CURRENT ROLE OF ICTAL SCALP EEG IN EVALUATION FOR EPILEPSY SURGERY

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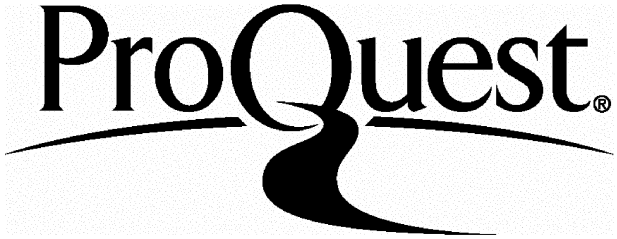

ABSTRACT

Scalp EEG-video telemetry, a time consuming and expensive investigation, is routine in all patients prior to surgery in the majority of epilepsy centres. With the introduction of MRI, which can usually identify the underlying pathological substrate associated with the patient's epilepsy, its role has become less clear.

The aim of this study was to clarify the current role of pre-surgical scalp EEG-video telemetry, by investigating whether specific ictal features were (i) associated with different pathologies, (ii) the likelihood of proceeding to surgery, or (iii) the post-operative outcome. This study also determined how often in this setting additional information was recorded that might modify the decision making process.

Four hundred consecutive patients undergoing scalp telemetry were studied, and the recordings analysed blind to the imaging data with regard to specific ictal EEG features. Seizure semiology was analysed separately.

The outcome was determined at least one year post-operatively (range 1- 6.5 years).

The presence of lateralised ictal temporal theta was significantly associated with a temporal location of pathology, and temporal lobe type seizure semiology. A combination of early and sustained lateralised theta was significantly associated with unilateral hippocampal sclerosis (UHS) (n=190) in comparison to the other imaging groups (n=210).

The combination of temporal lobe seizure type and UHS was the best predictor of proceeding to surgery (increasing the likelihood sixfold), but individual analysis of specific ictal EEG features did not predict post-operative outcome within specific imaging subgroups.

Overall video-EEG telemetry provided evidence of non-epileptic attacks in 3%, and grossly discordant electroclinical data compared to the neuroimaging findings in 10% of patients studied.

Therefore, ictal scalp EEG recordings have a relatively low yield of information that influences decisions concerning epilepsy surgery over and above the evaluation of seizure semiology and underlying pathology.

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Table of Contents

List of Tables

List of Figures

Page number

Chapter 1. Introduction

1.1 Overview

Epilepsy is amongst the most common serious neurological condition; overall in developed areas of the world the incidence i.e. the number of new cases diagnosed per year is 40-70 per 100,000 of the population (Sander and Shorvon, 1996) and the prevalence of epilepsy i.e. the number of patients with active epilepsy over all age groups within the same population is 500-1000 per 100,000.

Epileptic syndromes and seizure types can be divided and defined in different ways, and many types of epilepsy are amenable to medical control or remit naturally. Over two thirds of patients enter long-term remission. However some, in particular the epilepsies caused by more localised anatomical abnormalities are less easily treated medically; it has been estimated that 20% of all patients with epilepsy have seizures that are not adequately controlled by anti-epileptic medication, and that at least 50% of these patients could be candidates for surgical therapy (Engel and Shewman, 1993).

Epilepsy is not a benign condition; it carries both a risk of morbidity and mortality, which dictates the need for adequate control in the maximum number of patients. Medical morbidity due to epilepsy can be either primary – from the underlying aetiology of the epilepsy, or treatment-related; or secondary – as a direct result of the seizures. The increased mortality in patients with epilepsy is more marked within the younger patients and those with severe epilepsy (Nashef et al, 1995a). Nashef's study of mortality rates in patients with chronic severe epilepsy attending a specialist epilepsy clinic showed that these patients were five times more likely to die than the age and sex matched control group (Standardised mortality ratio of 5:1). This equated to a rate of 1 death per 200 patients per year of this adult cohort of patients with epilepsy (Nashef et al 1995b).

The need to achieve adequate seizure control and thus reduce morbidity and mortality in these patients with severe epilepsy has led to the development and increasing availability of neurosurgical techniques for those patients where medical treatment has not provided this control.

Neurosurgery for patients with intractable epilepsy demands a complex set of investigations in addition to a comprehensive clinical history to determine whether a particular patient is likely to benefit from surgical intervention. Over the years that epilepsy surgery has been practised these investigations have changed, with the development of technology and the accompanying techniques of data analysis. Currently several different tests are employed at most centres carrying out surgery for epilepsy, some of which are both time consuming and often labour intensive.

One of the key investigations performed is video–EEG telemetry, carried out in order to record the clinical and electrographic (EEG) features of the patient's seizures. In recent years, however, with the introduction of magnetic resonance imaging (MRI), which is able to identify underlying structural pathology pre-operatively, the role of the EEG has been brought into question.

The aim of this study was to consider specific features of the ictal scalp EEG in order to ascertain whether scalp EEG and video monitoring still adds significant information or alters the course of a presurgical assessment, given the current widespread and increasing availability of high resolution MRI. The study was done by retrospectively reviewing the ictal recordings of 400 consecutive patients who were monitored on the telemetry unit at the National Hospital for Neurology and Neurosurgery (NHNN) after January 1995. All of these patients would have had high quality Magnetic Resonance Imaging (MRI) scans as part of their pre-surgical evaluation which allows a comparison to be made of the usefulness of the video-telemetry in different pathologies as determined by the MRI.

1.2 History of surgical intervention for epilepsy

Surgery for epilepsy in the modern era dates back to just over 100 years ago. Victor Horsley carried out one of the earliest operations in 1886 at the National Hospital for Neurology and Neurosurgery (Horsley, 1886). Surgery was possible at that time because of the preceding advances in knowledge of the localisation of cerebral function formulated by his colleagues; Hughlings Jackson from observation of ictal semiology in patients with severe epilepsy and focal lesions identified at post-mortem; and David Ferrier who had confirmed these findings with electrical stimulation experiments carried out on the brains of monkeys.

However difficulties in localisation, operative hazards and the advent of anti-epileptic therapy led to a decline in the pursuit of epilepsy surgery during the next three decades.

The problems of post-traumatic epilepsy resulting from penetrating injuries sustained in the First World War, led to a resurgence of surgery based on the premise that focal epileptic seizures were associated exclusively with a structural lesion. Localisation prior to resection was based on the clinical features seen interictally e.g. focal neurological deficit, and characteristics of the seizures e.g. lateralised jerking.

In the years between the two World Wars the first papers by Foerster and Penfield (1930) appeared which detailed the use of intraoperative electrical stimulation of the human brain to map cortical function. These provided a better understanding of the correlation between anatomical areas and the motor and sensory functions associated with those different regions.

Surgery for epilepsy began to develop further with the advent of the ability to record the human electroencephalogram (EEG) and to thus identify epileptogenic areas, especially through the pioneering work of Herbert Jasper working at the Montreal Neurological Institute (Penfield and Jasper, 1954).

These early operations were mostly carried out on patients with focal motor seizures usually arising from lesions in extratemporal areas with motor manifestations of the seizures, which allowed clear pre-operative localisation. Surgery for temporal lobe seizures came later with the clinical recognition of focal seizures with predominantly experiential or behavioural rather than motor phenomena and the ability of the EEG to identify focal (usually interictal) epileptiform disturbances arising from the temporal areas of the brain (Jasper and Kershman, 1941).

Once recording human EEG became an established technique in the 1940s and 1950s, it was used extensively not only in the diagnosis of epilepsy but also to aid the surgeon in localisation pre-operatively. Initially only the interictal EEG was usually available, but as the ability to record for more prolonged periods was developed, it became possible to more often record seizures and to identify in some patients the probable area of ictal onset using the EEG. With the development of technology the recordings have progressed from limited recordings using paper or small numbers of channels of EEG recorded onto FM tape recorders (Roberts and Fitch, 1985) to the multiple channels of EEG and other physiological parameters being recorded digitally onto re-writable computer media that many epilepsy centres use today.

The numbers of patients undergoing surgery for epilepsy increased dramatically with the advent of improved neuroimaging techniques: computerised tomograms (CT) in the 1970s, and MRI in the 1980s. These investigations have allowed much more precise localisation of structural abnormalities to be identified pre-operatively and allowed many more patients to be considered as candidates for surgery. While the early MRI lacked the resolution to identify subtle pathologies such as hippocampal sclerosis technological advances in the late 1980s/early 1990s overcame many of these limitations.

One of the more significant developments in the analysis of the MRI was the ability to measure quantitatively the degree of hippocampal atrophy (usually reflecting sclerosis) that is known to be associated with temporal lobe

epilepsy. Cascino et al (1991) compared the MRI volume measurements of the hippocampal formation with the pathological findings after temporal lobectomy and found that the severity of the pathological abnormality correlated well with the volume loss determined pre-operatively on the MRI. The stereological principles needed for such detailed work and their application to MRI was studied by (Cook at al 1992). Such findings, together with the increased availability and understanding of MRI, has led to many more patients being referred for assessment for temporal lobe surgery.

Detailed measurements and improved sequencing techniques that help to enhance tissue characteristics have also meant that subtler abnormalities have been able to be detected, for example the identification of various malformations of cortical developmental. This has increased the number of patients referred for extratemporal resections as well as temporal lesionectomies, and substantially reduced the proportion of patients referred for presurgical telemetry in whom the underlying pathological substrate is unknown.

The scale of the rate of increase in numbers of patients being considered for epilepsy surgery since the 1980s can be obtained from the data gathered at two key international conferences on the surgical treatment of the epilepsies. In the interval between the first and second International Palm Desert conferences in 1986 and 1992, there was an increase in the number of centres carrying out epilepsy surgery. In the US the number of centres increased from 26 to 67, and the number of operation being performed, in the US - 500 vs. 1500 per annum, together with an increase in the type and complexity of those operations (Engel, 1993). These figures reflected the increase in availability of improved neuroimaging techniques.

1.3 Role of EEG recording

Initially the role of the EEG in epilepsy surgery was at the time of the operation when recordings from and stimulation of the cerebral cortex were used to guide the surgeon in localising the epileptogenic zone. The surgeon

would decide to operate using the clinical information available to him and any intra-operative recordings of the electrocorticogram (ECoG). However there were, and remain, many technical problems in both the recording and interpretation of the ECoG. Technically, for the surgical team recording directly from the cortical surface (ECoG) and performing intraoperative direct cortical stimulation requires light general anaesthesia and the duration of the operation is prolonged. For the neurophysiologists, the cortical area exposed by the craniotomy limits the sampling site. Negative findings are usually unhelpful and positive findings may represent propagation of electrical activity from areas not sampled, which make results difficult to interpret. The limited time available due to operative requirements prevents any more prolonged recording. There is little evidence that the extent of removal of areas of spiking cortex predicts post-operative outcome, with the possible exceptions of quasi ictal electrical patterns generated by areas of cortical maldevelopment (Palmini et al 1995) or quantitative methods of spike analysis (Alarcon et al, 1997).

As techniques developed firstly interictal and then ictal EEG recordings performed in the EEG laboratory or on specialist inpatient wards were increasingly used in the process of surgical assessment. Prior to the introduction of MRI the ictal EEG and the clinical semiology of the seizure recorded on video were the main source of pre-operative localisation. A review of early surgical series by Falconer and Serafetinides (1963) considered 100 patients who had temporal lobectomies, "Of these 53 patients have been rendered free of seizures or almost so, 30 have been improved at least 50%, and 17 show little or no improvement.....All but one patient before operation showed EEG evidence of an 'epileptic focus' confined to or predominant in one temporal lobe".

Patients would often have several repeated EEG studies in order to confirm both the interictal and ictal findings. The information gained from the interictal EEG comes from the distribution of the interictal spikes. This is referred to as the irritative zone (Lüders et al, 1993), as well as information from the

background abnormalities, which may reflect more widespread areas of cerebral dysfunction.

Initially when doubt remained about the electrophysiological data from the scalp recordings, the pre-operative neurophysiological assessment would end at this point and thus only a relatively small number of patients with medically intractable epilepsy were able to proceed to surgery. The ability to perform chronic intracranial recordings was developed in the 1960s and this increased the number of patients who could benefit from epilepsy surgery.

The results obtained from recordings made from implanted electrodes, both stereotactic depth electrodes and subdural strips and grids were for many centres the gold standard against which the other test results were compared, even though they were a relatively poor marker of eventual post-operative seizure freedom. The limited spatial sampling of intracranial studies necessitates the formulation of specific hypotheses prior to each individual patients study i.e. intracranial studies are relatively good at answering specific questions such as are seizures more likely to initially involve the right or left mesial temporal structures, but of much less value if the number of potential sites of ictal onset is large or uncertain. In the days before MRI became readily available such studies would be carried out in a high proportion of the patients being considered for surgery with most centres advocating that a policy of depth electrode implantation was essential except when all the other available data was concordant (Engel et al, 1981). The information obtained from these scalp and intracranial electrodes was used not only to plan surgery but also to predict the post-operative outcome.

Despite the reliance on MRI, the scalp EEG is still usually considered a routine and essential part of the presurgical evaluation process, and video-EEG telemetry is currently still carried out at the majority of centres when assessing patients for epilepsy surgery. Analysis of the ictal scalp EEG is often qualitative although certain ictal features have been associated with specific partial seizure types and are used when evaluating the ictal recordings. The mostly commonly used feature is the presence of rhythmic

temporal theta, which is significantly associated with temporal lobe seizures, described by Risinger et al (1989). Risinger et al described a pattern of unilateral rhythmic theta seen at the temporal/sphenoidal electrodes and occurring within 30 seconds of the seizure onset and found that this would correctly predict findings from subsequent depth electrode recordings in 82-94% of cases. They found that these patterns could be detected with excellent interrater reliability. Similar studies of ictal rhythmic temporal theta in patients with temporal pathology defined by MRI have confirmed these initial findings, e.g. Sadler and Desbiens (2000) and the definition has been further refined to distinguish between those patients with mesial as compared to lateral temporal pathologies, (Ebersole and Pascia 1996). Other ictal features have been described but have poorer inter-reviewer reliability or are not so strongly associated with either specific clinical seizure type or imaging defined pathology.

1.4 Justification of continuing to carry out ictal EEG recordings

Many authors have discussed the relative contributions of the various investigations currently carried out when assessing a patient for epilepsy surgery. More recently there have been several papers (Engel, 1999;Cendes et al, 2000;Pataraia et al, 1998; Gilliam et al, 1997; and Cascino et al, 1996) questioning the role of ictal scalp EEG recordings in the assessment for epilepsy surgery now that there is so much reliance on MRI techniques and also with the emergence of functional imaging, although there is little comparative data available with post-operative outcome.

Spencer (1994) discussed the use of MRI, Single photon emission computed tomography (SPECT) and positron emission tomography (PET) in the evaluation of epilepsy. Spencer concluded that these techniques were still changing rapidly; but at that time, whilst the MRI was able to demonstrate anatomical abnormalities likely to be associated with epilepsy it was not able to define the epileptogenic zone. SPECT and PET may give more information as regard to function of the cortex but need to be co-registered with the MRI

for the underlying anatomical structures and the practicalities of obtaining ictal scans remains difficult.

In the last five years however, more techniques have continued to be developed including MR spectroscopy, functional MRI studies (fMRI) and the ability to record the EEG in association with the MRI. Functional MRI is now established in its ability to provide information about the anatomical structures involved in primary motor and sensory functions, and compliments the information obtained from electrical cortical stimulation (Puce, 1995 and Yousry et al, 1995). However the use of functional MRI in assessment of epilepsy surgery patients has so far, been somewhat limited by practical considerations. Ictal recordings are rarely feasible, as they would rely on a patient having both frequent and predictable seizures that involved very little or no motor involvement. More recently techniques have been developed to allow spike-triggered or continuous simultaneous fMRI studies to be performed (Warach et al, 1996; Krakow et al, 1999, and Lemieux et al, 2001), and investigations undertaken to determine if comparison of the active fMRIs with resting baseline studies will help to identify the site of cerebral generators of the interictal spikes, given the much better spatial resolution of fMRI.

All of these developments mean that delineating the role of the EEG telemetry studies has become more necessary. Video-EEG telemetry usually involves prolonged inpatient assessment, utilises scarce resources and maybe associated with some risks if drug reduction is required in order to record seizures. The latter include injuries, psychosis, status epilepticus or rarely mortality from seizures precipitated by these means. Until very recently studies have continued to support the role of the EEG in the pre-surgical assessment but in a changing form. Fish and Spencer (1995) looked at the EEG findings in patients with MRI defined abnormalities. They reviewed data from several centres and discussed the fact that although the MRI had greatly improved the ability to identify the structural basis of epilepsy in the majority of patients, the lesion it identifies is not necessarily the site of epileptogenesis. The authors concluded that the use of ictal EEG should be refined and become more dependent on the type of imaging abnormality identified and its

location, in order to maximise the clinical relevance of the information obtained.

Engel (1999) discussed in a review article, the issue of when imaging investigations were enough to proceed to surgery. He considered several surgically remediable epilepsy syndromes and the role played by the various tests currently employed. Whilst recognising the important role played by MRI, PET and SPECT scans he concluded that as yet none of the tests can provide enough information on the epileptogenicity of areas of the brain, and that surgical decisions are made with the pooled information from all the tests carried out pre-operatively. He does however consider that in certain syndromes it may be possible to avoid prolonged monitoring in order to record ictal EEG if retrospective studies show it provides no new information.

It is only now, when the numbers of patients who have had surgery following assessments that include high quality MR imaging, are sufficiently large and the follow-up period is of several years that the relative contributions and current value of ictal EEG can start to be addressed.

Some recent studies have suggested that ictal EEG recordings in patients with mesial temporal lobe epilepsy are redundant. Cendes et al (2000) studied 184 patients with hippocampal atrophy, and looked at the localisation of the interictal and ictal discharges in the EEG. They found that if the patient had clear unilateral hippocampal atrophy there was a strong correlation between the side of atrophy and the lateralisation of interictal and ictal discharges. However in patients with bilateral asymmetric hippocampal atrophy 18% of the patients had discordant interictal and ictal EEG findings. They conclude that in patients with unilateral hippocampal atrophy an outpatient interictal EEG would be sufficient to confirm epileptogenicity. Their study group only included patients that met strict criteria with regard to the clinical features of the seizures and the interictal EEGs showed no abnormalities outside of the temporal regions. Their findings were supported by a similar study by Pataraia et al (1998). They analysed the ictal recordings in 24 patients who had mesial temporal lobe epilepsy as defined by MRI,

clinical seizure semiology and unitemporal interictal spikes. They found that the ictal recordings did not alter the surgical approach or correlate with outcome, and lateralisation, which was possible in 90% of the seizures, always corresponded to the side of the interictal spike focus and the MRI defined hippocampal atrophy. Again this is very select group, and the authors acknowledge caveats. They discuss the need to ascertain the semiology of the patient's typical seizures, to exclude non-epileptic seizures, and the duration of recording required to be confident that the interictal spikes are unitemporal (defined as a ratio of 9:1).

Gilliam et al (1997) looked at the post-surgical outcome of 90 patients who underwent assessment for temporal lobectomy. They found that concordance of the MRI and interictal EEG was most closely associated with a good post-surgical outcome, and therefore this information might be of use in refining the odds of a good outcome that might be given to a patient.

Other authors, however, are less confident about relying on interictal spikes as an indicator of ictal lateralisation (So et al, 1989) because of the high frequency with which bilateral interictal discharges are seen in patients with unilateral seizures, or the possibility of failure to localise from state-dependent interictal spikes (Sammaritano et al, 1991). Cascino et al (1996) discuss the need for serial EEGs or prolonged interictal studies to increase the likelihood of recording epileptiform abnormalities, but accept that in between 10-20% of patients interictal spikes may lead to false lateralisation. There is also evidence from animal models of chronic and acute focal epilepsy that the neuronal generators maybe different for ictal and interictal discharges. De Curtis and Avanzini (2001) concluded from animal experimental work that there is a " reverse relationship between the rate of interictal spikes and the susceptibility to generate ictal events". They also suggest that interictal spikes have a role in "antagonizing the precipitation of ictal activity". Other clinical studies have also suggested the difference between interictal spikes and ictal events and cautioned against the assumption that they have the same neural generators. Gotman (1991) proposes that the interictal spikes have little direct

effect on seizure generation and that the rate of spiking is "more a reflection of past seizures than an indication of the likelihood of impending seizures".

It may be that with the development of functional MRI giving more information about the interictal spikes that the need to record seizures may be reduced, but it is clear from these studies using interictal spikes to localise pre-operatively and support or confirm the MRI evidence, that they would require strict inclusion criteria to proceed to surgery without ictal scalp EEG studies. There will therefore, be patients who do not meet these criteria but nonetheless have intractable partial epilepsy and will still need to be further investigated for epilepsy surgery. In addition, for all patients there is a duty to provide a meaningful assessment of the probability of surgery rendering them seizure free or significantly improved so that they can make an informed decision whether or not to proceed to surgery given the associated risks.

None of the studies reported to date have investigated whether additional information of predictive value can be obtained from ictal scalp EEG recordings through analysis of the characteristics of the ictal onset and its evolution. Furthermore, virtually all EEG studies have relied upon retrospective reports often written by more than one specialist reviewing the EEG data with knowledge of the imaging findings. Despite the apparently negative findings from other recent studies, which have focused on ictal onset, uncertainty remains about the possibility of different ictal EEG patterns to refine the probabilities given to the patients of them benefiting from surgery. This would be particular important for different imaging categories of patients given the current practice of utilising high resolution MRI whenever possible as part of the presurgical evaluation.

1.5 Aim of study

The principal aims of this study therefore were to investigate whether, in patients being evaluated for epilepsy surgery, specific ictal scalp EEG features were associated (i) with the different pathologies underlying epilepsy, (ii) the likelihood of proceeding to surgery, or (iii) the post-operative outcome.

In particular these studies were to address whether in the setting of high resolution MRI, and video recording to confirm seizure semiology additional information was obtained from the EEG that might substantially change the decision making process.

The study was carried out prospectively from the patients selected by the epileptologists at NHNN for assessment for epilepsy surgery. The patients represent a reasonably typical population of adults with refractory focal epilepsy and thus any results obtained can be compared with findings from other epilepsy surgery centres. The start date of 1995 was chosen because standardised recording techniques were employed with the opening of the 6-bedded video-EEG telemetry unit at NHNN. The time period of the study also meant that all patients had standardised investigations particularly in respect of the imaging and neurophysiological investigations and there were no major changes in surgical techniques or procedures during this time.

Chapter 2: Patients and Methods

2.1 Patients

The patients in this study were recruited sequentially from those patients attending the video telemetry unit at the National Hospital for Neurology and Neurosurgery (NHNN). They were all patients who had been referred for video telemetry as part of their pre-surgical assessment and were under the care of one of the neurologists at NHNN. NHNN is a specialist hospital receiving referrals from a wide area throughout the UK, as well as some overseas patients. Only adult patients are admitted to the hospital, most will be older than 17 years of age but a very small proportion are seen in the 15-17 year age group. This study therefore does not include any children within the patient group. During their period of video-EEG telemetry all of the patients were under the clinical care of Professor Fish.

Patients referred for diagnostic reasons, and those referred from and whose other presurgical tests and continuing care remained at other centres were excluded from the study.

The patients presented with various epilepsy syndromes, representing the typical case-mix of the NHNN referrals for epilepsy surgery. They included patients being considered for temporal lobe surgery, extratemporal surgery, and hemispherectomy.

General and clinical information about the patients was entered on to a computerised anonymised database, obtained from the case notes usually at the time of entry into the study. This data included sex of the patient; age at the time of the recording; age at onset of seizures; aetiology of the seizures, if known; imaging results; history of status epilepticus; and other relevant clinical data. Details of the recording parameters were also included for example, duration of the recording; whether repeat studies were needed and

why; whether anticonvulsant medication was reduced; number of seizures recorded; whether any generalised tonic-clonic seizures were recorded. (See Appendix 1 for an example entry from the patient database).

