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MEDICAL SCIENCES AND TECHNOLOGY**
THIRUVANANTHAPURAM, KERALA



**Clinical profile, imaging features and
postsurgical outcomes of hypermotor seizures
originating from temporal lobe: A retrospective
observational study**

Dissertation submitted in partial fulfilment of the rules and regulations for

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By

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01/01/2021 to 31/12/2021

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DECLARATION

I, Dr. Pavan Kumar Rudrabhatla, hereby declare that this project was undertaken by me under the supervision of the faculty, R. Madhavan Nayar Center for Comprehensive Epilepsy Care, Department of Neurology, Sree Chitra Tirunal Institute for Medical Sciences and Technology.

Thiruvananthapuram,
Date: 14-12-2021.


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The candidate, Dr. Pavan Kumar Rudrabhatla, has completed the project under my guidance.

Thiruvananthapuram,
Date: 14-12-2021.



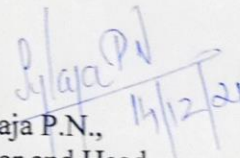
Dr. Ashalatha Radhakrishnan,
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SCTIMST.

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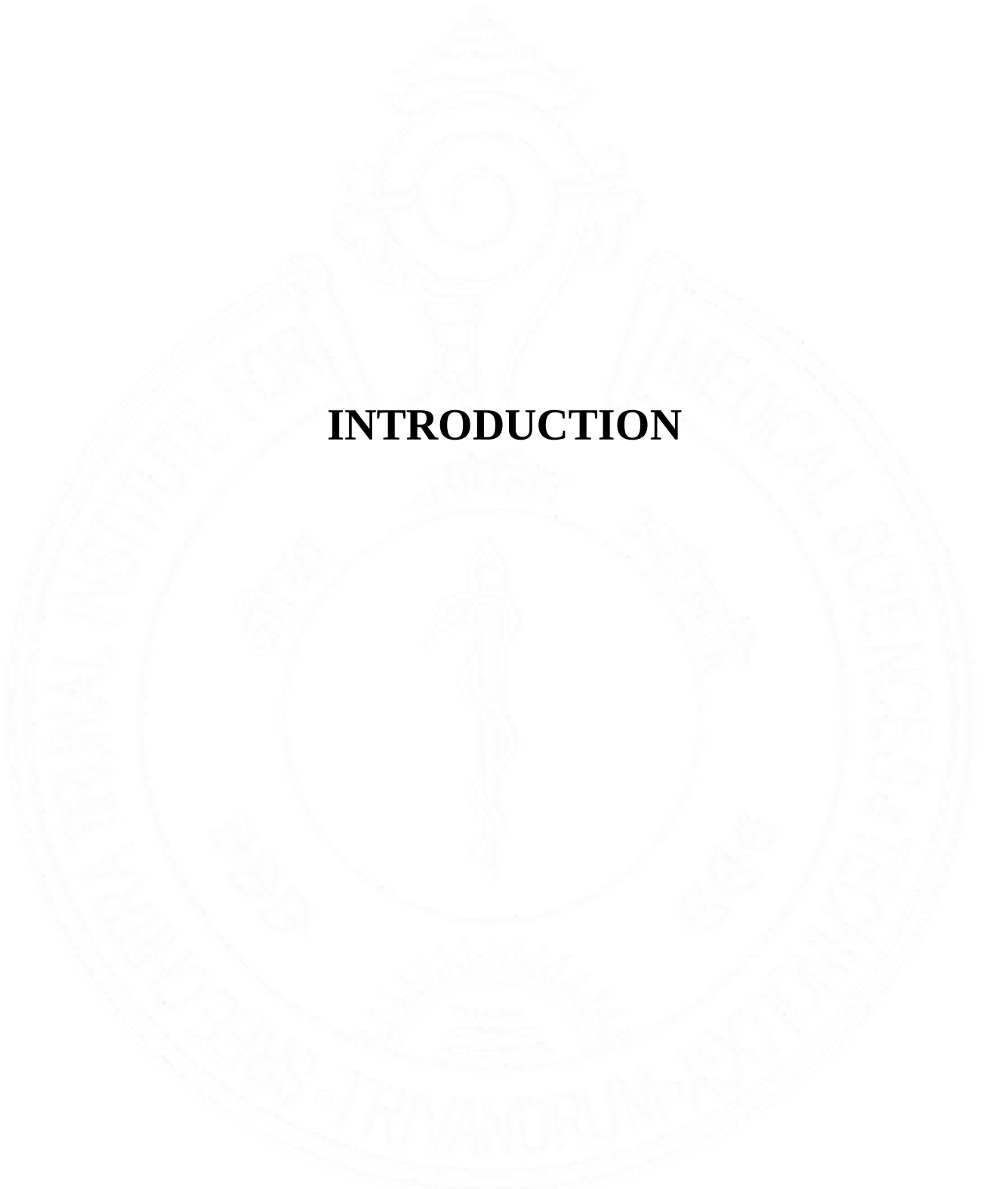
This candidate, Dr. Pavan Kumar Rudrabhatla, has carried out the minimum required project for post-doctoral fellowship.

Thiruvananthapuram,
Date: 14-12-2021.


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INTRODUCTION

INTRODUCTION

Hypomotor semiology with the classical 5As, Antecedent, Aura, Arrest, Automatisms, Amnesia is considered the garden variant of seizures originating from temporal lobe [1]. Similarly, hypermotor seizures [HMSs] which predominantly occur out of sleep, characterized by complex high amplitude movements involving proximal segments of the limbs or body axis resulting violent and inappropriate to the context movements, traditionally were associated with frontal lobe epilepsy [2,3,4]. However, hypermotor semiology is being increasingly reported in seizures originating from extra-frontal structures [5,6,7,8].

As opposed to the conventional thinking, temporal lobe epilepsy (TLE) can manifest with HMSs – ‘hypermotor TLE’ [6,7,8]. Knowledge regarding the seizures originating from various brain locations and the corresponding manifestations is important especially in the presurgical evaluation of drug resistant epilepsy (DRE). TLE is the most common type of focal epilepsy and drug-resistant TLE forms a substantial portion of the resective surgeries for DRE.

Evidence on hypermotor TLE is sparse which can result in the lack of knowledge regarding this entity among the treating neurologists/epileptologists. As a consequence, there can be a delay or even preclusion of surgical treatment in such patients leading to the continual risk of epilepsy related complications and poor quality of life (QOL).

We plan to study the demographic profile, clinical features, ictal semiology and electrical data, imaging features, histopathological findings, and postsurgical outcomes of patients with HMSs originating from temporal lobe who underwent surgery for DRE.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

HMS is defined by ictal complex motor agitation with proximal movements of the limbs and horizontal or rotatory movements of the trunk and pelvis while lying on the bed; associated movements include flinging, kicking, body rocking, body gyration, pelvic thrusting and might or not be associated with restless behaviour, dystonic posturing, head turning, or emotional symptoms [9]. Hypermotor semiology has been associated to frontal lobe seizures; especially those originating from the mesial frontal or orbitofrontal regions but hypermotor seizures have also been described in seizures originating from the dorsolateral frontal lobe, mesial and neocortical temporal lobe, upper and anterior aspect of insular cortex and parieto-temporal cortex [6-15].

Rheims et al. [3] described two subtypes of HMS: HMS1, characterized by marked agitation including one or several of the following motor behaviors: body rocking, kicking, boxing, associated with sitting up or standing up behaviors. Other features can include a mimic automatism like a facial expression of fear. In this type of HMS tonic or dystonic posturing are rare presented. The motor behavior looks like semipurposeful, as if the patients were trying to protect themselves against an external threat, reactive automatisms. Autonomic signs, ipsilateral head deviation and auras as described in temporal lobe seizures are frequently found. The authors primarily associated HMS1 with an epileptogenic zone (EZ) centered on the ventromedial frontal cortex. the ventromesial frontal cortex. Multidirectional spread was often observed into the frontopolar cortex and the temporal lobe. The same frontotemporal network has been previously described in NFLE [16,17]. Ictal fear was also found to correlate with discharges involving the anterior cingulate cortex, the orbitofrontal cortex, and the temporal neocortex [18]. In patients with sleep-related HMS of temporal lobe origin, HM manifestations started when discharge spread to the cingulate and frontal cortices [19]. Moreover, the non-HM signs observed in HSM1 are also consistent with the implication of this network.

HMS Type 2 seizures were characterized by mild agitation of the trunk than HMS1 while patients kept lying on the bed with frequent tonic/dystonic posturing, and rare changes of facial expression. HSM2 was associated with a more dorsal EZ than those resulting in HSM1, centered on the mesial premotor cortex and the dorsal anterior cingulate cortex. Moreover, the spreading of the ictal discharge was mostly unidirectional and less extensive than that of HMS1, possibly explaining why some patients may remain fully responsive during their seizures. Similarly, asymmetrical tonic posturing in nocturnal frontal lobe epilepsy (NFLE) was found to be associated with an involvement of the supplementary motor area and the dorsal anterior cingulate cortex [16]. Likewise, in patients with HMS of insular origin, which reproduce the typical features of HMS2 dominated by both horizontal movements of the trunk while lying on the bed and dystonic posturing, these ictal signs occur concurrently with the spread of the epileptic discharge over the supplementary motor area and the dorsal anterior cingulate cortex [2]. Alternatively, type 2 HM behaviours could reflect an ictal activation or dysfunction of the basal ganglia as they resemble previously described movements disorders [20].

Bonini et al., 2014, evaluated seizures from 54 patients with frontal lobe epilepsy (FLE) that were explored with stereo-electroencephalography (SEEG) during presurgical evaluation [4]. Semiologic features and concomitant intracerebral EEG changes were documented and quantified. Four main groups of patients were identified according to semiologic features and correlated with specific patterns of anatomic seizure localization. Group 1 was characterized clinically by elementary motor signs and involved precentral and premotor regions. Group 2 was characterized by a combination of elementary motor signs and non-integrated gestural motor behaviour and involved both premotor and prefrontal regions. Group 3 was characterized by integrated gestural motor behaviour with distal stereotypies and involved anterior lateral and medial prefrontal regions. Group 4 was characterized by seizures with fearful behaviour

and involved the paralimbic system (ventromedial prefrontal cortex – anterior temporal structures). The groups were organized along a rostrocaudal axis, representing bands within a spectrum rather than rigid categories. The more anterior the seizure organization, the more likely was the occurrence of integrated behaviour during seizures. Distal stereotypies were associated with the most anterior prefrontal localizations, whereas proximal stereotypies occurred in more posterior prefrontal regions.

Hyperkinetic seizures of temporal lobe origin preferentially occur in patients with structural epilepsy [19,21-23]. Wang et al. (2008) reported on four patients who presented with hyperkinetic seizures based on temporal polar lesions [6]. The authors of a retrospective stereo-electroencephalography (EEG) analysis described hyperkinetic seizures of temporal lobe origin in seven patients and claimed the existence of a consistent brain network including the temporal pole and the medial basal prefrontal cortex [24]. Besides the temporal pole, the temporal basal structures, especially the parahippocampal gyrus seems to be a region of interest in temporal lobe epilepsy (TLE) with hyperkinetic features [25]. Bidirectional connections between the temporal pole, amygdala, parahippocampal region, and the orbitofrontal and medial prefrontal cortex have been shown in primates [26,27]. The uncinate fasciculus, links rostral temporal, inferotemporal, and ventral temporal regions with the medial and orbital frontal cortices [28], which might allow fast seizure-spread. Another important white matter pathway, the extreme capsule, contains fibers connecting the medial and orbital prefrontal cortices, as well as the rostral cingulate gyrus with the rostral part of the superior temporal gyrus via the insula [29].

