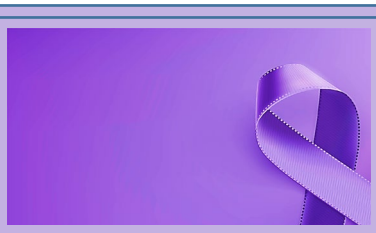

EPILEPSY

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Dear Doctor,

Greetings from Micro Labs. We are happy to bring you "EPILEPSY Newsletter'' which contains latest and interesting news in the field of Neuropsychiatry.

This issue contains:

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Ordinal regression improves the accuracy of epilepsy surgery outcomes prediction.

In recent years, epilepsy surgery has undergone various changes, demanding ongoing improvements to treatment strategies for this illness. This sector has made technological improvements in both diagnostic and therapeutic processes, as well as the introduction of previously inaccessible treatment choices.[1] For individuals who have failed to respond to treatment, surgical intervention is the next step.[2] Epilepsy surgery research frequently aims to find predictors of a positive outcome in order to better guide therapy. However, most studies describe seizure outcome as a binary variable of seizure freedom (Engel I) or not, ignoring the distinction between uncommon debilitating seizures (Engel II), worthwhile reduction in seizure frequency (Engel III), and no worthwhile reduction in seizure frequency (Engel IV) (Engel IV). Since the Engel surgical outcome is on an ordinal scale, the study advocated utilising ordinal logistic regression rather than typical binary logistic regression. The study particularly hypothesises that by utilising ordinal logistic regression, we would be able to detect the established relationship between mesial temporal sclerosis (MTS) and seizure outcome in each study with greater statistical power.

The study investigated the outcome of seizures freedom as a function of exposure to the presence or absence of MTS, using data from a previously published meta analysis that included 10 studies. The study turned the count data into independent vectors with the presence (1) or lack (0) of MTS, as well as dependent vectors of seizure freedom (1) or not(2), or the full Engel outcomes for each research. On the dependent vectors of seizure freedom and Engel result, the study used binary logistic regression and ordinal logistic regression, respectively. The p-value for the log-odds (or slope) coefficient was provided in the study.

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The observed Engel result distribution is compared to that anticipated by ordinal regression, stratified by the presence or absence of MTS (Figure 1). Because of the pooled odds ratio assumption, the anticipated difference in Engel I for MTS or not (65% vs 39%) is slightly greater than observed (64 vs 44%), whereas the predicted difference in Engel IV for MTS or not (5% vs 13%) is lower than seen (3% vs 18%). There is also a comparison of the pooled odds ratio and the odds ratios of the three binary logistic regressions (Figure 2). The 95% confidence range for each binary logistic regression has the pooled odds ratio of 2.97. A likelihood ratio test, however, revealed that the forecast of ordinal regression with non-proportional chances (Figure 1A) was a considerably better fit (P =.04) than the prediction of ordinal regression with proportional odds (Figure 1B).

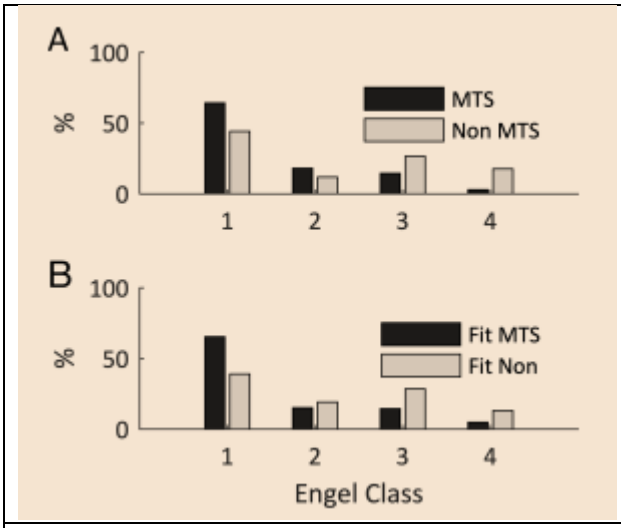
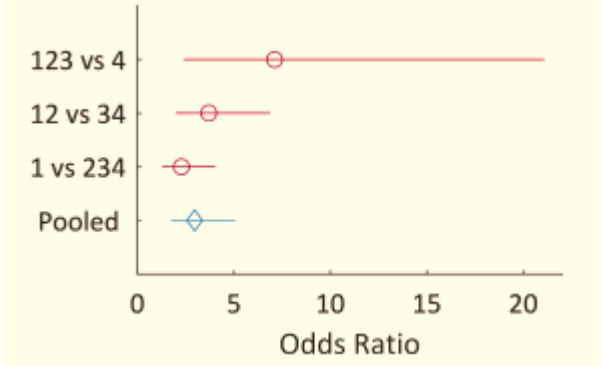