2.2 Study period

The period of recruitment was from January 1995 to October 1998. All patients had an initial period of video-telemetry in that period. However if any of the patients required repeated studies because insufficient data was obtained initially, such repeated studies were included until September 1999. No studies were included after that time, and therefore there are a small number of patients who had not completed their scalp video-EEG studies at the time the study period finished.

After the video-telemetry some patients required further tests before surgery could be performed, usually a sodium amytal or WADA test but in a small proportion (28/400 or 7%) intracranial studies were performed before definitive surgery. These patients are discussed in 3.5.5.

The end of the study period was September 1999 and this meant that the follow–up period on those patients who had surgery was at least one year post-surgery at the time of completion of data analysis.

2.3 Rationale for study size

There were 400 patients recruited into the study in the period January 1995 to October 1998, of these patients there were 218 females and 182 males. Their age at the time of the recording was an average of 32 years with a range of 16 to 61 years. Both the female: male ratio and age range was representative of the population being assessed at NHHN for epilepsy surgery.

This represented a convenience sample determined at the start by the opening date of the video-EEG telemetry unit. Whilst the largest possible sample was to be recruited it would not have been practical to continue

recruitment for significantly longer because of the need to obtain reasonable post-operative follow-up data on all patients prior to analysis.

Although the study involved 400 consecutive patients referred for pre-surgical video-EEG telemetry it was expected that about half of the patients in the overall group would have unilateral hippocampal sclerosis (UHS). A study group this large would allow comparisons to be made between the UHS and non-UHS group, furthermore while small predictive differences could fail to be identified with this sample size, such issues are unlikely to significantly influence clinical/patient decisions to proceed or not to surgery. While patients who have fully concordant data and unilateral hippocampal sclerosis (UHS) or a small clearly defined lesion are typically given pre-operatively a 70% chance of being seizure free, if there is evidence of more diffuse or widespread abnormalities prior to surgery or discordant test results, this figure can range down to 30% or less of seizure freedom following resective surgery. Given the mortality and morbidity of epilepsy and the relative risks of surgery it is differences of this order of magnitude that are important in the decision making process. A study group this large would allow comparisons to be made for example between the UHS and non-UHS group with a 90% chance of finding a 16% difference at the 5% significance level, furthermore while much smaller predictive differences could fail to be identified with this sample size such issues are unlikely to significantly influence the clinical/patient decision to proceed or not to surgery.

2.4 Methods - general

All of the patients underwent a sequence of standardised investigations as part of their pre-surgical assessment.

Initially they were all seen by experienced neurologists specialising in the treatment of epilepsy who assessed their suitability for epilepsy surgery. This clinical assessment included a description of the patient's habitual seizures and of the patients' medical history, in particular the time and nature of the first seizures and subsequent development of the habitual seizure type and

frequency. The patients also had a full medical examination to identify any other co-existing medical problems, which might influence the assessment and subsequent treatment for epilepsy.

Once considered suitable for the epilepsy surgery program the patients would then have a series of tests, usually carried out in the following order: - magnetic resonance imaging (MRI), neuropsychological assessment, video-EEG telemetry, and neuropsychiatric appraisal. Following completion of these tests the results were presented at a multi-disciplinary meeting and the patient's case would be discussed in the presence of the specialist consultants (neurologist, neurosurgeon, neuroradiologist, neurophysiologist, neuropsychologist and neuropsychiatrist) and the patients suitability for surgery or need for any other investigations considered. Some patients proceeded directly to surgery, other patients required a sodium amytal or WADA test before surgery, to determine language lateralisation or risk of post-operative amnesia, in 7.7% of patients intracranial EEG studies with either stereotactic depth electrodes or subdural strip electrodes were deemed necessary because of conflicting or inconclusive data.

2.5 Imaging

All of the patients had high resolution magnetic resonance imaging (MRI) carried out either at the Chalfont Centre for Epilepsy or at NHNN on a 1.5 Tesla GE Signa machine. Additionally some patients were scanned on a 1.5 Tesla Siemens SP63 Magentom scanner at the Hospital for Sick Children at Great Ormond Street Hospital. Similar protocols were used whichever scanner was employed.

The MRIs were performed using a specific epilepsy protocol. A sequence using T1 weighted coronal images in thin contiguous slices of 1.5mm or less which allows volumetric measurements of the hippocampus and amygdala to be made. A further sequence of T2 weighted images allows measurement of T2 relaxation times to be calculated, and 3 dimensional reconstructions can also be carried out to look for gyral abnormalities. The scanning techniques

used have been described by Cook et al (1992) and Van Paesschen et al (1995 and 1996).

In addition most patients also had fluid attenuated inversion recovery (FLAIR) sequences performed using protocols described by Wieshman at al (1996). The FLAIR sequences may help to identify or delineate areas of gliosis and foreign tissue lesions.

2.6 Neuropsychometry

All patients whose first language was English had a standardised set of psychometric tests designed to measure intellectual capacity, the relative strength of verbal and non-verbal memory, determine expressive and receptive language skills, and perceptual abilities. The testing is designed to be particularly sensitive to temporal lobe disturbance although measures of cognitive functions other than memory provide an indication of other localised cerebral disturbance, including some tests which are sensitive to frontal lobe dysfunction. The test battery has been described in detail elsewhere by Baxendale et al, (1998). The profile of the results allows assessment of lateralised and localised deficits and also to gauge the probable consequences on language, memory and overall ability of any possible surgical intervention. The need for a sodium amytal test prior to surgery was also determined by the baseline neuropsychology.

Non-English speakers were either tested via an interpreter or were tested in their own country using comparable tests as appropriate.

2.7 Neuropsychiatry

The majority of the patients being assessed for epilepsy surgery were seen by a Neuropsychiatrist whilst in hospital undergoing video-telemetry and if proceeding to surgery all patients were seen both prior and post operatively. The patients were assessed with a view to depressive symptoms and traits either current or in the past; any evidence of psychosis, post-ictal and/or inter-

ictal; and anxiety. Their expectations of surgery, and what level of support they would need pre-and post any surgical procedure was also explored.

2.8 Other Imaging techniques

A small proportion of the patients had PET (Positron Emission Tomography) scans at the Hammersmith Hospital and ictal and inter-ictal SPECT (Single Positron Emission Computerised Tomography) scans at Great Ormond Street. Both the PET and SPECT scans were performed as part of research projects looking at the findings in specific imaging groups and evaluation of any extra information obtained that could assist in the pre-surgical assessment. The protocols used have been described elsewhere (Richardson et al, 1998; Koepp et al, 2000; and Schmitz et al, 1995).

The ictal Neurolite SPECT scans were done whilst the patients were undergoing repeat video-telemetry, inter–ictal SPECT scans were carried out subsequently as an out-patient procedure, or during the telemetry if no seizure occurred during the test period i.e. whilst the tracer was active and the scanner was available. 9/400 patients had ictal SPECT studies attempted.

These functional scans were usually done after the initial video-telemetry if insufficient concordant data was available either to proceed directly to surgery or in order to plan out an intracranial study.

2.9.1 Video-EEG Techniques

2.9.1 General

All patients had video-EEG telemetry carried out on the Sir Jules Thorn unit at the National Hospital for Neurology and Neurosurgery. This is a dedicated 5-day, 6 bed unit (Scott et al, 2000). On the unit, patients are in individual rooms and they are asked to stay in their room area as much of the time as possible. To alleviate the boredom all the patient rooms are equipped with individually controlled cable TV and video recorders, and they are encouraged to bring in

books, puzzle books etc. The patients are allowed to leave the room to use the bathroom (they are shown how to disconnect the cable connecting the headbox to the recording equipment) but are encouraged to minimize the length of time spent outside their room.

2.9.2 Recording Equipment

The recording equipment used is a mixture of commercial transmitters/headboxes and encoders (Telefactor ™), in-house built transmitters using CED™ A-D converters and commercially available computers and recording drives using in-house developed software. The EEG is recorded continuously onto removable digital media (re-writable optical discs and more recently re-writable JAZ ™ discs).

The EEG is stored in digital format which allows post-acquisition manipulation of the data, for example re-formatting the data into bipolar or referential montages as necessary and the ability to change the filter, gain and timebase settings. There is rapid access to any part of the EEG recording. The EEG recording is time-locked to the video recording, which is an analogue recording onto high quality SVHS videotapes.

There is a simultaneous automatic spike and seizure detection program running using established algorithms for identifying seizure patterns and interictal spikes (Gotman et al, 1979, and Gotman, 1982). An experienced reviewer subsequently validates these detections allowing a quick first line review of the data.

All of the EEG recordings were reviewed by an experienced EEG technician in order to identify all seizures, whether or not they were reported or triggered an automatic detection, in addition to analysing the record for any interictal abnormalities.

2.9.3 Electrodes and Placement

Standard silver-silver chloride electrodes were used, they were attached using collodion glue with conducting gel (Dracard™) placed between the electrodes and the skin. Placement of the electrodes followed the standard 10-20 system of electrode placement (Jasper, 1958). This system devised by Jasper is based on the measurement of distance between bony landmarks on the skull then marking out points at 10% and 20% of the total distance, It allows a standardised system of placement which is adjusted for skull size and ensures reproducibility of placement both between technicians and centres. In addition superficial sphenoidal electrodes were used which were placed over the site of insertion for indwelling sphenoidal electrodes. This positioning of the electrodes ensures adequate coverage of the anterior temporal lobes without the discomfort of indwelling sphenoidal wire electrodes. Although historically all presurgical assessments would have included ictal recordings from indwelling electrodes in addition to the standard scalp electrodes,several studies have shown that with careful placement of anterior temporal electrodes on the scalp the extra information gained from indwelling sphenoidal electrodes is minimal and does not justify the patient discomfort (Homan et al, 1998; Sadler and Goodwin,1989; and Binnie et al, 1989).

The electrodes were checked regularly throughout the recording and always before any provocative procedure. If electrode to skin contact was poor, more conducting gel was inserted into the electrode and electrodes were re-applied, patient cables fixed as necessary.

2.10 Video-EEG telemetry: Protocols

2.10.1 Drug reduction

The telemetry unit operates a standard drug reduction protocol the use of which is determined according to the seizure frequency of the patient not the underlying pathology or neuroimaging abnormality. The standardised protocol

excludes those patients with frequent seizures (defined as 1 or more per day), those with frequent generalised seizures (defined as 1 or more per month), and those patients who have had any episodes of status epilepticus or serial seizures particularly occurring in the context of previous drug changes. The procedure is discussed with the patients when they are admitted to the unit, they are warned of the risks associated with reducing their anti-convulsant medication and their consent is sought for the procedure. It is also important that the nurses and technicians on the ward are certain that the patient will be able to co-operate with the telemetry recording procedure and not wish to leave the ward earlier than planned.

Medication is not changed in anyone that is pregnant at the time of the recording or who is currently in a prolonged seizure-free period. In the latter case the telemetry study is usually deferred and the patient advised to make contact if or when the seizures recur.

Drug reduction is initiated on the day of admission: on day one the drugs are reduced to a half the normal daily dose and on day two (if no complex partial seizures have been recorded) the drugs are reduced to a quarter of the daily dose. This reduction protocol does not apply to anticonvulsants with an inappropriately long half-life (e.g. barbiturates).

If, having had medication reduced, the patient has three or more complex partial seizures in a 24 hour period or a single secondary generalised seizure, they have a stat. dose which is equivalent to half (or three-quarters if the medication has been reduced twice) of the total daily dose of any medication which has been reduced. Their normal medications may then be re-instated depending on whether adequate electroclinical data has been obtained. Anti-convulsant medication must be re-instated at least 24 hours prior to discharge. At this time they will be re-commenced with a stat. dose (half of the total daily dose for any drug reduced once and three quarters of the total daily dose for any drug reduced twice) as an additional dosage, with the regular medication taken from that time onwards.

2.10.2 Sleep Deprivation

The majority of the patients were asked to be sleep deprived at least once during their stay on the unit. The standard procedure was that on the second night of their stay on the unit the patient would be asked to stay awake until 2 am and was then woken again 6 am, i.e. allowing them 4 hours of sleep. This procedure did vary according to the patient and how many hours they normally slept at home and the hour at which they went to bed. If no seizures were recorded on the third day the patient might be asked to stay awake a second subsequent night. Some patients did not feel able to comply with the procedure fully but were encouraged to try to stay awake a little later than their habitual bedtime.

2.10.3 Hyperventilation

All patients were asked to carry out a period of hyperventilation at least once during the recording. The patient was asked to relax and lie or sit with their eyes closed for one minute. The technician would then ask the patient to hyperventilate with their eyes closed for a period of five minutes, providing verbal encouragement when necessary. After five minutes they were asked to stop hyperventilating and breathe normally but remain with their eyes closed for a further period of at least one minute. The technician remains in the patient room throughout the procedure.

2.10.4 Photic stimulation

This was always carried out at least once during the course of the recording session. The patient was tested using a SLE™ (Model number CPS-10-luminance of light) photic stimulator with a grid placed over the lamp. The patient was tested at various frequencies with eyes open and closed. The lamp was positioned at 30 centimetres squarely in front of the patient, who was asked to look into the light when their eyes were open. For each frequency the patient was tested for 5 seconds with the eyes open, they were

then asked to close their eyes whilst the light remained flashing and continued for 5 seconds whilst their eyes were closed. Frequencies used were 18 Hz, 2,4,6,8,10,12,14,16,18,20,25 and 50 Hz. If the patient showed any photosensitivity or photoconvulsive response then the frequency was presented again to ensure repeatability and more detailed testing was carried out at the stimulation frequencies of interest.

2.10.5 Other provocative procedures

If the patient indicated that there were any specific triggers to their seizures, we tried to employ these. For example if the patient said that exercise sometimes brought on seizures we would encourage them to exercise in the room either using a static exercise bicycle or repeated "step ups" on and off a low step. Other patients mentioned food triggers, delaying a meal or eating larger meals.

There was no attempt to administer any drugs that were likely to provoke seizures, as chemically induced seizures can be potentially unreliable with the provocation of atypical seizures (Wieser,Bancaud and Talairach,1979).

2.11 Video Recording of Seizures

Video and audio recording is continuous during the time that the patient is on the unit. When they had an aura or warning of a seizure, patients were encouraged to press the event button. If they were unable to do this relatives or visitors were asked to press it for them when they realised that the patient was having a seizure. As soon as either the nursing and/or technical staff were aware that a seizure was taking place, because the event button had been pressed or from observation on either the video or EEG monitors, they would go into the patient room. The staff would then interact with the patient, asking them to remember a number or colour, calling their name etc. They would ensure that the patient was not likely to injure themself (for example removing sharp objects out of their grasp) and that they were in clear view of the camera. As the patient recovered from a complex partial seizure the staff

would ask the patient to perform simple motor tasks, assess whether they were orientated in time and place, and whether there was any aphasia or dysphasia. If the patient had a generalised seizure the patient was put into the recovery position as soon as possible and oxygen and suction administered as necessary. Patients were observed closely following all seizures to check recovery.

2.12 Methodology

2.12.1 Scoring of ictal features

All of the ictal recordings of the 400 patients were reviewed and scored by the author (CAS) blind to the MRI or other findings. All seizure recordings were reviewed once and in 143 (35%) patients the recordings were reviewed for a second time, in order to determine intraobserver reliability for each EEG feature analysed.

The features of interest within the ictal EEG were tabulated on a typed score sheet. The data from these score sheets was then entered onto an anonymised database (see Appendix 2 for example of score sheet).

For each patient all the seizures available were briefly reviewed and the first seizure without artefact was then reviewed in detail. Justification for this approach can be found in previous studies, which have shown that the first ictal recording is usually highly predictive of final results with respect to localisation and lateralisation when more than one clinically stereotyped seizure is recorded. Sum and Morrell (1995) studied 66 patients who had multiple seizures recorded on prolonged EEG monitoring and they found that the first seizure was well localised in 28 patients and predicted the final localisation in 26 patients, 2 patients having bilateral independent temporal seizures. In 38 patients the first seizure was non-localised and remained non-localised in 34. They concluded that the first seizure was highly predictive of localisation but could not exclude the presence of more than one independent epileptic focus.

In this study if the patient had more than one type of seizure electrographically or clinically then one of each seizure type was reviewed and the data tabulated. In analysing the ictal records of these patients there were three options (1) to count the first seizure only, (2) to count all the seizures and (3) to analyse these patients separately.

Employing option (2), i.e. including all the seizures could introduce a bias in the results with just a few patients who have multiple patterns of spread influencing the results disproportionately and clearly the number of patients who will be designated to the multiple seizure group is dependent upon the level of detail of the ictal EEG analysis. By discounting all the patients (option 3) valuable data is lost. A combination of option (3) and (1) was therefore employed. Patients who had both epileptic seizures and non-epileptic attacks (NEAs) were analysed separately, as these were clearly different clinical phenomena, although the finding was in itself useful and important information, and is discussed in the results.

Excluding the subgroup with recorded non-epileptic attacks, the number of patients with differing seizure types (either clinical or electrographic) represents a small proportion of the total cohort, 7% of patients having seizures (27/362). Of these only 4/27 had bilateral independent scalp EEG ictal onsets. There was no association with pathology (for example 15/27 had UHS compared to 190/400 of the total group) nor were they more likely to have had AED reduction (23/27 vs. 241/264). The proportion of patients proceeding directly to surgery was significantly lower ($p<0.01$) but the post-surgical outcome was similar to the group with a single seizure type (Table 1, below). The majority of the data analysis was therefore performed using the data from those patients with a single seizure type but for key features it was repeated to include those patients with multiple seizure types (but excluding those with seizures and NEAs). When including the multiple seizure patients the data from the first complex partial seizure was included. This would be similar to the approach adopted in the patients with a single seizure type and justified by data from studies such as Sum and Morrell (1995). The detailed findings of the patients with multiple seizures are discussed in the results.

Table 1: Comparison of patients with multiple and single seizure types

	Patients with multiple sz type	Patients with single sz type	
Direct to surgery	6/27 (22%)	156/323 (48%)	* $p<0.01$
Good post-op outcome	7/8 (88%)	124/168 (74%)	NS

Intraobserver reproducibility – the scores achieved by CAS in the 143 patient's records that were reviewed twice were compared. They were reviewed blind to the previous score and separated in time by at least one month. In 8 seizures there was a discrepancy between the two scores, the majority of which (7/8) related to minor differences on the initial EEG changes or post-ictal phenomena, only 1 seizure showed a substantive difference in the scoring of the rhythmic theta, relating to the distinction between rhythmic theta and repetitive sharp waves.

Interobserver validation – DF (supervisor) reviewed a random selection of 10 of the patient records. He reviewed this selection blind to the previous scoring and the results between the two reviewers were compared. Table 2 below shows the comparison of the scores achieved by the two reviewers, where a tick represents concordance and a cross discordant scores. Where values were assigned for duration and times of onset discrepancies are represented by plus or minus signs.

There was a high degree of concordance between the two reviewers. There was complete concordance in 6 categories and a better than chance concordance in the remaining further 6 categories. Table 3 shows the Kappa scores and significance levels for these measures.

There was less good agreement on timings of certain features, for example the duration of rhythmic theta showed a close (difference of 1 second or less) agreement in only 1/3 of the recordings. The difference in duration times

between the reviewers showed a median of –1.5s, range –9 to 3 s. As discussed later in the methods section (2.12.2 (d)) when analysing the duration of rhythmic theta, a value of 10 seconds or greater was taken as representing sustained theta. Using this value the reviewers disagreed in only one patient, 108, where the duration of rhythmic theta was given as 9 and 12 seconds, in all other patients there was complete agreement on whether the theta was sustained or not.

Similarly although there was disagreement on the time of onset of the rhythmic theta in 3/10 patients, the median of difference of onset times was 0s with a range of –1 to 4s. Using the definition of early theta as that occurring at or within 30 seconds the reviewers had complete agreement as to whether the rhythmic theta was early or late. There was a disagreement in 2/10 patients in the time taken for the discharge to be come bilateral, with a median difference of 0s and range of –1 to 7s.

Although this was a small sample of inter-observer comparison we are trying to identify robust readily usable measures that should be easily identified even with such a sample. The relatively favourable intra and inter-observer comparisons reflect the use and application of detailed and quantitative definitions.

These findings can be compared favourably with studies from other centres (Walczak et al, 1992). Walczak et al looked at accuracy and reliability when scoring scalp ictal EEG and found that rhythmic changes had good agreement between reviewers, as did post-ictal changes. The two reviewers here had a better than chance agreement on those features. The features such as timing where there was less good agreement were not discussed in Walczak's study. Another paper looking specifically at bilateral spread in scalp ictal EEG recordings gave a good interobserver reliability for the categorization of EEG seizure patterns with a kappa value equal to 0.729 (Schulz et al, 2000).

Table 2: Inter Observer Validation

Patient	1st change R	1st change L	F/R/H/BL	Time	Early /Late theta	RTP	RT 1st change	RT Evolves	F/R/H/BL	Duration	Sustained theta	BL	Syn	Off	PIS
101	✓	✓	✓	0	✓No θ	✓	✓	✓	✓	0	✓No θ	✓	✓	✓	✓
102	✓	✓	✓	0	✓	✓	✓	✓	✓	-9	✓	✓	-1	✓	✓
103	✓	✓	✓	-1	✓	✓	✓	?	✓	+3	✓	✓	✓	✓	✓
104	✓	✗	✗	0	✓	✓	✓	?	✓	-9	✓	✓	✓	✓	✗
105	✓	✓	✗ R/H	+4	✓	✓	✓	✓	✗ RFT/RH	-1	✓	✓	✓	✓	✓
106	✓	✓	✓	0	✓	✓			✓	-2	✓	✓	✓	✓	✓
107	✓	✓	✓	+1	✓	✓	✓	✓	✓	-5	✓	✓	✓	✓	✓
108	✓	✓	✓	0	✓	✓	✓	✓	✓	+3	✗	✓	✓+7	✓	✓
109	✓	✓	✓	0	✓	✓	✓	✓	✓	0	✓No θ	✓	✓	✓	✓
112	✓	✓	✗	0	✓	✓	✓	✓	✓	-9	✓	✓	✓	✓	✓

Table 3: Concordance of 2 reviewers scores of ictal features.

EEG feature	Kappa score	Probability
Rhythmicity of first EEG feature	1	.00157
Lateralisation of first EEG feature	.73684	.01573
Location of first EEG feature	.589	.001
Theta onset: early or late	1	.01573
Presence of rhythmic theta	1	.00157
Rhythmic theta first change	1	.00157
Rhythmic theta evolves from first change	1	.00468
Location of rhythmic theta	.855	.00001
Rhythmic theta: sustained or not	.78	.01123
Presence of bilateral changes	.736	.01573
Offset	1	.00157
Post-ictal lateralised slow	.615	.035

2.12.2 Ictal features – details

The ictal features that were considered are detailed below. The ictal features were chosen so that quantitative decisions could easily be made, e.g. presence or absence of features, onset and offset of changes in the EEG.

For some features such as asymmetry an arbitrary percentage difference was determined that could be readily identified by an observer. This would clarify the findings in the small proportion of patients where such differences would otherwise not be readily identified by qualitative visual inspection of the record and to enable replication of the study.

Onset:

It was noted whether or not the onset was obscured by physiological artefact such as movement or muscle at the onset of the seizure.

Then whenever possible it was noted whether the EEG or clinical onset was first or whether they occurred simultaneously. It was not always possible to judge the timing of the clinical onset as some patients may have had an aura prior to any motor phenomena, which they did not indicate either verbally or by pressing the event button. Where possible the clinical onset was taken as the patient indicating an aura or some clear clinical change, movement etc. The timing of the clinical onset was taken from the video-EEG telemetry report or from annotations on the ictal EEG recording.

If there was any change in the EEG at the onset it was described and divided into one of three groups (1) the presence of an alpha asymmetry, (2) a discharge or (3) attenuation of the background activity. These are similar categories to those used by Walczak (1992) when looking at interobserver reliability when scoring scalp ictal EEG. Alpha asymmetry was only included if the video-EEG telemetry report did not comment on any asymmetry in the resting record and the asymmetry persisted for longer than 3 seconds. With the attenuation of background activity efforts were made to exclude those instances where an arousal response or change of patient state, and only cases where there was a very marked (more than 50%) decrease in background activity and no obvious change in the patients level of alertness were counted.

