതുകൊണ്ട് താങ്കളുടെ ഒരവകാശവും നഷ്ടപ്പെടില്ല. ഇൻസ്റ്റിറ്റ്യൂട്ടിലെ താങ്കളുടെ തുടർ ചികിത്സയെ ഒരു വിധത്തിലും ബാധിക്കില്ല.പഠനത്തിന്റെ ഏത് ഘട്ടത്തിലും (സമ്മതപത്രം ഒപ്പിട്ടശേഷവും) താങ്കൾക്ക് പഠനത്തിൽ നിന്നും പിൻമാറാവുന്നതാണ്.

ബന്ധപ്പെടാനുള്ള വിവരങ്ങൾ

- താങ്കൾ ഈ വിവരങ്ങൾ വായിക്കുമ്പോൾ ചർച്ചചെയ്യാനും താങ്കൾക്കുണ്ടായേക്കാവുന്ന ചോദ്യങ്ങൾക്ക് ഉത്തരങ്ങൾ നൽകാനും താങ്കളെ ചികിത്സിക്കുന്ന ഡോക്ടർ ഉണ്ടാവും. താങ്കൾക്കെന്തെങ്കിലും ചോദ്യങ്ങളുണ്ടെങ്കിൽ ദയവായി ബന്ധപ്പെടുക

പഠനസംബന്ധമായ സംശയങ്ങൾക്ക് ഞാൻ ആരെ ബന്ധപ്പെടണം?

താങ്കൾക്കെന്തെങ്കിലും ചോദ്യങ്ങളുണ്ടെങ്കിൽ ദയവായി ബന്ധപ്പെടുക

ഫോൺ 9496937773, ഇമെയിൽ: viswanath248@sctimst.ac.in

ഗവേഷകന്റെ പേര്
ഡോ. വിശ്വനാഥ് കെ എസ് വിജി, സീനിയർ റെസിഡന്റ്, ഡിപ്പാർട്ടമെന്റ് ഓഫ് ഇമേജിംഗ് സയൻസസ് ആന്റ് ഇന്റർവെൻഷണൽ റേഡിയോളജി,
ശ്രീ ചിത്ര തിരുനാൾ ഇൻസ്റ്റിറ്റ്യൂട്ട് ഫോർ മെഡിക്കൽ സയൻസസ് ആന്റ് ടെക്നോളജി

പ്രധാന ഗവേഷകന്റെ ഒപ്പ്

ഗവേഷണത്തിന്റെ നൈതീക അനുവാദത്തെപ്പറ്റി താങ്കൾക്ക് ചോദ്യങ്ങൾ, ഉണ്ടെങ്കിൽ ദയവായി ബന്ധപ്പെടുക:
ഡോ. ശ്രീനിവാസ് ജി
മെമ്പർ സെക്രട്ടറി, ഇൻസ്റ്റിറ്റ്യൂഷണൽ എത്തിക്സ് കമ്മിറ്റി
ശ്രീ ചിത്ര തിരുനാൾ ഇൻസ്റ്റിറ്റ്യൂട്ട് ഫോർ മെഡിക്കൽ സയൻസസ് ആന്റ് ടെക്നോളജി
ഫോൺ 0471- 2524689, ഇമെയിൽ: iec.mem.sec@sctimst.ac.in

APPENDIX D-PLAGIARISM CHECK REPORT

RE-2022-142719-plag-report

ORIGINALITY REPORT

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