Fig. 1 - Results of ordinal logistic regression



Fig,2: Odds ratios for binary vs pooled ordinal logistic regression.

This is the first study to use ordinal logistic regression to analyse the results of Engel surgeries. Ordinal regression boosts statistical power while lowering the sample size required to achieve it. Using both proportional and non-proportional odds assumptions, the analysis found this to be accurate.[3]

When assessing ordinal outcomes (such as Engel surgical outcomes), ordinal regression should be addressed, especially for datasets with small sample sizes.

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Electroencephalography in Patients with Neurosyphilis and Viral Encephalitis-Induced Seizures

Syphilis is caused by a gram-negative bacterium, *Treponema pallidum* belonging to the Spirochaetaceae family. Clinical indications of infection appear in about a third of infected people. A chronic recurring condition (secondary syphilis) can occur after a regional infection at the entrance point (primary syphilis), with varying symptoms. After primary syphilis, neurological symptoms might emerge at any time. Early neurosyphilis, which develops months to years after infection, is distinguished from late neurosyphilis, which develops years to decades after infection.[1] Neurosyphilis has a wide range of clinical signs and imaging, which are known as "great imitators," especially in the presence of seizures, which can resemble the symptoms of viral encephalitis and lead to misdiagnosis. As a result, the goal of this study was to examine electroencephalography (EEG) in patients with seizures caused by the two disorders in order to aid in differential diagnosis.[2]

This was a retrospective analysis of patients who had seizures caused by neurosyphilis or viral encephalitis and had a video-EEG evaluation within the first week following the seizures and were treated. The existence of status epilepticus (SE) was defined according to the 2015 Report of the International League Against Epilepsy (ILAE) Task Force on Classification of Status Epilepticus, which comprised basic demographic variables (age, gender), early symptoms, seizure type, and the presence of SE. For all EEG experiments, an internationally established 10–20 electrode placement scheme was adopted.

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A total of 39 patients with neurosyphilis seizures and 40 patients with viral encephalitis seizures were included in the study. The discharge locations of patients with seizures induced by neurosyphilis were mostly in the temporal region, accounting for up to 89.7% (35/39), compared to 50.0% (20/40) of patients with viral encephalitis, and the difference was statistically significant ($p< 0.001$). Figure 1 shows typical LPDs, and the proportion of lateralized periodic discharges (LPDs) in the EEG of neurosyphilis patients was 46.2 percent (18/39), which was greater than the 27.5 percent (11/40) in viral encephalitis patients but did not achieve statistical significance ($p = 0.085$; Table 1). Patients with neurosyphilis were more likely than those with viral encephalitis to have temporal epileptiform discharges ($p = 0.002$), but there were no significant differences in LPDs ($p = 0.077$) or SE ($p = 0.088$).