First Change:

The first clear change in the EEG was then described several clearly defined parameters.
Was the first change rhythmic? Was it lateralised? The first change was considered to be lateralised if the amplitude over one hemisphere was more than twice the amplitude of the opposite hemisphere and was sustained over one hemisphere for more than two seconds before becoming bilateral, two seconds representing a realistic period during which lateralisation could be defined.

Location of the first rhythmic change? – Location was defined by the same criteria used for the rhythmic theta – see paragraph below.

If the first change was considered unilateral it was noted whether there was any change on the opposite side, for example attenuation of background activity, or any irregular or non-rhythmic activity.

Rhythmic Theta:

(a) The presence of rhythmic theta was noted, rhythmic theta was considered to have occurred when it lasted for two or more seconds and it could be bilateral or lateralised. If it was present it was noted if it was the first EEG change. It was also noted if the theta discharge evolved directly from the first change, i.e. if there was a slower or faster discharge or repetitive spiking in the same location as the theta activity that evolved without a break or period of attenuation into the rhythmic theta.

(b) Onset of the rhythmic theta.
If the theta was not the first EEG change the time difference between the first change and the rhythmic theta was calculated. This figure represented the onset time of the rhythmic theta, if the rhythmic theta occurred at or before 30 seconds from the ictal onset than this was classified as early and late if it occurred after 30 seconds. Williamson et al (1993) found that a lateralised

build up of rhythmic theta occurred within 30 seconds in approx. 80% of their patients with mesial temporal lobe epilepsy, and that this was a reliable sign of lateralisation of the seizure origin.

(b) Laterality of the rhythmic theta

The rhythmic theta was identified as Right, Left or Bilateral. To be described as unilateral the amplitude over one hemisphere had to be greater than twice the amplitude of the discharge on the opposite hemisphere and had to have been continuous on one hemisphere only for more than one second.

(c) Localisation of rhythmic theta.

For localisation purposes the electrodes applied using the 10-20 placement system were divided into groups. The midline electrodes (Fz, Cz, Pz) were identified separately.

- **Right frontal** (RF) or **Left frontal** (LF) included electrodes F4/F3 and Fp2/Fp1. F8/F7 were included if the discharge occurred only at those electrodes or in association with the other frontal electrodes.
- **Right Temporal** (RT) and **Left Temporal** (LT) included electrodes T4/T3 and sRSp/sLSp also F8/F7 when the discharge occurred at these electrodes in association with the other temporal electrodes. This group included the mid and anterior temporal electrodes. The posterior temporal electrodes (T6/T5) were for this purpose grouped with the occipital electrodes – see below. This allowed a distinction to be made between the mid and more posterior temporal discharges.
- **Right Central** (RC) and **Left Central** (LC) - electrodes C4/C3.
- **Right Parietal** (RP) and **Left Parietal** (LP) - electrodes P4/P3.
- **Right Occipital** (RO) and **Left Occipital** (LO) - electrodes O2/O1 and T6/T5.

All electrodes at which the discharge was occurring were marked. When entering the ictal features onto the database localisation was entered in two ways – by electrode groups as detailed above, and by the following categories: -

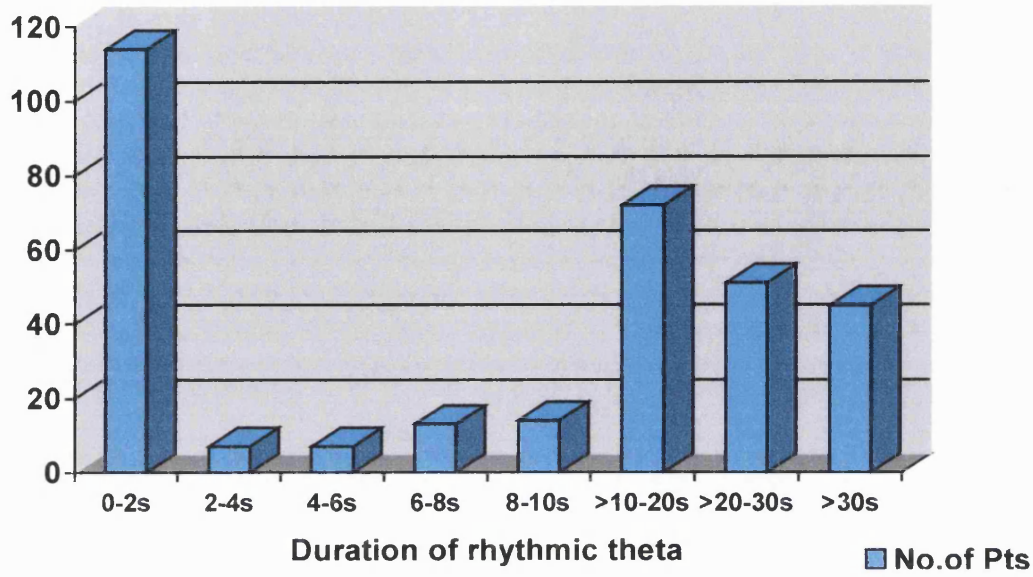
Focal – one electrode group as defined above.
Regional – two anatomically adjacent electrode groups (for example frontal and occipital electrodes would not be classified as regional but frontal and temporal electrodes would).
Hemisphere – three (or four) electrode groups all on the same side or two non-adjacent electrode groups in the same hemisphere (although this latter combination was very rare).
Nonlateralising, Nonlocalising – more than three groups and both sides involved.

(d) Duration of the rhythmic theta

The duration of rhythmic theta was calculated as the time from the appearance of the rhythmic theta to the time at which it stopped or became non-rhythmic. If the discharge remained within the theta range but become irregular and non-rhythmic it was not counted in the total duration of rhythmic theta.

When scoring this data for analysis the rhythmic theta was considered as sustained if the duration was 10 seconds or longer, and not sustained if less than 10 seconds. The value of 10 seconds has been used by other reviewers (Walczak et al, 1992) and represents a readily identifiable time period when reviewing the data with good interobserver reliability. Walczak used as his definition of rhythmic theta or alpha as a period of rhythmic activity lasting at least 10 seconds and occurring within 40 seconds of electrographic seizure onset. The histogram below shows the number of patients against duration of theta and it can be seen that, 48% of patients have either no rhythmic theta or theta lasting less than 10 seconds, 22% have theta between 10 and 20 seconds, 16% between 20 and 30 seconds and 14% have rhythmic theta greater than 30s. Thus duration of 10 seconds represents a median point if patients with no theta are included in the data set, although from the histogram it is clear that this is not a normal distribution.

Figure 1: Number of patients vs. duration of rhythmic theta



Evolution of ictal discharge:

Bilateral changes – if the discharge was unilateral at onset it was noted if the changes became bilateral and the time taken to become bilateral. It was also noted whether, when bilateral changes occurred if these were at the same (within 1 Hz) frequency over both hemispheres.

It was noted if the discharge changed side, i.e. if the discharge started unilaterally whether it switched to the opposite hemisphere at any stage in the seizure or if it was clearly more prominent on the opposite side.

Seizure offset:

It was noted if the seizure offset was abrupt i.e. whether a clear change in the EEG was identified or whether the discharge gradually reduced in amplitude and frequency and the exact end of the ictal EEG could not clearly be identified.

It was also noted if the offset was bilateral or unilateral, when the seizure discharge had been bilateral.

Post-ictal changes:

A reasonable period post-ictally was reviewed, usually about five minutes, although sometimes post-ictal recordings were marred by artefact or disconnection. The presence or absence of any post-ictal changes were noted, and the type of change was identified as, slow, spikes or other epileptiform discharges, attenuation of background activity and any asymmetry of background activity when it returned.

The location of these changes was also scored, whether the discharge was unilateral – in which case whether it was Ipsilateral or Contralateral to the side of seizure discharge, or whether the changes were bilateral. As in Walczak's study post-ictal slowing was only considered lateralised if the amplitude over one hemisphere was more than twice the amplitude over the opposite side.

2.12.3 Scoring of video description

The descriptions of the patient's seizures recorded during the video-telemetry and documented in the both the factual and conclusion of the clinical report were reviewed. The report was done at the time of the telemetry recording by a technician experienced in video-telemetry and checked by one of two Consultant Neurophysiologists (David Fish or Shelagh Smith). More than 25% of the reports were written at the time of the recording by the author, and more than 90% of the recordings were organised and supervised by the author. On the basis of this factual description the seizures were then divided into the following categories

Temporal lobe seizures, these were seizures identified using Engel's criteria (1993a) for mesial temporal seizure type. Engel in describing temporal lobe seizures has stated that there should be an aura; arrest of behaviour and/or a stare; oro-alimentary automatisms; posturing of 1 upper extremity and post-ictal confusion and/or disorientation. Other authors have extensively described the constellation of clinical features that are seen in complex partial seizures originating in the temporal lobe (Quesney, 1986; Quesney and Gloor, 1985; and Treiman et al, 1982). Seizures were subsequently further divided

into Typical temporal lobe seizures, abbreviated to tTLE where the clinical seizure included three or more of the features listed above; and Atypical temporal seizures, abbreviated to aTLE where the clinical seizure included only 1 or 2 of the above criteria but without any features that would suggest extratemporal localisation.

The differences and difficulties in distinguishing between mesial temporal and lateral temporal seizures were reviewed by Walczak (1995). Also the international classification of epilepsy syndromes has considered the frequency of the different automatisms and behaviours in these two groups. By restricting the number of criteria a distinction could be made when reviewing the ictal semiology allowing seizures to be classified as either typical (i.e. of mesial origin) or atypical (more likely to have a lateral origin). However this subdivision did not, for the most part, provide additional information and therefore for most of the analysis these two groups were considered together.

Extratemporal seizures, these were seizures with clear sensory or motor features to indicate localised activation of extratemporal structures. The exact nature of the motor and sensory features was dependent on the origin of the seizure focus. They were usually brief in nature, often bizarre and there was usually little or no post-ictal confusion. The features of extratemporal seizures can include bipedal automatisms and more complex motor automatisms which often appear semi-purposeful, there can be prominent bilateral posturing, and there is often vocalisation of varying complexity. Simple visual auras may occur as well as other non-specific auras, prominent blinking and forced eye deviation may be present particularly in seizures arising from a more posterior or occipital abnormality. These features have been well described by Williamson et al (1985); Williamson and Spencer (1986); and Quesney et al (1984).

Non-temporal and non-extratemporal seizures, these were seizures where there was a loss of awareness but there were no clear clinical features

pointing to either a temporal or extratemporal origin. They were usually fairly minor or had non-specific motor features.

Non-epileptic attacks, these were attacks where the patient was clincally unresponsive but a responsive alpha rhythm could be demonstrated and there were usually gross motor features, e.g. thrashing limbs, back arching etc. This group also included some attacks that may have resembled panic attacks.

Others

Simple partial seizures only, in these seizures the patient reported an aura or warning, there was no loss of consciousness and no motor features. There was no development into a complex partial or generalised seizure.

Electrographic seizures, where there was a clear EEG discharge which showed onset, evolution and offset but where there was no clinical change in the patient.

Generalised seizures where there was either no partial seizure preceding it or the partial seizure was very brief and could not be characterised.

Using these groups all of the seizures could be placed into one or other groups. As with the ictal EEG features because each patient could have more than one seizure reviewed it was possible that some patients had a mixture of seizure types.

2.12.4 Outcome

The outcome of all of the patients was reviewed. For the patients who did not proceed to surgery it was noted whether they were still awaiting further investigations, WADA tests or intracranial EEG studies; whether they were still attending the outpatient clinics at NHNN or whether they had died since the assessment.

For the patients who did proceed to surgery, Engel's standard classification for outcome was used (Engel et al, 1993). Class I was defined as seizure free

or non-disabling simple partial seizures only; Class II – rare disabling seizures; Class III – worthwhile improvement with some reduction in seizures from pre-operative levels and Class IV – no worthwhile improvement or seizure becoming worse post-operatively. The term "worthwhile" used by Engel is not standardised between epilepsy surgery centres but in this group of patients meant a reduction of more than 60-70% in the seizure frequency. It was also noted if the patient was awaiting further tests or more surgery because of continuing seizures. Retrospective data was not always complete enough to allow the newer proposed outcome classification to be used which with stricter definitions will enable a more standardised assessment of outcome between centres (Weiser et al, 2001).

2.12.5 Data Analysis

The statistical analysis was done using the SPSS package version 6.1.4. The tests performed depended on the type of data being analysed but consisted of chi-squared tests, Mann-Whitney and Logistic regression.

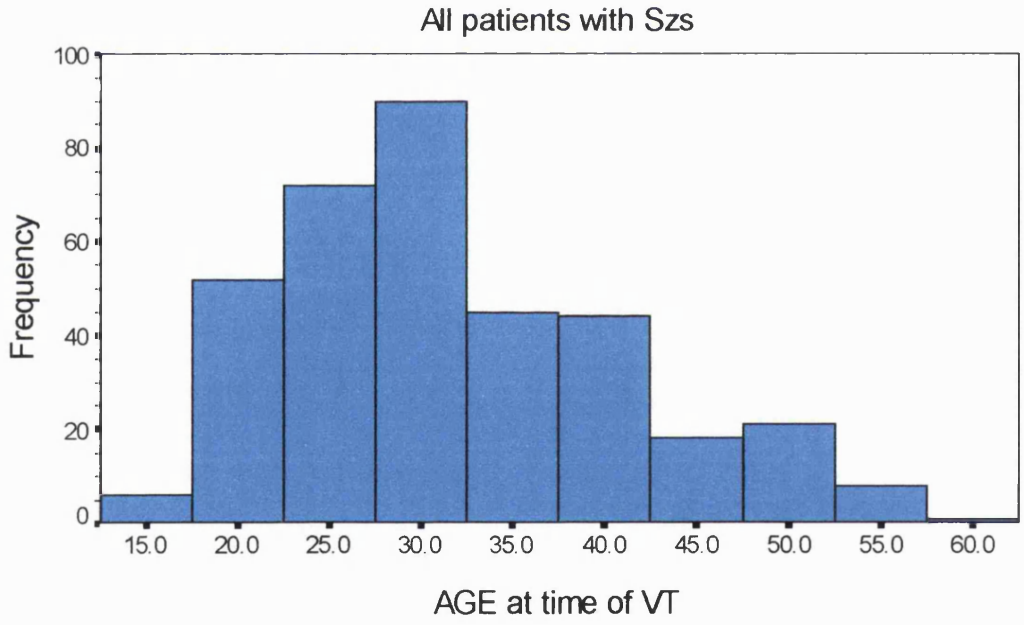
Chapter 3: Results

3.1 General and clinical data

3.1.1 Age at time of telemetry

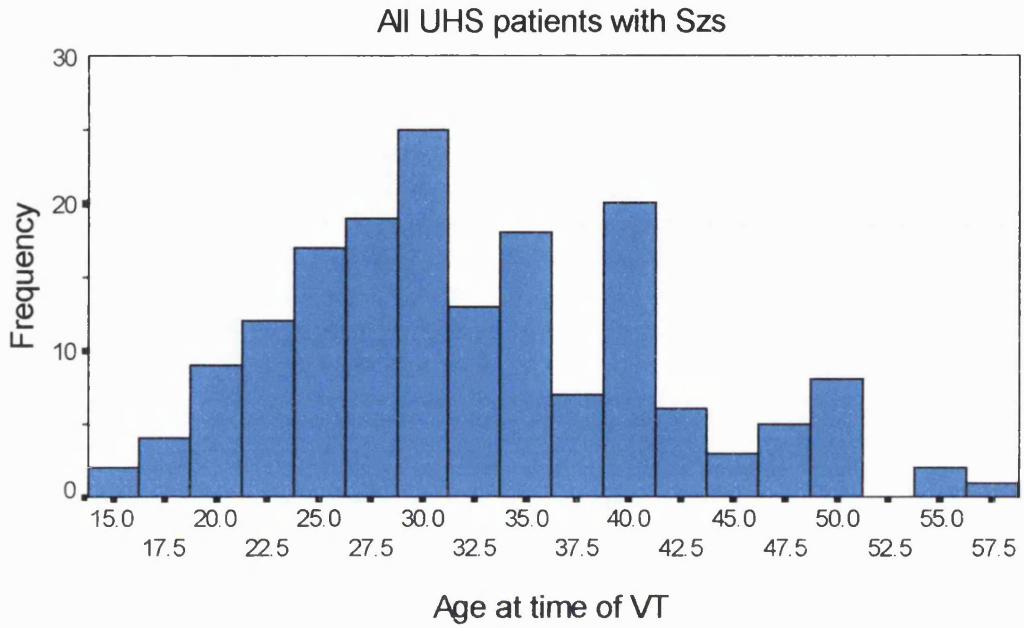
In the total group of 400 patients the mean age at the time of the final telemetry study was 32 years. In the subgroup of patients in whom seizures were recorded (number = 357) the mean age was 31.7 years, median 30 yrs with a range of 16-59 yrs.

Figure 2: Age at time of video-EEG telemetry



There were some differences between the different imaging groups and their ages. The patients with UHS were significantly older (Mann-Whitney $p<0.05$) with a median age of 31 yrs than those patients with other imaging abnormalities (median age of 29yrs).

Figure 3: All pts with UHS – age at time of video-EEG telemetry



However there was no significant difference in the age at time of the VT study between those patients with a single seizure type and those with multiple seizure types.

3.1.2 Febrile seizures

Wherever possible the history of whether or not a patient had a febrile seizure was obtained by the author reviewing the patients' case notes or the contemporary paperwork from the video-EEG telemetry admission.

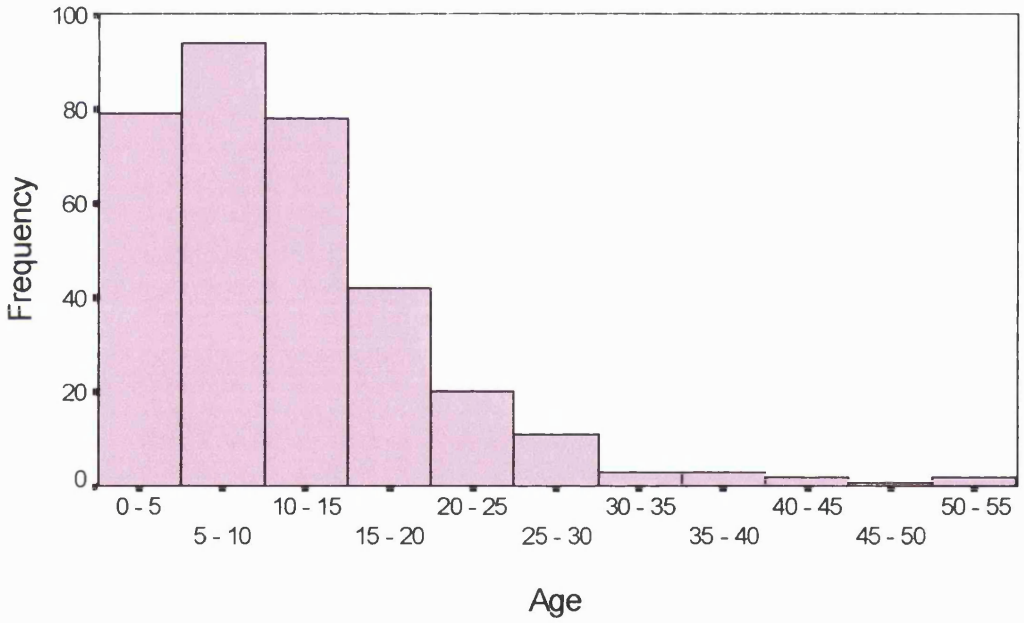
135 patients had febrile seizures clearly documented in their medical history and 237 did not have this documented, and in 28 patients the conclusive information could not be ascertained. As would be expected from earlier studies, (Kuks JBM et al, 1993) the presence of febrile seizures in the history was significantly associated with unilateral hippocampal sclerosis (98/176) in comparison to the other imaging groups (37/195) (Chi squared $p<0.00001$). Further analysis shows that the relationship is only significant if patients with UHS and only one electroclinical seizure type are considered i.e. those patients with multiple seizure types do not show the same a link between UHS

and febrile seizures (6/15 vs. 3/17), although the numbers are of course much smaller in this subgroup and therefore the lack of documented association may reflect a type 2 error.

3.1.3 Age of afebrile seizure onset

Considering only those patients who had seizures and in whom the data was available (n= 335); the median age of onset of afebrile seizures was 9 yrs, with a range of 0.1 – 53 yrs.

Figure 4: All patients with seizures – age of afebrile seizure onset

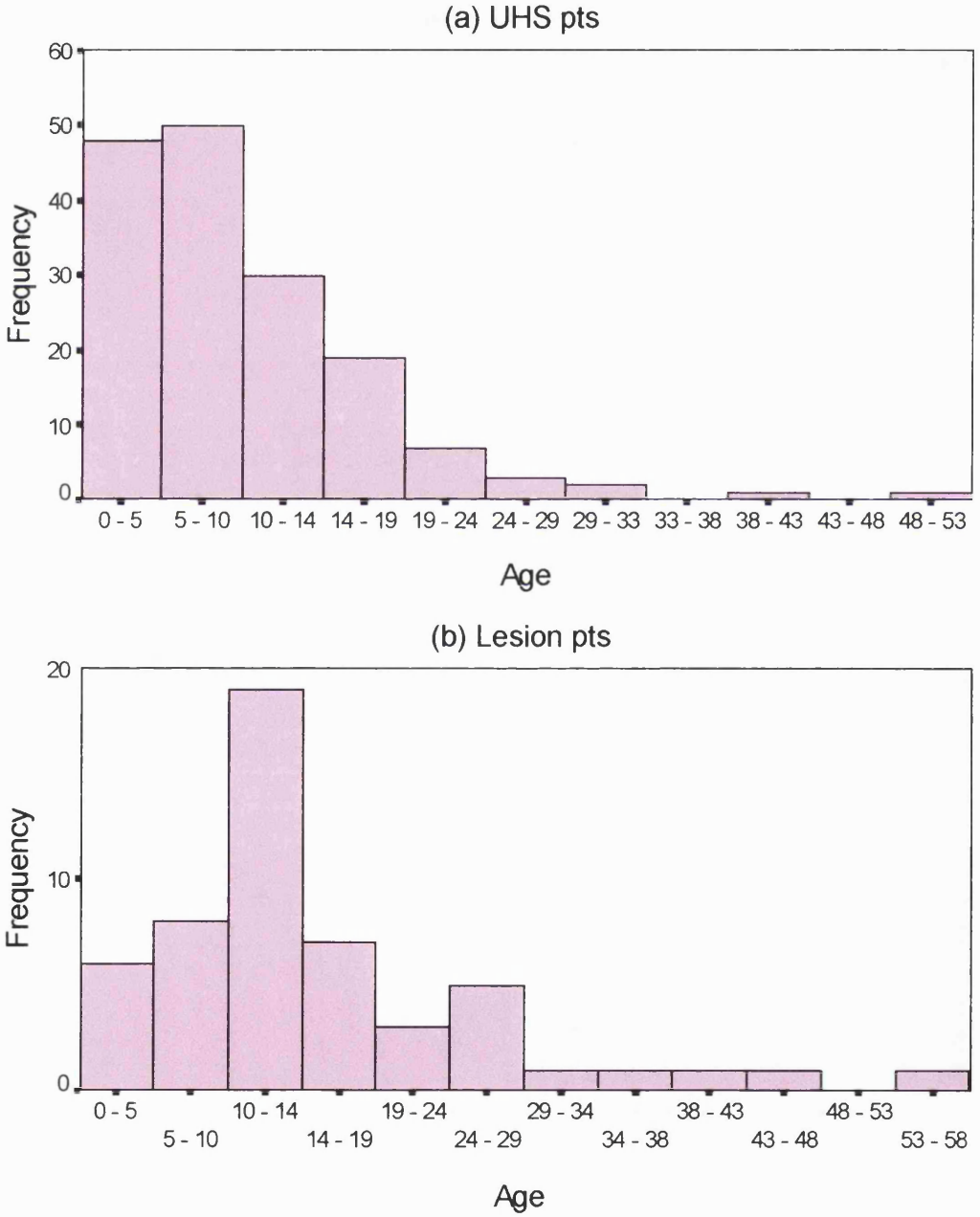


Looking at the different imaging groups those patients with UHS had a significantly earlier age of onset of afebrile seizures when compared with other patients, median age of 7yrs as compared to 11yrs (Mann-Whitney, $p<0.0005$). Patients with lesions had a median age of afebrile seizure onset that was older when compared to all other groups; 13 yrs compared to 8 yrs (Mann-Whitney, $p< 0.0005$) and patients with normal imaging were also slightly older in comparison to all other groups (Mann-Whitney, $p<0.05$).