Hypermotor manifestations such as bicycling movements were reported with TLE as early as 1890s [30]. Nobili et al, gave an account of three patients with sleep-related seizures characterized by frenetic, agitated, hyperactive movements (bimanual/bipedal activity, rocking, axial, pelvic, and hemiballistic movements), in whom stereo-EEG investigation and

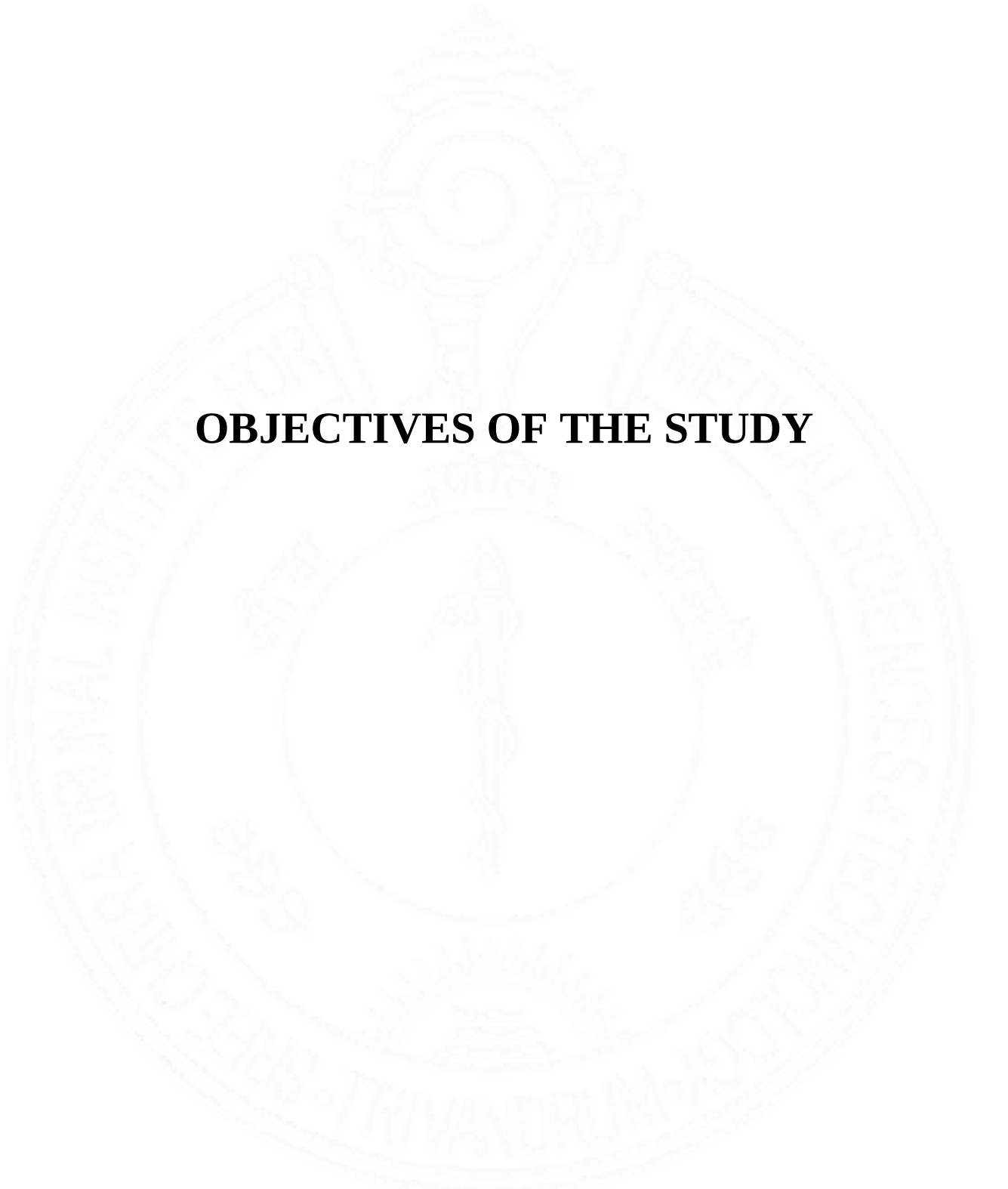
surgical outcome demonstrated a temporal lobe origin of the attacks [19]. A study of hypermotor TLE, defined as patients who were seizure free after surgical resection that involved the temporal lobe (lesionectomy/anteromedial temporal lobectomy) or those who had a well-defined temporal lesion on preoperative magnetic resonance imaging (MRI) together with characteristic interictal epileptiform discharges and regional ictal patterns over the ipsilateral temporal lobe on surface EEG included 12 patients (2.3% of the TLE group). Movements involved proximal limb segments (6) or body axis (6) and were often preceded by auras and followed by automatisms. Seven of 12 patients are seizure free after surgery. The other 5 patients declined surgery [22].

Staack et al, identified 6% of patients who were resected exclusively in the temporal region for refractory epilepsy to have hyperkinetic semiology. Most of the patients had a preceding aura. Ictal EEG activity was located in the corresponding temporal region, usually with a wide distribution over temporal electrodes with fast spread to unilateral frontal electrodes and to the contralateral side. Neuroimaging revealed extended lesions in the temporal lobe involving mesial and neocortical structures. Most of the patients underwent classical anterior temporal lobe resection including amygdalohippocampectomy. Fourteen patients (82%) became completely seizure-free (Engel class Ia). Histopathology showed mainly focal cortical dysplasia plus hippocampal sclerosis [7].

In a study on hypermotor TLE, 7 of the 9 patients completed intracranial recording and at least 3 seizures were recorded for each patient. The intracranial recordings showed ictal activity originating from mesial temporal lobe in 6 patients and the lateral temporal lobe in 1 patient. The time interval of ictal propagation from the temporal to frontal lobe was 15.0 ± 8.3 s. While the time interval from EEG origination to the beginning of hypermotor behavior was 21.0 ± 8.1 s favouring the fast spread of ictal activity to frontal lobe structures as the mechanism for hypermotor semiology. In this series, 0.7% of all patients who received surgical

treatment for TLE exhibited HMS. Most of these patients had auras that often occur in temporal lobe epilepsy and hypermotor behaviors were obvious later than the beginning of ictal EEG activities. Therefore, these behavioral traits imply temporal lobe origination and help to differentiate this group from the more common HMS arising from the frontal lobe [8].

We screened the 10-year data of patients who underwent surgery for refractory TLE from our institute, to identify patients with hypermotor seizures. The semiology of seizures, imaging findings, EEG data and surgical outcomes have been studied in detail and compared with patients with hypomotor TLE.



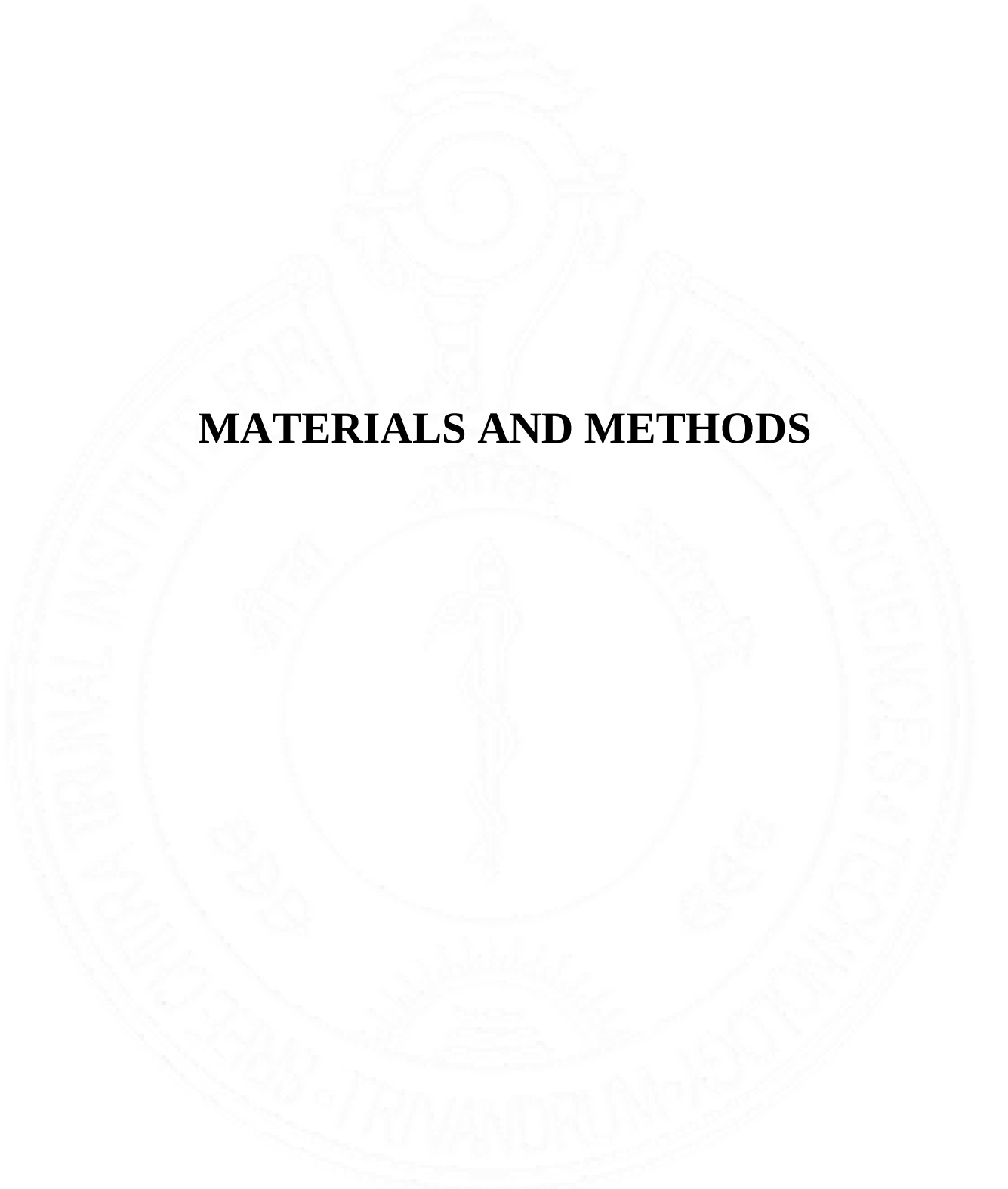
OBJECTIVES OF THE STUDY

HYPOTHESIS:

Carefully selected patients of hypermotor TLE with necessary presurgical workup would have good postsurgical outcomes.

OBJECTIVES OF THE STUDY

- To study the demographic, clinical, semiological, electrical, histopathological and postsurgical outcomes of patients with hypermotor TLE who underwent surgery for drug resistant epilepsy.
- To compare the hypermotor TLE group with hypomotor TLE patients (hypermotor:hypomotor = 1:2 ratio) to identify clinical, electrical and imaging differences between the groups.



MATERIALS AND METHODS

MATERIALS AND METHODS

This is a retrospective cohort study. This study was carried out in the R. Madhavan Nayar Centre for Comprehensive Epilepsy care in the Sree Chitra Tirunal Institute for Medical Sciences. This study was restricted to adult patients with Temporal Lobe Epilepsy who underwent surgery for drug-refractory epilepsy (DRE). DRE was defined as the failure of adequate trials of two tolerated, appropriately chosen and used antiepileptic drug schedules (whether as monotherapies or in combination) to achieve sustained seizure freedom [31]. These cases already underwent standard presurgical work up for epilepsy including clinical assessment, imaging, and video telemetry assessment.

Sample size:

Studies have shown that the in patients who underwent surgery for refractory TLE, 0.7 to 2.3% had hypermotor seizure semiology [8,22]. Considering the number of patients who underwent surgery for refractory TLE at our center (600 to 700 over the study period of 10 years) we expected a sample size of 10 to 16 patients with hypermotor TLE and the inclusion of double the number of hypomotor TLE as control group.

Sampling method:

The medical records for patients who underwent epilepsy surgery for TLE were screened and the recorded events of patients whose VEEG reports were suggestive of HMS were reviewed. After review of events all patients satisfying the participation criteria were included in the study.