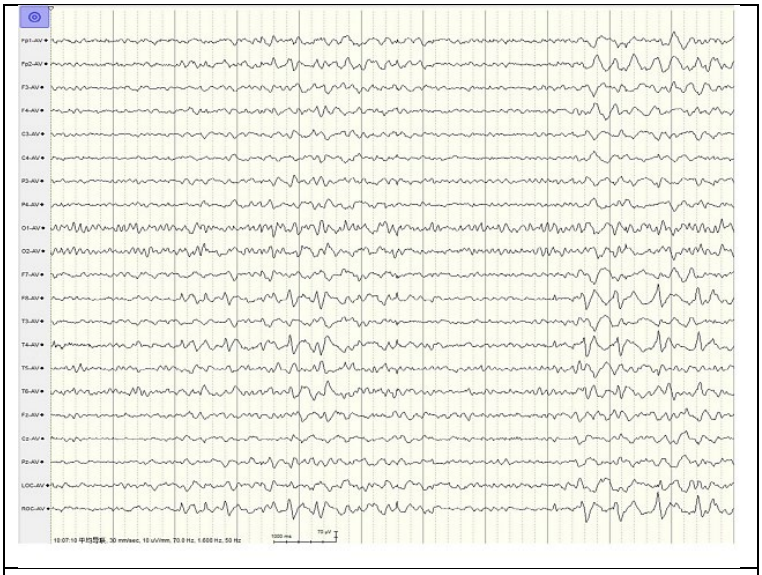

Fig. 1 | EEG in a 37-year-old male patient with neurosyphilis. LPDs were predominant in the right temporal region, appearing at a 1.5-Hz cycle.

Table 1 : Comparison of EEG characteristics between patients with seizures caused by neurosyphilis and viral encephalitis.

	Neurosyphilis (n=39)	**Viral encephalitis (n=40)**	**P-value**
Temporal epileptiform discharges, n (%)	35 (89.7)	20 (50.0)	0.000*
PDs, (%)	18 (46.2)	11 (27.5)	0.085
Rhythmic focal slowing, n (%)	19 (48.7)	24 (60.0)	0.314
Posterior dominant rhythm, n (%)			0.645
Decrease	23 (59.0)	25 (62.5)	
Absent	12 (30.8)	13 (32.5)	
Normal	4 (10.3)	2 (5.0)	
Degree of abnormal EEG, n (%)			0.673
Mild	14 (35.9)	12 (30.0)	
Moderate	13 (33.3)	15 (37.5)	
Severe	12 (30.8)	13 (32.5)	

Proportion of delta activities (%) (M, IQR)	30, 10-50	22.5, 5-50	0.587
Spike and wave index (%) (M, IQR)	30, 5-40	15, 5-30	0.249

The study evaluated two groups of individuals with seizures induced by neurosyphilis vs. viral encephalitis in this retrospective investigation. The two groups' temporal epileptiform discharges were considerably different, according to EEG. Although LPDs may differ, the sample size used was insufficient to obtain power. These findings imply that when EEG displays temporal epileptiform discharges, particularly in the form of LPDs, neurosyphilis should be considered. LPDs, according to Hirsch LJ et al, are characterised by recurrent, rhythmic lateralization or local spike and wave discharges that occur at a frequency of 1–2 Hz. LPDs are most commonly found in people who have suffered an acute brain damage, such as a stroke, tumours, or infections of the central nervous system.[3] Patients with seizures caused by viral encephalitis had considerably greater SE than those with neurosyphilis in this study.

Finally, EEG differs in patients with neurosyphilis and viral encephalitis seizures, particularly on temporal region discharges. Although LPDs did not differ significantly between the two disorders, it is indicated that when EEG displays temporal epileptiform discharges, particularly in the form of LPDs, neurosyphilis should be considered.

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A study on additional risks in older persons with epilepsy and intellectual disabilities

Intellectual impairment (ID) is a condition that occurs before adulthood and is described as a lack of intelligence that leads to decreased social functioning and has a long-term impact on development.[1] People with ID and epilepsy are a multifactorial group with a complex diverse aetiology. This covers the impact of specific genetic syndromes (for example, Down's syndrome) on morbidity as people get older. Multimorbidity (two or more chronic ailments) is common among people with ID and epilepsy, particularly mental and emotional disorders, neurodevelopmental disorders, and neurological conditions. The impact and complications of epilepsy in elderly individuals without ID are well understood. The clinical appearance and prognosis of epilepsy in the elderly vary from that of young persons. Physiological changes in metabolism that affect medicine, greater chances of pharmacological interactions, and higher polypharmacy burdens are all well-known. While studies have looked for differences in presentation in older adults with epilepsy in the general population and those in ID populations, no study has specifically looked to see if there is any difference in clinical risk characteristics between older adults with ID and epilepsy (aged 40 years and over) and younger adults.[2]