In addition patients with multiple seizure types were also slightly older at afebrile seizure onset in comparison to those patients with single seizure types (13 yrs vs. 10.5yrs) (Mann-Whitney $p<0.05$).

Figure 5:

Age of onset of afebrile seizures in patients with (a) UHS and (b) Lesions



3.1.4 Medication

At the time of the telemetry only 1 (0.25%) of the patients was on no anti-epileptic medication (AEDs). 38 (9.5%) were on one AED and the remainder, 361 (90.25%) were on 2 or more AEDs. The AEDs varied from patient to patient and included not only older AEDs but also newer anti-convulsants. The most common AED was Carbamazepine (in either the Retard or non-Retard formulation).

For the purposes of the video-telemetry, AEDs were often reduced in line with the protocol described in the methodology. Any other medication that patients were taking at the time of the recording, whether on a short or long-term basis was left unchanged.

Table 4: Number of telemetry sessions vs. no. of times AEDs were reduced

	Number of telemetry sessions				
AED reduction policy	1	2	3	4	Total no. of patients
Never	83	24	6	1	114
Once	196	35	4	0	235
Twice		32	3	4	39
Thrice			10	1	11
Four times				1	1
Total	279	91	23	7	400

Overall AEDs were reduced in 286 patients. The table above shows the breakdown of the number of telemetry admissions against the number of times the drug reduction policy was instituted. Of the patients only requiring one admission for telemetry nearly two thirds had their drugs reduced, overall

nearly half of the patients (196) were admitted only once and had their AEDs reduced on that admission.

3.1.5 Imaging

As described in the methods all of the patients had high resolution MR imaging. For the purposes of analysis the patients were then divided into categories determined by the MRI findings. The categories used were **Unilateral hippocampal sclerosis (UHS)** as determined by volume and T2 measurements; **Discrete Lesion** – the location of the lesion was noted but the data was not further divided by the type of lesion, and [illegible] were mostly DNETs, low grade cerebral tumours, and cavernomas; **Normal** – no abnormality detectable on the MRI and any measurements made were within the normal limits for both volumetry and relaxometry; **Dual pathology**- more than one abnormality at least one of which was potentially epileptogenic; **Bilateral hippocampal sclerosis (BHS)** – where both hippocampi were outside the normal limits for volumetry and relaxometry; and **Other,** usually widespread– this included patients who had more widespread abnormalities, e.g. diffuse cortical malformations, widespread atrophy, widespread cerebrovascular disease etc.

When determining UHS the values were considered abnormal if they fell outside of 2 standard deviations of the previously determined normal range for our institution using the current methodologies (Van Paesschen et al, 1995). This meant that the hippocampal volume ratio had to be less than 87%, more than 90% was definitely normal and 88/89% were equivocal findings. The hippocampal T2 relaxation times had to be longer than 93ms to be considered definitely abnormal, a T2 relaxation time of 91/92 ms was regarded as equivocal and under 91 ms definitely normal. Bilateral hippocampal sclerosis was determined using absolute values corrected for cranial volume (Free et al, 1995 and 1996).

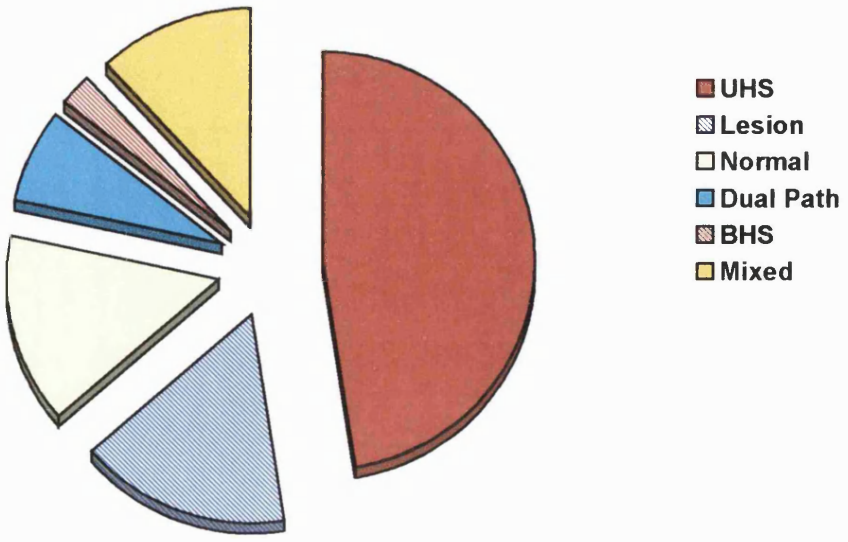
Table 5: MR imaging results

Imaging Results	Number of patients (% of total)
Unilateral HS	190 (47.5%)
Discrete Lesion	64 (16%)
Normal	59 (14.75%)
Dual Pathology	29 (7.25%)
Bilateral HS	10 (2.5%)
Other, usually widespread	48 (12%)
Total	**400**

It can be seen from Table 5 that the patients with hippocampal sclerosis, either unilateral or bilateral constituted half of the total group of patients (190+10). Although there was no bias in the selection of the patients into the consecutive study it could be argued that there is some bias inherent by the epileptologists, when they are deciding who should be assessed for epilepsy surgery, which will favour UHS and discrete lesions. However this practice and case mix is likely to be representative of other epilepsy centres.

The figure below shows graphically the division of the group by imaging.

Figure 6: Imaging v patient numbers



3.1.6 Recording duration

There were 400 patients in the study, who had a total of 558 periods of inpatient video-EEG telemetry each lasting for up to five days.

In 121 patients repeat studies were required, usually because no seizures had been recorded on the first admission (91 patients), but in some patients the telemetry was repeated so that further or more habitual seizures were recorded (21 patients), in order to perform additional investigations e.g. an ictal SPECT (8 patients) or in one patient the test was repeated so that psychometry could be carried out simultaneously with the telemetry.

The overall mean duration of the recording was 113 hours (range of 4 - 589 hours). The table below shows the average duration and range of patients with only one period of telemetry and those with more than one period.

Table 6: Duration of telemetry recording

	Patients with 1 period of telemetry	Patients with more than 1 period of telemetry
Average duration of recording (hrs)	82	183
Range (hrs)	4 – 192	44 – 589

3.1.7 Seizures

Overall there were more than 1300 seizures recorded in these 400 patients the table below shows the breakdown by type and number.

Table 7: Number of attacks and type

Number of Pts		No. of Seizures per pt	No. of Partial seizures	No. of GTCS
	38	0		
	79	1	58	21
	271	>1 sz	1194	65
Total	388		1252	86

Of the remaining 12 patients, five patients had pseudoseizures or non-epileptic attacks (NEAs) only and 7 patients had both seizures and NEAs recorded during the video-EEG telemetry.

The relatively small proportion of generalised seizures, just 7%, probably reflects the cautious drug reduction protocol used on our unit and the measures used to prevent serial seizures whenever possible. For example in a recent study from Yen et al (2001), where they rapidly reduced the AEDs, 36% of all their recorded seizures were secondarily generalised seizures in patients being assessed for temporal lobe surgery.

It is also probably relevant that less than half of the patients had either an extratemporal or more diffuse pathophysiology, which might predispose to more frequent generalised seizures.

3.1.8 Surgery

Out of the 400 patients 167 have proceeded directly to surgery. The table below shows the outcome following video-telemetry with respect to surgery in the different imaging groups.

Two clear findings can be seen in the table which will be discussed further in Part 3 of the results; namely that the percentage of patients with UHS proceeding to surgery is higher than all other imaging groups, and that very

few patients with normal imaging proceeded to surgery and none did so without first having an intracranial study (SEEG).

Table 8: Surgery by imaging group

MRI category	Direct to surgery		SEEG then surgery	No surgery		SEEG then no surgery	Total
	No.	%		No.	%		
UHS	116	61	9	64	34	1*	190
Lesion	25	39	6	33	52		64
Normal	0	0	4	53	90	2	59
Dual path.	11	38	1	17	59		29
BHS	3	30	1	5	50	1	10
Other	12	25	2	33	69	1	48
Total	167	42	23	205	51	5	400

* This patient died in a seizure in the interval between having an intracranial (SEEG) telemetry and the surgery that had been recommended following the intracranial study.

The type of operation performed was determined by the imaging abnormality, and could be divided as follows: - 152 (80%) temporal lobe resection; 31 (16%) lesionectomies; 5 hemispherectomies, 1 corpus callosotomy and 1 subpial transection. The large number of temporal lobe resections reflects the case mix and age of the patients studied.

More than 75% of the operations were carried out by one surgeon and all patients were operated on at the same site (NHNN) and received similar levels of post-operative nursing care it is reasonable to compare all the post-surgical outcomes together.

The temporal lobe resections were a modified Spencer procedure with a restricted anterior neocortical resection (up to 4 - 4.5 cm) sufficient to provide access for a mesial temporal resection (Spencer DD et al, 1984).

3.1.9 Follow-up

Follow-up information for the patients who had had surgery was available for almost all of them; only nine patients were lost to follow-up, usually due to transfer of long-term care from NHNN consultants to a local neurologist. The median follow-up time was 4 years with a range of 1 to 6 years. Details of the post-surgical follow-up are in the following sections.

Of the patients who had not had surgery it was noted whether or not they were still attending the outpatient clinics at NHNN but no further details were sought for this study.

3.1.10 Patient deaths

During the course of this study 8 of the 400 patients are known to have died. One patient had had surgery for his epilepsy and was making good progress when he died of an unrelated cause, carcinoma of the liver. Another patient had neurosurgery to debulk a cerebral tumour, which was the cause of his epilepsy, unfortunately there was a rapid recurrence of the tumour, a Grade 3 glioma, and he died within 2 months of the epilepsy surgery.

The remaining 6 patients all died during seizures (SUDEP). Two patients had had surgery, which as predicted pre-operatively, due to relatively unfavourable test results, had led to an amelioration of the seizures not their cessation. The other four patients were at various stages of the pre-operative process, either waiting for further tests or waiting for a date for surgery. The death of four patients (1%) following referral, prior to definitive treatment, emphasises the need to utilise the scarce resources with optimal efficiency.

These figures are similar to those found in larger cohort studies where the incidence of SUDEP in patients with medically intractable epilepsy is approx. 1:200 per year (Nashef et al, 1995b). Of the 6 SUDEP patients in this study there were equal numbers of men and women.

Of the 6 SUDEP patients, three had unilateral hippocampal sclerosis, one had a lesion, one diffuse imaging abnormalities and one had normal imaging. Of these six patients four were having frequent complex partial seizures and/or generalised seizures and one patient had a history of status epilepticus.

3.2 Ictal features and their relationship to MRI defined pathology

EEG ictal features

Firstly the results were analysed to see if any of the ictal EEG features studied were associated with a specific MRI defined pathology. If this were the case then the presence or absence of such features could help to predict in other patients whether similar MRI defined pathology was the likely cause of the epilepsy.

Initially analysis was performed on those patients with a single electroclinical seizure type. The analysis was then repeated for the key ictal EEG features to include those patients who had more than one electroclinical seizure type, as discussed previously in the methods section.

3.2.1 Rhythmic theta

The presence of rhythmic theta during the ictal discharge was noted, rhythmic theta was considered to have occurred when it lasted for two or more seconds and it could be bilateral or lateralised.

The presence of rhythmic theta during the ictal discharge was significantly associated with UHS (chi squared, $p<0.00001$) in comparison to all the other imaging groups, and the absence of any rhythmic theta was significantly associated (chi squared, $p<0.02$) with both the normal imaging group and the group with other, more widespread pathology, details are shown in the table below. In addition the presence of rhythmic theta was also significantly associated (chi squared, $p<0.00001$) with a temporal lobe type seizure (either typical temporal, tTLE or atypical, aTLE).

Table 9: Presence of rhythmic theta vs. imaging

Imaging	Rhythmic theta: Lateralised+ Bilateral	No rhythmic theta	
UHS	122	32	* $p<0.00001$
Discrete lesion	30	23	
Normal	23	23	
Dual Pathology	12	8	
BHS	8	2	
Others	15	25	
Total	210	113	

3.2.2 Onset of theta

The time of onset of the rhythmic theta during the seizure was considered, both in absolute terms and relative to other phenomena.

If rhythmic theta occurring at or before 30 seconds of the electrographic seizure onset is defined as an early onset (Williamson et al, 1993), there is a significant association between an early onset of theta and UHS ($p<0.00001$) when compared to all other imaging groups, this is the same whether or not the theta is lateralised. If the patient had either normal imaging or other, more widespread imaging abnormalities then there was a significant association with a later onset of rhythmic theta ($p<0.02$), again this was significant whether one considered either all early theta or only lateralised early theta. Table 10, below summarises these findings.

Table 10: Theta onset vs. imaging

	Theta onset ≤30 s	Theta onset>30s or no theta	
UHS	119	35	P<0.00001
Lesion	27	26	NS
Normal	21	25	P<0.02
Dual pathology	10	10	NS
BHS	8	2	NS
Other	12	28	P<0.0001
Total	197	126	

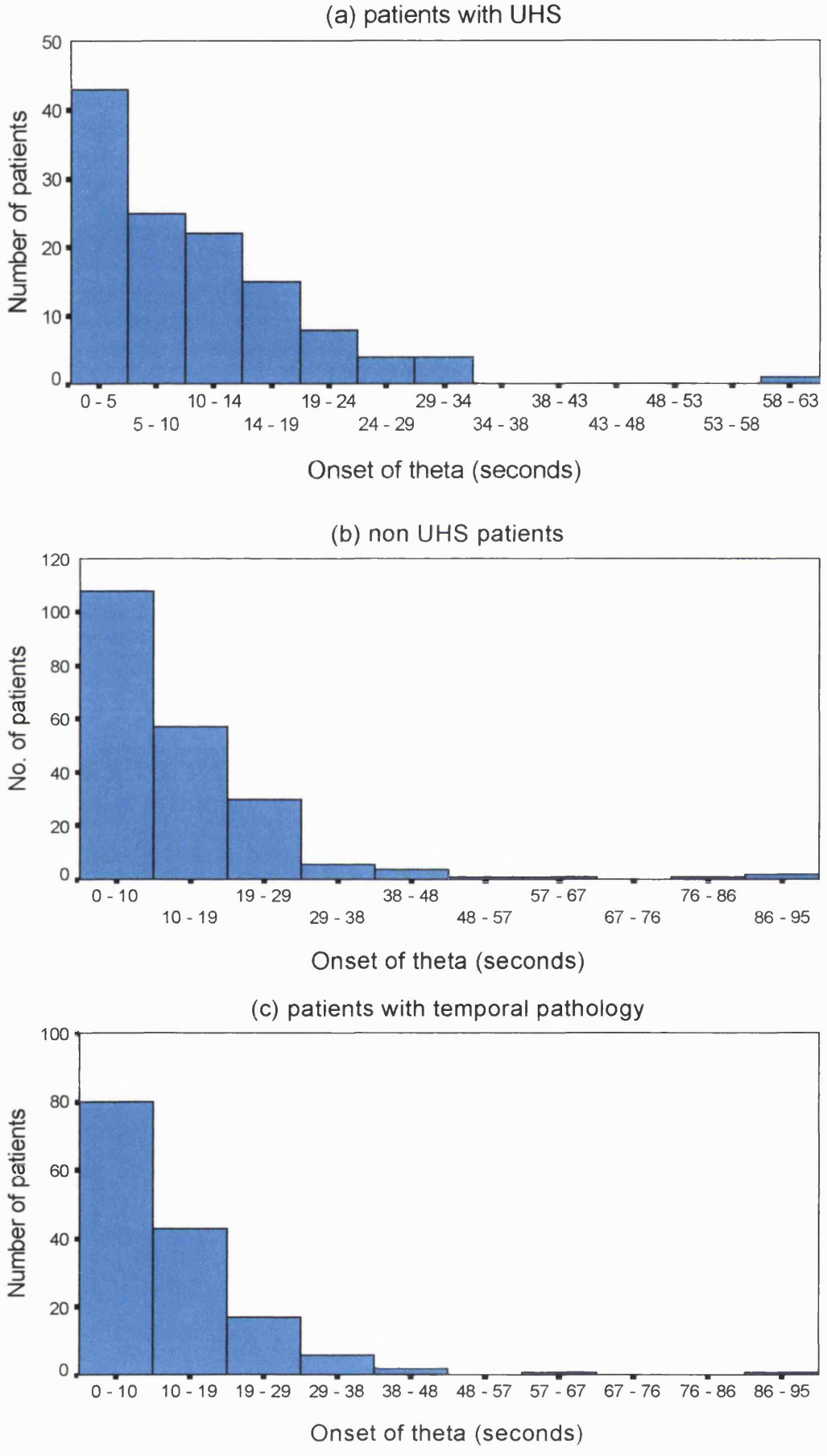
An early onset of rhythmic theta was also associated with a temporal type seizure (tTLE and aTLE) (Chi-squared p<0.00001) and a temporal location to the pathology (Chi-squared p<0.00001). There was a difference between those patients with UHS and those with temporal lesions, the patients with UHS being more likely to have an early onset of theta (Chi-Squared p<0.001). Table 11 below summarise these findings.

Table 11: Onset of theta vs. seizure type and pathology

	Theta onset ≤30 s	Theta onset>30s	
tTLE or aTLE sz	158	48	P<0.00001
All other sz types	39	78	
Temporal pathology	157	65	P<0.00001
Non-temporal pathology	40	61	
Pts with UHS	119	35	P<0.001
Pts with temporal lesions	24	23	

Looking at the absolute times of onset of the theta; the UHS group as compared to the non-UHS group showed a significant difference (Mann-Whitney $p<0.05$) with a median onset of rhythmic theta of 8 seconds in the UHS group and of 11 seconds in the non-UHS group. There is similarly a difference between those patients with a temporal location to their pathology (median 8.5s) compared with a non-temporal (11s), (Mann-Whitney $p<0.05$). Figure 7 below shows the onset of rhythmic theta in the different imaging groups.

Figure 7: Onset of rhythmic theta in different imaging groups



In contrast to the association of early theta to UHS when compared to temporal lesions, there is no significant difference between the median onset times of theta in these two groups (Mann-Whitney, p= 0.27).

Despite the significant association between a temporal type seizure (tTLE+aTLE) and the early onset of rhythmic theta i.e. within 30 seconds, there is no significant difference between the median onset time of rhythmic theta between the group who had a temporal type seizure and those who did not.

3.2.3 Duration of theta

In a similar manner to the onset of the ictal theta, the duration of the rhythmic theta was analysed.

Using 10 seconds as a cut off time, with duration of less than 10s being regarded as not sustained rhythmic theta, the different pathologies were compared. UHS was significantly associated with a duration of rhythmic theta equal to or more than 10 s (Chi-Squared $p<0.00001$) when compared with the rest of the patients.

Those patients with either a lesion on their MRI or normal imaging were more likely to have a shorter duration of rhythmic theta in comparison to the other patients (Chi-squared $p<0.05$). The patients with other, widespread abnormalities on imaging were also less likely to have sustained theta (Chi-squared $p<0.0001$). Table 10, below shows the association between imaging and duration of theta (lateralised or bilateral).

Sustained theta was also significantly associated with a temporal type seizure (tTLE+aTLE) and with a temporal location to the pathology (Chi-squared $p<0.00001$), whether the rhythmic theta was lateralised or bilateral. The sustained duration of rhythmic theta (lateralised or bilateral) also differentiated between those patients with UHS and a temporal lesion (Chi-squared $p<0.05$).

Table 12: Duration of ictal theta vs. imaging

	Theta duration <10s	Theta duration ≥10s	
UHS	44	110	P<0.00001
Lesion	31	22	P<0.05
Normal	29	17	P<0.05
Dual pathology	11	9	NS
BHS	4	6	NS
Other	30	10	P<0.0001
Total	149	174	

If one compares the duration of the rhythmic theta in the UHS group with the duration in all of the patients, it was significantly longer in the UHS group with a median of 21 seconds compared to 15 seconds (Mann-Whitney, $p<0.02$). There is also a difference when the UHS group is compared to the temporal lesion group, who have a median duration of rhythmic theta of 14 seconds, (Mann-Whitney, $p<0.05$).

There was however no significant difference in the median duration of rhythmic theta between those patients with a temporal type seizure (tTLE+aTLE) and those without and between those patients who had a temporal pathology and those who did not.

3.2.4 Lateralised theta

The presence of lateralised theta during the ictal discharge is significantly associated with UHS (chi squared, $p<0.00001$) in comparison to all other imaging groups and does distinguish between a temporal lesion and UHS ($p<0.02$). The imaging groups - lesion, normal and others/widespread are associated with an absence of lateralised theta ($p<0.02$ or less, in all cases) when individually compared in turn against all others.

Table 13: Lateralised ictal theta vs. imaging

	No lat theta or bilateral theta	Lateralised theta	Significance
UHS	44 (30%)	110 (63%)	P<0.00001
Lesion	33 (23%)	20 (11%)	P<0.005
Normal	28 (19%)	18 (10%)	P<0.02
Dual pathology	9 (6%)	11 (6%)	NS
BHS	4 (3%)	6 (3%)	NS
Other	27(19%)	13 (7%)	P<0.002
Total	145	178	

Ictal lateralised theta is also significantly associated with a temporal location to the pathology ($p<0.00001$) and both typical temporal (tTLE) and atypical temporal (aTLE) type seizures ($p<0.00001$) and further analysis was done to see if they were independently associated (see regression analysis below).

The onset of rhythmic lateralised theta was considered relative to other ictal phenomena, i.e. it was noted whether the lateralised rhythmic theta occurred as the first EEG phenomena, whether it evolved from the first EEG phenomena or if it was neither but did occur at some stage in the ictal discharge.

Analysis showed that lateralised theta was significantly associated with UHS, either when it occurred as the first phenomena (Chi-squared, $p<0.05$) or when it was the first feature or evolved from the first feature (Chi squared $p< 0.00001$).

If only those seizures with lateralised rhythmic theta were considered there was still an association between UHS and early, i.e. occurring at or before 30s of seizure onset, lateralised theta (108/110 vs. 2/110) (Chi-squared $p<0.005$). Looking at only the seizures with lateralised theta, patients with normal imaging no longer showed an association with a later (more than 30s) onset

of lateralised theta but those patients with other, more widespread imaging still showed an association with a later onset of theta (Chi-squared $p<0.05$).

There was no association between either a temporal seizure type (tTLE+aTLE), or a temporal location to the pathology, and an early onset of theta if only seizures with lateralised theta were considered. The significant association in these interactions (3.2.2) is therefore the presence of lateralised theta not the time of its onset.

Looking at the duration of rhythmic lateralised theta, there was still a significant association between the duration of lateralised theta of 10 or more seconds (sustained theta) and UHS although there was a reduced significance level ($p<0.01$) if only seizures with lateralised rhythmic theta were considered, compared to those seizures with sustained rhythmic theta which is bilateral or lateralised. ($p<0.0001$).

With the other imaging groups, if only seizures with lateralised theta were analysed no significant association was identified between the presence of sustained theta and either a lesion on the MRI or normal imaging. The patients with other more widespread pathology were still less likely to have sustained theta if only seizures with lateralised theta were considered ($p<0.05$) as compared to seizures with both lateralised and bilateral theta ($p<0.002$).

The sustained duration of rhythmic theta did not differentiate between those patients with UHS and a temporal lesion if only those seizures with lateralised theta were considered.