Controls:

We recruited double the number of hypomotor TLE-controls as the hypermotor-TLE group, matched for age and laterality of epileptogenesis (LOE) who underwent surgery for refractory TLE.

Inclusion criteria:**Cases:**

- All patients who underwent surgery for TLE having hypermotor semiology as documented in the video telemetry shall be included in the study.

(HMS which include movements involving the body axis or proximal limb segments, resulting in large amplitude movements [such as flinging, kicking, bicycling, body gyration, body rocking, pelvic thrusting]).

- These patients should be Engel class 1 at 1-year post-surgical follow up (as a confirmation of temporal epileptogenesis)

Controls:

- Age- and LOE-matched hypomotor TLE control patients who underwent surgery for DRE (hypermotor:hypomotor = 1:2 ratio) shall be included for comparison.

Exclusion criteria:

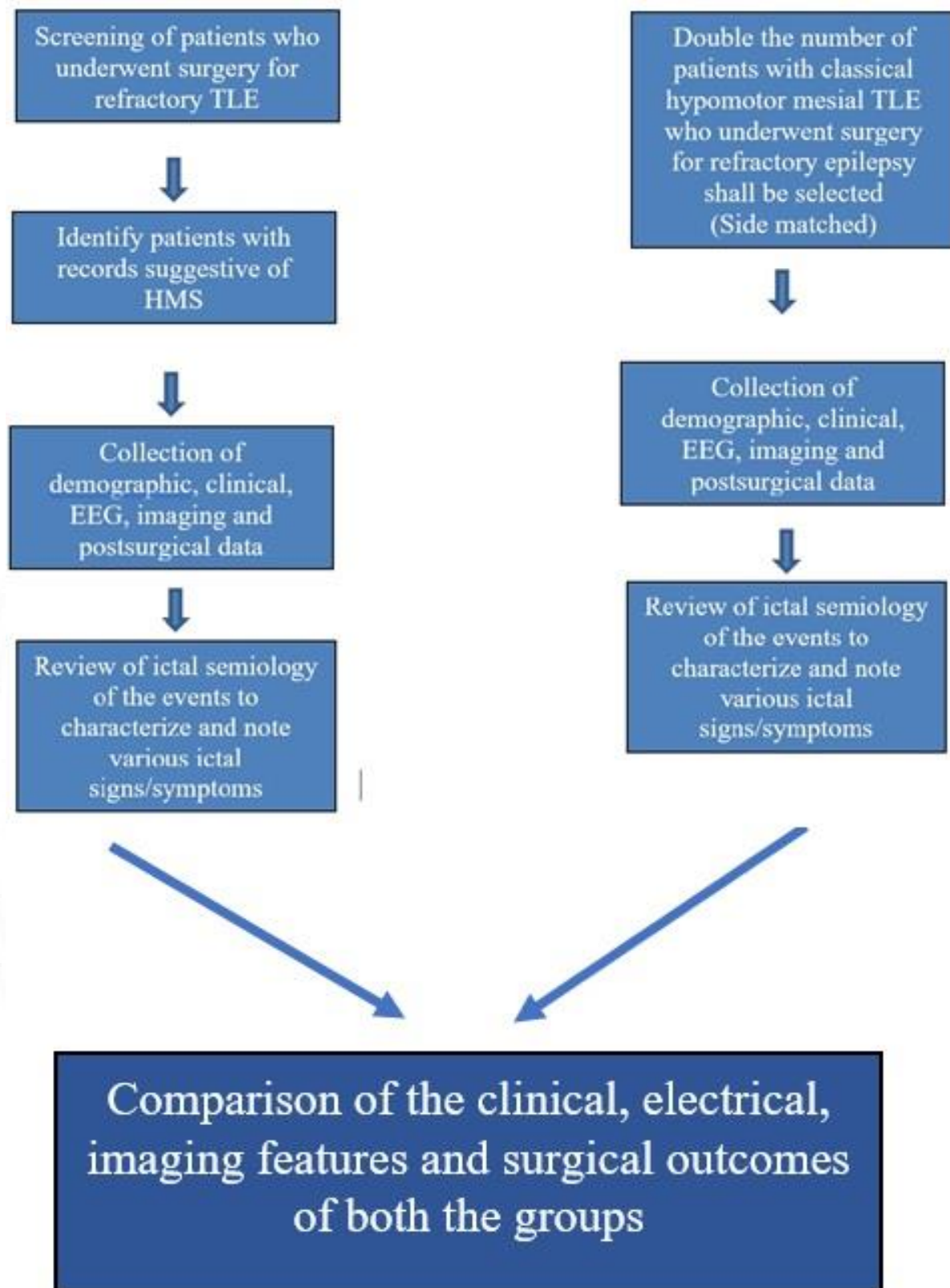
- In hypermotor TLE group, patients without Engel class 1 outcome were excluded.
- Patients with no available video electroencephalography (EEG) data to review were excluded.

Methodology:

We screened the medical records including video-EEG reports of patients who underwent surgery for refractory temporal lobe epilepsy (TLE) at R. Madhavan Nayar Centre for Comprehensive Epilepsy Care to identify patients with ictal semiology suggestive of HMS. The demographic data, seizure history, clinical characteristics, details of neuropsychological evaluation, imaging findings, interictal and ictal EEG data, operative notes, histopathological findings and postsurgical follow up data including Engel outcomes were collected. The video-EEG data of these patients was reviewed by an epileptologist to identify the various semiological symptoms/signs during the hypermotor events recorded. Details regarding the aura, time to onset of hypermotor features, duration of the events, frequency of secondary generalisation was collected. The frequency of various ictal symptoms in the total hypermotor seizures recorded was calculated.

We also included double the patients with classical hypomotor seizures originating from mesial temporal lobe for comparison with the hypermotor TLE group (hypermotor:hypomotor = 1:2 ratio). The hypomotor group were matched for age and in terms of LOE. Data collection and event reviewing was performed in this group similar to the hypermotor TLE group. A comparison between both the groups was performed to identify clinical, electrical and imaging differences between the groups.

Figure 1: Workflow of patient selection and data collection



Data collection:

The demographic data of the participants including age, gender, age of onset of epilepsy, age of undergoing video telemetry and age at surgery were collected. Clinical data regarding the presence or absence of antecedents, type of aura before the clinical events was collected. The type of MRI abnormality, presence or absence of hippocampal sclerosis and temporal neocortical changes, data on any other brain imaging available were analyzed. The histopathology reports were reviewed to collect data on the presence or absence of neocortical abnormalities, hippocampal sclerosis, or other abnormalities like a neoplasm.

Video EEG data was reviewed to collect data regarding the duration of recording, number of seizures recorded (including the number of events occurring out of sleep and events leading to generalized tonic-clonic seizures), duration of the events and the time-point of onset of hypermotor features into the event, details of the semiological features of each event recorded. The ictal electrical correlate including the onset and propagation, contralateral spread, the nature and location of the interictal epileptiform discharges were analyzed.

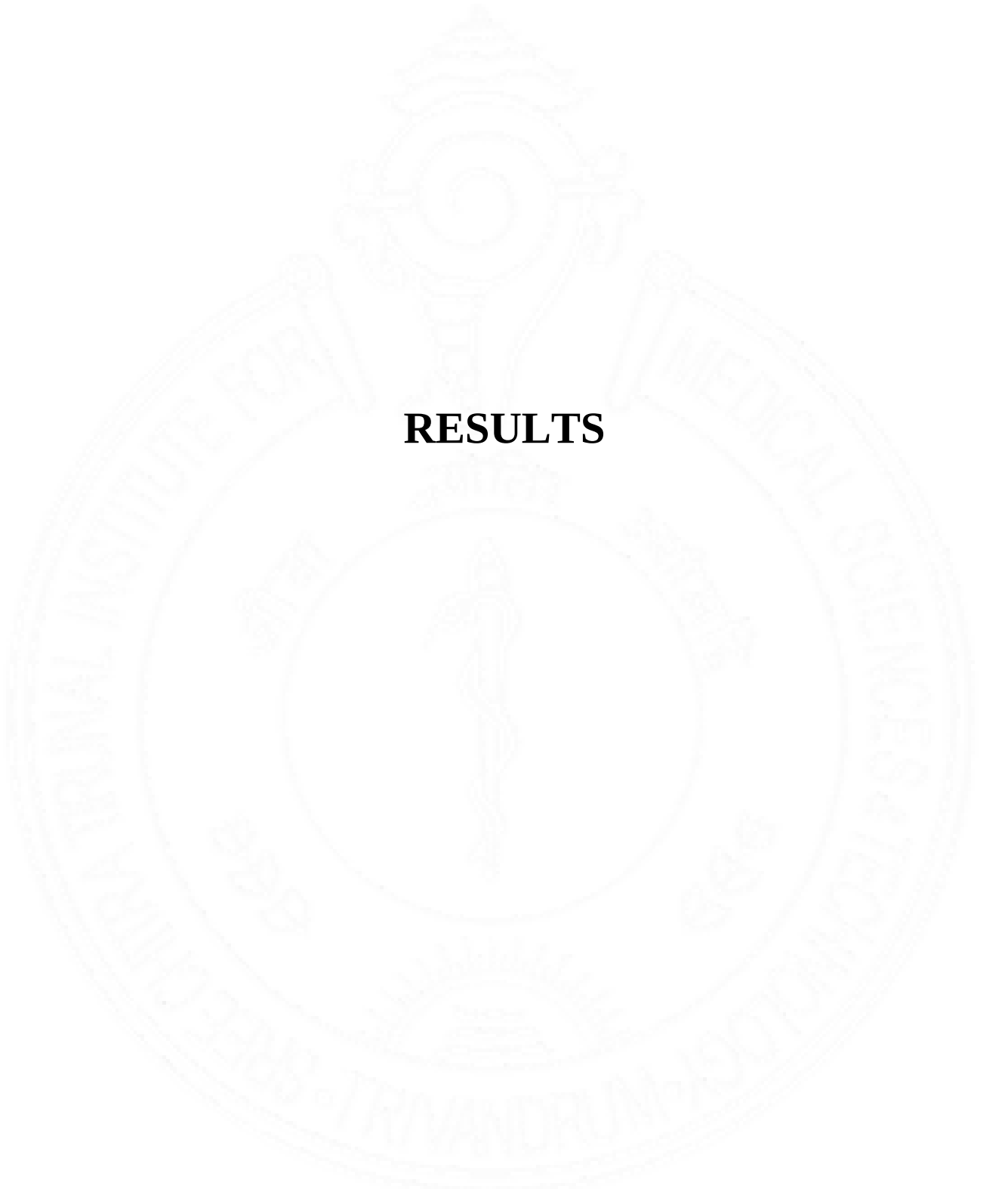
Data on the presence or absence of epileptiform discharges after surgery was analyzed. The post-operative outcome assessment included data on tapering or stoppage of anti-seizure medication (ASM) at 1 year follow-up in comparison to the presurgical treatment regimen, seizure outcome expressed as Engel surgical outcome scale [32].

Statistical analyses:

Analyses of all data sets were performed by using the Medical Statistics Software SPSS, Version 25.0 (IBM, Armonk, New York) with the help of a medical statistics expert. The comparison of baseline characteristics and different neuropsychological test variables between hypermotor and hypomotor TLE groups was performed using independent samples t-test or Mann–Whitney U test for continuous data and Chi square or Fisher's exact test for categorical data. The frequency with which various symptoms/signs occurred in the hypermotor TLE group was determined. A p value of ≤ 0.05 was taken as significant.

Ethical considerations:

This study has the approval of the Institutional Ethics Committee (IEC Regn No. ECR/189/Inst/KL/2013/RR-21, SCT/IEC/1778) and individual consent was waived as this was a retrospective study.