A total of 904 subjects with ID with epilepsy from 10 sites were identified in Epilepsy in ID National Audit (Epi-IDNA). The Epi-IDNA cohort was then analysed, including 405 subjects over 40 years old compared to 499 adults under 40 years old. The Sudden Unexpected Death in Epilepsy (SUDEP) and Seizure Safety Checklist were used to compare clinical characteristics to known risk factors.

Nearly two-thirds (62%) of the 405 older persons with ID and epilepsy had a comorbid physical illness, just under a third (28%) had a co-morbid neurodevelopmental problem, and just over a third (38%) had any mental health condition (Table 1). There was no significant difference in the proportion of those with mild ID compared to those with moderate to profound ID when comparing the older adult group (n=405) with the rest of the cohort (n=499) (Table 1).

Table 1: Characteristics of adults with Intellectual Disability (ID) and Epilepsy by age group (over 40 vs under 40).

ID severity			
Mild	179 (36%)	141 (35%)	0.78
Moderate to profound	320 (64%)	264 (65%)	
Diagnosis of ASD	225 (45%)	112 (28%)	<0.001
Diagnosis of ADHD	52 (10%)	7 (2%)	<0.001
Mental health disorder	151 (30%)	154 (38%)	0.02
Physical health disorder	278 (56%)	253 (62%)	0.04
Total medications: median (IQR)	4 (3)	5 (5)	<0.001
ASM: n (%) Number of ASM meds: median (IQR)	452 (93%) 2 (2)	389 (97%) 2 (2)	0.02
ASM type Generation 1 and 2 Generation 3 and 4	395 (79%) 220 (44%)	336 (83%) 216 (53%)	0.17 0.006

Antipsychotic meds: n (%) Number of anti-psychotic meds: median (IQR)	113 (23%) 0 (0)	123 (31%) (1)	0.02

The elder group had an epilepsy diagnosis for a longer time ($p<0.001$). Those in the younger age group were more likely to have epilepsy as a youngster (before the age of 16) ($p< 0.001$). In addition, the younger group was considerably more likely ($p=0.01$) to have had a seizure in the previous 12 months. The proportion of persons with an epilepsy care plan was lower in the older group ($p=0.057$). When applying logistic regression analysis to quantify the impact of age group on SUDEP risk factors, consistent results were obtained.

The findings show that there is a significant difference in clinical, prescription, risk, and service delivery features between persons aged 40 and up with epilepsy and ID and the younger adult sample. Prescription, physical, and mental health co-morbidities are all higher in older persons than in younger adults, as one might predict. Furthermore, when compared to the younger group, older adults with ID had lower levels of neurodevelopmental impairments.[2] Adults with ID had a higher anticholinergic burden and are more likely to be prescribed anticholinergic medication, according to a study of adults with ID and matched controls (OR 1.49, 95% CI: 1.38-1.59)[3]

This is the largest study of its kind, focusing on subjects with ID and epilepsy who have been diagnosed for more than 40 years. In comparison to the younger group, the 40-year-old cohort exhibits greater levels of clinical risk factors linked to multimorbidity, probable iatrogenic injury, and early mortality, as well as weaker clinical oversight mechanisms.

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An intracranial EEG recording case report of withdrawal seizures vs. on-medication seizures

Drug withdrawal can help people with well-controlled seizures improve their quality of life. Unfortunately, seizure recurrence is documented in roughly 46% of patients after medication cessation.[1] To improve the yield of long-term video EEG (LTVEM) monitoring, rapid withdrawal of anti-seizure drugs (ASMs) is used. Previous research, on the other hand, have shown that quick withdrawal of ASMs during pre-surgical LTVEM might be troublesome, compromising EEG validity and potentially leading to extra risks and investigations throughout the workup.[2]

The aim of this case study was to examine if epileptic patients' withdrawal seizures differed from their regular seizures in terms of semiology and electrophysiological.