Those patients with either a lesion on their MRI or normal imaging were more likely to have a shorter duration of theta in comparison to the other patients (Chi-squared $p<0.05$), whether or not the theta was lateralised, but if only seizures with lateralised theta were considered then a significant association was not identified. The patients with other more widespread imaging

abnormalities were also less likely to have sustained theta (Chi-squared $p<0.002$) whether or not the theta was lateralised, and if only those seizures with lateralised theta were considered then there was a decreased significance level ($p<0.05$).

If only seizures with lateralised theta were considered the association between sustained rhythmic theta and either a temporal type seizure (tTLE+aTLE), or a temporal location to the pathology, had a reduced level of significance at $p<0.002$ (compared to $p<0.00001$ when seizures with both lateralised and bilateral theta were considered).

3.2.5 Location of theta

The location of the rhythmic theta was then considered. If the rhythmic theta was divided into those seizures where the theta occurred in the temporal or fronto-temporal electrodes then there was no significant association between the location of the rhythmic theta and the pathology as defined by imaging.

If however the division was between those seizures where the theta occurred in the temporal electrodes and temporal plus any other combination of electrodes, as compared to seizures where there was either no theta or extratemporal theta then there was a significant association between the presence of temporal theta and UHS ($p<0.00001$). In the lesion, normal and other groups there was a significant association with no theta or extratemporal theta ($p<0.05$). It was probable that the numbers of seizures without any theta are introducing a bias and attempting to relate the localisation of rhythmic theta (temporal, fronto-temporal and other) did not help to further differentiate the findings by pathology.

3.2.6 Rhythmic changes at onset

The first clear EEG change during the seizure was considered and divided into those changes that were rhythmic regardless of the frequency of the discharge and those changes that were non-rhythmic for example spikes or

an irregular discharge. Only the mixed imaging group had an association that was significant; they were more likely than the other groups to have a non-rhythmic onset to the seizure ($p<0.05$). With the other imaging groups there was no significant difference between the selected group and the rest of the patients.

3.2.7 Bilateral changes

The evolution of the discharge during the seizure was considered. Seizures were divided into those where the discharge became bilateral, if it was unilateral at onset, those where there was no bilateral spread from a unilateral onset and those where there was no change because the discharge was bilateral at onset.

There was no significant association between any of the different imaging groups when the seizures that remained unilateral throughout were compared to those that were bilateral throughout or where there was bilateral spread.

If the seizures that were unilateral throughout were compared to those where the discharge changed from unilateral to bilateral there was a significant association between UHS and bilateral ictal spread (Chi squared, $p<0.05$). There was no other significant association between imaging group and the discharge becoming bilateral or remaining unilateral.

There was also an association between bilateral spread and patients with UHS (Chi-squared $p<0.05$) when compared against those where the discharge either remained unilateral or bilateral throughout. Patients with a lesion were more likely to have no change or no bilateral spread (Chi-squared $p<0.05$). None of the other imaging groups showed any significant association with bilateral changes. There was a significant association between a temporal pathology and the discharge becoming bilateral (Chi-squared $p<0.05$), but there was no difference between the UHS and temporal lesional group.

The discharge becoming bilateral was highly significantly associated with a temporal type seizure (Chi-squared $p<0.00001$).

3.2.8 Abrupt offset

For the purposes of the analysis the offset was divided into those seizures where the offset was abrupt and those where it was not. There was no significant association between any imaging group and the type of seizure offset.

Nor was there any association between seizure type and offset, or between location of pathology and offset.

3.2.9 Post-ictal changes

The types of post-ictal changes were compared across the imaging groups. The changes were divided into those patients with either attenuation or an alpha asymmetry (negative features) against those with post-ictal slow or spikes (positive features).

The only imaging group that showed any significant association was the mixed imaging group where there was an association with the more positive post-ictal features (Chi-squared, $p<0.05$). There was no association between the seizure type and the post-ictal changes or with the location of the pathology. However there was a significant difference between the patients with temporal lesion when compared to those with UHS; the patients with a temporal lesion being more likely to have post-ictal slow or spikes than the UHS patients (Chi-squared, $p<0.05$).

If the location of the post-ictal changes was considered, those patients with UHS were significantly associated with ipsilateral or bilateral changes as compared to no changes or contralateral changes (Chi-squared, $p<0.0001$). Ipsilateral and bilateral changes were also associated with a temporal location to the pathology ($p<0.005$) but UHS could be differentiated from temporal

lesions with the UHS group more likely to have ipsilateral/bilateral changes ($p<0.002$).

Amongst the other imaging groups the patients with lesions (both temporal and non-temporal) and those with mixed pathology were less likely to have Ipsilateral/bilateral changes ($p<0.05$).

There was also a strong association between having a temporal type seizure (tTLE+aTLE), and either Ipsilateral/bilateral changes post-ictally (Chi-squared, $p<0.00001$).

3.2.10 Clinical seizure type

The clinical seizure type was compared within the different imaging groups.

Considering only those patients who had a single electroclinical seizure type, the table below shows the seizure type divided by MRI groupings. Definitions of seizure types are given in the methods, tTLE – typical temporal seizure, aTLE – atypical temporal seizure), ETLE – extratemporal seizure, nonTLE/nonETLE – non-specific complex partial seizure and others. The tTLE and aTLE seizures were often grouped together for the sake of analysis to represent a temporal lobe type seizure.

Table 14: Seizure type vs. imaging

	Seizure Type				
MRI	tTLE	aTLE	ETLE	NonTLE/nonETLE	Other
UHS	93	33	5	2	21
Lesion	14	15	17	3	4
Normal	9	11	18	8	0
Dual pathology	4	4	4	6	2
BHS	3	7	0	0	0
Other	5	8	17	7	3

Analysis shows a significant association between the patients with UHS and either a tTLE or aTLE seizure type ($p<0.00001$). If the seizures are divided into typical temporal and atypical temporal there is a significant association between the tTLE type seizure as compared to the aTLE type seizure in the UHS group ($p<0.0005$).

If one looks at a subset of the patients and compares the UHS and the group with temporal lesions against seizure type, there is no significant difference between these two groups and seizure type if the tTLE and aTLE type seizures are grouped together i.e. UHS is not different from the temporal lesional group.

However if the seizure type is divided into tTLE and aTLE there is a significant association ($p<0.005$) between a typically temporal type seizure and UHS when compared to a temporal lesion. This might be expected from the definition of a tTLE type seizure, which is typically associated with a mesial temporal pathology as compared to a more lateral pathology. The patients with temporal lesions show no clear difference between temporal and atypical temporal seizures reflecting the fact that the lesions could be either mesial or lateral in location.

If the patients with more than one electroclinical seizure type are included in the analysis there is no change in the association, i.e. a temporal lobe type seizure (either tTLE or aTLE) remains significantly associated with the UHS as compared to any other imaging group ($p<0.00001$). This applies if either all or at least one of the seizures recorded falls into the tTLE/aTLE category. If the same analysis is done dividing the patients into those where all seizures are either tTLE/aTLE as compared to those where only one falls into that category then there is no difference between the UHS group as compared to all the other patients. This is because such patients have a multiple seizure pattern with at least one seizure not having a temporal semiology, and thus probably involving extratemporal areas.

As there are only two patients with multiple seizure types and a lesion on their MRI, no additional information would be obtained by comparing seizure type and temporal lesions against UHS. That is to say, tTLE seizure type as compared to aTLE would still be associated with UHS when compared with a temporal lesion.

3.2.11 Logistic Regression analysis

This allows the interactions between the various features to be analysed to see which if any EEG and clinical features are independently associated with a particular type of imaging.

Using this technique for each of the different imaging groups gives different predictive factors for each group.

There appears to be no feature of the ictal recording, which is significantly predictive of BHS or normal pathology. In contrast UHS is significantly predicted by lateralised theta, sustained theta, an early onset of theta and a temporal type seizure. Of the interactions early and sustained theta is predictive ($p<0.02$) as well as early and lateralised theta ($p<0.02$).

In the other imaging groups i.e. the lesional group, the dual pathology and the other group with more widespread abnormalities any predictive factors are reversed and do not clearly distinguish between them.

The table below summarises the predictive factors in the ictal recordings that are identified from the logistic regression analysis and also the significant associated features identified from the chi-squared analysis, for each of the imaging groups.

Table 15: Ictal features vs. imaging

Imaging	Associated ictal features (χ^2 analyses)	Independent predictive combinations of ictal features (Logistic regression analysis)
UHS	Lateralised theta ($p<0.05$) Early theta ($p<0.01$) Sustained theta ($p<0.00001$) Bilateral spread ($p<0.05$) Ipsilateral or bilateral post-ictal changes ($p<0.0001$) Temporal type seizure (tTLE+aTLE), ($p<0.01$)	Early and sustained theta ($p<0.05$) Sustained and lateralised theta ($p<0.01$) Early, sustained and lateralised theta ($p<0.01$)
Lesion	Absence of lateralised theta ($p<0.01$) Non-sustained theta ($p<0.05$)	
Normal	Absence of lateralised theta ($p<0.05$) Late onset of theta ($p<0.02$) Non-sustained theta ($p<0.05$)	
Dual Pathology	A non temporal type seizure ($p<0.05$)	
BHS	None significant	
Other	Absence of lateralised theta ($p<0.0001$) Late onset of theta ($p<0.05$) Non-sustained theta ($p<0.0001$) Non-rhythmic changes at onset ($p<0.05$) Spikes /slow post-ictally ($p<0.05$) A non temporal type seizure ($p<0.01$)	

Considering the UHS group in more detail the most significant features associated with this group are listed below along with the odds ratios. These are the features that were significantly associated using Chi-squared analysis and are also shown to be independently associated using logistic regression methods.

- Presence of lateralised theta; odds ratio of 3.71 (with 95% CI 2.3 – 5.9)
- Presence of sustained theta (lateralised or bilateral); odds ratio of 4.1 (95% CI 2.6 – 6.5)
- Presence of early theta (lateralised or bilateral); odds ratio of 3.9 (95% CI 2.4 – 6.4)
- Temporal lobe type seizure; odds ratio of 5 (95%CI 3-8)
- From logistic regression the odds of a patient having UHS if they have all these features i.e. lateralised rhythmic theta, early theta, sustained theta, a temporal type seizure and a non abrupt offset to the discharge, are **2.42:1.**

3.3 Do any specific features from the video-telemetry predict whether a patient proceeds to surgery?

Looking initially at those patients who only had one seizure type, the various features of the ictal EEG were analysed, and the analysis was repeated for key features in patients with both single and multiple seizure types. Analysis was done firstly using chi-squared tests and then using logistic regression methods.

3.3.1. Presence of rhythmic theta

The presence of rhythmic theta, lasting for at least 2 seconds, at any stage during a seizure is significantly associated with proceeding to surgery (Chi squared, $p<0.0001$); a total of 123/156 patients with lateralised or bilateral theta proceeding directly to surgery as compared to 33/156 with no theta proceeding to surgery.

If the patients are divided by the location of the pathology, then the association between the presence of theta and proceeding directly to surgery is only significant in those patients with a temporal pathology (mesial or lateral) ($p<0.0005$). The data can be further divided into those patients with a clinical temporal type seizure (tTLE+aTLE), and it can then be seen that the presence of rhythmic theta is significantly associated with proceeding directly to surgery only if the patient has a temporal location to their pathology and a temporal type seizure ($p<0.006$). That is to say if the patient has a non-temporal pathology and a temporal type seizure, or a temporal pathology and a non-temporal seizure, or neither then there is no significant association between the presence of rhythmic theta and proceeding to surgery.

Similar results are obtained if patients with UHS are considered i.e. there is a significant association, if the patient has UHS and a temporal type seizure (tTLE+aTLE), ($p<0.01$), between the presence of rhythmic theta and proceeding directly to surgery.

3.3.2 Onset of theta

The time at which the rhythmic theta occurred was analysed, as in Part 2 this was considered both in absolute terms and relative to the other phenomena. Using a cut-off time of 30s there is a significant association between theta occurring at of before 30s and proceeding to surgery ($p<0.00001$). If the cut-off point is decreased to 20s or 10s i.e. late onset theta is that occurring after 20s or 10s respectively then there is still a significant association (increasing values but still $p< 0.05$).

Table 16: Theta onset vs. Imaging

	Theta onset ≤ 10s	Theta onset ≤ 20s	Theta onset ≤ 30s	Lateralised theta onset ≤ 30s
UHS	73 (55; 75%)	107* (85; 79%)	119* (94; 79%)	108 (86; 80%)
Lesion	14 (6; 43%)	24 (11; 46%)	27 (13; 48%)	17 (12; 71%)
Normal	9	19	21	16
Dual Pathology	7 (4; 57%)	9 (5; 56%)	10 (5; 50%)	10 (5; 50%)
BHS	4 (2; 50%)	6 (2; 33%)	8 (3; 38%)	6 (2; 33%)
Other	8	11 (1; 9%)	12 (1; 8%)	10 (1; 10%)
Total	115* (67; 58%)	176* (104; 59%)	197* (116; 59%)	167 (106; 63%)

* Significance level of at least $p<0.05$

The numbers in brackets are those patients who have proceeded to surgery, followed by the percentage.

Looking at subsets of the patients, the significant association between an early onset and proceeding to surgery is present only in those patients with UHS but not in any other imaging subgroup. Although there is an association between early theta and surgery in those patients with a temporal pathology this is due to the effect of the patients with UHS and it is not seen in patients with temporal lesions.

Looking only at those patients with UHS (the largest imaging subgroup), and again using different cut-off points, there is still a significant association with proceeding to surgery, if the theta occurs at or before 20 seconds but not if the cut-off point is 10 seconds.

In all of the patients with a single seizure type, if only the seizures with lateralised theta are considered, then the time of theta onset is not significantly associated with proceeding to surgery, however the combination of lateralised and early theta compared to non-lateralised and/or late theta is strongly associated with proceeding to surgery ($p<0.00001$). This combination is also significantly associated with proceeding to surgery in patients with UHS and those with a temporal pathology.

3.3.3 Duration of theta

Using the definition of sustained theta as being duration of 10 or more seconds, then when considering the total group of patients there was a significant association between the presence of sustained theta and proceeding to surgery ($p<0.00001$).

Within the imaging subgroups duration of theta of more than 10 seconds was associated with proceeding to surgery in those patients with UHS and in those with a lesion. Table 17 shows the duration of theta in the different imaging groups, with the number of patients proceeding to surgery.

Theta onset also showed a strong association in those patients with a temporal pathology as compared to those patients with an extratemporal pathology or more diffuse abnormalities.

Table 17: Duration of theta vs. imaging

	Total number of pts (Number & % of patients going to surgery)		
	Duration of theta<10s	Duration of theta ≥ 10 s	
UHS	44 (22; 50%)	110 (89; 81%)	*
Lesion	31 (9; 29%)	22 (14; 64%)	*
Normal	19	17	NS
Dual Pathology	11 (3; 27%)	9 (5; 56%)	NS
BHS	4	6 (3; 50%)	NS
Other	30 (9; 30%)	10 (2; 20%)	NS
Total	149 (43; 29%)	174 (113; 65%)	*

* Significance level of at least $p<0.02$

Unlike the time of theta onset, the duration of the theta was significant both independent of whether the theta was lateralised and in combination. Thus a combination of lateralised and sustained theta was strongly associated with proceeding to surgery.

3.3.4 Lateralised rhythmic theta

If all patients are considered regardless of their imaging abnormality, the presence of unilateral theta was significantly associated with proceeding directly to surgery. For these purposes lateralised theta is included whenever it occurred during the seizure, i.e. whether it was the first feature or occurred later in the seizure.

If the patients are divided by the location of their pathology there was a significant association between lateralised theta and proceeding to surgery only in those patients with a temporal pathology ($p<0.00001$).

If the patients are split into the different imaging groups, it can be seen that the association between lateralised theta and proceeding directly to surgery appears to be dependent on the imaging but in fact this probably reflects the location of the pathology, i.e. those patients with a temporal pathology are more likely to proceed to surgery.

Analysing the subgroups further, in the patients with UHS, the presence of lateralised theta is dependent upon a temporal type seizure (tTLE+aTLE), ($p<0.005$), i.e. in patients with UHS who have a non-temporal seizure the presence of lateralised theta does not predict proceeding directly to surgery. Looking at only those patients with a temporal pathology gives a similar result, i.e. the presence of a temporal type seizure (tTLE+aTLE) is necessary for lateralised theta to predict proceeding to surgery.

Table 18: Lateralised theta vs. imaging

	No lateralised theta (Number & % going to surgery)	Lateralised theta (Number & % going to surgery)	Significance
UHS	44 (23; 52%)	110 (88; 80%)	$p<0.001$
Lesion	33 (9; 27%)	20 (14; 70%)	$p < 0.005$
Normal	28	18	NS
Dual Pathology	9 (3; 33%)	11 (5; 45%)	NS
BHS	4 (1; 25%)	6 (2; 33%)	NS
Other	27 (8; 30%)	13 (3)	NS
Total	145 (44; 30%)	178 (112; 63%)	$p<0.00001$

3.3.5 Location of theta

The location of lateralised theta does not appear to have any significant association with whether a patient proceeds to surgery or not. It makes no difference if the comparison is between patients where the discharge is only seen at the temporal electrodes as compared to all other locations and combinations; or if the data is analysed by considering temporal and temporo-frontal together and comparing it to all other locations. However if the seizures are divided into those in which rhythmic theta occurs at the temporal electrodes alone or in combination with any other electrodes as compared to those seizures with no theta or only extratemporal theta, then there was a highly significant association with proceeding to surgery ($p<0.00001$). In addition there is no difference if all imaging groups are considered together or individually.

Table 19: Location of theta vs. imaging

	Location of rhythmic theta (Number of patients going to surgery)				
Imaging	No theta	Temp. theta	Temp+frontal theta	Temp +*	Frontal+**
UHS	31 (14)	23 (17)	36 (26)	60 (50)	4 (4)
Lesion	23 (8)	4 (2)	8 (5)	14 (7)	4 (1)
Normal	23	6	6	10	1
Dual pathology	8 (2)	1	3 (2)	8 (4)	
BHS	2	2 (1)	2 (1)	4 (1)	
Other	25 (8)	4 (2)	3 (1)	8	
Total	112 (32)	40 (22)	58 (35)	104 (62)	9 (5)

*- theta seen in temporal regions and any area other than frontal.

** - theta seen in frontal regions and frontal and other areas except temporal

Numbers in brackets are those patients who have proceeded to surgery

3.3.6 Rhythmic changes at onset

The initial EEG changes were analysed and divided into those patients who had a rhythmic change at the onset of the seizure, irrespective of the frequency of such a discharge and those where there were no rhythmic changes at the onset, the initial changes being either irregular, consisting of spikes or there was attenuation of the background activity.

Overall there was an association between the presence of rhythmic changes and proceeding to surgery ($p<0.05$). Looking at subsets of the patients in

those without UHS on their imaging this association remained but patients with UHS showed no such association i.e. if the patient had UHS then it did not make any difference if they had rhythmic changes at onset or not. If one considered only those patients with a temporal pathology or a temporal type seizure (tTLE+aTLE) there was no significant association between the initial changes and proceeding directly to surgery.

3.3.7 Bilateral changes

Whether the discharge became bilateral during the course of the seizure was considered and for the purposes of the analysis divided into those patients where bilateral changes occurred and those where was either no bilateral spread or the discharge was bilateral from the onset.

There was an association between the ictal discharge becoming bilateral and proceeding directly to surgery ($p<0.05$) if all the patients were considered. Subsets of patients, those with UHS, those with a temporal pathology and those with a temporal type seizure (tTLE+aTLE) showed no association between bilateral changes in the ictal discharge and surgery i.e. the association is due to patients with UHS having bilateral spread and patients with UHS being more likely to proceed to surgery.

3.3.8 Abrupt offset

Was there any association between the nature of the offset of the ictal discharge and whether the patient proceeded to surgery? As in 3.2 the offset was divided into those seizures that ended abruptly and those that did not.

When considering all of the patients there appeared to be no significant association between the type of offset and proceeding to surgery. If the subset of patients with UHS was considered then there was a significant association (Chi-squared $p<0.02$) between an abrupt offset and not proceeding to surgery. There was no similar association if one looked at

subsets of patients with temporal pathology or with temporal type seizures (tTLE+aTLE).

3.3.9 Post-ictal changes

Two aspects of the post-ictal changes were considered, firstly the localisation of the changes and secondly the nature of the EEG features. The localisation was divided into those changes that were ipsilateral to the seizure discharge or bilateral and those that were contralateral to the seizure discharge or it was not applicable as there were no changes. The type of post-ictal changes were divided into negative phenomena i.e. attenuation or asymmetry of the alpha activity and more the positive phenomena of slow or spikes.

There was a significant association between ipsilateral or bilateral post-ictal changes and proceeding to surgery ($p<0.02$). There was no difference between those patients with ipsilateral changes when compared to those with bilateral changes. Nor was the difference significant if subsets were considered, for example only patients with UHS or those with a temporal location to the pathology.

Looking at the group overall there was no clear association between the nature of the post-ictal changes and whether the patient proceeded to surgery. However if one looked at the subset of patients with UHS there was a significant association with those patients with slow or spikes being more likely to proceed to surgery (Chi-squared $p<0.05$).

3.3.10 Clinical seizure type

The clinical seizure type was then looked at with respect to whether the patient proceeded directly to surgery or not.

If a patient had a temporal type seizure, i.e. either a typical temporal (tTLE) or an atypical temporal type (aTLE) seizure then this was significantly associated with proceeding to surgery.

If the seizure types are divided further the patients with typical temporal type seizures (tTLE) are more likely to proceed to surgery ($p<0.00001$) than those with atypical temporal seizures (aTLE) ($p<0.002$). The table below shows the relationship between seizure type and proceeding to surgery.

Table 20: Seizure type vs. proceeding to surgery

	Direct to surgery	Not direct to or no surgery	Significance
tTLE	92	36	p<0.00001
aTLE	39	39	
tTLE vs. aTLE			*p<0.002*
tTLE +aTLE	*131*	*75*	*p<0.00001*
ETLE	7	54	
NonTLE/NonETLE	5	21	
Others	13	17	
Total	156	167	

3.3.11 Imaging

The data was analysed by comparing one imaging group with all the remaining patients with respect to proceeding directly to surgery. As before those patients who required intracranial studies before surgery were classified for these purposes as not proceeding directly to surgery.

The table below outlines the relationship between imaging and surgery, in those patients with a single seizure type.

The presence of UHS on a patient's scan was significantly associated with proceeding to surgery and normal imaging was associated with not proceeding to surgery. Having other, more widespread imaging abnormalities

(the group that included CD, post-op and diffuse changes on the MRI) was also associated with not proceeding to surgery.

Table 21: Imaging vs. surgery

	Direct to surgery	Not direct to or no surgery	Significance
UHS	111	43	p<.00001
Lesion	23	30	NS
Normal	0	46	p<.00001
Dual Pathology	8	12	NS
BHS	3	7	NS
Other	11	29	p<.005
Total	156	167	

In addition having a temporal location to the abnormality seen on the MRI, whether this was UHS, BHS or a lesion was also significantly associated with surgery when compared with those patients who had either a non-temporal pathology, or diffuse abnormalities ($p<0.00001$).

Comparing temporal with extratemporal pathologies only, i.e. excluding those patients with normal imaging or mixed pathologies, the presence of a temporal pathology was significantly associated with proceeding to surgery ($p<0.002$).

3.3.12 Logistic regression analysis

Just considering those patients with a single seizure type if all the various EEG ictal features and the seizure type are entered into a logistic regression analysis program, independent features that are predictive of surgery are found.

In all patients, the independent predictors are sustained theta (p=0.0002); a non-abrupt offset to the seizure (p= 0.008); a temporal type seizure, tTLE+aTLE, (p= 0.006) and UHS on the MRI (p= 0.006). There is a significant interaction (p=0.038) between a temporal type seizure and UHS on the chances of proceeding to surgery after adjusting for duration and offset.

Table 22, below, shows the interaction between imaging and seizure type and the number of patients proceeding to surgery. The combination of a temporal type seizure (tTLE+aTLE),and UHS on the imaging has an odds ratio of 6.2:1 with a 95% confidence interval of 2.5-15.6.