RESULTS

RESULTS

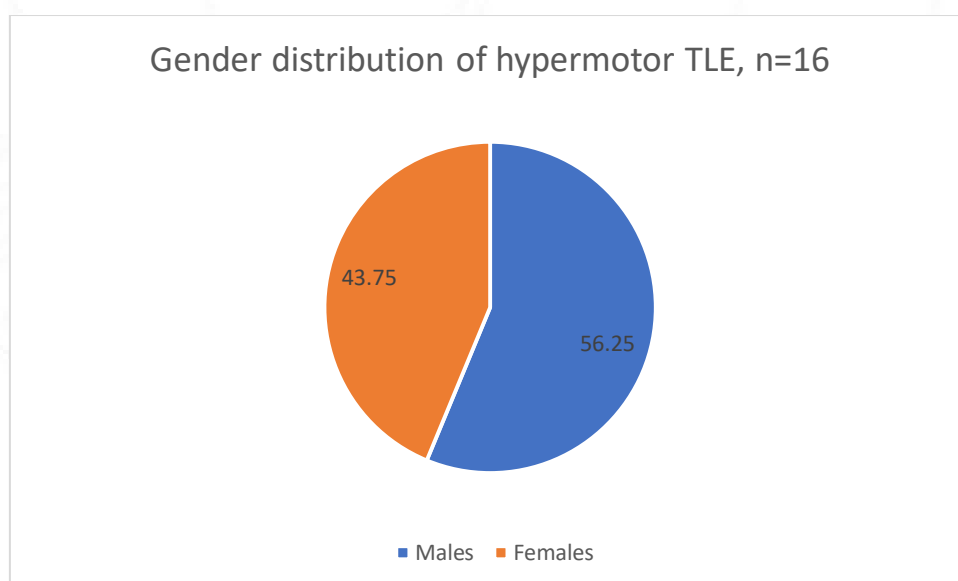
We retrospectively reviewed the data of 684 patients who consecutively received surgical treatment for TLE at the R Madhavan Nayar Center for Comprehensive Epilepsy Care of Trivandrum between January 2010 and December 2020. Sixteen patients (2.34%) were fulfilling the participation criteria and were included in the study. Thirty-two patients with hypomotor TLE from the 684 patients were included as controls (matched for age and laterality of seizure onset).

CHARACTERISTICS OF THE HYPERMOTOR TLE COHORT:

Gender distribution:

Out of the 684 patients with TLE who underwent surgery during the study period (389 males and 285 females), 16 cases had hypermotor seizures. Of these 16 patients, 14 (45.2%) were males and 17 (58.8%) were females.

Figure 2: Gender distribution of hypermotor TLE patients



Age, antecedent and aura:

The age of seizure onset was 7.56 ± 6.81 years, first event recording by telemetry was 18.25 ± 7.76 years, age at surgery was 19.69 ± 8.03 years and the mean duration of epilepsy was 12.125 ± 7.755 years.

Antecedent in the form of febrile seizures in early life was present in 5 (31.3%) of the patients and an aura was experienced in 11 (68.8%) of the 16 patients. Aura was reported by 10 (62.5%) of the patients.

Table 1: Aura observed in patients with hypermotor TLE

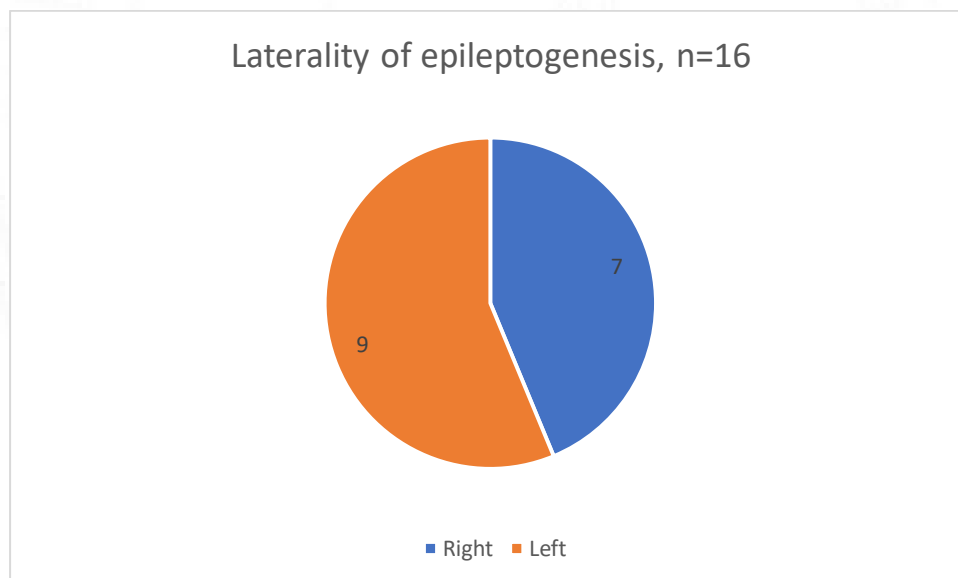
Type of aura	Number of patients experienced (n=16)
Epigastric aura	4 (25%)
Fear	5 (31.25%)
Jamais vu	1 (6.25%)
Elementary visual aura	1 (6.25%)
Choking sensation	1 (6.25%)
Thirst	1 (6.25%)
Vertigo	1 (6.25%)

Imaging findings, laterality of epileptogenesis and histopathology:

MRI brain showed temporal lobe abnormality in all patients with hippocampal sclerosis in 9 (56.3%) and neocortical abnormality was noted in 14 (87.5%) of the patients. Out of these 14 patients 11 had poor grey-white matter differentiation while the other 3 has features suggestive of developmental neoplasms in the temporal lobes extending into the neocortex.

The LOE was determined taking into consideration the clinical, imaging, video telemetry (semiology, ictal and interictal electrical data) and decision on surgery was taken after discussion in a patient management conference involving the epileptologists, neurosurgeons, neuroradiologists, neuropsychologists and speech therapists. All the 16 patients underwent anterior temporal lobectomy with amygdalo-hippocampectomy (right sided in 7 and left sided in 9 patients).

Figure 3: Laterality of epileptogenesis in hypermotor TLE patients



Histopathological examination of the resected specimens showed hippocampal sclerosis in 11 (68.8%), dysplasia in 4 (25%) (type IIa in all 4) and neoplasm in 3 (18.8%) (gaglioglioma, WHO grade I in all 3) of the patients.

VEEG data:

The mean total duration of VEEG recording as part of pre-surgical evaluation was 69.63 ± 40.44 hours and 5.13 ± 3.79 events were recorded on an average per patient with a total number of 82 clinical seizures recorded, all focal onset with a mean event-duration of 85.36 ± 57.06 seconds. Out of the total 82 events, 16 events (19.5%) resulted in bilateral tonic-clonic seizures (secondary GTCS) and 55 events (67.1%) occurred out of sleep. Hypermotor features started within 10 seconds of the clinical onset of seizures in all the recorded events.

Figure 4: Events recorded out of sleep and during wakefulness in hypermotor TLE

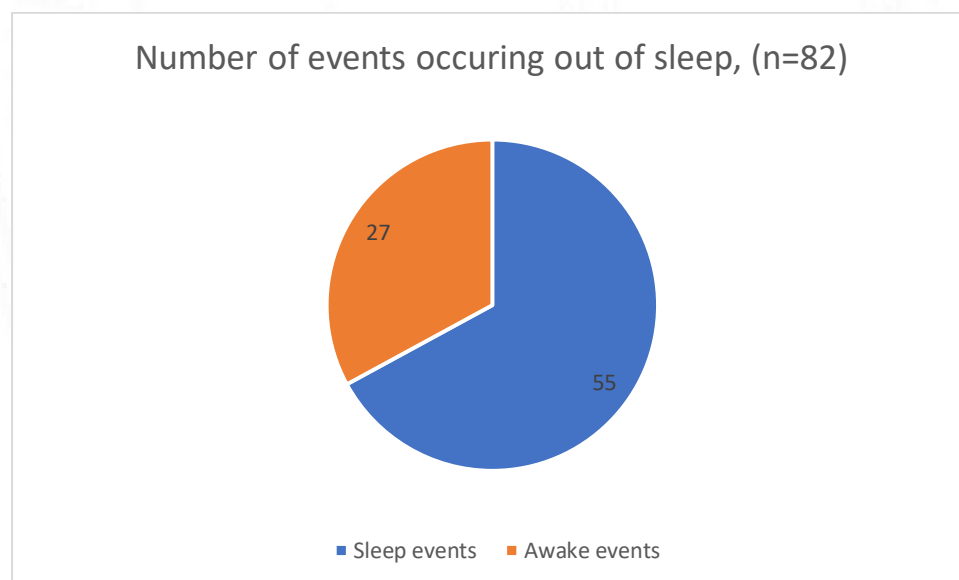


Table 2: Semiology of the events recorded in hypermotor TLE group and correlation to the previously described HMS semiology in landmark studies on frontal lobe epilepsy

Age in years/ Gender/ Total events recorded/ LOE	Clinical manifestations of the hypermotor seizures	Rheims et al., 2008 [3]	Bonini et al., 2014 [4]
15/M 8 events Left	Epigastric rising aura and choking sensation, marked restlessness, gets up from lying, tapping of hands over the bed R>L, fearful behaviour, kicking movements of lower limbs, leaving behaviour, oroalimentary automatisms seen in all events; additionally, side to side head movements, body rocking and pelvic thrusting seen in 2 events with tendency to pull out electrodes (no GTCS)	HMS type 1	Group 4 Distal stereotypies Hyperkinetic movements Fearful behaviour Integrated gestural motor behaviour
13/M 4 events Right	No aura, sudden marked restlessness, fearful behaviour, gibberish talking, side to side head movements, body rocking movements (in 2), right UL proximal flinging movements (in 3) followed by right hand distal stereotypies, left UL/LL dystonic posturing, perioral automatisms, left facial deviation with jerking, left UL clonic jerking (1 progressing to GTCS)	HMS type 1	Group 4 Proximal and distal stereotypies Hyperkinetic movements Fearful behaviour Integrated gestural motor behaviour
12/F 5 events Right	Aura of fear, sudden right UL tonic posturing with proximal flinging movements (followed by left upper limb posturing in 4 events), tonic vocalisation, eye deviation to right and unresponsiveness, oroalimentary automatisms (1 progressing to GTCS)	HMS type 2	Group 2 Elementary motor signs Non-integrated gestural motor behaviour
15/M 5 events Right	Arousal, vocalisation with fearful behaviour, marked restlessness, violent kicking movements of both LL, gets up from lying position, covers face with right hand, followed by rapid proximal flinging movements of the left UL and LL, left body gyration (in 2) tonic posturing left UL followed by all limbs, progressing to GTCS in all events	HMS type 1	Group 4 Proximal stereotypies Hyperkinetic movements Fearful behaviour Integrated gestural motor behaviour
37/F 4 events Left	Visual aura in some events, sudden tonic posturing of both UL (right in 1), pouting of lips and grimace, followed by behavioural arrest, stare, oroalimentary automatisms, right UL dystonic posturing and RINCH, left UL automatisms, left body gyration (in 1), confused behaviour and unresponsiveness (2 progressing to GTCS)	HMS type 2	Group 1 Elementary motor signs
30/M 2 events	Epigastric aura, grimace, head and eye deviation to left side, counter clockwise body gyration,	HMS type 2	Group 1