Case presentation:

Presurgical intracranial EEG was used to follow a 42-year-old lady with drug-resistant focal epilepsy. Positron Emission Tomography (PET) scan showed left anterior temporal hypo metabolism and fMRI showed left hemispherical dominance (Fig. 1). She had a left cortical intracerebral hemorrhage that was controlled, resulting in mild motor aphasia and right hemiparesis (Fig. 2). Anti-seizure drugs (ASMs) were interrupted as part of this regular pre-operative examination; as a result, several withdrawal seizures were recorded before ASM readministration.

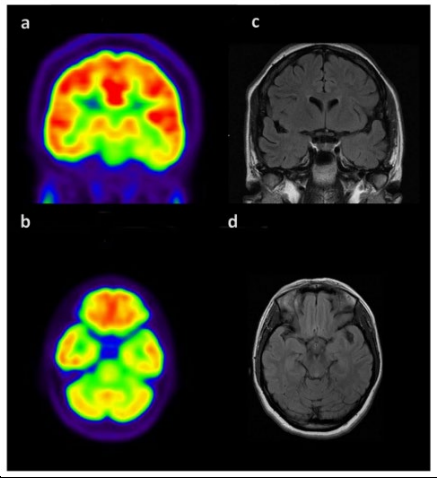

Fig 1: Presurgical phase 1 imaging results.

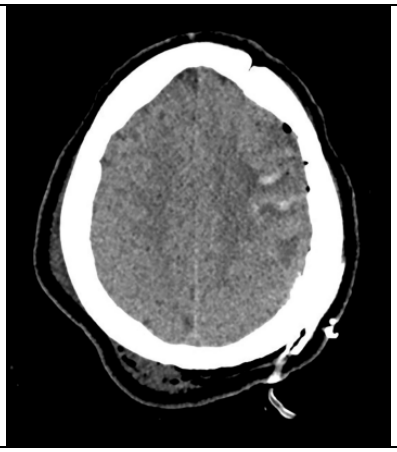

Fig 2: Left cortical intracerebral hemorrhage. Non-contrast CT showing left cortical intracerebral hemorrhage

The study identified three distinct phases in seizure organisation over the course of four days of invasive monitoring: Acute withdrawal seizures (AWS): the first recorded seizure 10 hours after implantation; stabilised withdrawal seizures (SWS): seven habitual seizures recorded

from 24 hours after implantation until ASM readministration; and non-withdrawal seizures (NWS): ten seizures recorded 24 hours after ASM readministration. The semiology and epileptic network in AWS and SWS were the same, but the propagation time from the temporal pole to the para-hippocampal gyrus (PHG) and hippocampus varied from no latency in AWS to up to 50 s in SWS. NWS were electrographic seizures that showed no clinical signs or symptoms. The temporal pole was the site of seizure onset in this type of seizure, as it was in the preceding two. NWS, on the other hand, can last up to 3 minutes without affecting the PHG or the hippocampus

Withdrawal of ASMs is thought to have a variety of effects on epileptic activity. We present the case of a 40-year-old woman who suffers from drug-resistant focal epilepsy originating in the left temporal pole. The ASMs were paused during intracranial LTVEM, resulting in numerous withdrawal seizures. There were no variations in the seizure organisation network after a thorough examination of these seizures. However, there was a noticeable shortening of activity propagation or dissemination.[2] According to a study conducted by Atalar AC et al, important factors such as ASM resistance and the presence of three seizure types must be considered before attempting an ASM switch/withdrawal in women.[3]

In conclusion, the epileptic activity propagation time is greatly shortened without having a significant impact on the epileptic organisation network or semiology. This suggests that ASM plays a critical function in preventing epileptiform activity from spreading from the initiation zone to other parts of the brain. Future research employing surface and intracranial EEG, as well as functional imaging techniques like fMRI, will be needed to confirm this finding and further investigate its underpinnings.

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