Table 22: Proportion of patients going onto surgery according to seizure type and UHS.

		Seizure type	
		Non-temporal Sz	Temporal type (tTLE+aTLE) Sz
Imaging	Not UHS	16/89 (18%)	29/80 (36%)
	UHS	9/28 (32%)	102/126 (81%)

It can be seen that having UHS and a temporal type seizure is significantly associated with and predictive of proceeding to surgery.

Repeating the analysis only on the patients with UHS, the independent predictive features are

(i) A non-abrupt offset, (an abrupt offset has an odds ratio of 0.14).

(ii) A temporal type seizure (tTLE+aTLE), with an odds ratio of 18.7.

Similarly in patients with temporal pathology, the independent predictive factors are

(i) A non-abrupt offset, (an abrupt offset has an odds ratio of 0.2).

(ii) A temporal type seizure (tTLE+aTLE), with an odds ratio of 23.5

(iii) Lateralised theta (odds ratio of 6.8)

(iv) The presence of UHS on the imaging, (odds ratio of 5.9).

3.4 Do any specific features from the video-telemetry predict a good outcome post-surgery?

3.4.1 EEG Features

Looking at the subset of patients who had a single seizure type the effect of various EEG and clinical features were considered as to whether they could predict a good outcome from surgery. A good outcome was defined as Engel class I or II and a poor outcome as Engel class III or IV (Engel J et al, 1993).

Initially just considering the EEG features and using chi-squared analysis there appeared to be no association between the following EEG features and a good outcome; the presence of lateralised theta ($p=0.187$); early onset of the rhythmic theta at or within 30 s ($p=0.053$); a duration of theta longer than 10s ($p=0.09$); the location of the theta ($p=0.258$); the presence of rhythmic changes at the onset of the seizure ($p=0.355$); whether the ictal discharge became bilateral ($p=0.338$); the type of seizure offset ($p=0.397$) or the type and location of any post-ictal changes ($p=0.296$ and $p=0.619$ respectively). However, of these, onset of rhythmic theta within 30 seconds is almost significant ($p=0.053$).

If the analysis is repeated including those patients with multiple seizure patterns then there is no association between post-operative outcome and the presence of sustained theta (duration greater than 10 seconds), the type of EEG changes at seizure onset, bilateral changes in the EEG, the type of seizure offset and the nature or location of any post-ictal changes. However the association between the presence of theta (lateralised or bilateral) within 30 seconds of the seizure onset and outcome becomes significant ($p=0.029$).

Table 23: Association between theta onset and post-operative outcome

		Theta≤ 30s	Theta >30s	
Single sz type				
	Engel Class I/II	94	30	
	Engel Class III/IV	27	17	NS p=0.053
Multiple and single sz type				
	Engel Class I/II	100	31	
	Engel Class III/IV	27	18	*p=0.029

Schultz et al (2000) have reported that bilateral spread of the discharge during a seizure in patients with UHS is a predictor of outcome. Our findings did not support this result. This is possibly due to the definition used by Schulz where in their study bilateral spread meant a switch of lateralisation or asynchrony whereas the analysis here considered any ictal EEGs where there was a contralateral discharge, synchronous or asynchronous. Although bilateral spread was associated with the finding of UHS on the imaging, there did not appear to be any significant association between bilateral spread and outcome. This was true whether only those patients with UHS and a single seizure type or those with multiple seizure types were considered.

Table 24: Bilateral spread and outcome (patients with UHS)

		Discharge becomes bilateral	No bilateral changes or no change/not applicable	
Single sz type				
	Engel Class I/II	58	35	
	Engel Class III/IV	16	6	NS p=0.3
Multiple and single sz type				
	Engel Class I/II	62	35	
	Engel Class III/IV	16	7	NS p=0.4

3.4.2 Clinical seizure type

Again just considering those patients with a single seizure type, having a temporal type seizure (i.e. either a typical or atypical temporal seizure) was significantly associated with a good outcome ($p<0.0005$). There was, however, no significant difference between those patients with a typical temporal type seizure, tTLE, compared to those with an atypical temporal seizure, aTLE. Table 25, below shows the outcome of patients against type of seizure.

Looking at patients with multiple and single seizure types there is still a significant association between a temporal lobe type seizure (typical and atytpical) and good post-operative outcome ($p<0.001$).

Table 25: Post-op outcome vs. Seizure type

	Good post-op outcome	Poor post-op outcome	Significance
TTLE	75	18	
ATLE	32	9	
tTLE vs aTLE			*NS*
tTLE +aTLE	*107*	*27*	*p<0.0005*
ETLE	5	7	
NonTLE/NonETLE	3	5	
Others	9	5	
Total	124	44	

3.4.3 Imaging and Location of pathology

Having UHS on the MRI was also significantly associated with a good outcome from surgery ($p<0.005$). None of the other imaging groups when compared in turn to the remaining patients showed any significant association with post-operative outcome. Table 26, below shows the numbers of patients with a good and poor post-operative outcome within each imaging group.

Table 26: Post-op outcome vs. imaging

	Good post-op outcome	Poor post-op outcome	Significance
UHS	93	22	P<0.005
Lesion	15	12	
Normal	2	1	
Dual pathology	5	3	
BHS	3	1	
Others	6	5	
Total	124	44	

Analysing the data for those patients with single and multiple seizure type shows a similar significant association between UHS on the MRI and post-operative outcome, ($p<0.005$). There was no other significant association with MRI defined pathology and outcome.

Looking in more detail at those patients with a single seizure type, having a temporal location to the pathology i.e. those patients with UHS, BHS and temporal lesions was associated with a good outcome ($p<0.01$). If the patients with normal imaging were excluded from the analysis and outcome was compared between those patients with a temporal and an extratemporal pathology, the significance level increases to $p<0.005$ of a temporal pathology being associated with a good post-operative outcome. There was no difference when right and left temporal pathologies were compared with outcome.

Considering those patients with a single seizure type who had UHS and a temporal type seizure (tTLE+aTLE) these patients were twice as likely to have a good outcome as those patients who had neither of these features. The table below shows the interactions between imaging and seizure type and the number of patients with a good outcome.

Table 27: Proportion of patients with a good outcome according to seizure type and UHS

		Seizure type	
		Non-temporal Sz	Temporal type (tTLE+aTLE) Sz
Imaging	Not UHS	9/23 (39%)	22/30(73%)
	UHS	8/11 (72%)	85/104 (82%)

3.4.4 Interactions between EEG and Clinical features with respect to outcome

Using logistic regression to analyse multiple EEG and clinical features against post-operative outcome, there was only one EEG feature that was significantly predictive of a good outcome i.e. Engel Class I or II. An early onset of theta i.e. rhythmic theta occurring at or before 30 s of the seizure onset irrespective of the duration provided it was longer than 2 seconds, did appear to be significantly predictive of a good outcome ($p<0.05$) with an odds ratio of 4.8, when all patients with a single seizure type were considered.

The same factor was found to be independently predictive of a good outcome if the logistic regression was repeated on those patients with both single and multiple seizure types. That is the onset of theta (lateralised or bilateral) within 30 seconds of the seizure onset was significant at $p=0.05$, with an odds ratio of 3.5:1.

Analysing in more detail those patients with a single seizure type, if only the patients with UHS are considered then an early onset of theta is not a predictor but duration of theta of more than 10 seconds was a significant predictor of a good outcome ($p<0.05$). If the patients with a multiple seizure type are included, theta of more than 10 seconds is not significantly predictive ($p=0.055$). The table below shows the relationship between duration of theta and outcome in patients with a single seizure type and UHS.

Table 28: Duration of theta vs. outcome.
(Patients with UHS and single seizure type)

	Post-operative outcome Engel Class I to IV					
	I	II	III	IV	No surgery	No follow-up
Non-sustained theta <10s	15 (34%)	3 (7%)	5 (11%)	1 (2%)	18(41%)	2(5%)
Theta ≥ 10s	65(59%)	10(9%)	15 (15%)	0	18(16%)	1(1%)
Theta ≥ 20s	50(53%)	7 (7%)	12(13%)	0	24(25%)	2 (2%)
Theta ≥ 30s	20(67%)	0	6(20%)	0	4(13%)	0

This table shows that there is no duration of theta that ensures a good outcome post-operatively. The percentage of patients with a Class I outcome remains similar whether the cut off point for the theta duration is 10 or 20 seconds, and although there is an increase if a duration of 30 seconds is used there are much smaller numbers involved. This table also adds support to the choice of 10 seconds as a suitable duration to represent sustained theta within a seizure. Using 10 seconds as a cut –off, just over half the patients have a Class I outcome and half do not.

As a duration of theta for 10 or more seconds is also significantly associated both with UHS on the imaging and a temporal type seizure (tTLE+aTLE) it is possible that the duration of theta is not adding any extra information in predicting a good outcome. The table below shows that if only patients with UHS and a temporal type seizure are considered then the percentage of patients with a good outcome with either sustained (10 or more seconds) or not sustained theta is not significantly different. The results are similar if patients with both single and multiple seizures are analysed or just single seizures. Similarly looking at patients with UHS and temporal type seizures (tTLE+aTLE) there is no significant association between a good or poor post-operative outcome and the presence or absence of lateralised rhythmic theta.

Table 29: Outcome vs. theta duration
(patients with UHS and temporal type seizures)

	%good outcome (Engel class I/II)	
Sustained theta (≥10s)	84%	NS p=0.12
Non-sustained theta (<10s)	70%	

Dividing the data from patients with a single seizure type by the imaging group did not reveal any other significant predictive features for the groups other than the UHS group as detailed above.

The combination of UHS on the imaging and temporal type seizure (tTLE+aTLE) although not independently predictive of a good outcome do show a significant association with a good outcome, the odds ratio of a patient having a UHS and a temporal seizure is nearly 7:1 in comparison to patients with neither of these features. A similar odds ratio can be seen if all patients with seizures are considered i.e. both single and multiple seizure types.

Thus there are some features that do help in predicting a good post-operative outcome. Having either UHS or other temporal pathology on the MRI, or having a temporal type seizure makes a good outcome more likely and while the individual EEG features do not appear significantly associated, an early onset of rhythmic theta is significantly predictive of good outcome. Early onset theta is also associated with temporal type seizures (tTLE+aTLE) and UHS.

If considering only those patients with a single seizure type and UHS then a sustained duration to the theta is predictive of a good outcome, but if the patients with multiple seizure types are included a sustained duration of theta is not significantly predictive.

3.5 Does Video-EEG telemetry provide any novel information?

The unexpected findings or other novel information that is gained from video-telemetry can be divided into four main categories: Recording NEAs during the video-EEG telemetry; Clinical seizure type being discordant with the pathology; Ictal EEG discharge being discordant with the pathology and multiple clinical seizure types. The recording of NEAs usually affects patient management with patients being referred for psychological therapy. If the NEAs respond to treatment patients may then sometimes proceed to surgery if the epileptic seizures remain refractory (Henry and Drury, 1995). The significance of the other three categories is less certain. The unexpected video-EEG telemetry findings could represent a true alternative localisation of the epileptogenic zone or raise false concerns because they instead represented seizure propagation. The former scenario would lead to the patient either being correctly rejected from the surgical program or correctly having surgery at a site distant to the MRI defined abnormality (with or without intervening intracranial monitoring). The latter scenario could lead to the patient unnecessarily undergoing intracranial EEG monitoring with the attendant risks and delays, having surgery at an inappropriate site, or being falsely rejected from the surgical program. Which of these is the basis for the novel findings can only be determined in those patients who either undergo intracranial monitoring or surgery. The results from these measures are therefore included for each group in the results below.

3.5.1 Recording non-epileptic attacks (NEAs) or pseudoseizures during the video-telemetry

There were only 12 of the 400 patients who had non-epileptic attacks. This represents 3.3% (12/362) of all patients in whom we recorded clinical events (both single seizure and multiple seizure type and NEAs). Four of these 12 had UHS i.e. only 2.3% (4/173) of patients with UHS in whom clinical events were recorded.

Overall seven of the twelve patients had a mixture of NEAs and seizures, with the epileptic seizures being clearly documented on either the same admission as the NEA or during a subsequent admission to the unit. Table 30, below gives some details about the patients with NEAs.

Table 30: Patients with NEAs

Type of attacks	Imaging (No. of pts	Surgery (No. of pts)
NEA only	Lesion: 2 Unilateral HS: 2 Normal: 1	0
NEA + tTLE	Unilateral HS: 2 Normal: 1 Dual pathology: 1	0
NEA+aTLE	Other: 1	0
NEA+ETLE	Normal: 1	0
NEA + Other	Dual Pathology: 1	1

Only one of these patients has proceeded to surgery. This was a patient with dual pathology on the MRI, widespread cognitive abnormalities and an IQ of approx. 70 who had seizures with rapid generalisation, and a prolonged period of apnoea with presumed substantial risk of SUDEP.

Of the remaining patients four of these had below average FSIQ and six had some psychological problems or an anxious personality that might have indicated problems prior to the video-telemetry.

With the patients in whom we recorded both epileptic and non-epileptic attacks the clinical semiology of the onset was similar in three of them. In the most of the remaining four cases the patients were unable to distinguish

between the two types of seizures even though the semiology was quite different.

3.5.2 Clinical seizure type discordant with the pathology

Fifteen patients had clinical seizure semiology clearly discordant from the pathology as determined by the MRI. This represents 5.5% (15/272) of all patients with an MRI abnormality in whom a single type of seizure was recorded (i.e. excluding those patients with NEAs and multiple seizure types).

There were 12 patients who had a temporal pathology (either HS or a temporal lesion) and extratemporal clinical seizure semiology, and 3 patients who had extratemporal pathology and a temporal type seizure (1 had typical temporal seizures, tTLE, and 2 patients had atypical temporal seizure, aTLE, (in each case with just one of the features normally associated with a temporal type seizure but no features to suggest an extratemporal seizure). By using the definition, described in the methods section, of typical temporal seizures (tTLE) and atypical temporal seizures (aTLE) there is a clear distinction from an extratemporal seizure.

5/12 patients with an extratemporal type seizure and temporal pathology had UHS, i.e. 2.89% (5/173). The remaining seven patients had a temporal lesion.

0/15 patients proceeded directly to surgery and 1/15 proceeded following an intracranial study. In this patient the intracranial video-EEG telemetry confirmed that the area of the lesion was epileptogenic and following a lesionectomy the patient has had a good outcome with occasional simple partial seizures.

A clinical seizure type discordant from the imaging could reflect either early cortical spread, and a wider area of involvement in the epileptogenic process than is indicated by the imaging alone, or non-overlapping functional and anatomical abnormalities. However in this study evidence from intracranial studies was available in only one patient and demonstrated that the clinical

seizure semiology was misleading and given a good post-operative outcome following a lesionectomy probably represented cortical spread. The true localisation in the remaining 14 patients is unknown.

3.5.3 Ictal EEG discharge discordant with the pathology

In those patients with a single seizure type there were 12 patients where the rhythmic theta seen during the ictal discharge was discordant with the pathology. None of the other ictal features studied in detail showed clear discordance with the imaging defined pathology. This represents 4.4% (12/272) of the group of patients with an imaging abnormality and where a single seizure type was recorded. All but two of the patients fell into the UHS group; the proportion of cases in this group was therefore 10/152 or 6.6%.

2/12 patients had an intracranial study and in both cases proceeded to surgery. In each case the intracranial study confirmed the localisation of the epileptogenic zone expected from the MRI finding and post-operative outcome in one patient is good, i.e. Class II, the other patient has been lost to follow-up.

4/12 patients proceeded directly to surgery. In each case the operation, either a temporal lobe resection for those patients with UHS or a lesionectomy for the remaining patient, was determined by the site of the MRI abnormality rather than the scalp ictal EEG. Two patients had a good outcome (Engel Class I/II) and two had a poor post-operative outcome (Engel Class III/IV). These findings are summarised in Table 32, together with some of the associated ictal EEG features.

Table 31, below, summarises the differences between these patients with discordant rhythmic theta and those with either concordant or bilateral theta with respect to outcome. Three of the six patients with frankly discordant theta had a good outcome (and one was lost to follow-up) from surgery at the site of the MRI abnormality. None of the patients with discordant scalp EEG findings had surgery at the site of the scalp ictal EEG localisation.

Table 31: Lateralisation of rhythmic theta and outcome

	Number of patients	Number proceeding directly to surgery	Number having surgery after SEEG	Good outcome
Discordant theta	12	4	2	3/5* (60%)
Concordant theta	166	108	3	84/108** (78%)
Bilateral theta	32	11	3	10/14 (71%)

* 1 patient was lost to follow-up; ** 3 patients lost to follow-up

There were two patients with right sided pathology (Rt HS) and left sided rhythmic theta and 10 patients with left sided pathology (1 dual pathology – both abnormalities on the same side; 1 lesion and 8 Lt HS) and right sided theta. There was a mixture of clinical seizures types, but more than half (7/12) had either a tTLE or aTLE seizure.

The table (No. 32) below shows the important ictal EEG clinical features of the patients who proceeded directly to surgery or following an intracranial study with this discordant data. Looking at the patients who proceeded directly to surgery in more detail, it can be seen in two of them the lateralised theta was only just sustained at 11s (the definition of sustained theta being a duration of 10 or more seconds), in one patient with sustained and discordant theta there is a change in side after only 16s and this patient has had a good outcome. The remaining patient, (pt 3 in table 32), had features that might be expected to predict a good outcome (temporal lobe seizure and sustained, lateralised rhythmic theta) if the rhythmic theta had been concordant with the imaging abnormality. This patient did not have a good outcome.

Table 32: Ictal features in patients proceeding to surgery with discordant data

Patient/pathology	Rhythmic theta	Sustained theta	Seizure type	Ictal evolution	Post-op outcome
1/Lt UHS	Rt – not first feature/nor evolving	Y – 11s	tTLE	No bilateral changes	III/IV
2/Lt UHS	Rt – evolves from 1st feature	Y – 11s	aTLE	No bilateral changes	I/II
3/Lt UHS	Rt - evolves from 1st feature	Y –37s	tTLE	Becomes bilateral	III/IV
4/Lt temp lesion	Rt – not first feature/nor evolving	Y- 65s	aTLE	Becomes bilateral + changes side at 16s	I/II
*5/Lt UHS	Rt - evolves from 1st feature	Y-19s	aTLE	Becomes bilateral	No follow-up
*6/Lt UHS	Rt– not first feature/nor evolving	Y- 25s	NonTemp/non extratemp	Becomes bilateral	I/II

* patients 5 and 6 were the two patients who had an intracranial study before definitive surgery.

In 4/12, there was rhythmic lateralised theta, which was either the first feature or evolved from it, and the theta was sustained. 4/12 had theta that was either first or evolved from first change but the activity was either not sustained or only just over 10 seconds in duration. In the remaining 4/12 of them, the theta activity was either not an early phenomena or not sustained.

3.5.4 The presence of multiple electroclinical seizure types

In total there were 34 patients where there was more than one type of electroclinical seizure type. These included 7 patients with NEAs and epileptic seizures (these have been discussed in section 3.5.1); 4 patients who had different clinical seizure semiology; and 23 patients where there was a difference in the scalp ictal EEG pattern. As discussed in the earlier methods section the majority of the analysis was carried out on the patients with a single seizure type but for all the key features the analysis was repeated to include these patients with multiple seizure types.

There were 4 patients who had clinically different seizure types, three of whom had UHS and the remaining patient had dual pathology on MRI. That is multiple clinical seizure types represented 4/362 or 1.1% in the group in whom a clinical event was recorded and 3/173 or 1.73% in the UHS group.

In all four of the patients one of the seizures was either a typical temporal lobe type seizures (tTLE) or atypical temporal (aTLE) and the other clinical seizure types varied. It is not surprising that the patient with dual pathology might have more than one clinical seizure type when both areas of abnormality are potentially epileptogenic, similarly a small proportion of patients with UHS may have more than one seizure type due to different patterns of ictal spread or multiple areas of ictal onset.

Of these four patients with differing clinical seizure semiology, the outcome following video-EEG telemetry was as follows:

- 1 patient proceeded directly to surgery – this patient had dual pathology, UHS and extrahippocampal abnormalities within the same temporal lobe. The patient had a temporal lobe resection for the UHS and subsequently has had a good post-operative outcome.

- 1 patient proceeded to surgery following an intracranial study. This patient showed both multiple clinical seizure semiology and different ictal EEG patterns on the scalp video-EEG telemetry. The intracranial study confirmed the findings of the scalp video-EEG telemetry, of more widespread areas of epileptogenicity than those normally associated with UHS both from the ictal EEG features and clinical seizure semiology, and the subsequent surgery was to remove the EEG defined area of abnormality not the MRI abnormality. This patient has subsequently had a poor post-operative outcome.

- 2 patients were rejected from the surgical program, without any further investigation.

2/4 patients proceeded to surgery, 1 had a good outcome and 1 a poor outcome.

In the remaining 23 patients the seizure semiology was consistent within an individual patient whilst the ictal EEG pattern differed.

These differences in ictal EEG patterns was varied and the significance uncertain.

- 6 patients had lateralised rhythmic theta in one seizure and no rhythmic theta in another.
- 1 patient had bilateral theta in one seizure and no rhythmic theta in another seizure.
- 2 patients had bilateral rhythmic theta in one seizure and lateralised rhythmic theta in another seizure.
- 3 patients had bilateral independent rhythmic theta in different seizures

- 1 patient had right sided rhythmic theta in one seizure, left in another and bilateral rhythmic theta in a third seizure.
- The remaining 10 patients showed different patterns of evolution, time of onset of rhythmic theta and the relative order of the features seen within the seizure.

3/23 proceeded to an intracranial study, and 2/3 of these patients then proceeded to surgery. The remaining patient died in a seizure between the intracranial study and surgery, which had been recommended.

- In 2 patients the intracranial study confirmed the MRI abnormality as the epileptogenic lesion.

- In 1 patient the imaging was normal and thus the intracranial study was necessary to identify rather than confirm the area of epileptogenesis.

5/23 patients proceeded directly to surgery. In each case the surgical procedure was carried out on the MRI defined abnormality.

The outcome of the 8 patients who either proceeded directly to surgery or following an intracranial study was: -
1 patient with an MRI abnormality was lost to follow-up;
6/6 patients with an MRI abnormality had a good post-operative outcome;
1 patient with a normal MRI had a good outcome.

3.5.5 Summary of novel data from video-EEG telemetry

Table 33, below shows the numbers of patients in both the overall group and those patients with UHS, who had the different types of novel data. Groups (a), (b), (c) and (d) are mutually exclusive.

Table 33: Types of novel data gained from video-EEG telemetry
in the total group and in the subset of patients with unilateral hippocampal sclerosis

	Total group	UHS group only
(a) Recording NEAS	12	4
(b) Clinical sz type discordant with pathology	15	5
(c) Ictal discharge discordant with pathology	12	10
(d) Multiple sz types	27	15
Multiple clinical sz types	*4*	*3*
Different EEG patterns	*19*	*10*
Bilateral independent EEG	*4*	*2*
Total	66	34

Considering the groups where there was novel information gained from the video telemetry other than those with NEAs, there were 54/362 or 15% in the total group and in the patients with unilateral hippocampal sclerosis 30/173 or 17%. It is not possible without evidence from either an intracranial study or post-surgical outcome to confirm or refute whether this information represents a false positive finding which may have disadvantaged the patient. The table below summarises the findings, using the groupings defined above. It should be noted that in the group of patients with multiple seizure types only those patients with frankly and consistent discordant data or normal imaging are included when attempting to determine the efficacy of scalp video-EEG telemetry in identifying the correct localisation.

Table 34: Summary of novel information

	Surgery based on MRI	Surgery based on scalp video-EEG telemetry	Correct localisation from scalp video-EEG telemetry	Incorrect localisation from scalp video-EEG telemetry
(b) Clinical sz type discordant with pathology	1	0	0	1*
(c) Ictal discharge discordant with pathology	6	0	2**	3*
(d) Multiple sz types	7	2***	1**	3*
Total	14	2	3	7

*based on intracranial findings and post-operative outcome

** based on poor post-operative outcome

*** one of these operations was on a patient with normal imaging.

The number of times that the scalp video-EEG telemetry findings provide useful information are made up of two elements

(i) The number of patients where the imaging was normal, the scalp EEG allowed an intracranial study to be performed and the outcome was good, i.e. the site of surgery was determined by the EEG not the MRI (n=3). This number relates to findings from the normal imaging group overall not just those with novel data.