Left	oroalimentary automatisms, right UL dystonic posturing, unresponsiveness, stare (1 progressing to GTCS with forced right HD, right ATLP)		Elementary motor signs
18/F 2 events Right	Aura of fear and jamais vu, loud cry, marked restlessness with fearful behaviour, tongue protrusion with open mouth, bilateral UL thrashing movements against bed, bilateral LL bicycling movements, followed by behavioural arrest, confused appearance, stare Followed by grimace, HD to right, left UL/LL paucity, right UL flinging/LL kicking movements in 1 event (no GTCS)	HMS type 1	Group 4 Proximal stereotypies Hyperkinetic movements Fearful behaviour Integrated gestural motor behaviour
25/F 3 events Right	Behavioural change, loud vocalisation fearful behaviour, marked restlessness, right UL flinging movements (in 1), bicycling (in 1), leaving behaviour - trying to jump out of bed, noisy blowing of air from mouth, oroalimentary automatisms, postictal cough (no GTCS)	HMS type 1	Group 4 Proximal stereotypies Hyperkinetic movements Fearful behaviour Integrated gestural motor behaviour
13/F 15 events Left	Sudden arousal, restlessness with vocalisation, pelvic thrusting movements, right hand tapping on bed, counter clockwise body gyration, HD to left, bicycling movements, right UL dystonic posturing, left UL automatisms (no GTCS)	HMS type 1	Group 4 Distal stereotypies Hyperkinetic movements Integrated gestural motor behaviour
14/M 13 events Left	Arousal, ED/HD to left, occasional counter clockwise body gyration, right UL dystonic posturing, bicycling movements (no GTCS)	HMS type 2	Unclassified Elementary motor signs Integrated gestural motor behaviour
25/F 5 events Left	Epigastric aura and fear, sudden shouting, marked restlessness with fearful expression on face, tapping of upper limbs on bed (R>L), violent flinging of left UL, violent kicking movements both LL, right forced HD, right UL tonic posturing, right ATLP and all progressing to GTCS	HMS type 1	Group 4 Proximal stereotypies Hyperkinetic movements Fearful behaviour Integrated gestural motor behaviour
9/M 4 events Right	Epigastric aura and feeling of thirst, arousal, right UL flinging movements, fearful behaviour, marked restlessness, pelvic thrusting, followed by stare, oroalimentary automatisms (no GTCS)	HMS type 1	Group 4 Proximal stereotypies Hyperkinetic movements Fearful behaviour Integrated gestural motor behaviour
11/M 3 events Left	Aura of vertigo, arousal, bicycling movements, left HD/ED, behavioural arrest, eye blinks, right facial deviation, face wiping with left hand (no GTCS)	HMS type 2	Unclassified Elementary motor signs Integrated gestural motor behaviour

23/F 4 events Right	Aura of fear, marked restlessness, shouting, clockwise body gyration (in 1), right upper limb flinging movements followed by oroalimentary automatisms, left hand dystonic posturing, left RINCH, right hand automatisms, behavioural arrest, stare (no GTCS)	HMS type 1	Group 4 Proximal stereotypies Hyperkinetic movements Fearful behaviour Integrated gestural motor behaviour
19/M 3 events Left	Marked restlessness, side to side head movements (in 1), counter clockwise body gyration, fearful behaviour and vocalisation, right hand dystonic posturing and RINCH followed by right UL flinging movements (in 2) (1 progressing to GTCS)	HMS type 1	Group 4 Proximal stereotypies Hyperkinetic movements Fearful behaviour Integrated gestural motor behaviour
13/M 2 events Left	Reports aura of fear verbally with fearful facial expression, marked restlessness, violent kicking movements, brief oroalimentary automatisms, right hand dystonic posturing, left hand automatisms (no GTCS)	HMS type 1	Group 4 Hyperkinetic movements Fearful behaviour Integrated gestural motor behaviour

LOE: Laterality of epileptogenesis, UL: Upper limb, LL: Lower limb, M: Male, F: Female, R: Right, L: Left, HMS: Hypermotor seizure, HD: Head deviation, ATLP: Asymmetric tonic limb posturing, RINCH: Rhythmic ictal non-clonic hand motions

Table 3: Frequency of the various hypermotor features

Semiological feature	Frequency of occurrence in the recorded hypermotor events (n=82)
Restlessness	60 (73.2%)
Bicycling/kicking movements	54 (65.85%)
Body gyration	37 (45.1%)
Tapping on bed with UL	32 (39%)
Flinging/thrashing movements of UL	31 (37.8%)
Pelvic thrusting movements	21 (25.6%)
Ipsilateral versive signs at onset	18 (21.95%)
Contralateral tonic posturing at onset	9 (11%)
Side to side head movements	7 (8.5%)
Body rocking movements	4 (4.9%)
Contralateral versive signs at onset	0

Electrical data:

Interictal epileptiform discharges were confined to temporal regions in 11 patients while in the other 5 patients they were seen over other regions as well. The ictal electrical onset was focal from the corresponding temporal region in 6 (37.5%), regional in 6 (37.5%) (5 patients it was frontotemporal, 1 patient it was centrottemporal), hemispheric in 2 (12.5%) patients and diffuse in 2 patients (12.5%). In all patients the subsequent evolution was best over the corresponding temporal region. In the later part the electrical rhythm was confined to the same hemisphere in 13 patients (81.3%), a late spread (after 10 seconds) was noted in 1 (6.3%) patient and the presence or absence of contralateral spread could not be assessed in 2 patients due to movement and myogenic artifacts. Clinical onset was soon after the electrical onset in 15 patients, while in 1 patient there was an average delay of 12 seconds.

Post-surgery outcomes:

Patients in the hypermotor TLE group were on an average of 2.5 ± 0.9 anti-seizure medications (ASM). All patients underwent anterior temporal lobectomy plus amygdalohippocampectomy (ATL plus AH). At 1 year postsurgical follow up, ASM were tapered and stopped in 10 (62.5%) patients, stopped in 2 (12.5%) patients and remained the same in 4 (25%) of the patients. All the 16 patients had Engel class 1 outcome at 1 year follow up. Post-surgery EEG at 1 week was normal or showed focal slowing in 13 patients and epileptiform discharges in 3 (18.8%) patients.

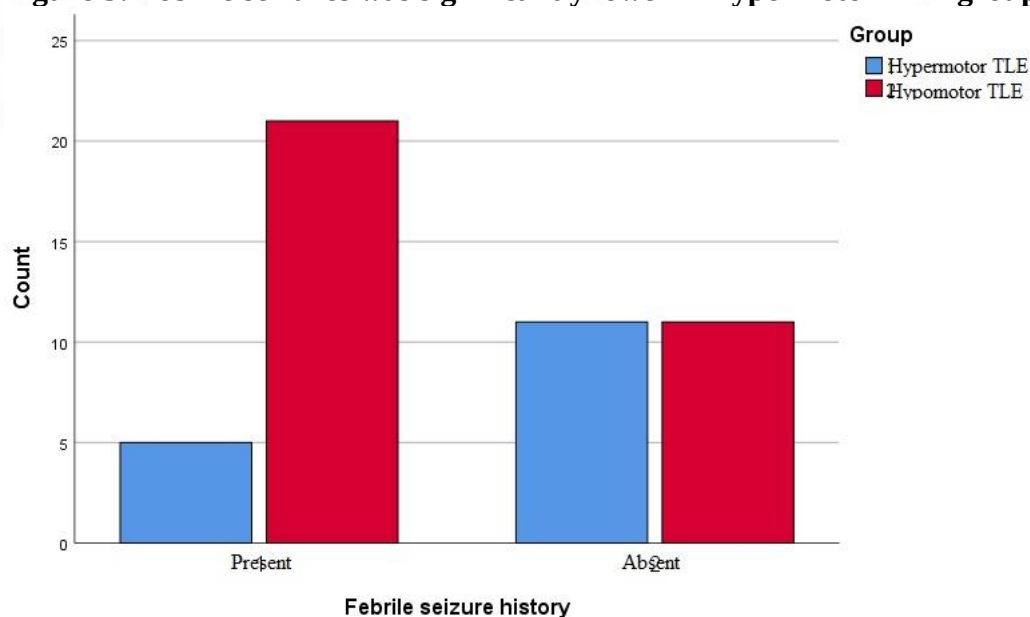
COMPARISON BETWEEN HYPERMOTOR-TLE AND HYPOMOTOR-TLE:

Age at epilepsy onset, age at video telemetry recording, age at surgery and duration of epilepsy at surgery were comparable between the two groups. Gender distribution was similar between both the groups (p-value of 1). History of febrile seizures (antecedents) was significantly lower in hypermotor TLE group (31.3%) compared to hypomotor TLE (65.6%), p-value of 0.024.

Table 4: Comparison of clinical details of both groups

Variable	Hypermotor TLE (n=16) Mean (SD)	Hypomotor TLE (n=32) Mean (SD)	p-value
Age of epilepsy onset	7.56 (6.81)	10.37 (5.74)	0.06
Age at video telemetry	18.25 (7.76)	21.44 (8)	0.105
Age at surgery	19.7 (8.04)	22.4 (7.8)	0.151
Duration of epilepsy before surgery	12.125 (7.76)	12 (7.5)	0.959
Males/Females	9/7	18/14	1.00
Febrile seizures	5 (31.3%)	21 (65.6%)	0.024

Figure 5: Febrile seizures was significantly lower in hypermotor TLE group (p=0.024)



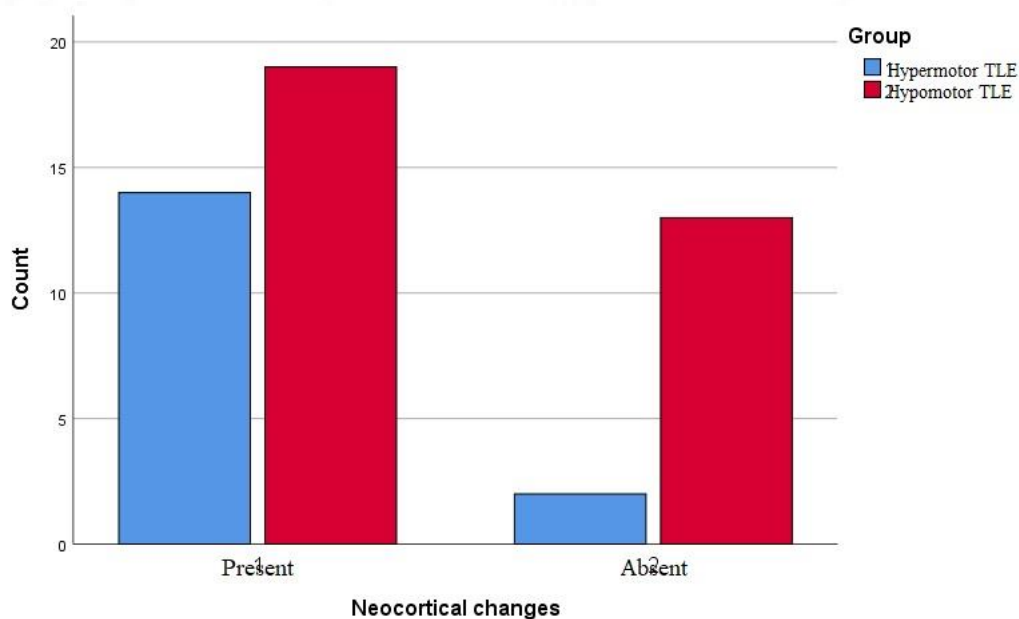
Comparison of imaging and histopathology data:

The presence of hippocampal sclerosis (HS) on MRI was significantly lower in hypermotor TLE group (56.3%) compared to hypomotor TLE (90.6%), p-value of 0.006 and temporal neocortical abnormalities were significantly higher in hypermotor TLE group (87.5%) compared to hypomotor TLE (59.4%), p-value of 0.048. Similar findings were noted in histopathological examinations as well (p-values of 0.005 for HS and 0.003 for dysplasia).

Table 5: Comparison of imaging and histopathology data

Variable	Hypermotor TLE (n=16)	Hypomotor TLE (n=32)	p-value
HS on MRI	9 (56.3%)	29 (90.6%)	0.006
Neocortical abnormality on MRI	14 (87.5%)	19 (59.4%)	0.048
HS by histopathology	11 (68.8%)	31 (96.9%)	0.005
Dysplasia by histopathology	4 (25%)	0 (0%)	0.003
Neoplasm by histopathology	3 (18.8%)	0 (0%)	0.011

Figure 6: Neocortical abnormalities significantly higher in hypermotor TLE (p=0.048)



Comparison of VEEG data:

The total duration of recording, events recorded (including events occurring in sleep and events with secondary GTCS) were similar in both groups. The mean duration of events was comparable in both groups, 85.36±57.06 secs in hypermotor TLE group and 88.57±27.5 secs in hypomotor TLE (p-value 0.301).

Table 6: Comparison of VEEG data

Variable	Hypermotor TLE (n=16) Mean (SD)	Hypomotor TLE (n=32) Mean (SD)	p-value
Total duration of VEEG	69.63 (40.44) hrs	73.22 (40.91) hrs	0.835
Number of events recorded	5.13 (3.8)	3.81 (1.57)	0.562
Events out of sleep	3.67 (4.72)	1.16 (1.42)	0.073
Secondary GTCS	1 (1.67)	0.59 (0.95)	0.536
Duration of events	85.36 (57.06)	88.57 (27.5)	0.301
Delay between electrical & clinical onset	0.75 (3) secs	3.75 (8.33) secs	0.225

The presence of aura was comparable, 66.8% and 71.9% in hypermotor and hypomotor TLE groups (p-value 0.822). The electrical ictal onset was focal over the temporal region in 6 (37.5%) and 29 (90.6%) patients, regional in 8 (50%) and 2 (6.3%) patients, diffuse in 2 (12.5%) and 1 (3.1%) patient in hypermotor and hypomotor TLE groups, respectively; there was a significantly lower number of patients with focal onset ictal pattern in hypermotor group compared to patients with hypomotor TLE (**p-value 0.0001**). In 13 (81.3%) and 21 (65.6%) patients in hypermotor and hypomotor TLE groups respectively, the ictal rhythm was confined to the hemisphere of origin without contralateral spread; late spread after a period of ipsilateral temporal evolution was noted in 1 (6.3%) and 10 (31.3%) patients, respectively. The exact

propagation and spread could not be assessed in 2 hypermotor TLE patients due to movement and myogenic artifacts. Overall, both the groups were comparable in terms of contralateral spread of ictal rhythm (p-value 0.51). Interictal epileptiform discharges were confined to temporal region in 11 (68.8%) and 25 (78.1%), extending to other regions in 5 (31.3%) and 7 (21.875%) respectively in hypermotor and hypomotor TLE groups, which was comparable (p-value 0.509). The time gap between electrical and clinical onset of events was 0.75 ± 3 secs and 3.75 ± 8.33 secs in the groups which was comparable (p-value 0.225).

Comparison of post-surgical outcomes:

The number of ASM was 2.5 ± 0.9 and 2.22 ± 0.42 , in hypermotor and hypomotor TLE groups respectively, which was comparable (p-value 0.297); in both groups 43.8% and 56.3%, underwent right and left ATL plus AH, respectively (p-value 1). ASM were tapered in 10 (62.5%) and 27 (84.4%) patients (p-value 0.089) and stopped in 2 (12.5%) and 2 (6.3%) patients (p-value 0.46), in hypermotor and hypomotor TLE groups, respectively, which was comparable. Engel class 1 outcome was noted in all patients (100%) with hypermotor TLE and in 31 patients (96.9%) in hypomotor TLE (1 patient had Engel class 2 outcome), which was comparable (p-value 0.475).

Comparison of hypermotor TLE and the entire cohort of TLE:

A total of 684 patients underwent resective surgery for refractory TLE between January 2010 and December 2020, out of which 16 patients with hypermotor TLE were identified. The mean age at the time of surgery was 19.69 ± 8.03 and 26.95 ± 9.45 years in hypermotor TLE group and whole TLE cohort, respectively ($p=0.002$); the mean duration of epilepsy at the time of surgery was 12.125 ± 7.755 and 17 ± 9.34 years, respectively ($p=0.038$). There was no significant difference in between groups with respect to the age of onset of unprovoked seizures.

Table 7: Comparison of hypermotor TLE and the entire cohort of TLE

Variable	Hypermotor TLE (n=16) Mean$\pm$SD	Entire TLE cohort (n=684) Mean$\pm$SD	p-value
Age at seizure onset	7.56 $\pm$ 6.81	9.96 $\pm$ 6.95	0.172
Age at surgery	19.69 $\pm$ 8.03	26.95 $\pm$ 9.45	0.002
Duration of epilepsy at surgery	12.125 $\pm$ 7.755	17 $\pm$ 9.34	0.038
Gender (Male/Female)	9/7	389/295	0.941



DISCUSSION

DISCUSSION

Our study tries to give a detailed account of the various clinical manifestations of HMSs originating from temporal lobe. The semiologic elements included violent vocalization, complex movements of the proximal segments of the limbs, rotation of the trunk, pelvic thrusting, or early tonic posturing or versive manifestations. Our study throws light on the imaging features, histopathological findings and post-surgical outcomes of this rare entity. We also did a comparison between the hypermotor TLE and hypomotor TLE groups, to identify the factors that are significantly associated with the occurrence of hypermotor seizures in TLE. We analyzed the post-surgical outcomes of hypermotor TLE and compared with the classical hypomotor group. Engel class 1 outcome at 1 year follow up was considered as the confirming factor of temporal lobe as the EZ in the hypermotor TLE group.

We have included 16 patients with hypermotor-TLE and 32 controls with hypomotor TLE (age- and LOE-matched) in this retrospective study screening the patients who underwent resective surgery for TLE between January 2010 and December 2020. All the patients were discussed in a patient management conference before surgery, where experienced epileptologists, neurosurgeons and neuroradiologists discuss the imaging and video telemetry data and take decision on the location of EZ and plan on the area of resection. Data of all the participants was included in the analyses and there was no attrition at 1-year follow up; video telemetry data of all the participants was available for review. Our study generated baseline data on the various hypermotor features of HMSs originating from temporal lobe.

The mean age at the time of surgery was 19.69 ± 8.03 and 26.95 ± 9.45 years in hypermotor TLE group and whole TLE cohort while the mean duration of epilepsy at the time of surgery was 12.125 ± 7.755 and 17 ± 9.34 years, respectively ($p=0.038$). However, there was no significant difference in between groups with respect to the age of onset of unprovoked seizures (7.56 ± 6.81 and 9.96 ± 6.95 years [$p=0.172$]). This shows that the disability experienced

by the hypermotor TLE group is higher when compared to the entire TLE cohort, probably due to the high frequency or severity of the clinical events; drug resistant hypermotor TLE patients can experience a poor QOL and the knowledge regarding this entity can avoid delay in considering surgical treatment. No difference in gender distribution noted between the groups (Male: Female = 9:7 and 389:295 respectively, $p=0.941$). Males were higher than females similar to previous studies [14].

The prevalence of hypermotor TLE was 2.34% in the TLE group who underwent surgery for DRE, similar to previous studies which ranges from 0.7 to 2.3% [8,22]. LOE was right in 7 (43.75%) and left in 9 (56.25%) patients. Antecedent in the form of febrile seizures was present in significantly lower number of patients with hypermotor TLE compared to hypomotor TLE group and aura was reported in 10 (62.5%) of the patients. In ten patients we found fearful behaviour and expression accompanying the seizures with intense emotional disturbances. These affective and behavioral changes may be due to the decrease of coupling between the anterior temporal and orbitofrontal regions and the lateral prefrontal cortex and cingulate gyrus [34]. The clinical manifestations were similar to HMS type 1 in 11 patients, as described by Rheims et al., [3] and similar to HMS type 2 in the rest 5 patients; comparison with the types described by Bonini et al., [4], 11 patients were similar to type 4, 2 to type 1, 1 to type 2, 2 could not be classified.

MRI abnormality was noted in all patients and was corresponding with the final EZ in all patients, with 87.5% having temporal neocortical abnormality. Neocortical abnormality involving the lateral temporal structures (dysplastic or neoplasm) were significantly higher in hypermotor TLE group, whereas mesial temporal abnormalities, namely hippocampal sclerosis was significantly higher in hypomotor TLE group; these findings were also confirmed by histopathological findings. Overall, HSMs were significantly associated with developmental lesions involving the temporal neocortex, similar to the findings of Elisak et al., 2013 and

Nobili et al., 2004 [14,19]. Previous studies have shown that hypermotor seizures are more common in patients with neocortical temporal lobe epilepsy (6%) (especially involving the temporal pole) than with mesial temporal lobe epilepsy (1%) [6,22,33]. These findings suggest that the classical antecedent followed by HS was associated with hypomotor TLE whereas the absence of antecedent and the presence of developmental lesion involving the neocortex was associated with hypermotor TLE.

Interictal epileptiform discharges were confined to temporal regions in 11 patients while in the other 5 patients they were seen over other regions as well. The ictal electrical onset was focal from the corresponding temporal region in 6 (37.5%), regional in 6 (37.5%) (5 patients it was frontotemporal, 1 patient it was centrottemporal), hemispheric in 2 (12.5%) patients and diffuse in 2 patients (12.5%). In all patients the subsequent evolution was best over the corresponding temporal region. In correlation with the lesion located in the temporal region in all of these patients and the interictal and ictal scalp-EEG results over the temporal area, we were convinced of a temporal seizure origin. It is certainly more difficult to distinguish between a frontal and temporal ictal onset zone in patients with hyperkinetic seizures when the MRI and the scalp EEG are less unequivocal. Considering that drug resistant patients with NFLE have been described, the actual localization of the epileptogenic zone becomes mandatory in a surgical perspective, and the information that hyperkinetic seizures may have a temporal lobe origin could be useful. In a previous study, sleep-related hyperkinetic seizures of temporal lobe origin were strikingly similar to those observed in NFLE (nocturnal frontal lobe epilepsy) [19]. Mai et al. (2005) reported that the sleep occurrence was also frequent in hyperkinetic seizures of temporal lobe origin and that they observed motor behaviour in the two conditions [23]. In our study 55 (67.1%) out of the 82 recorded events occurred out of sleep.

Wang et al. (2008) reported on four patients who presented with hyperkinetic seizures

based on temporal polar lesions [6]. The authors of a retrospective SEEG analysis described hyperkinetic seizures of temporal lobe origin in seven patients and claimed the existence of a consistent brain network including the temporal pole and the medial basal prefrontal cortex [24]. Besides the temporal pole, the temporal basal structures, especially the parahippocampal gyrus seems to be a region of interest in TLE with hyperkinetic features [25]. Bidirectional connections between the temporal pole, amygdala, parahippocampal region, and the orbitofrontal and medial prefrontal cortex have been shown in primates [26,27]. The uncinate fasciculus, links rostral temporal, inferotemporal, and ventral temporal regions with the medial and orbital frontal cortices [28], which might allow fast seizure spread. Another important white matter pathway, the extreme capsule, contains fibers connecting the medial and orbital prefrontal cortices, as well as the rostral cingulate gyrus with the rostral part of the superior temporal gyrus via the insula [29]. An example of seizure spread following this latter pathway might be found in two patients in our study, who had aura in the form of choking and thirst in addition to the epigastric aura.

Yu et al., 2013 [8], studied the intracranial EEG correlates of HMSs in TLE and found that the spike activity was the most common type of originating discharge, while rhythmic spiking and flattening were often recorded in the frontal lobe when ictal activity was propagated. The first activated area of the frontal lobe was variable between patients. The cingulate gyrus and orbitofrontal regions were not always the earliest activated area. This may imply that HMSs result from the activation of cortical or subcortical pathways and that a complex anatomic and functional network participates in the HMS genesis. Vaugier et al.'s study on the involved brain networks is a good supplement to this report [24]. They tried to define the neural structures involved in HMSs originating from the temporal lobe by stereo-EEG. They concluded that the temporal pole and its connexions with medio-basal prefrontal cortex represent the main structures involved in epileptogenic networks. A previous study of

ictal perfusion using single photon emission computed tomography (SPECT) demonstrated two distinct clusters of significant hyperperfusion in HMSs: one involving the bilateral frontomesial regions, cingulate gyri, and caudate nuclei, and the other involving the ipsilateral anteromesial temporal structures, frontoorbital region, insula, and basal ganglia [35]. According to some authors' hypotheses, a large neuronal network, comprising the anterior cingulate and temporolimbic cortices, could sustain these complex seizures with important affective symptoms [36-39].