(ii) The number of patients in whom there was discordance between the EEG and MRI, surgery is carried out on the MRI abnormality and there is a poor post-operative outcome (n = **2**). These are the two patients in group (c) where the EEG was discordant with the MRI.

It can be seen that these are very small numbers, 5 in total, 3 patients with normal imaging and 2 with UHS. In the patients with UHS this represents approx. 10% (2/23) of the patients with a poor post-operative outcome.

Performing an intracranial study can give the information needed to determine whether this novel and apparently discordant information is correct. A brief description and discussion of the patients from the study group who have had intracranial studies follows in section 3.5.6.

3.5.6 Intracranial studies

There were 28 patients in this study group in whom, following the scalp video-EEG telemetry, intracranial studies were performed. A further 15 patients were recommended to undergo intracranial studies following the scalp telemetry or this was a possibility once other non-invasive tests had been completed. These patients were all still considering whether to proceed or had declined this option.

Of the 28 patients in whom intracranial studies were performed, 11 patients had predominantly subdural strip or grid recordings, usually placed over a lesion, with the study being carried out for the dual aim of ascertaining from where the seizures originated and mapping eloquent cortex. The remaining 17 patients had depth implantations tailored to suit the clinical question. Table 35, below gives details about the patient's imaging and type of study.

Table 35: number of intracranial studies vs. imaging

MRI findings	Number of patients	No. proceeding to surgery
UHS	10	9* (90%)
Lesion	6 (all grids)	6 (100%)
Normal	6 (1grid)	4 (66.7%)
Dual Pathology	1 (1 grid)	1 (100%)
BHS	2	1 (50%)
Other	3 (all grids)	2 (66.7%)
Total	**28**	**23 (82%)**

* All UHS patients had been recommended to have surgery, one patient died between the intracranial study and surgery

It is not the aim of this study to include detailed discussion of the findings from these intracranial recordings, although their subsequent outcome is included in the overall analysis. However the rationale for suggesting the intracranial study in a proportion of the patients was a direct result of the findings of the scalp telemetry providing discordant information.

Of the patients with UHS, 4/10 had ictal scalp EEG findings discordant with the imaging; 4/10 had no rhythmic theta in the ictal discharge and the EEG pattern was thought not to represent a typical temporal (lateral or mesial) electrographic discharge but to indicate either a more widespread or extratemporal area of epileptogenicity. Of the remaining two patients one had bilateral and non-sustained theta and the other rhythmic theta, which met the criteria for sustained theta (with a duration of 14s) but the theta swapped sides during the seizure.

Each patient usually had more than one reason for proceeding to an intracranial study. Table 36 below lists the major reasons.

Table 36: Reasons for intracranial study

Reason for SEEG study	No. of patients
Discordance between ictal EEG and MRI	4
No rhythmic theta or other ictal EEG pattern of TLE szs	4
Wide field/bilateral/or non-sustained theta	4
Not TLE clinical pattern (as defined in methods)	6
Mix of Sz types (EEG or clinical)	3

In the patients with the subdural grid recordings the information from the scalp telemetry allowed the SEEG study to proceed i.e. the information obtained from the scalp video-EEG telemetry was not discordant. In all the patients with an imaging abnormality the grid was placed over the lesion, the epileptogenicity of the lesion confirmed and if appropriate functional mapping was carried out. In the majority of these cases the intracranial study would have been a strong possibility from the outset of the surgical assessment. In the patient with normal imaging and a subdural grid recording the placement was determined on electroclinical information from the scalp telemetry.

In 12/17 studies there were bilateral implantations of depth electrodes in the mesial temporal structures. This included 2 patients with bilateral HS and 10 with unilateral HS. The patients with bilateral HS also had bilateral problems on their psychometric testing, and in one patient although the electroclinical pattern was lateralised and would have fitted for a typical mesial temporal profile the interictal EEG abnormalities were bilateral and the volumetric analysis of the MRI did not show a clear difference between the two hippocampi. In the other patient with bilateral HS there was not a typical mesial temporal semiology to his seizure nor were there any lateralising features in the ictal EEG.

The remaining 5 patients who had bilateral depth studies all had normal imaging and the scalp telemetry was helpful in providing information from the electroclinical pattern that allowed the study to be planned.

The reasons why five patients were rejected following the intracranial study are briefly outlined below: -

The 2 patients with normal imaging; they were both found to have multi focal EEG onsets to their seizures, and in the absence of any imaging abnormality it was felt impossible to proceed any further.

The patient with bilateral HS; this patient had bilateral independent onsets to the seizures recorded with intracranial electrodes.

The remaining patient had had a previous neurosurgical procedure and at the time of the intracranial study it was found that the area of epileptogenicity was widespread and involved eloquent cortex making any further intervention inadvisable.

It should be noted that in 9/10 of the patients with unilateral HS who had intracranial studies, the findings from these studies confirmed or supported the MRI data and all (i.e. 10/10) were recommended to proceed to surgery. In 2/10 of the patients the intracranial study provided evidence for a wider area of epileptogenicity and one patient had a temporal lobe resection with the proviso of reduced odds of a good outcome and the other patient had a frontal lobe resection.

Of the patients with UHS 9/10 have subsequently had surgery and the outcome is good (Class I/II) in 6 patients, and less favourable in 2 patients. No follow-up was available for the remaining patient. In 9/10 of the UHS patients the surgery carried out (or proposed to be carried out) following the intracranial telemetry was on the side of the hippocampal sclerosis, therefore despite apparently discordant scalp ictal features the end result was an operation on the side indicated by the MRI. The novel information thus

obtained on these 9 patients did not ultimately change the operative procedure, and indeed prolonged the investigative process. In one case this led to the unfortunate result that a patient died during a seizure whilst awaiting surgery following the intracranial study.

3.6 Reasons why patients did not proceed to surgery - with particular with reference to the UHS group.

The reasons why patients do not proceed to surgery have, in essence, been discussed in 3.5 where the discordant findings from video-telemetry have been outlined. In the UHS group, which as can be seen from the previous sections in the results, are more likely to proceed to surgery and subsequently have a good outcome it is perhaps important to highlight the reasons why a third of these patients did not proceed to surgery. Table 37, below shows the reasons in the majority of cases, although it can be seen that there remains a small core of patients in whom it was their personal choice not to proceed either to surgery or to further investigations, their decision being based on information provided from all of the pre-surgical tests.

Table 37: Reasons for not proceeding to surgery in UHS pts

Reasons for not proceeding to surgery	No. of patients
Had no Szs and improved control or did not wish to proceed further	15
Had NEA or NEA+Szs recorded	4
Ictal discharge discordant with pathology and no further tests	5
Multiple electroclinical sz types	9
Discordant clinical Sz type	13
Patient died before surgery performed	1
Surgery recommended but pt declined either because of risk/benefit or improved Sz control	11
Various reasons including ongoing psychiatric and psychosocial reasons for not proceeding either to surgery or further investigations	7
	65

The reasons for not proceeding to surgery are similar in the remaining imaging groups; in many patients there is insufficient information to allow either a surgical procedure or at this time to plan an intracranial study. Some of the patients remain under review by the epileptologists and further studies may be undertaken if and when more information is obtained from novel imaging techniques that are under development. As with the UHS group of patients, in some the option to proceed to surgery or intracranial studies was declined due either to improved seizure control or the patient's concern about the risk/benefit ratio.

Table 38, outlines some of the reasons for not proceeding to surgery in the imaging groups other than UHS.

Table 38: Reasons for not proceeding to surgery

Reasons for not proceeding to surgery	No. of patients	Total
Had no Szs and improved control or did not wish to proceed further	Lesion: 6;Normal: 5; Dual Path: 3;Others: 5	19
Had NEA or NEA+Szs recorded	Lesion: 2;Normal: 3; Dual Path: 1;Others: 1	7
Ictal discharge discordant with pathology and no further tests	Dual Pathology: 1	1
Multiple electroclinical sz types	Lesion: 1;Normal: 4; Dual Path: 2;Others: 1	8
Discordant clinical Sz type	Lesion: 7; Dual Path: 2	9
Patient died before surgery performed	Lesion: 1	1
Various reasons including ongoing psychiatric and psychosocial reasons for not proceeding either to surgery; pt declining because of the risk/benefit ratio; improved sz control and insufficient evidence to plan an intracranial study.	Lesion: 16; Normal: 43; Dual Path: 8; BHS: 6; Others: 27.	100
		139

Chapter 4: Discussion

4.1 Review of the findings

4.1.1 Features from the video-EEG telemetry recording linked to pathology.

Firstly the results were analysed to see if there were any specific features that were significantly associated with different imaging abnormalities and whether these features were able to discriminate between the imaging groups.

Thus early, sustained and lateralised theta was found to be significantly associated with unilateral hippocampal sclerosis. The presence of lateralised theta at any time during the ictal discharge is more commonly seen in those patients with UHS than those with a temporal lesion, , i.e. the presence of lateralised theta was significantly associated with UHS but not with a temporal lesion. This finding is in broad agreement with other studies (Risinger et al, 1989). Risinger looked at the scalp ictal recordings from 110 patients who then had intracranial recordings and found that the presence of a 5Hz or faster rhythm at one sphenoidal electrode or temporally located electrode correctly predicted the temporal depth onset in 82% if the cases This association occurred regardless of whether it was the first or a delayed onset provided that the rhythmic theta was seen within 30 seconds of the seizure onset. A recent review article by Sadler and Desbiens (2000) reviewed the scalp ictal EEG features in temporal lobe epilepsy and states the consensus view of " a lateralised ictal change variably described as 'rhythmic 5-10 Hz sharp activity', a ' 5 cycles/second (or faster) rhythm maximum at a sphenoidal or temporal electrode position' or 'rhythmic theta-alpha' occurs within 30-40 seconds of seizure onset in 52-80% of patients. This pattern has a high specificity for TLE". These results were obtained from studies where the ictal EEG localisation was compared with either subsequent intracranial studies or post-operative pathology and seizure freedom (Walczak et al 1992, Williamson et al 1993, and Risinger et al 1989). Therefore the results here

confirm these earlier reports using the marker of preoperative high quality MRI rather than post-operative pathology or intracranial recordings.

In contrast the finding that rhythmic theta recorded specifically from electrodes over the temporal regions was not significantly associated with UHS was unexpected. This may be explained by the strict criteria used in the analysis. If rhythmic theta only occurred at temporal or fronto-temporal electrodes (standard electrodes Fp2, F8, T4 and right superficial sphenoidal or the homologous electrodes on the left), there was no significant association with UHS ($p=0.35$). However if one considered seizures with rhythmic theta at either the temporal electrodes alone or in any combination with other electrodes and compared them with seizures where was no theta or theta at only extratemporal electrodes, then there was a highly significant association with UHS ($p<0.00001$). This would be in keeping with previous studies mentioned above, where the presence of temporal theta has been found to be highly indicative of a temporal seizure or temporal location to the pathology. In those studies however the exact topography of the rhythmic theta is less clear. In Walczak's study he distinguishes between temporal, parasaggital and diffuse rhythmic theta, but does not distinguish between seizures where rhythmic theta is seen exclusively in those areas or in some combination e.g. fronto-temporal or centro-temporal. The present study therefore clarifies the earlier reports by demonstrating an association between rhythmic temporal theta and mesial temporal pathology (UHS) when a broader definition of temporal location is used but not with more limited criteria i.e. just temporal and fronto-temporal rhythmic theta. The importance of this finding can be seen for example when considering the ictal recordings of patients where rhythmic theta over more posterior temporal electrodes in addition to mid temporal electrodes is seen and is then often thought to be indicative of a more widespread pathology than isolated UHS. The reason for this finding is most likely due to the inherent difficulties in accurately determining the neuronal generators from the information obtained from the distantly located scalp electrodes (Gloor, 1985).

In this study comparing the location of theta with a temporal type seizure showed a similar distinction, i.e. a temporal type seizure was associated with temporal theta if all seizures with any temporal theta were compared to those where there was no theta or extratemporal theta only. Whereas if the comparison was carried out with temporal and fronto-temporal theta only then there was no association between temporal theta and a temporal type seizure.

A temporal type seizure was also significantly associated with UHS. If the temporal seizures were divided into those that were typically temporal and those that were atypical, a typical temporal seizure was still significantly associated with UHS albeit with a reduced level of significance ($p<0.000001$ compared to $p<0.0005$). In addition, dividing the clinical seizures into typical temporal and atypical allowed a distinction to be made between those patients with temporal lesions and those with UHS. This is not an unexpected finding; the features used when defining the typical temporal seizures are those features thought to be associated with more mesial temporal pathology in comparison to the atypical seizures which occur in patients who were more likely to have a lateral temporal pathology. The criteria used in this study to distinguish between typical and atypical temporal seizures was based on the number of features seen during the seizure; three or more of the features usually thought to be associated with temporal lobe seizures, for a typical temporal seizure and only one or two of the features for an atypical seizure. In Walczak's (1995) review of neocortical temporal lobe epilepsy he contrasts the ictal semiology of mesiobasal temporal lobe epilepsy and lateral temporal (neocortical) epilepsy. Distinctive characteristics are lacking in neocortical temporal epilepsy, with rare epigastric auras, and the significantly less frequent occurrence of ipsilateral limb automatisms, contralateral dystonic posturing and oro-alimentary automatisms.

With the other imaging groups in this study any of the ictal EEG features that are associated with individual pathologies represent the opposite of those features associated with UHS and thus are neither providing any new information nor do they allow discrimination between the other groups. The

only exception was that of the mixed imaging group where there was a significant association ($p<0.05$) with a non-rhythmic onset to the seizures. This is perhaps not unexpected as this group represents a mixed collection of different pathologies.

4.1.2 Features from the video-EEG telemetry recording linked to proceeding to surgery.

Looking at all of the variables which were analysed for predictors of proceeding directly from scalp video-EEG telemetry to surgery, the patients most likely to proceed to surgery were those with sustained rhythmic theta, a non-abrupt offset to the seizure discharge, a temporal type seizure and UHS on the MRI.

If a patient had the combination of a temporal type seizure and UHS, the odds ratio of proceeding to surgery is 6.2:1 (with a 95% confidence interval of 2.5-15.6) and the interaction between the two features is significant ($p<0.05$) after adjusting for duration of rhythmic theta and seizure discharge offset. This is in keeping with other studies. Patients with UHS are the commonest group of patients investigated for surgery, with mesial temporal lobe epilepsy being often resistant to drug therapy and these patients are most likely to have temporal lobe type seizures. In addition an anterior temporal lobectomy is the most frequently performed epilepsy surgery worldwide (Engel, 1996). With the wide experience in assessing this group of patients i.e. those with UHS, studies carried out since the more widespread availability of high quality MRI have questioned the need for intracranial studies when MRI can provide lateralising and localising information about the underlying pathology which allows patients to proceed directly to surgery. Thadani (1995) suggested criteria for successful epilepsy surgery without intracranial EEG, based on convergent findings on MRI scanning, interictal and ictal EEG, clinical seizure characteristics and the neuropsychological testing. The findings in this study confirm previous work and may enable us to further rationalise the pre-surgical assessment process, which is discussed in a later section.

The unexpected findings with respect to whether a patient had surgery or not, was the proportion of patients, in particular those with UHS, where a good outcome is more likely, who did not proceed to surgery. The reasons for this are summarised in the results section 3.6. It is clear that in some cases this decision was much influenced by personal factors either not to pursue the investigations or not to proceed to surgery. Given the cost and time implications of the pre-surgical assessment and in particular of the video-EEG telemetry, it is important that patients are counselled and fully understand all the issues before embarking on such a lengthy procedure. It is important that they do not put any possible medical treatments on hold whilst they wait for tests particularly if they are uncertain whether they will proceed with surgery, or unnecessarily risk the hazards of anti-epileptic drug reduction during video-EEG telemetry.

The number of patients who did not proceed to surgery because of novel or discordant data is a relatively small proportion, and they are discussed in more detail below in section 4.1.4.

4.1.3 Features from the video-EEG telemetry recording linked to a good post-operative outcome.

The finding that even the specific ictal EEG features studied had little relationship to the post-surgical outcome in comparison to the imaging is disappointing but confirms and extends other studies. Reports from the early series of surgical outcomes show conflicting information from the EEG data; in a follow-up study by Falconer and Serafetinides (1963) of temporal lobectomy cases, the best results were obtained from those patients who had either mesial temporal sclerosis or clearly defined small tumours regardless of what the EEG findings showed pre-operatively. More recent studies have shown that pathology either defined pre-operatively via MRI or post-operatively from pathology specimens provides the best indicator of post-surgical outcome. Berkovic et al, 1995 used actuarial methods to study outcome following temporal lobectomies in patients classified by the pre-operative MRI. They found that the MRI was a useful predictor of outcome and that the actuarial

analysis showed different patterns of post-surgical outcome with time in the different MRI groups. Garcia et al, 1994 also concluded that qualitative MRI provided important post-operative information, when they reviewed the findings of patients who had had temporal lobectomies and high-resolution MRI with volumetric and T2 signal measurements. However it has been suggested by Gilliam et al (2000) that the predictive value of MRI in patients with UHS may have been overestimated by retrospective studies that look at relatively small numbers of highly selected post-operative patients.

Some features of the ictal recording however were associated with a good post-operative outcome. When considering all the patients (i.e. those with both single and multiple electro-clinical seizure types) the presence of early rhythmic theta was significantly associated with a good outcome ($p = 0.03$). It just fails to reach significance if only the patients with a single seizure type are included in the analysis ($p=0.053$). Logistic regression shows that this is also an independent predictor of a good outcome when all patients (single and multiple seizure types) are considered together.

A similar lack of ictal features predictive of outcome has been reported in a study by Pataraia et al (1998). They looked at certain features of the ictal EEG in patients with unilateral mesial temporal lobe epilepsy and found that none of the ictal features they considered were predictive of post-operative outcome and did not add any additional localising information that was not already available from the MRI and interictal EEG. They were looking at a more selected group than in the study here: all patients had UHS on MRI, typical temporal lobe seizures and unitemporal spikes on interictal EEG. It is possible that the less proscriptive patient group in this study has led to the presence of early rhythmic theta being predictive of a good outcome. The lack of any other ictal EEG features being predictive would then be in agreement with Pataraia's study.

Other centres have looked at different EEG features in order to predict post-operative outcome. A recent paper (Schulz et al 2000) has looked at the propagation patterns of scalp EEG and suggested that these may be

predictive of outcome. They studied 58 patients with mesial temporal sclerosis or non-lesional TLE and found that 83% of patients without contralateral spread were seizure free as compared to 46% who did have contralateral propagation, and conclude that together with the presence of bitemporal interictal abnormalities bitemporal asynchrony in the ictal EEG probably represents bitemporal epileptogenicity and is thus associated with a worse post-surgical outcome. This was not a finding that we were able to confirm, in part due to the different definition of bilateral spread.

The other clinical features that in this study were significantly associated with a good outcome, for example a temporal type seizure and UHS help to confirm previous studies. Gilliam et al (1997) looked at the post-operative outcome in 90 patients and compared that with the interictal and ictal EEG findings. They concluded that the combination of concordant MRI and interictal scalp EEG was associated significantly with seizure cessation post-operatively in comparison to other combinations of EEG features, but that they were not independent predictor values.

Similarly Cascino et al (1996) looked at 159 patients with temporal lobe epilepsy, all of whom had ictal recordings and quantitative MRI. They conclude, "MRI-identified unilateral medial temporal lobe atrophy was a strong predictor of operative success". Although they found that routine (interictal) EEG findings significantly correlated with the temporal lobe of seizure origin and the results of the MRI, there was no relation between the routine EEG findings and the operative outcome. They suggest therefore that in patients with MRI-identified unilateral medial temporal lobe atrophy, concordant localised interictal EEG abnormalities may be adequate to confirm the epileptogenic zone and thus allow the patient to proceed to surgery. As all of their patients had ictal semiology consistent with medial temporal lobe epilepsy the results of this study can be seen to support their statement.

In this study if the patients with a single seizure type are considered then the odds ratio of a good post-operative outcome if the patient has both UHS on the imaging and a temporal type seizure (either typical temporal, tTLE or

atypical temporal, aTLE) are nearly 7:1, in comparison to a patient with neither of these features.

4.1.4 Novel data obtained from video-EEG telemetry

In a small proportion of patients novel or unexpected data was obtained from the EEG and video recordings that could make an impact on the decision to proceed to surgery.

Of these patients who had discordant data or other novel information there were some where this information either ruled them out of the surgical program or reduced the odds of a good outcome to such a level that they did not wish to proceed.

Only 3.3%, of our patients had non-epileptic attacks or NEAs during video-EEG telemetry, which is less than previously reported from epilepsy surgery programs (Henry and Drury, 1995). In their study Henry and Drury found 8% (12/145) of patients in a surgical program, these included patients who had both NEAs and epileptic seizures as well as patients who had only NEAs. They used strict criteria for inclusion of the attacks into their study and only considered those patients who were thought to have temporal type seizures, but not necessarily only those who had temporal pathology on MRI.

The discovery of NEAs in surgical candidates is often given as justification for carrying out video-EEG telemetry on all surgical candidates (Henry and Drury, 1995). However careful history taking with a particular reference to different seizure types, and any possible psychopathology that might predispose them to NEAs should identify a very high proportion of these patients. Identifying NEAs either prior to or during the video-EEG telemetry does not mean an automatic rejection from the surgical program rather that the issues of the NEAs should be identified and treatment with cognitive behavioural therapy (CBT) can be instigated. If the NEAs can be brought under control by these means, and the epileptic seizures remain genuinely intractable then epilepsy surgery can again be considered.

The reason for the smaller number in this study probably reflects selection prior to entry into the surgical program. As a tertiary referral centre the majority of patients will have had investigations at other centres (although not usually video-EEG telemetry) and their clinical history taken on several occasions. Some patients may therefore have been identified as possibly having either NEAs or a mixture before they are entered into the surgical assessment program at NHNN.

There were in total 17/66 (26%) patients who had novel data, including just one patient with NEAs, who proceeded either directly to surgery (11 patients) or after having an intracranial study (6 patients). In addition there was one patient who had an intracranial study but died before having definitive surgery. Although in these patients new information was gained from the scalp EEG video-EEG telemetry this did not always preclude surgery even if the data was apparently discordant.

Of the intracranial studies (n = 7) performed in this setting 5/7 cases confirmed the localisation expected from the MRI. Of these five patients 3 have a good outcome, one is lost to follow-up and one patient died before surgery. In the remaining two patients, the intracranial study supported the localisation predicted from the scalp ictal EEG and the surgery proceeded on that basis. Of these two patients one had normal imaging and has had a good outcome post-operatively, in the other patient the intracranial study showed more widespread areas of epileptogenicity, and a palliative operation was attempted. The patient has subsequently had a poor outcome.

Of the 11 patients proceeding directly to surgery, despite unexpected scalp EEG findings, in each case this was determined by the MRI localisation; 1 patient was lost to follow-up, 3/10 had a poor outcome (Engel Class III) and 7/10 had a good post-operative outcome. The three patients with the poor outcome included the patient with dual pathology who had NEAs in addition to epileptic seizures.

This is a highly select group and for the majority of the patients with unexpected findings we do not know without outcome from surgery or an intracranial study whether the scalp video-EEG telemetry correctly influenced the decision.

The relatively small percentage of discordant (as opposed to non-concordant) information obtained may in part reflect the patient case mix. Two factors should be considered; firstly the patients were all seen by NHNN neurologists specialising in epilepsy and so some of the potentially less favourable candidates for epilepsy surgery would have already been removed from the assessment program at an early level. Secondly as a tertiary referral centre the patient population is dependent on many factors and it is possible that with the increase in availability of video-EEG telemetry at more regional centres the case mix over time may have changed with the balance moving from relatively straightforward to more complex cases.