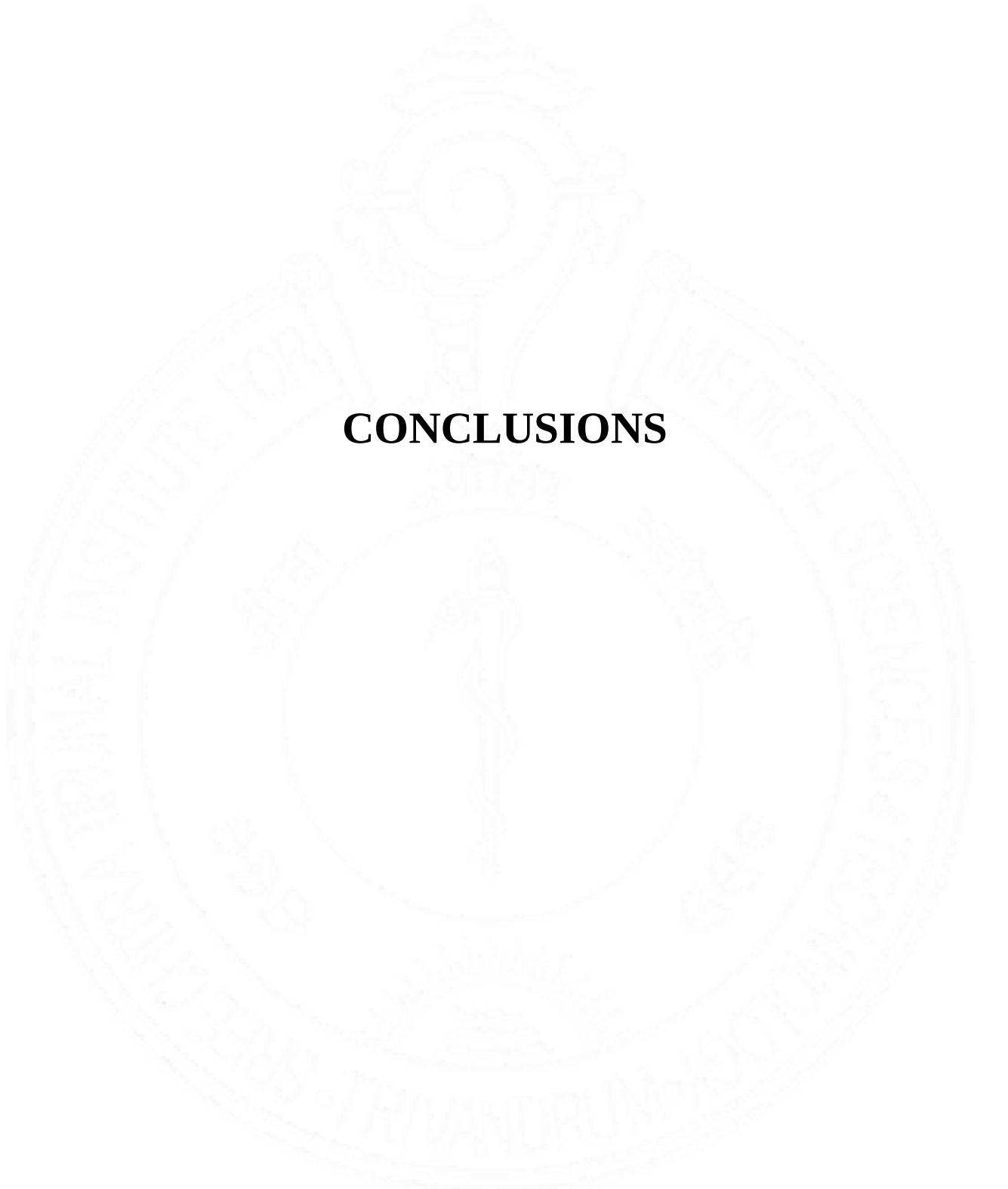
All patients underwent classical anterior temporal lobectomy plus amygdalohippocampectomy. At 1 year postsurgical follow up, all the 16 patients had Engel class 1 outcome and the ASM drug tapering or stoppage was also comparable to the hypomotor TLE group. Therefore, no contradiction to the hypothesis of TLE in a patient with HMSs, if scalp EEG patterns and neuroimaging findings correspond. The postoperative seizure outcome is favorable in such patients and not different from outcome data in classical TLE. . In conclusion, some HMSs can originate from the temporal lobe. Though the complex functional network contributing to HMSs is not clear, the frontal lobe may be involved. In carefully selected patients, surgical resection of temporal epileptogenic zones may lead to good outcomes.

Strengths of the study

1. Our study gives a detailed account of the semiological features, imaging findings and histopathology of patients with hypermotor TLE.
2. We included a control group (age and LOE matched) with hypomotor TLE for comparison.
3. The 1-year post-operative follow up data was available for all the patients without attrition.
4. Engel class 1 outcome at 1-year follow up in all the hypermotor TLE patients confirms the EZ to be in the temporal lobe.
5. This study has significant impact on the selection of patients with drug-resistant hypermotor TLE for surgical management.
6. We also compared the age of onset and the duration of epilepsy of the hypermotor TLE patients with the entire TLE group to demonstrate the disability of hypermotor TLE.

Limitations of the study

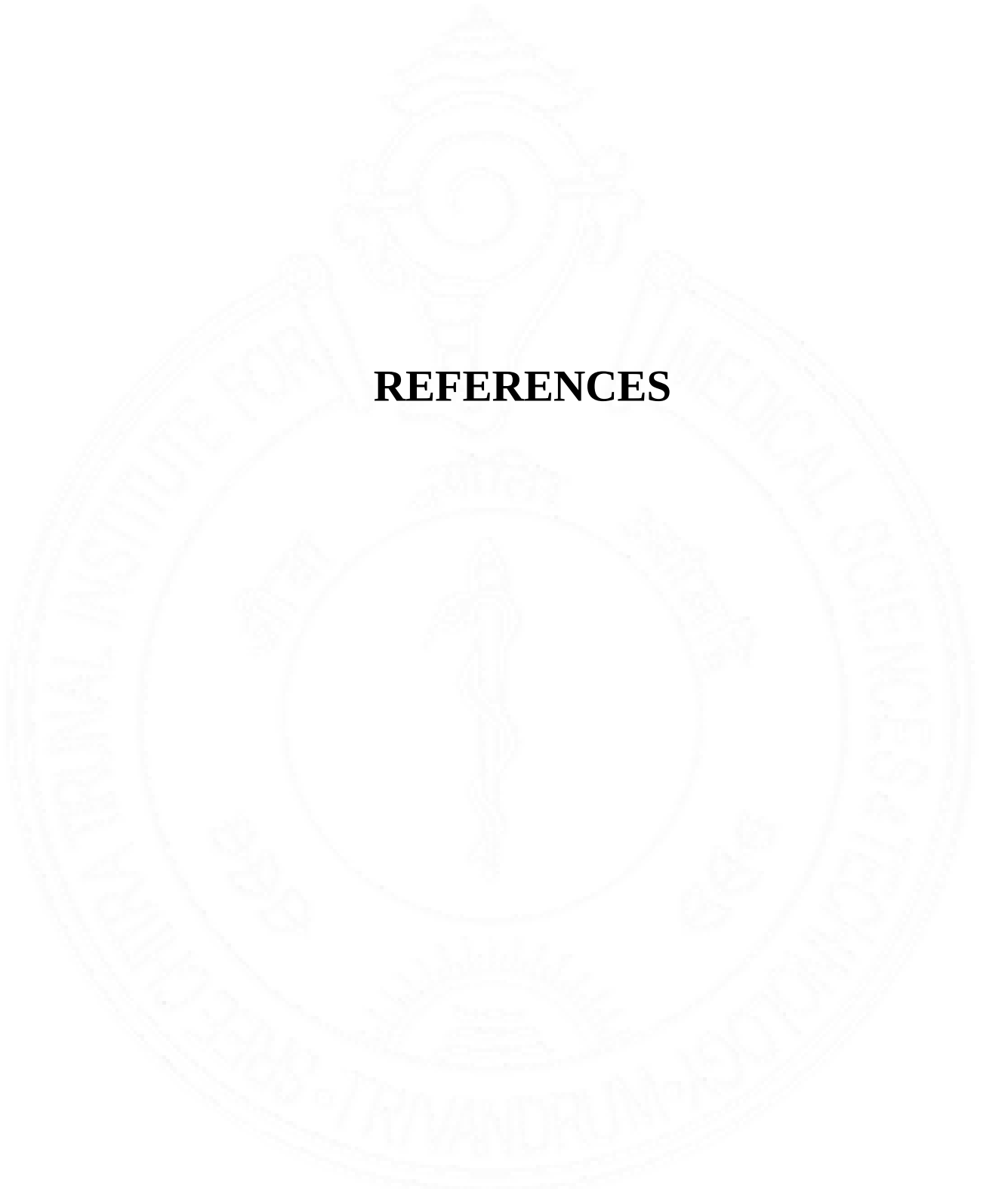
1. Functional imaging or invasive monitoring was not performed to study the nature of spread of electrical activity and networks involved during the seizures.
2. The sample size of the hypermotor TLE group is low.



CONCLUSIONS

CONCLUSIONS

- Our study provides a detailed account of the clinical manifestations, imaging findings, interictal and ictal EEG features, histopathological substrates and post-surgical outcomes of patients with hypermotor TLE.
- Absence of febrile seizures, neocortical involvement on imaging, dysplasia on histopathology were significantly associated with hypermotor seizures from temporal lobe, while history of febrile seizures and HS were significantly associated with hypomotor TLE.
- In our cohort the interictal ictal EEG features and imaging findings succoured in the diagnosis of TLE and hence the surgical management even though the semiologic features are not classical of TLE.
- Knowledge of hypermotor TLE among the treating neurologists is essentially to consider early surgical intervention in drug-refractory cases to improve QOL.
- Carefully evaluated and selected cases of drug-refractory hypermotor TLE can have good surgical outcomes, similar to the classical TLE.



REFERENCES

REFERENCES

1. Blair RD. Temporal lobe epilepsy semiology. *Epilepsy Res Treat*. 2012;2012:751510. doi: 10.1155/2012/751510.
2. Ryvlin P, Minotti L, Demarquay G, Hirsch E, Arzimanoglou A, Hoffman D, Guénot M, Picard F, Rheims S, Kahane P. Nocturnal hypermotor seizures, suggesting frontal lobe epilepsy, can originate in the insula. *Epilepsia*. 2006 Apr;47(4):755-65. doi: 10.1111/j.1528-1167.2006.00510.x.
3. Rheims S, Ryvlin P, Scherer C, Minotti L, Hoffmann D, Guenot M, Mauguière F, Benabid AL, Kahane P. Analysis of clinical patterns and underlying epileptogenic zones of hypermotor seizures. *Epilepsia*. 2008 Dec;49(12):2030-40. doi: 10.1111/j.1528-1167.2008.01675.x.
4. Bonini F, McGonigal A, Trébuchon A, Gavaret M, Bartolomei F, Giusiano B, Chauvel P. Frontal lobe seizures: from clinical semiology to localization. *Epilepsia*. 2014 Feb;55(2):264-77. doi: 10.1111/epi.12490.
5. Montavont A, Kahane P, Catenoix H, Ostrowsky-Coste K, Isnard J, Guénot M, Rheims S, Ryvlin P. Hypermotor seizures in lateral and mesial parietal epilepsy. *Epilepsy Behav*. 2013 Sep;28(3):408-12. doi: 10.1016/j.yebeh.2013.05.030.
6. Wang L, Mathews GC, Whetsell WO, Abou-Khalil B (2008) Hypermotor seizures in patients with temporal pole lesions. *Epilepsy Res* 82: 95-100.
7. Staack AM, Bilic S, Wendling AS, Scholly J, Kraus U, et al. (2011) Hyperkinetic seizures in patients with temporal lobe epilepsy: clinical features and outcome after temporal lobe resection. *Epilepsia* 52: 1439-1446.
8. Yu T, Zhang G, Wang Y, Cai L, Zhou X, et al. (2013) Surgical treatment of hypermotor seizures originating from the temporal lobe. *Seizure* 22: 862-866.

9. Kotagal P, Arunkumar G, Hammel J, Mascha E (2003) Complex partial seizures of frontal lobe onset statistical analysis of ictal semiology. *Seizure* 12: 268-281.
10. Tao Y, Guojun Z, Yuping W, Lixin C, Wei D, et al. (2010) Surgical treatment of patients with drug-resistant hypermotor seizures. *Epilepsia* 51: 2124-2130.
11. Yu T, Zhang G, Li Y (2013) Surgical treatment of hypermotor seizures originated from temporal lobe. *Epilepsia* 54: 81.
12. Dobesberger J, Ortler M, Unterberger I, Walser G, Falkenstetter T, et al. (2008) Successful surgical treatment of insular epilepsy with nocturnal hypermotor seizures. *Epilepsia* 49: 159-162.
13. Marusic P, Elisak M, Krijtova H, Tomasek M, Mohapl M, et al. (2011) Hypermotor seizures in temporal lobe epilepsy patients. *Epilepsia* 52: 191.
14. Elisak M, Amlerova J, Krijtova H, Tomasek M, Marusic P. Temporal lobe epilepsy and hypermotor seizures. *Epilepsy & Behavior*. 2013 Aug;28(2):328.
15. Proserpio P, Cossu M, Francione S, Tassi L, Mai R, et al. (2011) Insularopercular seizures manifesting with sleep-related paroxysmal motor behaviors: A stereo-EEG study. *Epilepsia* 52: 1781-1791.
16. Nobili L, Francione S, Mai R, Tassi L, Cardinale F, Castana L, Sartori I, Lo Russo G, Cossu M. Nocturnal frontal lobe epilepsy: intracerebral recordings of paroxysmal motor attacks with increasing complexity. *Sleep*. 2003 Nov 1;26(7):883-6.
17. Nobili L, Francione S, Mai R, Cardinale F, Castana L, Tassi L, Sartori I, Didato G, Citterio A, Colombo N, Galli C, Lo Russo G, Cossu M. Surgical treatment of drug-resistant nocturnal frontal lobe epilepsy. *Brain*. 2007 Feb;130(Pt 2):561-73. doi: 10.1093/brain/awl322.
18. Biraben A, Taussig D, Thomas P, et al. Fear as the main feature of epileptic seizures. *J Neurol Neurosurg Psychiatry*. 2001;70(2):186-191. doi:10.1136/jnnp.70.2.186.

19. Nobili L, Cossu M, Mai R, Tassi L, Cardinale F, Castana L, Citterio A, Sartori I, Lo Russo G, Francione S. (2004) Sleep-related hyperkinetic seizures of temporal lobe origin. *Neurology* 62(3):482–485.
20. Demirkiran M, Jankovic J. Paroxysmal dyskinesias: clinical features and classification. *Ann Neurol.* 1995 Oct;38(4):571-9. doi: 10.1002/ana.410380405.
21. Gil-Nagel A, Risinger MW. (1997) Ictal semiology in hippocampal versus extrahippocampal temporal lobe epilepsy. *Brain* 120(Pt 1):183–192.
22. Carreno M, Donaire A, Pérez Jimenez MA, Agudo R, Quilez A, Rumi J, Villarejo F, Bargallón N, Boget T, Raspall T, Pintor L, Setoain X. (2005) Complex motor behaviors in temporal lobe epilepsy. *Neurology* 65(11):1805–1807.
23. Mai R, Sartori I, Francione S, Tassi L, Castana L, Cardinale F, Cossu M, Citterio A, Colombo N, Lo Russo G, Nobili L. (2005) Sleep-related hyperkinetic seizures: always a frontal onset? *Neurol Sci* 26(Suppl. 3): s220–s224.
24. Vaugier L, Aubert S, McGonigal A, Trubachon A, Guye M, Gavaret M, Regis J, Chauvel P, Wendling F, Bartolomei F. (2009) Neural networks underlying hyperkinetic seizures of “temporal lobe” origin. *Epilepsy Res* 86(2–3):200–208.
25. Mirandola L, Badawy RA, Saunders AM, McIntosh A, Berkovic SF, Graeme DJ. (2010) Clinical features of seizures associated with parahippocampal/inferior temporal lesions compared to those with hippocampal sclerosis. *Epilepsia* 51(9):1906–1909.
26. Ghashghaei HT, Barbas H. (2002) Pathways for emotions: interactions of prefrontal and anterior temporal pathways in the amygdala of the rhesus monkey. *Neuroscience* 115:1261–1279.
27. Kondo H, Saleem KS, Price JL. (2005) Differential connections of the perirhinal and parahippocampal cortex with the orbital and medial prefrontal networks in macaque monkeys. *J Comp Neurol* 493(4):479–509.

28. Price G, Cercignani M, Parker GJM, Altmann DR, Barnes TRE, Barker GJ, Joyce EM, Ron MA. (2008) White matter tracts in first-episode psychosis: a DTI tractography study of the uncinate fasciculus. *Neuroimage* 39(3):949–955.
29. Schmahmann JD, Pandya DN. (2006) *Fiber pathways of the brain*. Oxford University Press, New York, pp. 409–410.
30. Sussman NM, Jackel RA, Kaplan LR, Harner RN. Bicycling movements as a manifestation of complex partial seizures of temporal lobe origin. *Epilepsia* 1989;30:527–31.
31. Kwan P, Arzimanoglou A, Berg AT, Brodie MJ, Allen Hauser W, Mathern G, Moshé SL, Perucca E, Wiebe S, French J. Definition of drug resistant epilepsy: consensus proposal by the ad hoc Task Force of the ILAE Commission on Therapeutic Strategies. *Epilepsia*. 2010 Jun;51(6):1069-77. doi: 10.1111/j.1528-1167.2009.02397.x.
32. Crumrine PK. Book Review: *Surgical Treatment of the Epilepsies*, 2nd edition, edited by Jerome Engel, Jr. Published in 1993 by Raven Press, New York, 786 pages, \$142.00. *Journal of Child Neurology*. 1994;9(4):457-458. doi:10.1177/088307389400900432.
33. Pfänder M, Arnold S, Henkel A, Weil S, Werhahn KJ, Eisensehr I, Winkler PA, Noachtar S. Clinical features and EEG findings differentiating mesial from neocortical temporal lobe epilepsy. *Epileptic Disord*. 2002 Sep;4(3):189-95.
34. Bartolomei F, Wendling F, Bellanger JJ, Régis J, Chauvel P. Neural networks involving the medial temporal structures in temporal lobe epilepsy. *Clin Neurophysiol*. 2001 Sep;112(9):1746-60. doi: 10.1016/s1388-2457(01)00591-0.
35. Wong CH, Mohamed A, Larcos G, McCredie R, Somerville E, Bleasel A. Brain activation patterns of versive, hypermotor, and bilateral asymmetric tonic seizures. *Epilepsia*. 2010 Oct;51(10):2131-9. doi: 10.1111/j.1528-1167.2010.02723.x.

36. Biraben A, Taussig D, Thomas P, Even C, Vignal JP, Scarabin JM, et al. Fear as the main feature of epileptic seizures. *Journal of Neurology Neurosurgery and Psychiatry* 2001;70:186–91.
37. Bartolomeil F, Guye M, Wendling F, Gavaret M, Re´gis J, Chauvel P. Fear, anger and compulsive behavior during seizure: involvement of large scale fronto-temporal neural networks. *Epileptic Disorders* 2002;4:235–41.
38. Tassinari CA, Tassi L, Calandra-Buonaura G, Stanzani-Maserati M, Fini N, Pizza F, et al. Biting behavior, aggression, and seizures. *Epilepsia* 2005;46:654–63.
39. Tassinari CA, Cantalupo G, Ho¨gl B, Cortelli P, Tassi L, Francione S, et al. Neuroethological approach to frontolimbic epileptic seizures and parasomnias: the same central pattern generators for the same behaviours. *Revue Neurolo-gique* 2009;165:762–8.

APPENDIX

ABBREVIATIONS

ILAE: International League Against Epilepsy

HMS: Hypermotor seizure

LOE: Laterality of epileptogenesis

TLE: Temporal lobe epilepsy

ASD: Anti-seizure medication

MRI: Magnetic resonance imaging

EEG: Electroencephalogram

AMI: Autobiographical Memory Interview

ATL plus AH: Anterior temporal lobectomy plus amygdalohippocampectomy

DRE: Drug-resistant epilepsy

QOL: Quality of life

FLE: Frontal lobe epilepsy

GTCS: Generalized tonic-clonic seizures

EZ: Epileptogenic zone

PARTICIPANT PROFORMA

Participant Number:

Participant Name:

Group:

Hospital Number:

Age of epilepsy onset:

Age at VEEG:

Age at surgery:

Duration of epilepsy at the time of surgery:

Sex:

Antecedent:

Aura:

VEEG data:

Duration of VEEG

Number of events

Duration and semiology of events

Interictal discharges

Ictal rhythm

Delay between electrical onset and clinical onset

Imaging findings:

Histopathological findings:

ASM details at the time of surgery and 1-year post-surgical follow up:

The side of surgery or LOE:

Engel outcome at 1-year post-surgical follow up:



श्री चित्रा तिरुनाल आयुर्विज्ञान और प्रौद्योगिकी संस्थान, त्रिवेन्द्रम
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Institutional Ethics Committee

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

SCT/IEC/1778/NOVEMBER/ 2021

14.12.2021

Dr. Pavan Kumar Rudrabhatla
Post Doctoral Fellow
Department of Neurology
SCTIMST, Thiruvananthapuram

Dear Dr. Pavan Kumar Rudrabhatla,

The Institutional Ethics Committee held on 26th November, 2021, reviewed and discussed your application to conduct the study titled "CLINICAL PROFILE, IMAGING FEATURES AND POSTSURGICAL OUTCOMES OF HYPERMOTOR SEIZURES ORIGINATING FROM TEMPORAL LOBE: A RETROSPECTIVE OBSERVATIONAL STUDY" (IEC/1778).

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	LLM, MBL	Female	Legal Expert	No
7.	Dr. Achuth Sankar S. Nair	Ph.D (i.Engineering ii.Music)	Male	Social Scientist	No
8.	Dr. Hari Krishna 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

The following documents were reviewed:

Original submission

1. Checklist Form
2. Covering letter addressed to the Chairperson, IEC, SCTIMST
3. Covering letter addressed to the Chairperson, IEC, SCTIMST from Dr. Ramshekhar N Menon, Additional Professor, Department of Neurology, SCTIMST
4. IEC Application Form
5. Project Proposal
6. Proforma
7. CV of PI and Co-PIs
8. Declaration Form
9. SRC Approval Letter

Revised submission

1. Covering letter addressed to the Member Secretary, IEC, SCTIMST dated 14.12.2021
2. Checklist Form
3. IEC Application Form
4. Project Proposal
5. Proforma
6. CV of PI and Co-PIs
7. Declaration Form

IEC Decision

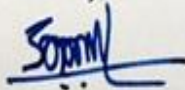
The IEC approved the conduct of the study in the present form.

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

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE (IEC)
SCTIMST, THIRUVANANTHAPURAM