4.2 The importance of the findings and their clinical significance.

It can be seen from the results that imaging does appear to be the dominant deciding investigation with respect to which patients proceed to surgery and which of those patients have a good outcome post-operatively. This may in part reflect the current practice at the National Hospital for Neurology and Neurosurgery where there have been many research projects aimed both at developing more sensitive techniques of analysis of the MR images and at relating imaging abnormalities thus found to different epilepsy syndromes. Previously other centres developed their epilepsy surgery assessment in different directions determined either by the expertise of the personnel or the resources available, and thus review of their data would not necessarily give the same emphasis and ictal EEG features might assume a greater level of importance. However there is increasing convergence of the imaging techniques in epilepsy surgery assessment and comparison between centres in terms of post-operative outcome and relative importance of all the investigations performed during the assessment program is more feasible than it would have been 10 years ago. Thus the results from this study can be

seen as having a broader relevance rather than relating solely to the practice at NHNN.

Clearly if one is going to utilise EEG ictal features to help predict post-operative outcome and thus counsel patients then the measures used need to be quantitative and easily identifiable so that inter-reviewer concordance is maximised. We have tried in this study to use only features that could be quantified and proved reliable, which is supported by the high inter-observer concordance. Other studies have also emphasised this point when reviewing specific ictal EEG features and relating them to either pathology or post-operative outcome (Pataraia et al, 1998, Schulz et al, 2000, Walczak et al, 1992, and Spencer et al 1985). In Spencer's study the authors reviewed ictal scalp recordings of patients who subsequently had depth EEG to determine lateralisation and localisation of seizure onset but who did not have MRIs performed. They found an interobserver agreement between 64-74% for seizure lateralisation but only 46-49% agreement with the lateralisation determined by the depth EEG, and conclude that more formal criteria are needed before scalp ictal records can be used reliably or accurately for localisation. In contrast, in Schulz' s study where the patient group and the ictal EEG features were more strictly defined, all patients had had MRIs, the interobserver reliability for EEG seizure patterns was good, and no discordance occurred in lateralisation of the ictal EEG.

There is support for the finding that MRI is an important influence in the decision making process from previous studies where researchers and clinicians have, when the scalp ictal recording is not completely concordant with the MRI, proceeded to an intracranial recording to confirm and support the MRI data. In the majority of cases the intracranial studies are in concordance with the MRI data. A study by King et al (1997) looked at 119 patients with hippocampal atrophy and of the 97 with unilateral atrophy 50 had intracranial studies and 78% showed results concordant with the MRI. Our own findings show that in those patients with an MRI showing unequivocal unilateral hippocampal sclerosis and the ictal scalp recording is non-concordant or frankly discordant, if the patient then proceeds to an intracranial

study with bitemporal stereotactic depth implantation to lateralise and localise the seizure onset, in 9/10 patients the intracranial study confirms that the seizure onset is concordant with the side of the hippocampal sclerosis. In the majority of these cases the seizure does not appear to be expressed clinically until there is a contralateral ictal discharge.

It is possible that the follow-up time in this study is too short to allow a true representation of post-operative outcome, however a median of 4 years post-operative is comparable to most similar studies where pre-operative assessment is reviewed with respect to post-operative outcome, however it is also true that there is less data available for more prolonged post-operative periods in patients whose pre-operative assessment included high quality MRI. One recent study (Foldvary et al, 2000) however would indicate that the follow-up time used in this study is acceptable. Foldvary et al looked at the long-term post-operative outcome in patients who had a temporal lobectomy. Their patients had a mean follow-up time of 14yrs and a range of 2 – 33.6 years. They found that the majority of recurrences occurred within 2 years of surgery, later recurrences did not tend to lead to medical intractability and that seizure freedom at 2 years was the best predictor of long-term outcome. However not all of these patients had an MRI and the pre-operative classification was made using other clinical and EEG data. There results are similar to those of the earlier study be Falconer and Serafetinides (1963) where after the second year there was little movement of patients between the good and poor outcome categories.

It is possible that in this study more patients may remit at a later date, for example after 5 years post-operation and then other factors from the ictal recording may be identified as being predictive of a poor outcome. One method of assessing this would be to serially review the post-operative outcome at say 1,2 and 5 years and determine which, if any patients changed from a good to a poor outcome and vice versa.

Another approach would be to consider reviewing in detail the pathology of the patients with good and poor post-operative outcome at 2 years and see if

there were any links between the EEG features and the pathology as determined by the surgical specimen. This was beyond the scope of the current study.

Does the fact that we are heavily dependent on the MRI mean that we can dispense with scalp video-telemetry? The number of patients who could be potential epilepsy surgery candidates is currently far greater than the number that can be assessed within a reasonable time frame and thus it becomes increasingly important to husband the available resources to maximise the benefit.

The rationale behind improving the throughput of patients being assessed is twofold. Patients are assessed for surgery because surgery may be a means of achieving seizure freedom or much improved control with or without continued use of AEDs for a proportion of patients with intractable partial epilepsy. This allows the patient a chance of a much improved quality of life, both medically and psychosocially. The patient may not need to continue taking any or so many AEDs and thus any possible side effects of medication are reduced.

Secondly patients with intractable epilepsy, particularly those where the seizures are poorly controlled run the risk of sudden death in epilepsy (SUDEP), and injuries during seizures. The fact that there is increased morbidity and mortality in this selected group of patient meant that there is also the chance that whilst waiting for video-EEG telemetry the patient may suffer severe injuries during seizures or even die as a consequence of their epilepsy. In the UK the waiting time for video-telemetry is typically a period of 12 months and the mortality in this group, i.e. patients with intractable partial seizures, is of the order of 1/200/year so by waiting a year for the test each patient has a 0.5% chance of dying due to the epilepsy. This data is from a study by Nashef et al (1995b) who found that in a cohort from a tertiary hospital, 1:200 per year were likely to die due to a sudden death caused by an epileptic seizure. This factor must be taken into consideration when one is

discussing with the patient the risks associated with epilepsy, the risks of the assessment and any subsequent surgery.

Given these figures of both the mortality and morbidity that may ensue whilst waiting for the test and the benefits of operating on patients that will have a good outcome the need to improve the throughput of the limited resource becomes clear.

By being able to "fast-track" selected patients, more patients would be able to be seen and assessed for surgery. Also by freeing up resources from patients that can be dealt with by alternative means the limited resources of both time and money can be directed at those patients who would benefit in terms of the data obtained from the video-EEG telemetry for example those patients where the seizure semiology is unclear, where the patient is suspected of having additional NEAs, or in patients with normal pathology where as much data as possible is needed in order to plan any intracranial study.

Several recent papers have discussed the option of not performing ictal recordings in carefully selected patients (Engel, 1999) and have suggested other measures that can provide confirmatory evidence for the MRI findings. Some authors have suggested that interictal EEG abnormalities may be an alternative to ictal data (Cascino et al, 1996 and Cendes et al, 2000). Cendes looked at 184 patients with temporal lobe epilepsy and an MRI compatible with mesial temporal sclerosis. They found a strong concordance between EEG and MRI volume lateralisation, with unilateral hippocampal atrophy predicting ipsilateral interictal epileptiform abnormalities and ipsilateral seizure onsets with no false lateralisation. In both studies the patient population was carefully selected; in Cendes's study the patients all had a clinical diagnosis of TLE with seizure semiology consistent with this diagnosis and no EEG features suggesting extratemporal partial epilepsy.

In contrast experimental work with animal models provides evidence that interictal spikes may not represent the area of ictal onset and may not suggest areas of epileptogenicity (de Curtis and Avanzini, 2001). They suggest from

their review of human and animal model work that the irritative area and the ictal-onset area are distinct and "that the size of these two areas and the boundaries between them are subject to continuous dynamic changes that reflect the underlying modulation of neuronal synchronisation". This would be in agreement with Gotman (1991) who proposed that " interictal spikes have little direct effect on seizure generation and that the rate of spiking is more a reflection of past seizures than an indication of the likelihood of impending seizures".

As temporal lobectomy is a well-established surgical procedure for treatment of medically refractory epilepsy and provides long-term benefits to these patients, it would be advantageous in terms of health care economics to be able to increase the number of patients undergoing this procedure without concomitant increase in expensive investigations. A recent study looking at long-term outcome in 79 patients following temporal lobectomies showed a percentage of 80% with Engel Class I or II outcome at a mean follow-up time of 14 years (Foldvary et al 2000). These and other studies showing the good outcomes that can be achieved emphasise the importance of pursuing investigations in patients with well-defined temporal lobe epilepsy.

4.3 Further studies

What is the way forward? Should we continue to record the ictal EEG in all patients being assessed for epilepsy surgery?

The findings here would suggest that in a selected group of patients the need for an ictal recording is declining. In patients with UHS and a temporal type seizure the added information from the ictal recording does not significantly alter the odds of either proceeding to surgery or of a good outcome. Patients are typically given odds varying between 30 and 70 % of a good outcome and it is differences of this size that are important and understandable in the clinical setting.

This would support the ongoing discussion from other similar centres where the need to perform video-telemetry in all cases has been questioned. Although in Engel's review article (1999) he concluded that at that time imaging was never enough because of the lack of information on function he emphasises the need to identify those epilepsy syndromes where the data obtained from ictal recordings might be replaced. He also discusses the important issue that equivocal results from ictal video-EEG telemetry in patients with UHS, might lead to the patients undergoing unnecessary intracranial studies or surgery being withheld inappropriately. This would be confirmed by the present study for those patients with isolated lesions or UHS.

If these patients with UHS who are more likely to benefit from surgery and to have a good post-operative outcome, were going to be "fast-tracked" i.e. the ictal video-EEG telemetry was eliminated from the pre-surgical assessment would any other parts of the assessment process need to be enhanced? The need for high quality MRI is paramount, and is already established, as the pre-eminent test when investigating a patient for epilepsy surgery. Also the importance of taking a good clinical history needs to be emphasised. Clearly if the important feature apart from the presence of UHS on the MRI is that the patient has either typical or atypical temporal lobe seizures then it is important that the clinician is very clear that the patients habitual seizure type fits into that category and that there is one seizure type, excluding the presence of isolated auras as well as complex partial seizures. There is also the possibility of recording the habitual seizures using home videos and thus obviating the need for an expensive hospital stay. This option would not be suitable for all patients, for example those who live alone, but it might prove an important alternative for those patients where seizures occur infrequently or in clusters and particularly where drug reduction for whatever reason is not possible. Although it might take several weeks or even months for an adequate home video to be obtained it would represent a low cost option in comparison to several weeks of expensive in-patient monitoring. It would need to be done in tandem with the patient being referred onto the waiting list for video-EEG telemetry so that should the home video either prove unsuccessful,

inconclusive or show unexpected seizure types then the patient would not be disadvantaged in terms of waiting time for video-EEG telemetry.

Sharborough and Gotman (1993) review a study done in Boston using home monitoring. In this study 15% of 150 operated patients had long-term monitoring entirely on an outpatient basis and 40% had some portion of their monitoring done in the home. They comment that home monitoring cannot substitute in all patients (medications were never reduced or withdrawn on an outpatient basis) but equally felt that not all patients needed the more expensive alternative of inpatient monitoring.

A potential risk of excluding video-EEG telemetry from the assessment process would be that one might occasionally operate on patients with NEAs. This could be largely avoided by careful psychiatric assessment looking for the specific features and profile associated with NEAs. It should be noted that all patients have a psychiatric assessment but this is usually done after the patient has had video-EEG telemetry and is a more broad based assessment examining patients general mood, their expectations of surgery, and any evidence of psychosis, post-ictal or interictal. A clear description of the seizures with or without a home video would also help in identifying those patients who have NEAS in addition to or instead of seizures. Supporting evidence from the patient's clinical history and interictal EEG abnormalities can help to identify patients who have a mixture of NEAs and seizures from those patients with NEAs in isolation (Raymond et al, 1999). If there were any possible indication that not all the patients' seizures were organic then one would err on the side of caution and perform ictal recordings being careful to get family members to confirm the habitual nature of any attacks subsequently recorded.

Even with careful screening however there will still be rare patients who will have NEAs post-surgery and did not have any prior to the operation, i.e. a de novo phenomenon. Post-operative management in these cases would be more difficult without the benefit of the pre-operative video-EEG telemetry assessment. However reports in the literature suggest that it may be possible

to identify such patients pre-operatively from a psychiatric assessment. Krahn et al (1995) reviewed six patients who had non-epileptic attacks following surgery for intractable partial epilepsy, three of whom had had both epileptic and non-epileptic attacks pre-operatively. Psychiatric assessment revealed common characteristics in these patients, and they suggest that psychiatric assessment may help to identify those patients at risk of developing post-operative NEAs.

It is also possible that other important and novel information will be lost. This represented 18% (66/362) of all cases and 20% (34/173) of those patients with UHS. Just looking at the patients with UHS however 10/34 of patients with novel data proceeded to surgery where with one exception the operative procedure was on the side of the imaging abnormality despite concerns raised by the video-EEG telemetry recordings and all nine of these had a good outcome. In 14% (24/173) of patients with UHS therefore scalp video-EEG telemetry provided novel information that may have contributed towards a decision not to proceed to temporal lobectomy.

Of the novel data aside from those patients in whom NEAs were recorded there were 19 patients (8 with UHS) in whom there were multiple clinical seizure types or the clinical seizure type was discordant with the imaging. This information could perhaps have been obtained from the clinical history and a thorough seizure description. This means that the new information provided by the video-EEG telemetry that did not relate to clinical seizure type was 9.6% (35/362) in the patient group overall and 12.7% (22/173) in those patients with UHS. The proportion of those patients with unexpected findings from the video-EEG telemetry who may have benefited from epilepsy surgery can only be determined if either an intracranial study or surgery is performed. In this study we are unable to determine, because of no further data or post-operative outcome, whether there may have been a benefit from surgery in 21/35 patients who had unexpected results from the video-EEG telemetry.

From this study we can identify 5/22 patients where the scalp video-EEG telemetry was clearly likely to have been correct in its localisation. This

number has two components. Firstly there were 6 patients who had normal imaging and who proceeded to an intracranial study, 3 of whom have also had definitive surgery and a good post-operative outcome. Secondly there were 16 patients in whom the imaging was discordant with the ictal scalp EEG and who proceeded to surgery based on the MRI results, 2 of whom have had a poor post-operative outcome.

In contrast there were 6/8 patients in whom the scalp video-EEG telemetry provided misleading information (i.e. discordance with the MRI) as judged by successful surgery on the MRI, or confirmation with an intracranial study (n=5) or unsuccessful surgery based on the EEG (n=1). One patient in this group was lost to follow-up.

It is possible that the major epilepsy centres i.e. those with most experience will start to rationalise their resources in their investigations/assessments. One centre has compared the post-operative outcome in monitored and non-monitored surgical candidates (Holmes et al, 1996). They looked at outcome at 5yrs after temporal lobectomy in 28 patients who proceeded to surgery on the basis of their interictal EEG patterns and 46 patients who had video-EEG telemetry prior to surgery. A good outcome was associated with consistent unilateral temporal interictal abnormalities and was similar in both groups if this was taken in to consideration.

By identifying those groups of surgical candidates who are more likely to have a good outcome and in whom an ictal recording may not be essential, will allow these patients to complete their pre-surgical assessment more efficiently. From the results of this study it would appear that patients with UHS and temporal type seizures are much more likely to proceed to surgery and are more likely to have a good outcome. It would therefore seem useful to ascertain whether they did have temporal type seizures on an outpatient basis by the use of home video recorders before admitting them for video-EEG telemetry and thus perhaps obviate the need for inpatient video-EEG telemetry. This might also have the advantage of screening out patients having non-epileptic seizures although one would have to exercise caution

when no concurrent EEG was available. Taking a clinical description of the seizures from relatives before and after showing them videos might also identify features which help to ascertain how reliable is the history taking.

4.4 Was the aim of the study achieved?

The stated aim of the study was to find out if video-EEG telemetry provided any additional and useful information in these days of reliance on MRI, and could we therefore justify continuing in the use of such an expensive investigation in all patients being assessed for surgery.

These aims were partially achieved; features of the ictal recording were identified that were associated with specific imaging groups, with proceeding to surgery and with achieving a good post-operative outcome. However in some but not all instances, the features that were best associated with or were significantly predictive of surgery and a good outcome were those features relating to either the clinical seizure type or the imaging abnormality. Scalp video-EEG telemetry did provide unexpected data in a relatively small proportion of cases – sometimes this correctly influenced decision making but sometimes may have disadvantaged patients by leading them to undergoing intracranial monitoring unnecessarily or having delayed surgery and the possibility that it led some patients being incorrectly rejected from the surgical program can not be excluded.

It is possible that, at times, a small sample size means that an association may have been missed, for example does early temporal theta enhance the chances of a good post-operative outcome in patients with UHS? However given the size of the two groups of patients, those with UHS and those without, the type II error for comparisons between UHS and non-UHS groups is small, there is a 90% chance of finding a 16% difference at the 5% significance level. However, for clinical purposes there needs to be a strong association in order to radically alter the odds to such an extent to influence patient choice. Patients are usually concerned about the difference between a 30 and 70% difference in the odds of seizure freedom or good outcome and

are not likely to be concerned about the difference of 10% given the hazards of epilepsy and the low complication rate of the operative procedure. It is also recognised that the multiple comparisons inherent in studies such as this may lead to occasional results appearing to be significant by chance alone. This is unlikely to have been a substantial factor in this study because most of the associations identified had very small p values.

The ictal EEG features are able to refine the odds of proceeding to surgery and of a good outcome and there does therefore currently appear to be a place for continued ictal recordings for some patient groups. However overall, the findings would lend support to the view that specific patient groups may be able to omit the video-EEG telemetry from their surgical assessment program. In the future patients with UHS who have clearly established and possibly documented on home-video temporal type seizures may be able to forgo video-EEG telemetry, particularly with developments in the field of functional imaging and in particular fMRI (functional MRI). Allowing some of the patients with unequivocal UHS to proceed to surgery without having video-EEG telemetry would mean that centres could spend more time and resource on those other more difficult or less straightforward cases.

In the setting of our evolving understanding and access to alternative technologies clear protocols could be instituted relating to which patients should/should not routinely undergo video-EEG telemetry prior to the surgery. The rationale for such decisions should be clearly explained to patients or their carers.

Caveats to any such protocols would be that they could only be instituted following

- A comprehensive clinical evaluation, which included a detailed description of habitual attacks.
- A high resolution MRI that should be completed prior to the video-EEG telemetry.

A suggested protocol follows:

1. If the MRI shows isolated UHS and there are well established temporal lobe type clinical seizures (ascertained from the clinical history and/or home videos), the risk: benefit ratio would be in favour of the patient proceeding to surgery, subject to a comprehensive psychiatric and psychological review and provided there is no evidence/question of non-epileptic attacks, rather than video-EEG telemetry.
2. In patients with isolated, indolent and well circumscribed lesions (i.e. there is no evidence of multiple pathology or additional HS) the risk: benefit ratio of video-EEG telemetry would support proceeding to surgery provided there is clear evidence that the lesion is epileptogenic, including a concordant seizure semiology and no evidence of non-epileptic attacks.
3. For all other patients there is still a need to perform video-EEG telemetry. Although for those patients with normal MRI the relatively low likelihood of proceeding to surgery and the complexity of the investigations needs to be carefully explained to the patient prior to the video-EEG telemetry

It is probable that both groups (1) and (2) should be reviewed at a multidisciplinary presurgical meeting to review and confirm all the findings obtained form the other investigations and then to make the decision whether or not to include video-EEG telemetry as part of that individual patient's assessment program. At the present time such decisions would still need to be taken on an individual case-by-case basis, while further evidence-based experience is obtained. Any introduction of such protocols would need to be subject to periodic audit of the results in order to refine the guidelines suggested. In addition comparison with results from other epilepsy centres that are using both similar investigations and rationale in determining suitability for surgery would strengthen the argument for or against proceeding to epilepsy surgery in certain well defined imaging subgroups without the need for video-EEG telemetry.

Chapter 5: References

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Appendix 1

Sample page from the database with patient information

Hosp Number:	XXXXXXXX
Ref Doctor:	Dr Duncan
Surgery:	Y
Imaging:	Unilateral HS: Lt HS RHCT2 103, LHCT2 105, AT2 normal, HC vol 78% L<R Rt HC -2SD control volume
Drugs Red:	Y
No of Szs:	3
GTCS VT:	0
Outcome:	Surgery:had amytal first
Question ans:	Y
Dov:	29/Jan/1996
Interictal EEG:	Bitemporal: Lt>Rt
Ictal EEG:	Lat: Lt
Number:	110
Febrile Szs:	Y
Afebrile sz onset:	10mths
Hist of SE:	N
GTCS freq:	Very rare
Dob:	29/Mar/1967
Handedeness:	Rt
Psychometry:	VIQ 70s - no deterioration, verbal memory better than non-verbal memory
Aetiology:	peri-natal?, prolonged labour also febirle convulsion
Duration:	95
Age at VT:	28
Sessions:	1
Dod:	
Cause:	

State: A

Date of surgery: 9/Sep/1996

Type of surgery: Temporal lobectomy: lt ant

Number of DR: 1

Postop outcome: 3yr sz free, 2yrs sz free

Pathology: HS

Sz type: ATLE

AEDs: 2

Sleep Dep: 2

Sex: F

Sample page from the ictal feature database

Hosp Number:	XXXXXXXX
Surgery:	Y
Imaging:	Unilateral HS: Rt HS and dilatation of Rt lateral ventricle
No. of Szs:	3
GTCS VT:	0
Number:	220
Sz type:	TLE
Rhythmic theta:	Y
Rhyth theta 1st:	Y
Loc of theta 1:	Lobar
Abrupt offset:	N
Postictal:	Slow/asymm alpha
Postictal loc:	Bilateral/ipsilateral
Bilat changes:	Y
Synchronous:	Y
Side change:	N
Sustained theta:	Y
Duration theta:	54
Theta evolves:	N/A
Side of theta:	Rt
Onset:	C
Onset of theta:	0
Loc of theta2:	F,T
EEG at onset:	Rhythmic theta

Appendix 2

ICTAL EEG

Number:

No of seizures: Archive disc:

Time of Clinical onset (if known):

Time of EEG onset:

			Notes
Onset			
			No change/attenuation/alpha asymmetry/ discharge
			before/with/after clinical change or uncertain
			Obscured by physiol.artefact
First Change			
Rhythmic: Y/N			
Lateralised: Y/N			
Location of 1st rhythmic change	Fz		
	Cz		
	Pz		
	RF	LF	F3/F4,*F7/*F8,Fp1/Fp2
	RC	LC	C3/C4
	RT	LT	*F7/*F8,T3/T4,sLSp/sRSp
	RP	LP	P3/P4
	RO	LO	O1/O2, T5/T6
Minimum time from clincial onset to 1st rhythmic change			time from pt indicating aura or something being seen
Any change on opposite side			
Rhythmic Theta			
Appearance of rhythmic theta			present or absent
			first change or not
			evolves from first change
			if not 1st change time from sz onset
Location of rhythmic theta	Fz		
	Cz		
	Pz		
	RF	LF	F3/F4,*F7/*F8,Fp1/Fp2
	RC	LC	C3/C4
	RT	LT	*F7/*F8,T3/T4,sLSp/sRSp
	RP	LP	P3/P4

	RO	LO	O1/O2 T5/T6
Duration of rhythmic theta			
Evolution			
Bilateral changes			whether discharge becomes bilateral if unilateral at onset
Synchronous changes ie at same frequency: Y/N			
Time to become bilateral			
Change of side			if unilateral at onset time to change sides
Seizure offset			
Abrupt offset			
Bilateral or unilateral			
Post Ictal Changes			
Absent or present			
			type of change eg slow or epileptiform discharges/spikes etc
			unilateral (ipsi or contra to Sz discharge) or bilateral

Type of seizure:

(1) Extratemporal

(2) Temporal (Engel's criteria) aura - arrest/stare,oraoalimentary automatisms,posturing of 1 upper extremity - post-ictal confusion /disorientation

(3) others ie not (1) or (2)